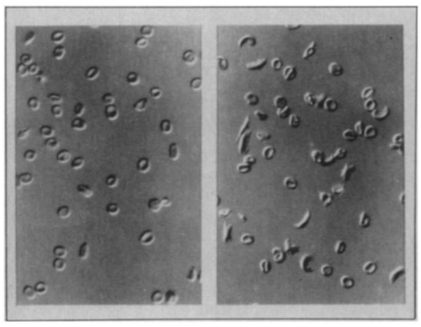
Making Blood Share More of Its Oxygen

Chemical modification of hemoglobin – the oxygen carrier in blood – shows promise for treating a range of conditions, including heart attacks and stroke, that can be caused by the reduced flow of blood to tissues. Two experimental approaches were reported last week in New York City at the spring national meeting of the American Chemical Society.

"There's a site on the hemoglobin molecule that can either weaken or tighten the bond with oxygen," explains Murray Weiner, acting director of clinical pharmacology at the University of Cincinnati Medical Center. Normally, the body fills that crucial site with a substance called 2,3-diphosphoglycerate (DPG). Weiner and Robert S. Franco have found a way to instead bind onto hemoglobin a natural analog of DPG – phytic acid – that keeps the oxygen more loosely bound than does DPG.



Weiner

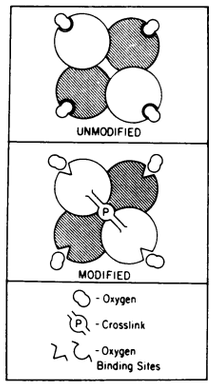
Two samples of sickle cell blood that gave up the same oxygen. Where oxygen preferentially came off modified hemoglobin (left), no sickling occurred.

The analog permits delivery of roughly twice as much oxygen per unit of blood to tissues, Weiner says, and with less work by the heart. That could prove especially useful in the treatment of ischemic disease – conditions caused by reduced or obstructed blood flow – because normal hemoglobin often cannot provide sufficient oxygen to prevent the death of affected tissues.

To incorporate phytic acid into red blood cells, the researchers bathe the cells in dimethylsulfoxide (DMSO), a small molecule that rushes into cells. Once the DMSO is inside, they rapidly dilute the bath, causing the cells to swell. The new bath also contains the phytic acid, a compound that can pass through the blood cell's membrane only when the cell is swollen. But as phytic acid enters the cells, the DMSO begins to leave. With DMSO's departure, the cells shrink back, trapping the phytic acid inside.

Weiner envisions that this process, in addition to modifying the blood of patients with ischemic disease, could help transfusion patients with sickle cell disease, because their painful sickling occurs only when affected blood cells give up their oxygen. Since the modified hemoglobin gives up its oxygen more readily than a sickle cell's does, he believes its presence could reduce the oxygen demand on cells with sickle cell hemoglobin. Weiner says he will soon begin human trials to establish the life span of blood cells with this modified hemoglobin.

In a second approach to the problem, at Columbia University's College of Physicians and Surgeons in New York City, Reinhold and Ruth Benesch, a husband-wife team of chemists, are incorporating an analog of vitamin B_6 into hemoglobin stripped from red blood cells. The compound, which permanently links one of the hemoglobin molecule's two pairs of subunits, works "akin to a built-in super DPG – one that is roughly 10 times more effective than DPG is at making oxygen available," according to Reinhold Benesch. Moreover, it keeps the hemoglobin from splitting in half and subsequently exiting through the kidneys – the normal fate of hemoglobin outside of blood cells.



John Mack

Outside red blood cells, hemoglobin quickly splits into two halves, each with an "alpha" (shaded) and "beta" portion. Forming a covalent bond across the two betas permanently locks the halves together and keeps oxygen from binding too tightly.

The Benesches envision their modified, out-of-blood-cell hemoglobin, which has already been tested on rats and rabbits, as a potential oxygen carrier that could be added to blood of trauma patients or persons with ischemic emergencies. And because, unlike other hemoglobins, it can still unload oxygen at low temperatures, they believe it could be used to oxygenate organ transplants during shipment or hearts during surgery. *– J. Raloff*

Launch problems spread to DOD

Even before the Jan. 28 explosion of the space shuttle Challenger, the Department of Defense (DOD) had been well along in planning a return to increased use of one-shot, "expendable" rockets for some of its launchings. Besides the limited size of the shuttle fleet, the craft's complexity raised concerns about its reliability among military planners, who cited a need to keep tried-and-true expendables around.

On April 18, however, DOD found itself in a launch-vehicle turmoil of its own, when one of its most reliable rockets – a Titan 34D, which is also the most powerful workhorse in the U.S. military stable – blew up only seconds after lifting off from Vandenberg Air Force Base in California. To make matters worse, this was the second failure of an Air Force Titan 34D. The other occurred last Aug. 28.

Both payloads were classified, but various nongovernment specialists speculated that in both cases it was a KH-11 reconnaissance satellite, a half-billion-dollar spy-in-the-sky of a type used to take high-resolution photos of the Soviet Union and other areas. Only one KH-11 is now believed to be operating in orbit, with but a single replacement in reserve on the ground.

The Air Force has launched 136 rockets (plus five earlier test flights) in the various versions that make up its Titan 3 series. Of these, nine have been 34Ds, most powerful of their kind. There have been only six failures among the 136, but they include the last two 34Ds. There are just six more 34Ds in stock, and the still more powerful version yet to come, called the 34D7, is not due to go into use until 1988.

All six 34Ds have payloads tentatively assigned to them, as do the ten 34D7s being built. But now the Air Force is confronted with uncertainties not only in the space shuttle but in its own expendables as well. "Priorities," says an Air Force spokesperson at Vandenberg, "could change." NASA, for example, has been attempting to work out a possible launch schedule for when the shuttle finally begins flying again, and several of the payloads were already going to be military. But if the 34D is also going to be delayed for a significant period (an investigation of last week's explosion is under way), NASA's post-Challenger planning efforts could well be overturned again.

Meanwhile, NASA's first post-Challenger launching is tentatively set for May 1. Its payload, the NOAA-G weather satellite, will be lofted by an expendable Scout rocket. *– J. Eberhart*