SCIENCE NEWS

THE WEEKLY NEWSMAGAZINE OF SCIENCE

AUGUST 2, 2003 PAGES 65-80 VOL. 164, NO. 5

confirming energy's dark side
genetic links to life span
speedy aerodynamic modeling
worm jaw: mighty and metallic

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# toxic dust

## BIG HARM FROM TINY POLLUTANTS

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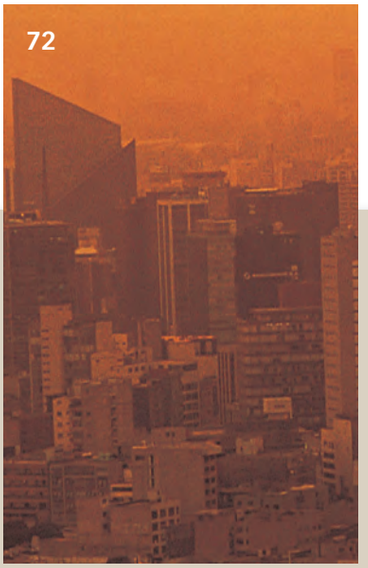


## Features



## This Week



**THIS WEEK ONLINE**
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**GREENER GROCERS** Proposed labels for fresh foods indicate how much fossil fuel was used to transport each item to the supermarket shelf. See Janet Raloff's Food for Thought.

## Of Note



## Meetings



## Departments



**Cover** The haze that frequently blankets Mexico City, shown here, consists primarily of tiny soot and other dust particles. New studies are uncovering surprising clues to how such microscopic bits of urban pollution trigger a broad range of diseases. Page 72



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**Science News** (ISSN 0036-8423) is published weekly on Saturday, except the last week in December, for $54.50 for 1 year or $98.00 for 2 years (foreign postage is $18.00 additional per year) by Science Service, 1719 N Street, N.W., Washington, DC 20036. Preferred periodicals postage paid at Washington, D.C., and an additional mailing office.

**POSTMASTER**
Send address changes to **Science News**, P.O. Box 1925, Marion, OH 43306. Change of address: Two to four weeks' notice is required—old and new addresses, including zip codes, must be provided.


**EDITORIAL, BUSINESS, AND ADVERTISING OFFICES** 1719 N St. N.W., Washington, D.C. 20036
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**SUBSCRIPTION DEPARTMENT** P.O. Box 1925, Marion, OH 43306. For new subscriptions and customer service, call 1-800-552-4412.

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# Repulsive Astronomy

## Strengthening the case for dark energy

**Astronomers have found new evidence for** one of the strangest properties of the universe. A mysterious substance, dubbed dark energy, appears to be ripping the cosmos apart, causing the universe to expand at an ever-faster rate.

The wrenching findings come from a correlation between two kinds of sky maps—one that denotes the positions of large numbers of galaxies and another, a snapshot of the cosmic microwave background, which is the remnant radiation from the Big Bang.

By comparing the maps, astronomers have found the imprint of dark energy, which pushes objects apart and thus counters gravity's familiar tug. Previous support for dark energy has been based on the brightness of distant stellar explosions known as supernovas (*SN: 3/31/01, p. 196*). With only one line of evidence, however, some researchers weren't convinced.

"Since the implications of dark energy are so profound for physics, having multiple, independent lines of evidence for its existence is absolutely essential," says Joshua A. Frieman of the Fermi National Accelerator Laboratory in Batavia, Ill., a coauthor of one of four dark-energy studies recently posted online. Each study uses data from the Wilkinson Microwave Anisotropy Probe (WMAP), a satellite that is generating detailed maps of the cosmic microwave background (*SN: 2/15/03, p. 99*).

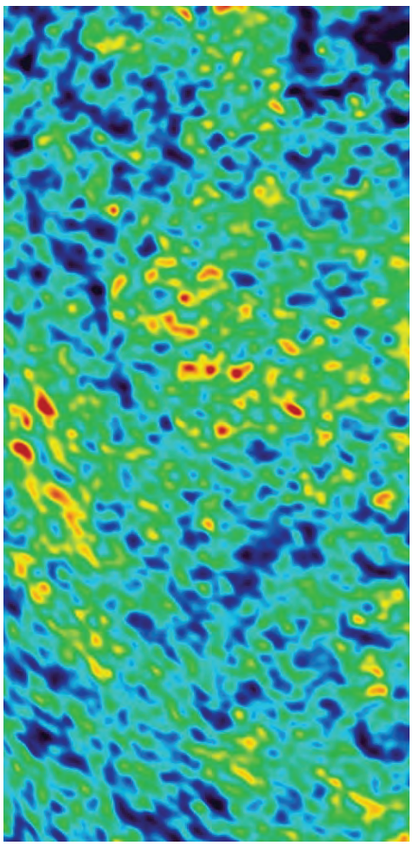
This remnant radiation is riddled with hot and cold spots, most of which reflect the lumpiness of the infant universe, from which galaxies grew. But some of the energy in the hot spots may have been acquired later, as light traveled for billions of years to reach Earth.

During their long journey, photons from the microwave background encounter huge concentrations of matter, such as superclusters of galaxies. As the photons fall into these clouds of matter, they gain energy, like a marble that speeds up as it rolls downhill. As the photons climb out of these areas, they lose energy.

If the universe were flat—so that parallel lines never meet—and contained no dark energy, photons traversing matter-filled regions would gain exactly as much energy as they lose. But in a flat universe containing dark energy, there would be no such cancellation, says Frieman.

Dark energy would spread matter out during the period in which photons traverse a supercluster or other large clump. The photons would therefore expend less energy leaving a supercluster than the amount they gained when they entered. So, wherever the universe harbors lots of matter, the microwave-background photons ought to be slightly more energetic than those in less-dense areas. This would be indicated by a shift of the photons toward bluer wavelengths.

That's exactly what Frieman, Ryan Scranton of the University of Pittsburgh, and their collaborators found when they compared data from WMAP with the positions of several million galaxies mapped by the Sloan Digital Sky Survey, a vast, visible-light survey of the heavens (*SN: 5/31/03, p. 341*). The blue shift was discernible on scales of 100 million light-years, or roughly one-hundredth the scale of previous studies. The scientists recently posted their findings online (*http://xxx.lanl.gov/abs/astro-ph/0307335*).



NASA/WMAP

**DARK FINGERPRINT** **Some of the color differences in this temperature map of the cosmic microwave background, researchers say, result from a mysterious substance called dark energy.**

Using a smaller sample from the same visible-light survey, Pablo Fosalba of the Institut d'Astrophysique de Paris and his collaborators observed a similar correlation (*http://xxx.lanl.gov/abs/astro-ph/0307249*). Relying on galaxies mapped at X-ray and radio wavelengths, Steven Boughn of Haverford (Pa.) College and Robert Crittenden of the Institute of Cosmology and Gravitation in Portsmouth, England, found the same blue-shifting effect (*http://xxx.lanl.gov/abs/astro-ph/0305001*). The same goes for Michael R. Nolta of Princeton University and his collaborators, who also worked with the radio-wavelength map (*http://xxx.lanl.gov/abs/astroph/0305097*).

"It is exciting that all these teams find the same correlation," says Wayne Hu of the University of Chicago.

Further studies with the Sloan data may help pin down the physical traits of the still-elusive dark energy, Frieman notes. —R. COWEN

# Extracting Estrogens

## Modern treatment plants strip hormone from sewage

**Reproductive hormones, both natural and** the synthetic ones in contraceptive drugs, sometimes survive sewage treatment and turn up in the environment where they can affect wildlife. Modern sewage-treatment facilities, about half of those used in Europe, break down these sex hormones more effectively than older plants do.

A new study shows why: Only the modern, multiple-chamber treatment plants subject the sewage to the gamut of chemical and biological conditions required to break down different hormones.

Sewage often contains two natural estrogens, estrone (E1) and 17-beta-estradiol (E2), as well as the synthetic estrogen 17-alpha-ethinylestradiol (EE2), used in birth-control pills and patches. Scientists have determined that some estrogen passes through U.S. water-treatment plants and reaches waterways (*SN: 6/17/00, p. 388*), where it can cause fish to develop sexual abnormalities (*SN: 1/8/94, p. 24*).

Older plants have a single tank designed to remove phosphate and nitrate from sludge, but newer facilities use several such tanks and retain sludge considerably longer, says environmental chemist Thomas A. Ternes of Bundesanstalt für Gewässerkunde in Koblenz, Germany. At a recently

updated plant in Wiesbaden, Germany, for example, sludge spends 11 to 13 days in a trio of tanks rather than the 4 days or less it took in a single tank before the renovation.

Different kinds of bacteria populate the various tanks because some tanks expose sludge to oxygen and others don't. To figure out where in the newer treatment process estrogens break down, Ternes and his colleagues in Denmark and Switzerland studied sludge removed from 10 different points along the flow of sewage in the Wiesbaden plant.

The scientists found that oxygen-deprived tanks remove most of the E1 and E2 that enter them, while oxygenated tanks remove most of the EE2. Most important, all three hormones were undetectable—though not necessarily entirely absent—in the plant's effluent, the researchers report in an upcoming *Environmental Science and Technology*.

Estrogen removal is a fortunate side effect of multiple-tank sewage treatment, says chemist Thomas Heberer of the Technical University of Berlin. The new research shows for the first time that subjecting sludge alternately to oxygenated and oxygen-deprived conditions is highly effective at eliminating the hormones, he says. He notes that with more-sophisticated measurement techniques, Ternes' team might have measured traces of estrogen that survived the treatment process.

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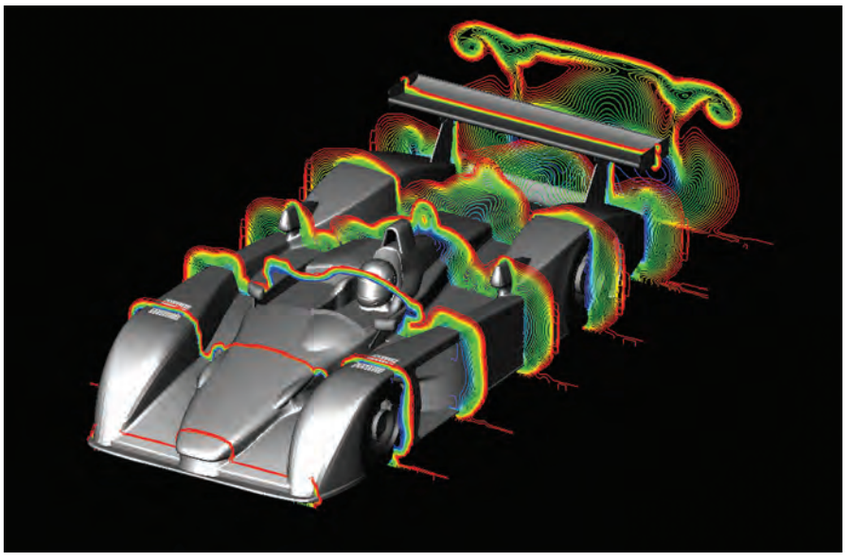

EXA CORP./AUDI AG

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The new method relies on a different equation, called the Boltzmann equation, which is typically employed to predict the behaviors of molecules in gases and liquids. More than a decade ago, researchers were surprised to learn that using the Boltzmann equation to calculate simple fluid flows didn't make the simulations more difficult or time consuming to carry out.

"It's the counterintuitive approach," says Steven A. Orszag of Yale University, a coauthor of the *Science* paper and an EXA consultant. "If you start from the very microscopic dynamics, you would think you'd have to compute much too much."

More recently, Orszag, Chen, and their colleagues found a way to include turbulence in their Boltzmann equation–based simulations at little additional computing cost. The trick was to invent a particular mathematical representation of disruption of particle motions by disorderly flows.

That last step was "really a breakthrough from my point of view," comments Roberto Benzi of the University of Rome Tor Vergata, a pioneer in the use of the Boltzmann equation for fluid flows. —P. WEISS

# Untangling the Brain

## Enzyme counters Alzheimer's-like snarls

**An enzyme prevents brain cells in aging** mice from developing knots of proteins resembling those that are a hallmark of Alzheimer's disease, scientists report. Known as Pin1, the enzyme could form the

basis of new treatments for the memory-stealing disorder.

In 1995, Kun Ping Lu of Beth Israel Deaconess Medical Center in Boston and Tony Hunter of the Salk Institute for Biological Studies in La Jolla, Calif., discovered Pin1. They subsequently showed that it interacts with a protein called tau, an important component of one of the two brain lesions seen in Alzheimer's disease. Known as tangles, these snarls of tau filaments turn up inside nerve cells. In contrast, the other lesion consists of an abnormal buildup outside nerve cells of a protein fragment known as beta-amyloid.

Most neuroscientists favor the hypothesis that beta-amyloid triggers the brain-cell loss in Alzheimer's disease, but some argue that tau is equally, if not more, important. Tau protein normally shapes a cell's interior skeleton, but in Alzheimer's disease, molecular tags called phosphates get added to tau. This embellishment seems to promote tangle formation.

Lu, Hunter, and their colleagues had shown that Pin1 binds to tau overloaded with phosphates. This alters the protein's shape in such a way that those tags get shed. "It's important for restoring the function of tau," says Lu.

This finding and others persuaded Lu that Pin1 can protect brain cells from the ravages of tangles. Some investigators, however, interpreted the data differently, arguing that the enzyme actually contributes to tangle formation.

In the July 31 *Nature*, Lu, Hunter, and their colleagues report that mice with an inactive Pin1 gene suffer nerve cell loss in the spinal cord and brain as the animals age. The mice show decreasing mobility and general loss of muscle coordination.

A close examination of the brains of the mice revealed that select regions exhibited nerve cell degeneration. In those areas, tau proteins were studded with phosphates and were tangled. Other researchers have induced tangle formation in mice by giving the rodents extra copies of the human tau gene but not by inactivating a gene, says Lu.

"This is the first demonstration that mouse tau can form structures similar to what we see in human brain," adds Mark Smith of Case Western Reserve University in Cleveland. "It will be a useful model to clarify the connection between tau and neurodegeneration."

While studying preserved brain tissue from people who had Alzheimer's disease, Lu and his colleagues also found that regions with the highest concentrations of Pin1 had the lowest percentages of nerve cells with tangles. Moreover, in healthy brains, the highest concentrations of the enzyme appear in areas that Alzheimer's disease doesn't normally destroy, the scientists report.

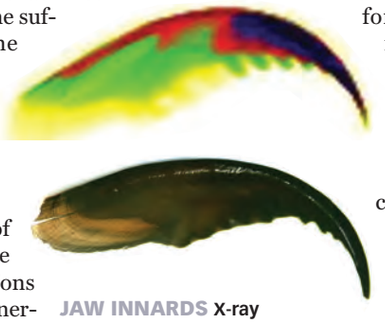
The animal and human data together create a "strong case" that Pin1 protects against Alzheimer's disease, says D. Stephen Snyder of the National Institute on Aging in Bethesda, Md.

Smith isn't quite as convinced, noting that the mutant mice experience nerve cell loss in brain regions different from those afflicted by Alzheimer's disease. "I'm not sure this [new study] shows the role of Pin1 in Alzheimer's disease as much as it shows a role in neurodegeneration," he says. —J. TRAVIS

# Worm's Jaws Show Mettle

## Worm's zinc links may inspire new materials

**Since biology excels at making strong and** hard substances, such as bone, teeth, and seashells, scientists who design new materials often try to emulate nature's inventions. For Galen D. Stucky of the University of California, Santa Barbara and his colleagues, the microstructures of marine worms' jaws harbor clues for making synthetic materials. Unlike the bony jaws of mammals, these worms' chops are made primarily of protein.



**JAW INNARDS** X-ray absorption (top) shows the highest concentration of zinc (dark area) near the tip of a clam-worm jaw. A light-microscope image of the jaw, about 3 millimeters long, appears at bottom.

H. LICHTENEGGER ET AL./PNAS

Stucky and his coworkers recently reported that the tiny jaws of the bloodworm, *Glycera dibranchiata*, contain the copper chloride mineral called atacamite, which makes the structures particularly strong (*SN: 11/9/02, p. 302*). In an upcoming issue of the *Proceedings of the National Academy of Sciences*, the researchers compare the bloodworm's jaws to those of the clam worm, *Nereis limbata*, a sand- and mud-dwelling scavenger. Although the protein compositions of the two worms' jaws are similar, the jaws of *Nereis* contain zinc instead of copper.

Using a variety of tests, Stucky and his coworkers found that the properties of the clam worm's jaw vary with its zinc content. As the concentration of zinc increases, so do the jaw's hardness and stiffness. The clam-worm jaws are especially hard near the tips, says Stucky, but even there, they're still softer than bloodworm jaws.

The researchers also found that the zinc in clam-worm jaws isn't in a mineralized form, as is the case for much of the copper in the tip of the bloodworm jaws. Instead, the team determined that clam-worm jaws are hard wherever zinc cross-links protein networks.

Stucky and his coworkers suggest that each animal's jaw composition suits the mechanical demands of its eating habits. The clam worm, which scavenges food, may not require jaws as hard as those of the bloodworm, which thrusts its jaws into prey to inject venom.

In the future, notes materials researcher Mehmet Sarikaya of the University of Washington in Seattle, investigators might discover more specifically how the zinc-based cross-linking occurs in clam worms and why the animals rely on zinc rather than on another metal. Within such knowledge, Sarikaya says, scientists might find clues for designing their own hardy composites of proteins and metals.

Stucky says his group is already taking steps toward creating flexible and lightweight materials inspired by the worm. The researchers are also examining the hard beaks of octopuses and squid, which are protein based like the worms' jaws yet contain little or no metal.

Materials scientists can learn a lot from animals, says Arthur Heuer of Case Western Reserve University in Cleveland, where he has studied the conch shell for clues to materials design. Says Heuer: "Nature has had hundreds of millions of years to experiment." —J. GORMAN

# Transplant Hope

## Thymus transplant jump-starts immune system in babies

**Babies born without a thymus gland—and** therefore bereft of a functioning immune system—are easy prey for disease-causing invaders. If untreated, this deficiency, called severe DiGeorge syndrome, is invariably fatal before a child's third birthday.

For babies with the syndrome, also called DiGeorge anomaly, a thymus transplant may present a life-changing option. But scientific information on such transplants has been limited to the results of sporadic case studies because the disease is rare, affecting only a handful of newborns each year in the United States. Researchers at Duke University Medical Center in Durham, N.C.,

now report the largest series of thymus transplants—in 12 children with DiGeorge syndrome over 8 years—and show success in establishing an immune system in many of these babies. The report appears in the Aug. 1 issue of *Blood*.

The babies received transplanted thymus tissue within their first few months of life. The grafted tissue takes a long time to build up a protective army of white blood cells called T cells, says M. Louise Markert, a pediatric immunologist at Duke, so the children remained especially vulnerable to infections for months after the surgery.

White blood cells begin in the bone marrow. Some of these migrate to the thymus gland, which sits above the heart, and there become T cells. Named for the thymus gland, T cells are frontline defenders in the immune system and champs at distinguishing the body's own tissues from foreign materials.

For the transplants, doctors salvaged some thymus tissue that otherwise would have been discarded from children undergoing heart surgery. The material was nourished in a lab dish, where the team removed existing T cells to keep them from attacking the babies who subsequently received the tissue. The doctors then implanted the thymus tissue into the recipients' thigh muscles.

Despite the transplant, five of the babies died within 5 months of surgery from infections and brain hemorrhages that were complications of DiGeorge syndrome, Markert reports. These deaths weren't caused by the transplants, she says.

Of the seven surviving children, all are free of infection and living at home. The children got their transplants between 1993 and 2001, and they now average 4 years since the surgery. Some of the older ones attend elementary school, Markert says.

While some of the children still have diminished hearing, mild mental retardation, and difficulty swallowing—all common to DiGeorge patients—the children are fending off infections, Markert says.

T cell concentrations in the children's blood are slightly below normal but not dangerously so, she adds. Three children tested 2 years after transplantation were all making antibodies, another good sign. In all seven children, the immune deficiency appears to be corrected, she concludes.

"This is a really scholarly piece of work," says Richard Hong, an immunologist at the University of Vermont in Burlington. Other scientists have investigated use of transplants of mature T cells for DiGeorge patients, but the Duke study validates thymus transplantation as the best treatment, he says. —N. SEPPA

**RUNNING START** **World-class sprinters are more likely than their marathon-running counterparts to have α-actinin-3 protein at work in their fast-twitch muscles.**

# Turbo Gene

## Getting a speed boost from DNA

**Whether you're better suited to run a** marathon or a 100-meter sprint correlates with a gene called *ACTN3*, researchers find.

The gene encodes the protein α-actinin-3, which functions in the so-called fast-twitch muscles. These muscles give the extra power needed for brief and vigorous bursts of activity, such as sprinting and speed skating.

Previous studies revealed that about one out of five white people in Australia has a variant of the *ACTN3* gene that cannot yield α-actinin-3. Because people with the deficiency seem healthy, the protein appears to be unimportant for day-to-day activities. Most likely, it's significant only "in the extremes of performance," says Kathryn North of the Children's Hospital at Westmead in Sydney, Australia.

That's where the athletic connection comes in. North and her colleagues theorized that because the protein affects fast-muscle fibers, a deficiency of α-actinin-3 might be detrimental to speedy running and thus less likely to occur in elite sprinters.

To test their theory, the researchers genetically screened a group of world-class athletes, including Australian Olympic competitors, and a control group of nonathletes. All the participants were white. The scientists divided the athletes into two groups: sprinters, which included speed skaters, and endurance athletes, such as marathon runners and rowers.

Of the sprinters, 6 percent had the gene variant leading to α-actinin-3 deficiency. That's one-third the rate for nonathletes, 18 percent of whom carried the variant. With a rate of 24 percent, endurance runners were similar to the nonathletes. The findings will appear in the September *American Journal of Human Genetics*.

"The unique finding of this study is that the sprint athletes are different," comments Tuomo Rankinen of the Pennington Biomedical Research Center at Louisiana State University in Baton Rouge. "The endurance athletes do not really differ from the nonathletes in terms of this genetic marker."

There is, however, a gender difference. None of the female sprinters was α-actinin-3 deficient. North thinks that in male sprinters lacking the protein, hormones such as testosterone may compensate for the protein deficiency.

Previous studies have shown ethnic differences. Some 25 percent of Asians are α-actinin-3 deficient, compared with only 1 percent of Bantu-speaking people in Africa. North says that the importance of α-actinin-3 protein for athletic performance may vary in different human populations.

"We know that at the moment, the best sprinters in the world are black," Rankinen says. "The next question is to compare the frequency of these *ACTN3* genotypes in black sprinters with [that of] the general African-American population, for example."

But North's first task is to establish how the gene's protein product, α-actinin-3, works in fast-twitch muscles. After knocking out mouse *ACTN3* genes, "we're going to be putting mice through little sprinting tests" and looking for structural changes in the muscles, she says. —S. MCDONAGH

updated plant in Wiesbaden, Germany, for example, sludge spends 11 to 13 days in a trio of tanks rather than the 4 days or less it took in a single tank before the renovation.

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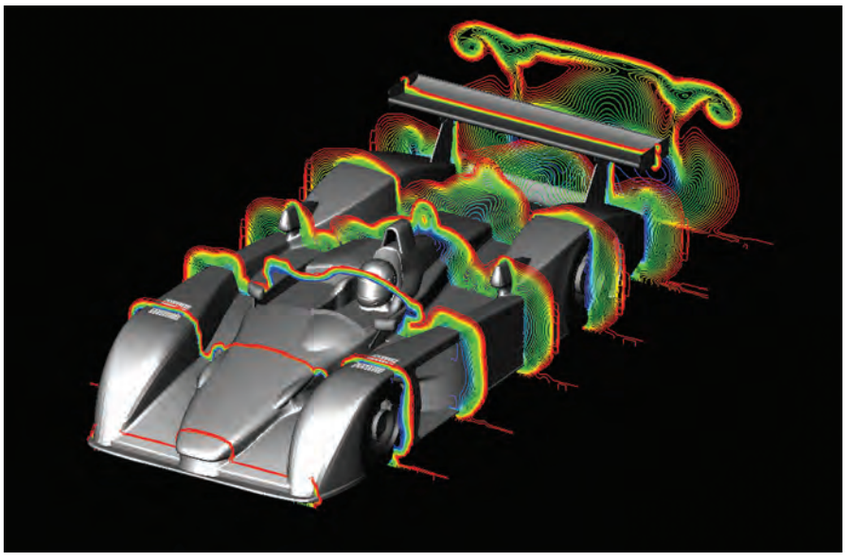

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Lu, Hunter, and their colleagues had shown that Pin1 binds to tau overloaded with phosphates. This alters the protein's shape in such a way that those tags get shed. "It's important for restoring the function of tau," says Lu.

This finding and others persuaded Lu that Pin1 can protect brain cells from the ravages of tangles. Some investigators, however, interpreted the data differently, arguing that the enzyme actually contributes to tangle formation.

In the July 31 *Nature*, Lu, Hunter, and their colleagues report that mice with an inactive Pin1 gene suffer nerve cell loss in the spinal cord and brain as the animals age. The mice show decreasing mobility and general loss of muscle coordination.

A close examination of the brains of the mice revealed that select regions exhibited nerve cell degeneration. In those areas, tau proteins were studded with phosphates and were tangled. Other researchers have induced tangle formation in mice by giving the rodents extra copies of the human tau gene but not by inactivating a gene, says Lu.

"This is the first demonstration that mouse tau can form structures similar to what we see in human brain," adds Mark Smith of Case Western Reserve University in Cleveland. "It will be a useful model to clarify the connection between tau and neurodegeneration."

While studying preserved brain tissue from people who had Alzheimer's disease, Lu and his colleagues also found that regions with the highest concentrations of Pin1 had the lowest percentages of nerve cells with tangles. Moreover, in healthy brains, the highest concentrations of the enzyme appear in areas that Alzheimer's disease doesn't normally destroy, the scientists report.

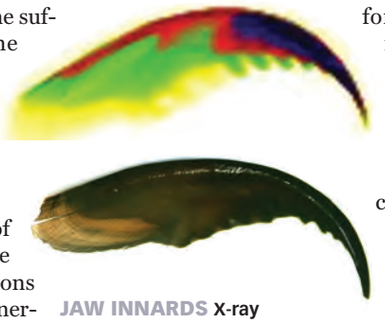
The animal and human data together create a "strong case" that Pin1 protects against Alzheimer's disease, says D. Stephen Snyder of the National Institute on Aging in Bethesda, Md.

Smith isn't quite as convinced, noting that the mutant mice experience nerve cell loss in brain regions different from those afflicted by Alzheimer's disease. "I'm not sure this [new study] shows the role of Pin1 in Alzheimer's disease as much as it shows a role in neurodegeneration," he says. —J. TRAVIS

# Worm's Jaws Show Mettle

## Zinc links may inspire new materials

**Since biology excels at making strong and** hard substances, such as bone, teeth, and seashells, scientists who design new materials often try to emulate nature's inventions. For Galen D. Stucky of the University of California, Santa Barbara and his colleagues, the microstructures of marine worms' jaws harbor clues for making synthetic materials. Unlike the bony jaws of mammals, these worms' chops are made primarily of protein.



**JAW INNARDS** X-ray absorption (top) shows the highest concentration of zinc (dark area) near the tip of a clam-worm jaw. A light-microscope image of the jaw, about 3 millimeters long, appears at bottom.

H. LICHTENEGGER ET AL./PNAS

Stucky and his coworkers recently reported that the tiny jaws of the bloodworm, *Glycera dibranchiata*, contain the copper chloride mineral called atacamite, which makes the structures particularly strong (*SN: 11/9/02, p. 302*). In an upcoming issue of the *Proceedings of the National Academy of Sciences*, the researchers compare the bloodworm's jaws to those of the clam worm, *Nereis limbata*, a sand- and mud-dwelling scavenger. Although the protein compositions of the two worms' jaws are similar, the jaws of *Nereis* contain zinc instead of copper.

Using a variety of tests, Stucky and his coworkers found that the properties of the clam worm's jaw vary with its zinc content. As the concentration of zinc increases, so do the jaw's hardness and stiffness. The clam-worm jaws are especially hard near the tips, says Stucky, but even there, they're still softer than bloodworm jaws.

The researchers also found that the zinc in clam-worm jaws isn't in a mineralized form, as is the case for much of the copper in the tip of the bloodworm jaws. Instead, the team determined that clam-worm jaws are hard wherever zinc cross-links protein networks.

Stucky and his coworkers suggest that each animal's jaw composition suits the mechanical demands of its eating habits. The clam worm, which scavenges food, may not require jaws as hard as those of the bloodworm, which thrusts its jaws into prey to inject venom.

In the future, notes materials researcher Mehmet Sarikaya of the University of Washington in Seattle, investigators might discover more specifically how the zinc-based cross-linking occurs in clam worms and why the animals rely on zinc rather than on another metal. Within such knowledge, Sarikaya says, scientists might find clues for designing their own hardy composites of proteins and metals.

Stucky says his group is already taking steps toward creating flexible and lightweight materials inspired by the worm. The researchers are also examining the hard beaks of octopuses and squid, which are protein based like the worms' jaws yet contain little or no metal.

Materials scientists can learn a lot from animals, says Arthur Heuer of Case Western Reserve University in Cleveland, where he has studied the conch shell for clues to materials design. Says Heuer: "Nature has had hundreds of millions of years to experiment." —J. GORMAN

# Transplant Hope

## New thymus tissue jump-starts immune system in babies

**Babies born without a thymus gland—and** therefore bereft of a functioning immune system—are easy prey for disease-causing invaders. If untreated, this deficiency, called severe DiGeorge syndrome, is invariably fatal before a child's third birthday.

For babies with the syndrome, also called DiGeorge anomaly, a thymus transplant may present a life-changing option. But scientific information on such transplants has been limited to the results of sporadic case studies because the disease is rare, affecting only a handful of newborns each year in the United States. Researchers at Duke University Medical Center in Durham, N.C.,

now report the largest series of thymus transplants—in 12 children with DiGeorge syndrome over 8 years—and show success in establishing an immune system in many of these babies. The report appears in the Aug. 1 issue of *Blood*.

The babies received transplanted thymus tissue within their first few months of life. The grafted tissue takes a long time to build up a protective army of white blood cells called T cells, says M. Louise Markert, a pediatric immunologist at Duke, so the children remained especially vulnerable to infections for months after the surgery.

White blood cells begin in the bone marrow. Some of these migrate to the thymus gland, which sits above the heart, and there become T cells. Named for the thymus gland, T cells are frontline defenders in the immune system and champs at distinguishing the body's own tissues from foreign materials.

For the transplants, doctors salvaged some thymus tissue that otherwise would have been discarded from children undergoing heart surgery. The material was nourished in a lab dish, where the team removed existing T cells to keep them from attacking the babies who subsequently received the tissue. The doctors then implanted the thymus tissue into the recipients' thigh muscles.

Despite the transplant, five of the babies died within 5 months of surgery from infections and brain hemorrhages that were complications of DiGeorge syndrome, Markert reports. These deaths weren't caused by the transplants, she says.

Of the seven surviving children, all are free of infection and living at home. The children got their transplants between 1993 and 2001, and they now average 4 years since the surgery. Some of the older ones attend elementary school, Markert says.

While some of the children still have diminished hearing, mild mental retardation, and difficulty swallowing—all common to DiGeorge patients—the children are fending off infections, Markert says.

T cell concentrations in the children's blood are slightly below normal but not dangerously so, she adds. Three children tested 2 years after transplantation were all making antibodies, another good sign. In all seven children, the immune deficiency appears to be corrected, she concludes.

"This is a really scholarly piece of work," says Richard Hong, an immunologist at the University of Vermont in Burlington. Other scientists have investigated use of transplants of mature T cells for DiGeorge patients, but the Duke study validates thymus transplantation as the best treatment, he says. —N. SEPPA

**RUNNING START** **World-class sprinters are more likely than their marathon-running counterparts to have α-actinin-3 protein at work in their fast-twitch muscles.**

# Turbo Gene

## Getting a speed boost from DNA

**Whether you're better suited to run a** marathon or a 100-meter sprint correlates with a gene called *ACTN3*, researchers find.

The gene encodes the protein α-actinin-3, which functions in the so-called fast-twitch muscles. These muscles give the extra power needed for brief and vigorous bursts of activity, such as sprinting and speed skating.

Previous studies revealed that about one out of five white people in Australia has a variant of the *ACTN3* gene that cannot yield α-actinin-3. Because people with the deficiency seem healthy, the protein appears to be unimportant for day-to-day activities. Most likely, it's significant only "in the extremes of performance," says Kathryn North of the Children's Hospital at Westmead in Sydney, Australia.

That's where the athletic connection comes in. North and her colleagues theorized that because the protein affects fast-muscle fibers, a deficiency of α-actinin-3 might be detrimental to speedy running and thus less likely to occur in elite sprinters.

To test their theory, the researchers genetically screened a group of world-class athletes, including Australian Olympic competitors, and a control group of nonathletes. All the participants were white. The scientists divided the athletes into two groups: sprinters, which included speed skaters, and endurance athletes, such as marathon runners and rowers.

Of the sprinters, 6 percent had the gene variant leading to α-actinin-3 deficiency. That's one-third the rate for nonathletes, 18 percent of whom carried the variant. With a rate of 24 percent, endurance runners were similar to the nonathletes. The findings will appear in the September *American Journal of Human Genetics*.

"The unique finding of this study is that the sprint athletes are different," comments Tuomo Rankinen of the Pennington Biomedical Research Center at Louisiana State University in Baton Rouge. "The endurance athletes do not really differ from the nonathletes in terms of this genetic marker."

There is, however, a gender difference. None of the female sprinters was α-actinin-3 deficient. North thinks that in male sprinters lacking the protein, hormones such as testosterone may compensate for the protein deficiency.

Previous studies have shown ethnic differences. Some 25 percent of Asians are α-actinin-3 deficient, compared with only 1 percent of Bantu-speaking people in Africa. North says that the importance of α-actinin-3 protein for athletic performance may vary in different human populations.

"We know that at the moment, the best sprinters in the world are black," Rankinen says. "The next question is to compare the frequency of these *ACTN3* genotypes in black sprinters with [that of] the general African-American population, for example."

But North's first task is to establish how the gene's protein product, α-actinin-3, works in fast-twitch muscles. After knocking out mouse *ACTN3* genes, "we're going to be putting mice through little sprinting tests" and looking for structural changes in the muscles, she says. —S. MCDONAGH

# AIR SICKNESS

## How microscopic dust particles cause subtle but serious harm

BY JANET RALOFF

On Oct. 26, 1948, a temperature inversion laid a blanket of cold, stagnant air over Donora, Pa., a tiny mill town on the Monongahela River. Over the next 5 days, the buildup of pollution cloaked the sun, sometimes restricting vision to just a few feet. Twenty people died outright and 50 more perished within a month from lingering health damage, says consulting epidemiologist Devra Davis, a former Donora resident whose own family survived the tragedy.

As bad as her hometown's pollution had been, its impact would pale against a 5-day killer smog that settled on London in December 1952. It killed some 12,000 people within 3 months, according to calculations in a June 2001 report by Davis and Michelle L. Bell of Johns Hopkins University in Baltimore. "With a death rate more than three times the norm for this period, the London fog of 1952 is widely regarded as a catalyst for the study of air pollution epidemiology," the pair noted.

That science would eventually show that even the diffuse dust wafting in seemingly clear air could kill. Its victims are just harder to identify than those in the London and Donora catastrophes because most who succumb are elderly or already in ill health. Indeed, a trailblazing 1991 analysis by Joel Schwartz, then at the Environmental Protection Agency, concluded that some 60,000 U.S. residents die from heart attacks and respiratory problems each year because of the effects of airborne dust at concentrations within federal pollution limits (*SN: 4/6/91, p. 212*).

Stunning as those numbers were at first, they're now accepted by most researchers. In that 1991 study and subsequent ones, Schwartz, now at the Harvard School of Public Health in Boston, has shown that community death rates rise and fall nearly in lock-step with local changes in concentrations of tiny dust particles—even when concentrations of those particulates are just one-quarter of the federal limit for outdoor air.

Yet more than a decade later, nagging questions remain: What makes dust and smoke particles, especially small ones, toxic? Is particulate matter, as scientists call it, inherently poisonous, regardless of its composition? Or does a large surface area per unit mass make those particles robust vehicles for ferrying toxicants such as metal atoms deep into the lungs?

In the past 2 years, a flurry of new data has finally begun answering these questions. The research links the greatest harm to the tiniest dust: particulate matter no more than 2.5 micrometers in diameter, called the PM-2.5 fraction. Some studies suggest that the most dangerous of all may be ultrafines, particles less than 0.1 micrometer across—a class of dust that environmental studies and regulations have generally ignored.

**LOOK HARD —** Fine, metal-laden particles from industrial sources in Hettstedt, Germany, are too diffuse to make the air hazy. When Environmental Protection Agency scientists collected and applied these particles to lung tissue from mice, however, they aggravated symptoms of asthma. Similar amounts of relatively metalfree dust had no such effect.

J. HEINRICH/ GSF INST OF EPIDEMIOLOGY

**REMODELED AIRWAYS** Although most people who die from particulate pollution had heart disease or respiratory problems, the new data are showing that even young and healthy people aren't immune to the violence that dust can perpetrate on lung tissue.

In Fresno, Calif., for instance, outwardly robust people routinely harbor damage in their lungs' small airways, setting the stage for respiratory and cardiovascular disease. These lung effects appear to trace to Fresno's high level of PM-2.5 pollution, which is as bad as that in Los Angeles and worse than that in nearly any other U.S. city, according to Kent E. Pinkerton of the University of California, Davis and his colleagues. They surveyed the airways of more than 80 men who had been longtime residents of Fresno—many of them in their 20s to 40s—who died from auto accidents and other events unrelated to pollution.

Pinkerton's team found that PM-2.5 has little effect on the lungs' larger passages but injures the deeper, smaller, thin-walled bronchioles that mark where the body begins to extract oxygen from air. The damage was apparently caused by the ravages of molecular fragments called free radicals. The affected tissue exhibited a kind of scarring called fibrosis and an abnormal thickening, two features that make breathing more difficult.

To confirm the role of particulate pollution in these subtle changes to the lung, Pinkerton's colleague Kevin R. Smith exposed young-adult rats for 4 hours on 3 consecutive days to

air deliberately concentrated with the particulates in Fresno's atmosphere. The amount of PM-2.5 in the test air, Pinkerton notes, reflected "what can exist in Fresno on bad-air days."

After the exposures, Smith examined areas of the rats' lungs and extracted unusually large numbers of inflammatory cells, called neutrophils, as well as hosts of dead cells.

"It's not unusual to see an occasional dead cell" in the lungs of rats that had breathed only clean air, Pinkerton notes, but the dust-exposed rats showed many dead lung cells, including macrophages—the organ's housekeeping cells. Because macrophages normally gobble up cellular trash such as pollutant particles, their loss could prove important, the Davis team notes in the June *Environmental Health Perspectives*.

In the May issue of that journal, Andrew Churg of the University of British Columbia in Vancouver and his colleagues report similar findings in the autopsied lungs of 11 nonsmoking women from Mexico City, but not in an equal number from Vancouver. Though the Canadian city's air is relatively clear of particulates, Mexico City's air carries a dense haze of fine dust much of the year.

The scientists focused on the lungs' smallest, oxygen-absorbing airways. Compared with those from the Canadian women, the tiny airways from residents of Mexico City "were very abnormal," Churg says. They were twisted and exhibited significantly more fibrosis and thickness than normal lung tissue. "A heavy smoker could have airways that look very much the same," he told *Science News*.

Churg's colleague David Bates plans to test whether the effects the team documented translate into breathing problems in healthy Mexico City adults.

Lilian Calderón-Garcidueñas of the University of North Carolina at Chapel Hill says she knows what Bates will find. At the Experimental Biology meeting in San Diego last April, she documented mildly obstructed breathing in 10 percent of the 174 ostensibly healthy Mexico City children she examined. All the children came from middle- to upper-class nonsmoking families living where the air wasn't the city's dustiest.

**HEART OF THE MATTER** Despite the natural expectation that lungs should be especially vulnerable to dust, "the worst effects, it turns out, are on the cardiovascular system," observes particle toxicologist Ken Donaldson of the University of Edinburgh.

Some of the most intriguing clues to what underlies these effects are emerging from studies on endothelin. This small protein, produced in healthy lungs, ordinarily prompts blood vessels to constrict to maintain proper blood pressure.

Renaud Vincent of Health Canada in Ottawa, Ont., and his colleagues had been wondering what makes some people particularly vulnerable to an increase in pollution, even in a relatively unpolluted Canadian city. To find out, the researchers exposed healthy volunteers to high concentrations of PM-2.5. They found that endothelin concentrations doubled in healthy people's blood when their exposures tripled from 50 micrograms per cubic meter ($\mu g/m^3$) to 150 $\mu g/m^3$, a range typical for the world's most polluted cities.

Although the endothelin jolt didn't hurt these healthy volunteers, previous studies have shown that people with artery-clogging atherosclerosis have a higher risk of dying after a heart attack if they had endothelin concentrations comparable to the spikes observed in the volunteers' blood.

Interestingly, Vincent notes, his team could trigger increases of endothelin only with the kind of dirty dust usually encountered outside—particles that carry some chemical hitchhikers, including metals and hydrocarbons. When the researchers washed the particles to remove those hitchhikers, the PM-2.5 exposures had no impact on blood concentrations of endothelin.

Harvard School of Public Health scientists also have begun exploring dust's cardiovascular effects. Gregory A. Wellenius and his colleagues exposed dogs to either clean filtered air or air seeded with 30 times the concentration of particulates that local outdoor air carried that day. The exposures lasted 6 hours on 3 or 4 consecutive days.

Right after each exposure, the researchers simulated a heart attack in the dogs by constricting a surgically implanted balloon that temporarily shut off a coronary artery. During this blockage, the researchers measured the heart's growing oxygen debt.

The debt was significantly larger in animals that had been exposed to fine airborne dust, the scientists reported in the April *Environmental Health Perspectives*. A dog's other coronary arteries couldn't dilate as well and couldn't compensate for the blocked vessel if the animal was inhaling particulates, Wellenius speculates. Such a reaction is "entirely consistent" with an endothelin boost from exposure to particulate pollution, he says.

**A NOSE FOR CLUES** The collective message from the 200-or-so Mexico City mongrels that Calderón-Garcidueñas and her colleagues studied is also alarming.

A neuropathologist, she was concerned that if dust could damage lung tissue, it might also break down the capacity of nasal passages to block substances from entering the brain. She now reports tracing metals associated with fossil fuel combustion—chiefly vanadium and nickel—from the dogs' nasal tissue, through the olfactory bulb, and into the frontal lobe and hippocampus of the animals' brains.

Because such metals can foster damage by generating free radicals, Calderón-Garcidueñas looked for signs of brain changes in dogs living in areas with heavy particulate pollution.

Dogs often serve as a model for human age-related cognitive impairments. Some dogs at age 10 and older develop the waxy brain plaques characteristic of Alzheimer's disease (*SN: 11/3/01, p. 286*). "In Mexico City," Calderón-Garcidueñas told *Science News*, "we are seeing [plaque] pathology in 11-month-old pups"—a dramatic acceleration in the development of the signature of Alzheimer's disease.

## Dust Rules

### A finer standard governing particulate pollution is on the horizon

Environmental agencies around the world today regulate dusty pollutants on the basis of mass—not chemistry—and most governments focus on the particles easiest to catch and quantify: those that are 10 micrometers across (the PM-10 fraction), rather than 2.5-micrometer particles (PM-2.5) and smaller ones.

Seven years ago, the U.S. Environmental Protection Agency announced it would soon require states to regulate airborne concentrations of PM-2.5 pollution in recognition of the smaller particles' significantly greater toxicity than larger particles and ability to move far deeper into the lungs, (*SN: 12/21/96, p. 410*). Almost immediately, the agency was sued by several industries that would be affected.

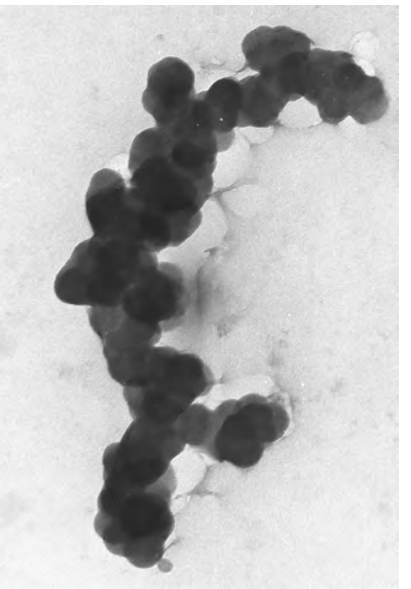
It took a Supreme Court ruling 2 years ago to get the regulations back on track (*SN: 3/10/01, p. 159*). Yet "we're definitely several years away" from enforcement of any regulation limiting PM-2.5 pollution, says EPA spokesman Dave Deegan in Washington, D.C.

So, for now, federal law prohibits PM-10 concentrations in air from exceeding an average of 150 micrograms per cubic meter ($\mu g/m^3$) over any 24-hour period or a 50 $\mu g/m^3$ daily average over an entire year. When PM-2.5 rules do go into effect, they'll restrict the 24-hour average air concentration of those small particles in any city to 65 $\mu g/m^3$ and the annual average concentration to just 15 $\mu g/m^3$. —J.R.

These data are "definitely worrisome," she says, especially in light of her preliminary findings of a similar breakdown in the nasal tissue of many people living in Mexico City.

Another new study in mice, this one by EPA scientists, suggests that particulates do their harm via the metals they sometimes carry. They found signs that exposure to metal-laden PM-2.5 aggravates asthma much more than does relatively metalfree dust.

Stephen H. Gavett of the agency's Research Triangle Park, N.C., laboratory and his colleagues used dust collected in two eastern German towns—one an industrial community polluted with metals and other combustion products and the other a farm village with relatively clean air. The metal-rich dust, gathered by Joachim Heinrich of the GSF Institute of Epidemiology in Neuherberg, Germany, proved far more potent in aggravating asthmatic constrictions of an animal's airways, the researchers will report in the September *Environmental Health Perspectives*.



**SOOTY RESIDUES** — This chain of ultrafine particles came from mucus lining an airway of a nonsmoking, lifetime resident of Mexico City. The sooty, submicron-scale spheres appear to be diesel-exhaust particles.

CHURG/UNIV OF BRITISH COLUMBIA

**ULTRAFINES, ULTRABAD?** If such studies suggest that the composition of inhaled particles affects their toxicity, other findings indicate that particle size can greatly exacerbate the problem.

In studies with isolated lung cells, for example, ultrafine particles proved to be between 10 and 50 times as potent as PM-2.5 or PM-10 particles in inducing free-radical damage, such as inflammation. Andre Nel of the University of California, Los Angeles and his team reported their findings in the April *Environmental Health Perspectives*.

Nel's team also found that ultrafine particles from urban air carry far more toxic combustion hydrocarbons on their surface, per unit mass, than larger particles do. Further probing showed that the smaller motes tend to lodge in cells' mitochondria, the organelles that generate power. The particles turn the mitochondria into "functionless bags," says Nel. And when these powerhouses die, he says, so do the cells they power.

Donaldson has tested "particles that are completely naked"—motes of pure carbon or titanium dioxide, for instance—and shown they cause no damage when delivered to rat lungs as 10-micrometer-wide particles. But crush them into submicron pieces, he says, and "they become highly inflammogenic to the lungs."

Why? Lung-defending macrophages can easily catch and discard the occasional big particle that gets lobbed their way. Exposing the lungs to large numbers of the smallest particles, however, "may completely overwhelm their defenses," Donaldson says. His team's data support that scenario.

After decades of research, says Donaldson, toxicologists are still discovering ways that fine dust particles can kill. And as the dust particles in their sights get ever smaller, the challenge of controlling their release gets ever larger. ■

*Continued from page 79*

toxic PTFE-derived gases." However, to fry items like eggs and pancakes, the pan has to be hot before you put oil and food into it. The article was enough to send me out to replace my nonstick frying pan.

**MARY SCHAER,** PORTLAND, ORE.

In the article, Günter Oberdörster makes the comment, ". . . you have to put it in perspective. . . . Cooking with such pans is less dangerous than driving a car." That's still quite frightening.

**BILL GALCHER,** REDWOOD CITY, CALIF.

Nonstick kitchen appliances such as waffle irons, Foreman grills, sandwich makers, and so forth have nonstick coatings and call for preheating prior to cooking. Though I suspect that such appliances wouldn't reach temperatures as high as pots or pans on a stove, appliance makers should be interested in ensuring safety in their preheating instructions.

**DAVE TRENDLER,** ALEXANDRIA, VA.

I read "Sticky Situation" with sorrowful remembrance. About 10 years ago, we let an unattended, coated pot overheat when we fell asleep. Fortunately, the incident didn't cause a major fire, but the artichokes and coating were charcoal crisp when we woke to the smoke alarm. We aired out the apartment and considered ourselves lucky until the next morning, when my lilac crested Amazon parrot was having trouble breathing and, within minutes, died in my hands. My lungs were sore and I had a headache and lack of energy for a few days. You didn't mention what fumes were given off by the overheated coating, but I was told at the time that it was similar to mustard gas.

**COLIN MESKELL,** BELLVUE, COLO.

## Love the one you're with

Your short piece "Findings puncture self-esteem claims" (*SN: 6/7/03, p. 365*) didn't say how self-esteem was assessed. Overdeveloped egotism is often a compensatory phenomenon in individuals with low self-esteem and can falsely present as high self-esteem. Self-reported self-regard taken at face value can lead to wrong conclusions about the effects of different levels of self-esteem on behavior, perception, relationships, and other aspects of life.

**LAURIE WINOGRAND,** SEATTLE, WASH.

**Corrections** *Species names were misspelled in two articles. In "Herbal Lottery"* (SN: 6/7/03, p. 359)*, the plant should have been called* Echinacea angustifolia *(not* augustifolia*). In the sidebar of "Phages Behaving Badly"* (SN: 7/12/03, p. 27) *the bacterium is* Streptococcus canis *(not* canus*).*

# OLD WORMS, NEW AGING GENES

## Biologists look into DNA for the secrets of long life

BY JOHN TRAVIS

For more than a decade, Cynthia Kenyon has watched microscopic worms of the species *Caenorhabditis elegans* live far longer than they should. She has seen mutant strains of this worm, which is normally dead and gone after a mere 2 or 3 weeks, last well into their second month. It's as if a person lived to be 200 years old. Kenyon's long-lived worms are a result of mutations in individual genes.

That's a radical notion to many scientists who have long thought of aging as an uncontrollable process of deterioration that isn't regulated by single genes.

"There have to be genes that affect life span," counters Kenyon of the University of California, San Francisco. Noting the dramatic differences in life span among various animals—a mouse may last for 2 years while a bat can live for half a century—Kenyon has become convinced that longevity has evolved in animals many times. She argues that her long-lived nematodes can reveal some of the fundamental molecular biology that controls longevity in more-complex organisms, even people.

In 1993, Kenyon and her colleagues jump-started the field of aging genetics when they reported on a mutant strain of *C. elegans* that lives twice as long as normal. It showed the largest proportional lifespan extension of any animal known at the time. Researchers eventually determined that this long-lived nematode strain arose from a defect in a hormone-triggered cascade of molecular signals that resembles one in people that is prompted by the hormone insulin. Mutations affecting a similar hormone-driven cascade in fruit flies can lengthen the lives of these insects as well.

Over the past few months, Kenyon's team and several other groups of worm researchers have documented an unexpectedly large number of genes controlled by this hormonal system, including genes involved in stress responses and antimicrobial actions. This aging pathway appears to be at work in mammals, also. Two research teams have shown that altering how mice respond to insulin or a related hormone can extend the animals' lives, raising the prospect that manipulating these hormones in people could slow aging or enable them to age with better health.

"There's a possibility in humans that a similar aging pathway is at work," says Catherine Wolkow of the National Institute of Aging in Bethesda, Md.

SANGER INSTITUTE/WELLCOME PHOTO LIBRARY

**AS THE WORM TURNS —** These microscopic worms typically live 2 to 3 weeks, but mutations in certain genes can more than double that life span. Biologists are examining whether these genes also control the aging process in more-complex animals, including people.

**WRINKLED WORMS** Some scientists challenge Kenyon's work by claiming that her long-lived nematodes aren't actually aging slowly. Perhaps, these critics say, the genetically altered worms become old and frail at the normal pace but simply have had a major cause of death eliminated. Settling that controversy requires a routine way of measuring the aging process.

In her initial work with *C. elegans*, Kenyon gauged the increasing age of a worm by its decreasing mobility. More recently, she and her colleagues trained high-powered microscopes on aging nematodes and documented many changes in various tissues. Among other signs of deterioration, cell boundaries become less distinct, and the insides of cells go from smooth to curdled and become filled with cavities. In complementary work, Monica Driscoll of Rutgers University in Piscataway, N.J., and her coworkers found that worm muscle fibers lose their organized appearance as worms age (*SN: 10/26/02, p. 260*).

Like elderly people, who have wrinkles and other signs of age, "old worms have a particular look to them," Kenyon says.

Now that biologists have an idea of what happens to a worm as it grows old, they may be able to make better sense of all the genes they've identified over the past decade that affect aging. Indeed, the number of these longevity genes continues to grow. At a recent annual international meeting of *C. elegans* researchers, Kenyon's group reported unearthing more than 30 previously unrecognized genes that, when mutated, extend the nematode life span.

At the moment, the best-characterized genetic pathway of worm aging is the one Kenyon's group described in 1993. In their original report, the scientists showed that mutations in two genes, dubbed *daf-2* and *daf-16*, had major effects on nematode longevity.

Worms with a certain mutation in *daf-2* had a doubled life span, but worms with mutations in both genes had a normal life span.

Kenyon's group was able to deduce from these observations that a working *daf-16* gene tends to trigger other worm genes that would promote longevity, while a functioning *daf-2* gene normally suppresses the activity of *daf-16* or its protein.

Why would the worm, or any animal, have a gene such as *daf-2* whose apparent purpose is to limit the organism's life span?

> "There's a possibility in humans that a similar aging pathway is at work."
>
> —CATHERINE WOLKOW

The gene appears to be part of a genetic system that allows worms to regulate their development—and, thereby, their lifespan—depending on whether environmental conditions are suitable for reproduction. When nutrients are scarce, growing worms don't develop fully, but instead take on a thinner, sexually immature form known as dauer. In this state, the organism can hang on for months and increase its chances of encountering richer living conditions. Worm biologists consider these long-lived dauers akin to the spores that bacteria form to ride out tough conditions.

Long before Kenyon's work, other researchers linked *daf-2* and *daf-16* to this arrested form of development. The genes' names derive from "dauer formation." Completely knocking out the activity of *daf-2* sends a developing worm right into the dauer state, whether or not nutrients are scarce. Kenyon found something more intriguing: Certain subtle mutations in the gene enabled a developing worm to bypass the dauer state but still have an abnormally long life span.

In 1997, a research group led by Gary Ruvkun of Massachusetts General Hospital in Boston finally identified the DNA sequence of *daf-2*. To everyone's surprise, the scientists found that its protein, DAF-2, resembles human cell–surface proteins, or receptors, that respond to insulin and another hormone known as insulinlike growth factor–1 (IGF-1). The worm's receptor is a primitive version of these human receptors, says Ronald Kahn, director of the Joslin Diabetes Center in Boston.

As for *daf-16*, it turned out to encode a DNA-binding protein that turns on other genes. Known as a transcription factor, this protein, DAF-16, is apparently suppressed when a hormone triggers DAF-2. The *daf-2* mutations, therefore, extend a worm's lifespan because they unleash DAF-16, enabling it to trigger genes that tend to promote longevity.

**PULLING OUT ALL THE STOPS** In their 1993 report, Kenyon and her colleagues speculated that the identification of genes under the sway of *daf-16* "could lead to a general understanding of how life span can be extended." In a flurry of recent publications, some of those genes have finally come to light.

In the April *Aging Cell*, a recently launched journal devoted to the molecular biology of aging, James H. Thomas of the University of Washington in Seattle and his colleagues identified several dozen *C. elegans* genes under the control of DAF-16. To do this, the scientists sought genes active in worms with mutations in *daf-2* and compared these to genes active in worms with mutations in both *daf-2* and *daf-16*.

The investigators also pinpointed genes containing a particular DNA sequence that DAF-16 binds to, implying that the protein controls the activity of those genes. Many of the genes governed by this protein are known to have roles in the metabolism and stress responses of worms.

In a paper published in the April 25 *Science*, Ruvkun's group unveiled its own list of genes regulated by the protein DAF-16. He and his colleagues searched the complete DNA sequences of *C. elegans* and the fruit fly *Drosophila melanogaster* for locations where DAF-16 might bind. They identified 17 cases in which the two animals have a similar gene with that characteristic sequence. They also found that the activity of six of those genes in the worms is affected by mutations of *daf-2* and *daf-16*. The data indicate that DAF-16 turns on some of the six genes and suppresses others.

Ruvkun's team used a technique called RNA interference to turn off these six genes, one at a time, in normal worms. Several of the inactivations extended the life span of *C. elegans*, but not as much as the doubling normally produced by *daf-2* mutations.

Through her own comparison of gene activity in worms with *daf-2* and *daf-16* mutations, Kenyon has also weighed in on the issue of DAF-16 targets. She and her colleagues found that DAF-16 turns on a variety of genes that make antimicrobial proteins. A DAF-16–boosted immune response may explain why long-lived mutant strains of *C. elegans* tend to be more resistant to death from bacterial infestation than normal worms are; Kenyon has found that aging worms typically die when the bacteria they eat overrun their bodies.

Kenyon's team also found that DAF-16 controls the production of many proteins that cells use to thwart damage to DNA and other molecules in response to factors such as heat or highly reactive molecules known as free radicals. A popular theory holds that aging is the result of a slow accumulation of free-radical damage.

Long-lived worms with a mutant *daf-2* make extra amounts of enzymes that defuse free radicals, experiments by Kenyon and others have shown. The worms also make more so-called heat shock proteins, which prevent other proteins from folding abnormally or aggregating into clumps. In the April *Aging Cell*, Gordon J. Lithgow of the Buck Institute for Age Research in Novato, Calif., and his colleagues demonstrated the importance of these protective proteins. The researchers introduced extra copies of the gene for one heat shock protein called hsp-16 into worms, and that alone increased the animal's average life span by more than 10 percent.

Last year, Kenyon and her colleagues added another character to the unfolding story. In the July 2002 *Genetics*, they revealed a key partner for DAF-16 in coordinating the worm's antiaging stress response: a transcription factor called heat shock factor (HSF). When the researchers used RNA interference to deactivate the gene for HSF, worms died earlier than normal. By monitoring the worms' tissues under microscopes, Kenyon's group showed that this premature death resulted from accelerated aging.

In the May 16 *Science*, the researchers flesh out the story yet more by showing that *daf-2* mutants don't have a doubled life span if the gene for HSF is also mutated. That raises HSF to DAF-16's level of importance. Indeed, Kenyon's group found a group of worm genes, including some that encode heat shock proteins, whose activities are influenced by both proteins working in concert.

Wolkow notes that some investigators had hoped that DAF-16 controlled just a few genes. If that were the case, it would in theory make it easier to extend people's life span by manipulating those genes. "It looks like it's much more complicated," Wolkow says. "I don't think we knew that at the outset."

"The worm seems to be pulling out all the stops. It's doing all sorts of things to increase life span," adds Kenyon. "It's a lot of little contributions from lots of genes."

**THE BIG QUESTION** Evidence is building that investigations into worm aging could have a payoff in mammals. Whereas worms have a single receptor matched to insulinlike signals, mammals have developed distinct hormonal pathways for insulin and IGF-1, each characterized by its own dedicated receptor.

In one series of experiments, Martin Holzenberger of Saint Antoine Hospital in Paris and his colleagues created strains of mice in which one or both copies of the rodent gene for the IGF-1 receptor had mutations. Mice lacking any normal copies died as embryos. However, mice with one working copy developed normally and lived, on average, 26 percent longer than did animals with two normal copies of the IGF-1–receptor gene. Holzenberger's group reported these results in the Jan. 9 *Nature*.

Similar results have emerged from the study of mice lacking some insulin receptors. A research team led by Kahn has created mouse strains that lack insulin receptors in specific tissues such as liver, brain, and fat. In the Jan. 24 *Science*, Kahn and his colleagues reported that mice missing the receptors in their fat tissue live 18 percent longer on average than typical mice.

The long-lived mice were also leaner, despite eating normal amounts of food, Kahn's group found. That's not surprising, because one of insulin's roles is to signal cells to store fat, but the researchers' findings could help uncover why severely calorie-restricted diets extend the life spans of many animals (*SN: 3/15/97, p. 162*). It may not be the reduction in calories that's crucial for boosting longevity, but rather the animals' leanness, says Kahn. His group is now putting the mutant mice on diets to see whether there's any additional life span extension.

> "There have to be genes that affect life span."
>
> —CYNTHIA KENYON

Kahn also plans to study the longevity of other mutant mouse strains to determine how insulin signaling in each tissue contributes to aging. He's particularly interested in mice that don't have insulin receptors in their brains, since studies in flies and worms have indicated that the nervous system has a key role in mediating insulin's impact on aging.

When she looks at the progress researchers have made on aging over the past decade, Kenyon admits she's stunned. "There wasn't a field when we started," she says. "Now, there are a lot of people working on aging. We've learned a huge amount."

For all their recent success, however, worm researchers have plenty of questions about the biology of aging that should keep them going for generations. Lithgow says he still can't answer a fundamental question: "Why do worms live 20 days and not 20 years?" ■



# OF NOTE

HEALTH PHYSICS

## Antiglare eye black is better than tape

Baseball and football players have claimed for decades that swiping black grease under their eyes helps them peer into a sunny sky to catch a ball. In recent years, the smudges have given way to tidier patches of black tape.

Brian DeBroff and his colleagues at Yale University School of Medicine now report that the black grease really does work—but that the newfangled black-tape patches don't stand up to the light of day.

The researchers used a standard test to assess how well 46 students could discern contrast against a sunlit background. Then the scientists randomly assigned the students to wear black grease, tape patches, or clear petroleum jelly. When retested, students sporting the black grease showed significant improvement in discerning contrast, whereas the other two groups didn't.

DeBroff says that he doubted that eye black works at all. "We thought it was a kind of psychological war paint," he says. Now, he suggests that the black grease cuts glare reflecting off the cheekbones. Exactly why grease works better than patches is unclear, he says. The findings appear in the July *Archives of Ophthalmology*. —N.S.

BIOMEDICINE

## Anthrax toxin curbs immune cells

Scientists have revealed yet another way in which the bacterium that causes anthrax disarms the immune system.

The microbe, *Bacillus anthracis*, produces a molecular complex that's called lethal toxin known to interrupt a cascade of signals inside macrophages, the immune cells that envelop and destroy bacteria (*SN: 5/9/98, p. 299*). This interference kills the macrophages.

The toxin also interrupts the same signaling cascade in dendritic cells, another class of immune cells, Bali Pulendran of the Emory Vaccine Research Center in Atlanta and his coworkers report in the July 17 *Nature*. Dendritic cells are crucial to an immune response since they alert antibody-producing cells and other protective cells to the presence of dangerous microbes.

Pulendran's team found that, unlike macrophages, dendritic cells exposed to the anthrax toxin don't die. However, the cells can no longer stimulate the activity of other cells of the immune system. Injections of the toxin into mice confirmed that it suppresses dendritic-cell function.

The investigators speculate that the anthrax toxin could be modified into a drug that dampens immune responses. Such a drug might alleviate autoimmune disorders or prevent transplanted organs from being rejected. —J.T.

FISH

## The secret appetite of cleaner wrasses

The little helpers known as cleaner fish, which nibble parasites off larger reef fish, actually prefer to nibble their clients.

Earlier experiments had already caught cleaner fish apparently cheating, taking nips of flesh and skin-covering mucus from their customers, says Alexandra Grutter of the University of Queensland in Brisbane, Australia. However, she says, it wasn't clear whether the cleaner fish actually had a taste for their clients or were just hungry enough to nip the customer when the search for parasites proved arduous.

Grutter and Redouan Bshary of Cambridge University in England administered a taste test. They trained the cleaner wrasses (*Labroides dimidiatus*) to eat off underwater trays and then offered an array of parasites and fish-mucus samples.

The cleaners ate significantly more mucus than parasites, the researchers report. What's more, parrotfish mucus proved more appealing than snapper mucus. The taste test feeds the speculation that cleaning developed from opportunistic nipping at other fish, Grutter says. No wonder client fish periodically dart threateningly at their cleaners, she says. —S.M.

QUAILS

## Some female birds prefer losers

When a female Japanese quail watches confrontations between two males, she later tends to choose the loser over the champ.

Studies of male clashes in other animals, such as Siamese fighting fish, have generally found that females prefer winners, says Alexander G. Ophir of McMaster University in Hamilton, Ontario. Scientists had reasoned that a winning male offers access to better territories, resources, and genes.

The males of the quail species *Coturnix japonica* scrap readily, and gamblers in Asia used to pit them against each other like fighting cocks, Ophir says. Canadian rules for animal research forbid staging actual fights, so Ophir and Bennett G. Galef, also at McMaster, used a confrontation in which males peck at each other through a clear partition. The male that pecked most often was declared the winner.

Ophir let a female view a sham fight and then monitored which male she chose to approach. The females spent more of their time close to the losers.

Ophir offers a possible explanation: Male Japanese quail play rough. During mating, they chase females, drag them around by their feathers, peck them, and try to mate with their heads. Ophir hypothesizes that by choosing the loser of a confrontation, a female reduces her risk of injury.

This protective behavior may derive from tough experience. The researchers did another version of the experiment, comparing females that differed in sexual experience. Previously mated females again tended to select the loser of the males' pecking competition, but virgins chose the winner. —S.M.

PARROTS

## Maybe what Polly wants is a new toy

Changing the toys frequently in a parrot's cage may reduce the bird's tendency to fear new things. Bird keepers grow anxious as their birds fidget, sometimes plucking their own feathers, says Rebecca Fox of the University of California, Davis. The fearfulness, or neophobia, also raises questions about bird development.

Research in rats linked neophobia to early separation from Mom, but experiments found no such link for parrots. Other studies even showed that nestlings fed by people were less afraid of new things until age 6 months than were birds reared by their parents. The effect doesn't last, though, and the hand-reared birds by 1 year of age show the typical neophobia.

**SCARY STUFF?** Young, hand-raised orange-winged Amazons cope with novelty better initially than parent-raised birds do.

FOX

Fox wondered whether hand rearing delayed neophobia because it exposed birds to extra novelty. Fox and James R. Millam of U.C.–Davis divided 32 young orange-winged Amazon parrots into two groups. For one group, she replaced two novel objects in their cages five times a week; parrots in the other group kept the same toys. After 11 weeks, she switched treatments.

To measure neophobia, she filled a dish with peanuts and apples, a treat that she calls "the Amazon equivalent of chocolate," then dangled an unfamiliar object above it and timed a bird's delay in approaching. The weeks of frequent toy changing brought a "moderate but significant" easing of neophobia, she reports. The frequent-change birds approached in about 6 minutes instead of 10 minutes.

Fox also found that some objects provoked more reaction than others. Of the 15 doodads she had purchased, three—a little stuffed pink elephant, a black plastic box, and a mesh shower puff—proved too scary to use in the experiments. "Not all novelty is equal," Fox says. —S.M.

LIZARDS

## Why do two-sex geckos triumph?

The smell of one invading species of gecko has a mysterious influence on the activity of the defending species, but the voodoo doesn't work on first exposure, reports a researcher in Hawaii.

The Hawaiian Islands and many other islands in the Pacific Ocean have long been home to *Lepidodactylas lugubris*, a species of unisexual lizards. These geckos, which are effective colonizers, probably reached Hawaii with the Polynesians. As more people moved around the Pacific during World War II, a bigger species (*Hemidactylus frenatus*) that has two sexes started spreading. When *H. frenatus* arrives on an island, the population of the unisexual species plummets. Susan Brown, a biologist at the University of Hawaii at Hilo, wonders why.

Scientists had speculated that because the geckos of *H. frenatus* are bigger, they poach the unisexuals' food. Brown doubts that explanation, since there seem to be plenty of bugs to go around, she says.

Instead, she proposes that *H. frenatus* inhibits the behavior of the smaller species. When the *L. lugubris* geckos are on their own, "these ladies are really aggressive," she says. But when she put the two species together, the *L. lugubris* were subdued. Moreover, the *H. frenatus* scent by itself could dampen aggression and reduce egg laying by the smaller geckos.

In new work, she raised the unisexual geckos in individual quarters and then exposed them to the dreaded scent. The first time a unisexual gecko encountered the other species, the smaller gecko attacked with her species' usual fervor. On her next exposure, however, she became subdued. Brown suspects that such a subtle interaction between the species is fueling the spread of *H. frenatus*. —S.M.

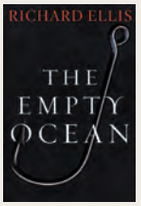
# Books

A selection of new and notable books of scientific interest

### THE EMPTY OCEAN

**RICHARD ELLIS**

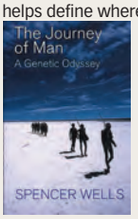
Ellis, a renowned marine illustrator and sea lover, explores the plight of the world's oceans and discusses what can be done to restore their bounty. He reports that overharvesting of the oceans has gone on for millennia. This, combined with the introduction of nonnative species and pollution to various seas, threatens the entire ocean ecosystem. Ellis presents sea creatures that either are extinct or are seriously threatened, including whales, great auks, cod, and coral. These profiles combine with abundant data and deftly written anecdotes to complete a portrait of the decline of the oceans. Overall, this book challenges people to rectify the problem. ***Island Pr, 2003, 367 p., b&w illus., hardcover, $26.00.***




### THE JOURNEY OF MAN: A Genetic Odyssey

**SPENCER WELLS**

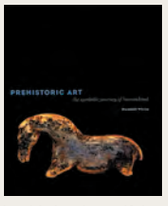
Advances in genetics help us understand who we are. Geneticist Wells explains how his field also helps define where we came from. He presents evidence supporting the notion that modern humans didn't descend from Neandertals. Rather, we trace our heritage to an Eve who lived about 150,000 years ago. Wells explains how scientists use chromosomes to trace the spread of humanity from Africa into Eurasia and around the globe. Data suggest that differing racial types emerged when mountain ranges split population groups and that the entire genetic diversity of Native Americans can be traced to just 10 individuals. Clear exposition and engaging detail make this an informative introduction into population genetics. ***Princeton U Pr, 2003, 224 p., color plates/b&w illus., hardcover, $29.95.***




### PREHISTORIC ART: The Symbolic Journey of Humankind

**RANDALL WHITE**

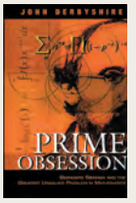
This rather scholarly yet beautiful book surveys images and objects that run through 40,000 years of prehistoric art. With an anthropologist's eye, White places these discoveries in context, discussing the possible uses and meaning of icons found around the globe. Hundreds of vivid photographs depict the representational systems of preagricultural societies. Some of these works are well known, such as the images on cave walls in Lascaux, France. But the bulk of what is presented here, including 5,000-year-old Japanese masks and terra-cotta figurines crafted 25,000 years ago in today's Czech Republic, is more exotic. This is a beautiful and comprehensive overview of the subject. ***Abrams, 2003, 239 p., color photos, hardcover, $45.00.***




### PRIME OBSESSION: Bernhard Riemann and the Greatest Unsolved Problem in Mathematics

**JOHN DERBYSHIRE**

Nearly 150 years ago, Bernhard Riemann posed a deceptively simple question to his peers at the Berlin Academy: Is there a general rule for figuring out how many prime numbers there are up to a given number? Three years ago, the Clay Institute agreed to award a million dollars to the person who can prove Riemann's hypothesis, which states that there is such a general rule. Derbyshire provides the historical background of the Riemann hypothesis and, for mathematically inclined readers, details of efforts to prove it so far. He also explains the impact that any solution to this problem will have on cryptography and other areas. Alternating between telling Riemann's life story and presenting a mathematical primer on the elements of his hypothesis, Derbyshire elegantly explores a vexing topic. ***Joseph Henry Pr, 2003, 422 p., b&w plates, hardcover, $27.95.***




### THE WATER GARDEN ENCYCLOPEDIA: The Ultimate Guide to Designing, Constructing, Planting, and Maintaining Garden Ponds and Water Features

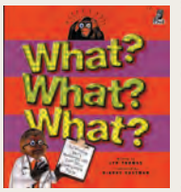
**PHILIP SWINDELLS**

Loaded with color photographs and illustrations and offering clear, step-by-step directions, this guide is a complete resource for creating a formal reflecting pool, fishpond, canal, or even a small water feature on a balcony. Opening chapters help readers assess what designs and features will work best for them, depending on the space they have and the maintenance they're willing to do. The second half of the book details how to build waterfalls, ponds, fountains, and streams, in addition to how to landscape with stepping-stones and bridges. One chapter is devoted to water-loving plants that thrive in these environments. That's followed by tips for maintaining the space. Forty projects are outlined. ***Firefly, 2003, 256 p., color photos/illus., flexibind, $29.95.***


### WHAT? WHAT? WHAT? Astounding Weird Wonderful and Just Plain Unbelievable Facts

**LYN THOMAS AND DIANNE EASTMAN**

"Your body is made up of around 100 billion living cells so tiny that thousands of them could be squeezed onto the period at the end of this sentence." So begins this tour of things you would have never guessed about your own body, inventions, animals, the weather, your house, and the clothes you wear. Children discover an utterly amazing variety of facts, including how much skin a body sheds, how many babies a mouse can produce, and how long it took to build the Taj Mahal. Clever illustrations and riddles add to the fun. Recommended for ages 9 to 12. ***Maple Tree, 2003, 128 p., b&w illus., paperback, $9.95.***

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# LETTERS

## Vocal on herbals

I find the ideas promulgated in "Herbal Lottery: What's on a dietary supplement's label may not be what's in the bottle" (*SN: 6/7/03, p. 359*) deeply disturbing. The idea of pulling out a couple of chemicals and standardizing them is a turning away from the holism that herbal remedies represent. This is the very essence of the complaint against conventional pharmaceuticals and why people are turning to herbals.

That there is a problem with consistency in marketed herbal products seems clear. However, requiring patentable, purified chemical combinations would be tantamount to making true herbal medicine illegal. In an age in which a leading cause of death in the United States is hospital-and-doctor-caused illness, I believe I have the right to choose a different path to health than conventional medicine and pharmaceuticals.

**VICTORIA BAKER,** REDWAY CALIF.

Several years ago, I corresponded with a physician at the University of Brussels about a disturbing rash of kidney problems in young European women who were taking Chinese herbs to lose weight. Some of them required kidney transplants. An unlisted contaminant, *Aristolochia*, turned out to be the source of the problem.

**JAMES A. ERDMAN,** CRESTONE, COLO.

Whoa! One of the attractions of herbal remedies is that they don't kill people. Pharmaceuticals kill around 2 million people a decade. The attitude of the Food and Drug Administration is to get rid of the competition. Destroying any industry is a bad idea, but that's what this monster is all about. Market forces take care of the shysters in time, but the FDA uses force and fraud to destroy legitimate concerns. My *Echinacea* works just fine, thank you.

**EDWARD G. ROBLES,** FRANKLIN, N.C.

*In fact, herbal remedies have been implicated in many deaths. See "When Herbs Bite Back"* (http://www.sciencenews.org/20020504/food.asp)*, "Honey of a Threat"* (http://www.sciencenews.org/20020427/food.asp)*, and "Homing in on Ephedra's Risks"* (http://www.sciencenews.org/20030419/food.asp). —J. RALOFF

## Nonstick Sticklers?

"Sticky Situation: Nonstick surfaces can turn toxic at high heat" (*SN: 6/7/03, p. 355*) noted that ". . . with food in it, a pan will never reach temperatures that produce

*Continued on page 74*

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