Non-Targeted Effects

Break out Session 1

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Non-Targeted Effects

The group discussed the non-targeted effects and their potential impacts on RP system. However, after a fruitful and fascinating discussion, we are not sure to bring clear answers but we are convinced that we have increased the number of questions.

Non-Targeted Effects….

..are characterised by Bystander Effect and Genomic Instability

By increasing our knowledge on these two biological mechanisms do we reduce uncertainties or do we increase confusion?

…….We are not sure to have a clear answer

Today, we have two dose-effect curves

- Targeted Effects are represented by LNT
  - Dose is linked to probability of occurrence
- NTE are represented by a strong early increase at low dose, then by a plateau, whatever the dose
  - What is the occurrence?

First Comment

- But when we compare and communicate on these dose-effect relationship, do we use the same endpoint ?
- For the LNT, it is clear that it is stochastic effects, cancer or potential hereditary diseases
- For the NTE, we describe a biological event, not a health effect

…….That is confusing

- First, the facts exist, the cancers observed after the A-bomb are more and more a solid database.
- Year after year, the scientists have tried to explain appearance of late effects after exposure
- But if we have better knowledge on mechanisms, do we reduce the uncertainties?

The foundations of LNT

- Physicist have given more and more information on energy deposit
- The question was to create a link between these physical basements and A-bomb survivors' observations
- And some created the DNA paradigm, the life was easy at this time.

……BUT

But opposition between two theories still exists after many years

- Is there a biological basis for non-threshold?
- Do we have evidence that threshold is not valid?

The first DNA paradigm break

- Mutations are the basis of the cell model
- But if cancer has a clonal origin, it is a tissue process
- And now the question is the part of epigenetic *vs* genetic aspect in cancer induction

Phenotypic stability trumps genomic alterations

- Oncogenic signaling is suppressed by normal tissue
- Carcinogenisis is promoted by the remodeling of the tissue
- Malignant genotypes can be ’reverted’ to normal phenotypes
- Extra-cellular signals are paramount

Other questions

- Are mechanisms the same
  - Higher than 100 mSv
  - Lower than 100 mSv
- Is extrapolation valid?

Now we know that there are exceptions to LNT, ….no more a taboo

- Results of an Oxford meeting in 2002
- ICRP 2007 recommendations accept that in some situations LNT could be not the best model, even if it remains the best tool for RP management

Genomic instability

- Is genomic instability an epigenetic effect?
- Not a clear answer by experts, two say yes one says no

- Genomic instability is a permanent event, produced by Ionising radiation but also by other agents.

……it is very difficult to maintain our genome

Bystander effect

Is the bystander effect specific to radiations?

It is premature to link bystander effect to cancer

For regulators, it is important to know whether a link exists between NTE and mutation, because we know that there is a link between mutation and cancer

We have to know the relationship between some Biological Effects *vs* Health Effects

- Chinese results published in 2000 (Radiat. res.) clearly show NO
- A gap between NTE and consequences in health-effect terms still exist, ***we don't know if NTE leads to health effects***

Is the NTE changing or not the extrapolated part of LNT--- the RP part ? The paradox is to discuss in a non-event area

If NTE are NOT linked to cancer, are NTE linked to non-cancer diseases ? To day it is pure speculation because no mechanism explanation exists.

But Let's Remember Stakeholder Questions

- What is the health effect ***for me*** if I eat Chernobyl-contaminated food every day?
- What will be the health effect ***for me*** if every day I eat food contaminated by radionuclides released from deep underground storage?

The internal contamination challenge

- Chronic exposure of long live radionuclides
- Very low dose and very low dose rate
- Is the dose a surrogate of risk (see EGIS report)

Level Zero of knowledge

(Except an experiment in Finland)

Conclusions

- This task group arise more questions than it brought answers
- But don't forget that the facts are robust
- And that the mechanisms are for explanation of these facts, not the reverse

- We apologise to the regulators because there are so many different opinions it is difficult to satisfy them!!

Conclusions 2

- Please don’t use scientific results before validation
- Don’t instrumentalise scientific results
- Don’t confuse radiation research and radiation protection research
- Be pragmatic
  - We have facts
  - We try to explain facts
  - Not the reverse