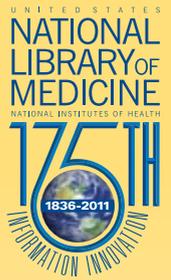


# NIH MedlinePlus

Trusted Health Information  
from the National  
Institutes of Health



Spring 2011

the magazine



Paula Abdul | Complex Regional Pain Syndrome



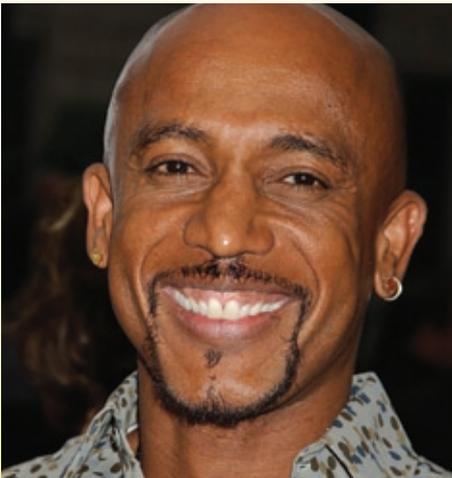
George Clooney | Spinal Cord Tear



Melanie Griffith | Chronic Knee Pain

**SAFELY  
MANAGING**

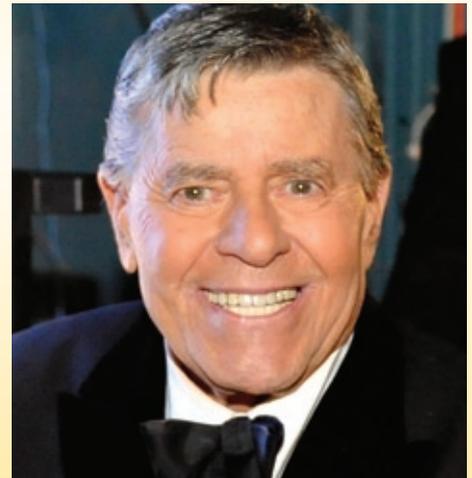
# CHRONIC PAIN



Montel Williams | Multiple Sclerosis



Bo Derek | Herniated Disc



Jerry Lewis | Chronic Back Pain

***Plus, in this issue!***

**Solving Medical Mysteries | Blood Clots That Kill | Coping with Food Allergies**



Photo: NLM

Donald West King, M.D.  
FNLN Chairman

## Support the Clinical Trials Conference

If you or your organization would like more information about supporting the 2011 Clinical Trials Conference or other NLM/FNLN programs, please contact Gage Lewis.

Email: [glewis@fnlm.org](mailto:glewis@fnlm.org)  
Phone: 202-683-2558

## June 6–7, 2011 Clinical Trials Conference: New Challenges & Opportunities

We are pleased to announce that the Friends of the National Library of Medicine (FNLN) and the National Library of Medicine (NLM), in association with the American Association for the Advancement of Science (AAAS), are cosponsoring a major conference to address the important topic of clinical trials: “Clinical Trials: New Challenges and Opportunities.”

On Monday and Tuesday, June 6–7, the 2011 NLM/FNLN Conference will explore the future of clinical trials, as part of the National Library of Medicine’s 175th Anniversary celebrations. Clinical trials are scientific studies that use human volunteers to help medical professionals find better ways to prevent, screen for, diagnose, or treat disease.

The conference, held at the Natcher Center on the NIH campus in Bethesda, Md., will convene key government, industry, academic, and patient advocate representatives to discuss pressing issues in clinical trials, including:

- Roles of NIH and ClinicalTrials.gov, the FDA, industry, and academia
- Registration and results reporting at ClinicalTrials.gov
- Effects of patient-driven digital networks on clinical research
- Novel methodologies to improve efficiency and quality
- Clinical research’s response to public health needs
- Forging government-industry partnerships
- Improving medical care by disseminating trial results

We hope that those members of the American public who are interested in the vital and evolving role of clinical trials will make plans to attend this conference.

Sincerely,  
Donald West King, M.D., Chairman  
Friends of the National Library of Medicine



## How to Attend

To sign up to attend the 2011 Clinical Trials Conference, visit [www.fnlm.org](http://www.fnlm.org) and fill out the attendance form on the Web site. Questions may be directed to [helen.harley@fnlm.org](mailto:helen.harley@fnlm.org); 202-679-9930 (8:30–5:00 ET)

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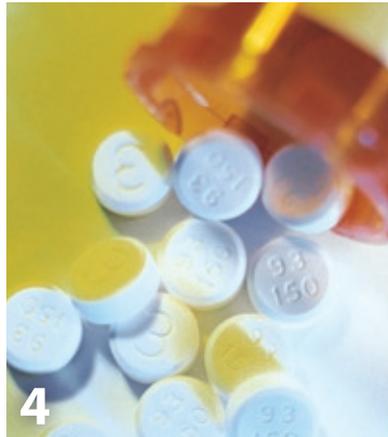
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**Joanna Karpinski and Josh Widzer manage food allergies—even cake.**

The National Institutes of Health (NIH)—the Nation's Medical Research Agency—includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical, and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit [www.nih.gov](http://www.nih.gov).

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Photos: (top of page) Comstock, (center) NIH Undiagnosed Diseases Program, (bottom) Michael Kent Photography (cover) Associated Press



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From NIH Director Dr. Francis S. Collins

# The Promise and Payoff of Rare Diseases Research

**Francis S. Collins, M.D., Ph.D., Director of the National Institutes of Health**, led the successful effort to complete the Human Genome Project, a complex multidisciplinary scientific enterprise to map and sequence human DNA. He spoke recently with *NIH MedlinePlus* magazine about the increasing promise of genetics research to the investigation and diagnosis of rare diseases.

## **Why should we focus on rare diseases when they affect so few people?**

If you or your family were affected, it wouldn't be rare for you. And the study of rare diseases has taught us more than most people realize. Furthermore, the opportunities to capitalize on what we have learned so far have never been greater. If you care at all about biology and about understanding medicine, rare diseases are critical.

## **How many rare diseases are there?**

Altogether, rare diseases affect almost 25 million Americans. Worldwide, there are more than 6,000 that have an impact on people.

## **How much progress has there been toward understanding rare diseases?**

The good news is that we have learned a lot about the molecular basis of many of those that are caused by single genes that have gone awry. The bad news is that treatments are available for fewer than 200 of them at the present time.

## **How much does the mapping of the human genome help?**

The Human Genome Project has provided many of the tools

that have made it possible to reach our current understanding about the molecular causes of disease. But, I think it's fair to say that most of what we've learned from the genome project has not yet been applied. We want to accelerate that process. And that's one of my goals.

## **What is the state of the art of genetics and disease now?**

The ability to identify the molecular basis of a disease, even a very rare one, has progressed rapidly. The challenge now is to develop clinical interventions in fewer than the 20 to 30 years it takes through traditional research methods.

## **Have you an example of a disease on which there has been substantial progress?**

It has been just eight years since the cause of progeria, a rare childhood disease that causes rapid aging, was discovered in my lab. And we now have kids in clinical trials, some of them for more than two years. We were lucky here because the gene involved turned out to be one that we knew a lot about. And we were particularly lucky because that information suggested use of a drug that was developed for an entirely different reason; a "repurposing," if you will. That will happen from time to time, and we should not miss such opportunities.



# More Information About Genetic and Rare Diseases

Two agencies at the National Institutes of Health (NIH)—the National Human Genome Research Institute (NHGRI) and the Office of Rare Diseases (ORD)—created the Genetic and Rare Diseases Information Center (GARD) to help people find useful information, in English or Spanish, about genetic and rare diseases.

Information is often hard to find for many genetic and rare diseases. Even if you can find information, it is often hard to know if it is correct. GARD can help you if you want to know more about a genetic or rare disease for yourself, a family member, a friend, or someone you take care of. GARD can provide you with timely and correct information.

## What can GARD do for you?

Information Specialists will search for answers to your questions and help you understand:

- What is known about the disease.
- What research studies are going on.
- What genetic testing and services are available.
- Which advocacy groups you can contact.
- What has been written recently about the disease in medical journals.

## How do I contact GARD?

You can talk to an Information Specialist, from noon to 6 p.m. Eastern time by:

- Telephone: 1-888-205-2311
- TTY: 1-888-205-3223
- International number: 301-251-4925

You can write to GARD anytime by:

- E-mail: [GARDinfo@nih.gov](mailto:GARDinfo@nih.gov)
- Letter:  
Genetic and Rare Diseases Information Center  
P.O. Box 8126  
Gaithersburg, MD 20898-8126
- Fax: 301-251-4911

“The challenge is to cross the gulf between the molecular understanding we now have of thousands of diseases and develop treatments for them. And this is where NIH can play a critical role in supporting the necessary translational research.”

### Any other diseases with similar progress?

Yes. Research is showing significant potential for cystic fibrosis, sickle cell anemia, Niemann-Pick Disease Type C, and Fragile X syndrome.

### What does the research future hold?

The challenge is to cross the gulf between the molecular understanding we now have of thousands of diseases and develop treatments for them. And this is where NIH can play a critical role in supporting the necessary translational research.

## Helping Americans be as healthy and active as possible

is a goal shared by all health professionals. But assisting people in managing chronic pain is tough. Strong medicines that relieve the pain can also create new problems and must be used with great care. Those who prescribe these medicines, and those who use them, must learn to do so safely and effectively. Sometimes, non-drug therapies, such as massage, acupuncture, or exercise, can help, as well.

# Safely Managing Chronic Pain

### FASTFACTS

- More than 76 million people in the United States live with chronic pain, but surveys show that almost half of them receive no treatment.
- The annual economic cost of chronic pain in the U.S. is estimated to be \$100 billion, including healthcare expenses, lost income, and lost productivity at work and at home.
- Research shows that almost 60 percent of older adults with pain have had it for more than a year.
- According to recent research, close to five million Americans report recently taking prescription pain medication in a potentially unsafe way.
- Although most people taking prescription pain medicines do so responsibly, there has been an increase in drug misuse or even abuse, especially of opioid pain relievers.

## The Two Faces of Pain: Acute and Chronic

What is pain? The International Association for the Study of Pain describes it as “an unpleasant sensory and emotional experience.” There are two basic types of pain, and they are very different.

- **Acute pain**, for the most part, has a physical cause, such as disease, inflammation, or injury to tissues. This type of pain generally comes on quickly, for example, after trauma or surgery, and may be accompanied by anxiety or emotional distress. Acute pain resolves when its cause is treated and healing occurs.
- **Chronic pain** lasts longer than acute, generally over three months. It may start with an injury or other cause, but it persists even after healing has occurred. Chronic pain is widely believed to be a disease, with known changes in the nerves that get worse with time. Due to its persistence, it can cause major problems in every aspect of a person's life, and is frequently resistant to many medical treatments. A person may even have two or more coexisting chronic pain conditions. Among the most common pain challenges for Americans are headaches, low back pain, arthritis pain, cancer pain, and nerve and muscle pain.

“Scientists are exploring the mystery of how and why acute pain sometimes transforms into chronic pain,” says Dr. Story Landis, Ph.D., Director of the NIH National Institute of Neurological Disorders and Stroke (NINDS). “This transformation is associated with changes—or plasticity—in the brain that we do not yet fully understand.”

In the forefront of pain research are scientists supported by the National Institutes of Health (NIH). Many of the NIH Institutes and Centers—including NINDS—are part of the NIH Pain Consortium, which is meant to enhance pain research and promote collaboration among researchers. (See “NIH Research...” on page 7.)



Photo: NINDS

Dr. Story Landis

## What Your Healthcare Provider Will Want to Know About Your Pain History

1. When did your pain start? What brings on your pain?
2. How long does your pain last? Does your pain come and go, or is it there all the time?
3. Where is your pain located? Does it move to other parts of your body?
4. What makes it better? What makes it worse?
5. How has your pain affected your mood and daily activities?
6. What words would you use to describe your pain; for example: burning, prickling, tingling, sharp, dull, stabbing, aching?
7. What have you tried to relieve your pain? Include prescription and over-the-counter drugs, as well as non-medicine treatments (meditation, acupuncture, etc.).
8. Are there any other symptoms with your pain?
9. What are your goals for pain relief and daily activity?
10. If you are taking any medicines, tell your healthcare provider the following:
  - The names of your medicines. Be sure to include any prescription and over-the-counter medicines, as well as herbal remedies.
  - How long you have been taking them.
  - How well they work.
  - How much you take and how often.
  - Any bad reactions or side effects, such as increased drowsiness, dry mouth, rash, or other reactions.

## Symptoms

- Chronic pain is often defined as any pain lasting more than 12 weeks. Whereas acute pain is a normal sensation that alerts us to possible injury, chronic pain is very different. Chronic pain persists—often for months or even longer.
- Chronic pain may arise from an initial injury, such as a back sprain, or there may be an ongoing cause, such as illness. However, there may also be no clear cause. Other health problems, such as fatigue, sleep disturbance, decreased appetite, and mood changes, often accompany chronic pain. Chronic pain may limit a person's movements, which can reduce flexibility, strength, and stamina. This difficulty in carrying out important and enjoyable activities can lead to disability and despair.

## Diagnosis

- Pain is a very personal and subjective experience. There is no test that can measure and locate pain with precision. So, health professionals rely on the patient's own description of the type, timing, and location of pain. Defining pain as sharp or dull, constant or on-and-off, or burning or aching may give the best clues to the cause of the pain. These descriptions are part of what is called the pain history, taken during the start of the evaluation of a patient with pain.
- Since chronic pain may occur in a variety of locations in the body and for many different reasons, patients and their health professionals need to work together to identify the causes and symptoms of that pain and how it can be relieved.
- Although technology can help health professionals form a diagnosis, the best treatment plans are tailored to the person, with input from healthcare team members, who each have different training backgrounds and understand chronic pain. The person with pain and his or her loved ones also must be actively involved in the treatment.

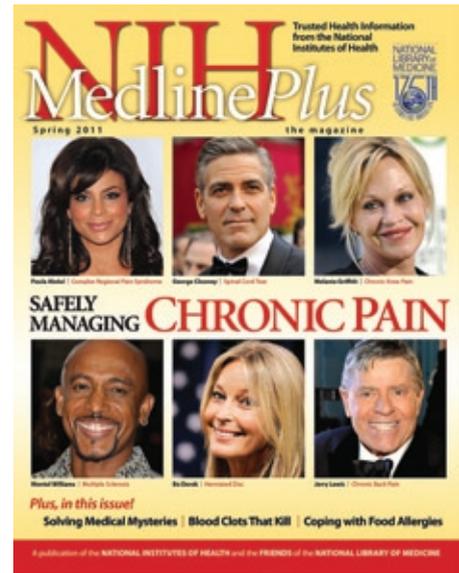
# Treatment

With chronic pain, the goal of treatment is to reduce pain and improve function, so the person can resume day-to-day activities. Patients and their healthcare providers have a number of options for the treatment of pain. Some are more effective than others. Whatever the treatment plan, it is important to remember that chronic pain usually cannot be cured, but it can be managed. The following treatments are among the most common ways to manage pain.

**Medications, acupuncture, electrical stimulation, nerve blocks, or surgery are some treatments used for chronic pain.** Less invasive psychotherapy, relaxation therapies, biofeedback, and behavior modification may also be used to treat chronic pain. These methods can be powerful and effective in some people. When it comes to chronic pain treatment, many people find adding complementary or alternative medicine (CAM) approaches can provide additional relief. These may include tai chi, acupuncture, meditation, massage therapies, and similar treatments.

**Self-management of chronic pain holds great promise as a treatment approach.** In self-management programs, the individual patient becomes an active participant in his or her pain treatment—engaging in problem-solving, pacing, decision-making, and taking actions to manage their pain. Although self-management programs can differ, they have some common features. Their approach is that the person living with pain needs help learning to think, feel, and do better, despite the persistence of pain. Improving communication with the healthcare provider is part of that empowerment.

Through NIH-supported research, starting successful self-management programs has reduced many barriers to effective pain management, regardless of the underlying conditions. Individuals who participate in these programs have significantly increased their ability to cope with pain. They improve their ability to be active, healthy, and involved members of their communities. In fact, new research suggests that the best self-management programs teach people different ways of thinking about and responding to pain, making their actions to relieve it more effective.



As noted earlier in this section, more than 76 million Americans suffer from some form of chronic pain. And yet, almost half of them receive no treatment.

The celebrities pictured on this issue's cover have all had to learn how to manage chronic pain associated with either an injury or a disease. They have previously spoken out about their own experiences with managing that pain, in hopes that the American public will gain a better understanding that chronic pain can happen to anyone.

**Paula Abdul**—The former *American Idol* judge has battled chronic pain since a cheerleading accident when she was 17, and subsequent car accidents and a plane crash. The result is a diagnosis of complex regional pain syndrome, which she continues to manage.

**George Clooney**—During filming of the movie *Syriana*, the internationally known actor tore the dura tissue that surrounds the brain and spinal cord. Despite several operations, he reportedly still has residual pain and memory loss because of the injury.

**Melanie Griffith**—A skiing accident was followed by three knee operations and a dependence on prescription pain pills. After rehab and with the support of husband Antonio Banderas and her family, Griffith has improved.

**Montel Williams**—A decade of misdiagnoses left Williams in constant pain. Finally, diagnosed with multiple sclerosis, the actor and TV host has been managing his pain with exercise and a healthy diet.

**Bo Derek**—The actress has spoken out publicly about her own chronic back pain and has supported the call for more education about pain management.

**Jerry Lewis**—No comedian took more tumbles and pratfalls than Lewis, and one of the results has been chronic back pain for the past 45 years—which he now manages with a nerve stimulator.

# NIH Research on Treating Pain

Among the many research projects related to chronic pain that are under way and funded by NIH Institutes are the following:

- **The NIH Pain Consortium is holding its 6th Symposium on Advances in Pain Research on April 14, 2011, at Natcher Auditorium on the NIH campus in Bethesda, Md. The event is free and open to the public.**
- The National Institute of Neurological Disorders and Stroke has funded the first human trial of gene therapy for pain. Researchers delivered a gene for enkephalin, a pain-easing chemical that is naturally produced in the body, to a precise site in the pain-processing pathway.
- An NIH clinical trial is currently testing resiniferatoxin, a plant toxin, which specifically targets pain-transmitting nerves to treat severe pain in advanced cancer patients.
- NIH-funded research finds that small molecules derived from the omega-3 fatty acids in fish can be used as a possible alternative treatment for inflammatory pain when other drugs prove inadequate.
- People with fibromyalgia may benefit from practicing tai chi, according to a study in the *New England Journal of Medicine*. The National Center for Complementary and Alternative Medicine helped fund the study.
- Scientists at the National Institute of Nursing Research (NINR) are analyzing genetic variations among individuals to understand responses to pain-reducing medications. They hope to develop diagnostic tools that use “biomarkers” that will allow researchers and clinicians to rapidly assess an individual’s pain response.
- Pain can be hard to assess in infants and children. NINR-supported scientists are carrying out a number of studies that examine the effects of pain and pain management in children of all ages—from preterm infants to children and adolescents after surgery, with sickle cell disease, or with other special medical needs.
- NINR-supported research has shown that successful self-management programs can reduce many barriers to effective pain management, whether cancer- or arthritis-related pain, back pain, or other chronic pain conditions.

# Opioids and Chronic Pain

Opioids are commonly prescribed because they are effective in relieving many types of pain. These medications are classified as narcotics and can be dangerous when abused. When used properly, opioids such as morphine have long been known to help the severe pain that follows surgery and to alleviate the suffering of people with advanced cancer. Recently, morphine and similar drugs have been used to treat chronic pain not caused by cancer. For many people, they have been remarkably helpful; for others, it either hasn’t worked or has created problems over time.

**Taken as directed**, opioids can manage pain effectively when used for a short amount of time. With long-term use, people need to be screened and monitored because a fraction of those treated will develop an addiction disorder, abuse the drugs, or give them to others. Long-term daily use of opioids leads to physical dependence, which is not to be confused with addiction disorder. An addiction disorder occurs in about 5 percent of people who take these pain relievers as directed over the period of a year. An addiction disorder can be treated, but like those who misuse or illegally distribute prescription drugs, the prescriber needs to be vigilant to identify and address these problems. That is why everyone who uses prescription opioids needs to be screened and closely monitored.

**When people have physical dependence** and the opioid use is stopped, withdrawal symptoms include restlessness, muscle and bone pain, insomnia, diarrhea, vomiting, cold flashes with goose bumps (“cold turkey”), and involuntary leg movements. Taken in large doses, or in combination with tranquilizers or alcohol, opioids can cause a deadly overdose that causes breathing to stop. To prevent an overdose, it is important to take opioids only as prescribed and to not combine them with other medications unless directed to do so by the prescriber. As clinicians and monitoring systems become more sophisticated, and opioids are better designed to be tamper-resistant or abuse-deterrent, healthcare providers believe that those who suffer because of a fear of addiction will receive the treatment they so desperately need.

# Medicines: Safe Storage and Disposal

Medicines, especially potentially dangerous drugs like opioids, must be safely stored. They should be in a locked container that does not allow others to gain access to them.

Unused portions of medicines must be disposed of properly to avoid harm to others and the environment. Certain medicines, such as opioids, may be especially harmful and, in some cases, fatal in a single dose if they are used by someone other than the person the medicine was prescribed for.

You may have received disposal directions for these medicines when you picked up your prescription. If not, instructions for proper disposal of your prescriptions can be found at DailyMed (<http://dailymed.nlm.nih.gov/>). If you properly dispose of these medicines, they cannot be accidentally used by children, pets, or anybody else.

It is important to note that disposal by flushing medicines down the toilet is not recommended for the vast majority of medicines. Unused or expired medicines that do not have flushing directions in the label can be disposed of safely in the household trash by:

1. Mixing them with something that will hide the medicine or make it unappealing, such as kitty litter or used coffee grounds.
2. Placing the mixture in a container, such as a sealed plastic bag.
3. Throwing the prescription bottle in your household trash.

If you have questions about disposing of your medicine, please call 1-888-INFO-FDA (1-888-463-6332).

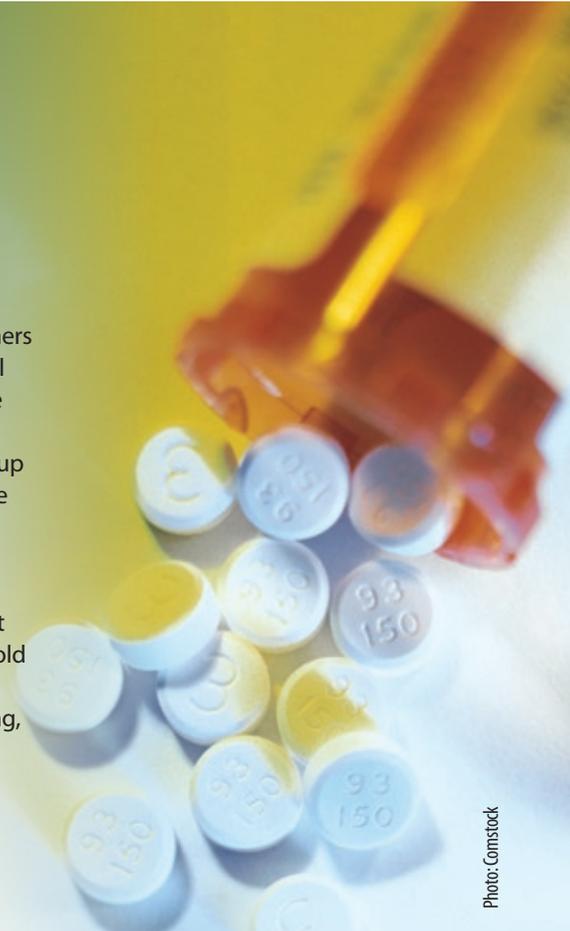


Photo: Comstock

## What Your Healthcare Provider Should Be Telling You

Safe and effective pain management must include clear and accurate information for patients about what the treatment includes, the expected results, and any dangers related to use of the prescribed medications, especially opioid pain relievers. The information should include the following:

- An overview of prescription and over-the-counter pain relievers, including what can and cannot be taken together.
- Specific instructions on use and misuse of pain relievers, including signs of impending addiction or related problems.
- Explanations of where to find professionals who will help them learn to be as healthy, high-functioning, and well-adjusted as possible, while living with daily pain that may be only partially relieved by medical treatments.

## Pain at End of Life

Chronic pain management at the end of life—in hospice, hospital, or home settings—is the focus of research and a graduate training program at the NIH Clinical Center.

The NIH Pain and Palliative Care Service conducts studies in pain and symptom management, quality of life, complementary therapies, and palliative medicine outcomes.

Hospice care is end-of-life care provided by health professionals and volunteers. They give medical, psychological, and spiritual support. The goal of the care is to help people who are dying have peace, comfort, and dignity. The caregivers try to control pain and other symptoms, so a person can remain as alert and comfortable as possible. Hospice programs also provide services to support a patient's family.

Hospice and palliative care is an expanding area of research within the NIH Pain Consortium.

## To Find Out More

- National Institute of Neurological Disorders and Stroke (NINDS): Contact NINDS's Brain Resources and Information Network (BRAIN) at (800) 352-9424  
[http://www.ninds.nih.gov/disorders/chronic\\_pain/](http://www.ninds.nih.gov/disorders/chronic_pain/)
- National Institute of Nursing Research (NINR) Pain Spotlight:  
<http://www.ninr.nih.gov/NewsAndInformation/NINRPainSpotlight.htm>
- NIH Pain Consortium: <http://painconsortium.nih.gov>  
The NIH Pain Consortium, a group made up of the many NIH Institutes and Centers with programs and activities addressing pain, was established to enhance pain research and promote collaborative efforts among pain programs. The Web site features pain-related health information, clinical trials, conference proceedings, funding opportunities, resources, and news releases.
- NIH Pain Consortium Index to NIH publications about pain symptoms, conditions, and treatments.  
[http://painconsortium.nih.gov/pain\\_index.html](http://painconsortium.nih.gov/pain_index.html)
- National Institute of Dental and Craniofacial Research:  
[www.nidcr.nih.gov/OralHealth/Topics/Pain/](http://www.nidcr.nih.gov/OralHealth/Topics/Pain/)
- National Institute of General Medical Sciences—Frequently Asked Questions about Pharmacogenetics:  
[www.nigms.nih.gov/Initiatives/PGRN/Background/pgrn\\_faq.htm](http://www.nigms.nih.gov/Initiatives/PGRN/Background/pgrn_faq.htm)
- Food and Drug Administration—Index to Drug-Specific Information:  
[www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111085.htm](http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111085.htm)
- MedlinePlus—Drug Information: Information on prescription and over-the-counter medicines and supplements:  
[www.nlm.nih.gov/medlineplus/druginformation.html](http://www.nlm.nih.gov/medlineplus/druginformation.html)

## We Need Your Help!

### Brief Surveys for Patients and Healthcare Providers

In order to help *NIH MedlinePlus* magazine better serve our readers, please take a moment to visit [www.surveymonkey.com/s/medpro](http://www.surveymonkey.com/s/medpro) (for healthcare providers) or [www.surveymonkey.com/s/medpat](http://www.surveymonkey.com/s/medpat) (for patients) and answer just a few questions about the information you received in this chronic pain section. It should take no more than five minutes of your time. Thank you!

# Ask Your Healthcare Provider

Working with your healthcare provider to understand and treat pain safely and effectively is the best way to approach pain. Ask the following questions, so that you fully understand your pain and the medications used to treat it:

1. What is causing my pain? What can I do about it?
2. Will you be treating my pain, the causes of my pain, or both?
3. What is the name of the pain medicine I will be taking? Why am I taking it?
4. How long will it take for the medicine to work?
5. What side effects should I expect? Should I report them to you?
6. If I forget to take the pain medicine, what should I do?
7. When should I take the pain medicine—on a regular schedule? Before, with, or after meals? At bedtime?
8. Are there any dangers to taking this pain medicine I should know about?
9. Will this pain medicine cause problems with any other prescription drugs or over-the-counter medicines I'm taking?
10. Is it possible to treat my chronic pain without medications?

# Solving Medical Mysteries



“This demonstrates that genomic tools are a powerful ally in our search to discover and understand rare diseases,” says Eric D. Green, M.D., Ph.D., director of the National Human Genome Research Institute (NHGRI).

## The NIH Undiagnosed Diseases Program

The National Institutes of Health (NIH) has been bringing sick people to its Bethesda, Md., campus for decades, usually to participate in clinical studies that have a defined focus, such as a particular cancer. Not only may they get helped, they also contribute to the overall understanding of disease.

But the Undiagnosed Diseases Program (UDP) is different. Instead of a single disease, UDP tackles the hardest-to-diagnose disorders, relying on NIH specialists in endocrinology, immunology, oncology, dermatology, dentistry, cardiology, genetics, and other areas to come up with insights about each case. A unified diagnosis is the optimal but often elusive endpoint.

Begun in 2008, the program is a clinical research initiative of the National Human Genome Research Institute (NHGRI), the NIH Clinical Center, and the NIH Office of Rare Diseases Research (ORDR). The UDP has responded to approximately 4,600 inquiries, received nearly 1,700 sets of medical records, and accepted roughly 380 cases from all over the country. Patients must be referred by a physician and provide all medical records and diagnostic test results requested by NIH. Those meeting program criteria then undergo an additional weeklong evaluation at the NIH Clinical Center.

Photo: iStock

# NIH Genetic Sleuths Diagnose Mysterious Inherited Disorder

Researchers for the National Institutes of Health's Undiagnosed Diseases Program (UDP) have pinpointed a genetic mutation as the cause of a rare and debilitating blood vessel disorder that had defied medical science for more than 100 years.

"This is the first novel disease discovered through the program's collaborative, interdisciplinary approach," says NIH Director Francis S. Collins, M.D., Ph.D. "The disorder had long-evaded conventional diagnosis."

Called ACDC, the condition is characterized by painful and debilitating calcium buildup in arteries below the waist and in the hands and feet, yet spares the coronary arteries. It blocks blood flow, making movement painful and difficult. UDP scientists examined members of two families with ACDC and identified a third case outside the country.

Suspecting a recessive gene was at fault in the five affected siblings of one family, researchers analyzed the DNA of the entire family (see "Thankful..." page 12). Each sibling had two copies of a particular mutation in a gene called NT5E, while each parent had only a single copy. When siblings inherit two such mutations, one from each parent, disease symptoms appear.

Similar mutations were detected in all the other affected patients studied. The NT5E gene normally makes the CD73 protein, which produces a small molecule, adenosine, which protects the arteries from calcifying. Calcification blocks blood flow, hampering normal, pain-free movement.

"This demonstrates that genomic tools are a powerful ally in our search to discover and understand rare diseases," says Eric D. Green, M.D., Ph.D., director of the National Human Genome Research Institute (NHGRI).

Manfred Boehm, M.D., lead investigator for the National Heart, Lung, and Blood Institute (NHLBI), says, "In addition to providing insight for this unique patient group and their physicians, it adds to our knowledge of vascular biology."

Concerning the patients, William A. Gahl, M.D., Ph.D., NHGRI clinical director, and director of the NIH Undiagnosed Diseases Program, adds, "We hope that an understanding of this faulty mechanism will guide us in providing helpful treatments for them."

Entering its third year, the UDP takes cases referred from around the country that challenge the diagnostic know-how and resources of the medical community at large. Participating patients undergo extensive diagnostic testing and evaluation at the NIH Clinical Center.



Photo: iStock



From left, Paula Allen and Louise Bengé, both from Brodhead, Ky., are sisters who participate in the NIH Undiagnosed Diseases Program. Their cases led to discovery of a rare disorder that causes calcification of their arteries in hips, legs, and feet.

Photo: Jeannine Mjoseph, NHGRI

# “Thankful They Found a Cause!”

## Kentucky sisters now have clues to lifelong, painful disorder

As a child, Paula Allen, 51, of Brodhead, Ky., loved to play “Kick the Can,” “Ghost in the Graveyard,” and other running games with her playmates. But then pain entered her life. By the time she was 18, pain in her hands drove her to the doctor—she thought arthritis—but the tests came back negative. By her 30s, the pain in her legs was so bad it prevented her from getting a good night’s sleep. Local doctors didn’t know the cause but suggested arterial surgery could help, although she would need to repeat it every five years. Paula declined.

The pain continued.

Her older sister, Louise Bengé, 56, also of Brodhead, was in her 20s when she first experienced similar, unexplained leg pain. Again, doctors could not identify the disorder but blamed blockage of blood vessels for her discomfort.

And the pain continued.

Finally, in 2009, Louise’s physician, Karen Saylor, M.D., of Mount Vernon, Ky., referred Louise and Paula to NIH’s Undiagnosed Diseases Program (UDP), a unique three-year-old NIH multidisciplinary initiative that seeks to provide answers to patients with mysterious conditions that have long eluded diagnosis, and advance medical knowledge about rare and common diseases.

Accepted into the UDP that May, the sisters, their three siblings, and their parents (who do not have the disease) visited the NIH Clinical Center for a week of intensive clinical and laboratory testing, evaluation, and consultation. It was worth it.

Clinical investigators from the National Human Genome Research Institute (NHGRI) and the National Heart, Lung, and Blood Institute (NHLBI) found that the pain Paula, Louise, and their siblings continue to suffer is due to ACDC, a rare genetic



Photo: Jeannine Mjoseth, NHGRI

**Louise Benge is monitored while walking, as part of testing for a rare genetic disorder, ACDC, at the Clinical Center on the NIH campus in Bethesda, Md. Annette Stine, research coordinator at the National Heart, Lung, and Blood Institute, monitors the treadmill test.**

disorder that permits calcium to build up in arteries below the waist and in the hands, blocking blood flow and making walking and other movements painfully difficult. Fortunately, ACDC spares the arteries of the heart.

ACDC is an inherited recessive disorder, meaning that Paula, Louise, and their siblings inherited two copies of the mutation, one from each parent, thus causing their debilitation.

While she continues to take medication to thin her blood and ibuprofen for pain, Paula now has hope a treatment may someday be found. "I am excited they found a cause and hope they can learn something that might help us or someone else," she says.

Back in Kentucky, Louise, too, remains hopeful. "It has impressed me that they want to help us at NIH," she says. "At a lot of places, they have said we should just go about our business."

## How to Participate in the Program

If you are interested in participating in the NIH Undiagnosed Diseases Program, discuss the option with your primary physician or healthcare provider (nurse practitioner or physician assistant). Information specialists at the Clinical Center's Patient Recruitment Call Center (1-866-444-8806) can provide more information about eligibility and what kinds of medical information referring physicians must submit for review. You or your healthcare provider may call.

Patients must be referred by a physician or other healthcare provider. Information that must go directly to NIH includes:

- A summary letter describing your condition, when it was first noted, and your current health status.
- A list of treatments and medications that have already been tried and their effects.
- Copies of reports and results of pertinent diagnostic tests, along with X-rays, MRI results, and other imaging records/studies. Copies of actual studies are preferred.

Request and keep copies of all materials. Because of confidentiality considerations, no e-mail submissions are accepted. Your referring physician must mail the summary and materials to:

**National Human Genome Research Institute**

**National Institutes of Health Undiagnosed Diseases Program**

**10 Center Drive - MSC 1851, Building 10, Room 10C103**

**Bethesda, MD 20892-1851**

## Call for More Information

Information specialists at the Clinical Center's Patient Recruitment Call Center can provide more information.

**Please call 1-866-444-8806.**



Photo: NHGRI

# “We feel deep compassion for patients...”

*NIH MedlinePlus* magazine talks with mystery-disease detective Dr. William Gahl, Director of the NIH Undiagnosed Diseases Program

## What kind of emotional support does your program offer patients?

For some, real hope and maybe even relief. As doctors, we feel deep compassion for patients who have been without hope because they are sick and no one has been able to help them. A principal mission, however, is the discovery of new diseases and variations of known diseases.

## Have your insights and research been able to help?

For some patients, we not only make a diagnosis but also can provide treatment or refer them elsewhere. But even when there is no treatment, simply having our diagnosis can be helpful. Many patients would rather know they have a fatal disease than go on with the uncertainty. Uncertainty is the major issue.

## Could you describe one of your cases?

We diagnosed a woman whose muscles had grown so much in the previous 10 years that people wondered whether she was training as a bodybuilder or was on steroids. But most exercise was painful, and eventually her muscle mass grew so heavy that she felt exhausted all the time. We diagnosed a potentially fatal protein buildup in the skeletal muscles. Once that was made—and it was made solely because of this program—she got a stem-cell transplant at the Mayo Clinic in Rochester, Minn., and is now recovering.

## What does a patient find with NIH that she may not find at another hospital?

First, we provide patients with coordinated access to many specialists. Second, different consultants can meet to discuss a given patient at the same time. Third, we offer state-of-the-art genetic analysis. Fourth, we plan to expand our basic research into the disorders we are seeing.

## Is there a unique part that genetics plays in the UDP?

Yes. Before coming here, our patients have gotten the standardized genetic tests that largely focus on a particular symptom. We consider those tests as a starting point.

## Can you give an example of how genetics has been applied?

Yes. We just discovered a new disease we've named ACDC. In nine individuals from three different families around the world, we found that a mutation in a gene called NT5E is inhibiting production of adenosine, which the body's large blood vessels need to avoid calcification. The large vessels of their bodies are calcifying, mostly below their waists, but the calcification also involves the joints of the hands and feet, making movement extremely painful.

## Are there any possible implications for other, more common disorders?

We won't really know how significant this discovery is for years. It could have all sorts of applications, including in the normal calcification of bone, and, possibly, abnormal calcification in other places, such as the blood vessels. But it's also possible it could only have implications for the affected family members we've studied. But knowing that adenosine has these functions is critically important for both basic and clinical research.

## Have you cured the people you were studying?

Although there may be some healing, our treatment probably won't reverse the calcification in our patients. Mainly, we want to avoid possible amputation. One person already has had to have an operation to bypass the femoral artery in the leg, so it's pretty serious stuff.

## Have you ever dealt with so many varied cases?

I'm not sure anybody deals with the diversity of cases that UDP does. We'll see anyone about anything as long as we have someone around here who knows a little bit about it. Even when we don't have the expertise, we do have the genetics. The good part is that we are helping people who wouldn't have been helped otherwise.

## Have you met your expectations for making diagnoses?

Yes. We have diagnosed 15 or 20 percent of the patients we admitted, which is a little more than we expected. We believe we'll be able to diagnose more as more basic research is performed.



Photo: NIH Clinical Center

## The NIH Clinical Center

houses 240 inpatient beds, 82 day-hospital stations, and more than 1,600 laboratories that conduct clinical and basic research. It has seen more than 400,000 patients since the hospital opened in 1953.

# NIH Clinical Center: There's No Other Hospital Like It

## Home to the NIH Undiagnosed Diseases Program

Patients in the National Institutes of Health's Undiagnosed Diseases Program are no strangers to hospitals, clinics, and doctors' offices. But their experience at the NIH Clinical Center—America's clinical research hospital and the world's largest hospital dedicated totally to clinical research—is a new one. Through clinical research, promising discoveries in the laboratory are translated into better health and health care for all.

### History of Medical Milestones

At the NIH Clinical Center, clinical research participants—more than 400,000 since the hospital opened in 1953—are active partners in medical discovery, a partnership that has resulted in a long list of medical milestones. Among these milestones has been the first cure of a solid tumor with chemotherapy, gene therapy, use of AZT to treat *(continued page 16)*

## Research at the NIH Clinical Center

happens from the bench to the bedside and back again, combining basic and clinical science to advance medical knowledge.

(continued from page 15) AIDS, and successful replacement of a mitral valve in the heart.

“Our patients come from every state and from around the world,” says John I. Gallin, M.D., Clinical Center director. “These partners in research and our specially trained staff collaborate to help advance medical knowledge that leads to new cures, therapies, and treatments.”

Currently, there are about 1,500 clinical research studies in progress at the NIH Clinical Center. About half are studies of the natural history of disease, especially rare diseases, which often are not studied anywhere else. What researchers learn by studying rare diseases often adds to the basic

understanding of common diseases. Most other studies are clinical trials, which often are the first tests of new drugs and therapies in people. The clinical trials at the NIH Clinical Center are predominantly Phase I and Phase II, often first-in-human to test safety and effectiveness.

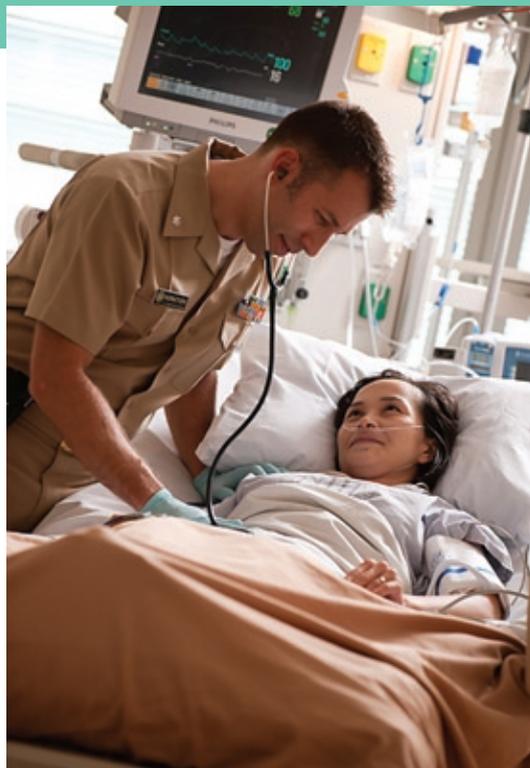


Photo: NIH Clinical Center



Photo: NIH Clinical Center

## Imagination and Collaboration of Specialists

Some 1,200 physicians, dentists, and Ph.D. researchers; 620 nurses; and 450 allied healthcare personnel work in patient care units and laboratories in numerous areas of clinical study. Specialists conduct research at the NIH Clinical Center in musculoskeletal and skin diseases; cancer; dental and craniofacial disorders; eye disorders; heart, lung, and blood diseases; infectious diseases; medical genetics; mental health; and neurological disorders.

All this expertise under one roof allows patients of the Undiagnosed Diseases Program to see specialists in one week that it would take months, if not years, to see elsewhere. At the NIH Clinical Center, investigators can make referrals for immediate testing and confer with peers across specialties to come up with the best approach for diagnosing and treating these patients.

**Patients are partners in research** and the NIH Clinical Center is built with their experience in mind. Each patient room features natural light, and patient services, such as the Main Playroom and patient library, provide recreation.

## Providing comfort and support

The NIH Clinical Center sees 10,000 new research participants a year. There are two types of research participants: patient volunteers and healthy volunteers. Patient volunteers are people with specific diseases or conditions who help medical investigators learn more about their condition or test new medications, procedures, or treatments. A healthy volunteer is a person with no known significant health problems who plays a vital role in research to test a new drug, device, or intervention.

There are many programs in place to ease the clinical research process for both patients and their families. Pediatric patients and their families stay at The Children's Inn, a 24-hours-a-day, seven-days-a-week, 365-days-a-year operation, where kids can be kids, instead of patients. There is also a school teaching kindergarten through high school, with a classroom and teachers who will go to the bedside.

For families and loved ones of adult patients, The Edmond J. Safra Family Lodge offers a home-like place of respite just steps away from the NIH Clinical Center, providing space for solitude, family meetings, and supportive fellowship.

## Training the next generation

The NIH Clinical Center offers an extensive range of clinical research training to help prepare the next generation of clinician-scientists. The innovative curriculum includes courses in pharmacology, principles and practice of clinical research, and bioethics.

Recently, the NIH Clinical Center launched the Sabbatical in Clinical Research Management program for clinical investigators, healthcare managers and administrators, and others who oversee clinical trials. The program focuses on what they need to manage a clinical or translational research effort.

Two new programs will bring early career investigators to the NIH Clinical Center. They include partnerships between the Damon Runyon Cancer Research Foundation and the National Cancer Institute and the NIH and the Albert and Mary Lasker Foundation.

"This is a first step toward opening the doors of the Clinical Center to clinician-scientists, further supporting the NIH mission to enhance health," says Dr. Gallin.



Photo: NIH Clinical Center

**Amanda Young**, a patient at the NIH Clinical Center, had an extremely rare disorder that was diagnosed by Dr. John Gallin, Clinical Center director.

# Blood Clots That Kill: Preventing DVT

Deep vein thrombosis (DVT) can be a killer. Here's how to understand and prevent DVT—at any age.

## FASTFACTS

- Deep vein thrombosis (DVT) is a blood clot that forms in a vein deep in the body. Most deep vein blood clots occur in the lower leg or thigh.
- A blood clot in a deep vein can break off, travel through the bloodstream to the lungs, and block blood flow. This condition is called pulmonary embolism (PE). PE is a very serious condition that can cause death.
- Only about half of the people who have DVT have signs or symptoms. Signs and symptoms occur in the leg affected by the deep vein clot. They include swelling of the leg or along a vein in the leg, pain or tenderness in the leg, increased warmth in the area of the leg that's swollen or in pain, and red or discolored skin on the leg.
- DVT is not just a condition of the elderly. It can strike anyone in any physical condition and at any age.
- DVT is treated with medicines that thin the blood, interfere with the blood clotting process, and dissolve blood clots. Other treatments include filters to catch blood clots.

## What Is Deep Vein Thrombosis?

Deep vein thrombosis (DVT) is a blood clot that forms in a vein deep in the body. Blood clots occur when blood thickens and clumps together. Most deep vein blood clots occur in the lower leg or thigh. They also can occur in other parts of the body.

A blood clot in a deep vein can break off and travel through the bloodstream. The loose clot is called an embolus. When the clot travels to the lungs and blocks blood flow, the condition is called pulmonary embolism (PE). PE is a very serious condition. It can damage the lungs and other organs in the body and cause death.

Blood clots in the thigh are more likely to break off and cause PE than blood clots in the lower leg or other parts of the body. Blood clots also can form in veins closer to the skin's surface. However, these clots won't break off and cause PE.

# Skater Tara Lipinski Speaks Out About DVT

Tara Lipinski has spent almost every day of her life ice-skating. At the age of 15, she became the youngest person ever to win a Gold Medal during a Winter Olympics. This was due, in part, to her signature move—a stunning but physically demanding triple loop/jump combination. However, by age 18, Lipinski was facing hip surgery, an event that would lead her to an awareness of deep vein thrombosis (DVT), a dangerous potential side effect of surgery. Ten years later, she is still on a mission to educate people about the realities of this condition—especially young people.

## **Tell us when you first became aware of your risk of DVT.**

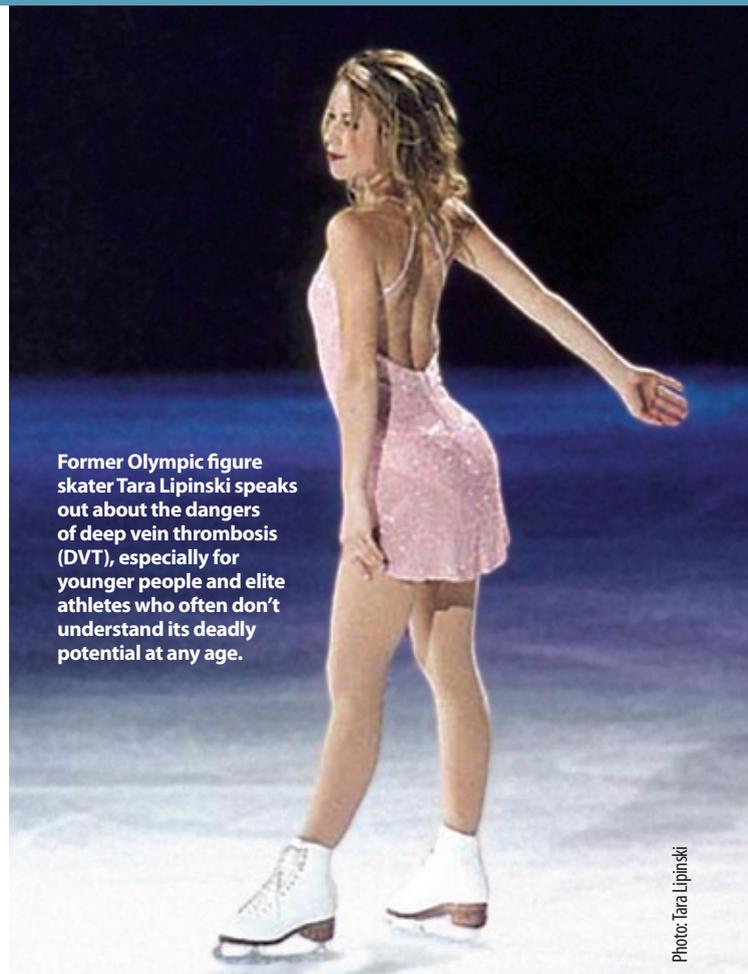
My hip had been hurting for a while. It had been misdiagnosed for about four or five years. Eventually, at the age of 18, I found out I had a torn labrum in my hip. It created a lot of joint pain and problems. So, I worked with orthopedic surgeon Dr. Marc Philippon, who was a pioneer in arthroscopic surgery. Dr. Philippon basically saved my career. The surgery really changed my life. And that's when I found out about DVT.

## **Were you surprised that DVT could be a complication of surgery for you?**

I never thought that DVT was something I'd have to worry about at that age; it wasn't on my radar. I thought "that's for older people or that's for people who don't exercise or who are sick and bedridden." I just never thought that a teenager—especially someone who was so active—would be at risk for something like DVT.

## **You became passionate about educating others on the topic. Why did it resonate so much with you?**

Here I am, an elite athlete; if there's a chance I can get it, anyone can. I just started thinking that if I never realized it was an issue, then my athlete friends probably didn't think it was an issue either. But it could be. It could happen to them. It could happen to someone my parents' age. It could happen to anyone.



Former Olympic figure skater Tara Lipinski speaks out about the dangers of deep vein thrombosis (DVT), especially for younger people and elite athletes who often don't understand its deadly potential at any age.

Photo: Tara Lipinski

## **Do you think young people and athletes are unaware they could be at risk?**

That's one of the main points of my campaign. I don't feel that most people do know about this risk—especially young, active people.

## **Tell us what you've been up to.**

Skating has always been the love of my life. Last year, I got into commentating. I worked with Universal and NBC in all of the skating competitions. I've become so passionate about it—just being back in the sport and watching these girls compete. I can definitely see myself doing this for a long time.

## **What's your main message for others when it comes to the risk of DVT?**

My message is that there isn't much of an awareness of this, and there should be. I'm very close with my family, so when I learned about this risk factor, I realized that my mom or dad could have had surgery, and I wouldn't have known before to even ask about the risk of DVT. I just want people to know about this when they go into surgery—and after—and that DVT can happen to the young and healthy, with or without surgery, as well.

## What Causes Deep Vein Thrombosis?

Blood clots can form in your body's deep veins if:

- Damage occurs to a vein's inner lining. This damage may result from injuries caused by physical, chemical, or biological factors. Such factors include surgery, serious injury, inflammation, and an immune response.
- Blood flow is sluggish or slow. Lack of motion can cause sluggish or slow blood flow. This may occur after surgery, if you're ill and in bed for a long time, or if you're traveling for a long time.
- Your blood is thicker or more likely to clot than normal. Certain inherited conditions (such as factor V Leiden) increase blood's tendency to clot. This also is true of treatment with hormone therapy or birth control pills.
- Sometimes, blood clots can form from no known cause.

## Risk

Many factors increase your risk for deep vein thrombosis (DVT). They include:

- A history of DVT.
- Disorders or factors that make your blood thicker or more likely to clot than normal. Certain inherited blood disorders will do this. This also is true of hormone therapy or birth control pills.
- Injury to a deep vein from surgery, a broken bone, or other trauma.
- Slow blood flow in a deep vein from lack of movement. This may occur after surgery, if you're ill and in bed for a long time, or if you're traveling for a long time.
- Pregnancy and the first six weeks after giving birth.
- Recent or ongoing treatment for cancer.
- A central venous catheter. This is a tube placed in a vein to allow easy access to the bloodstream for medical treatment.
- Being older than 60 (although DVT can occur at any age).
- Being overweight or obese.

Your risk for DVT increases if you have more than one of the risk factors listed above.

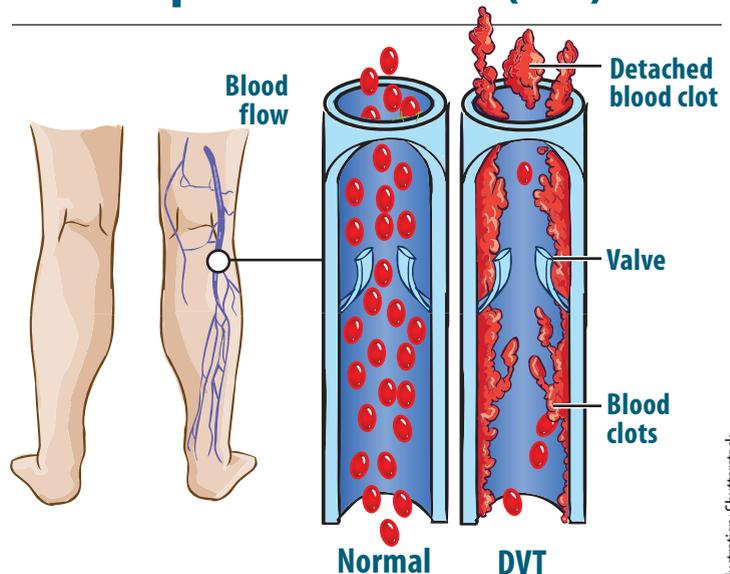
## Symptoms

The signs and symptoms of deep vein thrombosis (DVT) may be related to DVT itself or to pulmonary embolism (PE). See your doctor right away if you have signs or symptoms of either condition. Both DVT and PE can cause serious, possibly life-threatening complications if not treated.

**Deep Vein Thrombosis:** Only about half of the people who have DVT have signs or symptoms. These signs and symptoms occur in the leg affected by the deep vein clot. They include:

- Swelling of the leg or along a vein in the leg
- Pain or tenderness in the leg, which you may feel only when standing or walking
- Increased warmth in the area of the leg that's swollen or in pain
- Red or discolored skin on the leg

## Deep Vein Thrombosis (DVT)



Deep vein thrombosis, or DVT, is a blood clot that forms in a vein deep in the body. A deep vein thrombosis can break loose and cause a serious problem in the lung, called a pulmonary embolism, or a heart attack or stroke.

Illustration: Shutterstock

# Diagnosis

Your doctor will diagnose deep vein thrombosis (DVT) based on your medical history, a physical exam, and the results from tests. He or she will identify your risk factors and rule out other causes of your symptoms.

**Medical History.** To learn about your medical history, your doctor may ask about:

- Your overall health
- Any prescription medicines you're taking
- Any recent surgeries or injuries you've had
- Whether you've been treated for cancer

**Physical Exam.** During the physical exam, your doctor will check your legs for signs of DVT. He or she also will check your blood pressure and your heart and lungs.

**Diagnostic Tests.** Your doctor may recommend tests to find out whether you have DVT. The most common tests used to diagnose DVT are:

- **Ultrasound.** This is the most common test for diagnosing deep vein blood clots. Ultrasound uses sound waves to create pictures of blood flowing through the arteries and veins in the affected leg.
- **A D-dimer test.** This test measures a substance in the blood that's released when a blood clot dissolves. If the test shows high levels of the substance, you may have a deep vein blood clot. If your test is normal and you have few risk factors, DVT isn't likely.
- **Venography.** This test is used if ultrasound doesn't provide a clear diagnosis. Dye is injected into a vein, and then an x ray is taken of the leg. The dye makes the vein visible on the x ray. The x ray will show whether blood flow is slow in the vein. This may indicate a blood clot.
- **Other less common tests** used to diagnose DVT include magnetic resonance imaging (MRI) and computed tomography (CT) scanning. These tests provide pictures of your organs and tissues and are commonly used to diagnose pulmonary embolisms (PE).

## To Find Out More

- MedlinePlus: Deep Vein Thrombosis  
[www.nlm.nih.gov/medlineplus/deepveinthrombosis.html](http://www.nlm.nih.gov/medlineplus/deepveinthrombosis.html)
- MedlinePlus: Pulmonary Embolism  
[www.nlm.nih.gov/medlineplus/pulmonaryembolism.html](http://www.nlm.nih.gov/medlineplus/pulmonaryembolism.html)
- National Heart, Lung, and Blood Institute:  
"What Is Deep Vein Thrombosis?"  
[www.nhlbi.nih.gov/health/dci/Diseases/Dvt/DVT\\_WhatIs.html](http://www.nhlbi.nih.gov/health/dci/Diseases/Dvt/DVT_WhatIs.html)

# Treatment

Deep vein thrombosis (DVT) is treated with medicines and certain devices and therapies. The main goals of treating DVT include:

- Stopping the blood clot from getting bigger
- Preventing the blood clot from breaking off and moving to your lungs
- Reducing your chance of having another blood clot

Anticoagulants are the most common medicines for treating DVT. They're also known as blood thinners. These medicines decrease your blood's ability to clot. They also stop existing blood clots from getting bigger. However, blood thinners can't break up blood clots that have already formed. (The body dissolves most blood clots with time.)

Blood thinners can be taken as either a pill, an injection under the skin, or through a needle or tube inserted into a vein (called intravenous, or IV, injection).

Warfarin and heparin are two blood thinners used to treat DVT. Warfarin is given in pill form. (Coumadin is a common brand name for warfarin.) Heparin is given as an injection or through an IV tube. There are different types of heparin. Your doctor will discuss the options with you.

Your doctor may treat you with both heparin and warfarin at the same time. Heparin acts quickly. Warfarin takes 2 to 3 days before it starts to work. Once the warfarin starts to work, the heparin is stopped.

Newer anticoagulants are under development that will be easier to use than warfarin, because there is less bleeding risk without the monitoring required for warfarin.

## Latest NIH Research

- The National Heart, Lung, and Blood Institute (NHLBI) is conducting or sponsoring several studies looking at the relationship between a patient's genetic makeup and how the patient's body uses the anticoagulation drug warfarin. Better anticoagulation control could lead to a decrease in the rate of dangerous blood clots and bleeds among patients. Warfarin is a drug used to reduce the risk, but it must be dosed properly to avoid dangerous complications. NHLBI is also sponsoring studies looking at better ways to detect and treat DVT and PE. For more information about ongoing trials go to: [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
- NHLBI has been conducting studies on heart vein valve damage associated with DVT and how to preserve and/or replace the damaged valve function.
- Researchers are investigating whether there are genetic and other predispositions for DVT that occur without any known origin.

Photo: iStock



Allergic reactions to food can range from the uncomfortable to life threatening. Here are some useful tips and tools to avoid and treat them.

# Coping with Food Allergies

## FASTFACTS

- About one in 20 children and one in every 25 adults in the United States has a food allergy.
- In the United States, the most common food allergies are to eggs, milk, peanuts, tree nuts, wheat, crustaceans (shellfish), fish, and soy products.
- A severe, whole-body allergic reaction, known as anaphylaxis, can begin suddenly and may lead to death if not treated right away.

## What Is an Allergic Reaction to Food?

An allergy is an adverse health reaction triggered by your immune system to substances called allergens. A food allergy occurs when the immune system responds to a food as if it were a threat. The first few times a person at risk of developing a food allergy is exposed to the food, no symptoms are likely to occur. But the body has now been primed, and, in the future, that food may trigger an allergic response and one or more clinical symptoms. The symptoms of a food allergy can mimic those of a food intolerance, an unrelated disease that does not involve the immune system.

An allergic reaction to food usually takes place within a few minutes to several hours after exposure to the allergen. The process of eating and digesting food and the location of immune cells involved in the allergic reaction process affect the timing and location of the reaction.

## How Food Allergies Develop

Food allergies are more common in children than in adults. Most kids will naturally outgrow allergies to milk, eggs, soy products, and wheat. Allergies to peanuts or tree nuts often are lifelong. An allergy that begins in adulthood, such as to shellfish, also tends to be lifelong.

Food allergies often co-exist with other diseases, such as asthma, eczema (atopic dermatitis), and eosinophilic esophagitis, a disorder that causes severe heartburn, nausea, vomiting, weight loss, and difficulty swallowing food. If your family has a history of allergy, and you have eczema, then you are at greater risk for developing food allergies than someone who does not have them. The risk of harm to an individual with food allergy is hard to determine because the severity of any future reactions cannot be accurately predicted from the severity of past ones.



Photo: Michael Kent Photography

# Married... with Food Allergies

Joanna Karpinski and Josh Widzer share married life together and a common problem—severe food allergies. *NIH MedlinePlus* magazine's Naomi Miller caught up with them recently to learn more about how they cope.

## What foods are you allergic to?

**Joanna:** Tree nuts, peanuts, and cinnamon.

**Josh:** I am allergic to milk and all dairy products. This includes cream, cheese, butter, and milk.

## When did you start having problems with food allergies?

**Joanna:** My severe nut allergies developed when I was about 3 years old. The less severe peanut and cinnamon allergies began in my mid-20s.

**Josh:** I was too young to remember, but my Mom says that she fed me macaroni and cheese when I was around two years old. I immediately started swelling up and turning blue.

## How did you find out what the allergies were? Did you work with an allergist?

**Joanna:** We learned about my nut allergy the hard way: I had an anaphylactic reaction to a pecan treat when I was three. After that, my mother took me to an allergist, who used scratch tests to diagnose my other food allergies. As an adult, we used an elimination diet to diagnose my peanut and cinnamon allergies.

**Josh:** After the emergency room visit, we went to an allergist who diagnosed the milk allergy.

## What are your symptoms? What do you do when you feel them coming on?

**Joanna:** If I eat a tree nut, within about three minutes I'll develop anaphylaxis: my throat swells, it gets hard to breathe. I break out in a rash on my chest and hands, and can get itchy all over. I

immediately use an EpiPen (one type of epinephrine injector) and go to the ER. With cinnamon and peanuts, I get a bad rash on my hands and face within a day and have to take antihistamines.

**Josh:** If I just touch milk products, I itch and swell very badly. Benadryl usually clears up the skin reactions. I have a full anaphylactic reaction when I eat milk products, in which case an EpiPen and emergency room visit are required.

## How has having food allergies changed your lives?

**Joanna:** It's difficult to eat out because I can't trust food that I haven't seen prepared. Grocery shopping requires a bit more time because I have to read all of the labels thoroughly. Since Josh and I both have different allergies, it can be a challenge to make food we can both eat. But it has encouraged me to be very creative! I now have a hobby baking fancy cakes because no bakery could promise us an allergy-free wedding cake when we got married. So I learned to make my own wedding cake.

**Josh:** My allergies limit my choices of protein, so my meals contain more meat than average. Because most desserts contain milk products, I almost never eat them. Finding a cookie or cake I can eat is a special treat. Eating out also comes with some risk.

## What kinds of treatments and prevention have been helpful?

**Joanna:** There is no cure for adults with food allergies. Medications like epinephrine injections and antihistamines can treat symptoms, but avoiding the trigger foods and carrying my EpiPen at all times is how I stay safe and healthy.

## Symptoms

If you are allergic to a particular food, you may experience some or all of the following symptoms:

- Itching in your mouth and/or swelling of the lips
- Gastrointestinal (GI) symptoms, such as vomiting, diarrhea, or abdominal cramps and pain
- Hives or some other form of rash and reddening of the skin
- Tightening of the throat and trouble breathing
- Drop in blood pressure

### First Allergic Reaction

Usually, the first reaction to a food allergen occurs when you eat that particular food. Sometimes, exposure can occur without your knowledge, such as when a food allergen is a small part of a larger meal or a mixture of different foods. It is the first exposures that prime the immune system to the food.

In the case of peanut allergy, you may not have to eat peanuts or peanut-containing foods to have an allergic reaction. A person who experiences an allergic reaction may have had contact with peanuts in any of the following ways:

- Touching peanuts
- Using a peanut-containing skin care product
- Breathing in peanut dust, such as when in close proximity to people eating peanuts

### Cross-reactive Food Allergies

If you have a life-threatening reaction to a certain food, your healthcare professional can show you how to avoid similar foods that may also trigger the reaction. For example, if you have a history of allergy to shrimp, testing may show you are also allergic to other shellfish, such as crab, lobster, and crayfish. This is called cross-reactivity.



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## Diagnosis

If you have had an adverse reaction to a food, see a doctor for evaluation. Although you may think you have had an allergic response, only your doctor can determine if that has been the case.

The guidelines recommend that your doctor first takes your detailed medical history and then performs a physical examination. If a food allergy seems likely, there are tests—such as the skin prick test or a blood test to detect allergen-specific antibodies—that will help identify the possible allergenic foods. However, these approaches alone cannot conclusively diagnose a food allergy.

The only definitive test is an oral food challenge. Because this test can place you at risk for a severe allergic reaction, it must always be performed by a healthcare professional who has the appropriate training and experience with treating the symptoms of a severe allergic reaction.

## Acute Allergic Reactions

**An acute, or serious, allergic reaction that comes on rapidly and may result in death is called “anaphylaxis.” It can have many symptoms and affect different parts of the body. Symptoms can include itching, sneezing, difficulty breathing, and blood circulation problems. As a result, it is under-recognized and under-treated. The most common trigger foods for anaphylaxis are peanuts, tree nuts, milk, eggs, fish, and crustaceans (shellfish). To reduce the risk of anaphylaxis, it is essential that you avoid your specific trigger food. If you have a history of anaphylactic reactions to food, you should always carry an epinephrine auto-injector with you.**

# Prevention and Treatment

There is currently no cure for food allergies, and available treatments only ease the symptoms.

## Preventing a food allergy reaction

There are no drugs or treatments available that prevent food allergies. If you have food allergies, the only way to avoid allergic reactions is to avoid allergenic foods. After you and your healthcare professional have identified the food(s) to which you are sensitive, you must remove them from your diet.

## Read food labels

Read the list of ingredients on the label of each prepared food that you are considering eating. Many allergens, such as peanuts, eggs, and milk, may appear in prepared foods you normally would not associate them with.

Since 2006, U.S. food manufacturers have been required by law to list the ingredients of prepared

foods. In addition, they must use plain language to disclose whether their products contain (or may contain) any of the top eight allergenic foods—eggs, milk, peanuts, tree nuts, soy, wheat, shellfish, and fish.

## Treating a Food Allergy Reaction

### Unintentional exposure

When you have food allergies, you must be prepared to treat unintentional exposures. Talk to your healthcare professional and plan to protect yourself by taking the following steps:

- Wear a medical alert bracelet or necklace
- Carry an auto-injector device containing epinephrine (adrenaline), such as an EpiPen

- Seek medical help immediately if you are having symptoms

### Mild symptoms

Talk to your healthcare professional to find out what medicines may relieve mild food allergy symptoms that are not part of an anaphylactic reaction. However, be aware that it is very difficult to know which reactions are mild and which may lead to severe reactions (anaphylaxis).

Ways to manage your food allergy after a diagnosis:

- Is there a cure for food allergies? Not yet. The only way to prevent a reaction to a food is to avoid the allergenic food.
- The guidelines recommend that you read food labels carefully.
- If your child has a food allergy, the guidelines suggest seeking nutritional counseling.
- Remember, because some allergies can be outgrown, you should be re-tested periodically to see whether you are still allergic.



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## To Find Out More

- MedlinePlus: Food Allergy  
[www.nlm.nih.gov/medlineplus/foodallergy.html](http://www.nlm.nih.gov/medlineplus/foodallergy.html)
- National Institute of Allergy and Infectious Diseases:  
[www.niaid.nih.gov/topics/foodallergy](http://www.niaid.nih.gov/topics/foodallergy)
- FoodSafety.gov:  
[www.foodsafety.gov/poisoning/causes/allergens/](http://www.foodsafety.gov/poisoning/causes/allergens/)
- Centers for Disease Control and Prevention: Healthy Youth! Food Allergies  
[www.cdc.gov/HealthyYouth/foodallergies/](http://www.cdc.gov/HealthyYouth/foodallergies/)
- Food and Drug Administration: Food Allergies—What You Need to Know  
[www.fda.gov/Food/ResourcesForYou/Consumers/ucm079311.htm](http://www.fda.gov/Food/ResourcesForYou/Consumers/ucm079311.htm)

# Trusted Health Information for the Public

## MedlinePlus.gov: just a click away



For over a hundred years, the National Library of Medicine (NLM) served medical professionals by indexing the biomedical literature. The first indexes were printed volumes with titles like *Index-Catalogue of the Library of the Surgeon-General's Office*. Later, the index was called *Index Medicus* (IM). The library automated the production of IM in the 1960s, and in 1971 began making IM available for searching via a computer database called MEDLINE. In the 1990s, health professionals were able to search MEDLINE using a Web browser. But there were costs for using it.

When NLM made MEDLINE on the Web free of charge in June 1997, the general public immediately became an important NLM user group. A year later, 30 percent of MEDLINE searching performed from NLM's Web site was by students and the general public. But MEDLINE did not contain information for this audience. Its



MedlinePlus has a mobile version of the Web site that lets users access medical and drug information while on the go, available on any Web-enabled phones at [m.medlineplus.gov](http://m.medlineplus.gov) and, in Spanish, at [m.medlineplus.gov/espanol](http://m.medlineplus.gov/espanol).

MedlinePlus has an easy-to-use interface and highlights current health concerns and features on the home page—in English and Spanish versions.



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Keeping up with the latest health news and information is easier than ever now, with the MedlinePlus Twitter feed ([twitter.com/medlineplus4you](https://twitter.com/medlineplus4you)).

content was (and still is) information written by and for a health professional audience.

To address the needs of consumers, NLM developed a new Web site, MedlinePlus ([medlineplus.gov](http://medlineplus.gov)). MedlinePlus debuted on October 22, 1998, with 22 “health topic” pages—collections of links to reliable information on subjects like diabetes and heart attack. Since 1998, MedlinePlus has grown to become the most frequently visited government Web site for health information.

MedlinePlus offers authoritative, up-to-date health information, without advertisements, and is available anytime, anywhere for free. A Spanish-language version, MedlinePlus en español ([medlineplus.gov/spanish](http://medlineplus.gov/spanish)), is also available. A site for cell phones and other mobile devices is at [m.medlineplus.gov](http://m.medlineplus.gov).

MedlinePlus contains:

- Nearly 900 health topics pages that link to health information from NIH and other authoritative sources and include MEDLINE/PubMed searches, current news items

about the topic, and links to related topics

- Medical Encyclopedia—an extensive collection of medical images, as well as 4,000 articles about diseases, tests, symptoms, injuries, and surgeries
- Interactive Health Tutorials—narrated programs that use animated graphics to explain conditions and procedures in easy-to-read language
- Drugs, Supplements, and Herbal Information—prescription and over-the-counter medicines, plus herbs and supplements
- Current Health News—late-breaking stories about medicine and health
- Dictionary—spellings, definitions, and pronunciations of medical terms
- Multiple Languages—links to health information in over 40 languages
- Directories—locations and credentials of doctors, dentists, and hospitals, and much, much more.

## Breast Cancer & Lymph Node Removal

A new study suggests that some women with early stage breast cancer may not need to have radical surgery to remove a large number of lymph nodes from under the arm.

Typically, doctors remove one or two “sentinel” nodes, the first ones where cancer is likely to spread from the tumor. If cancer appears to have spread beyond these nodes, doctors usually recommend removing a large number of nodes. This can leave lasting pain and swelling in the arm, called lymphedema.

The study found that women who had only the sentinel nodes removed—and whose nodes were positive for cancer—lived just as long as women who had more nodes removed.

The findings apply to women who were eligible for the trial. They had relatively small tumors, five centimeters or less (about two inches), with only one or two nodes involved. Today, almost all women receive hormone therapy and/or chemotherapy, as well as radiation therapy to the whole breast after surgery. These treatments kill the cancer cells, which is why extensive surgery is not needed. NIH’s National Cancer Institute supported the research.

## Getting Stroke Patients Back on Their Feet

An estimated 4 million people who survive a stroke have trouble walking. What’s the best way to get them back on their feet? The largest stroke rehabilitation study ever conducted in the U.S. finds that intensive physical therapy done at home works just as well as more expensive, high-tech rehab in which patients practiced walking on treadmills while strapped in harnesses to support some of their weight. The study results show that rigorous physical therapy regimens like those used in the study are better than usual care physical therapy, which is less frequent and lower intensity.

Researchers also conclude that people can improve mobility up to a year after a stroke. This challenges previous thinking that recovery happens early and peaks at six months. NIH’s National Institute of Neurological Disorders and Stroke (NINDS) provided primary funding for the study.

## Cell Phones and Your Brain

Scientists have found that our brains are sensitive to the electromagnetic radiation from cell phone antennae. But it’s too early to say what the health impact may be.

Researchers used a PET scan to see what happens in the brain when people hold a cell phone to their ear for 50 minutes. The phone was either turned on, with the sound muted, or turned off. The scans showed more metabolic activity (glucose consumption) in the part of the brain closest to the antenna when the phone was on. More studies may be needed to determine any potential long-term effects. Dr. Nora Volkow, Director of NIH’s National Institute on Drug Abuse (NIDA), led the study.

## Two Pesticides Linked to Parkinson’s Disease

Researchers have linked two pesticides—rotenone and paraquat—to Parkinson’s disease, finding that people who used them were 2.5 times more likely to develop the incurable central nervous system disorder affecting muscle movement. Rotenone directly inhibits the function of the mitochondria, the structure responsible for cell energy production. Paraquat increases production of certain oxygen derivatives that may harm cellular structures. The results provide insight into mechanisms involved in Parkinson’s disease and may help develop approaches to intervention or prevention. NIH’s National Institute of Environmental Health Sciences (NIEHS) helped fund the study.



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# Info to Know

## NIH Quickfinder

For more information or to contact any of the following NIH institutes, centers, and offices directly, please call or go online as noted below:

### Institutes

- **National Library of Medicine (NLM)**  
www.nlm.nih.gov  
1-888-FIND-NLM (1-888-346-3656)
- **National Cancer Institute (NCI)** www.cancer.gov  
1-800-4-CANCER (1-800-422-6237)
- **National Eye Institute (NEI)** www.nei.nih.gov  
(301) 496-5248
- **National Heart, Lung, and Blood Institute (NHLBI)**  
www.nhlbi.nih.gov (301) 592-8573
- **National Human Genome Research Institute (NHGRI)** www.genome.gov (301) 402-0911
- **National Institute on Aging (NIA)** www.nia.nih.gov  
Aging information 1-800-222-2225  
Alzheimer's information 1-800-438-4380
- **National Institute on Alcohol Abuse and Alcoholism (NIAAA)** www.niaaa.nih.gov  
(301) 443-3860
- **National Institute of Allergy and Infectious Diseases (NIAID)** www.niaid.nih.gov  
(301) 496-5717
- **National Institute of Arthritis and Musculoskeletal and Skin Diseases** www.niams.nih.gov  
1-877-22NIAMS (1-877-226-4267)
- **National Institute of Biomedical Imaging and Bioengineering (NIBIB)** www.nibib.nih.gov  
(301) 451-6772
- **Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)**  
www.nichd.nih.gov 1-800-370-2943
- **National Institute on Deafness and Other Communication Disorders (NIDCD)**  
www.nidcd.nih.gov 1-800-241-1044 (voice)  
1-800-241-1055 (TTY)
- **National Institute of Dental and Craniofacial Research (NIDCR)** www.nidcr.nih.gov  
(301) 480-4098
- **National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)** www.niddk.nih.gov  
Diabetes 1-800-860-8747  
Digestive disorders 1-800-891-5389  
Overweight and obesity 1-877-946-4627  
Kidney and urologic diseases 1-800-891-5390
- **National Institute on Drug Abuse (NIDA)**  
www.nida.nih.gov (301) 443-1124
- **National Institute of Environmental Health Sciences (NIEHS)** www.niehs.nih.gov  
(919) 541-3345
- **National Institute of General Medical Sciences (NIGMS)** www.nigms.nih.gov  
(301) 496-7301
- **National Institute of Mental Health (NIMH)**  
www.nimh.nih.gov 1-866-615-6464
- **National Institute of Neurological Disorders and Stroke (NINDS)** www.ninds.nih.gov  
1-800-352-9424
- **National Institute of Nursing Research (NINR)**  
www.ninr.nih.gov (301) 496-0207

### Centers & Offices

- **Fogarty International Center (FIC)**  
www.fic.nih.gov (301) 402-8614
  - **National Center for Complementary and Alternative Medicine (NCCAM)**  
www.nccam.nih.gov 1-888-644-6226
  - **National Center on Minority Health and Health Disparities (NCMHD)** www.ncmhd.nih.gov  
(301) 402-1366
  - **National Center for Research Resources (NCRR)**  
www.ncrr.nih.gov (301) 435-0888
  - **NIH Clinical Center (CC)**  
www.cc.nih.gov (301) 496-2563
  - **Office of AIDS Research (OAR)**  
http://www.oar.nih.gov (301) 496-0357
  - **Office of Behavioral and Social Sciences Research (OBSSR)**  
http://obssr.od.nih.gov (301) 402-1146
  - **Office of Rare Diseases Research (ORDR)**  
http://rarediseases.info.nih.gov  
Genetic and Rare Disease Information Center  
1-888-205-2311 Toll-free
  - **Office of Research on Women's Health (ORWH)**  
http://orwh.od.nih.gov (301) 402-1770
- Marin P. Allen, Ph.D.**, Office of Communications and Public Liaison, NIH
- Joyce Backus**, National Library of Medicine (ex-officio)
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- Vicky Cahán**, National Institute on Aging
- Kym Collins-Lee**, National Eye Institute
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- Carol Krause**, National Institute on Drug Abuse
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