Dermatomyositis
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ABSTRACT
Dermatomyositis (DM) is an idiopathic inflammatory myopathy with unique cutaneous features. When it appears in adulthood, it may foreshadow several different forms of cancer. Up to 25% of DM patients will go on to develop a malignancy, and, therefore, early recognition and screening are critical. The purpose of this article is to provide an overview of the signs and symptoms of DM, guidance in diagnostic testing and treatment of the disease, and recommendations related to preventive screening in order to reduce morbidity and mortality associated with related systemic disease.

Keywords: cancer, dermatomyositis, myopathy, paraneoplastic, rash

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Cancer that conveniently announces itself? Lung disease that provides fair warning? For primary care providers, a disease that reveals its intent before it attacks is a disease that can be cured. Dermatomyositis (DM) is one such illness. DM often foreshadows critical systemic illness with hallmark signs well before it strikes.

Dermatomyositis (derma meaning skin, myo meaning muscle, and sitis meaning inflammation) is an idiopathic inflammatory myopathy with unique cutaneous features. Approximately 20,000 people in the United States have DM,1 with women affected at 2 to 3 times the rate of men.2 The onset of the disease shows a bimodal distribution of 5 to 14 years old and 45 to 60 years old.2 However, it is the adult-onset version of DM that has been labeled a paraneoplastic syndrome because this form may act as the harbin-ger of cancer.3,4 DM is progressive, chronic, and autoimmune in nature. Patients present with a skin rash, along with symmetric, proximal muscle inflammation and weakness.5 Typically, the cutaneous signs appear first, but they may also coincide with or follow the muscle inflammation.4,6 In fact, changes in the skin can occur more than a year before muscle symptoms appear.3 In approximately 21% of cases, the disease is amyopathic, meaning there is little to no muscle involvement at all.6 Because DM is a connective tissue disease (CTD), it shares the common characteristics of multisystem involvement and autoimmune etiologies similar to other CTDs, including rheumatoid arthritis, eosinophilic fasciitis, Sjogren syndrome, scleroderma, and lupus erythematosus.4 However, unlike the other CTDs, in DM the skin rash is typically the first presenting symptom.4

Systemic involvement in DM manifests itself in a diverse manner, from minor constitutional symptoms like fever and malaise to life-threatening cancer. Up to 25% of DM patients will go on to develop a malignancy,6 giving DM patients a 6-fold increase in cancer risk during the first year after diagnosis.3,5 The increased risk of cancer is only associated with adult-onset patients who exhibit skin manifestations. The risk is greatest in the first couple of years after diagnosis.3,7

The types of malignancies vary and include ovarian, lung, pancreatic, stomach, and colorectal cancers and non-Hodgkin lymphoma. Sixty percent of patients will present with symptoms of DM before any malignant neoplasm is present.3 Up to 50% of patients will develop pulmonary disease in the form of interstitial lung disease.3 Furthermore, thoracic muscle weakness may lead to dyspnea in some patients, whereas skeletal muscle weakness leads to dysphagia. Because the skin lesions and/or muscle weaknesses typically occur well before systemic...
disease is present, it is imperative to diagnose early and begin screening tests in order to reduce systemic complications and morbidity.1

PATHOPHYSIOLOGY
The etiology of DM is largely unknown. As with many of the autoimmune diseases, the complement system appears to be the force behind endothelial and muscular damage induced by the collaboration between genetic susceptibility and the environment. Genetic studies point to a polymorphism of tumor necrosis factor promoter and an allele of the HLA-DQA gene as risk factors.8 Whether these genes or others are the culprits, with a genetic foundation in place, environmental stressors initiate changes that set the stage for disease. Some of the known environmental triggers include drugs (hydroxyurea, phenytoin, nonsteroidal anti-inflammatory drugs, and statins), viruses (human immunodeficiency virus, Escherichia coli, and Coxsackei virus), malignancy, and ultraviolet radiation.8 With genetic and environmental prompting, autoreactivity (reaction against our own cells) begins. Complement pathways produce enzymes, activate immune complexes, and, ultimately, produce membrane attack complexes.9 Because the complement system has the ability to lyse cells, clear debris, activate cytokines, and initiate inflammatory mediators, the most important component for such a powerful system is regulation. Complement deficiency leads to autoantibody proliferation, whereas complement overactivation causes tissue damage.9 When complement safeguards fail, as seen in DM, the body’s own cells, which are not normally antigenic, begin to attack. Autoantibodies begin to form.

As expected, components of the complement system and membrane attack complex cells can be found in patients early in the disease process. These components act on endothelial cells to cause cell death.1 Histologic samples reveal a condition known as interface dermatitis, which originates in the interface between the dermoepidermal junction. Common findings include basal cell vacuolization (spaces and cavities between basal cells and dermis), apoptotic keratinocytes (dying keratinocytes and the waste of their remains), and inflammatory infiltrate.10 There is an overproduction of cytokines, including type 1 and 2 interferons. Interferons are implicated in most autoimmune diseases and chronic inflammation and may damage both endothelial cells and myofibers in DM.2,11

The complement system is also implicated in the generation of inflammation, which damages capillaries and causes ischemic muscle damage.6,7 Myositis-specific autoantibodies have been found in 50% to 70% of patients with DM.2 Abnormal muscle enzyme levels are routinely found in DM patients, leading to muscle weakness, disability, and contractures. Further research is needed to determine precisely how these disease markers fit together to produce DM.

Sixty percent of patients will first seek treatment when both muscle and skin symptoms become problematic; 30% of patients will present with skin rash only.7 This means that 90% of DM patients will have the characteristic cutaneous features upon initial presentation. DM rash causes severe pruritus and burning, which can be refractory to treatment even when muscle weakness is suppressed.7 A recent study found that quality of life, energy level, depression, and mood scores were significantly worse for DM patients than for patients with comparable inflammatory skin diseases and patients with chronic health conditions like hypertension, recent myocardial infarction, or diabetes.12 Patients complaining of muscle weakness describe increasing difficulty getting up from a chair, combing their hair, or climbing the stairs.5

PRESENTATION
Fortunately, this skin rash can be quite unique, providing the lifesaving diagnostic clues that make early recognition and subsequent screening possible. Table 1. Mnemonic to Remember the Signs of Dermatomyositis

| D | Dispigmentation of poikiloderma |
| M | Macular reddish purple rash on eyelids *pathognomic |
| S | Scaling alopecia |
| K | Knuckles and bony prominences with Gottron papules *pathognomic |
| I | Itchy rash mainly in sun-exposed areas; appears as confluent, reddish purple macules |
| N | Nail fold telangiectasia and dystrophic cuticles |
The 6 hallmark skin manifestations of DM are as follows (Table 1):

1. Gottron papules (Figure 1) are raised, smooth, indurated, reddish violet lesions that appear mainly on bony prominences like the knuckles, elbows, or knees. They may also appear along the side of fingers. As a note for differential diagnosis, Gottron papules on the knuckles are present in 60% to 80% of DM patients; conversely, cutaneous lesions on the knuckles are rare in lupus. This symptom is pathognomonic to DM.

2. Heliotrope rash (Figure 2) is a macular, reddish purple rash on the eyelids named for the small purple flower Heliotrope penuvianum. It may present with periorbital edema. Up to 60% of patients will have heliotrope rash, ranging from dilated eyelid veins to violet, edematous rash. Scaling may also occur. This symptom is also pathognomonic to DM.

3. Violaceous/erythematous pruritic macular rash (Figures 3-5) may occur over any portion on the body but tends to concentrate in sun-exposed areas. The bony prominences of knuckles, knees, and elbows can be involved as well as the face, neck (V-sign), back (Shawl sign), lateral hips (holster sign), and extensor arms. The macules occur in a diffuse, confluent, or patchy distribution; are usually symmetrical; and are associated with severe and sometimes debilitating pruritus. There may be scaling. Over time, hyperkeratosis, pigment changes, and ulcerations may occur secondary to the initial assault.

Figure 1. Gottron papules.

![Gottron papules](Source: IMACS)


Figure 2. Heliotrope rash.

![Heliotrope rash](Source: IMACS)


Figure 3. Erythematous rash on sun-exposed areas.

![Erythematous rash](Source: IMACS)

diagnosis, lupus erythematosus does not present with pruritus.

4. Periungual telangiectasias (Figure 6) are visible blood vessels that appear like irregular splinters on the proximal nail folds and are often accompanied by ragged, dystrophic cuticles.

5. Alopecia (Figure 7) with scaly, reddish violet lesions may occur on the scalp.

6. Poikiloderma (Figures 8 and 9) (poikilo meaning irregular and derma meaning skin) is a condition in which the skin becomes finely variegated with areas of hyper- and hypopigmentation, telangiectasia, and atrophy. This typically occurs in the same sun-exposed spots where the violaceous/erythematous rash occurred in late-stage disease.

RISK FACTORS
DM is considered an autoimmune disorder and, thus, there are few identifiable or modifiable risk factors for this disease. Research does show that it affects women 2 to 3 times more than men, and onset usually occurs between the ages of 5 to 14 for juvenile DM or 45 to 64 for adults. There is speculation that viruses, illness, or tumors have potential to cause the inflammatory response linked to its development, but there is no evidence to support this claim.

DIFFERENTIAL DIAGNOSIS
With the clinical presentation of DM, there are many differential diagnoses that can be made. Often, when a patient presents with DM, it is confused with polymyositis (PM) given that both are classified as idiopathic inflammatory myopathies, and both are
also characterized by muscle abnormalities. However, in DM, cutaneous involvement is the differentiating factor from that of PM. In addition, DM is more frequently associated with an underlying malignancy than PM with reported ranges from 15% to 23%.7

One study revealed that in those with PM, 9% of the population study was diagnosed with 1 of 42 cancers at the same time or after PM was diagnosed. Of those who died in the study, cancer was the principal cause in 14% of the PM cases. In that same study, 15% of the DM population was diagnosed with cancer, but in contrast, a striking 40% had cancer as the primary cause of death.13 In addition to PM as a differential diagnosis, many cutaneous diseases need to be ruled out in order to successfully diagnose DM. These include, but are not limited to, systemic lupus erythematosus, dermatitis, tinea corporis, psoriasis, or rosacea.14 Other than the use of diagnostic testing, DM differentiates itself from many of these skin disorders by its pathognomonic heliotrope rash and proximal muscle weakness involvement.

**DIAGNOSIS**

Early diagnosis of DM is imperative to prevent further disease progression. Studies have associated older age at the onset of disease and more severe skin and muscle involvement with a higher risk of malignancy.8 In 1975, researchers Bohan and Peter proposed a set of 5 criteria to assist in the diagnosis of DM (Table 2); this is the common criteria still used in today’s practice. One is the progressive, proximal symmetrical weakness of muscles.15 This criterion requires a thorough history taking, including the onset of muscle weakness, effects on activities of daily living, and associated symptoms. Most patients will complain of difficulty climbing stairs, brushing hair,
or rising from sitting or squatting that has progressively worsened over weeks to months. The 2nd criterion is the evidence of elevated levels of muscle enzymes, particularly serum creatine kinase concentrations. In those diagnosed with DM, the creatine kinase may be up to 50 times the upper limit of normal. Thirdly, classic electromyographic findings in active myopathy are increased spontaneous activity with fibrillations and sharp waves. Electromyographic studies are useful early in DM and show abnormal findings in 70% to 90% of cases, but they are nonspecific and can be seen in other muscle diseases. Imaging with magnetic resonance imaging is a sensitive, noninvasive technique that can help in the early diagnosis of DM and monitoring response to treatment. It is useful in assessing the extent of muscular inflammation; for example, fatty infiltrates are indicative of chronic muscular inflammation, and these patients might be less responsive to therapy. Magnetic resonance imaging can also detect muscle edema or fluid retention in the muscles. The 4th criterion from Bohan and Peter requires an abnormal muscle biopsy. Such a sample can be diagnostic and would reveal perivascular and interfascicular inflammatory infiltrates with adjoining groups of muscle fiber degeneration/regeneration. Lastly, the cutaneous findings are DM specific. These include a pathognomonic heliotrope rash, poikiloderma, and Gottron papules.

Although creatine kinase is the most sensitive and specific indicator of muscle disease, other laboratory data may yield abnormal results, including aspartate aminotransferase or lactic dehydrogenase. In addition, anti-Mi2, which is highly specific but not sensitive to DM, is an autoantibody that is directed against a nuclear adenosine triphosphatase autoantigen present in 25% to 30% of DM patients. It is associated with the hallmark cutaneous manifestations; its presence carries better overall prognosis, with milder muscle disease and a heightened response to steroid therapy.

 DM is associated with an increased risk of malignancy; most cancers are diagnosed within 3 years of the diagnosis of myositis. For this reason, patients should be instructed to closely monitor and immediately report any onset of new symptoms for 2 to 3 years after their diagnosis of DM. During this time, patients should also have routine computed tomographic scans, pulmonary functions tests, and screenings to detect early cancers. Screenings include, but are not limited to, mammographies, colonoscopies, and pelvic examinations that should be performed every 6 to 12 months. In 2000, 1 study conducted in Taiwan found a strong correlation between DM patients and malignancies of nasopharynx cancer. Thus, in addition to thorough history taking and physical examination, the recommendation has been made to include nasopharyngeal examination as part of screening for the adult DM patients of Asian descent, especially those of Chinese ethnicity.

Table 2. Bohan and Peter’s 5 Criteria for Diagnosing Dermatomyositis

<table>
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<tr>
<th>Criteria</th>
<th>Diagnostic Pearls</th>
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<tr>
<td>1. Progressive, proximal symmetrical weakness of muscles</td>
<td>1. Obtain a thorough history, including onset and effects on activities of daily living</td>
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<tr>
<td>2. Elevated muscle enzymes</td>
<td>2. Particularly serum creatine kinase levels</td>
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<tr>
<td>3. Electromyography or magnetic resonance imaging findings</td>
<td>3. Assess the involvement and extent of muscular inflammation</td>
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<td>4. Abnormal muscle biopsy</td>
<td>4. Reveals inflammatory infiltrates</td>
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<td>5. Cutaneous findings</td>
<td>5. Heliotrope rash, Gottron papules</td>
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**TREATMENT**

Therapy for DM involves general and specific measures to control both components of muscle disease and skin disease (Table 3). In those patients with cutaneous disease of DM, photoprotection is the first-line approach for management and reduction of skin lesion exacerbations. Patients should be strongly encouraged to practice diligent photoprotection year round, including wearing protective clothing, wide-brimmed hats, and broad-spectrum sunscreen. For the associated pruritus and burning that can occur with skin manifestations, various topical agents, including bland moisturizers and emollients, can help alleviate this. For further control of erythematous and pruritic skin changes, topical corticosteroids are also frequently used to combat cutaneous inflammation.
Prednisone’s anti-inflammatory and immunosuppressive pharmacokinetics makes it the initial drug of choice for systemic pharmacologic therapy for both skin and muscle manifestations of DM.\(^1\) It should be given as a daily dose until the serum creatine kinase level is normalized and then slowly tapered over the following 12 months; after that, this low dose should be continued for 1 year.\(^1\) If there is no reported improvement in muscle strength after 3 months of therapy, other immunosuppressive agents should be considered. It is important to note that approximately 25% of patients will have no response to prednisone therapy.\(^1\) Methotrexate is a well-known antimetabolite and is considered first-line adjuvant therapy in patients with more resistant manifestations of DM or for those failing to respond to prednisone.\(^1\) Supplemental folic acid should also be initiated daily in order to help minimize the side effects of methotrexate.\(^1\)

**THE FUTURE OF DM**

DM patients may find relief in the future from some interesting clinical trials being conducted with new biologic agents. These drugs will enable clinicians to mount a more targeted assault than our present immunosuppressive agents allow. For example, rituximab has been approved for use in rheumatoid arthritis, one of the autoimmune cousins to DM. This drug is a monoclonal antibody that attacks the CD20 antigen on B lymphocytes. Researchers recently conducted clinical trials using rituximab on a group of 200 refractory DM and PM patients, and 83% showed improvement within 20 to 22 weeks.\(^17\) Although that is promising, the new biologic agents are antigen specific and are therefore useful in very specific circumstances. Consequently, researchers evaluated specific subsets of the DM population who would benefit from rituximab.\(^18\) Those with the autoantibodies anti-Jo-1 and anti-Mi-2 showed the most improvement from rituximab therapy.\(^18\) It seems that there will not be 1 “magic bullet” to tackle DM but rather an arsenal of many biologic agents that are called on as antibody-specific testing warrants. This new biologic treatment, and others, will need to be investigated further before they can be integrated into routine treatment.

With the variability of clinical presentation and multisystem involvement, it is necessary that the DM patient be managed within a multidisciplinary team including rheumatologists, dermatologists, neurologists, and pulmonologists and regular input from physical and occupational therapists as well as speech and language therapists.\(^15\) It is imperative that clinicians collaborate and show vigilance in their assessments for potential visceral manifestations and underlying malignancies. With early treatment, reported survival rates are as high as 80% at 5 years and 73% at 8 years after diagnosis.\(^1\) Early treatment can also reverse the late complications of calcinosis involving the skin, muscle, and fascia seen in areas of inflammation, which can evolve into devastating contractures.\(^2\)

**RECOMMENDATIONS FOR NURSE PRACTITIONER PRACTICE**

DM is a unique disease falling into the category of idiopathic inflammatory myositis with distinct cutaneous involvement. In years to come, more research will be necessary to help further distinguish this disease (ie, its pathogenesis, susceptibility, and progression). The nurse practitioner should be aware of the hallmark pathognomonic cutaneous manifestations and muscle involvement that can be seen with DM. With unsettling skin changes and potential systemic limitations, it is imperative for the provider to approach the DM patient holistically. In order for successful diagnosis of DM, it is key for them to be familiar with the 5 criteria established by Bohan and Peter. Once a diagnosis is made, a collaborative effort should be established between the NP and a multidisciplinary team. Nurse practitioners should be prepared to diagnose early, treat appropriately, and refer as necessary to ensure the most effective and successful outcome of the DM patient.

<table>
<thead>
<tr>
<th>Table 3. Managing the Dermatomyositis Patient</th>
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<td>Photoprotection</td>
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<tr>
<td>Topical corticosteroids to control cutaneous inflammation and irritation</td>
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<tr>
<td>Prednisone for both skin and muscle manifestations</td>
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<td>Collaboration with a multidisciplinary team</td>
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