Attributing Health Effects and Inferring Risks at Low Doses

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Challenges for the Next Decades

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Basic remarks

- First of all, one has to be very careful to distinguish „health effect“ (something that is actually observed) and „health risk“ (something that is expected).
- In general, health effects are related to the past and health risks to the future.
- It makes a difference to attribute in the individual case or in the case of a population.

Definition of very low, low, moderate and high doses

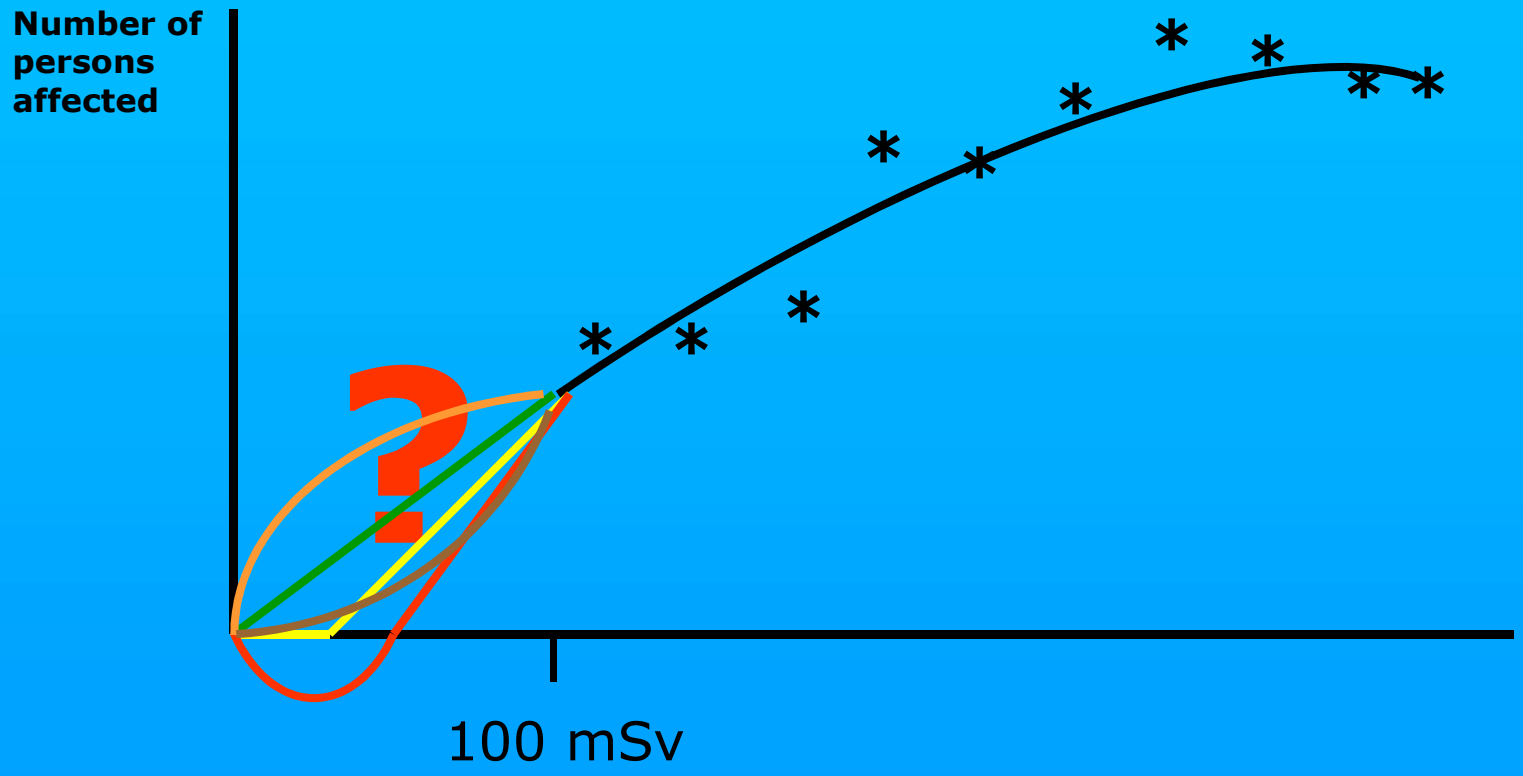
Dose category	Range of absorbed dose (for low-LET radiation)
High dose	> 1000 mGy
Moderate dose	100 mGy – 1000 mGy
Low dose	10 mGy – 100 mGy
Very low dose	< 10 mGy

(Source: UNSCEAR 2012)

Consequence of restricting to doses below about 100 mGy

- Due to the threshold dose of about 1 Gy for deterministic effects, deterministic effects will not be addressed.
- Focus will be on:
  - malignant tumours,
  - leukaemia.
- A few remarks will be on:
  - hereditary effects,
  - cataracts,
  - cardiovascular diseases.

The well-known problem



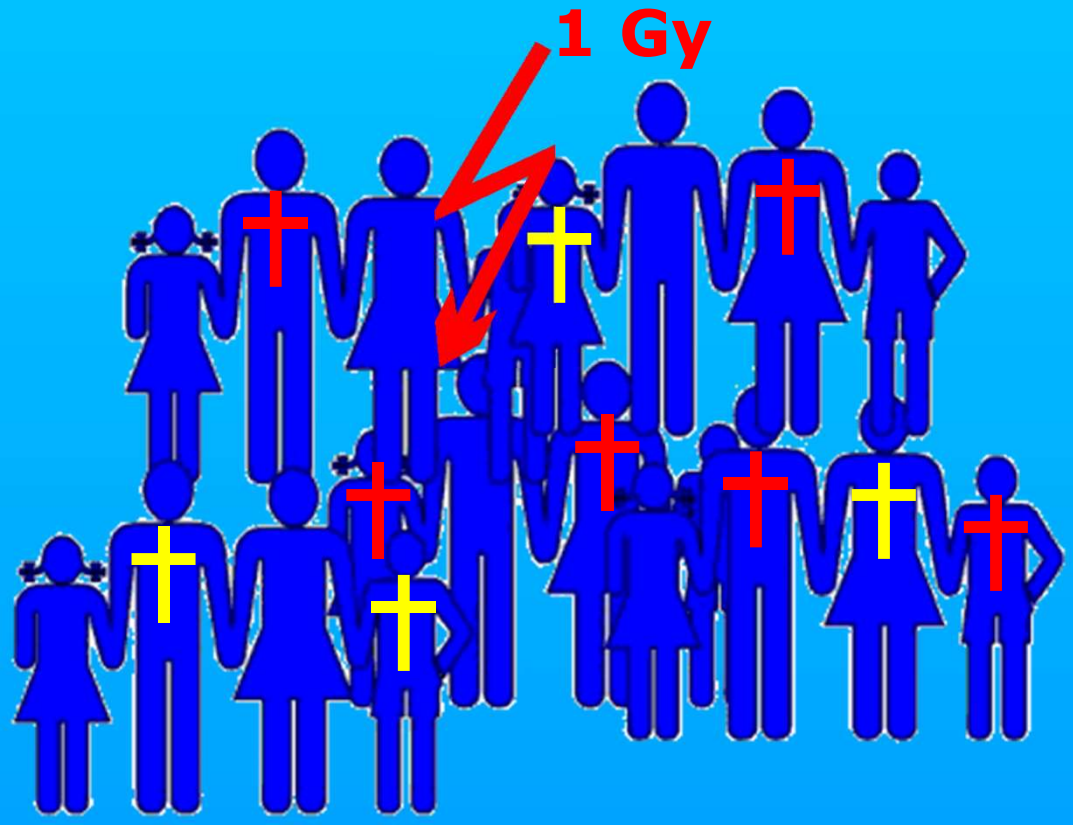
Conclusions regarding LNT

- A lot of biological mechanisms are affecting the response of organisms in the low dose range.
- Most, if not all, of these mechanisms show a **non**-linear dose response.
- In addition, individual differences are to be expected.
- Thus, an exactly linear, non-threshold response is highly unlikely.

But!:

- For practical reasons, the convention to use the LNT approach in radiation protection is justified.

Common problem of stochastic effects:
lack of a biomarker



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20% spontaneous cancer deaths
10% additional cancer deaths due to 1 Gy

Is attribution possible in population studies?

- Yes, it is possible to attribute stochastic health effects in populations to ionizing radiation.
- But:
  - A serious problem in population studies is to overcome the statistical fluctuations.
  - With decreasing dose uncertainty increases (not linearly, but to the square!).
  - Thus, it is not surprising that for a mixed population a statistically significant increase in radiation-induced cancer deaths is seen only from about 100 mSv upwards.

Is attribution possible when individuals are affected?

- No, it is not possible to attribute a stochastic health effect in an individual to ionizing radiation.
- The major reason: up to now, no biomarker has been found that clearly tells us, which agent caused a specific cancer.

What can be done in the individual stochastic case?

- One can try to calculate probabilities.
- „Assigned share“ (frequently called „Probabilty of causation“) can be estimated based upon individual characteristics (type of cancer, gender, age at exposure, age at diagnosis, dose ...).
- Using this concept, you never can be sure that the specific individual cancer was indeed caused by radiation, meaning that you cannot attribute with certainty.
- This is particularly true in the low dose range (i.e. below about 100 mSv).

Conclusions (1)

- An observed health effect in an individual could be unequivocally attributed to radiation exposure if the individual were to experience tissue reactions (often referred to as “deterministic” effects), and differential pathological diagnosis were achievable that eliminated possible alternative causes.
- Other health effects in an individual that are known to be associated with radiation exposure — such as radiation-inducible malignancies (so-called “stochastic” effects) — cannot be unequivocally attributed to radiation exposure, because
  - radiation exposure is not the only possible cause and
  - there are at present no generally available biomarkers that are specific to radiation exposure.

Conclusions (2)

- An increased incidence of stochastic effects in a population could be attributed to radiation exposure through epidemiological analysis — provided that, inter alia, the increased incidence of cases of the stochastic effect were sufficient to overcome the inherent statistical uncertainties.
- Although demonstrated in animal studies, an increase in the incidence of hereditary effects in human populations cannot presently be attributed to radiation exposure; this may be due to the large fluctuation in the spontaneous incidence of these effects.

Conclusions (3)

- In general, increases in the incidence of health effects in populations cannot be attributed reliably to chronic exposure to radiation at levels that are typical of the global average background levels of radiation.
- The reasons are:
  - the uncertainties associated with the assessment of risks at low doses,
  - the current absence of radiation-specific biomarkers for health effects and
  - the insufficient statistical power of epidemiological studies.
- Therefore, it is not reasonable to multiply very low doses by large numbers of individuals to estimate numbers of radiation-induced health effects within a population exposed to incremental doses at levels equivalent to or lower than natural background levels.

Conclusions (4)

- One has to keep in mind, however, that public health bodies need to allocate resources appropriately, and that this may involve making projections of numbers of health effects for comparative purposes.
- This method, though based upon reasonable but untestable assumptions, could be useful for such purposes provided that
  - it were applied consistently,
  - the uncertainties in the assessments were taken fully into account, and
  - it were not inferred that the projected health effects were other than notional.

An example of calculation of low dose risk for comparison reasons

- Scientific knowledge can be applied to compare the potential benefits and risks of various types of imaging procedures used in medicine.
- The specific task may be to estimate the potential future impact in terms of cancer risk from the population exposure due to CT scanning in a specific year in a particular country.
- The current use of CT scanning in the United States may result in a future increase of about 1.8% (95% CI: 0.9%, 2.7%) above the current cancer rate.
- This estimate can be used to compare it with the potential impact on health effects by alternative diagnostic procedures.
- It is, however, not clear that this increase will actually happen or could be observed.

Challenges for the next decades

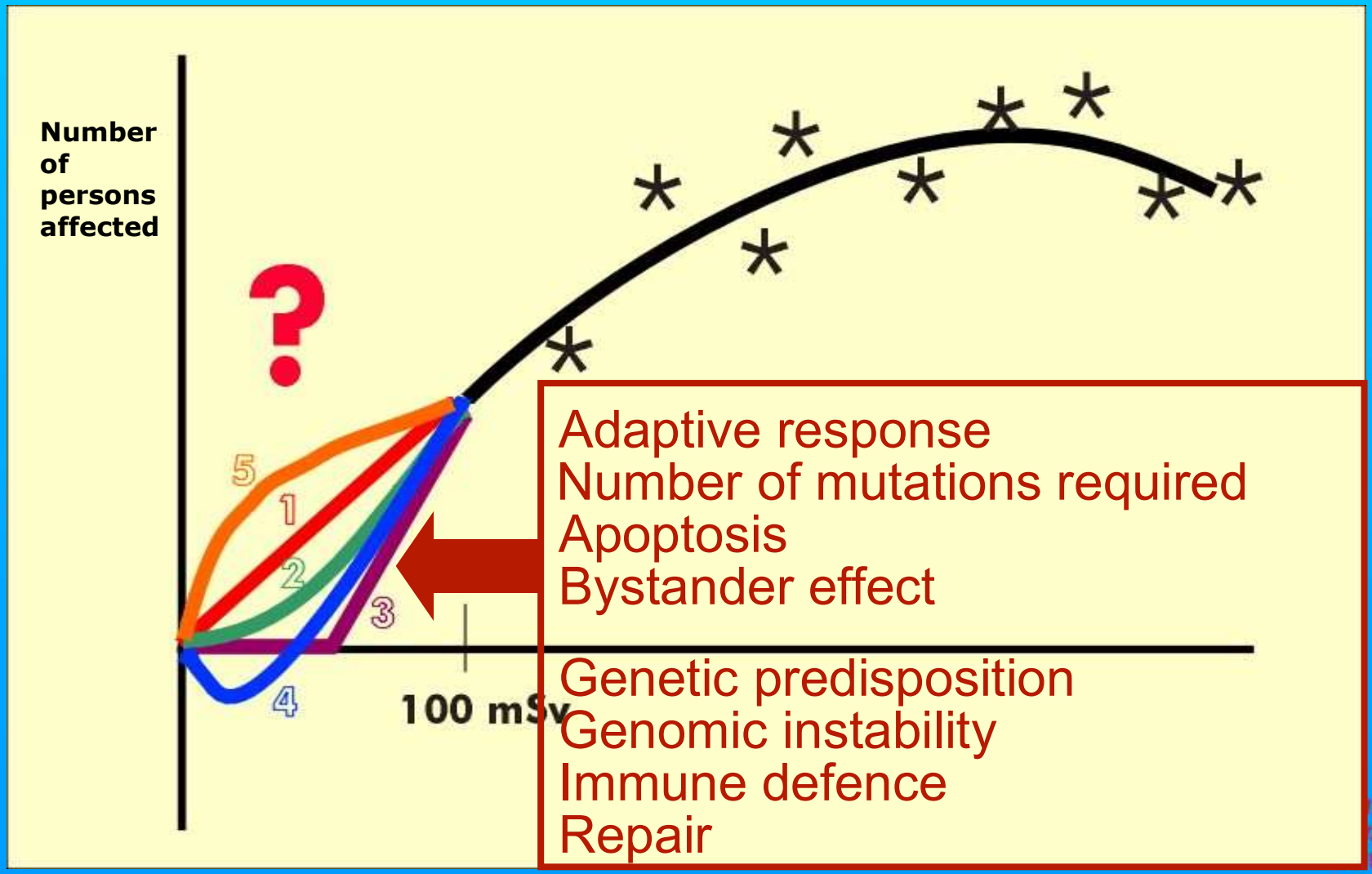
What we do not know in the low and very low dose range:

- Is there a tumour risk below about 100 mSv (general public) or about 10 mSv (fetus)?
- What does it mean for health effects that doses in the range of some mSv can induce biological effects, such as damage to the DNA?
- Do we know already all relevant biological mechanisms in the low and very low dose range and what can we conclude from the known mechanisms?
- How does the dose response curve look like for cataracts and circulatory diseases? Is there a risk in the low and very low dose range?

Combined effort of radiation epidemiologists and biologists (1)

- Study of biological mechanisms, in particular in the low dose range.
- Advantage for the epidemiologist: This may help to decide which shape of the dose-response relationship in the low dose range is correct (e.g. linear or linear-quadratic).

Biological mechanisms relevant in the low dose range



Combined effort of radiation epidemiologists and biologists (2)

- Identification of people who are prone to develop a cancer.
- Advantage for the epidemiologist: this might narrow the high variability of the spontaneous rate of malignancies.

Combined effort of radiation epidemiologists and biologists (3)

- Identification of a biomarker of radiation induced malignancies.
- Advantage for the epidemiologist: avoidance of „dilution“ of the number of cases due to other agents.

But: Can we expect to find a biomarker indicating causation by ionizing radiation?

- There is strong evidence that carcinogenesis is a multistep process;
- Most likely, ionizing radiation can induce all necessary steps;
- But in many (all?) cases other agents may do part of the job;
- Thus, we cannot expect to find a pure radiation-specific biomarker, but, at best, a biomarker indicating some contribution by ionizing radiation;
- Is it realistic to find such a marker?

In depth information on
„Attributing Health Effects to Ionizing Radiation Exposure and Inferring Risks“
(not only at low doses)
may be obtained from the

UNSCEAR 2012 Report, Annex A

(http://www.unscear.org/unscear/en/publications/2012.html)