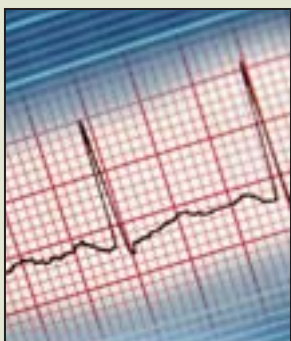


In a Heartbeat

Low-birthweight babies get a difficult start in life, usually spending their first months in a hospital neonatal intensive care unit (NICU). One-quarter of these very tiny infants (those under 3 pounds) develop sepsis within a few days of birth. Sepsis is a bacterial infection that spreads through their blood, leading to organ failure and sometimes death. Currently, diagnostic tests for sepsis in



these newborns are imperfect, and often the problem is detected too late. If doctors could better monitor the onset of sepsis, many lives could be saved.

NIGMS grantee **Randall Moorman** of the University of Virginia Health System in Charlottesville is testing the idea that heart rate irregularities may signal the

onset of sepsis in these high-risk babies. Along with UVA neonatologist Pam Griffin, Moorman studied two groups of approximately 300 infants who had been admitted to NICUs at two different hospitals for a period of at least 1 week. At the first NICU, the researchers continuously monitored the infants' heart rates while watching for symptoms of sepsis. By correlating these two types of information, the scientists were able to develop a mathematical model of sepsis risk based on abnormal heart rate characteristics.

When the scientists applied their model to similar measurements gathered from babies at the second NICU, they accurately identified which infants were at highest risk for sepsis. The new approach could enable doctors to easily and more accurately predict the onset of sepsis through noninvasive heart rate monitoring.

Natural De-Icer

Sometimes, medical clues come from unexpected places. For example, scientists who are interested in preserving cells and organs for transplantation are learning from fish that can swim in icy polar waters. To survive the frigid conditions, these animals produce a natural antifreeze that keeps their organs supple and functioning rather than frozen solid. If scientists could design similar molecules to preserve the function of chilled human organs, it would be a boon to organ transplantation.

Natural antifreeze works by lowering the freezing point of biological fluids, so that ice crystals will not form until the

surrounding temperature dips to sub-zero levels. Years ago, researchers such as Robert Feeney of the University of California, Davis, became fascinated with the antifreeze molecules present in Antarctic fish. However, despite lots of hard work since Feeney's pioneering experiments, chemists have been unsuccessful in making antifreeze in large enough amounts to be medically useful.

Now, NIGMS grantee **Robert Ben**, a chemist at the State University of New York in Binghamton, has gone one step further toward achieving this goal by making customized versions of natural antifreeze. Beginning with specialized proteins that have sugar molecules attached to them, Ben applied a new method to substitute one of the chemical bonds in natural antifreeze with a sturdier chemical bond. With further refinements, synthetic antifreezes will be an important aid to storing human cells and tissues for organ transplants and other medical procedures.

A Breath of Fresh Air

Remember what your parents said about taking off the bandage on your skinned knee to let the cut "breathe?" Turns out they were right. After the bleeding stops, most wounds—even serious, slow-healing ones—heal better when aired out properly.

NIGMS grantee **Chandan Sen** of the Ohio State University Medical Center in Columbus evaluated a simple method to deliver oxygen, a component of air, directly to slow-healing skin wounds. These wounds are an unfortunate but common complication of surgery, burn recovery, and diseases like diabetes. Sen and his coworkers filled specialized plastic bags with pure



(100 percent) oxygen and attached the bags directly around the wounds of 32 patients. The researchers applied the oxygen-filled bags for periods ranging from 3 weeks to 7 months, depending on the severity of the wound. Their results showed that three-quarters of the stubborn wounds responded to the treatment and healed.

Delivering pure oxygen this way holds promise as a cost-effective, safe way to treat serious wounds. Not only does it seem to be as effective as current treatments, but it also has several advantages. The treatment could be easily used at home and it is simple enough to be used by many people at once, such as during a public health emergency or at war.

Stuck on Mom

After fertilization, an embryo has just a few days to settle into a woman's uterus, implant, and start growing into a baby. Researchers have learned that during the fertile period in a woman's menstrual cycle, cells in her uterus acquire a sticky sugar coating.

Recently, NIGMS grantee **Steven Rosen** of the University of California, San Francisco, teamed up with fellow UCSF scientist Susan J. Fisher to make an important discovery about implantation, which Fisher had been studying for many years. The researchers found that a molecule on the surface of embryos appears to help them adhere to the sticky uterine lining. Rosen's earlier research had revealed that white blood cells use a sugar-grabbing protein called L-selectin to crawl along the surfaces of blood vessels. Rosen and Fisher reasoned that embryo cells might use a similar method to roll to a stop and implant inside a woman's uterus. They found that trophoblasts, cells that ball up around a developing embryo, were indeed studded with molecules of L-selectin. The scientists performed experiments that mimicked the environment and blood flow conditions inside the uterus. They learned that trophoblasts stuck most tightly to samples of uterine tissue collected from women in a fertile period of their menstrual cycle.

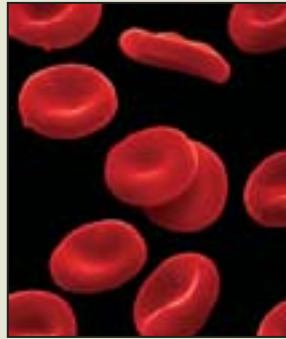
The research holds promise for understanding and treating infertility, since the failure of an embryo to implant properly is a common cause for problems in conceiving a baby and in many types of pregnancy loss.

PC, M.D.?

It's unlikely that computers will ever replace doctors. But computer-based methods are doing their part to help researchers understand health and disease. Recently,

NIGMS grantee **Bernhard Palsson**, a bioengineer at the University of California, San Diego, created a computer (*in silico*) model of how red blood cells work, based on the results of thousands of previously published experiments on red blood cells. He then used the model to study how genes play a role in a disorder called hemolytic anemia. In this type of anemia, red blood cells self-destruct and bone marrow is unable to replenish the supply. People who have the condition are prone to fatigue, shortness of

breath, and a host of other health complications.



Palsson used the *in silico* model to simulate the altered chemical reactions that take place in the cells of people with hemolytic anemia. Scientists know that deficiencies in two critical red blood cell enzymes can cause the disorder. These deficiencies

can be inherited, meaning that they are caused by variations in a person's genes. Palsson and his coworkers used their model to look for links between gene sequence variants and clinical measurements from people with hemolytic anemia. The model accurately predicted which gene variants would cause a more severe, chronic form of hemolytic anemia and which variants would cause a less serious form of the disease.

Palsson's model shows that a mathematical approach can help scientists understand how a genetic change can cause a disease. Palsson predicts that in future years, *in silico* models will be commonly used for discovering new drugs as well as for diagnosing and treating disease.