Biological indicators for radiation exposures

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The experience with accidental radiation exposures has frequently shown that the physical dosimetry does not give sufficiently good results for dose estimations. Therefore the determination of biological effects is necessary in order to get some additional information about the absorbed radiation dose. Several biological systems have been studied under these circumstances and interest for biological indicators for radiation damage has increased appreciably. There are two main reasons for this interest:

1. Biological indicator can be used in addition or even in substitution to physical dosimetry. It is an advantage that biological indicators can be determined for biological dosimetry after a radiation exposure has taken place which is in contrast to physical dosimetry.

2. Biological dosimetry gives not only information about the range of the absorbed (radiation dose) but it is also possible to get information about the individual radiosensitivity which can vary considerably from person to person. Therefore biological indicators are also a measure of the biological-medical radiation damage. By determination of such indicators it is possible to give a prognosis about possible radiation damage. It is further possible to start therapeutical procedures under these conditions earlier.

A number of methodologies have been studied for these purposes:

1. Electronspin resonance,
2. Biochemical indicators,
3. Chromosomal aberrations,
4. Hematopoetic changes,
5. Studies of spermiogenesis.

The most efficient and widely used techniques are those which measure chromosomal aberrations. Several methodologies are used in this connection: The evaluation of structural chromosomal aberrations in metaphases,

premature chromose condensation, the determination of micronuclei and recently the use of molecular biological techniques like fluorescence in situ hybridization (FISH).

A useful biological indicator should fulfil the following features:

1. The measured radiation effect should be dose dependent in a certain dose range. It would be desirable that this dose range covers radiation doses of occupational exposures at working places (20 - 50 mSv) up to accidental exposures of several sievert.

2. A certain specificity should exist for the changes by ionizing radiation.

3. It should be possible to get some information about dose rate effects.

4. The results should be available within a few days after radiation exposure.

5. The radiation damage should be measurable over a certain time period.

6. It should be possible to determine a partial body irradiation and to measure the localization of radiation exposure.

7. The biological material which is needed for the determination should be easily obtained.

These demands are maximal and cannot be fulfilled by any indicator up to now. Ionizing radiation induces free radicals in many biological materials. These free radicals can be quantitatively determined by electronspin resonance. The measurements can only be performed with materials with a low water content. Several studies have shown that teeth are very well suited for such studies. But also in hair and bone free radicals can be measured. After the nuclear accident in Tschernobyl this technique has been used for dose estimation in several cases. It is also possible by this technique to measure radicals in bricks, stones and other material in order to estimate local radiation doses.

A number of studies have been performed in order to use biochemical systems for dose estimation. In this connection the excretion of metabolites after the

break down of proteins and nucleic acids has been mainly investigated. It was observed that in a dose range between 0.5 to 2.5 Gy a good dose response can be obtained for taurine and other amino acids as well as with metabolites of DNA. However, there is a very high individual variability with respect to these parameters and therefore it is difficult to obtain a reasonable dose estimation with the biological systems which have been used up to now.

Most experience for biological dosimetry has been obtained with cytogenetic techniques through which chromosomal changes can be measured. Most widely the determination of the socalled dicentric chromosomes has been used. These chromosomes are formed after chromosome breakages and subsequent connection of these breaks in such a way that a chromosome with two centromeres results. The formation of dicentrics shows a certain specificity for ionizing radiation. The conventional technique has been found useful for dose ranges between 0.1 to several sieverts. The dependence on radiation quality and dose rate has been studied. Again the spontaneous rate of dicentrics can differ individually considerably. This has to be taken into consideration and complicates dose evaluation in the low dose range. Usually chromosomal aberrations are determined in metaphases of proliferating lymphocytes from blood after cell proliferation has been stimulated. Dicentric chromosomal aberrations have to be measured within a few weeks after a radiation exposure. Otherwise the cells with such chromosomal aberrations get lost and an estimate is no longer possible.

For these disadvantageous reasons a new technique has been introduced: The fluorescence in situ hybridization (FISH). With this technique it is possible to paint specific chromosomes by the corresponding DNA probes and to study not only instable chromosomal aberrations like dicentrics or chromosome breaks but also to determine stable chromosomal aberrations like translocation, deletious etc. As DNA probes for all human chromosomes are available today this technique can be widely used. With this technique it is possible to determine chromosomal aberrations even are several years after a radiation exposure. Thus chromosome aberrations could be measured in survivors after the atomic bombing in Japan even today. Further the potential of this technique allows to study a number of fundamental radiobiological questions.

Besides these techniques for which a lot of experience and expertise is necessary an easier method has been developed: The determination of

micronuclei. With this technique it is not necessary to push the cells into the metaphase but micronuclei can be determined also in interphase cells. However, the cells have to go through mitosis before micronuclei are expressed. Micronuclei originate also from chromosome breaks with acentric fragments and from whole chromosomes which are located in the cytoplasm.

During last years a technique has been developed which includes a proliferation control. Cytochalasin B has been used in concentrations which allow the division of the cell nucleus but not the division of the cell itself. Under these conditions cells with two cell nuclei develop. The micronuclei which consist of chromatin particles in the cytoplasm are only determined in such bionucleated cells. The specificity of the expression of micronuclei is less than with dicentrics. Cells with micronuclei get lost with in a few weeks like cells with dicentrics. Therefore an exact measurement can only performed within a few weeks after radiation exposure. Although the sensitivity for the micronucleus determination is less than for other cytogenetic techniques it has been found very useful that the results are obtained quickly and comparatively easily. Further the micronucleus test can be used with an automated cell system.

With all these cytogenetic techniques it has been shown that besides estimates of radiation dose it is also possible to get a measure of the individual radiosensitivity. For instance in a number of persons with genetic syndromes like ataxia telangiectasia, Franconi anaemia and others which show a high degree of radiosensitivity it has been found that the expression of chromosomal aberrations including micronuclei is increased. Most of these genetic syndromes are expressed only in persons who have the mutation in both genes (homozygotes), the genetic mechanism is recessive and not dominant. However, it has been found that an increased radiation effect can also be seen in heterozygotes (mutation only in one gene) although the increase of the radiation effect is less in these individuals than in the homozygotes. This variability of individual radiosensitivity certainly will play a significantly larger role for radioprotective measures in the future. Therefore it is desirable to have such techniques available which give an information about the extent of radiation damage and to use this information for the decision whether therapeutic measures have to be applied or can be excluded.

It can be suggested from these experimental experiences that the comparative simple micronucleus assay is used for screening if many persons have been exposed by an accident. Under these circumstances quite a number of results can be obtained in a very few days after blood samples have been taken from the exposed individuals. The micronucleus assay can be used again in a dose range of 0.1 to several sieverts. As with chromosomes evaluations of micronuclei have been described for fast neutrons, also dose rate effects have been studied. After such a screening the blood of the exposed people can be investigated by looking for conventional chromosomal aberrations or using the FISH technique. Especially in the low dose range these methodologies certainly can give more exact data. In one accident it was possible to measure the radiation effect by the micronucleus test and the formation of dicentrics. Comparable results were obtained.

With these techniques it is certainly possible to get an information about a radiation exposure including the individual radiosensitivity which will be very useful for judgements of accidental situations.

References

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