Inflammatory Myopathies

The inflammatory myopathies represent the largest group of acquired and potentially treatable causes of skeletal muscle weakness. They are classified into three major groups:

- **polymyositis (PM)**
- **dermatomyositis (DM)**
- **inclusion body myositis (IBM).**

PATHOLOGY AND PATHOGENESIS

- Dermatomyositis is thought to be an autoimmune disease, but there has been no consistent evidence of either antibodies or lymphocytes directed against specific muscle antigens.
- However, muscle histologists have agreed that dermatomyositis is ***humorally mediated vasculopathy*** with deposits of complement in blood vessels of skin and muscle, with infiltrates characterized by ***more B cells than T cells***, and this contrasts with the predominance of T cells in polymyositis, which is considered a disorder of lymphocyte regulation.
- Polymyositis is considered an autoimmune disease of disordered ***cellular immunity*** .

Clinical Features

PM as a stand-alone entity is a rare disease affecting adults.

DM affects both children and adults and women more often than men.

IBM is most likely to affect persons >50 years of age with male to female ratio of 3:1.

- These disorders present as progressive and symmetric muscle weakness except for **IBM**, which can have an asymmetric pattern.

- Weakness is mainly proximal, such as getting up from a chair, climbing steps, lifting objects, or combing hair.

- Fine-motor movements that depend on the strength of distal muscles, such as buttoning a shirt, sewing, or writing, are affected only late in the course of PM and DM, but fairly early in IBM.

- Falling is common in IBM because of early involvement of the quadriceps muscle with buckling of the knees

- **Ocular muscles are spared**, even in advanced, untreated cases; if these muscles are affected, the diagnosis of inflammatory myopathy should be questioned.

- Facial muscles are unaffected in PM and DM, but mild facial muscle weakness is common in patients with IBM.

- In all forms of inflammatory myopathy, pharyngeal and neck-flexor muscles are often involved, causing **dysphagia** or difficulty in holding up the head (*head drop*).

- Sensation remains normal.

- The tendon reflexes are preserved but may be absent in severely weakened or atrophied muscles

- Myalgia and muscle tenderness may occur in a small number of patients, usually early in the disease

- Weakness in PM and DM progresses subacutely over a period of weeks or months; by contrast, IBM progresses very slowly, over years.

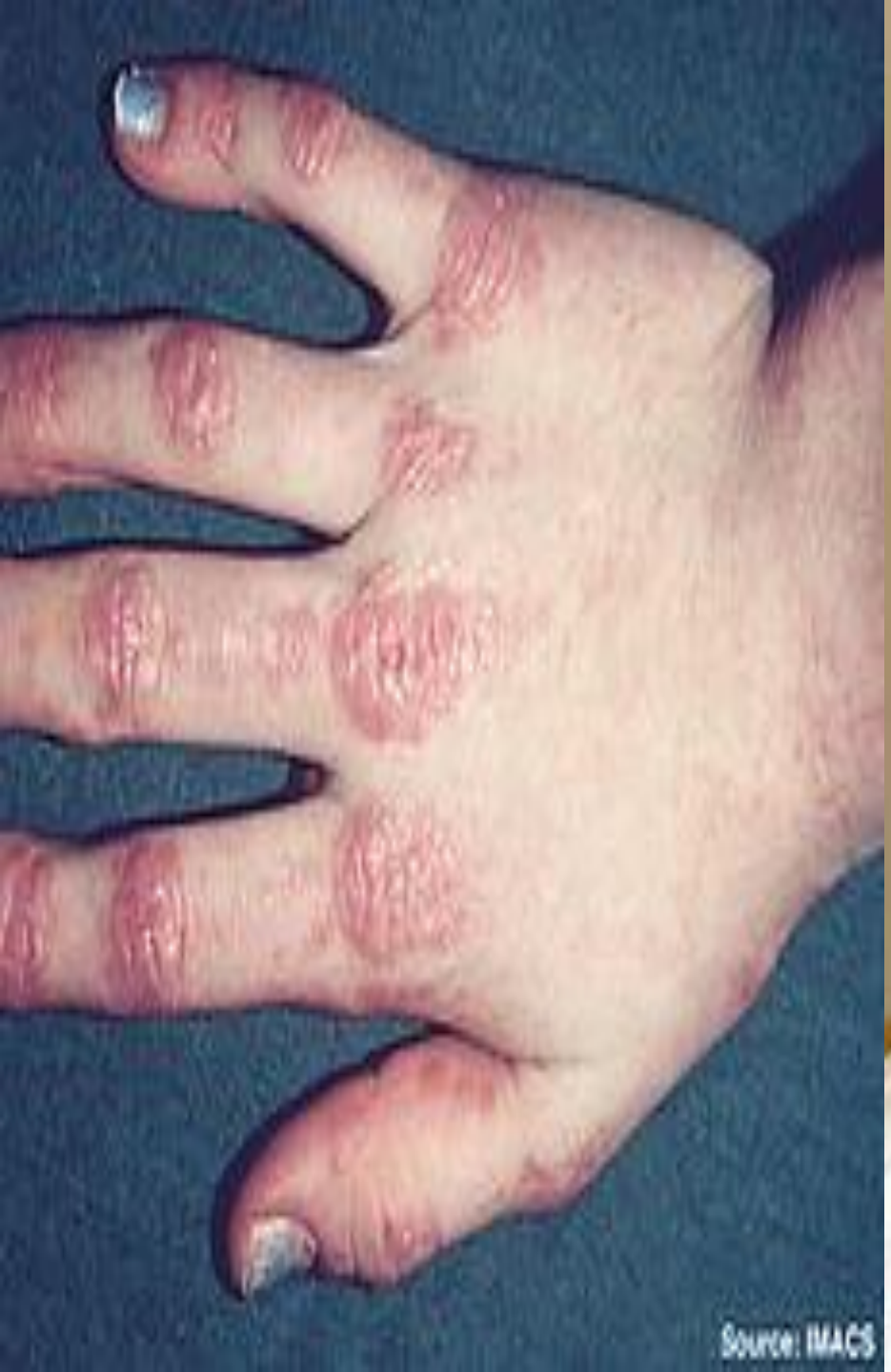
Polymyositis

- As an isolated entity, PM is a rare (and overdiagnosed) disorder; more commonly, PM occurs in association with a systemic autoimmune or connective tissue disease, or with a known viral or bacterial infection. Drugs, especially D-penicillamine or zidovudine, may also produce an inflammatory myopathy similar to PM.

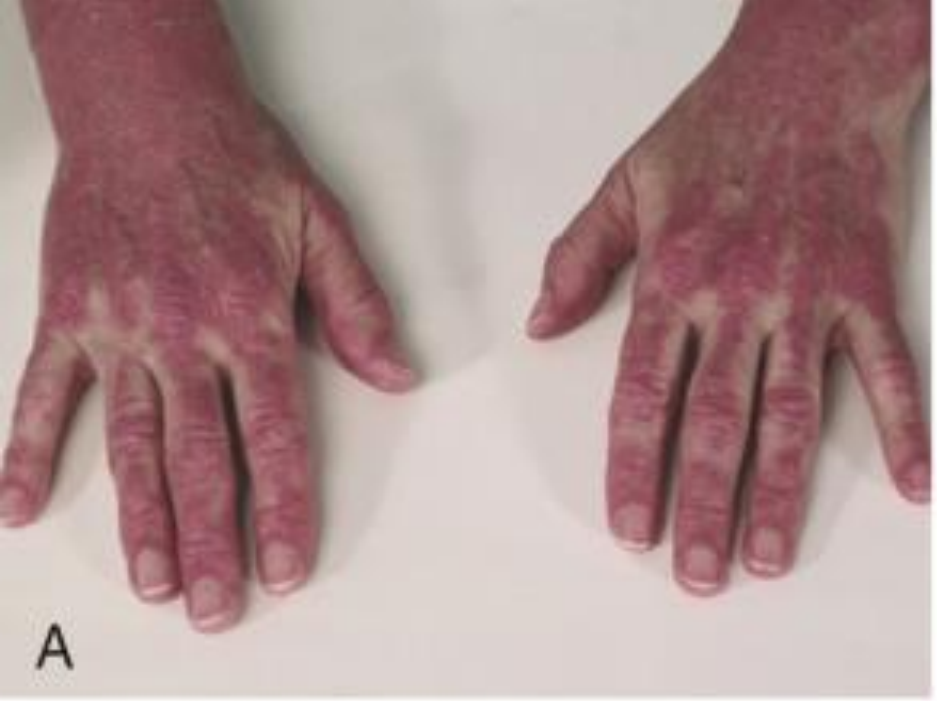
Dermatomyositis

DM is a distinctive entity identified by a characteristic rash accompanying, or more often preceding, muscle weakness.

- blue-purple discoloration on the upper eyelids with edema (***heliotrope rash***),
- a flat red rash on the face and upper trunk
- erythema of the knuckles with a raised violaceous scaly eruption (***Gottron's sign***)


Source: IMACS

- The erythematous rash can also occur on other body surfaces, including the knees, elbows, malleoli, neck and anterior chest (***V sign***), or back and shoulders (***shawl sign***)
- The cuticles may be irregular, thickened, and distorted, and the lateral and palmar areas of the fingers may become rough and cracked, with irregular, "dirty" horizontal lines, resembling ***mechanic's hands***.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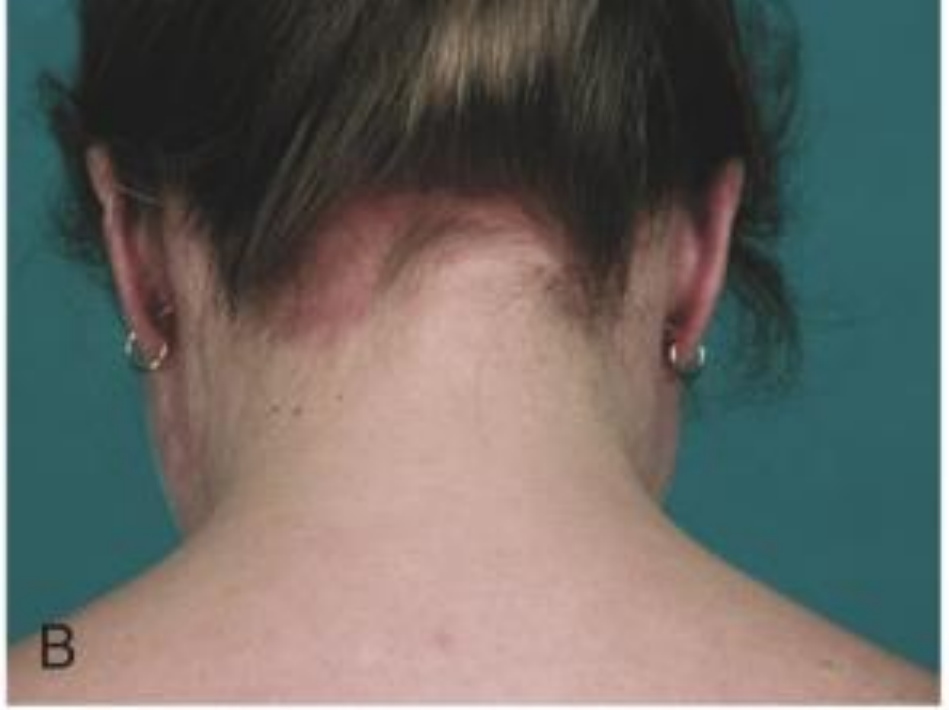
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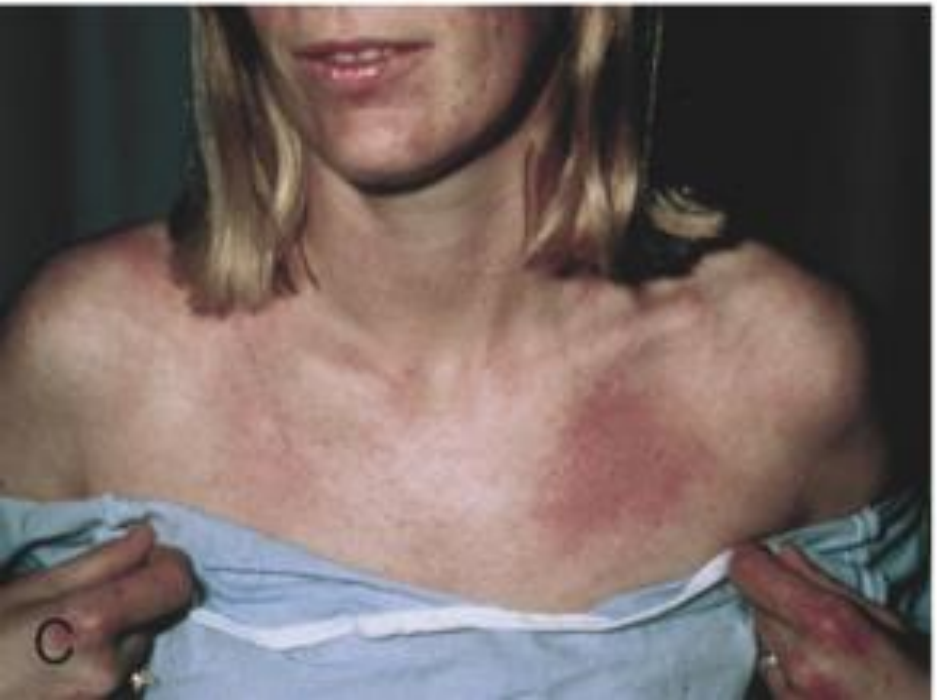
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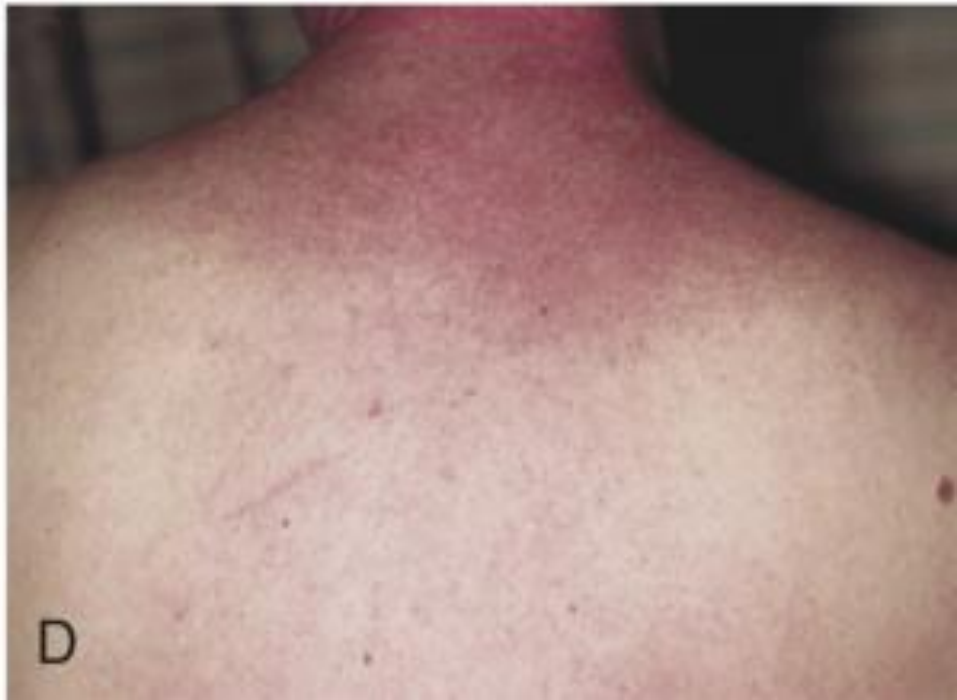
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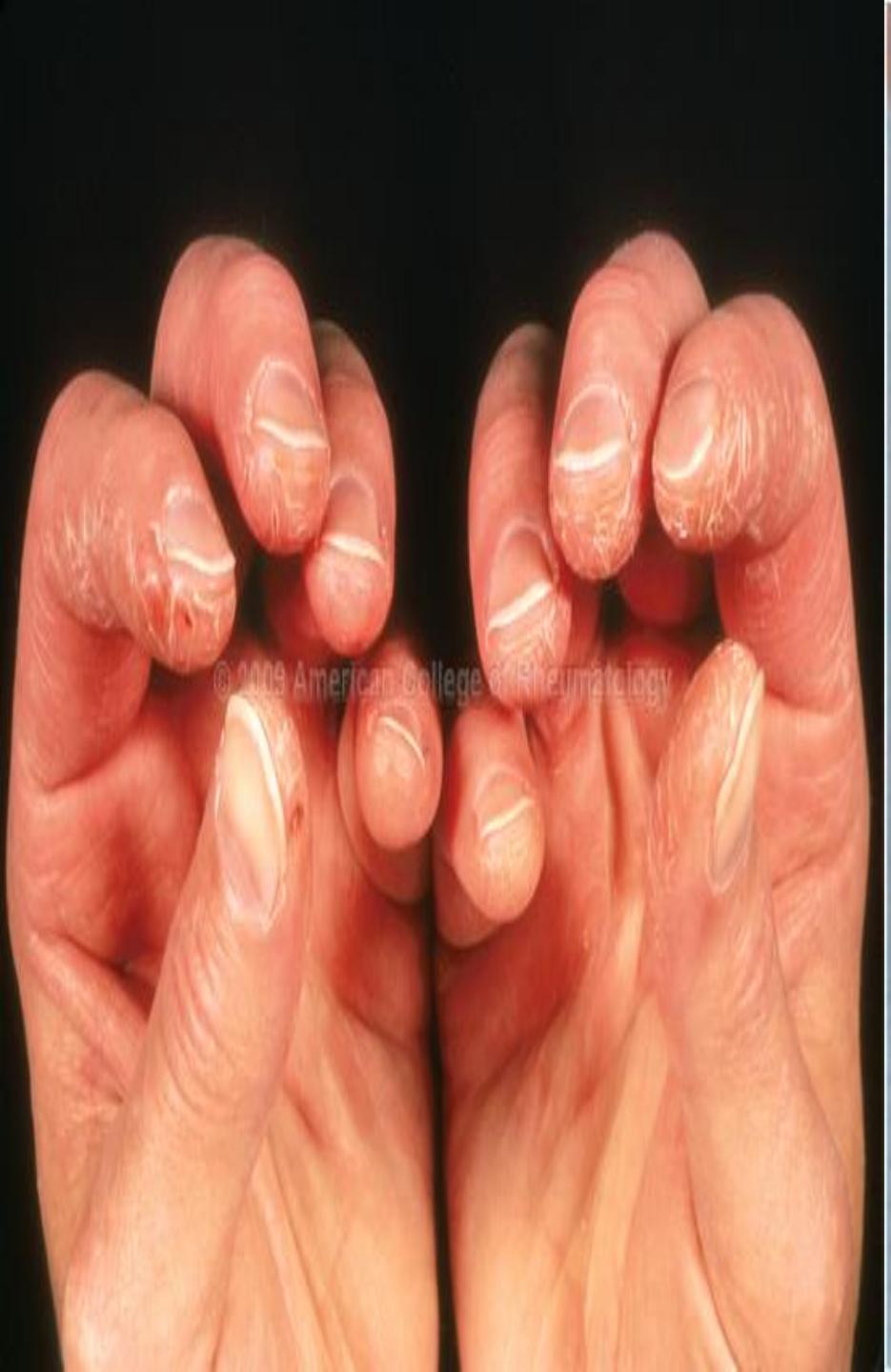
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Source: IMACS

Inclusion Body Myositis

- Weakness and atrophy of the distal muscles, especially foot extensors and deep finger flexors, occur in almost all cases of IBM and may be a clue to early diagnosis.

- Some patients present with falls because their knees collapse due to early quadriceps weakness.

- Others present with weakness in the small muscles of the hands, especially finger flexors, and complain of inability to hold objects or perform tasks such as turning keys or tying knots.

- On occasion, the weakness and accompanying atrophy can be asymmetric and selectively involve the quadriceps, iliopsoas, triceps, biceps, and finger flexors.

- Dysphagia is common, occurring in up to 60% of IBM patients, and may lead to episodes of choking.

- Disease progression is slow but steady, and most patients require an assistive device such as cane, walker, or wheelchair within several years of onset.

Extramuscular Manifestations

These may be present to a varying degree in patients with PM or DM, and include:

- ***Systemic symptoms***, such as fever, malaise, weight loss, arthralgia, and Raynaud's phenomenon, especially when inflammatory myopathy is associated with a connective tissue disorder.
- ***Joint contractures***, mostly in DM and especially in children.
- ***Dysphagia***, due to involvement of oropharyngeal striated muscles and upper esophagus, especially in DM and IBM.
- ***Cardiac disturbances***, including atrioventricular conduction defects, tachyarrhythmias, dilated cardiomyopathy, a low ejection fraction, and congestive heart failure, may rarely occur.

- ***Pulmonary dysfunction,*** due to weakness of the thoracic muscles or interstitial lung disease, which may cause dyspnea, nonproductive cough, and aspiration pneumonia. Interstitial lung disease may precede myopathy or occur early in the disease and develops in up to 10% of patients with PM or DM.
- ***Subcutaneous calcifications,*** in DM, sometimes extruding on the skin and causing ulcerations and infections.
- ***Arthralgias,*** synovitis, or deforming arthropathy can occur in some patients with DM and PM.

Association with Malignancies

- The incidence of malignant conditions appears to be specifically increased only in patients with DM and not in those with PM or IBM.

- The most common tumors associated with DM are ovarian cancer, breast cancer, melanoma, colon cancer, and non-Hodgkin lymphoma.

- A complete annual physical examination with pelvic, breast (mammogram, if indicated), and rectal examinations (with colonoscopy according to age and family history); urinalysis; complete blood count; blood chemistry tests; and a chest film should suffice in most cases.

Diagnosis

- Serum **CK levels** are elevated (3–30 times above normal).
- The **EMG** demonstrates a myopathic changes and signs of denervation from the associated inflammation
- **Muscle biopsy** demonstrates muscle changes in the perifascicular region. Myopathic changes include necrosis and regeneration, muscle fiber atrophy
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Treatment

The goal of therapy is to

- improve muscle strength, thereby improving function in activities of daily living, and
- ameliorate the extramuscular manifestations (rash, dysphagia, dyspnea, fever).
- When strength improves, the serum CK falls concurrently; however, the reverse is not always true.(we should treat muscle strength rather than CK level)

Agents used in the treatment of PM and DM include:

1. *Glucocorticoids*.

- Oral prednisone is the initial treatment of choice;

- The efficacy of prednisone is determined by an objective increase in muscle strength and activities of daily living, which almost always occurs by the third month of therapy.

- A feeling of increased energy or a reduction of the CK level without a concomitant increase in muscle strength is not a reliable sign of improvement.

- If prednisone provides no objective benefit after ~3 months of high-dose therapy, the disease is probably unresponsive to the drug and tapering should be accelerated while the next-in-line immunosuppressive drug is started.

2. ***Other immunosuppressive***

Approximately 75% of patients ultimately require additional treatment.

This occurs when

- a patient fails to respond adequately to glucocorticoids after a 3-month trial,
- glucocorticoid-related side effects appear,
- attempts to lower the prednisone dose repeatedly result in a new relapse,
- rapidly progressive disease with evolving severe weakness and respiratory failure develops.

The commonly useddrugs are: *Azathioprine*, *Methotrexate*, *Mycophenolate mofetil* and *Cyclosporine* .

3. *Immunomodulation*.

intravenous immunoglobulin (IVIg) improved not only strength and rash but also the underlying immunopathology. The benefit is often short-lived (<8 weeks); repeated infusions every 6–8 weeks are generally required to maintain improvement. IVIg may also be beneficial for patients with PM.

Note: IBM is generally resistant to immunosuppressive therapies.

Prognosis

- The 5-year survival rate for treated patients with PM and DM is ~95%;
- death is usually due to pulmonary, cardiac, or other systemic complications.
- DM responds better to therapy than PM and thus has a better prognosis.
- IBM has the least favorable prognosis of the inflammatory myopathies.