RADIATION CAUSES BONE LOSS

The scientific world has been shaken by a report from Clemson University that a single therapeutic dose of radiation can cause appreciable bone loss. Senior author Ted Bateman, PhD, a professor of bioengineering, and his South Carolina colleagues showed that when mice were given a dose of just two Gy (two gray, a radiation dosage formerly designated as 200 rads), between 29 and 39 percent of their interior bone mass was destroyed.

It did not particularly matter which kind of radiation the mice were exposed to. Gamma rays, protons, high-speed carbon and iron nuclei all had a similar and markedly destructive effect. Dr. Bateman and his colleagues reached these figures by creating 3D computer scans of the spongy interior of the bones and then calculating how much bone mass these irradiated mice had lost compared to a control group.

"We were surprised at how large the difference in bone mass was," Dr. Bateman told the weekly magazine, *New Scientist* (Barry 2006).

Two Gy of radiation is similar to a single therapeutic dose of radiation given to human cancer patients, while a full course of therapeutic radiation typically delivers as much as 70 or even 80 Gy. It had previously been known that patients receiving therapeutic radiation suffered some bone loss and were put at a greater risk of fractures. But until now it was unknown that just a single dose of radiation could trigger such severe bone loss. This news is doubly disturbing since chemotherapy (often now given with radiation as part of a one-two punch) can also independently cause bone loss. The cumulative effects of radiation and chemotherapy delivered to the same patient may therefore be significantly more damaging.

The Clemson scientists demonstrated what they called "profound changes in trabecular architecture." (The term "trabecular" describes the microscopic bony latticework that characterizes the interior of skeletal bones. The trabecular pattern of bony tissue is what gives bones their structural strength.)

Significant losses in bone volume were observed for the four types of radiation that were studied: gamma (volume down 29 percent), proton (down 35 percent), carbon (down 39 percent), and iron (down 34 percent). Several measurements of bone health, including trabecular connectivity, density, thickness, spacing, and number were also adversely affected.

"These data have clear implications for clinical radiotherapy," the Clemson scientists said, "in that bone loss in an animal model has been demonstrated at low doses" (ibid.)

Dr. Bateman agreed, however, that making a direct extrapolation of these findings to humans could be difficult. The bones of the mice in the experiment were still growing, making them more susceptible to radiation damage. (This is also the case in young human patients.) Although the Clemson findings have caused a stir particularly in space research circles, NASA's chief radiation health officer, Dr. Frank Cucinotta, pointed out that the gamma ray dose in these mouse experiments was 40 times greater than space station astronauts would experience over a period of months, and 2 to 4 times what astronauts on a Mars mission would encounter. However, astronauts are also exposed to high-energy and iron nuclei in addition to gamma radiation.

Bone Death: A Long History

It has been known for quite some time that radiation could cause "serious and permanent injuries" to growing bones as well as localized but incapacitating diseases (Fajardo 2001: 365). In fact, the real surprise in the latest study was that relatively small doses caused such a significant amount of damage.

The basic concept of 'bone death' was probably known to the ancient Greek physician, Hippocrates.

Necrosis of the bone (i.e., osteonecrosis) was fully described as early as 1794. In 1903, just a few years after the 1895 discovery of X-rays, the German surgeon Georg Clemens Perthes (1869-1927) exposed one wing of a day-old chicken to X-rays. Just 12 days later he noted that growth of the irradiated wing was retarded and that the feathers were abnormally formed. In 1905, two French scientists, Joseph Recamier and Louis Mathieu Tribondeau (1872-1918), described similar growth retardation in kittens.

In the intervening decades, various tumors, especially sarcomas, were found with increased frequency in patients who had undergone irradiation. James Ewing, MD (1866-1943), the celebrated American pathologist (after whom the bone tumor called 'Ewing's sarcoma' is named), was extremely interested in the reactions of bones to radiation. He was impressed by the ability of radiation to shrink the size of bone tumors and, along with surgery and Coley's toxins (a fever-causing, mixed bacterial vaccine), to effect prolonged remissions in some cases (Ewing 1940:370). He described three patients who had been irradiated for bone cancers and whose irradiated bones then became brittle and easily fractured. Ewing also observed thickening in the outer layer (known as the cortical plate) of bone at the expense of the marrow cavity and noted the increased susceptibility of irradiated bones to infection (Fajardo 2001).

The most famous instance of radiation damaging bones, however, occurred in the first decades of the 20th century. Industrial engineers learned that by adding a small amount of radium to a zinc sulfide solution (at a ratio of 1:30,000) they could create a luminescent paint that glowed in the dark. This seemed to be a harmless product. Around the time of World War I, approximately 2,000 young women in New Jersey were employed painting the dials of clocks and watches with luminous paint. In order to create fine brush tips for this detailed work they would frequently lick the tip of the brushes. Over the years, these women either ingested radium itself or breathed in radon gas in sufficient quantities to cause serious medical problems for many of them. A New York dentist, Theodore Blum, DDS, was the first to observe an unusual number of jaw-bone injuries in these unfortunate dial painters, a condition he called 'radium jaw.'

The medical examiner of Essex County, NJ, at the time, Harrison Marland, MD, then became alarmed and launched a thorough investigation. He found severe anemia in most of these women. At autopsy, many of these women had necrosis of the bones, especially the mandible (lower jaw). Marland also recounted how the damaged bone marrow, excised osteosarcomas (cancers) of their bones, or even organs removed at autopsy literally glowed in the dark (Fajardo 2001: 366). These women were so radioactive that, even after death, their bodily organs would fog photographic film!

The most incredible part of this saga is that despite the fact that the danger of luminous paint was well established in the 1920s, it was not until nearly 20 years later - in the run-up to World War II - that action was finally taken to bar the use of radium in watch dial paint (Caufield 1989). It was a most shameful episode in public health, but it did make the general public aware that radiation could seriously damage bones and organs.

What is the Tolerance Dose?

Medical dictionaries define a 'tolerance dose' as the largest quantity of a substance or treatment that an organism can endure without exhibiting unfavorable or injurious effects. The tolerance dose of radiation to the bones has traditionally been set quite a bit higher than is implied by the recent Clemson article. There are many variables, but generally speaking when the dose is from 70 to 80 Gy the incidence of osteoradionecrosis (bone death caused by radiation) is in the range of 14-22 percent. It is 4 percent when the dose is under 70 Gy. The tolerance dose for the adult human femur (thigh bone) is said to be 38 to 43 Gy.

In the 1950s, Michael Bonfiglio, MD, of the University of Iowa, found a 1.2 to 1.9 percent increase in the incidence of fractures of the femur after pelvic irradiation for cancer (Fajardo 2001:373). Among patients who still have their teeth, the bone necrosis rate caused by radiation is 24 percent. Among those lacking teeth the rate is less - 14 percent. In studies involving patients who still had teeth, this bony necrosis developed on average 10 months after completion of radiation therapy. In those without teeth, it occurred on average 22 months later.

As noted above, if the bone is growing (as in the Clemson experiment) the tissues are ultra-sensitive to radiation. Clinical observations suggest a tolerance range of 15-30 Gy for growing bones.

In conclusion, exposing bone to radiation can result in four major types of complications: necrosis (a type of cell death), fractures, severe alterations in bone growth, and radiation-induced cancers. The topic of radiation-induced cancers in particular has not received the attention it deserves. Radiation itself is called a "complete carcinogen," in that it can cause the four phases of cancer's formation: (a) initiation, (b) promotion, (c) progression and (d) metastatic activity of transformed cells. While radiation-induced tumors of bone are not common, they do occur, as the case of the radium-dial painters dramatically showed.

Luis Fajardo, MD, who recently retired as a professor of pathology at Stanford University, California, has documented many such cases. "Irradiation from both external and internal sources is associated with an increased risk of osteosarcoma," or bone cancer, he wrote in his classic textbook, Radiation Pathology (Fajardo 2001:128). The minimum latency period for radium-caused tumors is 3.5 years with a peak time of about 8 years, although cases were documented as long as 25 years after initial exposure. Children who receive radiation for cancers (other than those of bony origin) are at particular risk if their growing bones receive large doses of radiation.

Although the danger of therapeutic radiation always seems to come as a surprise to the general public, most of the risks of radiation to the bone were recognized soon after Roentgen discovered X-rays. Yet, astonishingly, in the 21st century some patients receiving radiation are still not told about the full extent or true likelihood of the harmful side effects of radiation therapy.

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