Chapter 13

Radiation and health — Cancer

We are living in a "sea" of radiation. Radioactive isotopes have always been present, and since 1895 we have also had x-rays which is extensively used for diagnostic purposes. In the beginning very little was known about the health effects and the pioneers made a lot of experiments which we today consider as dangerous and foolhardy.

It is quite interesting to read about the pioneers and their work.

The interested reader can consult a new book with the title;

" Radioactivity: A History of a Mysterious Science"

by Marjorie Caroline Malley (published 2011).

In spite of the fact that several of the pioneers were burned due to handling of the radioactive sources with their hands, the radiation was in the beginning of the 20th century considered positive which would bring you good health. For example a number of spas where the water contains low levels of radon was visited by a number of people assuming that the radioactivity can cure ailments such as rheumatism. Places like Bad Gastein, Carlsbad (Karlovy Vary), Marienbad (Mariánské Lázně) and Joachimsthal (Jáchymov) have a large number of guests that appreciate the radioactivity.

The "pendulum" of public opinion with regard to radiation was on the positive side through the first part of the 20th century, and then started to move back after 1945 with the atomic bombs. After Chernobyl the pendulum of opinion was far out to the negative side.

Today, 25 years after Chernobyl the "pendulum" of opinion has started to go back again, mainly due to the work carried out by the cell culture scientists. All this is very interesting and we would all benefit if we could base our opinion and use of radiation on scientific knowledge.

In 1899, Stenbeck and Sjögren from Sweden used radiation to remove a tumor from the nose of a patient (see chapter 10). This demonstrated the positive effect of radiation. Furthermore, the x-ray pictures, which fascinated a whole world, gave more evidence to the positive use of radiation. A more doubtful use of radioactive isotopes is the above mentioned spas, and on the negative side we can mention the use of radioactive isotopes in drinking water, in tooth paste as well as the use of radium and luminous substances in show business. Let us look into some of the foolish use of the radioactive isotopes in the early part of the 20th century.

RADIUM THERAPY

The only scientific apparatus for the preparation of radio-active water in the hospital or in the patient's own home.

This apparatus gives a high and measured dosage of radio-active drinking water for the treatment of gout, rheumatism, arthritis, neuralgia, sciatica, tabes dorsalis, catarrh of the antrum and frontal sinus, arterio-sclerosis, diabetes and glycosuria, and nephritis, as described in Dr. Saubermann's lecture before the Roentgen Society, printed in this number of the "Archives."

DESCRIPTION.

The perforated earthenware "activator" in the glass jar contains an insoluble preparation impregnated with radium. It continuously emits radium emanation at a fixed rate, and keeps the water in the jar always charged to a fixed and measureable strength, from 5,000 to 10,000 Maché units per litre per diem.
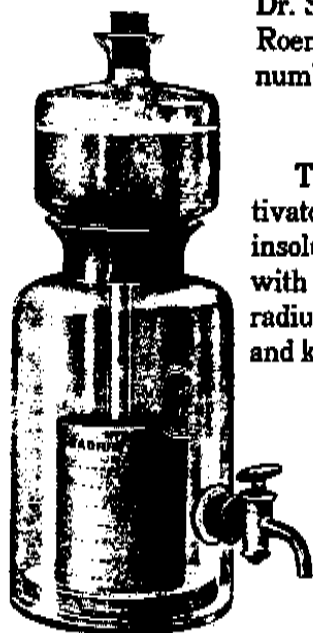
SUPPLIED BY

RADIUM LIMITED,

93, MORTIMER STREET, LONDON, W.

Left:

An advertisement from 1913 for radioactive drinking water.

A jar with water, a cylinder and some radium salt was used. When Ra-226 disintegrates, radon is formed and is released into the water. When the tap was opened, radon was found in the water. The radiation doses were small and the whole system was rather harmless.

From R. F. Mould (1980)

In the advertisement it is mentioned that the activity in the water could be kept at a strength of 5000 – 10,000 Mache. An activity of 10,000 Machè per liter correspond to 3.64 µCi/l or 130 000 Bq/l.

Below:

Radithor was manufactured from 1918 to 1928 by the Bailey Radium Laboratories in New Jersey. The bottle contained 1 µg of both Ra-226 and Ra-228 (mesothorium) with activity of 37,000 Bq for each of the isotopes.

Some doctors prescribed Radithor – it was supposed to cure by stimulating the endocrine system. Instructions on the bottle suggested patients drink from the bottle itself, and swallow an entire bottle after a meal.

It is known that a patient consumed over 1400 bottles of Radithor (more than 100 MBq of these isotopes). Radium works like Barium and Calcium in the human body. When digested, they travel to the bone marrow and remain there to the end of life.

The isotopes and their decay products yield both α, β and γ-radiation. Another sad story with radium is the "dial painters" –mainly young girls that painted the dials with a mixture of radium and fluorescent materials. Some of these girls got bone cancer. We shall return to this later.

Health effects of radiation

Because large doses of radiation are known to kill cells, there is the possibility of using radiation to treat cancer when localized to a small area of the body. Similar large whole-body doses can lead to death, which occurs in the course of days or weeks.

When considering medium and small doses, the biological effect is considerably more difficult to predict. The reason for this is the time lag between the exposure and the observable biological effect. For solid cancers it is usually several years, even decades.

Marie Curie, and a number of the other radiation pioneers died from cancer. Their working habits involved little or no protection and they may have attained *large* radiation doses – which may have caused their sicknesses.

On the other hand, recent experiments have claimed that *small doses* may even have a positive health effect since radiation has the possibility to stimulate defense mechanisms as well as repair processes(see chapters 11 and 12).

In all discussions on the biological effects of radiation, the radiation dose is a key issue. ***Without knowledge about the size of the dose it is meaningless to discuss the effects.*** The relationship between the dose and effect is also a hot issue in the community of research scientists. Knowledge about the dose-effect curve is a requirement when discussing mechanisms and health risks of radiation.

Large and small doses

The large dose region can be characterized in the following way:

An acute whole body dose of more than 1 to 2 Gy is considered to be large and a dose smaller than 0.1 to 0.2 Gy (100 to 200 mGy) is considered to be small.

Annual doses in the region 2 – 10 mGy (such as those attained from natural background radiation) are considered to be very small.

A very important aspect is the doserate – whether the dose is given acute or spread out over time i.e. years.

The Use of Large Doses

- **Sterilization of medical equipment.**

Co-60 and Cs-137 γ-radiation are used to sterilize medical equipment. The doses delivered are of the order of 20 to 40 kGy. The purpose of the radiation is to kill bacteria, viruses, and fungi that contaminate equipment.

- **Radiation of food products**.

The purpose is almost the same as for sterilizing equipment. The doses are, however, smaller, on the order of 5 to 10 kGy. Larger doses may change the taste of certain foods.

- **Radiation therapy**.

In Chapter 10 we discussed radiation treatment of cancer. The purpose is to kill the cancer cells while allowing nearby healthy cells to survive. Much effort is carried out to achieve treatment protocols that will give the most effective treatments. The total dose given to a tumor is 10 to 80 Gy. A treatment protocol may include daily doses of 2 Gy, given 5 days per week.

- **Bone marrow transplantation.**

In combination with bone marrow transplantation which is used for the treatment of certain illnesses, whole-body radiation is sometimes used to deplete the original bone marrow. The dose used is about 12 Gy (6 days with a daily whole body dose of 2 Gy). This dose is sufficient to completely destroy the bone marrow and would kill the patient if it were not for the immediate transplant of new compatible bone marrow. A number of people have been treated in this way.

LD_{50} Dose

By definition, an LD_{50} dose (abbreviation for " Lethal Dose to 50 percent") is the dose that could kill 50 percent of the individuals exposed within 30 days. To arrive at a determination of the LD_{50} dose, experiments like the following must be carried out.

In typical experiments, rats, about 15 animals in each group, were given different whole-body doses. The number of animals dying in the course of 30 days was observed for each group. The result is given in the figure below.

The dose is given along the horizontal axis and the number of animals dying (in percent for each group) is given along the vertical axis. The results show that no animals survived a dose of 10 Gy, whereas all rats survived a dose of 5 Gy. It can be seen that the LD_{50} dose is approximately 7.5 Gy.
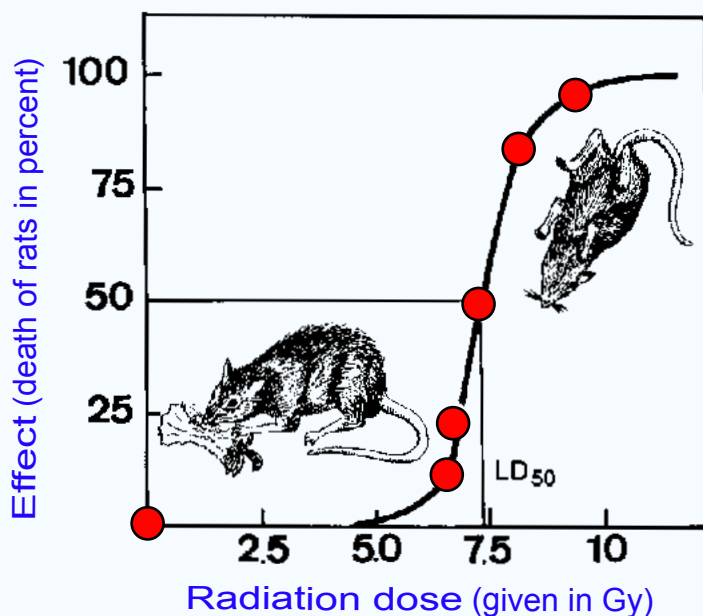

Adapted from A. P. Casarett (1968) with permission of A. P. Casarett

Dose-effect curve for radiation-induced death in rats.

When humans and animals are irradiated, the blood-forming organs (in the bone marrow) will be the first to react. For doses of the order 1 to 2 Gy the number of white and red blood cells will decrease and as a result of this, the immune system will fail and, after one to two weeks, life threatening infections may occur. If the radiation doses are smaller than 4 to 5 Gy, there is a good chance the bone marrow will recover and resume the production of blood cells. This takes place after 3 to 4 weeks and, consequently, 30 days is a reasonably chosen limit for the name *acute radiation death*.

In the radiation accident in Norway in 1982 the whole body dose was determined by ESR to be 22.5 Gy (see page 78 – 81). The man survived for 13 days and the blood values observed in the period are given in the figure below.
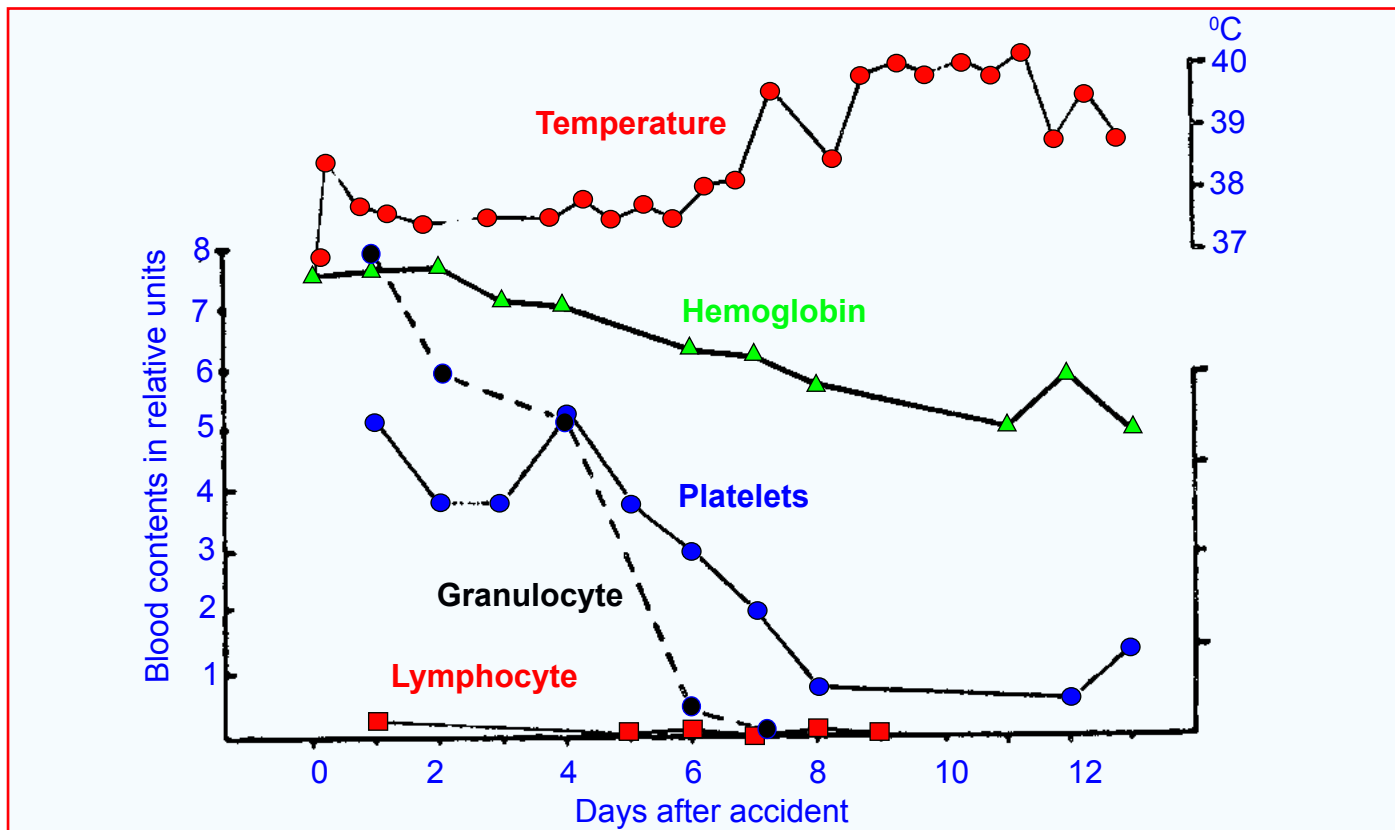
In the figure is given temperature (above) and the different blood values for the technician involved in the radiation accident in Norway. The lymphocytes were already knocked out after 24 hours. He was treated with antibiotics.

The LD_{50} doses for a number of animals have been determined and some values are given in the table below. Single cell organisms (for example bacteria, paramecium, etc.) may survive doses of the order 2,000 to 3,000 Gy. (This is taken into consideration in radiation treatment of food).

In the case of humans there is not enough information to determine a precise LD_{50} dose. The only information available has come from radiation accidents and the lethality depends not only on the dose and dose rate but also the post-exposure treatment given to the victims.

Type of animal	Dose in Gy
Dog	3.5
Monkey	6
Rat	7.5
Frog	7
Rabbit	8
Tortoise	15
Goldfish	23
Human	3 – 5 ***

***

On page 156 the data from Chernobyl is given. 115 were hospitalized with acute radiation syndrome and 28 died. Doses were estimated based on ESR and biological criteria (chromosome aberrations).

From these data a LD_{50} dose can be estimated. The dose is about 6 Gy! This is somewhat larger than that given in the table.

It can be mentioned that the survival time for the 28 was from 10 days to 3 months – more than the 30 days.

Acute Radiation Sickness

The information on acute radiation sickness is mainly attained in animal experiments. For humans we have only had a few accidents (below 100) were large doses (above 1 Gy) are involved.

In 1906, Bergonie and Tribondeau found that there were different radiation sensitivities for different types of mammalian cells. Cells which grow rapidly (high mitotic rate), as well as undifferentiated cells, are the most sensitive. This implies that bone marrow, testes, ovaries and epithelial tissue are more sensitive than liver, kidney, muscles, brain and bone. Knowledge about this is of great importance for those exposed to ionizing radiation. The bone marrow and the epithelial cells of the intestine and the stomach as well as the gonads, the lymphocytes and skin develop the greatest damage. Damage to the bone marrow is the cause of death for whole-body doses in the region 3 to 10 Gy, whereas damage to the epithelial cells of the stomach and intestine is the cause of death for doses in the range from 10 to 100 Gy. For large doses, above 100 Gy, damage to the central nervous system causes death.

Adapted from A. P. Casarett (1968) with permission of A. P. Casarett
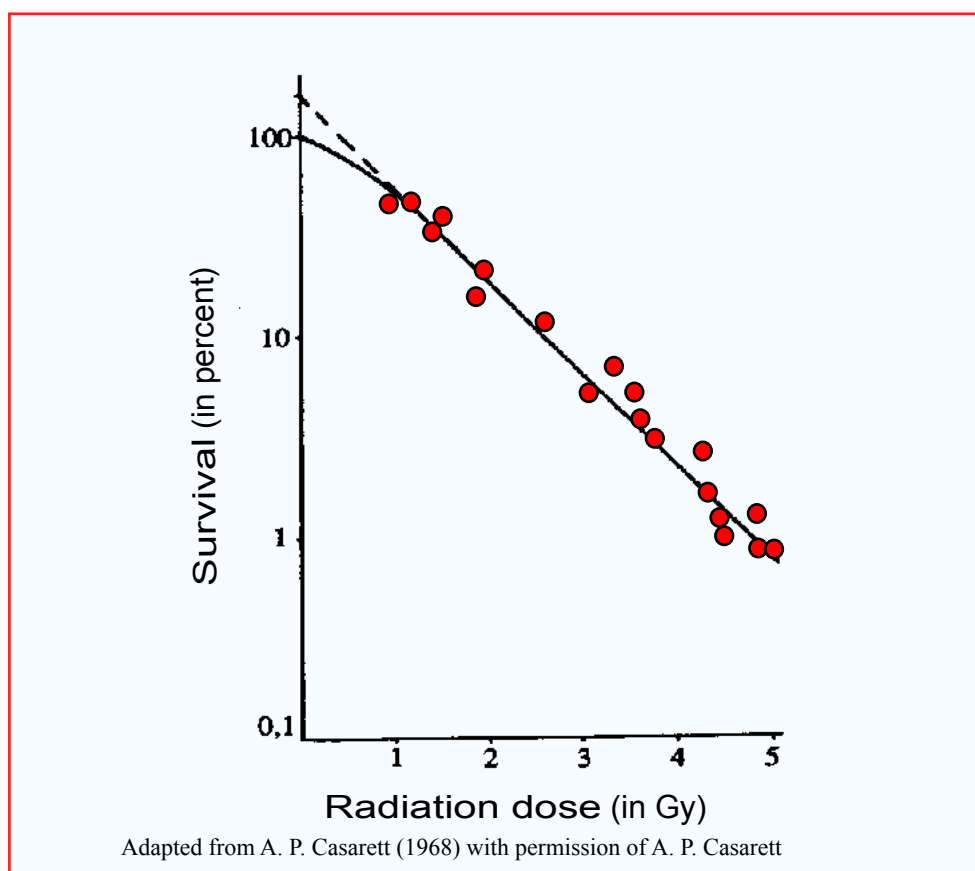
Survival curves for bone marrow cells of the mouse after irradiation with Co-60 γ-radiation.

- **Hematopoietic syndrome**

As mentioned above, the failure of the bone marrow is the cause of death for whole-body doses in the range of 3 to 10 Gy. The radiation may either kill these cells or arrest their development. A dose of 5 Gy will kill about 99% of the hematopoietic stem cells in mice. These stem cells are necessary for the production of circulating blood cells (erythrocytes, granulocytes and platelets). A reduction of these cells will result in anemia, bleeding and infections.

The first sign of such radiation sickness is nausea, vomiting and diarrhea. This situation may disappear after a couple of days. Then, the consequences of lost blood cells become evident. Again, significant diarrhea may take place, often bloody, and a fluid imbalance may occur. This, together with bleeding, occurs in all organs. In addition, if infections occur, death may take place in the course of a few weeks.

- **The gastrointestinal syndrome**

For whole body doses of 10 to 100 Gy, the survival time is rarely more than one week. Damage to the epithelium of the intestine results in significant infections from the bacteria in the intestine itself. The production of blood cells is almost completely stopped, and those remaining in the blood disappear in the course of a few days. After 2 to 3 days almost all granulocytes will have disappeared from the circulation.

The symptoms are pain in the stomach and intestine, nausea, vomiting and increasing diarrhea. A considerable loss of liquids and electrolytes will change the blood serum composition. There is an increased chance of infections.

- **Central nervous system syndrome**

For radiation doses above 100 Gy, the majority may die within 48 hours as the result of the central nervous system syndrome. The symptoms are irritability and hyperactive responses (almost like epileptic attacks) which are followed rapidly by fatigue, vomiting and diarrhea. The ability to coordinate motion is lost and shivering occurs followed by coma. Then respiratory problems occur which eventually lead to death.

The symptoms described are due to damage to the brain, nerve cells and blood vessels. Immediately, permeability changes take place in the blood vessels resulting in changes in the electrolyte balance. The loss of liquid from the blood vessels leads to increased pressure in the brain. It is possible that the respiration center in the brain is particularly damaged. Autopsies have shown that some animals die without visible damage to the brain.

Small Doses and Risk Estimates

With regard to human health it is rather difficult to describe the effect of small doses – both acute doses and protracted. We consider a small dose to be below about 200 mGy acute, and about 1 Gy given in the course of 5 to 10 years.

In most experiments with cells, plants and animals, large doses have been applied with clear and significant results. When the doses become smaller the effects decrease and become less clear. In order to compensate for this, the number of subjects (e.g., animals) can be increased. However, for the region where very small doses are involved (e.g., from an annual dose of a few mGy up to an acute dose of about 50 mGy), the number of animals or humans must be so large that it is very difficult (usually impossible) to conduct experiments and/or epidemiological studies. In epidemiological studies, attempts are made to correlate the radiation dose to the incidence of biological effects such as cancers in a large group of people. Some examples are the populations that have been exposed to radon, those exposed to the bombs at Hiroshima and Nagasaki, and those exposed during the Chernobyl accident. Such studies have yielded both conflicting and confusing results. They are, however, of considerable interest to scientists and to the public.

With regard to human health we shall discuss two effects where we know something about the mechanisms – namely ***cancer*** and ***genetic damage***. The startpoint for both is a DNA-damage resulting in a mutation – either in a somatic cell or in an ovary or sperm producing cell.

Since the number of sex cells is small compared to somatic cells, the number of damage would be very different. For both these mechanisms all the defense processes we have outlined in chapter 12 comes into play.

The studies involving both cancer and genetic effects started a long time ago, before the mechanisms involving DNA was known. Consequently, in the beginning and all the way up to present the epidemiologists were the frontfigures and they tried to ascribe the dose-effect curves in a simple way like the LNT-model.

We shall first discuss genetic effects and then see in more detail into cancer.

Genetic Damage

Fruit fly

In 1927, Hermann Muller observed that ionizing radiation causes mutations. He worked with the fruit fly ("*Drosophila melanogaster*") and used x-rays and found an increased mutation frequency in the X-chromosome. This was the starting point for radiation genetics.

Drosophila melanogaster was a major workhorse behind the early 20th century genetic revolution. Thomas Hunt Morgan used the fly's fast reproductive cycle and simple care requirements to elucidate the fundamentals of heredity.

The fruit fly is an excellent model system; it is inexpensive, easy to work with and exhibits genetic changes that are easy to observe (see an example below).

Normal fruit fly   and   a mutation
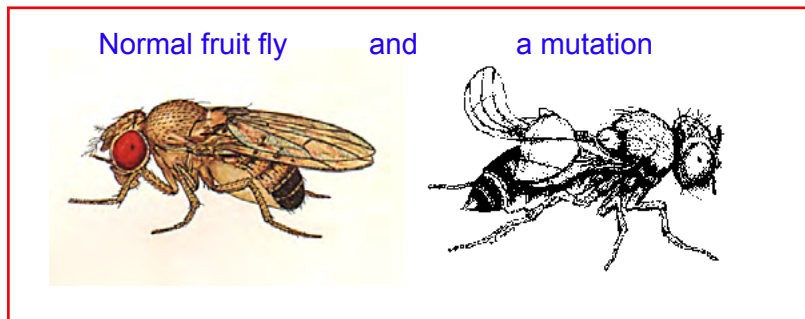
The observable genetic changes are, for example, the color of eyes and defects to the wings (as in the figure). If you compare this fly with the normal one, you can easily observe curled wings.

The fruit flies are rather small and the observations are made using a magnifying glass. The flies can be kept in glass jars, and may be anesthetized with ether in order to keep them quiet during observation.

Hermann Joseph Muller
(1890 − 1967)

Hermann Muller started his career with T.H. Morgan studying mutations in fruit flies. He used X-rays for inducing the mutations.
In 1927 he published the work; "*Artificial Transmutation of the Gene*" in *Science.* Here he described how the radiation yields observable mutations in the X-chromosome.

The Nobel Prize in Physiology and Medicine for 1946 was awarded to Hermann J. Muller;
"*for the discovery of the production of mutations by means of X-ray irradiation*".

Mice – "The megamouse experiment"

Most of the knowledge about radiation-induced mutations was obtained through laboratory experiments. For example, irradiated mice have been studied extensively for years.

At Oak Ridge Liane and William Russell carried out an experiment including altogether about 7 million mice. "***The mega mouse experiment***" provided evidence for seven different types of mutations (changes in the fur color, the ears, etc.). Radiation had increased the number of mutations, and the results can be summed up as follows:

Liane B. Russell
(1923)

William L. Russell
(1911 – 2003)

1. The radiation sensitivity for the different types of mutations varied by a factor 20.

2. With mice, a significant dose-rate effect was found, the mutation frequency increases with increasing dose rate. Consequently, a protracted dose yielded a smaller effect. This result was not found in the fruit fly experiments.

3. Male mice were more radiosensitive.

4. The number of mutations for a certain dose decreased with the lapse of time between radiation and conception. This seems to be equal for the two sexes.

5. Spontaneous mutations always take place. One possible source of these mutations is background radiation. The animal experiments seem to indicate that background radiation accounts for about 2% of the spontaneous mutations.

A significant question in these early days was the socalled "*doubling dose*" which is the dose that doubles the mutation frequency. The experiments with mice indicated a doubling dose of $1 - 2$ Gy.
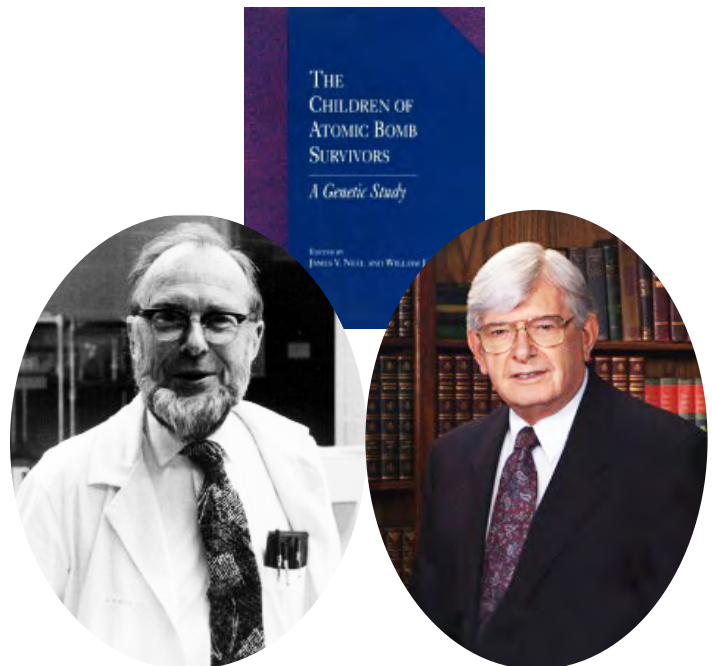
Children of the atomic bombs

For a number of years the two Americans James V. Neel (1915 – 2000) and William J. Schull have studied the children of the atomic bomb survivors in Japan.

Approximately 70,000 children have been registered where the parents received radiation doses of about 350 mSv. This cohort has been studied carefully for the incidence of; stillborn, child death, deformities, death before the age of 26, an abnormal number of chromosomes, and changed ratio of girl/boy.

The conclusion is that no genetic effects have been detected. This implies that there is no detectable radiation-related increase in congenital abnormalities, mortality (including childhood cancers), chromosome aberrations, or mutations in biochemically identifiable genes.

James V. Neel   William J. Schull
The two authors of the book:
The Children of Atomic Bomb Survivors

J. V. Neel and W. J. Schull concluded that the doubling dose for humans is about 2 Sv for acute radiation and about 4 Sv for protracted radiation. In the view of these results, genetic effects from the Chernobyl accident are not expected to be detected. Furthermore, "chromosomal structural changes are likely to be of comparatively little importance among the radiation hazards to man"

If a genetic study should be carried out today it would include studies at the DNA level. It must also include most of the components of the study in Japan, such as; frequency of congenital malformations and still births, death rates among live-born children, growth and development of surviving children, cancer and chromosomal abnormalities in children of those exposed. A study of the genetic effects of ionizing radiation must include a DNA component.
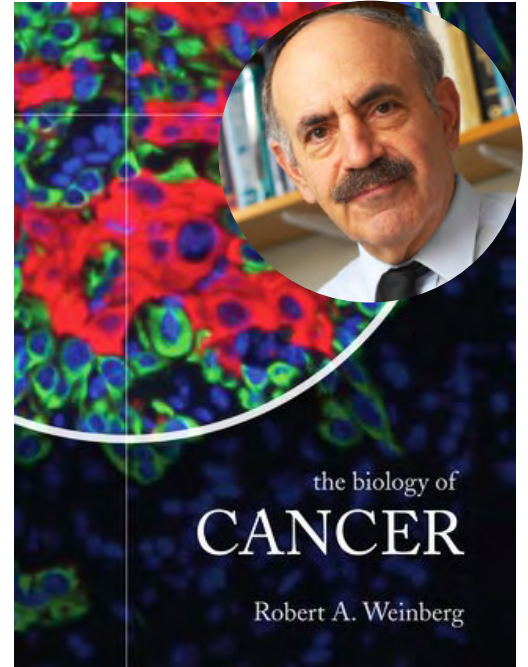
Cancer

Cancer is a disease in which abnormal cells divide without control. Behind this basic definition is a complex and unpredictable spectrum of over 100 types of cancer. When a cellular mechanism goes wrong, the resulting damage, if not repaired, may contribute to a cell's evolution into malignancy. Cancers begin with a DNA-damage in a single cell. The damage may be due to both endogenous as well as exogenous processes. A useful picture is that we have a pool of damaged cells that can be trigged into a cancer development.

It's impossible to comprehensively review current cancer research; the amount of information is enormous and the rate of discovery is increasing. In the preface to the book "***The Biology of Cancer***", Robert Weinberg writes; "*we are deluged with a vast amount of genetic, biochemical, and cell biological information about cancer development, far more almost than any human mind can assimilate and comprehend*".

Carcinomas which comprise more than 90% of human cancers, arise from epithelial cells of either endodermal or ectodermal origin. They are further classified according to tissue of origin, or divided into different histologic types that differ in their patterns of growth and metastasis.
Sarcomas and the leukemias/lymphomas develop from cells of mesodermal origin, including muscle, bone, blood vessels, fibroblasts, and circulating cells of the blood and lymph systems.

the biology of
CANCER
Robert A. Weinberg

The goal

During the years we have had individuals that have got cancer due to ionizing radiation. Some of the pioneers and some of the doctors that used radiation without protection are among these individuals. In all these cases it is not possible to arrive at any dose determination. With regard to the use of radiation and to the use of nuclear energy it is important to have some knowledge about the dose-effect curve for radiation. The goal is to get information on "***the dose-effect curve for small radiation doses***" and how we (the radiation authorities) should establish a protection system. Today the protection system is based on the LNT-hypothesis (Linear No Threshold), assuming that all radiation is deleterious.

Up to now the major source of information for evaluating health risks from exposure to radiation is the LSS-group (Life Span Study) of survivors after the Hiroshima and Nagasaki bombs. The LSS cohort consists of approximately 87,000 survivors who were in the city at the time of the bombings and for whom it is possible to estimate the doselevel. The size of the cohort in Hiroshima which was within 2000 m from the hypocenter was approximately 28 000. They may have attained doses above 8 mGy.

Great efforts have been made to determine the radiation dose, which consisted of γ-radiation and neutrons. The dose was given at a very high doserate together with the blast. ***This implies that some of the protection and repair processes discussed in Chapter 12 are not working.*** Consequently, the results form the bombings would not be valid in other situations where the doses are given with a low doserate – including the cohorts exposed in and after reactor accidents.

We shall first go through some of the available information we have on irradiated groups, including the LSS cohort. We mentioned above that some of the pioneers in the radiation field died from cancer. Furthermore, a number of first radiologists got skin cancer and that uranium miners suffered from lung cancer. In these cases the radiation doses must have been large.

Different irradiated cohorts

The dial painters

In the first part of the 20th century, the numerals and hands on some clocks were painted with radium. Radium paint was still used in dials as late as the 1960s. Women were employed to do the painting. Sometimes they ingested small amounts of radium because they "pointed" their brushes by licking them.

Radium is a bone seeker and some of the women contracted bone cancer later in life.

A large amount of work has been carried out with the purpose to determine the intake, doses and health effects for all those exposed to Radium. A report from R.E. Rowland from Argonne National Laboratory was published in 1994. In the 1990s three books about the dial painters have been published: *"Radium Halos", "Radium Girls" and "Deadly Glow".*

An illustration of radium painters

Let us try to give some of the main points. From about 1917 it became an industry in USA to paint the dials and numbers on the clocks with a mixture of radium and fluorescent materials. It was mainly young girls (20 – 30 years old) that did the painting. On this page is an illustration from D.W. Gregorys play "***Radium girls***", and on the next page you can see a picture from a studio in Illinois in 1925.

The radioactive paint consisted of a mixture of Ra–226 (from the Uranium series) and Ra–228 (from the Thorium series). The α-particles from the radioactive isotopes bombarded luminous materials such as barium bromide (BaBr), zinc sulfide (ZnS) and others – which resulted in a constant glow that could be seen in the dark.

More than 2000 young women were engaged. Each girl handled about 1 mCi radium per month (37 MBq). In this work the girls were exposed to external as well as internal radiation which including both α, β and γ-radiation. We are faced with the following radiation scenario:

1. The radium isotopes resulted in radon. The radon level in the working room was about 2000 Bq/m³.

2. The girls were exposed to external γ-radiation from the radium sources. The dose level has been calculated to be up to 460 mGy/year. The breasts are most exposed.

3. The girls were exposed to α-radiation from the intake of Ra–226 and Ra–228.
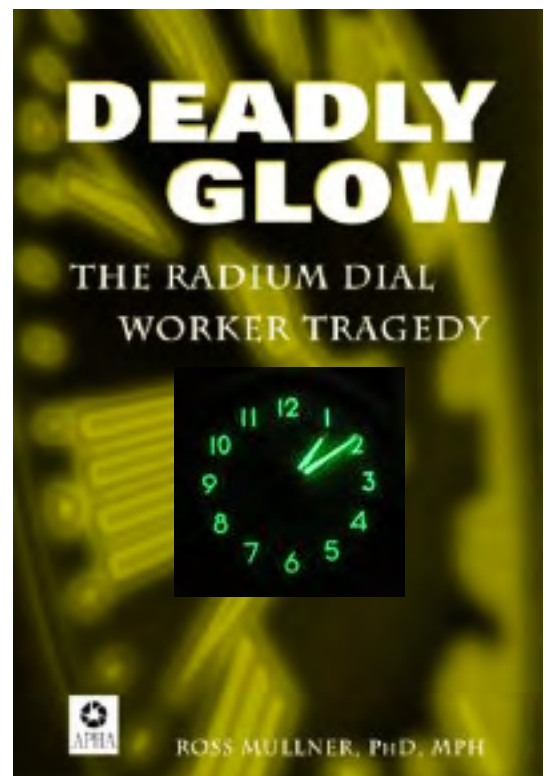
Dial painters 1925

Ra-226 from the Uranium series has a half-life of 1600 years. It ends up in the stable isotope Pb–206. In the decay processes 10 α-particles are involved. Ra 228 from the Thorium series has a half-life of 5.8 years. It ends up in Pb–208. In the decay scheme 6 α-particles are involved.

We can conclude that the doserate is rather low, and completely different from the atomic bombs in Japan.

When these isotopes are inside the body it is the α-particles that give the main contribution to the radiation dose. However, it is the γ-radiation from the decay processes that can reach the outside and consequently give the basis for measurements (in recent years whole body measurements).

A large amount of work has been carried out to localize those working in this industry and which have been exposed to radiation. The total number identified was 4133 (3637 women). Approximately 2500 were measured in order to determine the radiation doses. A significant part of the work has been carried out by Robley D. Evans. He introduced the method to use the γ-radiation to determine the radium in the body.

Evans established "***Center for Human Radiobiology at Argonne National Laboratory***" in 1968. They published the work on "***Radium in humans***" in 1994. The radium dial painters, mainly young girls, were a considerable part of this work.

The work with the dial painters (all those exposed to radium) included the following items;
a). To identify all the dial painters,
b) To measure the radioactivity in the body and thus estimate the total intake and
c). To determine the health history for those exposed.

Robley D. Evans
(1907 – 1995)

Let us note that a significant intake in the case of the dial painters was due to the fact that the girls licked the brushes to sharpen the tip. In 1926 it was urged that the girls should stop this licking – which certainly helped. No cancers were observed for those starting after 1930.

Measurements

Radium is taken up and deposited mainly in the bones. In order to calculate total doses to the individuals, both radioactive decay as well as biological excretion must be considered, i.e. we try to find a biological half-life. A decay curve has been found and used – the retention of Ra–226 is about 2.5 % at 1 year and about 0.33 % after 50 years. This implies that the intake of radium can be estimated from measurements at later times – and this again can give an estimate of the accumulated body dose. The total skeletal dose varied considerably with the highest values up to 280 Gy.

In the large Argonne work altogether about 6000 people are included. The names of about 5000 are known, 3500 have been localized and about 2500 have been measured.

Health effects

In spite of the large doses to all parts of the body only two types of cancer have been diagnosed – 64 bone sarcomas and 32 head carcinomas. The total doses for those with bone sarcomas varied from 11 to 278 Gy – and for those with head and neck carcinomas the total calculated dose varied from 8.6 to 158 Gy.

From a population of 2,383 cases for whom reliable body content measurements have been done – all the 64 bone sarcoma cases occurred in the 264 cases with more than 10 Gy, while no sarcomas appeared in the 2,119 radium cases with less than 10 Gy.

The great majority of exposed individuals went through life with no recognizable consequences of their exposures. They lived as long as, and apparently in as good health as, their unexposed neighbours. This fact seems to have been little appreciated and seldom mentioned, but it may be the most important finding of the entire study. No leukemias, no breast cancer and no lung cancer in spite of the rather large doses given at a low dose rate.
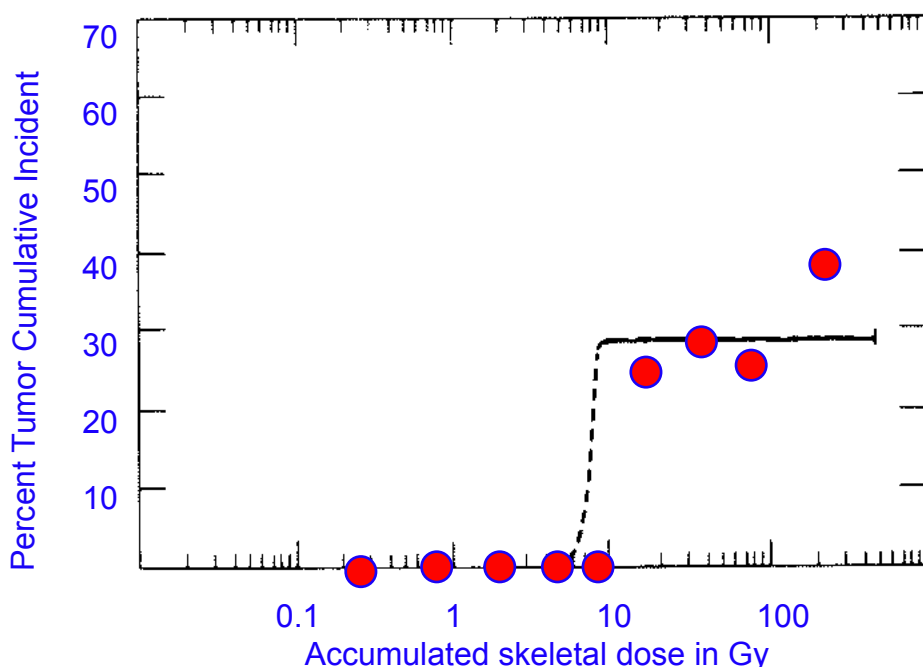
The figure above is the dose-effect curve for the relation between radium intake (resulting in skeletal dose) and cancer (Evans data).

Radon and lung cancer

Radon and lung cancer was treated on pages 110 – 123. It was concluded that for miners working in an atmosphere of radon + a number of other carcinogens including smoking it was a connection that could be ascribed by a linear curve *with a threshold*. The data for the miners can not be used for radon in homes. The newer studies of radon in homes and lung cancer has been described both by a linear dose-effect curve and by a curve including a hormetic region up to a radon level of about 1000 Bq/m^3 (see page 120 – the Schneeberg data).

Chest fluoroscopy and breast cancer

Several years ago when tuberculosis was more frequent, patients were examined with x-rays. A number of x-rays and fluoroscopies were performed in combination with pneumothorax treatment (see Chapter 9, page 214). The idea was to give the lungs some rest which was accomplished by collapsing the lung with air. The treatment could last for several years and the patient needed more air every second week. Each fill of air required more x-rays and the doses could be significant.

The weak point here is that no dosimetry was done at the time, and reconstructions give only an idea of the dose involved. The total dose was spread over time. Some observations done in recent years indicate an increase in breast cancer for the largest doses (page 214). The same figure indicate hormesis for the lower dose region.

For a while, a radioactive material (thorotrast) was used as a contrast medium in x-ray diagnoses. Increased cancer incidence (liver cancer) has been observed among patients so treated, particularly in Germany and Japan.

Atomic bombs – Hiroshima and Nagasaki

The only two atomic bombs dropped in an area with people are those in Hiroshima and Nagasaki in August 1945. Large amount of work has been performed to determine the biological effects of these bombs. We have several places through the book described effects and discussed physical and genetic consequences. We shall now once more discuss the radiation from the bombs and the occurance of cancer that can be attributed to this radiation.

A model of Hiroshima and the first nuclear bomb 6th of August 1945. The bomb exploded 600 meters above ground. The fire ball is indicated by the red ball. The explosions released a large amount of energy in the form of; 1) heat (about 35 %), 2). blast or pressure (about 50 %) and 3) radiation (about 15 %). About 5 % is promt radiation consisting mainly of γ-radiation and a small fraction of neutrons, and about 10 % is delayed (i.e. fallout isotopes). The prompt radiation is given within seconds. In all the subsequent discussion about the radiation effects it is the promt irradiation we are discussing.

1945

Today

The picture to the left is taken in 1945. It shows the ruins of the former Hiroshima Prefectural Industrial Promotion Hall (called Genbaku Dome) close to "Ground zero". Below you see Genbaku Dome in August 2010. In 1996 this memorial was included in UNESCOs "World Heritage List"

The radiation quality

Approximately 3 – 5 percent of the energy released in a nuclear bomb is prompt irradiation, i.e. γ-radiation and neutrons. This radiation decreases rapidly with the distance from the point of explosion (inverse square law) as well as by absorption, scattering, and capture by the atmosphere.

The dose level in air as a function of the distance from the hypocenter has been obtained by calculations, and also from observations of thermoluminescence (γ-radiation) as well as induced radioactivity from neutron reactions (n,γ reactions). The neutron intensity decreases rapidly and becomes negligible in comparison with the gamma component.

The range for significant levels of radiation does not increase markedly with the weapon yield. For Hiroshima and Nagasaki the dose levels 1 m above ground in the open field 1 km from the "ground zero" (at the surface below the blast), were estimated to 4.22 Gy (Hiroshima) and 8.62 Gy respectively, while at 2 km the doses were 0.08 and 0.14 Gy (Dosimetry System from 2002). Thus, only within a distance of about 1 km the radiation itself may be fatal. However, in this zone the blast and thermal effects are much more important than the prompt irradiation.

In the table below is given the estimated population size and number of acute (within 1945) deaths in Hiroshima and Nagasaki after the atomic bombings.

City	Estimated city population at the time of the bombings	Estimated number of deaths within 1945
Hiroshima	340,000 – 350,000	140 000
Nagasaki	250,000 – 270,000	70 000

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The cause of death was flash or flame burns and falling debris. During the following months, several died from the effect of burns, and other injuries. From what we know about acute radiation death, very few were exposed to doses large enough to cause death alone. For those that attained such large doses would be killed by the blast and heat.

Dose calculations

In 1950 it was assumed that about 280,000 people have been exposed to radiation because of the bombs. It is an impossible job to determine individual doses to all these people. However, a tremendous job has been done and dose estimations have been published in 1966, 1981 and 1986 – and again in 2002. Small changes in the position of the blast have been introduced between DS86 and DS02.

Let us mention some of the problems with regard to doses.

1). Neutrons are readily absorbed by water. Consequently, the weather conditions and humidity are of importance for the dose evaluation.

2). The bomb material which envelopes the fissionable material (U-235/Pu-239) is important. In Hiroshima and Nagasaki iron was used and a heavier metal in the nose and tail. This would slow down some of the neutrons and absorb some of the γ-radiation. Some years ago the assumption was that the neutron doses were large in Hiroshima compared to those in Nagasaki. Later, new calculations showed that the neutron doses in Hiroshima had to be reduced and the γ-doses set higher.

3). To estimate individual doses, knowledge is needed about the location of the person during the blast and what kind of protection he or she had (being indoors, outdoors, etc.). These reconstructions are based on the survivor's testimony, taken some years after the bombs fell. At times, the stories were vague, and some doses were immediately deemed impossible to calculate.

4). Some years ago, it was found that the estimated position of the centre of the explosion at Nagasaki had to be changed by 37 meters. This may sound trivial, but the result was that some persons had to be moved from one dose group and placed into another. Similar small differences were also introduced in the DS02 calculations.

Health effects

All the time since the bombs were dropped the health of those survived has been followed. In 1947 the "***Atomic Bomb Casualty Commission***" (ABCC) was established. The purpose was to study the health of the A-bomb survivors. This organization was reorganized in 1975 when RERF ("***Radiation Effects Research Foundation***") was formed.

The objective of the RERF is to conduct research, for peaceful purposes, on the medical effects of radiation on man, with a view to contributing to the health and welfare of the atomic-bomb survivors and to the enhancement of the health of mankind.

Information on early effects of the radiation was obtained by interviewing more than 100,000 atomic-bomb survivors, primarily from 1956 to 1961. Among the acute radiation symptoms recalled by survivors, epilation (hair loss) is regarded as the most reliably reported. In general, acute radiation symptoms do not appear at low-dose radiation exposures. That is, below a certain radiation dose, no acute symptoms occur.

In order to investigate late effects, 94,000 survivors were selected and registered as a cohort, LSS (Life Span Study). Individual doses to 86,611 survivors were determined. In the period from 1950 – 2000 it was 47,685 that died from all causes. With regard to cancer it was 10,127 that died from solid cancer and 296 from leukemia. It is quite uncertain how many of these cancers were due to the radiation in 1945, but the number is assumed to be approximately 500. In 1990 the number was assumed to be 429 and in 2006 it was assumed to be 527, – of them 87 from leukemia and 440 from solid cancers.

Dose effect curve

Using the latest dosimetry system (DS02) the statistical analysis supports a linear-quadratic dose response model for solid cancers. Previous analysis have been interpreted in accordance to the LNT model. For leukemia a linear-quadratic model gives the best fit – even a hormetic region can be suggested.

Studies on the LSS cohort have shown an increase in cancer for the group with doses in the range of 200 – 500 mSv. Hazard values for doses below 200 mSv are speculations.

It can be noted that the doses calculated are given in sievert (Sv). The radiation here is mainly γ-radiation and consequently the radiation weight factor is 1. This implies that we attain the same numerical value if the dose is given in gray (Gy).

Comments

1. Little information exists about the accumulated doses received, as well as of the variation in doses from one person to another **after** August 1945. It is reasonable to assume that in the period since 1945 the accumulated equivalent dose is on the order of 150 to 300 mSv. This equivalent dose, and in particular its variation, is very difficult to take into consideration.

2. Health end points other than cancer have been linked to radiation exposure in the LSS cohort. A dose-response relationship with mortality from nonneoplastic disease was demonstrated in 1992, and subsequent analyses in 1999 and 2003 have strengthened the evidence for this association. Statistically significant associations were seen for the categories of heart disease, stroke, and diseases of the digestive, respiratory, and hematopoietic systems. The data were inadequate to distinguish between a linear dose-response, a pure quadratic response, or a dose-response with a threshold as high as 0.5 Sv.

3. The doses in free air out from the hypocenter have been calculated with rather high quality. However, individual doses are a quite different story. Since the uptake of the individual stories were made several years after the bombing a lot of errors will be present. We have no way of calculating the dose for a person exposed in a street car. We're not sure how many people were standing between a person and the bomb. When the bomb hit, some persons were standing, some sat and so on.

4. There were no radiation monitors in the cities, of course, so the number of gamma rays and neutrons released by the bombs had to be estimated. This was easy for the Nagasaki bomb, since this type was used in numerous weapons tests, while leaving lasting traces in the atmosphere, provided a wealth of data. Nuclear scientists even built replicas of Japanese homes in the bombs' radius.

5. Hiroshima's bomb, "Little Boy," was the challenge. The bomb was unique, shooting two uranium cores together for its explosion. The Manhattan Project had never tested it, and the United States never built a similar bomb. This left doubts about the theoretical estimates made of Little Boy's radiation, especially the neutrons it released. There seemed to be disagreements between concrete activated by the bomb and calculated doses. It was called the "Hiroshima discrepancy." There was only one possible solution: They had to resurrect Little Boy in 1982.

6. The doserate was very large. Consequently, we can not expect that all the defense mechanisms, discussed in Chapter 12, took place.

The conclusion of this is that the LSS cohort and the radiation effects to this group have very limited value with regard to a protection system that can be used by the radiation authorities in the case of reactor accidents, and for protection threshold values in general.

The picture above is from the 6th of August 2011 the 66th anniversary of the world's first atomic bombing in Hiroshima. People pray after releasing paper lanterns on a river facing the Genbaku Dome.

The Taiwan cohort

In 2006, W.L. Chen and coworkers published the paper "*Effects of Cobalt-60 Exposure on Health of Taiwan Residents Suggest New Approach Needed in Radiation Protection*"[1].

The paper is about an almost unbelievable story from Taipei in Taiwan. It was observed, accidentally, that a number of apartments had been contaminated with Co-60 gamma-radiation.
Approximately 10,000 people occupied these buildings and received a rather large radiation dose during a period of up to 20 years.

The above mentioned paper is about all the work carried out to determine dose level and accumulated doses as well as the medical work connected to this irradiated group. Some unexpected results were obtained.

The apartments were built mainly in 1983 and they used recycled steel, accidentally contaminated with cobalt-60. The first "radioactive" apartments were discovered in 1993, and later more apartments, altogether more than 1700 were found. The contaminated buildings included both public and private schools as well as some small businesses, in Taipei City and nearby counties. About ten thousand people occupied these buildings for 9 to 22 years.

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1 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2477708/

Co-60 has a half-life of 5.27 years. It decays by emitting one β-particle – followed by the emission of two γ-ray photons with energy of 1.17 MeV and 1.33 MeV respectively. On page 24 in Chapter 2 you can see the decay scheme.

The γ-radiation is "whole body irradiation". Considerable work was carried out in 1996 to determine the dose-rate at that time. Ionization chambers as well as thermoluminescence dosimeters (TLD) were used. In order to explore the doses to the residents a Rando phantom was used. This phantom is divided into 2.5 cm slices that can be filled with dosimeters.

In December 1996, the AEC estimated that 20% of the residents received an annual (1996) dose in the range from 5 to 160 mSv (or mGy). This implies that 80% of the residents received a dose of less than 5 mSv. The dose level in the houses during the period 1983 to 1996 can be determined very good by the measurements in 1996. However, the whole body doses to the residents are very uncertain and depends on the time spent in the different apartments. This implies that we have limited information about individual doses.
A crude estimate of the average 1996 dose for 3 different cohorts is as follows:

      1. High cohort (~ 1100 people) = 87.5 mGy
      2. Medium cohort (~ 900 people) = 10 mGy
      3. Low cohort (~ 8000 people) = 3 mGy

The calculated mean annual dose received by all the residents in 1996 was about 13 mGy. You can easily calculate that this dose level corresponds to approximately 74 mGy/year in 1983.
We can use this and get an information of ***accumulated doses*** to the residents in the three groups or cohorts.

Number of exposed people and doses are given in the table below:

Cohort	Number of people	Mean annual dose 1983 (in mSv)	1983 – 2003 individual dose (in mSv)	1983 – 2003 Collective dose (person-Sv)
High	1 100	525	4000	2,260*
Medium	900	60	420	378
Low	8 000	18	120	960
Averaged	10 000	74	600	6 000
Adjusted	10 000	49	400	4 000

* From July 1996, 50 % of the residents relocated.
Approximately 10 000 people are involved altogether. The adjusted doses are calculated on the assumption of the residency factor of about 0.7.

Let us made this short by saying that the the size of the cohort is 10 000 and they got a "collective dose" in the period 1983 – 2003 of approximately 4000 person-Sv and individual doses up to 3 – 4 Gy.

Health effects

Residents with annual doses above 5 mSv were examined in AEC (Atomic Energy Commission) hospitals. Some residents were later examined in Hiroshima.
The examinations revealed no harmful radiation sicknesses. When the residents in one of the highly radioactive buildings sued the government for compensation, the concerned hospitals testified that they had no evidence that the radiation had caused any harmful effects.

The harmful effects in question were cancer and congenital malformations (birth defects). The mean cancer mortality in Taiwan in the period 1983 – 2002 is 116 deaths per 100,000 person-years. It increased in this period as seen in the figure below. In Norway the cancer mortanlity is higher with about 220 deaths per 100 000 person-years.

For a population of 10,000 the number of cancer deaths expected for the 20 year period 1983 –2002 is 232. The observed cancer deaths for the Taiwan cohort is given in the figure below. The total cancer deaths for the cohort was 7 – only 3 % of that expected for the general population.
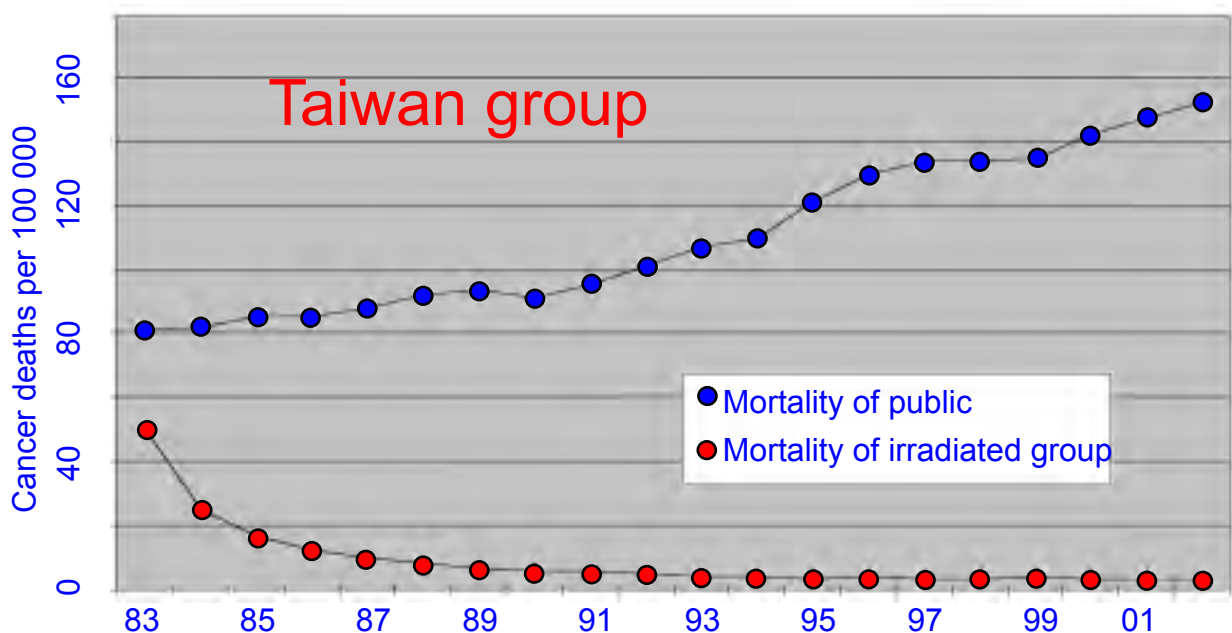
Congenital malformation was the other harmful effect studied. There is no official statistics with regard to the rate of congenital malfunctions in Taiwan, but an incidence of 46 children was expected. It was found only 3 children with congenital malformations in the cohort (heart disease). This is about 6.5 % of the rate for the general population.

Summary

The results of the Taiwan study strongly suggest that whole-body chronic irradiation, in the dose rate range that the apartment residents received, *caused no symptomatic adverse health effects*, such as radiation sickness, or the increased cancer or increased congenital disease such as predicted by ICRP theories. On the contrary, those who were exposed had lower incidences of cancer mortality and congenital malformations.

The results from the Taiwan cohort demonstrate the beneficial health effects from chronic exposures to low dose rates of ionizing radiation. We have in this book demonstrated that low dose-rate irradiation stimulate the cells defense mechanisms – and that small doses can be beneficial. These results must be analyzed and will hopefully introduce a change in our view on radioactivity and radiation in general.

We quote from Chen et al. article.
The medical evidence from this study clearly suggests that current radiation protection policies and standards are inappropriate. We therefore recommend that the radiation protection authorities change them to accurately reflect the actual benefits and hazards of exposures to radiation. This would have very important consequences for all the nuclear risk assessments carried out and the public attitudes toward all applications of nuclear and other technologies that involve ionizing radiation. Fear of small doses of radiation is the basis for political barriers blocking the construction of nuclear power plants and nuclear waste management facilities.

Risk calculations – dose-effect curves – LNT-theory

The international body for radiation protection is the ***"International Commission on Radiation Protection"*** (**ICRP**).

ICRP was established in combination with the second international congress in radiology in Stokholm, Sweden, in 1928. Rolf M. Sievert was one of the founders and later became chairman. The ICRP makes suggestions and recommendations for radiation protection, which are followed in most countries that have established a national protection board.

Since 1928, ICRP has developed, maintained, and elaborated the International System of Radiological Protection used world-wide as the common basis for radiological protection standards, legislation, guidelines, programmes, and practice.

Rolf M. Sievert
(1896 –1966)

We can mention that the first recommendation is from 1934. People working with radiation should not attain doses above 0.2 R (roentgen) per day. In our dose-system this is about 1.86 mGy to soft tissue per day or about 680 mGy per year. Since then the maximum allowed doses have been smaller and smaller and today the ICRP limits are:

Group	Annual dose
Radiation worker	20 mSv
General public	1 mSv

LNT

The most important aspect with regard to recommendations is that ICRP uses the principle of linear dose-effect-curves (LNT) with no threshold doses to estimate the health effects from small radiation doses. This principle was introduced in the late 1950s and is still the basis for all dose limits recommended.

Back in the 1950s the "target theory" dominated the evaluation of radiation data. It was assumed that the biological result was due to a "hit" – and the number of hits increases linearly with dose. A few years later it was accepted that the initial step for carcinogenesis (the initiation) is a damage to the DNA in a cell. Again the initial number of DNA-damages increase linearly with dose. Thus as long as we can keep the biology with all its defense and repair mechanisms out – it is reasonable to assume the LNT-model.
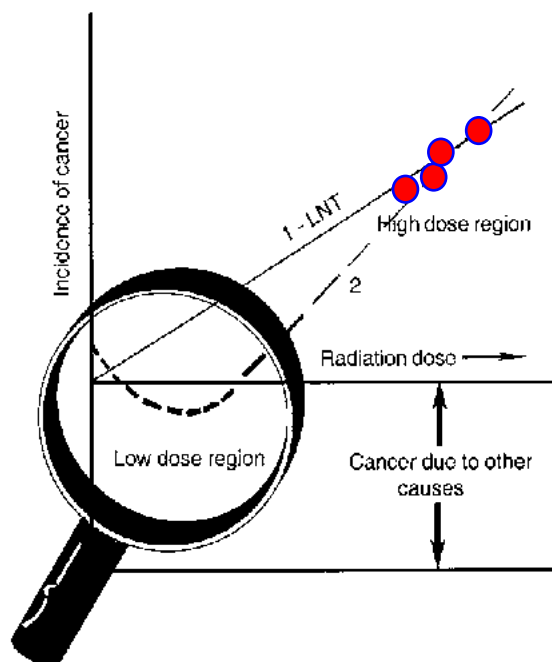
The figure to the left give you an idea of the basics behind the dose-effect curve.

The curve marked 1-LNT is the well known "linear no-threshold model" for radiation damage.

The curve marked 2 has an alternative form, including both a threshold as well as a "hormetic" part for the smallest doses. The filled circles indicate assumed observed data for the large dose region. The two alternatives are drawn to fit observations in the high dose region.

In 1957 P. Armitage and R. Doll published a paper about carcinogenesis. They suggested that the promotion step must be considered to be a stochastic process – i.e. it takes place by chance. From the pool of cells with DNA-damage the cell that is the origin for a tumour is picked out by chance. If radiation was the only carcinogen and if no biology is included, we can use the collective dose conception in risk analysis.

Sir Richard Doll (1912 – 2005) was a British physiologist and epidemiologist. Around 1950 he found a strong correlation between smoking and lung cancer. This was a surprise at the time and Doll was knighted for his work.

ICRP have not included the biological processes with repair and apoptosis that is stimulated by small doses given at a low doserate and the LNT-model is still used. Thus in the 2007 recommendations we quote:

*"T*he 2007 recommendations of the International Commission on Radiological Protection (ICRP) take account of the latest biological and physical information and consolidate the additional guidance provided by ICRP since 1990. The changes to the scientific data are not substantial. ICRP has retained its fundamental hypothesis for the induction of stochastic effects of linearity of dose and effect without threshold and a dose and dose-rate effectiveness factor (DDREF) of 2 to derive nominal risk coefficients for low doses and low dose rates."

Based on the above considerations and conclusions the radiation authorities in most countries (including "Strålevernet" in Norway) have used the " *Linear No Threshold*" (LNT) -model for the deleterious effect of ionizing radiation. The model simply assume that all radiation is bad and that the deleterious effect increases linearly with dose with no threshold (start at zero dose). Since zero dose is not attainable the ALARA – principle (As Low As Reasonable Achievable) was introduced.

The risk model chosen by ICRP and the other radiation authorities is excellent for setting up a protection system for all use of ionizing radiation. The ultimate goal is zero dose. Furthermore a linear dose-effect curve makes it possible to use collective doses and opportunities to calculate the detrimental effects to an irradiated cohort.

Risk estimates are based on the form of the dose-effect curve – and is by definition the steepness (the derivative) of the dose effect curve.

Total risk = risk factor • dose

For a straight line this implies a constant risk factor (independent of dose)!

The calculated total effect using the LNT-model is the product of the risk factor and the collective dose. Such simple calculations have been extensively used and have attracted the interest of the public. For all other forms of the dose-effect curve, however, risk calculations are far more complicated and, for the most part, impossible.

All regulations with regard to radon in houses, radioactivity in the drinking water, radioactivity in food products after Chernobyl have been set in line with the LNT-theory. ***All these regulations are very costly.***

If we take biology into account

As long as we only are concerned about physical processes with radicals and DNA-damage the linear dose-effect curve is expected. However, we have seen in Chapter 12 that when living cells are irradiated a number of biological processes are intitiated that will strongly influence the end result such as the induction of cancer. In particular the research during the last two decades are very interesting and show that small doses of radiation given at a low doserate stimulate the defense mechanisms.

We can safely conclude that: "***the LNT-model is not valid".*** In fact, small doses are necessary for life.

Radiation hormesis

During the last years a lot of research show that small doses of radiation are beneficial to life. We shall first mention an experiment carried out with ***Paramecium.***

Planel and coworkers (1987) studied the growth of *Paramecium* (the small "slipper shaped" cells living in water) by carrying out the following experiments:

A. Cultures of paramecium were put into a 5 to 10 cm thick lead chamber that reduced the background radiation to almost zero. The result was that cell growth was reduced. The same result was obtained when the experiment was carried out in an underground laboratory where the radiation background was very small.

B. The next step in the experiment was the introduction of radioactive sources.
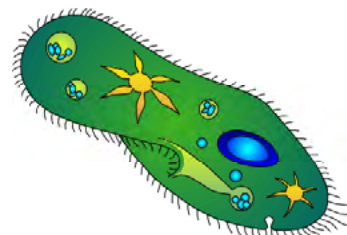
A drawing of Paramecium

The radiation from the sources resulted in a radiation level which yielded an annual dose of from 2 to 7 mGy (comparable to normal background radiation). The result was that the cell growth increased back to "normal." These and similar experiments indicate that small doses of radiation may stimulate a number of processes such as cell growth and cell repair.

Radiation Hormesis and the Linear-No-Threshold Assumption
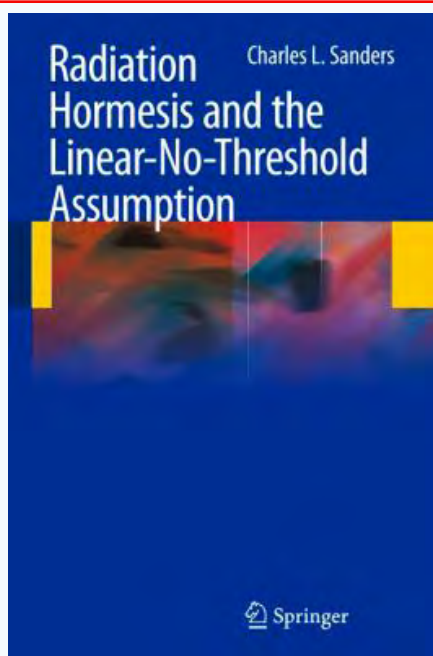
Charles L. Sanders

*In 2009 Charles Sanders published the book **"Radiation Hormesis and the Linear-No- Threshold Assumption."***

We quote from the introduction to this book

"Ionizing radiation is considered to be a weak carcinogen. Negative uncertainty about carcinogenic effects from ionizing radiation have influenced decommissioning of the existing nuclear facilities, long-term storage for reactor waste, construction and placement of new nuclear power plants, increased fears of "dirty bombs," and utilization of diagnostic radiology to find and treat disease. The decades-long moratorium on new construction of nuclear power plants in the U.S., a pervasive resentment of anything "nuclear," and a delay or refusal to obtain needed medical radiation exposures are some of the societal consequences to radiophobia among the American public.

Springer

While regulatory decision making was designed to protect the public health, in some ways it has become punitive and burdensome. The idea that any exposure to radiation may be harmful has led to public anxiety and enormous economic expenditures that are disproportionate to the actual radiation risks involved. In the United States and some other countries, regulatory compliance costs are steadily growing, while desired public health benefit from added regulation are increasingly difficult to measure.

A position paper of the Health Physics Society calls the regulatory systems for determining and enforcing public health standards "inconsistent, inefficient, and unnecessarily expensive".

For those interested in the vigorous discussion going on with regard to the LNT-theory should also read the summary article from 2000: "*It's Time to Tell the Truth About the Health Benefits of Low-Dose Radiation*" by James Muckerheide.

http://www.21stcenturysciencetech.com/articles/nuclear.html