Framework protein for blood cell flex

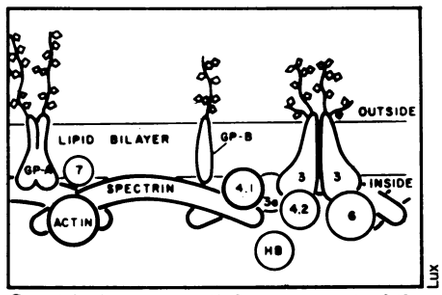
Flexibility and durability are requirements for red blood cells. Continually accepting and delivering their oxygen loads, they travel 300 miles through circulatory system conduits during a typical lifespan of 120 days. Each time around they must squeeze their 7-micron widths through spleen passages as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

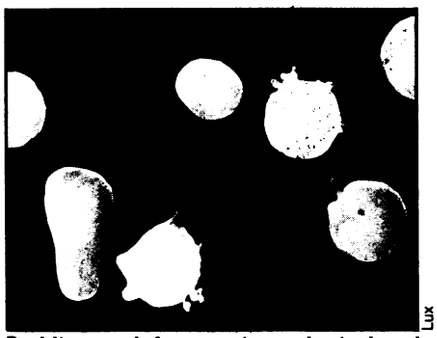
Lux finds that membranes of the spherical cells are less stable than normal. Closer analysis reveals that all the abnormal mice are deficient in one protein, called spectrin, intrinsic to the membrane skeleton. The severity of the spectrin deficiency parallels the severity of the mouse's disease. Jaundice 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

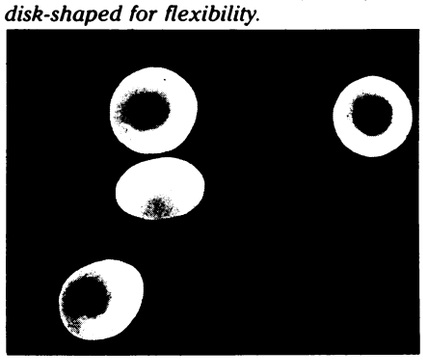


Lux

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


Lux

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


Lux

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. □

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

want any more. A third reason that birth rates are falling in the 14 countries is that more and more women of reproductive age are using modern methods of birth control — especially the pill, male or female sterilization or an intrauterine device. In fact, the current drop in birth rates appears to tally closely with how many women of reproductive age are using contraceptives. For instance, Costa Rica is enjoying an impressive reproduction curtailment, and 78 percent of Costa Rican women of reproductive age are currently using contraception, whereas in Pakistan or Bangladesh, which are experiencing only minor birth rate drops, only 10 percent or fewer of fecund women are using birth control. Nepal's continuing high birth rate can be attributed largely to Nepal's limited family planning programs, particularly in remote areas of the country. Only 22 percent of Nepalese women of reproductive age have ever heard of contraception, and only 10 percent of them are currently using it. □

Atomic clock keeps super-cool time

Keeping time has been one of man's obsessions since the dawn of civilization. At first, it was done by a wedge-shaped imprint on a clay tablet to keep track of the lunar cycles or a slab of stone stuck in the ground to mark the arrival of the solar equinox. As science progressed, so did its methods of timekeeping — from sun dials and water clocks, to pendulums and balance wheels.

During the last three decades, timekeeping has been dominated by atomic clocks, instruments that provide a frequency standard by measuring the oscillations of atoms or molecules. These devices brought time into the realm of the ultra-precise. Millions of years might pass before such clocks would lose one second. But researchers at the Harvard-Smithsonian Center for Astrophysics are trying to improve on that precision.

The accuracy of present-day atomic clocks is limited by the thermal noises inherent at room temperatures. Those noises can be reduced by entering the world of the super-cold, where temperatures approach absolute zero (−273.16°C). There is one problem, however, in doing this. Atomic clocks, like hydrogen maser clocks, may stop oscillating when they are cooled. Robert F. C. Vessot, Edward M. Mattison and Eric L. Blomberg recently overcame this obstacle by coating the super-cooled maser cavity with carbon tetrafluoride. With the CF_4 frozen on the interior surfaces of the cavity, the oscillating hydrogen atoms could be reflected off the walls without becoming perturbed, thus preserving the phase of the oscillations. By doing this, the three researchers were able to keep a hydrogen maser clock working at temperatures as cold as 25° Kelvin (−248.16°C).

"The clock was going like gangbusters," says Vessot. "It finally quit oscillating at 25°K, but we believe that was due to our running out of helium in the cryostat [apparatus for maintaining the low temperature]." The researchers cannot measure the accuracy of their super-cooled clock until they have a second clock with which to compare. They are now in the process of doing that. But calculations show that a hydrogen maser clock cooled to 25°K would have to run 300 million years before it would lose one second of time. This is six times better than the hydrogen masers currently in use. "We're now aiming to get it down to 4°K where the accuracy would be even better," Vessot told SCIENCE NEWS.

The Center for Astrophysics has been developing such maser clocks for long-baseline interferometry and satellite-tracking systems. Three years ago Vessot, in collaboration with NASA, launched one such clock into space to see how its frequency changed as gravity changed, an outcome predicted by Einstein's theory of general relativity. It was the first atomic clock sent into space for a relativity test.

One application of a cryogenic maser lies in the field of experimental gravitation. Such a super-cool clock could be put on a space probe to help in the search for gravity waves and provide clues toward understanding the sun's mass distribution and angular momentum. □

NOAA-6 satellite aloft

The TIROS-N satellite launched last Oct. 13 for the National Oceanic and Atmospheric Administration has been more than just another conventional weather-watcher. Besides providing twice-daily scannings of the land, sea and air, it monitors solar radiation above the atmosphere (which can affect events ranging from long-distance communications to the descent of Skylab) and relays data from numerous other sensors such as balloons and buoys. And now TIROS-N has a twin.

Called NOAA-6, the newcomer was launched on June 27, underwent a check-out period and was declared operational on July 16. The two satellites provide data for use in predictions by the National Weather Service, timed so that TIROS-N's information aids in preparing afternoon forecasts, while that from NOAA-6 is assigned to the morning line. The devices are the first two in a planned series of eight satellites in the program, with the next launching scheduled for 1980. NOAA hopes to keep two such satellites in orbit at all times through 1985. Besides their daily tasks related to periodic forecasting, TIROS-N and NOAA-6 also have research roles in the ongoing Global Weather Experiment of the Global Atmospheric Research Project (GARP). □