Fundamentals of Nuclear Power Generation
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Module - 10
Biological Effects of Radiation
Lecture - 02
Stochastic & deterministic effects of human cells

Hello friends, today we are looking to finish the tenth module of our course, where we are talking about the biological effect of radiation. You definitely have gone through the first lecture by now and actually I am having a quite a bit of gap between the time I record to the previous lecture and this one has I was down a bit with fever and cough and cold. And even today also my voice is quite a bit restricted hopefully I can Skype through.

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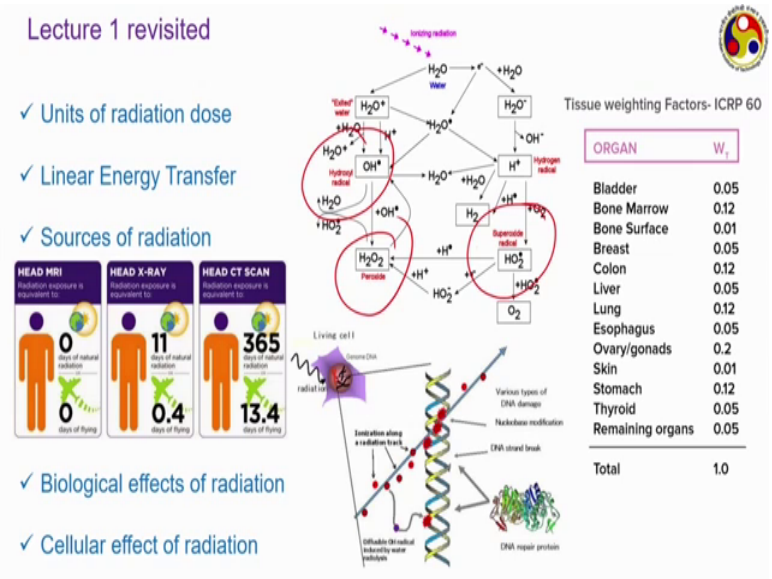

Just to have a recap of what we have done in the previous lecture first you are introduced to the different units of radiation doses that we generally use like. Just to associate with radioactivity, you are very early we are associate you were introduced to the units like urieo bacral which are associate with the radioactive disintegration. But when we are talking about the biological effects of radiation we have to look for new units and their units like rongio red and (Refer Time: 01:30) that came into picture which are conversion

in one of the three arts of radiation or the SI versions of them gray and Sievert. So, you are introduce to those.

And also several associated factors like different tissues respond differently to radiation accordingly we use some kind of tissue infector these are introduced. Then you are introduced the concept of linear energy transfer, which is actually some kind of potential or stopping power of a tissue against radiation. Or against a as different tissues respond differently or the same tissue I can say respond differently to different particle depending on their mass and energy level which is given measurement above in terms of the LET.

Then you have to you are introduce to different sources of radiation, living being can receive radiation from infinite number of sources like we can we are always subjected to some kind of so called background radiation which inverse the cosmic radiations and the rays coming from the outside atmosphere. Also there can be radiatic particle there are going interior to our body or inside our body through the foods that you are taking. There can be particles which are going with air during the inhalation process.

And also nowadays with increase in the medical equipments, there are significant fraction of radiation being contributed by different kind of medical instruments like where instruments like MRI which does not require any kind of radiation dose introduces any radiation does not introduce any kind of radiation effect. Very general or simple kind of technique like an x-ray can impose radiation equivalent to 11 days of natural radiation. Whereas CT scan which is again a quite common technology nowadays that just one sitting of hit CT scan can lead to radiation exposure to your body which is equivalent to 365 days that is one full year of natural radiation or more than 13 days of flying.

Of course, when you are flying or you are at higher altitude you are exposed to larger amount of cosmic radiation and that is why flying also induces quite a bit of radioactive effect. Now, in our on our body, but this modern medical equipments which involves radiation like-x rays or any kind of scans, they also can have significant effect and therefore, we need to be very very careful before undergo any such kind of them.

Then we have discussed about the biological effects of radiation and the cellular effect of radiation. You have seen the cellular effects of radiation can be of two types, primarily one is the indirect effect which leads to the particle radical formation as our cell primarily comprises of cytoplasm and water is the main component of the cytoplasm. So,

the radiation generally breaks the H 2 O molecule there leading to the formation of several very dangerous kinds of radicals such as the peroxide the hydroxyl and also so called the superoxides. They all can have important effects or important detrimental effects on the cell. And there can be direct effect also whether radiation can change the demorphidology or the morphology of the DNA itself we shall be looking more into them in today's lecture.

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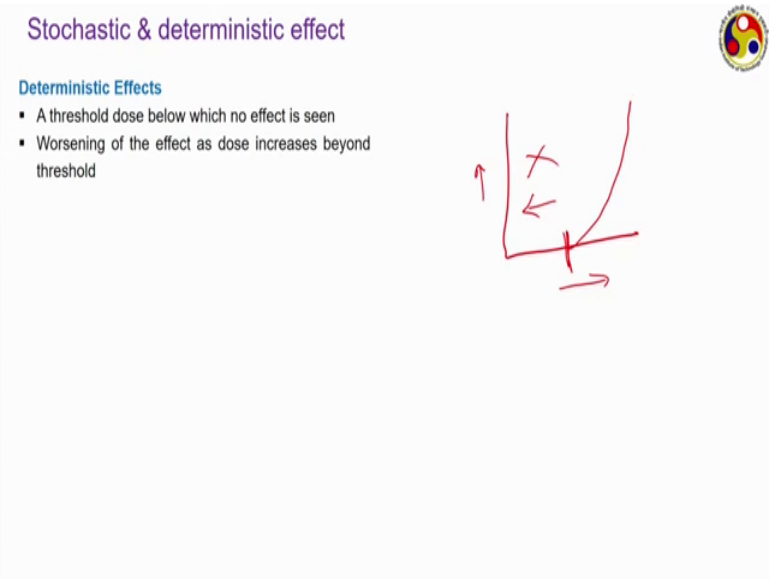

Now, the terms for introduce in a last lecture itself, but let us look a bit more into this two terminologies that is what where the biological effects radiation may have they are generally classified into two categories, one is stochastic, and other deterministic or sometimes called the nonstochastic effect. The deterministic effect generally refers to those kind of phenomenon where or which appears only once a threshold dose of radiation is based that is if the radiation exposure is less than the threshold, then you will not find any kind of effect or only when the threshold is reached the effect becomes prominent.

But once you have reach the threshold increasing the dose beyond that keeps worsening the effect. So, the behavior can be means if we plot something like this, where effect on this side and the dose on this side tills if this is a threshold then below this threshold you will not find any kind of effect, but above the threshold effect keep some increasing very

very shortly. So, this is what we called the deterministic effect. Deterministic effects generally are immediate effects or short-term effects.

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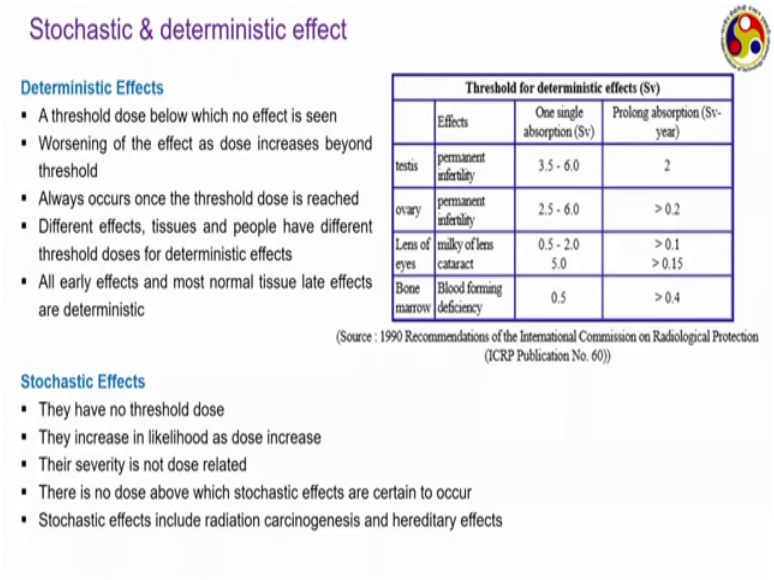

Once the threshold is reached they are guaranteed to appear. And also the threshold value actually depends upon the particular person or particular place which is subjected to radiation because different person or in fact, the different tissues of the same person have different values for this threshold. And also which kind of effect is going to appear accordingly the threshold is also going to vary. And any early effect as I have mentioned and most of the normal tissue late effects are deterministic or non-stochastic in nature.

These are some typical values of the threshold corresponding to the deterministic effect like generally the genital organs are the most affected by the radiation. And as you can see here when they are subjected to say the testis is subjected to a single absorption dose of strength 3.5 to 6 Sievert as be then that is actually quite high dose or a prolonged absorption of measuring to (Refer Time: 07:36) year then that will lead to a permanent infertility. Ovaries even more sensitive generally the female genitalia is much more sensitive to the male genitalia that is why the value is even smaller even 10 times smaller to this.

The lens of eye that is also very very sensitive to this when it is subjected to a radiation dose of something like 0.5 to 2 Sievert only, it can result to a milky of lens. For a scatter lock function may appear with a dose of 5 Sievert or greater than 0.15 Sievert here for

prolongment radiation dose. And bone marrow probably is the most sensitive kind of tissue or sensitive kind of part of the body related to radiation effects with a very relatively smaller radiation dose of only 0.5 Sievert it can lead to the blood forming deficiency.

So, and also this data are quite a bit old, but still very much valid. These are recommendation given by the well known ICRP that is International Commission on Radiation Protections who generally says the standard for any kind of radiation based guidelines. Now, putting this in comparison with stochastic effect, first stochastic effect there is no such threshold dose. So, stochastic effect whether that will appear or not that does not depend upon the magnitude of the radiation that the object is being subjected to. Rather there more likely with increasing the dose. Or I can say that the severity of the stochastic effect does not depend upon the intensity of the dose, but as the dose intensifies their appearance is more likely.

So, we cannot say that for this particular dose, this kind of stochastic effect is going to appear or not. But of course, they are more likely. And also there is no dose; however, stochastic effect starting to occur, they may not at all appear, but also they can appear with quite a small dose, because generally the effect is cumulative when someone is subject to a occur small dose for a very prolong period, then the stochastic effect can appear.

But I repeat if the strength of the dose is more, then there more likely to appear, but the severity of the diseases severity of the effect is has no relation with the strength of the dose. And stochastic effect actually concerns much larger or more catastrophically affects of radiations such as the carcinogenesis and also the gene defects or DNA nutritions leading to hereditary effects. So, stochastic effects are long term effects, and they are also quite difficult to spot, whereas deterministic or non-stochastic effects are immediate effects and they appear once their threshold is breached.

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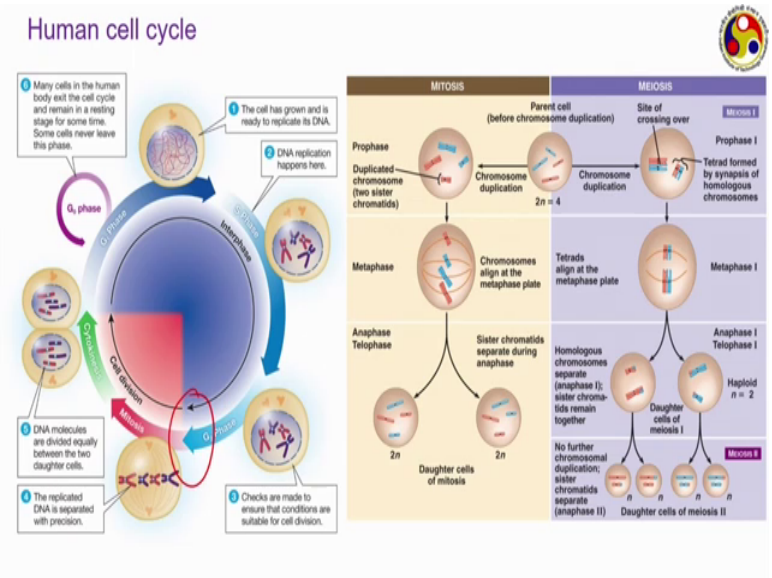

Now we need to gets some idea about the human cell cycle. Each human cell undergoes quite a few difference stages of development. The first stage of importance is the G 1 stage like shown in the diagram they are principally four or five stages. Once the first stage is the G 1 phase, which is the growth phase or growth phase one during the cell growth. And at the end of G 1 phase, it is ready to replicate the DNA then is the S phase when the DNA replication happens. Then because to the G 2 phase where the DNA replication is already done, so they makes further growth and ensures that it is ready for cell division and then the most important one the mitosis during which the cell divides into two.

And cytokinesis actually is a follow up step of mitosis sometimes called a part of the mitosis itself. And some cells may have an intermediate G naught stage as well, where many human body cells may exit the cell cycle remain in a resting position or some kind of neutral position for some time into some cells may remain there for a very, very long time and that is referred to as a G naught phase.

Now, scientist have done some experiments to understand which particular phase of this human cell cycle is most vulnerable to radiations. And to facilitate that what they have done they have chosen different cell samples and applying some kind of sophisticated techniques, they have ensured that their cell cycles are exactly following the same timings that is they are perfectly synchronous with each other. Once they have developed

quite a few cell colonies which are perfectly synchronous with each other then different cell colonies were subjected to different amounts of radiation and also in different phases of their individual cell cycles.

And it has been observed that a cell is the most vulnerable to radiation when that is going to the mitosis process or about to go through the mitosis process. When we subjected to radiation in the other phases like G 1 phase or S phase or early part of G 2 phase, effect of radiation is quite small, but when it is going to the mitosis then only it is most vulnerable or it is about to start the mitosis somewhere here then also it is very much vulnerable. And there is a reason also.

Like we know that inside the cell there are different kinds of components. Now, if radiation effects some of the components say if it is effects a mitochondria, the mitochondria may get permanently damaged, but inside a cell there can be several mitochondrion and therefore, just damaging one may not affect the cell performance too much, but once the radiation effects the nucleus then the radiation is definitely going to be the very important and the cell is going to suffer, because nucleus is a main part of the cell and that is unique.

And the nucleus is in the most vulnerable position when it is going to the mitosis. This is a very rough schematic representation of cell division where both mitosis and meiosis are shown. Meiosis is a one during which the chromosomal exchanges happens, but that is not of our interest. Let us focus on mitosis only. There are principally four different phases, prophase, metaphase, anaphase and telophase, and sometimes also fifth follow phases cytokinesis which is more like a post processing phase.

During the prophase phase the chromosomes are duplicated this is where the chromosomes are duplicated. So, initially if there are if there are n pairs of chromosomes like it this is a parent cell where there are in this diagram, there are four chromosomes. The chromosomes are initially duplicated in the prophase phase leading to four chromosomes. And now our four pairs of chromosomes I should say.

And then this chromosomes align each other along the metaphase plane during the metaphase process, and then they subsequently separate out to develop to new daughter cells during the anaphase getting completed during the telophase process. Accordingly we get two different daughter cells which are identical to the parent cell. Mitosis is the

most common type of cell division that we can see and that is the one that is responsible for development of our body from a single cell embryo to a fully grown human person human body.

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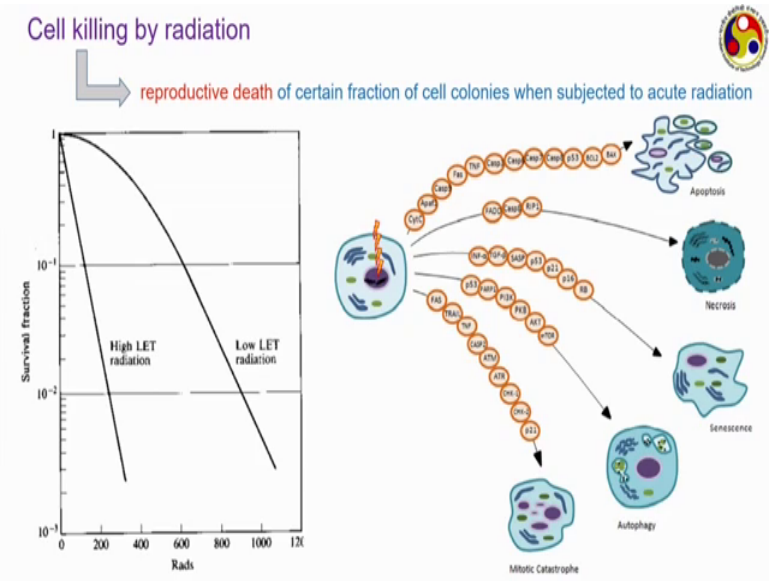

So, if mitosis is affected by radiation then there can be real catastrophe effect and something known as cell killing. Cell killing refers to reproductive date of a certain fraction of cell colonies when subjected to acute radiation. Like when a cell is affected by radiation, then the cell may loses reproductive power, and accordingly it is terminology wise it is called the cell is being killed that is cell killing or causing the reproductive death that depends and upon the level of the dose. Again experiments are conducted with different cell colonies being subjecting them to different levels of radiation, and then observing what fraction of that has suffered this cell killing. And it has been found to be proportional to the LET again.

Like in case of high LET radiation it is a very, very short decline. You can see it is a vertical straight line which is going down very very rapidly. Here one thing of importance here is a vertical scale is a logarithmic scale and so the change is extremely rapid. Whereas for low LET radiation, the change is very small particular in this part, there is very little change, it is increasing only later on. So, for a high LET radiation dose, the effect of for radiation causing the cell killing is very, very prominent.

And now this cell killing can be of five different types which are shown here. (Refer Time: 17:21) subjective radiation can follow different kinds of roots all accessories several kinds of enzymes and chemical processes. One thing you have to remember here is that the while we are talking about the effect of radiation on cell killing, actually all the effects are more or less chemically in nature particular the indirect effect of radiation. Because a cell compresses a several kinds of chemicals and as we have already seen the indirect effect of radiation is to develop free radicals. And once the radicals develop, then the next part is just chemistry. So, from that point of view, the effect after that pre radical formation has taken place is the same as with any kind of chemical poisoning.

So, the way the cell is going to react to a nuclear accident, and the way it is going to react to some chemical accident, there may not be too much different. But of course, the fact is that for a nuclear accident, the affect may be very very prolonged because the radioactivity may remain in the surrounding for a few hundred years as well. So, these are the five different kinds of mechanisms of cell may undergoes apoptosis, necrosis, senescence, autophagy and mitotic catastrophe.

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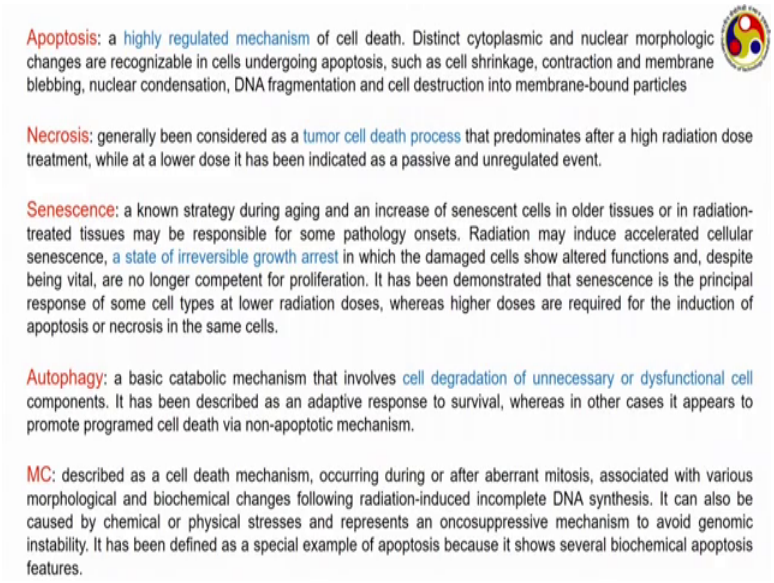

Apoptosis is a highly regulated mechanism of cell death. Distinct cytoplasmic and nuclear morphological changes are recognizable in cells undergoing apoptosis, such as shrinkage of the cell, contraction and membrane blebbing, nuclear condensation, fragmentation of the DNAs, and also cell destruction into membrane-bound particles.

So, apoptosis is the most common type of cell killing process in fact, a body to replace the old cell by the new one also follows apoptosis, apoptosis. But apoptosis is the first most prominent kind of effect cell killing mechanism that radiation can lead to there is an necrosis, necrosis is generally is considered as a tumor cell death process that predominates after a high radiation dose treatment. While at a lower dose, it has been indicated as a passive and unregulated event. One thing we have to understand here the all the effect of radiation may not be bad because treatment of carcinogenesis such kind of things also you makes use of high dose radiations. And they are the objective radiation is to kill the affected tumor cells. So, necrosis general is a primary mechanism there which leads to the cell killing.

Then senescence is a non-strategy during aging and increase of senescence cells in older tissues or in radiation treated tissues maybe responsible for some pathological onset. Radiation may induce accelerated cellular senescence, a state of irreversible a growth harassed in which the damage cell show altered functions and, disagreeing or no longer competent for proliferation. So, cell is not able to grow any further and also not able to divide any further. It has been demonstrated that senescence is the principal response of some cell types at lower radiation doses, whereas at higher doses they may lead to apoptosis or in certain cases necrosis.

So, this theory the primary types of cell killing mechanism that you can find when that is subjected to radiation, apoptosis is the most common one, necrosis can also be found, but when the radiation dose is low then the most common one that you will find is this senescence. But when the dose is high it is more likely to be apoptosis or in certain cases necrosis.

Autophagy is basic catabolic mechanism that involves cell degradation of unnecessary or dysfunctional cell components. Again it is a very natural process, the dysfunctional cell components are being eaten up by the cell itself or some other part of the body whose function is to clean the unnecessary portions, thereby cleaning the body itself. It has been described as an adaptive response to survival, whereas in other cases it appears to promote programmed cell death via non apoptotic mechanism.

And finally, MC or metabolic catastrophe; it is described as cell death mechanism occurring during or after obedient mitosis associated with various morphological and

biochemical changes following radiation-induced incomplete DNA synthesis. It can also be caused by chemical or physical stresses and represents and oncosuppressive mechanism to avoid geometric instability. It has been defined as a special example of apoptosis because it shows several biochemical features which are quite similar to apoptosis only.

Now, as we have repeatedly mentioning that the way different tissues respond to radiation and not same. Of course, when a cell is subjected to radiation particularly when is above to mitosis that is very much likely to go for cell killing that is reproductive death. However, that likelihood that is individual to the tissue itself.

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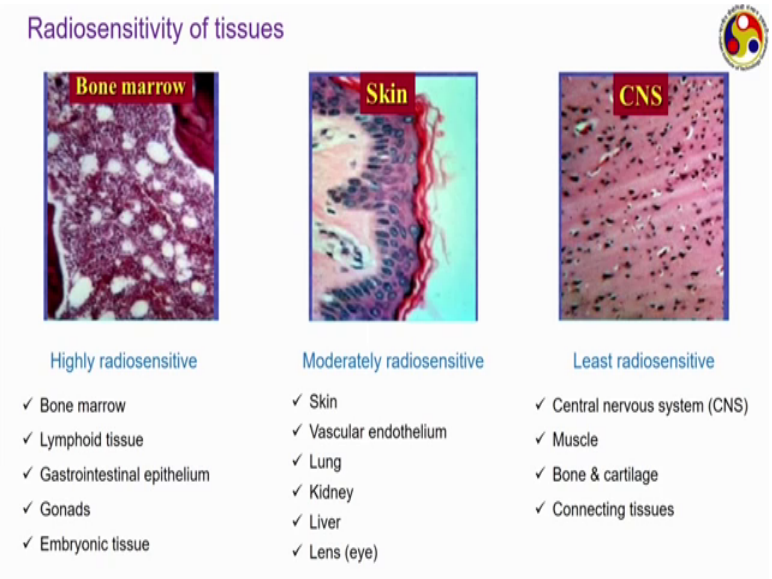

Based upon the radio sensitivity tissues can be defined in to or divide into three categories highly radiosensitive, moderately radiosensitive and least radiosensitive. Highly radiosensitives are those who is generally a very important tissues of the body and their also affected strongly by the radiation. The most important one of them maybe bone marrow. This is a picture of bone marrow being suffered by radiation. The lymphoid tissue can be there. The gastro intestinal epithelium is also very important which actually forms the inner layer of our GI tract, those cells are very very active and they are going to continuous mitosis process. So, they are very likely to get affected by radiations. The gonads I kept on mention repeatedly there also very much affected by radiation, even small amount of radiation also can also lead to permanent infertility for

both male and female. The embryonic tissue that is the fetus that is also highly sensitive to radiation.

The under moderates moderately radiosensitive tissues, you can get skin. Skin is always subject to radiation particular the background radiation or cosmic radiation. It is being subjected to the effect of radiation on skin can be in the form of radiation is of the skin appearance small pimple kind of structures or rashes etcetera. And can be even more severe depending upon what level of radiation it is being subjected to. This is a picture where you can clearly see here there are lots of disintegrations of the internal cells and in this part as well because of the effect of radiation they are strongly affected. The vascular endothelium, lung, kidney, liver and also the lens of our eyes, they can also be strongly affected by radiation.

But the parts which are very less affected for most of the normal radiation dose there almost immune to radiation can be the nervous system, thankfully on nervous system is hardly affected by radiation, and therefore, therefore, even when someone is subjected to radiation for a prolongation of time, he is nervous system keeps on working properly. The muscles the heart tissues like muscles, and bones, and cartilage and several connecting tissues there also very less affected by radiations.

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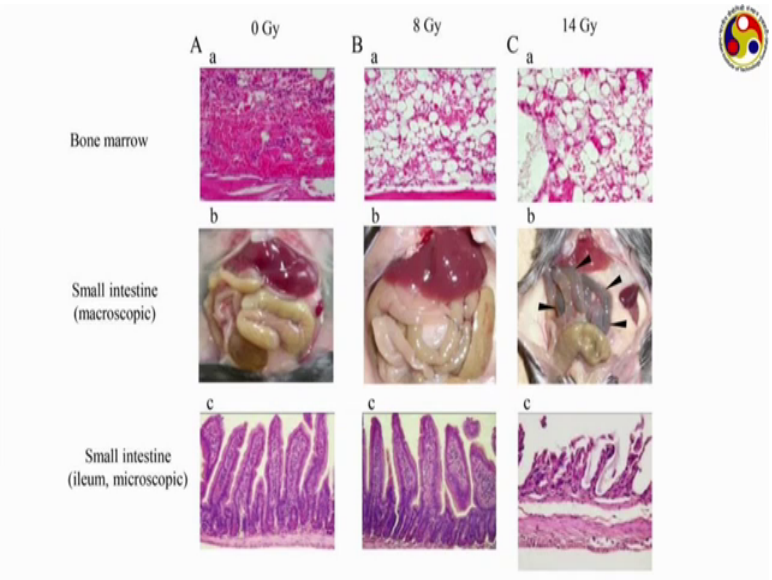

This is a set up pictures which shows the effect of radiation on some highly sensitive tissues. This one is the normal picture of a bone marrow; it is not subjected to radiation.

It is subjected to radiation dose of 8 gray, you can see there are very less number of cells appearing. And the when you subjected to higher radiation dose of 14 gray, the complete structure has changed. And accordingly most of the bone marrows have suffered the cell killing or reproductive death not being able to cause develop newer blood cells, and therefore may lead to the formulate to leukemia.

Small intestine, if it is macroscopic view then you can see with 8 gray of this the muscles are corresponding to tissues are elongated, when only subjected to a 14 gray dose then this cells have already died, this tissues whether they have already died and severely affected. And if you take a microscope view of the same thing, then you can see with 8 gray dose, they have already started to get affected. Their shape has got distorted and also some of them some discontinuous started to appear in this zones, they have started to get separated from the base. And when it is much higher dose of radiation, they are completely separated from the base, and their shape is also extremely different from what we initially had. So, these are the effects radiation may have on highly sensitive tissues.

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Radioactive effect of foetus

Gestational age	Effect	Threshold dose
0-2 weeks	Death or no consequence	50-100 mGy
2-8 weeks	Congenital anomalies	200 mGy
	Growth retardation	200-250 mGy
	Childhood leukemia	
8-15 weeks	Severe mental retardation	60-310 mGy
	Intellectual deficit	200 mGy
	Microcephaly	200 mGy
16-25 weeks	Severe mental retardation	250-280 mGy

And radiation can have even severe effects on the fetus or embryo. Particularly during the first eight weeks of pregnancy. You can see within first two weeks if it is subjected to a dose or threshold dose of 50 to 100 milligray then it can lead to the death of the fetus. Whereas, within 2 to 8 weeks, with the threshold dose of 200 or 250 milligray, it can lead to congenital anomalies, growth retardation and childhood leukemia. For later part the

chances are much lesser threshold also keeps increasing, but there the effect of radiation primarily not fetus death, but severe effects on the mental part that is it can lead to mental retardation, it can lead to intellectual deficit or in severe mental retardation may also appear in very in the later part of pregnancy.

And that is one primary reason that nowadays pregnant ladies are not suggest to go for x-rays. Earlier x ray was the most common mechanism that was used by the doctors to test the status of the fetus, but nowadays everyone is ask to go for ultrasound, because it is almost the use of x rays almost banned for pregnant ladies that is pre precisely to avoid these effects of radiation. Of course, ultrasound does not involve any kind of radiation effects as that is a sound waves the techniques and hence that is completely that can completely avoid any of this kind of effects.

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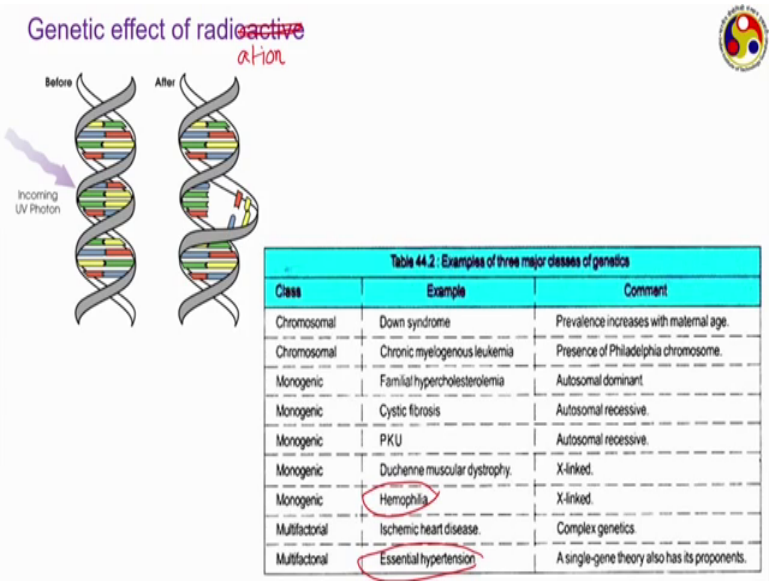

Table 44.2 : Examples of three major classes of genetics

Class	Example	Comment
Chromosomal	Down syndrome	Prevalence increases with maternal age.
Chromosomal	Chronic myelogenous leukemia	Presence of Philadelphia chromosome.
Monogenic	Familial hypercholesterolemia	Autosomal dominant.
Monogenic	Cystic fibrosis	Autosomal recessive.
Monogenic	PKU	Autosomal recessive.
Monogenic	Duchenne muscular dystrophy.	X-linked.
Monogenic	Hemophilia	X-linked.
Multifactorial	Ischemic heart disease.	Complex genetics.
Multifactorial	Essential hypertension	A single-gene theory also has its proponents.

Then we come to the genetic effects of radiation. It should be genetic effect of radia radiation not radioactive. Now, that is where you are talking about the direct effect. Direct effect refers to when the DNA structure is directly being subjected to incoming radiation something like an UV photon or an IR photon. Again that is very likely to appear during the mitosis process itself, because during others stages of the cell division or cell cycle I should say the DNA is not exposed, the DNA is kept inside the nucleus and it has very less chance to get exposed to the radiation. But during the cell division process the DNAs are open and that is why the DNAs make it subjected to radiation. And

there can be several kinds of effects of radiation, and the primary effect may can be the causing the nutrition to the DNAs thereby completely changing the characteristic of the offspring who are going to come from the same from that person um.

If the jam cells are subjective to such kind of radiation, generally they lose the power to reproduce, but if any of those jam cells which are affected by radiation, they are able to survive and then lead to the formation of a zygote, then there is a high chance that the next generation will be affected by radiation. There can be several kinds of effect that we can find very commonly the down syndrome is one of the effects we can have chronic myelogenous leukemia or we can have also cystic fibrosis, we can have hemophilia. And we have essential hypertension. These are all different kinds of effects that may come because of radiation.

Again these effects are also similar to any other kind of genetic effects like we have mentioned in case of indirect effect, the effect of radiation is took is to cause the radical formation and then rest part is similar to any kind of chemical effect. Similarly, here also here radiation is causing a nutrition to the DNA or causing a changing in the structure of the DNA, and then next part is similar to any kind of genetic defects genetic defects I should say.

So, there are several models of gene theory that are available which tries to predict this, but still very less is known and also this genetic effects of radiation are more stochastic type that is they are long term effect. It is very difficult to understand whether they are going to appear or not, very difficult to understand immediately whether they are going to appear or not. Only with a observing over a prolong period time, we shall be able to make ensure that they are going to appear. Particularly if the effects comes in the next generation then that is quite difficult to correlate, because the defect can the effect or genetic nutrition that is getting caused that can be from any of the parents, can be from the father, can be from the mother and how much effect is getting transferred that is also quite difficult to practice difficult to predict.

So, this takes us towards the end of this particular module, actually there are several other factors that could have been added here, and the length of the module itself is also quite short. But any further discussion that I would like to have about the effects of radiation, it can have on human cells or on the DNA that requires the much more

knowledge about the biology and also genetics which I am I am not at all converse into it. And also that is not relevant to understand from the point of view of this course that is why you are keeping this module quite short.

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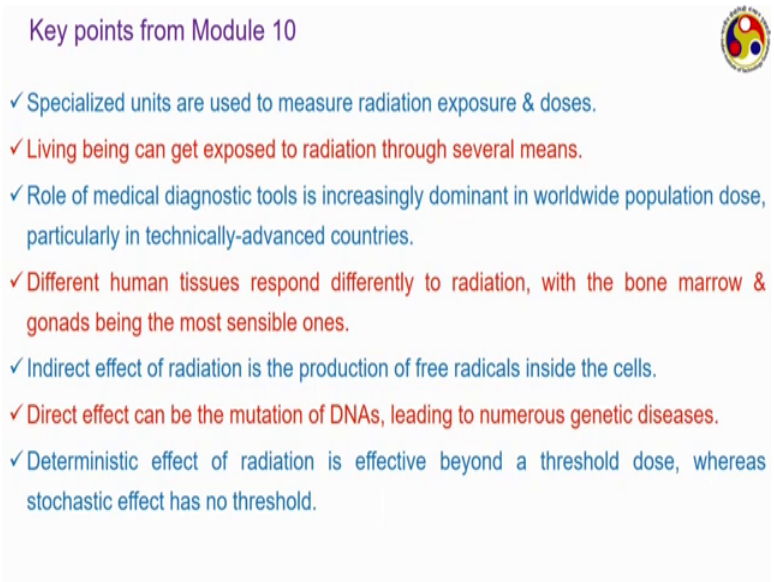

Now, just to summarize the key points from this particular module; here your interest to specialized units for measurement of radiation exposure and doses units like Sievert and gray. Then living being can get exposed to radiation to several means. Role of medical diagnostic tools is increasingly dominant in worldwide population dose, particularly in technically-advanced countries like we have seen in 1980s where medical instruments are contributing only ultra function in total immunity doses. In early 2000s, it is all contributing nearly half of the total radiation dose in United States alone.

Different human tissues respond different radiation, with the bone marrow and gonads being the most sensible ones. And also I should mention about the fetus. Indirect effect of radiation is the production of free radicals inside the cell and subsequent chemical effects. Direct affect can be the nutrition of DNAs leading to numerous genetic diseases. Deterministic effect of radiation is effective beyond a threshold dose, but once the threshold is breached, then the severity of the effect is directly proportional to the dose itself. Whereas, the stochastic effect has no threshold, it may appear may not appear it is very difficult to predict, but larger the strength of the dose, the more likely are this stochastic effect appear of this stochastic effects, so that is all for this tenth module.

This probably is the shortest possible module that we have in this intercourse because most part of the relevant discussions are related to biology and medical sciences which I have tried to avoid in this. But something that I could have could have added rather that is whatever we have discussed here are the bad effects of the radiation, but there can be several good effects also made the use of radiation in cancer treatments or similar kind of other fix again some medical terminologies and medical knowledge is required. So, I have not gone there.

And finally, that something that I must have included that is how can we get how can we get protected can get ourselves protected from this radiation. Particularly from the very beginning of the course we repeatedly saying that whenever there is any discussion of setting up a nuclear power stations, the major discussion is to protect the surroundings from the dose of radiation, but whether that is at all important or what kind of protection we should have in a nuclear power stations but that discussions I have not putting this, because that will be the topic of our next week where we are going to discuss about the safety and security of a nuclear power plant and there we shall we starting to disc starting with the discussion of how we can get ourselves protected from radiation itself.

So, thanks to all of you for listening. If you have any query please write to us we are shall be happy to answer you.

Thanks a lot. Bye.