

Biomedicine

Diane D. Edwards reports from Washington, D.C., at the 29th annual meeting of the American Society of Hematology

Upping cell counts: On clinical trial

"Too little, too late" can be the unhappy ending of a patient's medical history if he or she has too few white blood cells. Normally, growth factors made by the body stimulate the adequate production of white cells like granulocytes and macrophages. But white-cell production, which is part of the immune system's arsenal against infection, often drops after exposure to anticancer drugs or to infectious agents like the AIDS virus. Researchers say that injecting more of a particular growth factor might "artificially" boost cell numbers and fight infection. Granulocyte-macrophage colony stimulating factor (GM-CSF) and granulocyte colony stimulating factor (G-CSF) are two such factors currently being tested.

Biotechnology companies now can manufacture human GM-CSF and G-CSF in yeast or bacteria, and researchers have begun testing the usefulness of these two recombinant growth factors in various medical conditions, including AIDS (SN: 9/12/87, p.165). The factors might be used as, among other things, a supportive therapy for cancer patients undergoing chemotherapy or radiation. Current cancer treatments can suppress the bone marrow's production of needed cells, necessitating that physicians wait until cell numbers increase before beginning another cycle of treatment.

At the meeting, several groups reported on early clinical trials using one of the factors in cancer patients. At the Sloan-Kettering Cancer Center in New York City, 18 patients with a cancer called transitional-cell carcinoma were given G-CSF after a standard chemotherapy regimen that depletes cell numbers. Traditionally, 70 percent of patients receiving this chemotherapy have too few white cells to withstand the next cycle of chemotherapy, usually scheduled two weeks after the previous cycle, says Sloan-Kettering's Janice Gabrilove. All 18 patients treated with G-CSF, however, were able to receive chemotherapy on schedule, and their white blood cell counts at the end of the first therapy cycle increased three-fold over those not receiving G-CSF. Other preliminary clinical trials of GM-CSF suggest that it also may be useful in cancer patients.

Results of an unusual "clinical trial" involving GM-CSF agree with the promising findings of more formal studies, says Robert P. Gale of the University of California at Los Angeles. In September, two men in Goiania, Brazil, took a lump of cesium-137 from an abandoned radiation therapy facility. Intrigued by the radioactive material's blue glow, several people broke open the cesium and showed it to friends, some of whom ate part of the grainy material. By the time health officials realized what had happened, about 250 individuals had been exposed. Isolating the most seriously ill became "both a scientific and a political nightmare," says Gale, one of an international team of scientists who treated the patients. Because radiation can kill bone marrow, infection is a major concern following such an accident. Gale gave GM-CSF to eight patients; he reports that seven responded to GM-CSF with increased cell counts. Four of those patients later died, two from infections present before the GM-CSF treatments.

How much and when GM-CSF should be given after a radiation accident remains unclear, Gale says. He adds that it is also unclear how often a patient will need GM-CSF infusions.

Other studies of GM-CSF in custom-designed mice have also indicated that excessive stimulation of cell production could cause problems (SN: 12/12/87, p.375), and some researchers question whether overproduction could lead to leukemia. But data from the various human clinical studies indicate that toxicity is "uniformly mild," says Joseph H. Antin of Brigham and Women's Hospital in Boston. Thus far, he and other scientists have seen no evidence that using the factors could lead to leukemia. But, Antin says, "the range of patients likely to benefit from this therapy remains to be established."

Earth Sciences

Richard Monastersky reports from San Francisco at the fall meeting of the American Geophysical Union

Point of impact: Manson, Iowa?

Since 1980, scientists have debated whether a meteor is responsible for the extinctions of the dinosaurs and many other forms of life at the end of the Cretaceous period. But if such an apocalyptic impact did occur, where is the big hole in the ground?

According to some scientists at the U.S. Geological Survey (USGS), the answer is in Iowa. In the cornfields of the western part of the state, buried under 30 meters of glacial gravel, there is a 35-kilometer-wide crater called the Manson, Iowa Impact Structure. In 1985, scientists tested the rock in the crater and determined that the crater's maximum age is about 70 million years, putting the impact in the ballpark of the Cretaceous-Tertiary (K-T) boundary, which is 66 million years old. In the sedimentary record, this boundary is a thin layer of clay and mineral fragments, which some say was formed by a globe-circling cloud of dust that would have followed a large impact.

Using a refined dating technique, USGS researchers Michael Kunk and John Sutter of Reston, Va., and Glen Izett of Denver have now determined the Manson crater is 66 million years old. Within the resolution of this technique, the Manson impact was contemporaneous with the K-T boundary, says Kunk.

Did the Iowa impact produce that huge cloud blocking out the sunlight and extinguishing much of the life on earth? The Manson crater is too small to satisfy most planetary geologists who study craters; they estimate that the K-T impact would have produced a crater over 100 km wide. But Eugene Shoemaker of the USGS in Flagstaff, Ariz., resolves this by invoking a currently popular idea that at least two meteors hit earth at the end of the Cretaceous.

The Manson crater's revised birthday makes it an attractive possibility as a site of one of the impacts. "It's the best candidate I know of so far," says Kunk. Several researchers have formed a consortium to study the structure of the crater and the kinds of rocks created by the heat of that impact. By comparing them with the fragments found at the K-T boundary and by refining the date of that boundary, they hope to determine whether the crash in Iowa created at least some of the evidence found at the K-T boundary.

Stressed-out holograms

Stress isn't what makes the world go 'round, but it does make the world shake, at least during earthquakes. To study quake-producing stresses, which are simply the forces within the crust, geophysicists use a range of techniques that can determine the direction of these forces. Historically, however, it has been much more difficult to measure the *size* of the stress.

Now scientists are adding holograms to their bag of stress-measuring tricks—a promising technique that can resolve both the direction and size of crustal stress, says Catherine L. Smither, who is working with Thomas J. Ahrens at the California Institute of Technology in Pasadena and with Douglas R. Schmitt of Stanford University.

In a trial of this technique, Smither and her colleagues inserted a holographic camera into a borehole in the wall of a mine and took a reference picture of the area. Then, after drilling a small hole in the side of the wall, they used the same photographic plate to take a second picture of the area. Since the hole reduced the stress on the borehole wall, the wall moved a minute distance between the two pictures, creating an interference pattern on the hologram. By analyzing this pattern and repeating the technique on different sides of the borehole, Smither's group could measure the size of the stress in all three dimensions. They hope to reduce the size of the camera so that they can soon test the technique in other locations.



Smither