ducing alternatives to burning fossil fuels.

The Bellagio report recommends some immediate responses to the greenhouse threat, many of which can be justified solely on other grounds. At the top of the list is prompt approval and implementation of the Montreal Protocol on ozone. Chlorofluorocarbons both destroy stratospheric ozone and act as a greenhouse gas. The Protocol's provisions would lead to a 15% to 25% decrease in the rate of warming.

Long-term energy policies should be reexamined, the report says. Increased efficiency in the consumption of energy would reduce carbon dioxide emissions. So would a shift toward alternative energy sources such as solar energy and nuclear power. Emissions per unit of energy would decrease with a shift away from coal, a high carbon dioxide–emitting fuel, toward natural gas.

Deforestation has numerous drawbacks, the release of carbon dioxide being one that should now be considered. Reforestation would remove carbon dioxide from the atmosphere, among other benefits.

The report also advocates immediate steps to improve understanding of the greenhouse effect and clarify the options for dealing with it, including consideration of a law of the atmosphere, like the Law of the Sea, or a convention such as the one for ozone. The likely effects of the greenhouse are so large that "a coordinated international response seems inevitable and rapid movement towards it is urged," the report concludes.

Momentum in that direction seems to be building. The biggest push has come from a surprise in the stratosphere, the Antarctic ozone hole. No computer model of ozone destruction included the voracious chemical reactions mediated by ice particles that are wiping out half the ozone over Antarctica each spring. Scientists even had trouble noticing that anything was amiss. The hole has everyone wondering whether greenhouse models might be missing a surprise as well.

The ozone hole is among the reasons that major environmental groups such as the Environmental Defense Fund and the World Resources Institute are starting to put time and money into the problem. But environmentalists will still have their hands full raising the public's consciousness. A recent poll found that two-thirds of Americans believe that the greenhouse effect presents a somewhat to very serious danger. But that placed it thirteenth out of 16 problems, beating out only x-rays, indoor radon, and radiation from microwave ovens. What would be handy is a crisis. No one is willing to call the current drought a greenhouse effect, but it could still become the ozone hole of the movement to control the greenhouse. ■ RICHARD A. KERR

Blood-Forming Stem Cells Purified

Having a pure population of bone marrow stem cells opens the door to treatments for blood diseases and basic research advances

ONE OF THE MAJOR OBSTACLES to understanding how different types of blood cells are formed has been not knowing what cells produced them. Now researchers have found a way to isolate the bone marrow stem cells in mice that give rise to all blood cell types. On page 58, Irving Weissman and Shelly Heimfeld of Stanford University School of Medicine in California and Gerald Spangrude, presently of the Royal Melbourne Hospital in Victoria, Australia, report that as few as thirty of these stem cells can restore blood cell production in a mouse subjected to a lethal dose of radiation.

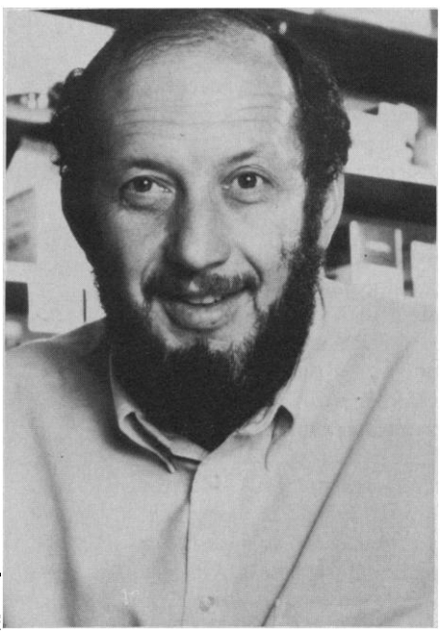
The new findings represent a culmination of ideas and efforts by many investigators to identify which cells in the bone marrow ultimately form the eight or nine different lineages of cells in circulating blood. "This is the end of the particular road that was the search for the stem cell," says Weissman. The information should lead to better treatments for blood disorders as well as advancing basic research on blood-forming tissues.

For example, if a similar cell can be identified in humans, researchers may be able to transplant stem cells instead of whole bone marrow into people who receive large doses of radiation. Also, it may be possible to maintain the stem cells in vitro, transfer genes into the cells, and then reinject the altered cells into a person who has a specific genetic or acquired blood cell defect such as sickle cell anemia, thalassemia, severe combined immune deficiency, or leukemia.

Weissman and his colleagues had to separate the stem cells from many other populations of cells in the bone marrow. "It was like searching for a needle in a haystack," says Heimfeld. "These stem cells are incredibly rare [about 0.05% of total bone marrow cells] and they have no other distinguishing characteristics."

To obtain the stem cells, the researchers used monoclonal antibodies against surface proteins. First they selected out bone marrow cells that were already differentiated or committed to become a certain kind of blood cell—T or B lymphocytes, macrophages, or granulocytes, for example. They then enriched the remaining cells for blood-forming or hematopoietic stem cells, which are not yet differentiated and which can regenerate themselves throughout the animal's lifetime.

They also tracked the fate of the stem cells in mice given a dose of radiation that, under usual experimental conditions, would be lethal. After intravenous injection, the cells divided, differentiated, and migrated to different blood-forming tissues, including the spleen and thymus gland. In the spleen one cell could form an entire colony of precursors for red blood cells, macrophages, and granulocytes. Thirty stem cells could rescue 50% of lethally irradiated mice, and 6 weeks after receiving the cells, about half of the circulating blood cells were from the donated stem cells.



Ron May

Irving Weissman. *"This is the end of the road that was the search for the stem cell."*

Jan Klein and Yukoh Aihara of the Max Planck Institute in Tübingen, West Germany, generated the monoclonal antibody that ultimately allowed the Stanford group to isolate a population of pure stem cells. "They were trying to find T cell precursors in the bone marrow and they gave us a whole set of antibodies," says Weissman. The German group's Sca-1$^+$ antibody

marked a subpopulation of stem cells that Weissman, Christa Muller-Sieburg, and Cheryl Whitlock, also of Stanford, had partially purified in 1986, yielding what Weissman now thinks is a pure population of cells.

Other groups of investigators have used different methods to isolate mouse stem cells including separation techniques based on differences in cell density and labeling type I major histocompatibility antigens. These proteins are important in immune system recognition and are found on stem cells. As yet, these approaches have not yielded a pure population of stem cells, says Heimfeld.

In March, Irwin Berstein, Robert Andrews, and Ronald Berenson of the Fred Hutchinson Cancer Research Center in Seattle, Washington, and their colleagues reported progress in isolating human stem cells. They found that a protein on the surface of 1% to 4% of bone marrow cells appears to be a marker for a stem cell population in both humans and baboons. "This CD34 antigen is expressed by cells that will establish hematopoeisis [blood cell formation] in vivo," says Bernstein. When the researchers inject 15 to 19 million of bone marrow cells enriched for $CD34^+$ cells into lethally irradiated baboons, the animals regain their ability to form all blood cell types.

A major difference between this experiment in primates and those done by the Stanford group in mice is that the human stem cells are clearly not a homogeneous population. As part of a new collaboration, the Stanford and Seattle researchers hope to purify the human stem cells. Then they may be able to test whether the cells can generate all the different blood cell types in an experimental mouse just developed by Weissman's group.

The new information should answer some basic questions about the development and differentiation of hematopoietic cells. For instance, a running debate has been whether bone marrow stem cells are already programmed to become a certain kind of cell—a T lymphocyte for example—or whether the biological environment dictates the cell's final differentiated state.

Weissman's data support the latter hypothesis. The stem cells are obviously capable of producing all lineages of blood cells when injected intravenously, a procedure that exposes them to many different biological environments in the body. But if they are injected directly into the thymus gland, they differentiate only into T lymphocytes. This result implies that something about the microenvironment of the thymus gland directs their differentiation into T cells.

■ DEBORAH M. BARNES

Near-Field Microscopes Beat the Wavelength Limit

Normal optical microscopes are limited to resolutions no better than the wavelength of visible light, but a new technique gives a tenfold improvement in detail and should open new vistas to viewing with visible light

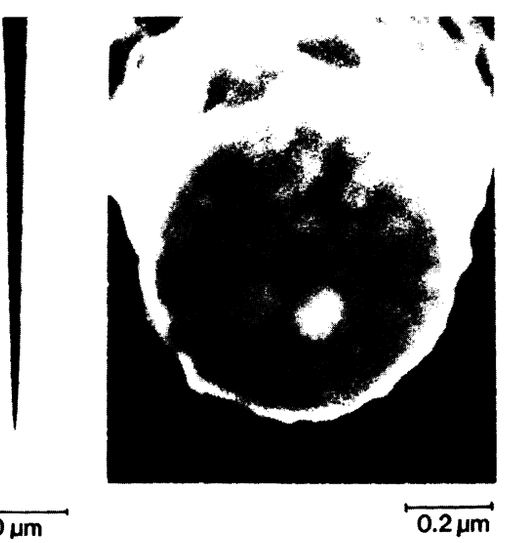
THE QUEST TO BUILD microscopes that see the world in smaller and smaller detail eventually runs into a Catch-22. Better resolution requires using probe particles of increasingly smaller wavelengths, which means increasingly higher energies, but higher energy particles damage the object under view and often require special preparation of the sample.

X-ray microscopes, for example, give up to 50 times better resolution than visible light microscopes, but their ionizing x-ray radiation harms a sample considerably. Electron microscopes are yet another 25 times more powerful than x-ray microscopes, but they work only on samples put in vacuum and they too damage the sample. Scientists would like a microscope as benign to samples as a light microscope but with as much resolving power as an x-ray microscope.

Enter the near-field scanning optical microscope. Cornell University physicist Michael Isaacson says this new microscope, which he developed with Aaron Lewis, now at Hebrew University in Jerusalem, can make out details as small as one-tenth the wavelength of visible light. Eventually its resolution might be pushed to one-fiftieth of a wavelength, Isaacson says, which would put it on a par with current x-ray microscopes.

The laws of physics make such resolution impossible with normal lens-based light microscopes. No matter how carefully such a microscope is designed or built, the diffraction of light restricts its resolution to no better than the wavelength of the light used by the microscope. (Visible light has wavelengths between about 400 and 700 nanometers, or 400 to 700 billionths of a meter.) By using x-rays, which have much shorter wavelengths, microscopists have achieved resolutions as good as 10 to 20 nanometers, and electron microscopes can make out details as small as 0.2 nanometer. (With electron microscopes, the limiting factor is the focusing ability of the electromagnetic lenses and not the wavelength of the electrons, which can be made very small by increasing the energy.)

Isaacson has developed a lensless light microscope that sidesteps this wavelength resolution limit. The basic idea is to use a tiny probe and bring it right up next to the sample, so that the probe is seeing only a very small part (less than a wavelength across) of the sample at any given time. Then by scanning the probe over the sample, the microscope can piece together an entire image.



The tip of the probe. *Electron micrographs show the profile of a pipette (left) and its tip, which has a 100-nanometer-diameter hole.*

The most obvious way to do this is to illuminate only a small part of the sample at a time. By putting a subwavelength hole in a mask, say, and shining a light through the hole, one gets a spot of light less than a wavelength across. Shining this light through the sample one point at a time eventually images the whole sample.

The key to this technique is keeping the sample within the so-called "near field" of