with cord blood in the spring of 1993 and announced his results at a gene therapy meeting in Steamboat Springs last month. Kohn's aim was to introduce a missing gene into three children suffering from adenosine deaminase deficiency, or ADA, a potentially fatal defect that cripples the immune system. His team separated the CD34 cells from each child's cord blood just after birth and then used a retrovirus as a vector to carry the adenosine deaminase gene into the CD34 cells. Kohn reinfused the cells back into the children when they were 3 days old.

The children have been followed for 23 months, and so far the experiment has been partially successful: The gene is expressed in about 1% of the bone marrow population, and messenger RNA for the enzyme is being produced—a sign that the gene is being expressed and that the enzyme is being made in the cells. "We probably only got the gene into 1% of the stem cells we treated, and they were probably diluted another 100 times by the rest of the bone marrow. Our main concern is to optimize the number of cells with the gene," Kohn says. Researchers in Amsterdam, Netherlands, carried out a similar procedure on children with ADA last year and are awaiting the results.

Many other therapies are in the pipeline, although large obstacles remain before some of the most exciting can be put into practice. Chris Walsh of NHLBI wants to treat Fanconi's anemia and thalassemia, but he needs to figure out, he says, how to turn on the relevant gene only in the right blood cells—for example to get red blood cells to express hemoglobin in anemia sufferers. "You'd like to know the regulatory mechanisms for these genes so they are turned on in the appropriate lineages," he says.

Perhaps the most ambitious proposed therapy comes from Anthony Ho and Flossie Wong-Staal of the University of California, San Diego, who would like to use Kohn's technique to treat children with AIDS. Stem cells are not infected by HIV, so the researchers' idea is to extract CD34 cells from the cord blood of babies born to HIV-positive mothers and insert into those cells an anti-HIV gene—for a ribozyme that can cleave HIV RNA. Expression of this gene would inhibit the reproduction of HIV in the child's cells. If the child eventually became HIV-positive, the HIV-resistant stem cells could be transfused back into the child, where they should produce HIV-resistant T cells and macrophages. The team hopes to start a clinical trial early next year.

Despite the obstacles, the components of cord blood look set for some close scientific scrutiny. Indeed, it's already true that doctors should think twice before discarding them.

–Clare Thompson

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CHEMISTRY

New Compounds Make Light of Pests

Low-flying helicopters, on a regular basis, spew dense clouds of a necessary evil across the California countryside. The clouds contain the insecticide Malathion, necessary because it kills Mediterranean fruit flies (Medflies) that threaten billions of dollars of California crops, but evil in the eyes of many Californians, who fear that Malathion—a nerve toxin—poses a threat to human beings as well as flies. Although toxicologists believe the health threat from the typical exposure to the insecticide is minimal, growing public outrage over Malathion's use has sent state officials scrambling for alternatives.

At last month's American Chemical Society meeting in Anaheim, California, researchers from the U.S. Department of Agriculture (USDA) reported that they may have found one. Field tests of two compounds that become toxic in the digestive tract of insects—but not mammals—showed they are highly effective against the Medfly and its equally destructive cousin, the Mexfly, or Mexican fruit fly.

The compounds, the chemical dyes phloxine B and uranine, have been used for decades to color drugs and cosmetics; they have already been deemed safe by the U.S. Food and Drug Administration. "We're excited about the potential of using these dyes as alternatives to Malathion," says Ted Batkin, a physicist who heads California's Citrus Research Board.

The dyes' selectivity stems from the fact that they turn toxic only after exposure to light. "Insects like fruit flies have translucent guts" that are easily penetrated by sunlight, says James Heitz, a biochemist at Mississippi State University. As a result, when flies eat a protein-based bait laced with the dyes, the compounds are activated in the flies' digestive systems. But in humans, other mammals, fish, or birds, the dyes pass through the digestive system without seeing the light of day.

The dye molecules' facility at absorbing

Powerful protest. Controversy over the insecticide Malathion has spurred development of a light-sensitive replacement.

energy from photons starts a deadly chain of reactions in the insect, Heitz says. That excess energy gets nabbed by nearby energy-hungry oxygen atoms. The energy excites and destabilizes one electron orbiting the oxygen, transforming the atom into a form known as "singlet oxygen" that more easily binds to surrounding molecules. In insect tissues, singlet oxygen typically binds with lipids in cell membranes and amino acids in proteins, changing their structure and therefore interrupting their functions. This process, once started, kills cells and eventually the organism itself. (In cosmetics or on leaf surfaces this chain of events is broken, Heitz thinks, because reactive oxygen doesn't have a chance to penetrate cells before it reacts with other airborne compounds.)

Although these compounds don't kill Medflies as quickly as Malathion does, in lab tests the dyes—which seem to work best together—have proven quite lethal. At the Anaheim meeting, two groups of researchers from the USDA reported that the dyes appeared to be very effective in small field trials as well. One group, led by Bob Mangan and Daniel Moreno at the USDA's Agricultural Research Service in Weslaco, Texas, hung bait consisting of plant proteins laced with the dyes from grapefruit trees in a large cage containing 2000 Mexican fruit flies. Nearly 90% of the flies were killed within 4 days.

In the first uncaged field trial, Nicanor Liquido, a research entomologist with the USDA's Tropical Fruit and Vegetable Research Laboratory in Hilo, Hawaii, reported that on a 10-acre plot of coffee bushes sprayed with a mixture containing the dyes, the fruit fly population dropped 50% compared with an unsprayed plot. The population of flies in the sprayed plot would have dropped even further, notes Grant McQuate, a technician on the project, but the plot was surrounded by 1000 acres of untreated plantation, allowing flies from untreated areas to migrate into the test site.

Despite these promising results, the dyes are not ready to replace Malathion, according to David Bergsten, a toxicologist at the USDA's Animal and Plant Health Inspection Service in Riverdale, Maryland. Researchers need to show that the dyes don't break down into compounds that can harm crops. If they can, sunlight may soon not only help fields grow but keep them fly-free as well.

–Robert F. Service