Recognizing
The National
Bone and Joint Decade
2002–2011

Questions & Answers about . . .

Juvenile Arthritis

(Juvenile Idiopathic Arthritis, Juvenile Rheumatoid Arthritis, and Other Forms of Arthritis Affecting Children)

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
National Institutes of Health
Public Health Service • U.S. Department of Health and Human Services

For Your Information

This publication contains information about medications used to treat the health condition discussed in this booklet. When this booklet was printed, we included the most up-to-date (accurate) information available. Occasionally, new information on medication is released.

For updates and for any questions about any medications you are taking, please contact the U.S. Food and Drug Administration at 1–888–INFO–FDA (1–888–463–6332, a toll-free call) or visit their Web site at www.fda.gov.

For updates and questions about statistics, please contact the Centers for Disease Control and Prevention's National Center for Health Statistics toll free at 1–800–232–4636 or visit its Web site at www.cdc.gov/nchs.

Additional copies of this booklet are available from:

National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIAMS/National Institutes of Health
1 AMS Circle
Bethesda, MD 20892–3675

You can also find this booklet on the NIAMS Web site at www.niams.nih.gov.

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What Is Juvenile Arthritis?

"Arthritis" means joint inflammation. This term refers to a group of diseases that cause pain, swelling, stiffness, and loss of motion in the joints. Arthritis is also used more generally to describe the more than 100 rheumatic diseases that may affect the joints but can also cause pain, swelling, and stiffness in other supporting structures of the body such as muscles, tendons, ligaments, and bones. Some rheumatic diseases can affect other parts of the body, including various internal organs. **Juvenile arthritis (JA)** is a term often used to describe arthritis in children. Children can develop almost all types of arthritis that affect adults, but the most common type that affects children is juvenile idiopathic arthritis.

Both **juvenile idiopathic arthritis** (JIA) and **juvenile rheumatoid arthritis** (JRA) are classification systems for chronic arthritis in children. The JRA classification system was developed about 30 years ago and had three different subtypes. More recently, pediatric rheumatologists throughout the world developed the JIA classification system, which includes more types of chronic arthritis that affect children. This classification system also provides a more accurate separation of the three JRA subtypes.

Prevalence statistics for JA vary, but according to a 2008 report from the National Arthritis Data Workgroup,[1] about 294,000 children age 0 to 17 are affected with arthritis or other rheumatic conditions.

[1] According to the National Arthritis Data Workgroup, the actual number of new cases of JA is higher than previously reported because the statistic includes conditions not previously captured, as cited in Helmick CG, Felson DT, Lawrence RC, Gabriel S, Hirsch R, Kwoh CK, et al.; National Arthritis Data Workgroup. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. *Arthritis & Rheumatism*, 58(1):15-25, January 2008.

What Is Juvenile Idiopathic Arthritis?

JIA is currently the most widely accepted term to describe various types of chronic arthritis in children.

In general, the symptoms of JIA include joint pain, swelling, tenderness, warmth, and stiffness that last for more than 6 continuous weeks. It is divided into seven separate subtypes, each with characteristic symptoms:

1. **Systemic arthritis (formerly known as systemic juvenile rheumatoid arthritis).** A patient has arthritis with, or preceded by, a fever that has lasted for at least 2 weeks. It must be documented as an intermittent fever, spiking for at least 3 days, and it must be accompanied by at least one or more of the following:
   - generalized enlargement of the lymph nodes
   - enlargement of the liver or spleen
   - inflammation of the lining of the heart or the lungs (pericarditis or pleuritis)
   - the characteristic rheumatoid rash, which is flat, pale, pink, and generally not itchy. The individual spots of the rash are usually the size of a quarter or smaller. They are present for a few minutes to a few hours, and then disappear without any changes in the skin. The rash may move from one part of the body to another.

2. **Oligoarthritis (formerly known as pauciarticular juvenile rheumatoid arthritis).** A patient has arthritis affecting one to four joints during the first 6 months of disease. Two subcategories are recognized:
   - *persistent oligoarthritis*, which means the child never has more than four joints involved throughout the disease course
   - *extended oligoarthritis*, which means that more than four joints are involved after the first 6 months of the disease.

3. **Polyarthritis – rheumatoid factor negative (formerly known as polyarticular rheumatoid arthritis – rheumatoid factor negative).** A patient has arthritis in five or more joints during the first 6 months of disease, and all tests for rheumatoid factor are negative.

4. **Polyarthritis – rheumatoid factor positive (formerly known as polyarticular rheumatoid arthritis – rheumatoid factor positive).** A patient has arthritis in five or more joints during the first 6 months of the disease. Also, at least two tests for rheumatoid factor, at least 3 months apart, are positive.

5. **Psoriatic arthritis.** Patients have both arthritis and psoriasis (a skin rash), or they have arthritis and at least two of the following:
   - inflammation and swelling of an entire finger or toe (this is called dactylitis)
   - nail pitting or splitting
   - a first-degree relative with psoriasis.

6. **Enthesitis-related arthritis.** The enthesis is the point at which a ligament, tendon, or joint capsule attaches to the bone. If this point becomes inflamed, it can be tender, swollen, and painful with use. The most common locations are around the knee and at the Achilles tendon on the back of the ankle. Patients are diagnosed with this JIA subtype if they have both arthritis and inflammation of an enthesitis site, or if they have either arthritis or enthesitis with at least two of the following:
   - inflammation of the sacroiliac joints (at the bottom of the back) or pain and stiffness in the lumbosacral area (in the lower back)
   - a positive blood test for the human leukocyte antigen (HLA) B27 gene
   - onset of arthritis in males after age 6 years
   - a first-degree relative diagnosed with ankylosing spondylitis, enthesitis-related arthritis, inflammation of the sacroiliac joint in association with inflammatory bowel disease, Reiter's syndrome, or acute inflammation of the eye.

7. **Undifferentiated arthritis.** A child is said to have this subtype of JIA if the arthritis manifestations do not fulfill the criteria for one of the other six categories or if they fulfill the criteria for more than one category.

What Causes Juvenile Arthritis?

Most forms of juvenile arthritis are autoimmune disorders, which means that the body's immune system – which normally helps to fight off bacteria or viruses – mistakenly attacks some of its own healthy cells and tissues. The result is inflammation, marked by redness, heat, pain, and swelling. Inflammation can cause joint damage. Doctors do not know why the immune system attacks healthy tissues in children who develop JA. Scientists suspect that it is a two-step process. First, something in a child's genetic makeup gives him or her a tendency to develop JA; then an environmental factor, such as a virus, triggers the development of the disease.

Not all cases of JA are autoimmune, however. Recent research has demonstrated that some people, such as many with systemic arthritis, have what is more accurately called an autoinflammatory condition. Although the two terms sound somewhat similar, the disease processes behind autoimmune and autoinflammatory disorders are different.

When the immune system is working properly, foreign invaders such as bacteria and viruses provoke the body to produce proteins called antibodies. Antibodies attach to these invaders so that they can be recognized and destroyed. In an autoimmune reaction, the antibodies attach to the body's own healthy tissues by mistake, signaling the body to attack them. Because they target the self, these proteins are called autoantibodies.

Like autoimmune disorders, autoinflammatory conditions also cause inflammation. And like autoimmune disorders, they also involve an overactive immune system. However, autoinflammation is not caused by autoantibodies. Instead, autoinflammation involves a more primitive part of the immune system that in healthy people causes white blood cells to destroy harmful substances. When this system goes awry, it causes inflammation for unknown reasons. In addition to inflammation, autoinflammatory diseases often cause fever and rashes.

What Are Its Symptoms and Signs?

The most common symptom of all types of juvenile arthritis is persistent joint swelling, pain, and stiffness that is typically worse in the morning or after a nap. The pain may limit movement of the affected joint, although many children, especially younger ones, will not complain of pain. JA commonly affects the knees and the joints in the hands and feet. One of the earliest signs of JA may be limping in the morning because of an affected knee. Besides joint symptoms, children with systemic JA have a high fever and a skin rash. The rash and fever may appear and disappear very quickly. Systemic arthritis also may cause the lymph nodes located in the neck and other parts of the body to swell. In some cases (fewer than half), internal organs including the heart and (very rarely) the lungs, may be involved.

Eye inflammation is a potentially severe complication that commonly occurs in children with oligoarthritis but can also be seen in other types of JA. All children with JA need to have regular eye exams, including a special exam called a slit lamp exam. Eye diseases such as iritis or uveitis can be present at the beginning of arthritis but often develop some time after a child first develops JA. Very commonly, JA-associated eye inflammation does not cause any symptoms and is found only by performing eye exams.

Typically, there are periods when the symptoms of JA are better or disappear (remissions) and times when symptoms "flare," or get worse. JA is different in each child; some may have just one or two flares and never have symptoms again, while others experience many flares or even have symptoms that never go away.

Some children with JA have growth problems. Depending on the severity of the disease and the joints involved, bone growth at the affected joints may be too fast or too slow, causing one leg or arm to be longer than the other. Overall growth also may be slowed. Doctors are exploring the use of growth hormone to treat this problem. JA may also cause joints to grow unevenly.

How Is It Diagnosed?

Doctors usually suspect JA, along with several other possible conditions, when they see children with persistent joint pain or swelling, unexplained skin rashes, and fever associated with swelling of lymph nodes or inflammation of internal organs. A diagnosis of JA also is considered in children with an unexplained limp or excessive clumsiness.

No single test can be used to diagnose JA. A doctor diagnoses JA by carefully examining the patient and considering his or her medical history and the results of tests that help confirm JA or rule out other conditions. Specific findings or problems that relate to the joints are the main factors that go into making a JA diagnosis.

Symptoms – When diagnosing JA, a doctor must consider not only the symptoms a child has but also the length of time these symptoms have been present. Joint swelling or other objective changes in the joint with arthritis must be present continuously for at least 6 weeks for the doctor to establish a diagnosis of JA. Because this factor is so important, it may be useful to keep a record of the symptoms and changes in the joints, noting when they first appeared and when they are worse or better.

Family history – It is very rare for more than one member of a family to have JA. But children with a family member who has JA are at a small increased risk of developing it. Research shows that JA is also more likely in families with a history of any autoimmune disease. One study showed that families of children with JA are three times more likely to have a member with an autoimmune disease such as rheumatoid arthritis, multiple sclerosis, or thyroid inflammation (Hashimoto's thyroiditis) than are families of children without JA. For that reason, having an autoimmune disease in the family may raise the doctor's suspicions that a child's joint symptoms are caused by JA or some other autoimmune disease.

Laboratory tests – Laboratory tests, usually blood tests, cannot alone provide the doctor with a clear diagnosis. But these tests can be used to help rule out other conditions and classify the type of JA that a patient has. Blood samples may be taken to test for anti-CCP antibodies, rheumatoid factor, and antinuclear antibodies, and to determine the erythrocyte sedimentation rate (ESR), described below.

- **Anti-cyclic citrullinated peptide (anti-CCP) antibodies** – Anti-CCP antibodies may be detected in healthy individuals years before onset of clinical rheumatoid arthritis. They may predict the eventual development of undifferentiated arthritis into rheumatoid arthritis.

- **Rheumatoid factor (RF)** – Rheumatoid factor, an autoantibody that is produced in large amounts in adults with rheumatoid arthritis, also may be detected in children with JA, although it is rare. The RF test helps the doctor differentiate among the different types of JA.

- **Antinuclear antibody (ANA)** – An autoantibody directed against substances in the cells' nuclei, ANA is found in some JA patients. However, the presence of ANA in children generally points to some type of connective tissue disease, helping the doctor to narrow down the diagnosis. A positive test in a child with oligoarthritis markedly increases his or her risk of developing eye disease.

- **Erythrocyte sedimentation rate (ESR or sed rate)** – This blood test, which measures how fast red blood cells fall to the bottom of a test tube, can tell the doctor if inflammation is present. Inflammation is a hallmark of JA and a number of other conditions.

X rays – X rays are needed if the doctor suspects injury to the bone or unusual bone development. Early in the disease, some x rays can show changes in soft tissue. In general, x rays are more useful later in the disease, when bones may be affected.

Other tests – Because there are many causes of joint pain and swelling, the doctor must rule out other conditions before diagnosing JA. These include physical injury, bacterial or viral infection, Lyme disease, inflammatory bowel disease, lupus, dermatomyositis, and some forms of cancer. The doctor may use additional laboratory tests to help rule out these and other possible conditions.

Who Treats It?

Treating juvenile arthritis often requires a team approach, encompassing the child and his or her family and a number of different health professionals. Ideally, the child's care should be managed by a pediatric rheumatologist: a doctor who has been specially trained to treat the rheumatic diseases in children. However, many pediatricians and "adult" rheumatologists also treat children with JA. Because there are relatively few pediatric rheumatologists and they are mainly concentrated at major medical centers in metropolitan areas, children who live in smaller towns and rural areas may benefit from having a doctor in their town coordinate care through a pediatric rheumatologist. Many large centers now conduct outreach clinics, in which doctors and a supporting team travel from large cities to smaller towns for 1 or 2 days to treat local patients.

Other members of your child's health care team may include:

- **Physical therapist.** This health professional can work with your child to develop a plan of exercises that will improve joint function and strengthen muscles without causing further harm to affected joints.

- **Occupational therapist.** This health professional can teach ways to protect joints, minimize pain, conserve energy, and exercise. Occupational therapists specialize in the upper extremities (hands, wrists, elbows, arms, shoulders, and neck).

- **Counselor or psychologist.** Being a child or adolescent with a chronic disease isn't easy, for the child or his or her family. Some children may benefit from sorting out their feelings with a psychologist or counselor trained to help children in this situation. Members of the child's family may benefit from counseling as well.

- **Ophthalmologist.** If your child's medications or form of arthritis can affect the eyes, catching problems early can help keep them from becoming serious. All children with JA need to have regular exams by an ophthalmologist (eye doctor) to detect eye inflammation.

- **Dentist and orthodontist.** Dental care can be difficult if a child's hands are so affected by arthritis that thorough brushing and flossing of the teeth becomes difficult. In addition, children with involvement of the jaw may have difficulty opening the mouth for proper brushing. Therefore, regular dental exams are important. Because JA can affect the alignment of the jaw, it is important for children with this disease to be evaluated by an orthodontist.

- **Orthopaedic surgeon.** For some children, surgery is necessary to help minimize or repair the effects of their disease. Orthopaedic surgeons are doctors who perform surgery on the joints and bones.

- **Dietitian.** For children with chronic diseases, good nutrition is particularly important. A dietitian can help design a nutritious diet that will benefit the whole family.

- **Pharmacist.** A pharmacist is a good source of information about medications, including possible side effects and drugs that have the potential to interact with one another. If a child has trouble swallowing large pills or taking other medication, the pharmacist may have suggestions for different ways to take the medication or may be able to formulate or help you get kid-friendly versions of some medications.

- **Social worker.** A social worker can help a child and his or her family deal with life and lifestyle changes caused by arthritis. A social worker also can help you identify helpful resources for your child.

- **Rheumatology nurse.** A rheumatology nurse likely will be intimately involved in a child's care, serving as the main point of contact with the doctor's office concerning appointments, tests, medications, and instructions.

- **School nurse.** For a school-age child, the school nurse also may be considered a member of the treatment team, particularly if the child is required to take medications regularly during school hours.

How Is It Treated?

The main goals of treatment are to preserve a high level of physical and social functioning and maintain a good quality of life. To achieve these goals, doctors recommend treatments to reduce swelling, maintain full movement in the affected joints, relieve pain, and prevent, identify, and treat complications. Most children with JA need a combination of medication and nonmedication treatments to reach these goals.

Following are some of the most commonly used treatments.

Treatments With Medication

- **Nonsteroidal anti-inflammatory drugs (NSAIDs)** – Aspirin, ibuprofen, naproxen, and naproxen sodium are examples of NSAIDs. They are often the first type of medication used. All NSAIDs work similarly: by blocking substances called prostaglandins that contribute to inflammation and pain. However, each NSAID is a different chemical, and each has a slightly different effect on the body.

  Some NSAIDs are available over the counter, while more than a dozen others, including a subclass called COX-2 inhibitors, are available only with a prescription.

  All NSAIDs can have significant side effects, so consult a doctor before taking any of these medications. For unknown reasons, some children seem to respond better to one NSAID than another. A doctor should monitor any child taking NSAIDS regularly to control JA symptoms as effectively as possible, at the optimal dose.

- **Disease-modifying anti-rheumatic drugs (DMARDs)** – If NSAIDs do not relieve symptoms of JA, the doctor is likely to prescribe this type of medication. DMARDs slow the progression of JA, but because they may take weeks or months to relieve symptoms, they often are taken with an NSAID. Although many different types of DMARDs are available, doctors are most likely to use one particular DMARD, methotrexate, for children with JA.

  Researchers have learned that methotrexate is safe and effective for some children with JA whose symptoms are not relieved by other medications. Because only small doses of methotrexate are needed to relieve arthritis symptoms, potentially dangerous side effects rarely occur. The most serious complication is liver damage, but it can be avoided with regular blood screening tests and doctor followup. Careful monitoring for side effects is important for people taking methotrexate. When side effects are noticed early, the doctor can reduce the dose and eliminate the side effects.

- **Corticosteroids** – In children with very severe JA, stronger medicines may be needed to stop serious symptoms such as inflammation of the sac around the heart (pericarditis). Corticosteroids such as prednisone may be added to the treatment plan to control severe symptoms. This medication can be given either intravenously (directly into the vein) or

by mouth. Corticosteroids can interfere with a child's normal growth and can cause other side effects, such as a round face, weakened bones, and increased susceptibility to infections. Once the medication controls severe symptoms, the doctor will reduce the dose gradually and eventually stop it completely. Because it can be dangerous to stop taking corticosteroids suddenly, it is important that the patient carefully follow the doctor's instructions about how to take or reduce the dose. For inflammation in one or just a few joints, injecting a corticosteroid compound into the affected joint or joints can often bring quick relief without the systemic side effects of oral or intravenous medication.

- **Biologic agents** – Children with JA who have received little relief from other drugs may be given one of a newer class of drug treatments called biologic response modifiers, or biologic agents. Five such agents – etanercept, infliximab, adalimumab, abatacept, and anakinra – are helpful for polyarthritis, extended oligoarthritis, and systemic arthritis. Etanercept, infliximab, and adalimumab work by blocking the actions of tumor necrosis factor (TNF), a naturally occurring protein in the body that helps cause inflammation. Anakinra works by blocking a different inflammatory protein called interleukin-1. Abatacept works by blocking the activation of certain inflammatory cells called T cells.

Treatments Without Medication

- **Physical therapy** – A regular, general exercise program is an important part of a child's treatment plan. It can help to maintain muscle tone and preserve and recover the range of motion of the joints. A physiatrist (rehabilitation specialist) or a physical therapist can design an appropriate exercise program for a person with JA. The specialist also may recommend using splints and other devices to help maintain normal bone and joint growth.

- **Complementary and alternative therapies** – Many adults seek alternative ways of treating arthritis, such as special diets, supplements, acupuncture, massage, or even magnetic jewelry or mattress pads. Research shows that increasing numbers of children are using alternative and complementary therapies as well.

  Although there is little research to support many alternative treatments, some people seem to benefit from them. If a child's doctor feels the approach has value and is not harmful, it can be incorporated into the treatment plan. However, it is important not to neglect regular health care or treatment of serious symptoms.

How Can the Family Help a Child Live Well with Juvenile Arthritis?

Juvenile arthritis affects the entire family, all of whom must cope with the special challenges of this disease. JA can strain a child's participation in social and after-school activities and make schoolwork more difficult. Family members can do several things to help the child physically and emotionally.

- **Get the best care possible.** Ensure that the child receives appropriate medical care and follows the doctor's instructions. If possible, have a pediatric rheumatologist manage your child's care. If such a specialist is not close by, consider having your child see one yearly or twice a year. A pediatric rheumatologist can devise a treatment plan and consult with your child's doctor, who will help you carry it out and monitor your child's progress.

- **Learn as much as you can about your child's disease and its treatment.** (The resources listed at the end of this booklet can help.) Many treatment options are available, and because JA is different in each child, what works for one may not work for another. If the medications that the doctor prescribes do not relieve symptoms or if they cause unpleasant side effects, you and your child should discuss other choices with the doctor. A person with JA can be more active when symptoms are controlled.

- **Insist that your child take the treatment.** Although it can be difficult to give your child a weekly shot or unpleasant-tasting medication, it's important that you do so – for his or her sake. If your child truly has a problem with one form of medication, speak with the doctor. He or she may be able to recommend a different medication or at least suggest ways to make taking the medication a little easier.

- **Consider joining a support group.** Try to find other parents and kids who face similar experiences. It can help you – and your child – to know you're not alone. The Juvenile Arthritis Alliance (JAA), a membership organization of the Arthritis Foundation, has support groups for people with JA and their families. The organization also has national meetings at which families can learn the latest about pediatric rheumatic disorders, share ideas, and form friendships. To contact JAA, see the Arthritis Foundation entry under "Where Can People Find More Information About JA?" on page 27.

- **Treat the child as normally as possible.** Don't cut your child too much slack just because he or she has arthritis. Too much coddling can keep your child from being responsible and independent and can cause resentment in siblings.

- **Encourage exercise and physical therapy for the child.** For many young people, exercise and physical therapy play important roles in managing JA. Parents can arrange for children to participate in activities that the doctor recommends. During symptom-free periods, many doctors suggest playing team sports or doing other activities. The goal is to help keep the joints strong and flexible, to provide play time with other children, and to encourage appropriate social development.

- **Work closely with your child's school.** Help your child's school to develop a suitable lesson plan, and educate your child's teacher and classmates about JA. For information about Kids on the Block, Inc., a program that uses puppets to illustrate how arthritis and other conditions can affect school, sports, friends, and family, see "Where Can People Find More Information About Juvenile Arthritis?" on page 27. To learn more about Federal laws that ensure access to education for special needs students, refer to Public Law (P.L.) 93-112, P.L. 94-482, and P.L. 99-457. Some children with JA may be absent from school for prolonged periods and need to have the teacher send assignments home. Some minor changes – such as having an extra set of books or leaving class a few minutes early to get to the next class on time – can be a great help. With proper attention, most children progress normally through school.

- **Talk with your child.** Explain that getting JA is nobody's fault. Some children believe that JA is a punishment for something they did. Let your child know you are always available to listen, and help him or her in any way you can.

- **Work with therapists or social workers.** They can help you and your child adapt more easily to the lifestyle changes JA may bring.

Do These Children Have to Limit Activities?

Although pain sometimes limits physical activity, exercise is important for reducing the symptoms of juvenile arthritis and maintaining function and range of motion of the joints. Most children with JA can take part fully in physical activities and selected sports when their symptoms are under control. During a disease flare, however, the doctor may advise limiting certain activities, depending on the joints involved. Once the flare is over, the child can start regular activities again.

Swimming is particularly useful because it uses many joints and muscles without putting weight on the joints. A doctor or physical therapist can recommend exercises and activities.

What Are Researchers Trying to Learn About Juvenile Arthritis?

Scientists are investigating the possible causes of juvenile arthritis. Researchers suspect that both genetic and environmental factors are involved in development of the disease, and they are studying these factors in detail. To help explore the role of genetics, the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) has a research registry for families in which two or more siblings have JA.

The JRA Affected Sib-Pairs Registry is located at the Cincinnati Children's Hospital Medical Center. Established in 1994, the registry continually lists new cases and is systematically updated. The focus of the registry is on genetic susceptibility in families whose siblings have JA. Current NIAMS-funded research is looking at genes that can predispose people to diseases and perhaps help predict their outcome. Eventually, gene therapy, or therapy based on the functioning of genes, may be used to treat pediatric rheumatic disorders by monitoring children's response to treatment or by predicting who is most likely to respond to a particular treatment regimen.

Researchers keep trying to improve existing treatments for children and find new medicines that will work better with fewer side effects. That effort received a major boost with the passage of the Pediatric Research Equity Act of 2003, which requires drugs that might be used in children to be

tested in children. As a result of the act, increasing numbers of medications are being tested for safety and effectiveness in children. Consequently, doctors will have more information on appropriate medications and doses to prescribe for their pediatric patients. (For information on specific drugs studies in children, visit www.clinicaltrials.gov.)

Other areas of research supported by the National Institutes of Health are widely varied and include studies of the following:

- the causes and consequences of sleep disruption in children with JA
- the causes of and potential treatments for anemia that often occurs in children with chronic inflammatory diseases such as JA
- the effectiveness of daily calcium supplementation for increasing bone mineral density in children with JA. A randomized, controlled trial of calcium supplementation was conducted among children with JA. The trial found that supplementation resulted in a small, but statistically significant, increase in total body bone mineral density, compared with a placebo in children with JA.

- the safety and usefulness of the combination of intravenous methylprednisolone (a corticosteroid medication) and intravenous cyclophosphamide (a drug that suppresses the immune system) compared to treatment with intravenous methylprednisolone alone for children with severe systemic JA

- the impact of chronic and recurrent pain on children

- ways to limit the impact of pain on children's functioning

- the role of an inflammatory chemical called interleukin-15 (IL-15) in the growth of new blood vessels in the tissue lining of the joint tissue. This increase in blood vessels contributes to the overgrowth of the tissue (called pannus) and damage in JA.

- a randomized, controlled trial of the effectiveness of a combination of methotrexate, corticosteroids, and etanercept compared to the standard therapy of methotrexate in keeping disease inactive in children with new onset polyarthritis.

Where Can People Find More Information About Juvenile Arthritis?

- **National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)**
  National Institutes of Health
  1 AMS Circle
  Bethesda, MD 20892–3675
  Phone: 301–495–4484 or
  877–22–NIAMS (226–4267) (free of charge)
  TTY: 301–565–2966
  Fax: 301–718–6366
  E-mail: NIAMSinfo@mail.nih.gov
  www.niams.nih.gov

  NIAMS provides information about various forms of arthritis, rheumatic disease, and bone, muscle, joint, and skin diseases. It distributes patient and professional education materials and refers people to other sources of information. Additional information and updates can be found on the NIAMS Web site.

- **NIH Osteoporosis and Related Bone Diseases ~ National Resource Center (NIH ORBD~NRC)**
  2 AMS Circle
  Bethesda, MD 20892–3676
  Phone: 202–223–0344 or
  800–624–BONE (2663) (free of charge)
  TTY: 202–466–4315
  Fax: 202–293–2356

E-mail: NIAMSBoneInfo@mail.nih.gov
www.niams.nih.gov/bone

The NIH Osteoporosis and Related Bone Diseases ~ National Resource Center provides patients, health professionals, and the public with an important link to resources and information on osteoporosis and other metabolic bone diseases. The mission of NIH ORBD~NRC is to expand awareness and enhance knowledge and understanding of the prevention, early detection, and treatment of these diseases as well as strategies for coping with them. The center has a wide range of publications on osteoporosis, including Bone Health and Osteoporosis: A Report of the Surgeon General and an accompanying booklet written for the general public. Fact sheets on osteoporosis include more detailed information on topics such as prevention of falls and fractures, calcium supplements, exercise, quality-of-life issues, and osteoporosis in men and various ethnic groups. Fact sheets on bone health and osteoporosis are also available in Spanish and Chinese. These and other fact sheets are available by mail and on the center's Web site, which also provides links to other sources of information on osteoporosis.

- **American Academy of Orthopaedic Surgeons (AAOS)**
  6300 North River Road
  Rosemont, IL 60018–4262
  Phone: 800–824–BONE (2663) (free of charge)
  www.aaos.org

The academy provides education and practice management services for orthopaedic surgeons and allied health professionals, including those who treat children. It also serves as an advocate for improved patient care and informs the public about the science of orthopaedics. The orthopaedist's scope of practice includes disorders of the body's bones, joints, ligaments, muscles, and tendons. For a single copy of an AAOS brochure, send a self-addressed, stamped envelope to AAOS or visit its Web site.

- **American College of Rheumatology/Association of Rheumatology Health Professionals**
  1800 Century Place, Suite 250
  Atlanta, GA 30345–4300
  Phone: 404–633–3777
  Fax: 404–633–1870
  www.rheumatology.org

  The American College of Rheumatology (ACR) is an organization of doctors and associated health professionals who specialize in arthritis and related diseases of the bones, joints, and muscles. The Association of Rheumatology Health Professionals, a division of ACR, aims to enhance the knowledge and skills of rheumatology health professionals and to promote their involvement in rheumatology research, education, and quality patient care. The association also works to advance and promote basic and continuing education in rheumatology for health professionals who provide care to people with rheumatic diseases.

- **Arthritis Foundation**
  P.O. Box 7669
  Atlanta, GA 30357–0669
  Phone: 800–283–7800 (free of charge) or call your local chapter. (To find your local chapter, check your phone directory or visit the foundation's Web site.)
  www.arthritis.org

  The Arthritis Foundation is devoted to supporting arthritis research and providing educational and other services to individuals with arthritis. The foundation publishes a free pamphlet on rheumatoid arthritis and a magazine for members on all types of arthritis. It also provides up-to-date information on research and treatment, nutrition, alternative therapies, and self-management strategies. Chapters nationwide offer exercise programs, classes, support groups, doctor referral services, and free literature. The foundation also has free information about lupus, scleroderma, and other autoimmune and rheumatic conditions on its Web site.

- **Kids on the Block, Inc.**
  9385-C Gerwig Lane
  Columbia, MD 21046
  Phone: 410–290–9095 or
  800–368–KIDS (5437) (free of charge)
  Fax: 410–290–9358
  www.kotb.com

  Kids on the Block, Inc., is an educational program that uses puppets to show how juvenile arthritis can affect school, sports, friends, and family. A package is available

(for a fee) that includes a set of large puppets representing a diverse group of children, as well as audiocassettes, a training guide, four different program scripts, props, follow-up activities, and other resources. The program is designed so that anyone can be a puppeteer, and workshops to train puppeteers are available.

Key Words

Antinuclear antibody (ANA) – A type of antibody directed against the nuclei of the body's cells. Because these antibodies can be found in the blood of children with lupus and some other rheumatic disorders, testing for them can be useful in diagnosis.

Corticosteroids – Powerful anti-inflammatory hormones made naturally in the body or synthetically for use as medicine. Corticosteroids may be taken by mouth or intravenously, or they may be injected into the affected joints to temporarily suppress the inflammation that causes arthritis-related swelling, warmth, loss of motion, and pain.

Disease-modifying antirheumatic drugs – A class of medication that can slow or potentially stop the activity of rheumatic disorders, such as rheumatoid arthritis, often by suppressing the overactive immune system.

Erythrocyte sedimentation rate (ESR or sed rate) – A test that measures how quickly red blood cells fall to the bottom

of a test tube of unclotted blood. Rapidly descending cells (an elevated sed rate) indicate inflammation in the body.

Flare – A period in the course of disease in which symptoms become worse. In most children, JA is characterized by periods of remission punctuated by flares.

Immune response modifiers – A relatively new class of medications used in arthritis treatment that are based on compounds made by living cells. These compounds modify the action of the immune system by blocking chemicals that fuel inflammation and tissue destruction.

Juvenile arthritis (JA) – A term often used to describe arthritis in children.

Juvenile idiopathic arthritis (JIA) – A term for various types of chronic arthritis in children. Arthritis is an inflammation of the tissues lining the joints of the body. JIA can cause swelling, pain, damage to the joints, and, in some cases, damage to other parts of the body. Juvenile idiopathic arthritis has replaced juvenile rheumatoid arthritis as the preferred term for the same condition.

Juvenile rheumatoid arthritis (JRA) – A term used to describe the most common types of arthritis in children. It is characterized by joint pain, swelling, tenderness, warmth, and stiffness that lasts for more than 6 weeks and cannot be explained by other causes. Previously, juvenile rheumatoid arthritis was the preferred term, but recently it has been replaced by juvenile idiopathic arthritis.

Nonsteroidal anti-inflammatory drugs (NSAIDs) – A class of medications that work to reduce pain, fever, and inflammation by blocking substances called prostaglandins. Some NSAIDs, such as ibuprofen (Motrin) and naproxen sodium (Aleve), are available over the counter, while many are available only with a doctor's prescription.

Oligoarthritis (formerly known as pauciarticular juvenile rheumatoid arthritis) – Refers to a form of JIA that affects four or fewer joints.

Pericarditis – Inflammation of the pericardium, the membrane that surrounds the heart. Pericarditis is a feature of some rheumatic disorders, including systemic arthritis.

Pleuritis – Inflammation of the pleura, the membrane that covers the lungs and lines the inner chest wall. Pleuritis is a feature of some rheumatic disorders, including systemic arthritis.

Polyarthritis (formerly known as polyarticular juvenile rheumatoid arthritis) – Refers to a form of JIA that affects five or more joints.

Remission – A period when the symptoms of JA improve or disappear completely. Sometimes remission is permanent, but more often it is punctuated by flares of the disease.

Rheumatic disorders – Disorders that affect the joints and soft tissues, causing pain, and sometimes inflammation, tissue damage, or disability.

Rheumatoid factor – An antibody that is found often in the blood of adults with rheumatoid arthritis and once in a while in children with JA. For these children, testing for the antibody may be useful as a diagnostic tool.

Systemic – Refers to a disease that can affect the whole body, rather than just a specific organ or joints. For example, the JIA subtype systemic arthritis (formerly known as systemic juvenile rheumatoid arthritis) can affect the skin, blood vessels, bones, and membranes lining the chest wall, as well as the joints.

Tendonitis – The inflammation of tendons, which are strong bands of connective tissue that attach muscles to bones.

Vasculitis – Inflammation of the blood vessels. Vasculitis is a feature of a number of rheumatic disorders.

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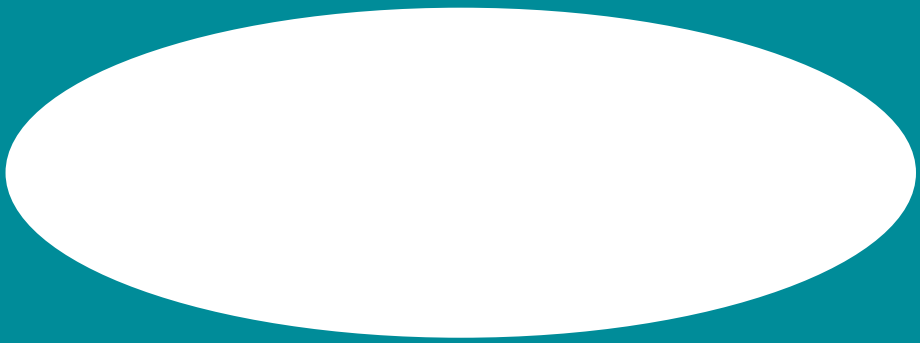
The mission of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), a part of the U.S. Department of Health and Human Services' National Institutes of Health (NIH), is to support research into the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases; the training of basic and clinical scientists to carry out this research; and the dissemination of information on research progress in these diseases. The NIAMS Information Clearinghouse is a public service sponsored by the Institute that provides health information and information sources. Additional information can be found on the NIAMS Web site at www.niams.nih.gov.



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