

# Space Life Sciences Research Highlights

## Space Flight Experiments Lead to Discovery of Previously Unknown Process that Causes Destruction of Red Blood Cells

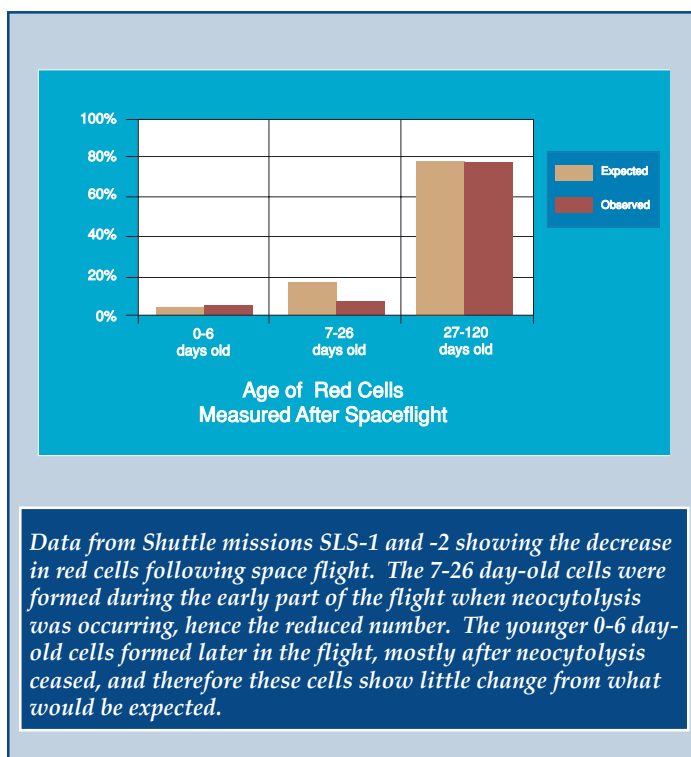
*Clarence Alfrey has found the explanation for why there are fewer red blood cells in individuals who travel in space. In doing this, he discovered a previously unknown phenomenon called “neocytolysis,” which is the destruction of young red blood cells under certain conditions. This discovery not only explains why there are fewer red blood cells in space, it also has clinical implications in the treatment of the anemia that accompanies renal disease.*

One of the more puzzling observations in astronauts returning from space is a decrease in the quantity of red blood cells circulating in the blood stream. This anemia invariably occurs, even after flights of only a few days.

Clarence Alfrey of the Methodist Hospital, Baylor College of Medicine, and his colleagues finally found the explanation. They carefully characterized red blood cells in experiments performed on the Spacelab Life Sciences-1 and -2 missions in 1991 and 1993. The analysis showed that the decrease is due to the *destruction* of red blood cells that were either newly released into the blood or that would be released soon from bone marrow. The number of red blood cells declined too rapidly to be explained by a change in the *production* of new red cells, and older cells were not affected.

Dr. Alfrey believes that the cause of the destruction of the newly formed cells starts with the decrease in blood plasma volume that occurs in microgravity. Without gravity, there is less pooling of blood in peripheral blood vessels and less dilation of fine blood vessels such as capillaries, resulting in a central pooling of blood plasma in the body. Because of this plasma volume decrease, the mass of existing red blood cells in the blood is suddenly inappropriately elevated for the new environment. The level of erythropoietin (a hormone that controls red blood cell production) decreases.

The mass of red blood cells then decreases—via the destruction of recently formed cells—as the body adapts from a condition of excess red blood cells to a level more appropriate for the microgravity environment. The sequence of events reverses itself upon return to Earth when the quantity of red blood cells returns to normal.



What is significant about this new finding is that, prior to this research, it had generally been thought that red blood cells were controlled by erythropoietin regulation of the production of red cells. A physiological mechanism that could hasten the removal of circulating red cells wasn't known.

Destruction of the youngest circulating cells—when there is an “excess” of red cells in the blood—was the only plausible explanation for the space flight results. Alfrey called this process neocytolysis, meaning destruction (*lysis*) of the youngest (*neo*) cells (*cytes*).



*Dr. Alfrey and co-workers measuring the red cell mass of an altitude study volunteer from Cerro de Pasco, Peru. Dr. Wilson Ruiz is on the left, Ms. Theda Driscoll is in the center, and Dr. Alfrey is on the right.*

Additional support for this idea came from studies of individuals who had become acclimatized to high altitude, in Peru. When these people descend to a lower altitude, they experience a rapid decrease in red blood cells, similar to the decrease observed in astronauts during space flight. High altitude individuals moving to lower altitude also exhibit a rapid and large suppression of erythropoietin. When erythropoietin falls below a certain minimum level, this triggers neocytolysis. Dr. Alfrey found that low doses of erythropoietin given subcutaneously to high altitude-acclimatized individuals who moved to lower altitude prevented the decrease in red blood cells.

These changes in high altitude individuals demonstrate, as did the space flight experiments, an adaptive reaction of the body. What we now know about neocytolysis is that it begins in less than 24 hours, is limited to a 10-15% reduction in red blood cells, and is completed within 7-10 days. It appears to be initiated when erythropoietin levels are depressed below a threshold level. If further adaptation by the body is necessary, changes proceed more slowly through alteration in red blood cell production.

Dr. Alfrey is now investigating whether neocytolysis is present in individuals with impaired kidney function. Patients on dialysis typically have low erythropoietin levels, and they have an accompanying anemia that is ameliorated by erythropoietin therapy.

In a recent experiment, Dr. Alfrey withheld erythropoietin therapy from dialysis patients who had low

erythropoietin levels. An analysis of survival patterns of red blood cells strongly indicated that neocytolysis was occurring. He concluded that neocytolysis contributes to the anemia that accompanies renal disease.

A prediction of neocytolysis is that the manner in which erythropoietin is administered to renal disease patients—intermittent doses administered intravenously—would result in peaks and nadirs of effective erythropoietin in the body. The low levels of erythropoietin occurring at the nadirs would bring about neocytolysis. Other researchers have shown that erythropoietin given at lower levels but administered daily and subcutaneously is more effective than the higher but more transient peaks associated with intravenous injection—avoidance of the nadirs that precipitate neocytolysis explains this nicely, adding a rational basis to changing the way erythropoietin is given. “Changing will save money,” Dr. Alfrey points out.

“Knowledge of the changes in blood in space flight has increased our understanding of adapting to high altitude and the anemia related to renal disease,” according to Alfrey. Further research is needed to understand exactly how neocytolysis works and to determine the optimal levels of erythropoietin administration to renal disease patients. It would also be of great interest to learn whether neocytolysis plays a role in any other heretofore unexplained anemia, such as the anemia commonly observed in acute infections.

The title of a commentary accompanying one of Dr. Alfrey’s recent scientific publications summarized his research this way: “Neocytolysis: From Outer Space to the Dialysis Unit.” As the title suggests, this series of studies shows the progression of scientific discovery from one avenue of scientific research to another. It is a textbook demonstration of how using the unique environment of space as a laboratory can not only further our understanding of fundamental scientific processes, it also illustrates how this research can benefit life on Earth.

#### References

1. Rice L; Alfrey CP; Driscoll T; Whitley CE; Hachey DL; Suki W. Neocytolysis contributes to the anemia of renal disease. *Am J Kidney Dis* 33(1):59-62, 1999.
2. Means RT Jr. Neocytolysis: from outer space to the dialysis unit. *Am J Kidney Dis* 33(1):140-1, 1999.
3. Alfrey CP; Rice L; Udden MM; Driscoll TB. Neocytolysis: physiological down-regulator of red-cell mass. *Lancet* 349(9062):1389-90, 1997.