Joint Pain in Children: An Algorithmic Approach

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Musculoskeletal and joint diseases appear to have increased in the last decade. Confusion over terminology and a lack of awareness of these conditions have probably contributed to their under-recognition. In a survey of primary care pediatricians in upstate New York, about 5% of all patient visits were attributed to arthralgias and injuries. These patients frequently pose a diagnostic dilemma because of the extremely broad differential diagnoses that must be considered. Typical of the many presentations might be a child with knee pain, no fever, and a questionable history of trauma. The pain may begin slowly; the child may limp but deny any pain. Moving the joint produces pain, and normal motion may be limited because of it. Early in the examination it is important to determine that the pain is in the joint itself rather than the soft tissue around the joint or the muscle close to it. It is also important to distinguish between pain in the joint itself and referred pain. If there is actual swelling of the joint or pain on motion with tenderness and with limitation of motion, we can safely assume that particular joint is involved. Presented here is a semi-algorithmic approach to the diagnosis of joint pain in pediatric practice.

The first step in initial screening is to establish whether a single joint or multiple joints are involved. The second important step is to determine whether or not there is associated fever. For practical purposes, this initial screening should lead to the following four possible groups of diagnoses: a) single-joint involvement with associated fever, b) single-joint involvement without fever, c) multiple-joint involvement with associated fever, and d) multiple-joint involvement without fever. (Figure 1)

Single-joint involvement associated with fever

When a single joint has pain or swelling and fever is present, the next step is to quickly and efficiently rule in or out a number of immediately treatable infectious conditions [1].

Septic arthritis. This condition classically presents with a severely painful, swollen, warm and red joint in a febrile child. The join must be aspirated for Gram's stain, cultures, and examination of the synovial fluid and cell count. In the absence of Gram's stain or culture, a cell count of 40,000/mm^3 is regarded as evidence of bacterial infection.

Osteomyelitis. With reactive arthritis or sympathetic arthritis, this is an arthritis with effusion in a nearby joint as a reaction to osteomyelitis. A technetium or gallium joint-bone scan often reveals an osteomyelitis in the adjacent bone.

Presence of foreign body in the joint. A thorn, shard of glass, or other foreign body may cause a secondary infection or sterile synovitis. A xerogram or computerized tomographic scan is superior to a radiograph in demonstrating a non-opaque foreign body.

Traumatic arthritis. Traumatic serosanguineous effusion can cause fever secondary to blood within the joint. There is almost always a history of trauma. Aspiration usually reveals sterile synovial fluid. The effusion may continue or recur. Arthroscopic

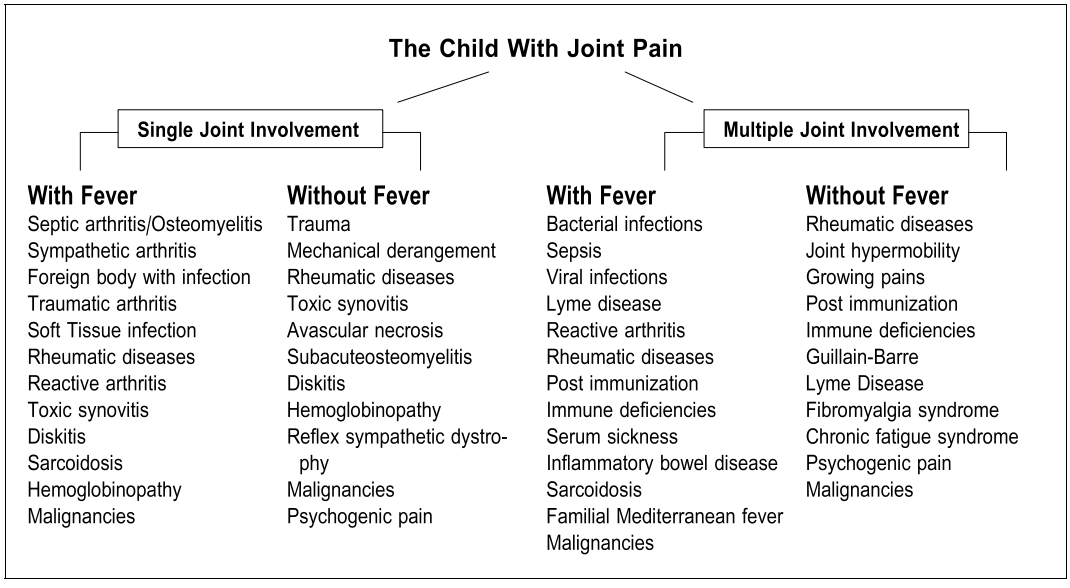

Figure1. The Child With Joint Pain

surgery will reveal the nature of this condition. In addition, clotting abnormalities must be ruled out.

Soft tissue infection (cellulitis). This condition can mimic arthritis when located near a joint. If the above possibilities have been eliminated, consider other groups of diseases, beginning with the rheumatic diseases.

Rheumatic diseases. Pauci-articular onset of juvenile rheumatoid arthritis may present with single-joint disease (Table 1). Usually, one of the large joints is affected, and the patient is either afebrile or has a low grade fever. Very rarely, children with systemic onset JRA may also present initially with monoarticular disease, usually in the knee or hip. In that case, look for other manifestations of the disease such as rheumatoid rash, hepatosplenomegaly, lymphadenopathy, pericarditis and, in rare instances, iritis. It is unusual for children with systemic lupus erythematosus to present with single-joint involvement. Occasionally, rheumatic fever, Kawasaki's disease, juvenile dermatomyositis and certain viral infections may begin with arthritis affecting one joint [2].

Post-infectious reactive arthritis. This includes post-viral or post-bacterial diseases such as poststreptococcal reactive arthritis and post-*Salmonella*, *Shigella*, and *Yersinia* reactive arthritis. These post-viral or post-bacterial conditions have a benign, self-limited course that may require symptomatic and supportive therapy.

Toxic synovitis. If the hip joint is affected, toxic synovitis must be taken into account. Also called transient synovitis, it occurs in children aged 8–10. Most of the patients are boys, and there is often a history of respiratory infection. Within a few weeks a limp and pain referred to the knee develop along with a low grade fever. The erythrocyte sedimentation rate may be mildly elevated. The disease usually subsides after 1–2 weeks and does not commonly recur. However, Legg-Calve-Perthes disease is occasionally a sequela.

One of our recent patients demonstrated the transient nature of this disease. This 8 year old girl with pain in the right hip was unable to bear weight on her right leg. A joint-bone scan showed avascularity of the right femoral head. Four days later she became asymptomatic, at which time a repeat joint-bone scan revealed a normal hip. The likely explanation is that a transient vascular spasm of unknown etiology had occurred.

Diskitis. This clinical entity can present with single-joint pain with or without fever. It is a rare condition that may occur in young children, with peak onset at 4–6 years of age. It is discussed in more detail in the section on single-joint pain without fever.

Hemoglobinopathy. In a black child, sickle cell anemia must be ruled out by hemoglobin electrophoresis. In the very young child it causes a dactylitis that may mimic true arthritis; in older children it causes micro-infarcts that give rise to periostitis and periarthritis that are responsible for the pain crises in this disease.

Table 1. Analysis of a pediatric rheumatology clinic population, 1997-2001, at Children's Hospital of New Orleans

Diagnosis	No. of patients	Percent
Rheumatic diseases	**821**	**54**
Juvenile rheumatoid arthritis	324	21
Systemic lupus erythematosus	119	8
Juvenile dermatomyositis	36	2.4
Vasculitis:		
Kawasaki disease	71	4.6
Henoch-Schönlein purpura	51	3.4
Polyarteritis nodosa	9	0.6
Takayasu	1	<0.1
Rheumatic fever	15	1
Linear scleroderma	6	0.4
Mixed connective tissue disease	3	0.2
Reactive arthritis	31	2
Sarcoidosis	20	1.3
Inflammatory bowel disease	10	0.7
Psoriatic arthritis	8	0.5
Sjögren's syndrome	2	0.1
Behçet's disease	4	0.25
Positive antinuclear antibodies	69	4.5
Raynaud's phenomena	19	1.3
Serum sickness	23	1.5
Unclassified diseases	**707**	**46**
Fibromyalgia syndrome	258	17
Joint hypermobility	202	13
Growing pains	34	2.2
Reflex sympathetic dystrophy	11	0.8
Chronic fatigue syndrome	13	0.9
Transient synovitis	11	0.8
Idiopathic Iritis/uveitis	8	0.5
Fever of unknown origin	4	0.2
Periodic fever syndrome (FMF)	11	0.8
Viral disease	19	1.3
Conversion reaction	6	0.4
Malignancy	6	0.4
Other non-specific referrals	124	8
Total no. of patients	**1,528**	**100**

Malignancies. Leukemia is the most common malignancy in childhood. However, it rarely presents with single-joint involvement. Tumors such as synovial cell sarcoma or bone tumors such as osteosarcoma and Ewing's sarcoma can rarely present as single-joint involvement with fever. In any malignancy, bone pain is usually prominent, and other features such as weight loss and fatigue are commonly present [2].

The proper diagnosis of these disorders can be made by a comprehensive history and physical examination along with step-by-step laboratory tests, as follows:

- Tests to rule out infections should include the following: complete blood count, ESR, urinalysis, blood culture; synovial

JRA = juvenile rheumatoid arthritis

ESR = erythrocyte sedimentation rate

fluid analysis to include Gram's stain, culture and cell count; streptococcal antibodies such as ASO titer. Pure protein derivative and other tests such as radiograms, joint-bone scan, CT scan and magnetic resonance imaging may also be needed.

- After infectious conditions have been ruled, laboratory tests that can be helpful in the search for a rheumatic disorder include: rheumatoid factor, antinuclear antibody, immunoglobulins, human leukocyte antigen B27, and components of the complement (C3, C4 and CH50). Angiotensin-converting enzyme serum level, slit-lamp examination, chest radiogram, echocardiogram, and electrocardiogram may also be necessary.
- Tests to rule out malignancy should include the following: In addition to complete blood count, bone marrow aspiration and/or biopsy, non-invasive procedures such as joint-bone scan, CT scan and MRI, and other tissue biopsies when needed.

Single-joint pain without fever

Single joint pain or swelling in the absence of fever usually occurs in the larger joints.

Trauma. If there was a history of trauma, local injury is the most obvious possible cause.

Mechanical derangements. Specific injuries such as injury to the meniscal or cruciate ligaments are uncommon in young children but have a much higher incidence in teenagers. When trauma has been ruled out, arthritis associated with rheumatic disease or inflammatory bowel disease must be considered.

Rheumatic diseases. When trauma has been ruled out in the case of single-joint arthritis in a child, pauci-articular JRA is the most common disorder, followed by inflammatory bowel disease.

Toxic synovitis. If the hip is involved, toxic synovitis should be considered.

Avascular necrosis of the femoral head. If the pain in the hip persists, osteochondritis (Legg-Calve-Perthes disease) is a possible diagnosis. This condition is particularly common in children on chronic steroid therapy (such as SLE patients) and in children with sickle cell anemia.

Sub-acute osteomyelitis. Low grade infections such as osteomyelitis and septic arthritis are rare without fever but can occur. Bacterial infections are most likely causes, followed by viral infections, tuberculosis, and fungal infections.

Diskitis. Diskitis is a rare condition in young children. The peak onset is at age 4–6. The disease appears with back pain and stiffness or with pain referred to the abdomen or lower extremities. The child usually refuses to walk or to bear weight on one or both legs. The ESR is usually elevated. Xray changes may not be apparent for several weeks or months, but a joint-bone scan and MRI can be helpful for the diagnosis early in the course of the disease.

Blood dyscrasias and hemoglobinopathies. Blood dyscrasias such as hemophilia can affect a single joint, especially the knee.

Reflex sympathetic dystrophy. Reflex sympathetic dystrophy is one of the under-recognized disorders in the pediatric population. The diagnosis is based on features of a localized pain syndrome and additional signs of dysautonomia. The skin of the involved limb has episodic cyanotic discoloration with a purple mottled appearance. The skin temperature may be reduced. Slow capillary filling and soft tissue swelling are common manifestations. The patient can appear seemingly indifferent to his problem. The French term "la belle indifférence" has been used to describe this particular clinical situation. Those affected with RSD are usually teenage girls. A history of minor trauma is found in many of these patients, followed by disuse of the involved limb. Symptoms may last from one week to months. When the condition persists, chronic changes with skin atrophy, pigmentation, hyperhidrosis and muscle atrophy may be seen. Several studies found many of these children to have difficulties at school, a dependent personality with avoidance of responsibility, low pain threshold, anxiety and depression. In addition, stressful psychological events, such as physical or sexual abuse or divorce of the parents, were often documented as preceding the onset of RSD. Of the 70 patients studied by Wilder et al. [3], 84% were girls with a mean age of 12.5 years. The lower extremity was involved in 87%. The average time from initial injury to diagnosis was one year. The etiology and pathogenesis of RSD is not well understood, although there is clear evidence for local sympathetic nervous system over-activity. The diagnosis is based on the clinical signs and symptoms. Bone scan with technetium 99m perfusion study may be helpful, showing decreased blood flow in the involved limb in a significant number of these children, although increased flow was reported mostly in adult patients. In more chronic cases, a radiogram may reveal evidence of osteoporosis. There is no laboratory marker for this disorder and tests such as complete blood count and ESR are normal. Tests for rheumatic diseases such as antinuclear antibodies and rheumatoid factor are negative.

Malignancies. These are less likely but must be included in the differential diagnosis. Again, bone tumors need to be considered. In approximately 10–15% of all patients with leukemia, the presence of joint or bone pain is an early clue. Here a bone marrow analysis is helpful.

Psychogenic pain. This is a possibility when there is a suggestive background and an unremarkable physical examination.

Multiple-joint pain with fever

As in patients with single-joint involvement, we start by considering infection.

Sepsis. In patients who have fever and polyarthralgia or polyarthritis, sepsis with seeding of the bacteria to the joints is an important differential consideration. Disseminated staphylococcal disease with multiple-joint involvement has been reported but is relatively uncommon. Other bacteria such as

SLE = systemic lupus erythematosus

RSD = reflex sympathetic dystrophy

Mycobacterium tuberculosis and brucellosis can involve multiple joints. Pyelonephritis can cause a reactive polyarthralgia. This infection ran occur without pyuria and can be detected only by carefully performed urine cultures. In most children with fever and polyarthralgia or arthritis who are not seriously ill, the joint symptoms resolve, along with remission of the fever, upon treatment of the underlying condition.

Viral diseases. Many of the viruses can cause a clinical picture of reactive arthritis. Most common is the arthritis associated with rubella virus and vaccine. Mumps virus, hepatitis B virus, adenovirus, Epstein-Barr virus, cytomegalovirus, parvovirus B19 and herpes are known to cause arthritis, and in recent years human immunodeficiency virus has been implicated.

Reactive arthritis. In culturing, the organisms that need to be considered most frequently are salmonellae, shigellae, *Neisseria* species, brucellae, and *Yersinia enterocolitica*.

Rheumatic diseases. If intermittent high fever, rheumatoid rash, hepatosplenomegaly, lymphadenopathy and pericarditis occur, a diagnosis of systemic onset of JRA can be established. If the joint involvement persists for at least 6 weeks, even in the absence of these additional manifestations, a diagnosis of polyarticular-onset JRA can be made. But if there are other symptoms, consider other rheumatic diseases such as SLE, juvenile derrnatomyositis and scleroderma. Classic or atypical Kawaski disease and Henoch- Schönlein purpura can present with joint involvement and should be included in the differential diagnosis.

Lyme disease. In endemic areas in the United States and Europe, you must consider Lyme disease in any child with arthritis. The arthritis is usually preceded by a skin lesion or rash known as erythema chronicum migrans. Detection of antibodies to *Borrelia* (and confirmed by Western blotting method) is helpful for the diagnosis. In addition, detection of *Borrelia* by polymerase chain reaction is available in some centers [4].

Post-immunization. Arthritis and arthralgia are common manifestations that follow immunization, particularly mumps-measles-rubella, and are most likely a reaction to the rubella component.

Immunodeficiency syndromes. The most common immunodeficiency conditions seen in association with chronic arthritis are selective immunoglobulin A deficiency, agammaglobulinemia, and hypogammaglobulinemia, and complement component deficiencies. The arthritis is indistinguishable from that seen in children with pauci-articular JRA. Erosive joint disease, rheumatoid nodules, and circulating rheumatoid factors are usually not present.

Serum sickness. This is the result of an immune reaction, especially to medications. Serum sickness-like disorders have been reported in association with viral illness. The clinical signs of serum sickness include fever, arthritis and an urticarial rash. Other manifestations such as nephritis do not always occur.

Inflammatory bowel disease. When in addition to the joint symptoms the patient develops gastrointestinal symptoms such as abdominal pain, diarrhea and weight loss, consider Crohn's disease or ulcerative colitis. Arthritis occurs in up to 30% of these patients, usually in the weight-bearing joints. In a few patients arthritis precedes the bowel symptoms by months or years. A small number of patients will develop ankylosing spondylitis; most are HLA-B27 positive [2].

Sarcoidosis. Childhood sarcoidosis is a rare granulomatous disorder of unknown origin that can affect any organ of the body, including the joints. The clinical presentation can vary greatly depending upon the organs involved. Two distinct forms of sarcoidosis exist in children. Older children usually present with a multisystem disease similar to the adult manifestation, with frequent hilar lymphadenopathy and pulmonary infiltration. Early-onset sarcoidosis is a unique form of the disease and is characterized by the triad of rash, uveitis and arthritis in children less than 4 years old. The diagnosis of sarcoidosis is confirmed by demonstrating a typical non-caseating granuloma on a biopsy specimen. Elevated serum angiotensin-converting enzyme may be seen in 80–85% of the patients and is a valuable tool for monitoring disease activity. Other granulomatous diseases should be reasonably excluded [5].

Familial Mediterranean fever. This is one of the known periodic fever syndromes. Patients with this condition present with recurrent short episodes of fever and polyserositis (including arthritis, peritonitis and more rarely pleuritis and pericarditis), which are the predominant features of FMF. This condition is relatively rare in the USA. As the name implies, it occurs primarily in children of Mediterranean origin including Turks, Armenians, and Sephardic Jews. It is inherited as an autosomal recessive trait. The gene responsible for FMF was mapped in 1992 to a small interval on the short arm of chromosome 16, and was identified and cloned in 1997. Haplotype and mutational analyses showed ancestral relationships among carrier chromosomes that have been separated for centuries. The gene encodes a 781 amino acid protein known as pyrin, which has a role in inflammation. Over 29 mutations have been found so far. The five most common mutations (V726A, M694V, M694I, M680I and E148Q) were found in more than two-thirds tested Mediterranean FMF patients. The most common missense mutation is methionine-694-valine mutation (occurring in 20–67% of cases), which is associated with a higher disease severity index and also a higher incidence of amyloidosis followed by the valine-726-alanine mutation (7–35%), which is associated with milder disease and a lower incidence of amyloidosis. Genetic screening using restriction analysis PCR systems on a DNA isolated from peripheral blood lymphocytes is now available in commercial genetic clinical laboratories. These tests should be performed in any patient from an ethnic origin at risk who presents with recurrent fever and musculoskeletal symptoms. However, genetic laboratories usually screen for the 5–10 most common mutations, and rare mutations will be missed. Therefore, the

HLA = human leukocyte antigen
FMF = familial Mediterranean fever
PCR = polymerase chain reaction

diagnosis of FMF is still based on clinical grounds, and genetic screening should be used as a confirmatory test.

In addition, when considering FMF as the possible diagnosis, other periodic fever syndromes such as familial hibernian fever and hyper-IgD syndrome need to be ruled out [6].

Malignancies. When bone pain occurs in addition to the joint involvement, neoplastic diseases such as leukemia, lymphoma and neuroblastoma must be considered. Such patients may develop arthralgia and even arthritis before other manifestations of their illness become evident. Sometimes a definite diagnosis of leukemia or lymphoma can be established only after bone marrow aspirations and biopsies. When needed, lymph node and/or liver biopsies may be valuable tools in the process of seeking the correct diagnosis.

Multiple-joint involvement without fever

Rheumatic diseases. When there is multiple-joint pain or swelling in the absence of fever, first consider the rheumatic diseases – including acute rheumatic fever – in patients with polyarthralgia or polyarthritis. The arthritis of SLE may be impossible to clearly differentiate from JRA unless there is synovial thickening or erosive changes that are more typical of JRA. Patients with early Henoch-Schönlein purpura may complain of arthritis before the characteristic purpuric lesions develop.

Joint hypermobility. We previously described juvenile episodic arthralgia/arthritis as recurrent episodes of shortlived joint pain or swelling with normal laboratory findings; more than 60% of these children had hypermobility of the joints. Joint hypermobility may predispose children to the development of arthralgia or arthritis. It is a benign condition with an excellent prognosis. In a normal school population of 260 children, we found that 18% of the girls and 6% of the boys had hypermobile joints. Thus, it is important to check for hypermobility in patients with unexplained joint complaints. Hypermobility that produces excessive stretching of ligaments is the probable cause of the symptoms in many patients with juvenile episodic arthralgia/arthritis. The causes of symptoms in those who are not hypermobile are still to be determined. The association between joint hypermobility and articular complaints was based on many anecdotal reports. We have confirmed this observation in a controlled study of Israeli schoolchildren, where as many as 40% of hypermobile children manifested symptoms of arthralgia. These symptoms are benign and usually resolve without sequelae. The normal child with symptomatic joint hypermobility presents with recurrent pain and, more rarely, swelling in the knees. Often, the pain is limited to one or two joints and recurs in the same joints. The hips, ankles and elbows are less frequently involved. Many of these children will experience pain following exercise and others will manifest pain late in the afternoon or in the evenings. A family history of joint hypermobility was found in more than 50% of these children. It is suggested that children with unexplained joint pain should be evaluated for joint hypermobility. However, it should be emphasized that this is a diagnosis of exclusion and serious forms of joint diseases such as juvenile rheumatoid arthritis, infection or malignancy must be ruled out before considering the diagnosis of this benign condition. In addition, joint hypermobility is a well-known manifestation of a number of conditions such as Ehlers-Danlos, Marfan's osteogenesis imperfecta, homocystinuria, trisomy 21, and pseudoxanthoma elasticum. These conditions should be ruled out before establishing the label of benign joint hypermobility. The mechanism by which joint symptoms develop in joint hypermobility is not well understood. The clinical impression is that the episodes of pain in the hypermobile child correlate with physical activity. Therefore, we may speculate that pain could be related to excessive stretching of the ligaments, joint capsule and other soft tissue constituents around the joint. These micro-injuries are manifested by pain [7].

Growing pains. In a European study, 15% of all schoolchildren had poorly understood myalgia, bone pain, or arthralgia. These are the non-specific aches or "growing pains" that are commonly seen in childhood. Most growing pains occur in children with an age range of 3–13 years and girls seem to be more affected than boys. Pain is described as cramps that are often deep in the thighs, shins and calves. It is usually localized to the lower extremities. Pain in the groin, back and upper extremities is unusual. The pains occur in the evening or at night and may interrupt sleep, but they disappear by morning. The pains may be precipitated by exercise and are usually relieved by massage. Growing pains are usually not associated with limping. These children are otherwise healthy and have normal growth and development. This is a diagnosis of exclusion. Physical examination, laboratory studies and radiographs are within normal limits. Skeletal growth has no effect on the incidence of growing pains. Historically, the French physician Duchamp, in 1823, was the first to describe growing pains as "Maladies de la croissance" (diseases of growth). In 1939, Hawksley introduced his anatomic theory, based on the notion that children with growing pains have anatomic abnormalities such as "scoliosis, pes planovalgus, genu valgum or varum, tibial torsion, femoral anteversion, or leg length discrepancy." He emphasized that faulty posture due to these abnormalities may cause limb pain at the end of the day or at night. This theory was refuted by repeated evaluations of children with growing pains that revealead no abnormal physical findings. In 1951, Naish and Apley in Britain proposed the emotional theory and established the current definition of growing pains. In their study of 721 children, 30 (4.2%) gave a history of intermittent limb pain not related to joints, occurring late in the day or at night for at least 3 months. Using Apley's criteria, Swedish investigators Oster and Neilsen, in a 1970 study of schoolchildren, found a higher prevalence of growing pains (13% of boys and 18% of girls). In addition, these investigators found that over 40% of the girls and less than 30% of the boys had suffered simultaneously from growing pains and episodic headaches and/or abdominal pain. They found that children with

IG = immunoglobulin

growing pains demonstrated the same growth velocity as did children without growing pains. No correlation was found between the frequency of growing pains and growth as measured by height, weight and weight/height ratio. Although the nature of growing pains is still unknown, it is well accepted is a benign and non-crippling condition that resolves spontaneously. The pathogenesis of growing pains remains unknown. Still, very little is known about the nature of growing pains, although a great deal has been learned about what they are not [7].

Fibromyalgia syndrome

Fibromyalgia syndrome is more common in young adult females. This condition is manifested by diffuse musculoskeletal aching and tenderness on multiple tender point sites detectable on physical examination and is often accompanied by characteristic sleep disturbances. This syndrome is now established as a recognizable clinical entity in adults and children. The prevalence of FMS in children is not well documented, although we found a frequency of 6.2% in Israeli schoolchildren. Of 338 schoolchildren evaluated (age range 9–15 years), 21 (6.2%) fulfilled the criteria for FMS, namely widespread pain on digital palpation in 11 or more of the specific tender point sites in combination with tenderness. Another seven children without diffuse aching met the criteria of the tender points. More girls (8.8%) than boys (3.9%) were found to have FMS, although the difference was not statistically significant. Most interesting were the dolorimetric findings in this study. Boys were found to have a lower tenderness threshold than girls. Moreover, children with FMS had a lower tenderness threshold both at control and tender point sites than those without FMS. Many children diagnosed with FMS complain of pain and stiffness at the knees, ankles, elbows, wrists, fingers, cervical spine, thighs and feet. Some of them may have a feeling of joint swelling without obvious swelling or effusion in the joints. Symptoms of sleep disturbances, fatigue, migraine headaches, depression and irritable bowel syndrome are frequently associated. In patients with FMS, diffuse aching and fatiguability go along with sleep disturbances. The diagnosis of FMS is based on the currently accepted 1990 American College of Rheumatology criteria. Fulfillment of these criteria requires at least a 3 month history of widespread musculoskeletal pain, and physical examination revealing tenderness on digital palpation in at least 11 of 18 (9 pairs) tender point sites:

- occiput, at the suboccipital muscle insertion
- trapezius muscles, at the upper border and midpoint of the muscles
- neck, at the intertransverse spaces C5-C7, on the anterior aspect
- supraspinatus muscles, at the origin of the muscles, above the spine of the scapula
- parasternal region, at the second costochondral junction
- distal humerus, 2 cm distal to the lateral epicondyles
- lower back, at the upper outer quadrant of the buttocks
- femoral greater trochanter, at the posterior prominence
- knees, at the medial pad fat.

All of the above tender point sites are bilateral. Although the etiology of FMS is unknown, studies have implicated a number of mechanisms. These include sleep disturbances in stage 4 non-REM sleep, biochemical changes in the upper spine and lower back, alteration in immune responsiveness, overactivity of the sympathetic nervous system, alteration of plasma catecholamines, changes in neurotransmitters (substance P, endorphins, serotonin), infectious agents, and repeated microtrauma to skeletal muscles. Recent endocrinologic studies demonstrated several abnormalities in subsets of patients with FMS, including low somatomedin-C levels, cortisol non-suppression to dexamethasone, hypothalamic-pituitary-adrenal axis perturbations, and a hyperprolactinemic response to thyroid-releasing hormone. Although patients with FMS have normal basal prolactin levels, a recent study found that FMS was very common in a subset of women with hyperprolactinemia and that the frequency was directly associated with the degree of hyperprolactinemia [7].

Post-immunization. Arthritis or arthralgia after immunization is another possibility when there is no fever.

Neurologic conditions. These include post-infectious polyneuritis (or Guillain-Barre syndrome) that may be present with pain in the extremities, but this is not a real arthritis.

Malignancies. When all the above conditions have been ruled out, consider malignancy.

Psychogenic arthralgia

Hysteria can occur in teenagers, and those who have anxiety or depression may develop pain in the foot or ankle and refuse to walk or bear weight. In time this leads to atrophy of the muscles and decreased range of motion without any evidence of swelling or signs of inflammation. This may become a difficult problem and requires collaboration with a social worker, psychologist or psychiatrist.

FMS = fibromyalgia syndrome

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