

## Framework protein for blood cell flex

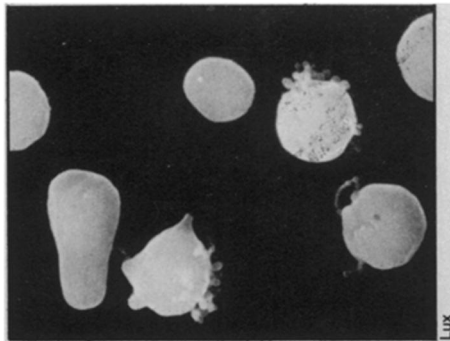
Flexibility and durability are requirements for red blood cells. Continually accepting and delivering their oxygen loads, they travel 300 miles through circulatory system conduits during a typical lifespan of 120 days. Each time around they must squeeze their 7-micron widths through spleen passages as small as 3 microns.

A scaffolding made up of many proteins gives the red blood cells their shape and pliancy. Now scientists have identified components of that skeleton and have hypothesized how they fit together. They find that some human hereditary blood diseases involve abnormalities of a framework component. A series of mutations in mice has aided analysis of these anemias down to the molecular level.

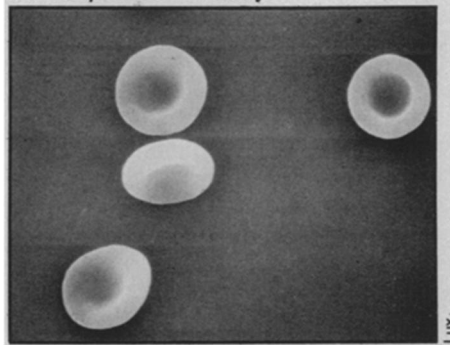
Samuel Lux of Children's Hospital in Boston described four types of mutant mice with red blood cell disorders. He was speaking at the 50th Anniversary Symposium of the Jackson Laboratory in Bar Harbor, Maine. Mice with the most serious condition, called "jaundice," seldom survive to weaning. In all four conditions the red blood cells are deformed from the normal shape (disks with pressed-in centers) to spheres with budding and fragmenting membranes. "You see rosaries of membrane vesicles and budding into the membrane," Lux says. The more membrane a cell sheds, the rounder it becomes. In the most severe mouse anemia, there is little budding; most of the cells observed are already spherical.

Lux finds that membranes of the spherical cells are less stable than normal. Closer analysis reveals that all the abnormal mice are deficient in one protein, called spectrin, intrinsic to the membrane skeleton. The severity of the spectrin deficiency parallels the severity of the mouse's disease. Jaundice anemia mice have no detectable spectrin, while those with the mildest disease, normoblastic anemia, have half of the normal amount.

Two populations of abnormal red blood cells were detected among the mice with spherocytic anemia, a condition of intermediate severity. Bryan Smith and Paul Lacelle examined the mechanical properties of those cells. One group of cells are



Budding and fragmenting spherical red blood cells (above) appear in mouse genetic anemias. Normal cells (below) are disk-shaped for flexibility.

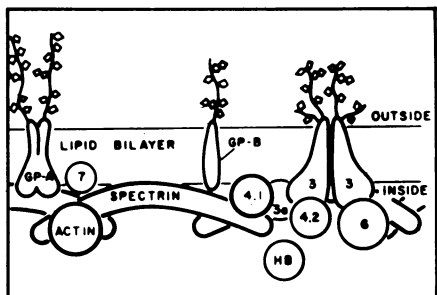


easily deformed. "Their membranes pull out into long nipples that can't snap back into place when the stress is removed," Lux says. Cells of the other set are rigid. They burst without first deforming.

These findings led the researchers to suspect there is something wrong with skeletal proteins in several human hereditary blood diseases. In the many types of elliptocytosis, the red blood cell membrane skeleton, as well as the cell, is elliptically shaped. Lux and collaborators examined red blood cells and found that in half the families with hereditary elliptocytosis, spectrin was less stable than normal. This finding indicates that there are two distinct types of the disorder.

In another human disease, hemolipic anemia, fragmentation and budding of red blood cells (similar to the mouse disorders) also seem to correlate with defective spectrin. Lux finds in this case that the spectrin denatures more easily than normal and contains fewer than normal phosphate groups. Finally, in the disease hereditary spherocytosis, pieces of membrane fragment, leaving the cell a rigid sphere. The abnormal red blood cells linger in narrow constrictions of the spleen, where macrophages destroy the trapped cells. The therapeutic treatment for many patients is to remove the spleen. Although the cells circulating in the blood become spherical, they still carry enough oxygen for the patients to survive.

Spectrin's presence in red blood cells seems long established, spanning mammals, reptiles and birds. Even in the most primitive worm to have red blood cells, the cells contain a spectrin-like component, Lux says. □



Spectrin is an essential component of the structure underlying cell shape.

## World population decline documented

Last year Harvard University's Center for Population Studies reported that the world's population growth rate has begun to decline (SN: 2/25/78, p. 116). Now, similar findings are reported by the World Fertility Survey in the July POPULATION REPORTS: Population growth is declining at a dramatic rate in many developing countries.

The World Fertility Survey, an international research program funded by the United Nations and the U.S. Agency for International Development, is designed to assist countries, particularly in the developing world, in carrying out scientifically designed surveys of human reproductive behavior. Since the project got underway in 1974, it has been gathering information on birth rates, marriage trends and birth control practices in 15 developing countries.

The survey has found decreasing birth rates in 14 out of the 15 developing countries studied by comparing the average size of families among married women ages 45 to 49 with the average size of completed families expected for all women now of reproductive age. In Costa Rica, for example, women aged 45 to 49 have had an average of 7.2 live births during their lives, but younger women are now expected to average only 3.8 births by the time they reach the same age. In Sri Lanka, women aged 45 to 49 had an average of 6.0 live births, but women of reproductive age are now expected to have only 3.4 births by the time they reach their late 40s, an equally sharp decline. Somewhat less dramatic drops can also be seen in South Korea, Fiji, Indonesia, Panama, Colombia, Malaysia and Thailand. Birth rates in Peru and the Dominican Republic are somewhat lower. There is even a modest reduction in three extremely populated developing countries — Bangladesh, Pakistan and Mexico — from 7.1 births to 6.3 or 6.1 births. The only country surveyed that is not experiencing a decline in birth rates is Nepal.

Why should birth rates be falling in 14 of the 15 developing countries? There are several factors, the survey reveals. For one, women in the 14 countries are marrying later than they used to. (However, while a delay in marriage can and usually does produce a decline in birth rate, the overall impact on reproduction of increased age at marriage is less than might be expected.) For another, women in the 14 countries are more interested than women of previous generations were in limiting the size of their families. In fact, a two-child family is even becoming the ideal for many of these women. In Bangladesh, South Korea, Sri Lanka, Thailand, Colombia and Peru, half or more of women with two children state that they don't