A Stimulant for Red Cell Formation

Caltech biologists work on a substance which may eventually be useful in treating radiation injuries and anemias.

Caltech biologists are working on the isolation of a substance called erythropoietin, which stimulates the bone marrow to produce more red blood cells. This substance, a protein, may eventually be useful in treating certain anemias and radiation injuries. Samples of erythropoietin, obtained from the blood of anemic rabbits, have been sent to laboratories in various parts of the nation and Europe, where further research on the isolation and purification of the protein will be made.

Henry Borsook, professor of biochemistry at Caltech, is credited with being the first to learn how to prepare erythropoietin so that it could be injected into other animals. The injection causes a marked increase in red cell production in normal as well as in starving or anemic animals. Red blood cells transport oxygen from the lungs to body tissue and carry away carbon dioxide wastes. Anemia and radiation injuries reduce the red blood count necessary for health.

Erythropoietin has not yet been used on humans. Though all existing forms of purification have been tried, the substance has not been refined enough to try it on people. For another thing, it is not known whether there would be harmful immunological side effects. And finally, there is the problem of a supply source. The only practical way in sight at present to obtain the large amounts required for clinical use would be as a by-product, perhaps from large slaughter-house animals. No assay method has, as yet, been reliable or sensitive enough to detect erythropoietin in normal, healthy, large animals, If biologists could be sure that there is a detectable amount in unconcentrated normal blood, then it would be practical to extract and concentrate the substance from such blood.

Caltech scientists point out that perhaps the difficulty of finding evidence of the protein in the blood or urine of healthy humans and animals may mean that it is an emergency product synthesized only when the body needs more oxygen than it is getting – as in the case of anemias or sudden changes to high altitude. In a research done by Joseph Scaro at the Institute of Altitude Biology at San Salvador de Jujuy, erythropoietin was detected for several days in the urine of Argentine soldiers after they had been taken from sea level to 15,000 feet altitude in the Andes Mountains. However, most scientists believe that it does exist in healthy bodies, but in such minute quantities that its detection by present methods is uncertain.

Erythropoietin works by persuading embryonic blood cells in the bone marrow to become red blood cells faster. Subcutaneous injections of it cause an observable increase in the reddening of the bone marrow, where blood cells are born.

Erythropoietin is easy to keep; dehydrated material remains active for several months or longer at room temperature and it will remain active in frozen plasma for over a year.

If erythropoietin can be purified sufficiently, the indications are that it can be used on humans. For instance, it is known that the protein from humans works on rats, mice and monkeys; and that material from dogs works on rats; and rabbit erythropoietin works on rats, mice and monkeys. For some strange reason, the only case where the substance from other animals doesn't work is in guinea pigs.

Although the present research is a large step toward a practical use of this precious substance, many questions remain to be answered. Caltech biologists will try to discover how to isolate the protein in a more pure form; how to detect small quantities of it to find out if there is more than one type; and to study its physiology.

Working with Dr. Borsook on the project are Drs. Geoffrey L. Keighley, senior research fellow in biology; Peter Lowy, research fellow in biology; and George Hodgson, MD, visiting National Academy of Sciences research fellow from the University of Chile in Santiago. The project is wholly supported by the American Cancer Society.