Juvenile Dermatomyositis: A Clinical Overview

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The questions below should help focus the reading of this article.

1. What criteria are necessary to establish the diagnosis of juvenile dermatomyositis (JDMS) or polymyositis?

2. What antibody studies are commonly positive in children with JDMS?

3. What are characteristic features of the rash of JDMS?

4. How are children with JDMS appropriately treated?

The spectrum of inflammatory muscle disease in children includes juvenile dermatomyositis (JDMS), polymyositis (PM), inflammatory myopathy associated with other connective tissue diseases, and acute viral myositis, in addition to inflammatory myopathies associated with bacterial and parasitic infection. On a worldwide basis, most inflammatory myopathies accompany bacterial or parasitic infections, while in North America a viral etiology is more common. A review of JDMS and PM in children, the epidemiology of these diseases, their clinical and laboratory aspects, and the most recent evidence of genetic and infectious factors that may play a role in disease susceptibility is provided in this article.

The primary clinical feature of both JDMS and PM is chronic and progressive proximal muscle weakness. In the case of JDMS, the vasculitis and distinctive skin manifestations are associated with progressive muscle weakness; with PM, the skin is spared. Fulfillment of the criteria of Bohan and Peter[1] is needed to establish the diagnosis of either JDMS or PM (Table 1). A child can be diagnosed with definite JDMS if, in addition to the typical rash, 3 of the 4 criteria are found. A definite diagnosis of PM can be made if 3 of the 4 criteria are found and there is no evidence of skin involvement. Because myositis is often a component of other connective tissue diseases, it is essential to exclude such conditions as systemic lupus erythematosus (SLE), mixed connective tissue disease, juvenile rheumatoid arthritis (especially of systemic onset), the spondyloarthropathies, and Sjögren syndrome.

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EPIDEMIOLOGY

A bimodal age distribution of the combined populations of patients with PM and DMS has been identified. One peak occurs at 5 to 14 years of age, the other at 45 to 64 years of age. The combined frequency of JDMS and PM in the United States is estimated to be 1 to 3.2 cases in 1 000 000 in whites and 7.7 cases in blacks. JDMS is 10 to 20 times more frequent than PM in childhood. In the case of JDMS, there is a 2:1 female predominance.

ANA: Antinuclear antibodies
CK: Creatine kinase
GLA: γ-Carboxyglutamic acid
JDMS: Juvenile dermatomyositis
HLA: histocompatibility locus antigens
PM: Polymyositis
SLE: Systemic lupus erythematosus

EDUCATIONAL OBJECTIVE

Readers may also want to reread the article on "Rheumatic Diseases of Childhood" by Rennebohm, published in the December 1988 issue of *Pediatrics in Review* (1988;10: 183–190). R.J.H.

28. The pediatrician should have knowledge to make an appropriate evaluation of a 4-year-old girl with progressive muscle weakness, differentiating among dermatomyositis, polymyositis, muscular dystrophy, an endocrinopathy (thyroid disease, Cushing disease), Guillain-Barré syndrome, trichinosis, toxoplasmosis, myasthenia gravis, toxic exposure, and a metabolic disease (hypophosphatemia, hypokalemia), and develop a plan for management. (Topics, 90/91)

There appears to be a cluster of the pediatric cases in February through April of some years. In the Midwestern United States, there was an increase in children with definite JDMS whose symptoms first appeared in the months of June through January in each of 7 years (1974 to 1980). These children were diagnosed within 4 months of the onset of symptoms, and the seasonal cluster suggested an environmental influence. There is some ambiguity about

TABLE 1. Criteria for Diagnosis of Juvenile Dermatomyositis and Polymyositis in Childhood*

	Juvenile Dermatomyositis	Polymyositis
Characteristic rash	+	–
Symmetrical proximal muscle weakness‡	+	+
Elevated muscle-derived enzymes	+	+
Muscle histopathology†	+	+
Electromyographic changes: inflammatory myopathy	+	+

* In addition to presence (or absence) of characteristic rash and exclusion of other rheumatic diseases, 3 of 4 criteria must be met to confirm diagnosis.
† The histology of childhood polymyositis is different from juvenile dermatomyositis.
‡ Exclusion of other rheumatic diseases.

this point, for others in a different latitude have looked at children with PM (including an unknown number with JDMS) and have not reported a cluster of onset in any one season.

Although malignancy is reported to be associated with adult dermatomyositis and PM, there does not appear to be any association of malignancy with JDMS or childhood PM.

CLINICAL FINDINGS (Table 2)

Skin Manifestations

The rash characteristic of JDMS may precede or follow the onset of proximal muscle weakness. Periorbital erythema and eyelid telangiectasia, which accompanies periorbital edema in 50% to 90% of affected children can be discerned. Telangiectasis on the eyelid (and elsewhere) may persist long after other signs and symptoms of disease activity have resolved. The rash has a violaceous or heliotrope hue and is often most prominent on the eyelid. Like the rash seen in SLE, it may cross the bridge of the nose (Fig 1). The rash may be precipitated by a brief unprotected exposure to the sun, and the child may develop erythema involving the upper torso or the extensor surface of the arms and legs. The rash may occur in the absence of elevation of serum levels of muscle-derived enzymes. Exposure to sunlight may cause exacerbation of skin inflammation alone or may precipitate activation of the myositis as well. Recurrent photosensitive dermatitis may precede muscle weakness in the case of JDMS. The skin over the knuckles may be either hypertrophic or pale red, evolving into colorless bands of atrophic skin (Gottron sign, Fig 2). Similar patches fre-

Fig 1. Periorbital rash of juvenile dermatomyositis. Some areas of infarction are present in nasolabial folds, and capillary thrombosis is present.

Fig 2. Gottron sign in juvenile dermatomyositis, characterized by erythema and thinning of the skin over metacarpal and intraphalangeal joints (see arrow). On occasion, there can be a thickening of involved skin, resulting in redundancy.

TABLE 2. Signs Suggesting Juvenile Dermatomyositis

Symmetrical proximal muscle weakness
Vasculitis with capillary thrombosis
Nasal speech
Oral ulcerations, abdominal pain, and weight loss
Persistent rash over pressure points, shawl area, and face

quently occur over the elbows, knees (Fig 3), and medial malleoli of the ankles. Inflamed skin over the buttocks may make it difficult for the child to sit on a firm surface. Diffuse vasculitis (nailbed telangiectasia, infarction of oral epithelium, skin folds, or digital ulceration) is clearly associated with more severe disease, and children with such symptoms may experience an unremitting course associated with the development of soft tissue calcifications. These calcifications, which occurred in approximately one third of the children in our series in contrast to 70% in others, are often located at pressure points (Fig 4, A and B) and are a consequence of the severity and duration of the disease.[2]

Musculoskeletal Symptoms

Proximal muscle weakness as evidenced by difficulty in climbing stairs, getting up from a chair, or combing hair, or by using hands to push off body in an attempt to stand (Gower sign). Neck flexor weakness is a particularly sensitive indicator of muscle impairment. In the younger child, weakened abdominal muscles are common. Occasionally, there are complaints of pain on muscle compression but, unlike bacterial related myopathies, pain is not a frequent symptom in children with JDMS. As active inflammation subsides, one of the residual findings on physical examination is neck flexor weakness, which may persist for 1 or 2 years after therapy has begun. Usually, the child is more comfortable when the limbs are held in the flexed position. This promotes the development of flexion contractures and soft tissue calcification, often with unfortunate consequences. Combined medical therapy to suppress inflammation and physical therapy (gentle passive stretching) is required in the early phase of the disease, and more intensive graded physical therapy is required at later stages in the disease. The shorter the interval between onset and therapy, the less likely the child is to have soft tissue calcifications, because they appear to be related to disease severity and duration. Decreased bone density (associated with suppressed serum levels of osteocalcin and significantly impaired bone mineral analysis) may also be identified, even in the untreated child, and may result in an increased rate of bone fracture. Scanning with technetium-99m may reveal early sites of massive muscle destruction and soft tissue calcification, in addition to localized bone changes that herald early avascular necrosis or spinal cord compression fractures.

Fig 3. Involvement of skin over knees in juvenile dermatomyositis, showing thinning and atrophy as well as erythema.

Gastrointestinal Symptoms

Difficulty in handling secretions is usually associated with decreased esophageal motility and can be demonstrated using radiographic contrast studies, in which one finds retained barium in a widened atonic pyriform sinus. An associated finding is nasal, high-pitched speech, which is easily detected (for example by asking patients to recite the alphabet) and which usually resolves with a decrease in the inflammatory component of the myositis. The patient may not be able to swallow liquids comfortably; esophageal reflux may result in aspiration pneumonia, and appropriate precautions should be used to prevent this, including thickened feedings, elevation of the head of the bed, and bronchial drainage. In addition, involvement of the masseter may be associated with difficulty in chewing food. Vasculitis can also affect any part of the gastrointestinal tract in a spectrum that ranges from decreased D-xylose absorption, which may be associated with weight loss, to frank ulceration with perforation, which can threaten life.

Cardiorespiratory Symptoms

Results from an electrocardiogram are abnormal in more than half of the children with definite JDMS. Asymptomatic conduction abnormalities predominate (for instance, one of our patients had a complete right bundle branch block). These conduction derangements often resolve when the activity of the disease abates. A decrease in ventilatory capacity in the absence of respiratory complaints was found in 78% of our patients with definite JDMS. Pulmonary fibrosis may occur in both adults and children with inflammatory myopathy, but it is associated more often with those who develop antibodies to Jo-1 (dis-

Fig 4 . A, soft tissue calcifications (see arrows) in a child with juvenile dermatomyositis. B, radiological confirmation of soft tissue calcifications seen in left fourth finger in part A.

cussed below) and who have symptoms of overlap syndrome. One of our patients, who now has an inflammatory myopathy but not JDMS, has highly positive antinuclear antibodies (ANA) and a special kind of autoantibody, called Jo-1. She was first seen at the age of 12 years with shortness of breath and radiographic evidence of interstitial fibrosis, but she did not develop myositis until 6 years later.

Ophthalmologic Symptoms

The eye may also be involved in JDMS, most commonly with evidence of thrombosis of vessels at the eyelid margin. In addition, "cotton wool" spots may occur as a result of small vessel occlusion, and intraretinal edema may result in injury to retinal nerve fibers, resulting in optic atrophy and sustained visual loss.

Other Disease Manifestations

Vasculitis involving the central nervous system may be associated with depression and sometimes with wide mood swings. It is not common for a child with JDMS to have Raynaud phenomenon or fever; these symptoms are more frequently found in overlap syndrome.

DIFFERENTIAL DIAGNOSIS OF JDMS

Skin

Laboratory findings in the presence of JDMS are summarized in Table 3. Other autoimmune diseases may exhibit some of the cutaneous manifestations found with JDMS. The tendency for sun exposure to exacerbate the erythema of the skin is seen with SLE as well as JDMS. A malar rash, which more commonly crosses the bridge of the nose with SLE, also develops in some children with JDMS. The Gottron sign can be mimicked by psoriatic lesions, accompanied by healing foci of hypopigmentation found in areas usually unaffected by JDMS, such as the pretibial region. A further clue that the lesions are not part of the spectrum of JDMS is that they clear with exposure to sun rather than becoming more prominent. Telangiectasia is a prominent feature of scleroderma and occurs in overlap syndromes in which myositis is a disease component. For example, a child with mixed connective tissue disease may have rashes seen with JDMS as well as proximal muscle involvement, but can be distinguished from the child with JDMS by the presence of antibodies to ribonucleoprotein in their sera.

Assessment of endothelial cell damage may give an indication of active disease.

Muscle-Derived Enzymes

Skeletal muscle is rich in enzymes and, in the case of an inflammatory myopathy, damage to the muscle either as a consequence of reduced vascular supply or direct immunological cytotoxicity results in the release of enzymes from the sarcoplasm to the peripheral circulation. Elevation of enzyme levels does not distinguish between necrosis of tissue and cell membrane leak, and sera to be analyzed must be free of hemolysis.

TABLE 3. Laboratory Findings in Juvenile Dermatomyositis

Antinuclear antibodies	Positive speckled
DNA	Normal or negative
Smith antigen	Normal or negative
Ribonucleoprotein	Normal or negative
SSA-Ro/SSB-La	Normal or negative
Von Willebrand factor-related antigen	Elevated
Creatine kinase	Elevated
Aspartate aminotransferase	Elevated
Lactic acid dehydrogenase	Elevated
Aldolase	Elevated
Erythrocyte sedimentation rate	Normal or elevated
White blood cell count	Normal or elevated
Hemoglobin	Normal or depressed
D-Xylose	Impaired

Functional myopathies and myopathies that are a consequence of denervation are accompanied by decreased muscle mass, weakness, pain, loss of function or paralysis, and usually result in muscle atrophy. With these diseases, the serum levels of creatinine kinase (CK), the muscle (M) and brain (B) isoenzymes of CK, as well as pyruvate kinase (PK), lactic acid dehydrogenase, and aldolase are normal. In contrast, some forms of dystrophies may result in CK and aldolase levels being increased as much as 30 times normal, and CK-MB (increased in acute myocardial infarction, back surgery) also being elevated with Duchenne muscular dystrophy. In contrast, the BB form of CK is elevated with central nervous system disease and injury to smooth muscle (as is seen in genitourinary surgery). The CK-MM isoenzyme can be elevated as a result of myocardial and skeletal muscle disease or trauma.

Trauma to muscle resulting from vigorous physical exercise (eg, marathon running), surgical and accidental crush injury, and intramuscular injections can also increase serum levels of CK. Drugs that increase muscle membrane permeability also may result in increased levels of CK (ie, aminocaproic acid, D-penicillamine, halothane (hyperpyrexia), and quinidine). Drug overdose with amphetamines, barbiturates, ethanol, and heroin all result in massive increases in CK. Disorders of the calcium metabolism, such as hypocalcemia (either isolated or associated with rickets), hypoparathyroidism, and chronic renal failure, can be associated with increased CK levels. Once the low ionized calcium are normalized, the elevated CK levels usually normalize as well.

All four muscle enzymes should be measured in the sera.

Aldolase has a short half-life and can be increased with viral hepatitis, metastatic liver disease, some prostate tumors, and some forms of leukemia and anemia. Lactic acid dehydrogenase has five isoenzymes, the anodal forms are increased in cardiac renal erythrocytes and some diseases of skeletal muscle, whereas the cathodal forms are increased in dysfunction of skeletal muscle and liver. Other less specific enzymes that can also be elevated as a result of muscle damage are aspartate aminotransferase, which frequently is increased in association with liver damage, and alanine aminotransferase. Myoglobin is present only in skeletal and cardiac muscle. This oxygen-binding heme protein is present in the serum in elevated levels with myopathies; persistent myoglobinuria can result in renal failure.

Muscle Complaints

Children with JDMS may complain of muscle cramps or of pain on compression of the proximal muscles, but proximal muscle weakness is still the predominant symptom. Other conditions that may be associated with muscle cramps and contractures include hypothyroidism, uremia, and electrolyte imbalance (such as hypokalemia). Pretibial tenderness is seen with erythema nodosum and not with JDMS; pain that wakes the child at night should be investigated for other causes, such as malignancy, osteoid osteoma, or osteomyelitis. Muscle weakness can be seen in hormonal derangements, either endogenous (eg, adrenal dysfunction) or iatrogenic (eg, administration of high-dose steroids). In addition, thyroid, pituitary, and parathyroid dysfunction may be accompanied by skeletal complaints. Metabolic muscle diseases include defects of glycolysis (eg, phosphofructokinase deficiency) and are associated with contractures, exercise intolerance myoglobinuria, and a positive ischemic lactate test. There may be a defect in lipid metabolism, such as a carnitine deficiency state (which may be exacerbated by nonsteroidal anti-inflammatory drugs), or a myalgia syndrome, which can be documented by a positive ischemic ammonia test.

Acute infectious viral myositis in children, most frequently attributed to Influenza A or B, is distinguished clinically from chronic myositis by its propensity for calf muscles, severe pain, and rapid resolution in 1 to 4 weeks. This acute myositis may be accompanied by myoglobinuria, electromyographic changes, elevation of CK, and an increase in viral antibody titers.

Other connective tissue diseases may insult muscle. Children with systemic onset juvenile rheumatoid arthritis may have spiking fevers and an evanescent rash. Often they do not wish to be held and have elevated levels of muscle enzymes, making the specific connective tissue diagnosis imperative. The myositis of SLE is usually accompanied by an elevated anti-double-stranded DNA, reduction in serum levels of complement, and the presence of immune complexes to a degree not usually found in JDMS.

Electromyogram

Evidence of an inflammatory myopathy is not specific for JDMS. The electrodes are placed in an area where the child has proximal weakness (not the site of a future biopsy),

and insertional irritability is often observed followed by spontaneous electrical activity at rest. This may also be seen with muscular dystrophy and with early acute inflammatory myopathy, but may not be present with chronic acquired illness. Abnormal early full recruitment of muscle fibers with moderate effort occurs in 45% of patients with JDMS, and bizarre, high-frequency discharges may be seen in 15% to 20% of patients tested. Reduced motor unit activity can be seen with Duchenne muscular dystrophy as well as JDMS. Furthermore, myasthenia gravis can coexist with an inflammatory myopathy, resulting in a greater degree of motor unit potential instability than found in the uncomplicated inflammatory myopathies. The pattern of inflammation in muscle as detected by electromyography can be found with other connective tissue disease, such as rheumatoid arthritis, progressive systemic sclerosis, SLE, Sjögren syndrome, and sarcoidosis.

PATHOPHYSIOLOGY OF JDMS

Vascular lesions can occur in the absence of a prominent inflammatory component and may be unique to children with JDMS,[3] although other investigators have found lesions with polymyositis that appear to be similar to those seen with JDMS. Capillaries, venules, and small arteries are damaged with loss of muscle capillary network and structural changes in the nailfold capillary bed, which may persist despite clinical improvement. The primary lesion occurs in the endothelial cell, which contains reticulotubular inclusions that are the site of thrombosis and vessel obliteration. In some cases, increased collagen deposition in skin has been reported.

We have tested children with active disease and found that increased serum levels of muscle-derived enzymes may be associated with increased levels of von Willebrand factor-related antigen released from damaged endothelial cells. When we studied 10 children with active JDMS, we found that increased levels of von Willebrand factor-related antigen are usually correlated with decreased gastrointestinal absorption of D-xylose. This suggests that medication given orally will be absorbed poorly and provides the rationale for the intravenous administration of methylprednisolone or other immunosuppressive agents.

During active disease, increased levels of fibrinopeptide A (a measure of thrombin generation) have been documented in conjunction with activation of the complement cascade, despite normal serum levels of complement components. In addition, there is some evidence that the terminal attack complex of the complement system may be involved in damage; the C5b-9 membrane-attack complex has been localized in the intramuscular microvasculature in 10 of 12 patients with JDMS.[4] Several studies have suggested that immune complexes may play a role in inflammatory myopathies. The usual indicators of an acute phase reaction may be absent; the sedimentation rate, white blood cell count, and differential are often normal, but they may be altered in cases of massive involvement. This suggests that there are elevated levels of acute early phase reactants with decreases in those patients who respond to therapy, and persistence of elevation in those patients who have soft tissue calcification. In our own series, children with persistent skin inflammation often have elevated levels of IgE, despite other evidence that the disease has become less active. The muscle pathology in JDMS reflects vascular compromise and capillary dropout, with perivasicular atrophy of both type I and type II fibers (as opposed to steroid-induced myopathy, in which there is atrophy of type II fibers), and inflammatory infiltrates of mononuclear cells and plasma cells. Muscle biopsy of some children who have JDMS with normal serum enzyme levels and elevated levels of von Willebrand factor-related antigen can reveal a surprising extent of inflammation. In contrast, with PM there appears to be less primary vessel involvement; vessels are normal in number and structure, and soft tissue calcification does not occur. In the case of dermatomyositis, the infiltrate is composed of Ia+ B cells and the T-4 to T-8 ratio is increased, but few children have been studied extensively. There appears to be a close relationship between T4+ cells to B cells as well as macrophages, suggesting a cytotoxic cellular mechanism, perhaps directed against immune complex-modified endothelial cells.[5] There have been sporadic reports of cellular reactivity of pediatric mononuclear cells to muscle (or its fragments), which we were not able to confirm using cultures of peripheral blood lymphocytes from five untreated children with active disease.

A muscle biopsy may reveal more extensive disease than expected clinically.

Those children with JDMS who do develop calcifications may have one of several outcomes. The calcifications may resolve spontaneously, draining as a white cheesy exudate, leaving dry pitted scars. We and others have found that calcifications do not decrease when chelating agents are given. In some children with persistent active disease, the calcifications can progress to become a sheath in fibrotic muscle, impairing flexion and function and breaking the barrier of the skin, which forms a potential site of entry of infection.

This soft tissue calcification is accompanied by urinary excretion of γ-carboxyglutamic acid (GLA), which is a component of the vitamin K-dependent coagulation pathway; this GLA excretion is increased in comparison to controls matched for age and sex. Increased GLA excretion was present both in the nine children with JDMS who had no clinical or radiological evidence of ectopic calcification and whose mean values for GLA excretion were twice that of normal, as well as in seven patients with JDMS who did have soft tissue calcifications with mean values three times that of normal. Routine measures of coagulation (including prothrombin time and activated partial thromboplastin time) are normal, but the perturbation of endothelial cells and thrombin generation may be linked in an as-yet-undefined manner to the increased urinary GLA excretion. GLA-containing calcifications have the same diffraction pattern

seen on x-ray crystallography as those found in scleroderma. The calcifications are not correlated with the presence of autoantibody, immune complexes, or known histocompatibility antigens. Treatment with anticoagulants has been suggested but poses a considerable hazard for the active child, and it has not yet been proven to be effective in a case-control study.

If appropriate monitered therapy is begun once the diagnosis is confirmed, it is less likely that soft tissue calcifications will occur. A pediatric rheumatologist may be helpful in management.

GENETIC FACTORS

Reports of JDMS in more than one family member are sporadic, but the disease has occurred in monozygotic twins who developed muscle-related abnormalities 2 weeks after an upper respiratory tract infection. In a large cross-sectional study of children with JDMS and their families, a marked increase of the histocompatibility locus antigens (HLA) B8 (relative risk 2.8, $P < .01$) and DR3 (relative risk 3.8, $P < .01$) was found in whites. In Latin Americans, the relative risk for DR3 was 18.5 ($P < .05$).[6] The association of the supratype, A1, Cw7, B8, and DR3 suggests that there might be a genetic component to disease susceptibility or expression. Other autoimmune diseases associated with increased HLA and DR3 include myasthenia gravis, type I (insulin-dependent) diabetes mellitus, and Graves disease. Tests for a wide array of antibodies with tissue or organ specificity were negative when comparing sera from 89 patients with JDMS to 105 controls matched for age and sex. Only the ANA and antibody to PM-1 were more frequent in patients with JDMS than controls ($P < .005$ and $P < .001$, respectively).[7] There was no association with the presence of any other tissue- or organ-specific autoantibody and HLA B8 and DR3 among white patients with JDMS, documenting that, in this group, HLA B8 and DR3 were not associated with generalized nonspecific autoimmunoreactivity. The ANA-positive sera from these children, unlike blood from adults with myositis and pulmonary fibrosis, does not have specificity for the Jo-I antigen found in sera from patients with adult dermatomyositis. Furthermore, when sera from 39 children newly diagnosed with JDMS were studied, none had a nucleolar pattern on HEp2 substrate (seen in scleroderma), and over 63% were positive at a titer greater than 1:80 in a pattern that was predominantly speckled (53%) (a homogeneous pattern was found in 10% of cases). Assays for antibodies to nuclear antigens: Scl-70, SSA-Ro/SSB-La, DNA, RNP, and DNP were all negative. We have found recently that sera from children with primary Coxsackievirus B cardiomyopathy have an ANA that is similar to that of JDMS in a speckled and anticytoskeletal pattern.

Viral Infection and JDMS

A possible infectious relationship in JDMS is suggested by the observation that sera from children newly diagnosed with JDMS from the Chicago area had increased frequency of antibodies (both neutralizing and complement-fixing) to Coxsackievirus B, as well as increased frequency of the HLA B8 and DR3.[8] In a recent report, an RNA probe was used to identify Coxsackievirus B2 persistence in muscle of patients with PM or dermatomyositis, suggesting that this may be a fruitful approach to this problem.[9] Other infectious agents have been implicated in the case of chronic myositis, including toxoplasmosis and hepatitis B. Both skeletal and cardiac myopathies have been found with active human immunodeficiency virus infection. Using electron microscopy and viral isolation, Coxsackievirus A-9 was identified in a child with a chronic myopathy. Of note is that Coxsackievirus A-9 shares a group antigen with the Coxsackievirus B strains. Coxsackievirus B2 has been isolated from the stool, the complement-fixing titer of antibody increased in a child with chronic myositis, and an increase in antibody titers to Coxsackievirus B4 has also been documented by several investigators. We have just embarked on a 3-year nationwide study of the epidemiology of JDMS to obtain confirmation of the hypothesis that response to Coxsackievirus B plays a role in the pathophysiology of JDMS. Newly-diagnosed cases (within 5 months of onset) are sought for this project (Hotline: 312–880–3333).

Newly diagnosed cases of juvenile dermatomyositis (within 5 months of onset) are sought for clinical research. Hotline: 312–880–3333.

THERAPY AND COURSE OF TREATMENT

Steroids are the therapy of choice for children with JDMS. With severe gastrointestinal involvement or vasculitis, intravenous administration of methylprednisolone is preferred until serum levels of muscle-derived enzymes have normalized. It is important to monitor for some of the known side effects of prednisone therapy: retardation of growth, changes in bone density, cataract formation, and avascular necrosis (usually of the femoral head). Several factors may be used to detect inflammation. Levels of muscle-derived enzymes, CK, aspartate aminotransferase, alanine aminotransferase and aldolase may all be elevated, or a single value may be abnormal.[10] Not uncommonly, the elevated serum levels of muscle-derived enzymes will normalize after the first bout of therapy, but there may be clues of persistent disease activity. We have found that the von Willebrand factor-related antigen is a reasonable indicator of vasculitis. Newer assays of macrophage activation, such as neopterin, may be a more sensitive indicator of persistent inflammation.

Assessment of the degree of the child's clinical activity and choice of therapy may require the help of a pediatric rheumatologist. Pulse doses of methylprednisolone are effective (maximally, 30 mg/kg per dose up to 1 g/d) given every other

day until muscle enzymes have normalized. On the alternate day, small maintenance doses of prednisolone may be needed. On occasion, when muscle enzymes are normal in the presence of clinically active disease, we have continued therapy until von Willebrand factor-related antigen has returned to normal levels, thus aborting flares once the steroids are tapered. If there is a prominent cutaneous component to the disease, treatment with hydroxychloroquin (no more than 7 mg/kg per day) may be used in conjunction with topical steroids and lubricants. In all children, use of a sunscreen (level 16 or more) will diminish exposure to the ultraviolet light spectrum, in an effort to decrease disease activation. Finally, some children with longstanding chronic disease have normal levels of muscle derived enzymes, normal levels of von Willebrand factor-related antigen and elevated levels of neopterin, suggesting immune stimulation. These children may have too much fibrosis to benefit from a short course of steroid therapy and intensive physical therapy; in these children, a muscle biopsy may be helpful to assess the potential for repair. Low dose intravenous methotrexate has also been of some use in the treatment of children with refractory symptoms, and cyclosporin has been used in England and France with moderate success. There have been no comparative studies of the efficacy of these drugs in children in the United States. Cytoxan has been found to be ineffective against PM in adults, and has not been well studied as a treatment for childhood myositis.

During the past 5 years, we have been using von Willebrand factor-related antigen as a guideline to therapy in conjunction with intravenous methylprednisone at the onset of therapy. We have not had the development of soft tissue calcifications in any of the 11 children managed in this way. A concern that accompanies the use of oral steroids is the development of compression fractures as a consequence of osteopenia. We have found that children with JDMS have low levels of osteocalcin and that the levels of osteocalcin rise when the disease becomes less active. This means that bone mineral density should be determined and, if it is low, institution of vitamin D therapy and an assessment of dietary calcium intake should be considered to document the need for supplemental calcium. With respect to therapies other than steroids, a single case report suggests that intravenous γ-globulin therapy may diminish disease activity, perhaps in a manner similar to that documented for Kawasaki syndrome. Others have suggested the evaluation and use of methotrexate. Evaluation of the use of cyclosporin for treatment in this country has been hampered by coexisting therapies.

Children have several types of disease course (monocyclic, recurrent, continuous), and it is difficult to predict outcome at the onset of illness, although some studies indicate that prognosis is directly related to the degree of vasculitis. Overall, the greatest mortality appears to be in the nonwhite adult female patient group; improved survival has been documented for children, with less than 7% mortality in the past few years as compared to over 30% mortality 25 years ago.[11] Relapse in a child with an apparent monocyclic course is not common, but has been observed 8 years after apparent complete recovery from the initial insult. There is sporadic evidence that, despite apparent clinical quiescence, there may be continued histological evidence of inflammatory muscle disease. Graded physical therapy is very important to loosen contracted muscles. Local skin care and sun protection using blocking agents (level 16 or more, *p*-aminobenzoic acid-free may be needed), as well as avoidance of strenuous exercise during the active phase of disease all hasten recovery.

SUMMARY

The child who develops the symptoms of the specific rash, proximal muscle weakness, and fatigue should seek medical care promptly. With the advances in physical and medical therapy, many of the consequences of the disease can now be ameliorated. There are suggestive data that JDMS and PM may each have a different pathophysiology, but more evidence is needed. The next few years should be exciting as there is increased effort to determine if there is, in fact, a causal relationship between Coxsackievirus B or other enterovirus and genetic factors that alter the susceptibility to or severity of the course of the disease—JDMS.

Self-Evaluation Quiz

12. Similar diagnostic criteria for juvenile dermatomyositis (JDMS) and polymyositis include each of the following, *except:*

A. Characteristic rash.
B. Symmetrical proximal muscle weakness.
C. Elevated muscle-derived enzymes.
D. Electromyogram typical of an inflammatory myopathy.
E. Exclusion of other rheumatic diseases.

13. Assays for which of the following antibodies are commonly positive in children with JDMS?

A. Scl-70.
B. SSA-Ro/SSB-La.
C. DNA.
D. Antinuclear antibodies.
E. Ribonucleoprotein.

14. A 7-year-old girl develops proximal muscle weakness and a rash. Which of the following features of her rash would not be consistent with a diagnosis of JDMS?

A. Periorbital erythema and edema.
B. Eyelid telangiectasia.
C. History of improvement after exposure to sun.
D. Atrophic skin over knuckles, elbows, and knees.
E. Violet or reddish purple color.

15. True statements about management and therapy for children with JDMS include each of the following, *except:*

A. Corticosteroids are of primary importance.
B. Systemic corticosteroids increase the risk for soft tissue calcification.
C. Repeated determinations of the von Willebrand factor-related antigen are helpful in monitoring therapy.
D. Physical therapy is helpful.
E. Bone mineral density should be determined.

REFERENCES

1. Bohan A, Peter JB. Polymyositis and dermatomyositis. *N Engl J Med.* 1975; 292:344–347, 403–407
2. Pachman LM, Friedman JM, Maryjowski MC, et al. Immunogenetic studies of juvenile dermatomyositis III: a study of antibody to organ-specific and nuclear antigens. *Arthritis Rheum.* 1985;28:151–157
3. Banker QB, Victor M. Dermatomyositis