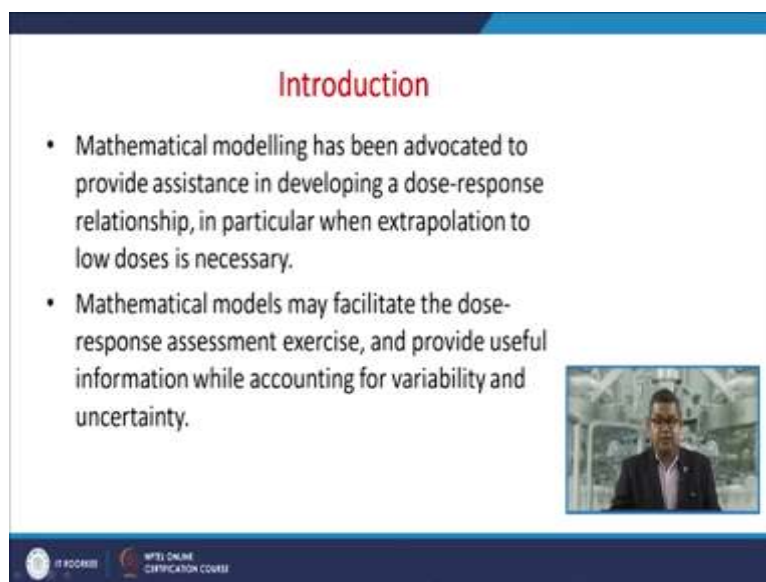



**Chemical Process Safety**  
**Professor Shishir Sinha**  
**Department of Chemical Engineering**  
**Indian Institute of Technology Roorkee**  
**Lecture 09**  
**Dose-Response and Threshold Dose**  
**Predictive Models and Extrapolation**

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**Introduction**

- Mathematical modelling has been advocated to provide assistance in developing a dose-response relationship, in particular when extrapolation to low doses is necessary.
- Mathematical models may facilitate the dose-response assessment exercise, and provide useful information while accounting for variability and uncertainty.



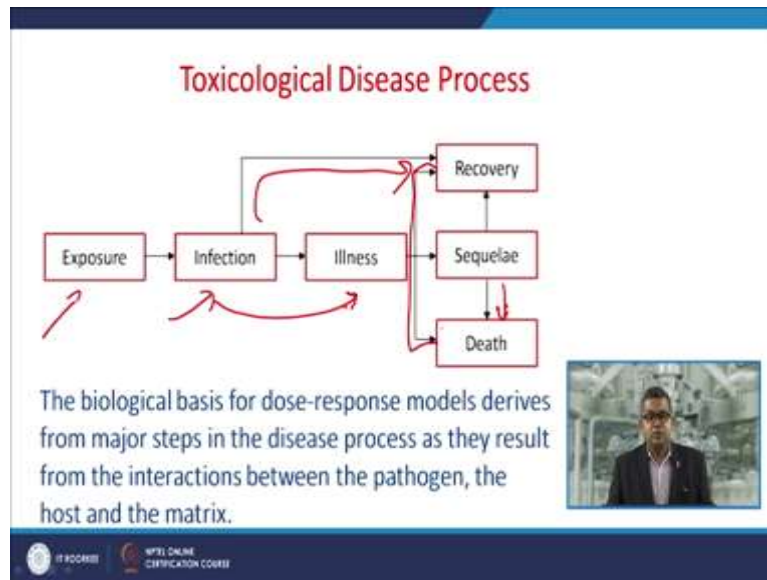
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Welcome to the Dose-Response and Threshold Module. In this particular module we will discuss the different predictive models and we will learn that how we can extrapolate those data to the real time things. Now, mathematical modeling has been advocated to provide assistance in developing a dose response relationship in particular when extrapolation to low doses is necessary.

Now, the reason is that as we discussed in the previous module we cannot overlook the importance of dose versus response because the dose is directly applies to the various parameters like age, different environmental condition, physique, et cetera. So and every time you cannot perform the experimentation or you cannot utilize the previous data available. So the best way is to perform the mathematical modeling and you can extrapolate all those modeling data to the to the industry or to the real-time situations.

So the mathematical models may facilitate the dose response assessment exercise, and provide the useful information while accounting for variability and different type of uncertainty. Now, remember these kinds of things, they are always governed by the different parameters.

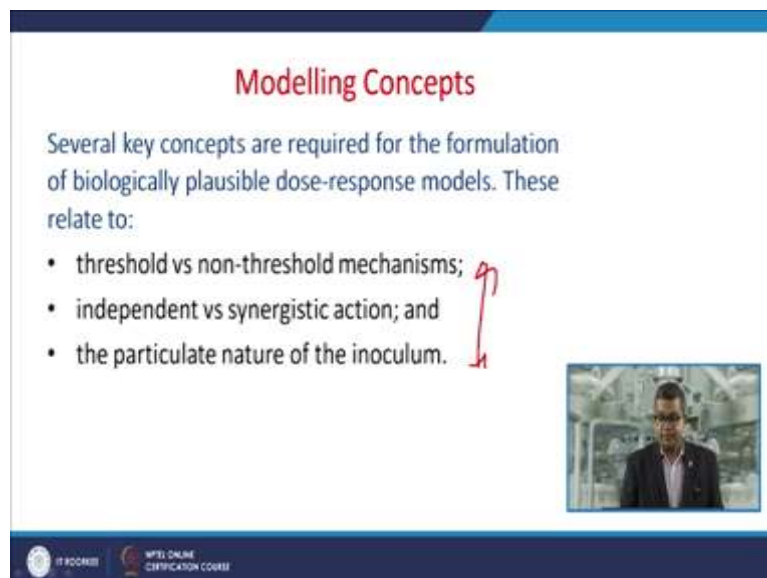
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So, let us take one by one the toxicological disease process usually we follow a set pattern or a set protocol once a particular person get exposed then based on the exposure it gets infection and this may lead to the illness and sometimes directly it may get recover. Now, after illness there are certain skill and sometimes it may lead to death or sometimes it may recover.

So, biological basis for dose-response model derives from major steps in the disease process as the result from the interaction between the pathogen and host and the matrix. So these three-four different things we must encounter while go for this type of modelling.

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So, first let us understand that what is modeling concept, several key concepts they are required for formulation of biological things in dose response model these relate to the threshold versus non-threshold mechanism. We have gone through this threshold aspect in the previous modules, independent versus synergistic action and the particular nature of inoculum. So we must know these concepts a priori.

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### Modelling Concepts

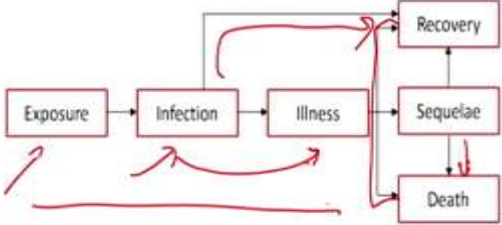
Ideally, the dose-response models should represent the following series of conditional events:

- the probability of infection given exposure;
- the probability of acute illness given infection; and
- the probability of sequelae or mortality given acute illness.




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### Toxicological Disease Process



The biological basis for dose-response models derives from major steps in the disease process as they result from the interactions between the pathogen, the host and the matrix.



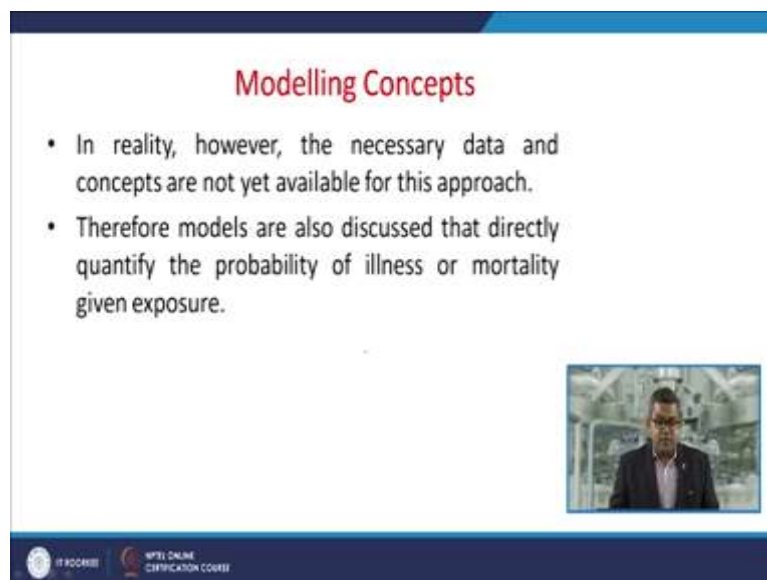
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Ideally the dose-response models should represent the following series of conditional event, one is the probability of infection given exposure (go back to this previous slides all these things they are under the representative conditions). The probability of infection given exposure and then the probability of acute illness given infection. Because sometimes you may

recover and sometimes you may not, so what is the probability of this acute illness given infection and the probability of sequel or mortality given the acute illness?


Remember if you recall the first module, we have discussed the accidental pyramid, then the number of responses on the bottom of the pyramids on the larger side and it goes on diminishing and there may be one or two fertility for every kind of scenario. So you must find out all three aspects that is the probability of infection, acute illness, and mortality et cetera so that you can have perform the model analysis adequately.


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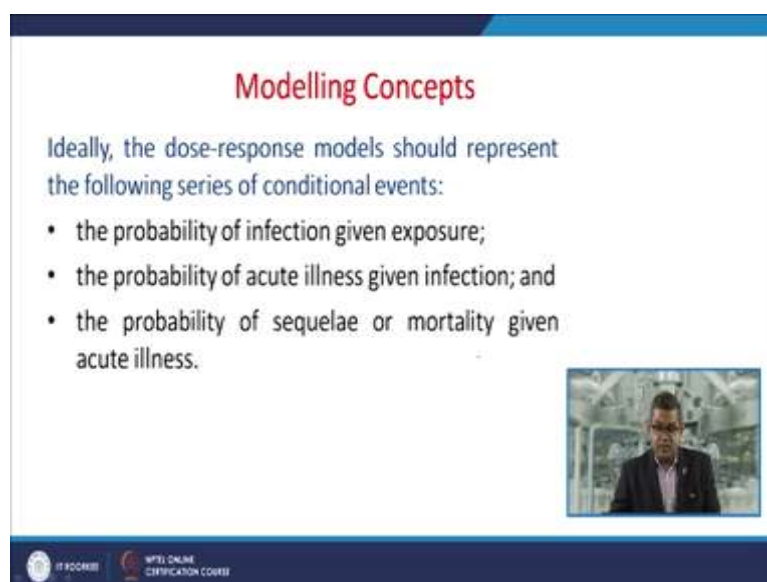


**Modelling Concepts**

- In reality, however, the necessary data and concepts are not yet available for this approach.
- Therefore models are also discussed that directly quantify the probability of illness or mortality given exposure.






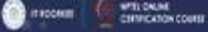


**Modelling Concepts**

Ideally, the dose-response models should represent the following series of conditional events:

- the probability of infection given exposure;
- the probability of acute illness given infection; and
- the probability of sequelae or mortality given acute illness.





In reality, the necessary data and concepts are not yet available for these kinds of approach therefore, you require a model which is discussed that directly quantify the probability of illness and mortality for a given exposure.

(Refer Slide Time: 05:07)

**Modelling Concepts**

Threshold vs non-threshold mechanisms

- The traditional interpretation of dose-response information was to assume the existence of a threshold level of pathogens that must be ingested in order for the microorganism to produce infection or disease.
- A threshold exists if there is no effect below some exposure level, but above that level the effect is certain to occur.

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Go back to the threshold versus non-threshold mechanism the traditional interpretation of those response information was to assume the existence of threshold level of pathogen that must be ingested in order for microorganism to produce infection or disease. A threshold exists if there is no effect below some exposure level, but above that level the effect is certain to occur.

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**Modelling Concepts**

Threshold vs non-threshold mechanisms

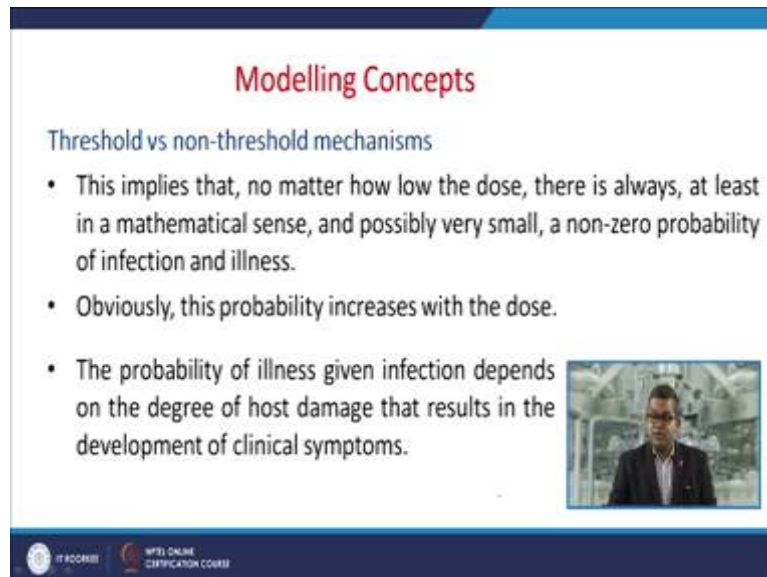
- Attempts to define the numerical value of such thresholds in test populations have typically been unsuccessful, although the concept is widely referred to in the literature as the "minimal infectious dose".
- An alternative hypothesis is that, due to the potential for microorganisms to multiply within the host, infection may result from the survival of a single, viable,  
– infectious pathogenic organism  
– "single-hit concept"

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Now, there are attempts to define the numerical values of such threshold in test population have typically been unsuccessful because you will not find all those testing modules, et cetera, although the concept is widely referred in the literature as the minimal infectious dose. So an alternative hypothesis is that due to the potential for microorganism to multiply within the host

infection may result from the survival of a single viable. Now, infectious pathogenic organisms that is called a single hit concept.


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**Modelling Concepts**

Threshold vs non-threshold mechanisms

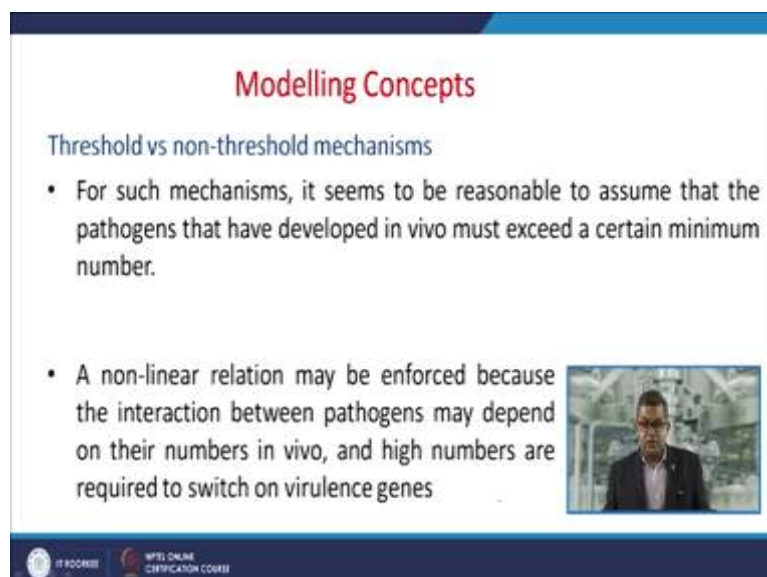
- This implies that, no matter how low the dose, there is always, at least in a mathematical sense, and possibly very small, a non-zero probability of infection and illness.
- Obviously, this probability increases with the dose.
- The probability of illness given infection depends on the degree of host damage that results in the development of clinical symptoms.



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Now this implies that no matter how low the dose, there is always at least a mathematical sense, and possibly very small, a nonzero probability of infection and illness. Obviously, this probability increases with the dose, so you are taking more and more than definitely the probability will be no on the higher side. The probability of illness given the infection depends on the degree of host damage that results in the development of clinical symptom.


(Refer Slide Time: 06:47)



**Modelling Concepts**

Threshold vs non-threshold mechanisms

- For such mechanisms, it seems to be reasonable to assume that the pathogens that have developed in vivo must exceed a certain minimum number.
- A non-linear relation may be enforced because the interaction between pathogens may depend on their numbers in vivo, and high numbers are required to switch on virulence genes



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For such mechanisms, it seems to be reasonable to assume that the pathogens that have developed in vivo must exceed a certain minimum number. A non-linear relation may be enforced because of because the interaction between pathogen may depend on their number in vivo, and high number are required to switch on virulence genes.


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**Modelling Concepts**

Independent action vs synergistic action

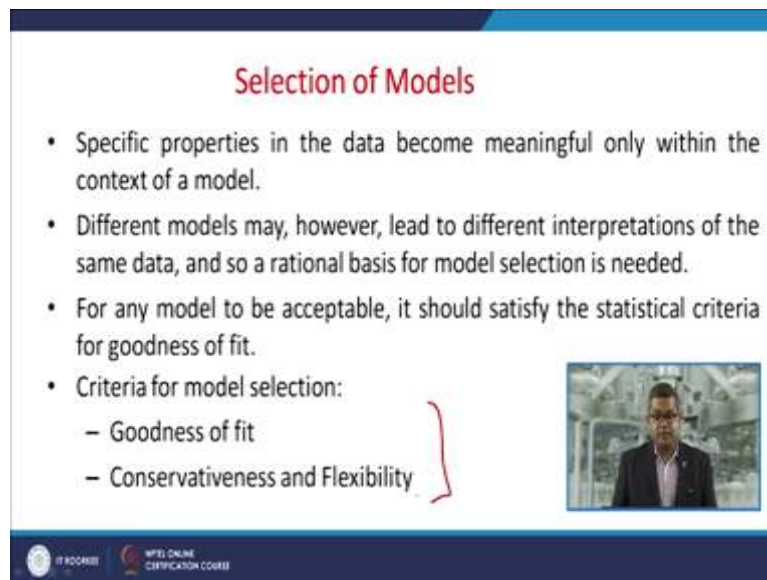
- Hypothesis: the mean probability "p" per inoculated pathogen to cause (or help cause) an infection (symptomatic or fatal) is independent of the number of pathogens inoculated, and for a partially resistant host it is less than unity.
- **In contrast**, the hypotheses of maximum and of partial synergism postulate that inoculated pathogens cooperate so that the value of "p" increases as the size of the dose increases. —



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Now, go to the independent action versus synergistic action. The hypothesis says that the mean probability “p” that is per inoculated pathogen to cause or help cause an infection symptomatic or fatal is independent of the number of pathogens inoculated and for a partially resistant host it is less than unity. In contrast, the hypothesis of maximum and of partial synergism postulates that the inoculated pathogen cooperate so that the value of “p” increases as the size of dose increases.


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**Selection of Models**

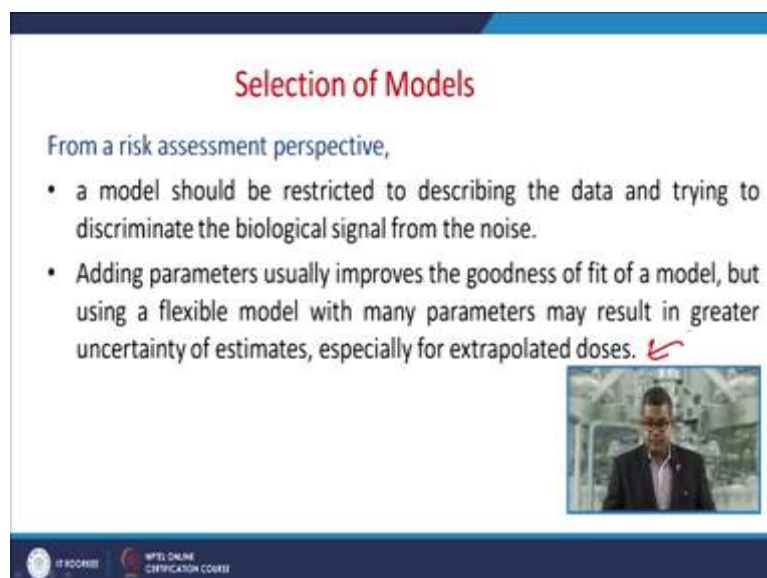
- Specific properties in the data become meaningful only within the context of a model.
- Different models may, however, lead to different interpretations of the same data, and so a rational basis for model selection is needed.
- For any model to be acceptable, it should satisfy the statistical criteria for goodness of fit.
- Criteria for model selection:
  - Goodness of fit
  - Conservativeness and Flexibility





Now, how do we select the models and that depends on certain factors like specific properties in the data become meaningful only within the context of model; one thing. Second is a different model may, however, lead to different interpretations of the same data. So a rational basis of model selection is always needed. For any model to be acceptable it should satisfy the statistical criteria for goodness to fit. Now the criteria for model selection this is based on two things, goodness of fit and conservativeness or and flexibility.


(Refer Slide Time: 8:40)




**Selection of Models**

From a risk assessment perspective,

- a model should be restricted to describing the data and trying to discriminate the biological signal from the noise.
- Adding parameters usually improves the goodness of fit of a model, but using a flexible model with many parameters may result in greater uncertainty of estimates, especially for extrapolated doses. ↪



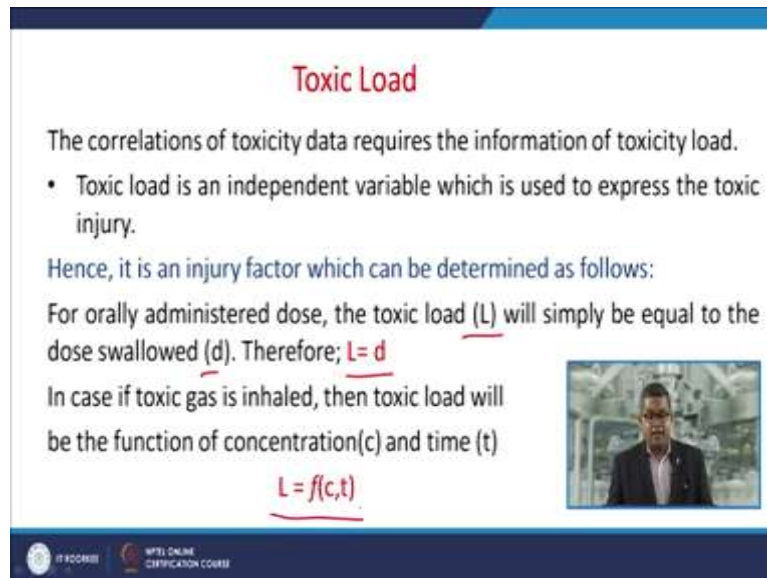


From a risk assessment perspective, a model should be restricted to describing the data and trying to discriminate the biological signal from the noise. Now adding parameters usually



improves the goodness of fit of a model, but using a flexible model with many parameters may result in greater uncertainty of estimates, especially for extrapolated doses.

(Refer Slide Time: 9:14)



**Toxic Load**

The correlations of toxicity data requires the information of toxicity load.

- Toxic load is an independent variable which is used to express the toxic injury.

Hence, it is an injury factor which can be determined as follows:

For orally administered dose, the toxic load (L) will simply be equal to the dose swallowed (d). Therefore;  $L = d$

In case if toxic gas is inhaled, then toxic load will be the function of concentration(c) and time (t)

$L = f(c,t)$

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Now, we go to the toxic load.

For the correlations of toxicity data requires the information about the toxic load. Now toxic load is an independent variable which is used to express the toxic injury. Hence, it is an injury factor which can be determined as follows. For orally administered dose, the toxic load “L” will simply be equal to the dose swallowed “d”.

So therefore,  $L = d$ .


In case if toxic gas is inhaled, then toxic load will be the function of concentration “c” and a time “t”. So “L” is a function of “c” and “t”.

(Refer Slide Time: 10:00)

### Toxic Load

- ❖  $L = f(c,t)$ 
  - ❖ This can be simply a product of both terms as;  
 $L = ct$  —
  - ❖ Or it can be of complex form  
 $L = ct^m$

For acute inhalation toxicity of irritant gases the value of  $m$  for animals tends to be less than unity and is often in the order of 0.5



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Now, this “L” is a function of “c” and “t”, this can be simply a product of both terms as

$$L = c.t;$$

like this, or it can be in the complex form

$$L = ct^m$$

For acute inhalation the toxicity of irritant gases the value of  $m$  for animal tends to be less than unity and is often in the order of 0.5.

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### Toxic load- response relation

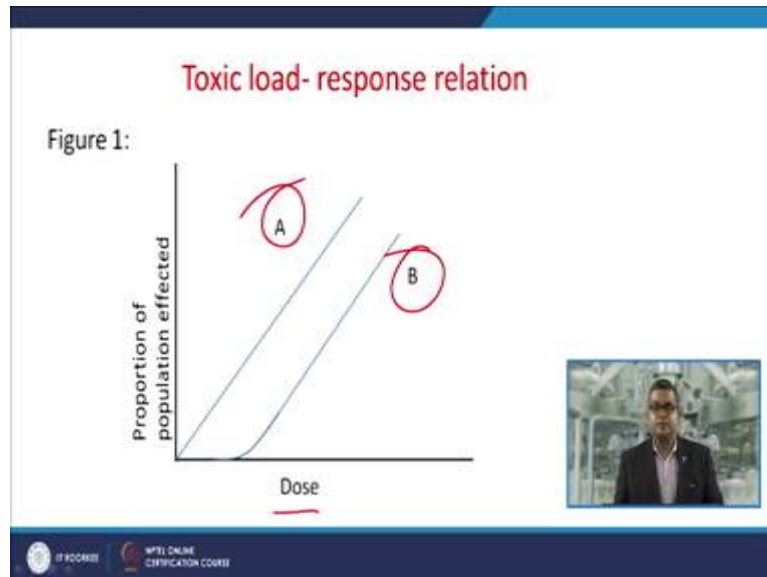
- A distribution which is used to correlate data for toxic injurious, as for injury of other kinds is the Log normal distribution. Associated with the lognormal distribution is the probit equation.
- A particular problem arises at low levels of toxic load because the precise relationship between toxic load and the proportion affected is a critical issue in setting exposure limit.



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Now, you must establish the toxic load response relations. A distribution which is used to correlate data for toxic injuries, as for injury of other kind is log normal distribution associated with the log normal distribution is the probit equation. So a particular problem arises at low level of toxic load because the precise relationship between toxic load and the proportion affected is a critical issue in setting exposure limit.

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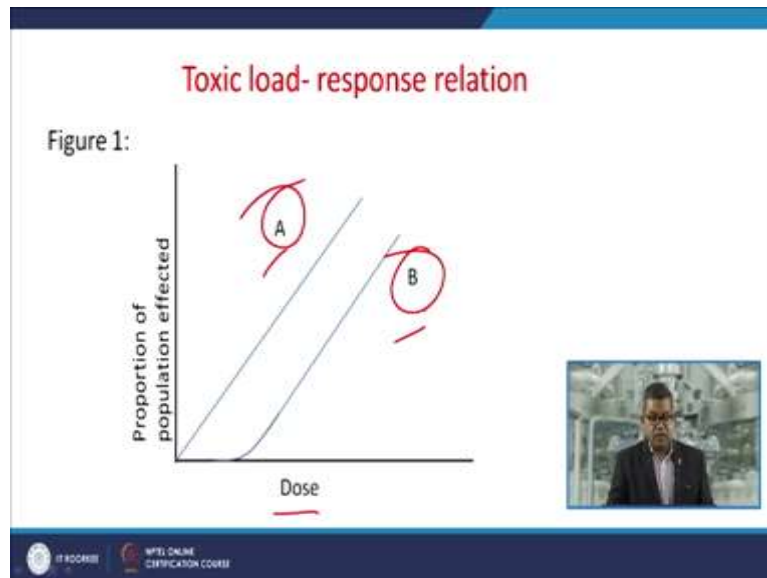


Now, here you can see the toxic load response relation, this figure. The proportion population affected and dose and there are two responses A and B.

(Refer Slide Time: 11:25)

The slide is titled "Toxic load- response relation". It contains a bulleted list of points explaining the two curves from Figure 1. A small video inset of a man is in the bottom right. The slide footer includes logos for "IPR 100838" and "WPI ONLINE CERTIFICATION COURSE".

- Figure 1 illustrates two possible relations with relations
  - "A" there is no lower limit below which there is no noxious effect, whereas
  - with Sigmoidal relation "B" be there may be said to be a "threshold" below which the effect of toxic load is negligible
- It is frequently difficult to distinguish between these two type of curves to establish whether there is or is not a threshold
- This is the case particularly where the number of workers involved are small and the conditions of exposure are variable.



Now, this particular figure illustrates the two possible relations with relations, “A” there is no lower limit below which there is no noxious effect this one. Now with sigmoidal relation “B” there be many may be said to be the threshold below which the effect of toxic load is negligible. Now it is frequently difficult to distinguish between these two type of curves to establish whether there is or not a threshold. Now, this is the case particularly where the number of workers involved are small and the conditions of exposures exposure are variable.

(Refer Slide Time: 12:14)

### Toxicokinetic Modelling: One- Compartment Model

- Two Cases
  - Impulse Response ↙  
Refers to instantaneous introduction of the chemical
  - Step Response ↙  
Refers to constant input of chemical to the body

The original concentration being zero for both the cases

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Now, toxicokinetic modelling, this is the one compartment model, another modeling concept. There are two cases, one is the impulse response refers to the instantaneous introduction of chemical sometimes all of sudden the concentration is increases, then step response refers to

the constant input of chemical to the bodies. So this is this based on the frequency. So the original concentration is being zero for both the cases.

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**Toxicokinetic Modelling: One- Compartment Model**


- For Impulse response;

$$\frac{dX}{dt} = -k_e X$$

With,

$$X(0) = D_0$$

Where  $D_0$  is the dose of chemical ,  $k_e$  is the elimination constant and  $X$  is the mass of chemical in the body.



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Now, for impulsive response we may utilize this mathematical equation

$$\frac{dX}{dt} = -k_e X$$

With,

$$X(0) = D_0$$

Where, “ $D_0$ ” is the dose of chemical and “ $k$ ” is the elimination constant and “ $X$ ” is the mass of chemical in the body.

(Refer Slide Time: 13:08)


**Toxicokinetic Modelling: One-Compartment Model**

- For Step response;  $\frac{dX}{dt} = D - k_e X$

Concentration C is given by,

$$C = x/V_d$$

Where  $V_d$  is the apparent volume of distribution of chemical in the body.



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For step response this mathematical equation prevails

$$\frac{dX}{dt} = D - k_e X$$

Concentration “C” is given by,


$$C = x/V_d$$

Where, “ $V_d$ ” is the apparent volume of distribution of chemical in the body.

(Refer Slide Time: 13:28)

**Toxicokinetic Modelling: One-Compartment Model**

- The chemical is distributed between the bloodstream and other body matter, both aqueous and non-aqueous, and the total effective capacity constitutes the apparent volume of distribution.
- For elimination after an instantaneous input of chemical  $C = C_0 e^{-k_e t}$
- The half life of chemical can be calculated as,  $t_{0.5} = 0.693/k_e$



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Now, the chemical is distributed between the bloodstream and other body matter, both aqueous and non-aqueous and the total effective capacity constitutes the apparent volume of distribution. For elimination after an instantaneous input of chemical



$$C = C_0 e^{-k_e t}$$

The half-life of a particular chemical can be calculated as

$$t_{0.5} = 0.693/k_e$$

(Refer Slide Time: 14:02)

**Typical half life of some drugs in our body**

- Aspirin 0.3h
- Morphine 3h
- Quinidine 6h
- Diazepam 50h
- Phenobarbital 86h

The model describes the elimination of chemical with time and it is totally based on the assumption that body has a tendency to eliminate the chemical. Elimination occurs by metabolism or secretion.

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Now, these are the typical half-life of some drugs in our body like Aspirin 0.3 hour, Morphine 3 hour, Quinidine 6 hour, Diazepam 50 hour, Phenobarbital 86 hours. So the model describes the elimination of chemical with the time and it is totally based on assumption that body has a tendency to eliminate the chemical. So elimination occurs by metabolism or secretion.

(Refer Slide Time: 14:35)

**Dose-infection models**

- for microbial pathogens, dose-infection models based on the concepts of single-hit and independent action are regarded as scientifically most plausible and defensible.
- When the discrete nature of pathogens is also taken into account, these concepts lead to the single-hit family of models


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Next is the dose infection model, for microbial pathogens dose infection model based on the concept of single hit and independent action are regarded as scientifically most plausible and defensible. So when the discrete nature of pathogens is also taken into account, these concepts lead to the single hit family of models.



(Refer Slide Time: 15:04)

**Dose-infection models**

- Empirical (or tolerance distribution) models, such as the **log-logistic, log-probit and Weibull(-Gamma) models**, have also been proposed for dose-response modelling.
- The use of these alternative models is often motivated by the intuitive argument that single-hit models overestimate risks at low doses.



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Now, empirical or tolerance distribution models such as log-logistic, log-probit, or weibull-gamma model have also been proposed for dose response modelling. The use of these alternative models is often motivated by the intuitive argument that a single hit models overestimate risk of low doses.


(Refer Slide Time: 15:28)



**Hit- Theory Models**

- the probability of infection of a host that ingests exactly n pathogens can be expressed as:  

$$- P_{inf}(n; P_m) = 1 - (1 - P_m)^n$$
- Where,  $P_m$  = Probability of pathogen to survive  
n = no. of pathogens
- the probability of infection as a function of the dose is given by: (D= mean ingested dose)  

$$- P_{inf}(D; P_m) = 1 - e^{-D \cdot P_m}$$



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Now, this is a hit theory model. The probability of infection of a host that ingest exactly n pathogens can be expressed at this particular mathematical relations like

$$P_{inf}(n; P_m) = 1 - (1 - P_m)^n$$

Where, P m is the probability of pathogen to survive and number of pathogens. So the probability of the infection as a function of dose is given by this particular mathematical equation,

$$P_{inf}(D; P_m) = 1 - e^{-D.P_m}$$

where D is equal to mean ingested dose.

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**Hit-Theory Models**

- If  $P_m$  is considered as constant value "r" then
  - $P_{inf}(D; r) = 1 - e^{-D.r}$
- When  $D.r \ll 1$ 
  - $P_{inf}(D; r) \approx D.r$
- If the probability of starting an infection for any organism in any host, and is assumed to follow beta- distribution, then:
  - $P_{inf}(D; \alpha, \beta) = 1 - {}_1F_1(\alpha, \alpha + \beta, -D)$

Now, if p m is considered as a constant value "r" then the equation can be represented like this,

$$P_{inf}(D; r) = 1 - e^{-D.r}$$

when  $D;r \ll 1$ , then this particular equation reduces to this one,

$$P_{inf}(D; r) \approx D.r$$


If the probability of starting an infection for any organism in any host and is assumed to follow the beta distribution, then that particular equation becomes like this.

$$P_{inf}(D; \alpha, \beta) = 1 - {}_1F_1(\alpha, \alpha + \beta, -D)$$

(Refer Slide Time: 16:40)

**Hit- Theory Models**

- For  $\alpha \ll \beta$  and  $\beta \gg 1$ , the Beta-Poisson formulae:  
$$-P_{inf}(D; \alpha, \beta) \approx 1 - \left(1 + \frac{D}{\beta}\right)^{-\alpha}$$
- When  $\frac{\alpha}{\beta} \cdot D \ll 1$ , this formulae is approximated by  
$$P_{inf}(D; \alpha, \beta) \approx \frac{\alpha}{\beta} \cdot D$$
- For both  $\alpha \rightarrow \infty$  and  $\beta \rightarrow \infty$ , while  $\frac{\alpha}{\beta} \rightarrow r$ ,  
the Beta-Poisson formulae converts to exponential  
model.  
$$P = r \cdot D$$



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Now, if  $\alpha \ll \beta$  and  $\beta \gg 1$ , the beta Poisson formula becomes like this

$$P_{inf}(D; \alpha, \beta) \approx 1 - \left(1 + \frac{D}{\beta}\right)^{-\alpha}$$

or another alternative is that

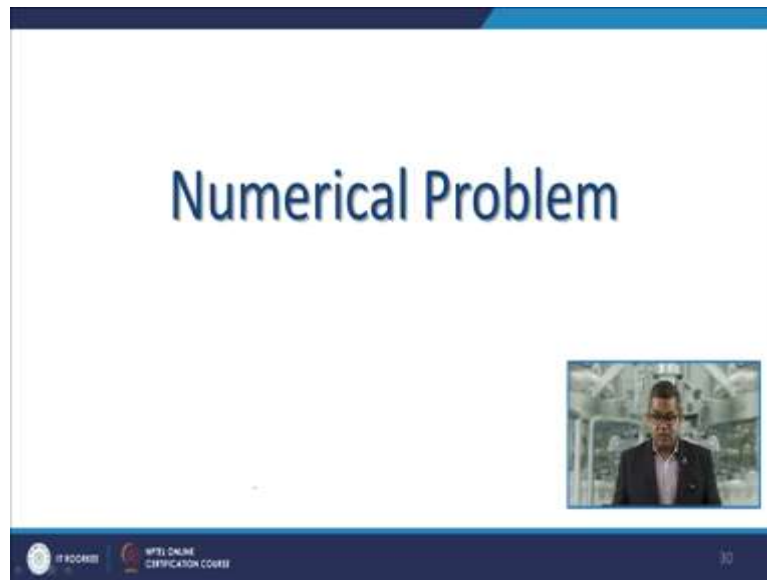
When  $\frac{\alpha}{\beta} \cdot D \ll 1$  in this particular aspect, this formula is approximated by

$$P_{inf}(D; \alpha, \beta) \approx \frac{\alpha}{\beta} \cdot D$$

For both  $\alpha \rightarrow \infty$  and  $\beta \rightarrow \infty$ , while  $\frac{\alpha}{\beta} \rightarrow r$ . ; the Beta-Poisson formula is converted to the exponential model

$$P = r \cdot D$$

(Refer Slide Time: 17:28)

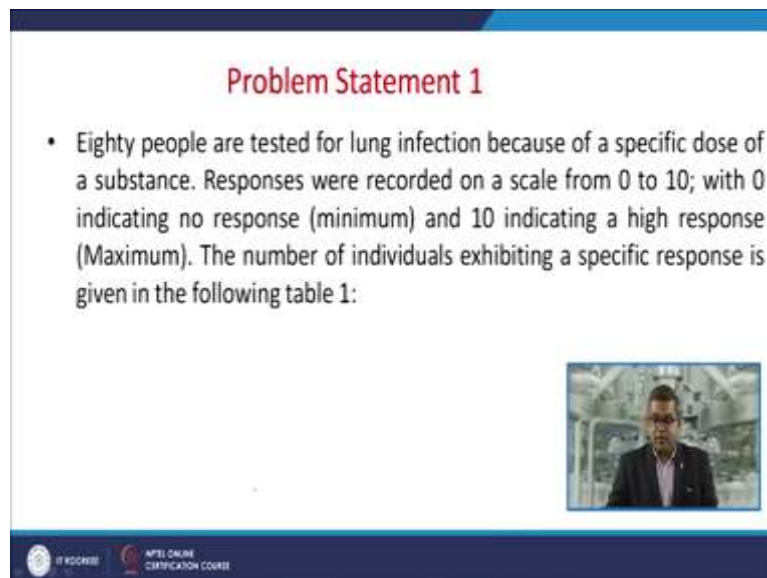


Numerical Problem

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Problem Statement 1

- Eighty people are tested for lung infection because of a specific dose of a substance. Responses were recorded on a scale from 0 to 10; with 0 indicating no response (minimum) and 10 indicating a high response (Maximum). The number of individuals exhibiting a specific response is given in the following table 1:

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Now, to prove this, we will discuss, we will discuss one numerical problem.

The problem statement is that; eighty people they are tested for lung infection because of a specific dose of a substance. Responses were recorded on a scale from 0 to 10, with 0 indicating no response minimum, and 10 indicating a high response that is maximum.

(Refer Slide Time: 18:01)

**Table 1: Specific Response from Individuals**

Response	Number of Individuals affected
0	0
1	6
2	12
3	14
4	11
5	12
6	9
7	6
8	4
9	3
10	3
Total	80



The number of individual exhibiting a specific response is given in the this table, that is 0 number of individual affected null, 1 response 6, 2 12, 3 14, 4 11, 5 12 and again 6 9, 7 6, 8 4, the 9th response 3 and 10th response is 3, so total number of individual affected 80.


<b>Response</b>	<b>Number of Individuals affected</b>
0	0
1	6
2	12
3	14
4	11
5	12
6	9
7	6
8	4
9	3
10	3
<b>Total</b>	<b>80</b>



(Refer Slide Time: 18:34)

### Problem Statement

- i) Determine the mean and the standard deviation.
- ii) Plot a histogram of the number of individuals affected versus the response.
- iii) Plot the normal distribution on the histogram of the original data.



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Now, you have to determine the mean and standard deviation, you need to plot a histogram of the number of individual affected versus the response and you need to plot the normal distribution on histogram of the original data.

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$$\mu = \frac{\sum_{i=1}^n x_i f(x_i)}{\sum_{i=1}^n f(x_i)}$$

here  $i = 1, 2, 3, \dots, 10$  total affected persons are 80  
 $\sum_{i=1}^{10} f(x_i) = 80$

$$\mu = \frac{(0 \times 0) + (1 \times 6) + (2 \times 17) + (3 \times 17) + (4 \times 11) + (5 \times 13) + (6 \times 9) + (7 \times 6) + (8 \times 4) + (9 \times 2) + (10 \times 3)}{80}$$
$$= \frac{361}{80} = 4.5125 \approx 4.51$$

$\mu = 4.51$

$$\sigma^2 = \frac{\sum_{i=1}^n (x_i - \mu)^2 f(x_i)}{\sum_{i=1}^n f(x_i)}$$

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So, now I am giving you the solution of this problem statement. So you can calculate the mean by using the equation  $\mu = \frac{\sum_{i=1}^n x_i f(x_i)}{\sum_{i=1}^n f(x_i)}$  where  $i$  is equal to 1, 2, 3, up to 10 that is the number of responses and the total affected persons 80 that is the affected persons which is listed in the table. So  $\sum_{i=1}^{10} f(x_i)$  is equal to 80, so we can calculate the  $\mu$  by this way this is response multiplied by the number

of person affected 2 into 12 plus 3 into 14 plus 4 into 11 plus 5 into 12 plus 6 into 9 plus 7 into 6 plus 8 into 4 plus 9 into 3 plus 10 into 3 and the whole divided by 80.

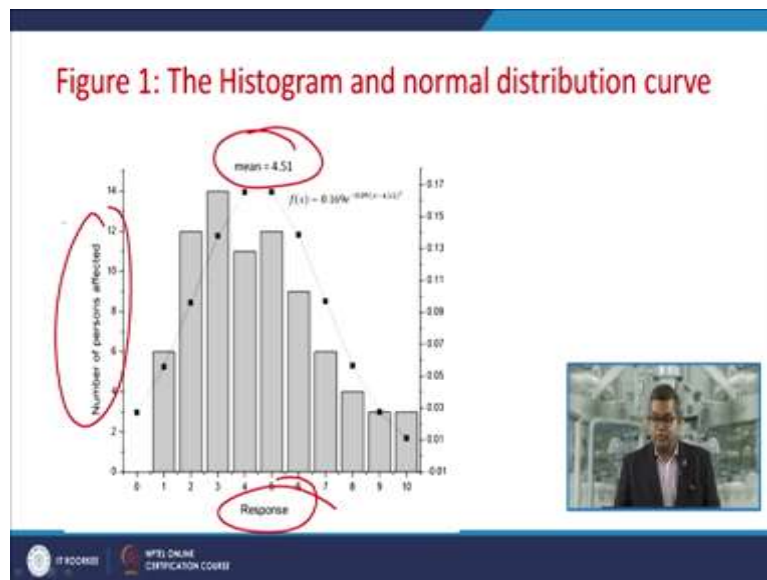
So it comes out to be 361 by 80 which is 4.5125 and approximately 4.51, so Mu is equal to 4.51. So you can calculate the standard deviation by this particular formula small Sigma square is equal to i summation i is equal to 1 to n xi minus Mu square f xi divided by summation i is equal to n f xi, so we have calculated Mu from here and we will calculate the standard deviation.

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$$\begin{aligned} \sigma^2 &= \frac{(1-4.51)^2(6) + (2-4.51)^2(12) + (3-4.51)^2(14) \\ &+ (4-4.51)^2(11) + (5-4.51)^2(12) + (6-4.51)^2(9) \\ &+ (7-4.51)^2(6) + (8-4.51)^2(4) + (9-4.51)^2(3) \\ &+ (10-4.51)^2(3)}{80} \\ \sigma^2 &= 5.54985 \\ \sigma &= \sqrt{5.54985} \\ \sigma &= 2.3558 \approx 2.36 \end{aligned}$$

So this small Sigma square is equal to 1.4.51 square multiplied by 6 plus 2 minus 4.51 square 12 plus 3 minus 4.51 square into multiplied by 14 plus 4 minus 4.51 square multiplied by 11 plus 5 minus 4.51 square 12 plus 6 minus 4.51 square multiplied by 9 plus 7 minus 4.51 square 6 plus 8 minus 4.51 square 4 plus 9 minus 4.51 square 3 plus 10 minus 4.51 square multiplied by 3 the whole divided by 80. So this comes out to be 5.54985 and standard deviation is equal to 5.54985, 2.3558 approximated to 2.36, so this is the standard deviation of the problem statement.

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Now, we can see the histogram, so based on your calculation and based on the formula in question we have plotted the histogram and the normal distribution curve, so this is your mean and these are the various responses and the number of persons affected. So you can have a look of this histogram.

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$$\begin{aligned} f(x) &= \frac{1}{\sigma \sqrt{2\pi}} \exp \left[ -\frac{1}{2} \times \left( \frac{x - \mu}{\sigma} \right)^2 \right] \\ &= \frac{1}{2.36 \times \sqrt{2\pi}} \exp \left[ -\frac{1}{2} \times \frac{(x - 4.51)^2}{2.36^2} \right] \\ f(x) &= 0.169 \exp \left[ -0.09(x - 4.51)^2 \right] \end{aligned}$$

80


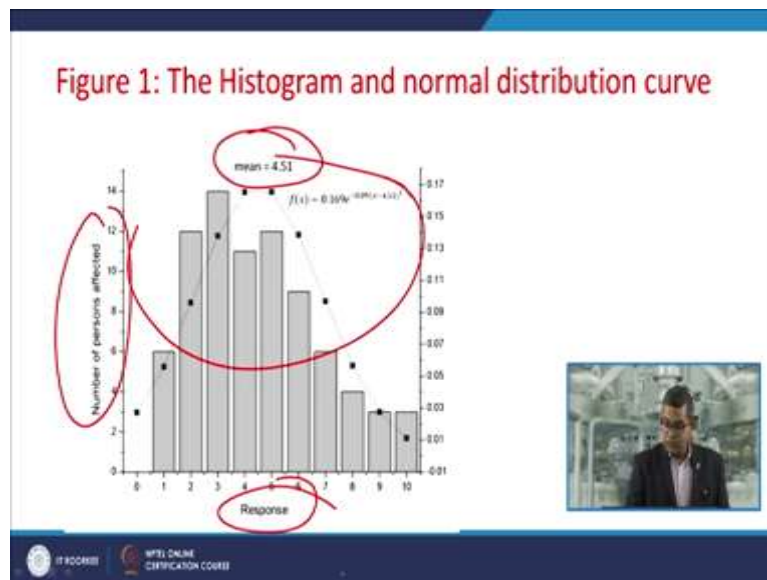
Now, in the third part first we need to calculate the normal distribution with the equation. A normal histogram, a normal distribution can be calculated using this equation  $f(x)$  equal to  $\frac{1}{\sigma \sqrt{2\pi}}$  exponential minus  $\frac{1}{2}$  into  $\frac{(x - \mu)^2}{\sigma^2}$  which is already being calculated in the previous slides  $2.36^2$ . So this comes out to be  $f(x)$  is equal to  $0.169$  exponential minus  $0.09(x - 4.51)^2$ . So the calculated distribution

can convert a function representing the number of individual affected by multiplying with the total number of individuals that is 80. So the corresponding values these are tabulated in table 2 and normal distribution curve is plotted in figure 1 which are which I am going to show you.

(Refer Slide Time: 25:18)

**Table 2: Theoretical Frequency and Number of People Affected for Each Response**

x	f(x)	80*f(x)
0	0.2373	2.1784
1	0.05595	4.476
2	0.09605	7.684
3	0.13779	11.0232
4	0.16518	13.2144
4.51	0.169	13.52
5	0.16548	13.2384
6	0.13853	11.0824
7	0.09691	7.7528
8	0.05665	4.532
9	0.02768	2.2144
10	0.0113	0.904

So the calculated distribution are converted to a function representing the number of individuals affected by multiplying the total number of individual that is 80, so the corresponding values are tabulated in this particular table, you can see that the x and f x values which has been calculated by the formula which we have just now achieved and this is the 80 multiplied by f x. And the normal distribution curve is this one. So by this way you can analyze that how we can calculate the different models and in different slides, in next modules we will discuss the other models, thank you very much.