CHAPTER 5

Systemic JRA

CW Boynton writing sample

Systemic (pronounced sis-TEH-mick) JRA is the least common, but most severe, form of juvenile rheumatoid arthritis. It strikes about 20 percent of patients—boys and girls equally—and is characterized by long-term joint pain, fevers of 103 degrees or higher, and an intermittent pink rash that can last for weeks, or even months. In many children, the outer lining of the heart and lungs becomes inflamed, and the lymph nodes, liver and spleen become enlarged. Kidney damage can occur. Because of this wide-spread and potentially dangerous inflammation, powerful medications are usually prescribed, along with a strict exercise regime. For some children, systemic symptoms disappear completely within a few months or years, although joint-related symptoms may remain or worsen. Roughly one-quarter carry the disease into adulthood. Doctors sometimes call this condition Still's disease.

This chapter details the symptoms, treatments, possible complications, and outcomes experienced by most children with systemic JRA. The newest option for hard-to-treat systemic patients—stem cell transplant—is explained in the treatment section.

What it is

The name systemic means "system-wide." Thus, in this type of JRA, the entire body is affected—the skin and internal organs, as well as the joints. Because of this, children with systemic JRA are generally much sicker than those with pauciarticular or polyarticular forms of the disease.

Cindy Price says her daughter Marian, 11, became so weak, sore, swollen, itchy, and dehydrated during two systemic JRA flares that she couldn't pull herself out of bed, walk to the bathroom or hold her fork:

> *It was totally horrible. She was waking up in pain or with a fever every night—none of us got much sleep—lost 12 pounds and missed three months of school. Her rash itched terribly. At dinner I'd give her a baked potato, and she couldn't mash it with her fork. She couldn't hold her sandwich at lunchtime; my husband or I would have to put it to her mouth. Her throat was sore, and her mouth hurt. Liquids were all we could really get down her.*
>
> *Both flares like this went on for months They were eventually brought under control with medication. And to keep the arthritis under control now, she takes about a dozen pills a day. But do you know what I remember most about her flares? That not once during these times did my daughter smile. Imagine your child being so sick—in so much pain all the time—that she can't laugh or smile. Her smile is something I don't take for granted anymore.*

In addition to being the most severe form of juvenile rheumatoid arthritis, systemic is the most difficult to diagnose. No lab test, or series of test, can confirm any type of JRA. But clues often show up in blood work. Up to 60 percent of children with pauciarticlar and polyarticular JRA, for example, test positive for high levels of anti-nuclear antibodies. Children with systemic JRA, however, almost always test ANA negative. Few systemic children also test positive for the rheumatoid factor protein, which is often found in children with severe polyarticular disease. Other blood tests (such as the erythrocyte sedimentation or "sed" rate; see Chapter 2, *Diagnosing JRA*) usually do show the presence of high levels of inflammation in most children with systemic JRA. But none pinpoint the cause. Compounding problems is the fact that many systemic children don't experience joint pain or swelling early in the disease. Spiking fevers and a salmon-colored rash are often the only symptoms for several days or weeks—at times perplexing parents and doctors alike. A definitive systemic JRA diagnosis cannot be made until arthritis appears and remains active for at least six straight weeks.

Undoubtedly, the time involved in diagnosing this disease is frightening for most parents. But was "pure hell" for Angie Mace. It took doctors almost four years to diagnose her daughter Kelli with systemic JRA. Kelli

was just an infant when she developed a 105-degree fever that wouldn't go away and started dragging one leg, remembers Angie:

> *Now, the diagnosis makes perfect sense. She had all the classic signs of severe systemic JRA: high fever, joint pain and now an enlarged spleen and kidney damage, among other problems. But getting that diagnosis was pure hell. We saw doctors in five hospitals across the United States, and every one of them had a different opinion. She had countless blood test, countless hospital stays. And I just wanted to pull my hair out, because there was nothing I could do for her. She couldn't eat, couldn't sleep. I couldn't eat, couldn't sleep. My stomach was sick all the time. I searched the Internet daily for any information that could help. I just about drove myself crazy. Today, Kelli's on medication and feeling better -- not great, but better. We know what we're fighting now, which is at least somewhat comforting. The "what ifs" are finally gone.*

How it strikes

Hallmarks of the disease are high, spiking fevers that usually start late afternoon or early evening, and a pale, blotchy pink rash on the chest and thighs—or other parts of the body—that comes and goes. When Stacy Portko's fifteen-months-old son, Bryan, first showed signs of systemic JRA, he was waking up from his afternoon nap with a rash all over his body:

> *It was like clockwork. At first, we thought he was having an allergic reaction and went crazy trying to figure it out. We cut strawberries from his diet; changed the laundry detergent and then the dryer sheets; removed all the plants from our house; steam cleaned his room; tried lactose-free milk—it was nuts. We did this for two weeks. But the rash continued and then the fevers came, reaching as high as 104 during the evening. By this point, Bryan was miserable, crying non-stop, and we were all scared. I prayed for him then, and still pray for him every day.*

During a flare, your child's temperature may go up to 103 degrees or higher, return to normal within a few hours, and later spike up again. With the fever can come chills and shaking. This cycle can go on for several days, weeks or months. During this time, many children lose weight, become weak and pale, and develop anemia.

Severe joint pain and swelling may accompany fever and rash from the get-go. But often, children first feel only flu-like aches in their joints, without any swelling. In fact, many children with systemic JRA don't experience actual arthritis inflammation—pain and swelling—until weeks or months after their first fever strikes. Because of this, many parents and doctors mistake initial signs of systemic JRA for a virus, infection, or even the measles. Once arthritis does appear, it can range from mild to severe, attacking one joint or several joints. It can strike symmetrically—affecting the same joints on both sides of the body—or asymmetrically—affecting a specific joint on one side of the body. The neck, back and jaw can become inflamed. Some children with systemic JRA experience severe joint pain when their fever spikes, then relief when their temperature goes down. It's different for each child.

David Moore says his three-year-old son, Skyler, usually develops the blotchy pink rash just minutes before his temperature starts to rise:

> *Sometimes, he gets 106-degree fevers that last all night. We fight it with ice packs and even with feeding him frozen veggies—which helps him get nourishment, too. And he needs all the nourishment he can get. He hasn't grown in over a year, and his joint problems are getting progressively worse. Although let me stress here that Skyler is one of the more severe cases. It took months and months for specialists to diagnose him, and a host of other health problems have had him in and out of the hospital—pneumonia and meningitis among them. But it's scary any time your child is sick.*

Particularly scary with systemic JRA is how this disease can affect internal organs, especially the heart and lungs. Pericarditis—inflammation of the outer layer of the heart—and pleurisy—inflammation of the outside membrane of the lungs—are both common in children with systemic JRA. Pericarditis is an inflammation of the pericardium, the sac-like membrane that encloses the heart. Classic symptoms include fever and chest pain. Chest pain may be either brief and sharp or steady and constricting. It usually centers under the breastbone, but it can also spread to the neck and shoulders. Taking a deep breath, swallowing, coughing or lying down can sometimes cause the pain to worsen, while sitting up or leaning forward often offers relief. Other less common symptoms include a dry cough, abdominal or overall swelling, anxiety, sweating and fatigue.

In some cases, fluid can accumulate within the pericardium, causing a condition called pericardial effusion. If the pericardial effusion is large enough, it can interfere with the heart's ability to pump blood—a condition called cardiac tamponade. When this happens, low blood pressure and shortness of breath often accompany the symptoms mentioned above. In other cases, pericarditis can progress to the more severe constrictive pericarditis, in which the inflamed pericardium thickens and contracts around the heart, interfering with heart function. Breathing difficulties and swelling of the ankles, legs and abdomen often signal constrictive pericarditis has formed.

Many children with pericarditis find relief from the same nonsterodial anti-inflammatory drugs prescribed to help treat their arthritis. For persistent inflammation, corticosteroid medications, such as prednisone, may be prescribed. Detailed information on these, and other, medications is included in Chapter 6, *Drug Therapy*. In patents whose pericarditis has evolved into cardiac tamponade, excess fluid around the heart may be withdrawn with a sterile needle—a procedure called pericardiocentesis. When constrictive pericarditis interferes with heart function, the thickened pericardium may be surgically removed in a procedure called a pericardiectomy. For most systemic children, pericarditis persist as long as system-wide JRA symptoms are present, and needs to be closely monitored.

Two great sources for more detailed information on pericarditis are the American Heart Association (AHA) and the National Heart, Lung and Blood Institute (NHLBI). Contact the Dallas-based AHA at (800) 242-8721 or via the Internet at www.americanheart.org. Reach the NHLBI in Bethesda, Md., at (301) 592-8573, or online at www.nhlbi.nih.org.

Pleurisy, also called pleuritis, is caused by inflammation of the pleura—the membrane that covers the lungs and lines the inside of the chest cavity. In some patients, fluid accumulates in the space between the lungs and chest wall, causing a condition called pleural effusion. Most children with systemic JRA, however, experience "dry" or "plastic" pleurisy, with no fluid buildup. Like pericarditis, pleurisy typically causes chest pain that worsens with breathing or coughing. The pain may originate and remain in one area of the chest wall or spread to the shoulders and back. In rare cases, pleurisy pain manifests as a constant, dull ache.

The nonsterodial anti-inflammatory drugs used to treat pericarditis, and arthritis pain and swelling, can help relieve pleurisy symptoms, as well. Corticosteroids like prednisone are generaly prescribed for more difficult cases. Lying on one side—which limits chest wall movement—can also help ease pleuritic pain. For most children, the condition generally persists as long as system-wide JRA symptoms are present and should be closely monitored. For more information on pleurisy, contact the NHLBI or the American Lung Association at (800) 586-4872 or www.lungusa.org.

Twelve-year-old Joshua suffers from both pericarditis and pleurisy, plus severe joint pain. He was diagnosed with systemic JRA in 1995 after a series of hospitalizations and examinations, which included him being flown from his home in Maui, Hawaii, to a Honolulu medical center, explains his mother, Georgina McKinley:

> *None of the doctors on our island knew what was wrong with him, and he almost died. He was burning up at 107 degrees, became anorexic, and when I asked nurses to look at their text books—to try to help figure things out—their books dated back to the '60s and '70s. Even once Josh was diagnosed, I had a hard time finding good information. The public library was no help. Few friends or family members even knew children could get arthritis—and I had so many questions.*

Her answer, like for so many others, was to turn to the Internet. But even there, solid medical information was lacking. So she did what any resourceful single mother would do, she says. She started her own Web site for parents of children with JRA to share information, thoughts, and feelings at www.geocities.com/Heartland/Village/8414/. Here she shares Josh's story in detail, plus offers links to other JRA-related sites. You can also access her page through the International Still's Disease Foundation at www.members.tripod.com/stillsfoundation/. Says Georgina:

> *I started the site just for systemic parents. But then parents of kids with every form of JRA started posting messages, and I realized it needed to be open to everyone. Parents need to know if other children are experiencing what their children are going through. They need to play a role in their child's care. And for this to happen, we need to learn all we can, and from one another. When your child goes from having well-doctor visits*

once a year to constant sick visits—sometimes as much as twice a week—your whole world changes. You need support and to know you're not alone.

Like Joshua, many systemic children also develop an enlarged spleen or liver; some develop both. Splenomegaly is the medical term for an enlarged spleen, and hepatomegaly for an enlarged liver. Hepatosplenomegaly is the enlargement of both organs. As a rule, none of these conditions cause any outward symptoms. They're usually detected by a physician during a physical exam. Treatment varies. But generally, strenuous activities are limited to avoid ruptures—although for many systemic children, it's a moot order. Joint pain and stiffness prohibit the majority from taking part in contact sports, or any activity that puts them at risk of being hit, falling or damaging their joints.

Painfully enlarged lymph nodes (better known as swollen glands) are also common, as are rheumatoid nodules—painless, rubbery, pea-sized bumps that often occur during flares. They form where bone lies close to the skin, and pressure is likely. Elbows, heels, knees, knuckles, and ankles are usually affected. Nodules may be single or multiple, and vary in size from a few millimeters to as much as 2 centimeters. Children with glasses often get them on the back of the ears and bridge of the nose. They typically come and go and are more of an annoyance than a problem. They can, however, occasionally ulcerate. When this happens, the nodules need to be watched for infection. Internal rheumatoid nodules can also form on the lungs, abdominal wall, esophagus, and vocal cords, but usually don't produce any symptoms.

Rheumatoid nodules most often occur in children with a positive rheumatoid factor, and in those taking strong medications. Methotrexate, for example, a powerful anti-rheumatic drug, can increase their occurrence. Although there's no specific treatment for rheumatoid nodules, decreasing pressure on susceptible areas can help.

Twenty-year-old Monika no longer suffers from fevers, rashes, or other systemic symptoms. But her joints still flare—sometimes as bad as when she was first diagnosed with systemic JRA as a high school freshman. Today, she knows increased medications and exercise will eventually help ease the pain. But as a teen-ager, facing JRA was a nightmare, she says:

I didn't understand why this was happening, and thought my entire body had launched some kind of terrible coupe. My wrists were immobile. My fingers were swollen and painful. My ankles and knees were full of fluid, and my jaw stiff and cracking. I felt that sitting and watching television were the only things I could do—everything else was too painful. I could barely turn a doorknob without debilitating pain, and inflammation in my hip made it impossible to walk. Because of all this, I could only attend school sporadically. And when I did attend, I felt left out because I couldn't do so many things—like stand up and walk at the end of class. When I wanted to move, my sore, stiffened hips and ankles wanted to stay put. It the worst.

I saw my life like a Monopoly game: I was the player stuck in jail, while all my friends were moving around the board buying, trading, and having a good time.

How it's treated

Most children with systemic JRA need to take several medications for many months or years. Disease-modifying anti-rheumatic drugs (DMARDs) and nonsterodial anti-inflammatory drugs (NSAIDs) are the most commonly prescribed to fight both arthritic and organ-related inflammation.

As the name suggests, DMARDs work by modifying the course of inflammatory conditions like JRA, slowing or all together stopping their progression. NSAIDs block the production of hormone-like substances called prostaglandins, which cause inflammation. But it's the more powerful DMARDs that usually help systemic patients most.

Methotrexate is the most frequently prescribed DMARD. Originally used as a chemotherapy drug to treat certain kinds of cancer, it slows the progression of JRA by altering the way the immune system works. Most children taken between 7.5mg and 20mg once a week, either by mouth or injection. Higher doses may be used to treat more severe cases. But like other DMARDs, it can take weeks or months for relief to appear.

Monika underwent eleven months of weekly Methotrexate injections before feeling any substantial relief:

Gradually, I was able to reclaim more and more movement. It wasn't the full recovery I was magically hoping for. But the arthritis symptoms became manageable. The trick at this point was to remember that even though I was feeling better, I wasn't cured. Remission—or even partial remission—can lull you into forgetting about your disease; into not remembering the arthritis is there. But you still need to follow doctors orders and take your medicine, exercise, go to physical therapy—whatever you're supposed to do. Otherwise, you face damaging your joints and the possibility of worse flares or needing surgery.

Methotrexate side effects can range from annoying to life-threatening. So children taking this drug must be monitored closely. The most common side effects are nausea and vomiting, skin rash, mouth sores, diarrhea, sensitivity to sun, loss of appetite, mood swings, and hair loss. More serious side effects that should be immediately reported to your child's doctor include skin discoloration, bowel inflammation, confusion, fainting, kidney problems, unusual bleeding or bruising, shortness of breath, and yellow skin or eyes. Methotrexate is also known to cause miscarriages, and has the potential to cause lung disease, kidney or liver damage and bone marrow problems. Despite these risks, most children at least try methotrexate or other DMARDs, and many find significant symptom relief.

Corticosteroids like prednisone are strong, effective medications also prescribed to help control severe inflammation. They can be taken orally, injected directly into joints, or through intravenous infusions—and for many children offer tremendous relief. But they can also cause serious side effects, such as a swollen face, weakened bones, weight gain, excessive hair growth, irritability, and increased susceptibility to infections. Long-term use can also interfere with a child's growth. In fact, many children with systemic JRA tend to be small and thin for their age because of extended prednisone use. To keep tabs on growth, doctors often ask parents to track their child's height and weight with a standardized growth chart. There's one for boys and one for girls. (See Appendix XX.) It's important to watch your child's rate of growth. It should be steady—no matter how slow—with no dramatic jumps or stops.

The many prescription and non-prescription medications used to control symptoms are explained in detail in Chapter 6, *Drug Therapy.*

Other treatments—like physical and occupation therapy and splints and crutches—are described in Chapter 7, XX.

Most children find substantial relief from these treatments. Indeed, about 75 percent of systemic patients eventually go into complete remission—some within a few months, others after several years, explains David Sherry, MD, a pediatric rheumatologist at the Children's Hospital Medical Center at the University of Washington, Seattle:

> *To me, systemic is the best and worst form of JRA. It's the worst because the fever, rash and pain can go on for many, many months–years even—and really be devastating. Systemic children can get so, so sick. But it's also the best because once these symptoms are brought under control, most children are usually fine. For whatever reason, systemic children tend to have fewer recurrent flares than those with polyarticular or pauciarticlar disease. However, those who don't find relief can end up in pretty bad shape. Joint pain can worsen and even develop into polyarticular disease. And for many of these kids, nothing seems to help. Although some of the worst of these children are now finding relief through stem cell transplant—a risky procedure that should only be used as a last resort, but that has shown results.*

Stem cell transplant is a high-tech, complicated procedure traditionally used to treat aggressive cancers. Adult arthritis patients who've failed to find relief from conventional therapies have turned to it as a last resort. But it was never an option for children.

Then, in November 1999, eleven-year-old Mollie Hauck of Canby, Oregon, made national headlines for being the first child in the United States to undergo a stem cell transplant for JRA. Government approval for her to try to the procedure came after medical studies in the Netherlands, Europe and Australia showed 20 children with JRA experienced remission from stem cell transplant[1], and doctors here petitioned it was her own chance for relief.

Diagnosed with systemic JRA when she was two, Mollie's joint pain and swelling only worsened over the years. She spent most days laying in bed, or sitting in a wheelchair, with joints so swollen that even the slightest movement caused her to scream and cry. No treatment

helped. At the time of the stem cell transplant, she was taking twelve to fifteen different medications each day and going for weekly prednisone injections—sometimes having as many as 29 injections at one time. Explains her mother, Kathy:

> *Mollie had no options left. We tried every prescription drug, every possible alternative and experimental drug, and nothing worked. As a last resort, we even tried horse pills—real horse pills designed for treating pain in animals. But there was no relief, and Mollie had no life. Over a period of five years, she was well enough to attend school just 30 days. She couldn't play or have fun with friends. The pain was so constant that she basically shut down. If we treated her by taking her out to lunch, or for a wheelchair ride around the mall, she would end up being totally wiped out for three or four days after. So we didn't hesitate when stem cell became an option. And really, the results have been miraculous. She can pick up a plate, carry a glass of water, walk around the mall, sit crisscross-applesauce on the floor—all things she could never do before. She can hold a pencil in her hand and dress herself. It's like a dream come true.*

Health experts like Sherry agree Mollie's transformation was, indeed, miraculous. But they also stress the importance of people understanding stem cell transplant and its risks.

Stem cells are immature blood cells that haven't yet become red or white cells. During a stem cell transplant for JRA, stem cells are extracted from the patient's own bone marrow for an autologous transplant—meaning the patient will get back her own stem cells. The immune system is then "zapped" or cleaned with a high dose of chemotherapy or radiation to kill the malfunctioning immune system, and the harvested stem cells re-implanted—with the hope that they'll create a new strong, healthy immune system.

Because this procedure leaves the patient defenseless against fighting even the mildest diseases, most spend several weeks or months in the hospital, as their new immune system grows back. Mollie spent 37 days at Doernbecher's Children's Hospital at Oregon Health Sciences University, including fifteen days in isolation. Two return trips were also needed to help fight a cold a virus. Like other stem cell patients, she faced the risk of becoming seriously ill, or even dying, from infection as

her immune system recovered. There was also the possibility that the transplanted cells would only form a partially effective immune system – which thankfully was not the case with Mollie, says her mother:

> *For the first time in nine years, Mollie has a normal life—we all do. She still takes some medications, but nothing like she used to. And we're all hopeful that this will last. Unfortunately, we can't predict what will happen; whether the arthritis will come back. If it does, at least we know we've tried everything. But I don't think negatively. Even at Mollie's worst, I tried to think positively. You've got to believe.*

However, calling stem cell transplant a cure for systemic JRA is still under debate, experts stress. Says the Children's Hospital Medical Center of Cincinnati's Dr. Daniel Lovell in an Arthritis Foundation statement:

> *It may be a cure, but it's too early to say for sure. We need more long-term follow-up. Yes, there are tremendous success stories like Mollie's. But some successful transplant recipients have also experienced a recurrence of JRA symptoms, although not as serious as before. So right now, it's really for people who have no other options.*

The Arthritis Foundation's complete and official stance on stem cell transplant can be found online at www.arthritis.org/resources/news/news_stemupdate.asp. The treatment is also discussed further in Chapter 7, XX.

Possible complications

Since JRA impacts every child differently, there are as many possible complications as there are systemic patients. The worse complication systemic children face is that their arthritis develops into polyarticular disease. In other words, that joint pain and swelling spreads and becomes progressively worse and destructive. This happens to roughly to 25 percent of systemic patients.[2]

About 2 percent of children with systemic JRA also develop a dangerous eye inflammation called uveitis. It's a condition most common in those who have a positive ANA level—rare with systemic JRA—but it can

appear in children with a negative ANA level, too. If left untreated, it can cause permanent vision damage, including blindness. If detected early, however, it is easy to treat.

Uveitis is discussed in detail in Chapter 3, *Pauciarticular JRA*, because these children are most at risk. Essential here, however, is the fact that the American Academy of Pediatrics recommends that children with systemic JRA have eye exams every three months. These screenings should continue for at least ten years after the arthritis has gone into remission. Uveitis can develop at any age, even after active joint symptoms are gone. In fact, some rare cases of uveitis were diagnosed more than twenty years after JRA symptoms went into remission.[3]

The usual outcome

No one can tell for sure what your child's outcome will be. Long-term outcomes vary and are unfortunately impossible to predict. Some systemic children experience only one flare or episode of the disease, followed by complete remission. Others experience periods of flares and remission over several months or years, which vary in length and intensity. In yet others, systemic symptoms like fever, rash and pleurisy disappear, but the arthritis continues. Many recover completely. Others carry severe, persistent arthritis symptoms into adulthood.

Twelve-year-old Cameron has had systemic JRA for six years now. Despite taking heavy medications, having hip and shoulder surgery, and following a strict four-day-a-week physical therapy routine, he has never gone into remission. Following doctors' orders, however, has helped Cameron manage his pain—and for the most part allows him to keep up with his friends, says his mother Christine Johnson:

> *Cameron will never be as physical as before JRA struck. Then, he went to gymnastics twice a week and played T-ball—so active that he'd get hollered at by the coach for doing cartwheels and flips in the outfield. Now, we mainly get glimpses of what he could do if he didn't have JRA, but are grateful for everything he can do: swim, ride around on his scooter, even ice skate and run and jump with his friends sometimes. That's pretty incredible when you realize that three years ago, he could barely walk and had to crawl to get around.*

He's a trooper—and proof that with faith, determination, and good medical care, our kids can do amazing things.

-End-