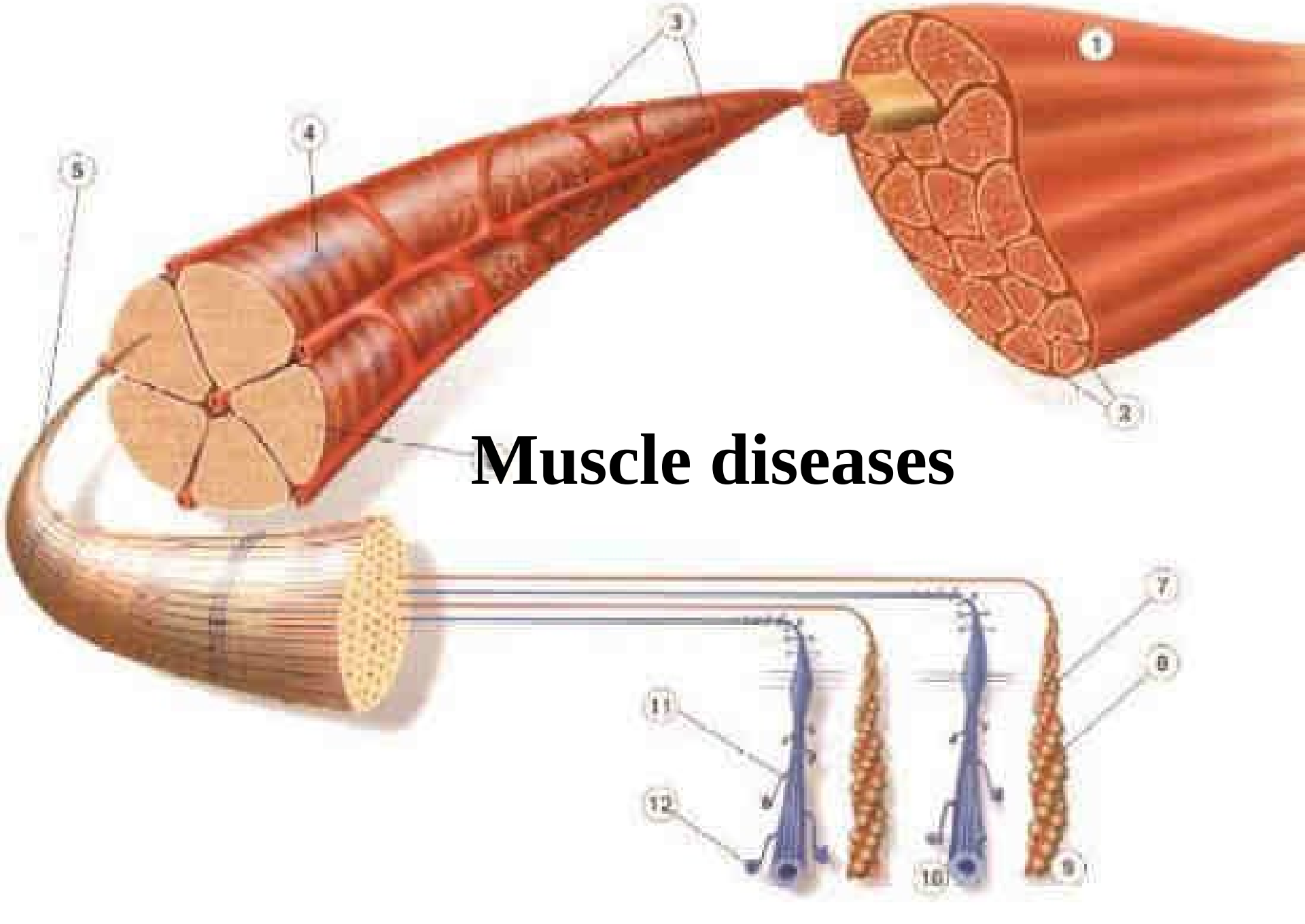
بسم الله الرحمن الرحيم

رب أوزعنى أن أشكر نعمتك التى انعمت على
وعلى والدى وأن أعمل صالحا ترضاه وأدخلنى
برحمتك فى عبادك الصالحين

صدق الله العظيم

سورة النمل آيه ١٩

Muscle diseases



Classification of muscle diseases

A. **inherited**

- **Muscular dystrophies.**
- **Myotonia.**
- **Congenital myopathies.**
- **Channelopathies.**
- **Primary metabolic.**

Classification of muscle diseases

A. **Acquired**

- **Drug-induced.**
- **Endocrinal.**
- **Inflammatory.**
- **Paraneoplastic.**
- **Secondary metabolic.**

Symptoms of muscle disease

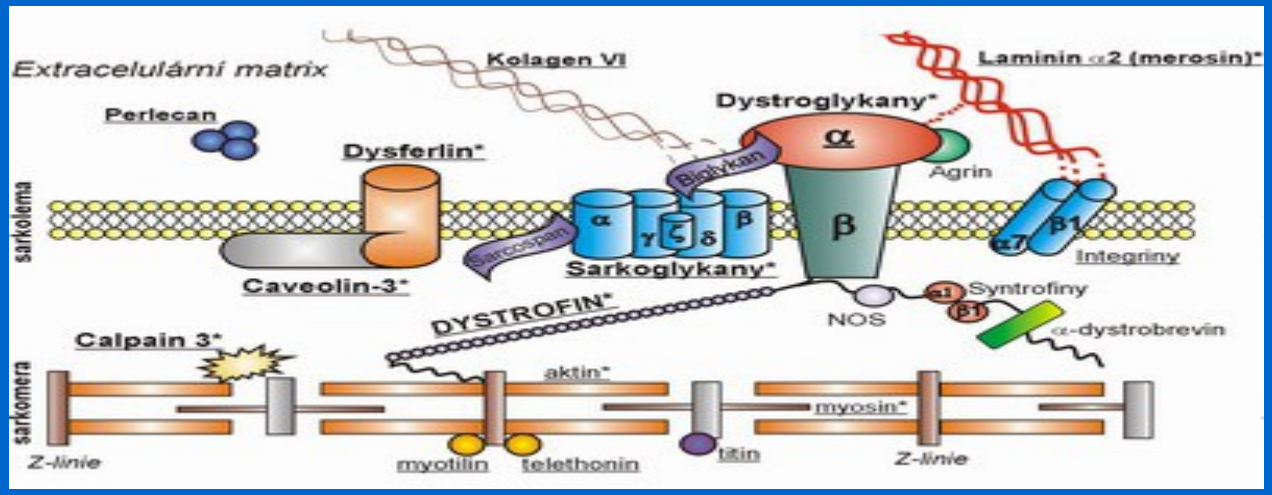
- Muscle fatigue, exercise intolerance in general
- Proximal and symmetric weakness
  - Waddling gait; difficulty of rising from sitting, climbing stairs; Gower's sign
  - Hyperextension of the knee
  - Increased lordosis of the lumbar spine, scoliosis
  - Contractures, tight Achilles tendons
- Myopathic face
- Muscle atrophy; pseudohypertrophy of calf
- Myotonia
- Tendon reflexes are normal or decreased

Diagnosis of muscle diseases

- Creatinine kinase levels increased in many myopathies (sign of muscle fiber necrosis)
- ENG / EMG: differentiation between neurogenic and myogenic weakness
- Muscle biopsy: signs of muscle fiber abnormality, inflammation, immunostaining of muscle constituents
- Genetic testing

Muscle dystrophies

- Hereditary myopathies, characterized by progressive weakness and muscle atrophy
- Genetic defect of **proteins constituting the sarcolemma-associated cytoskeleton system**



Muscle dystrophies

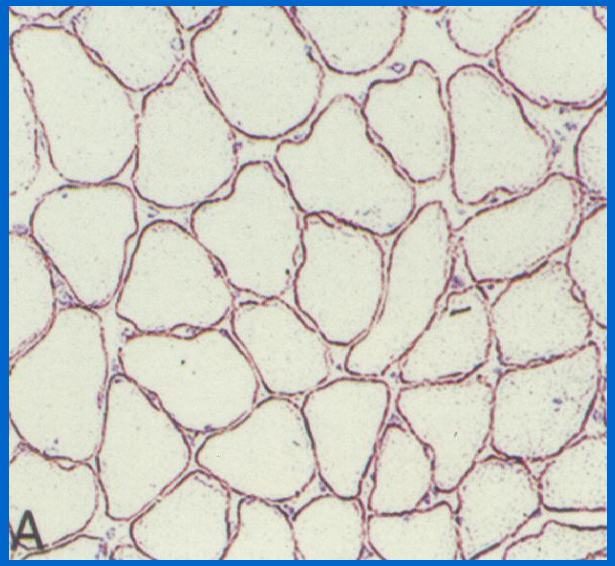
X-linked	AD	AR
• Duchene • Becker's • Emery-dreifuss	• Limb-girdle • FSH • OP • Distal	• Limb-girdle • Congenital

Duchenne muscular dystrophy

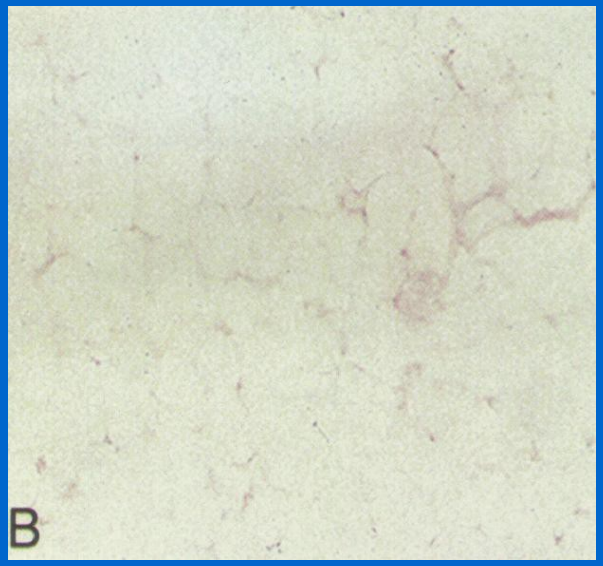
Dystrophinopathy

- Cause: deficiency of dystrophin, resulting in progressive loss of muscle fibers
  - Becker's type: reduced amount of dystrophin; more benign course
- X-chromosome linked
- 1 in 3500 live births, occurs in boys, girls are carriers

Duchenne muscular dystrophy



Normal



Duchenne dystrophy

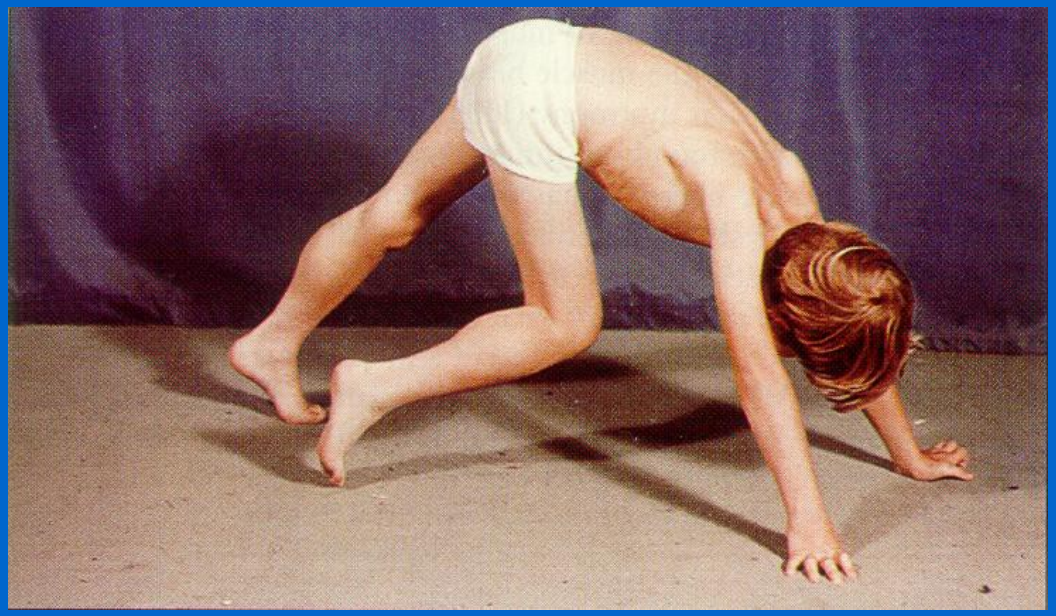
Diagnosis:

- Lack of immunostaining of dystrophin in muscle biopsy specimen
- Demonstration of deletion in the dystrophin gene

Duchenne muscular dystrophy

- Onset at 3-5 years
- Initial symptoms: difficulty getting up from deep position and climbing steps, waddling gait
- Weakness most pronounced in limb-girdle muscles, trunk erectors; **craniobulbar muscles are spared**
- Skeletal deformities
- Contractures.
- Cardiac.
- Inability to walk by 9-11 years
- Death occurs usually in the 3rd decade due to respiratory insufficiency

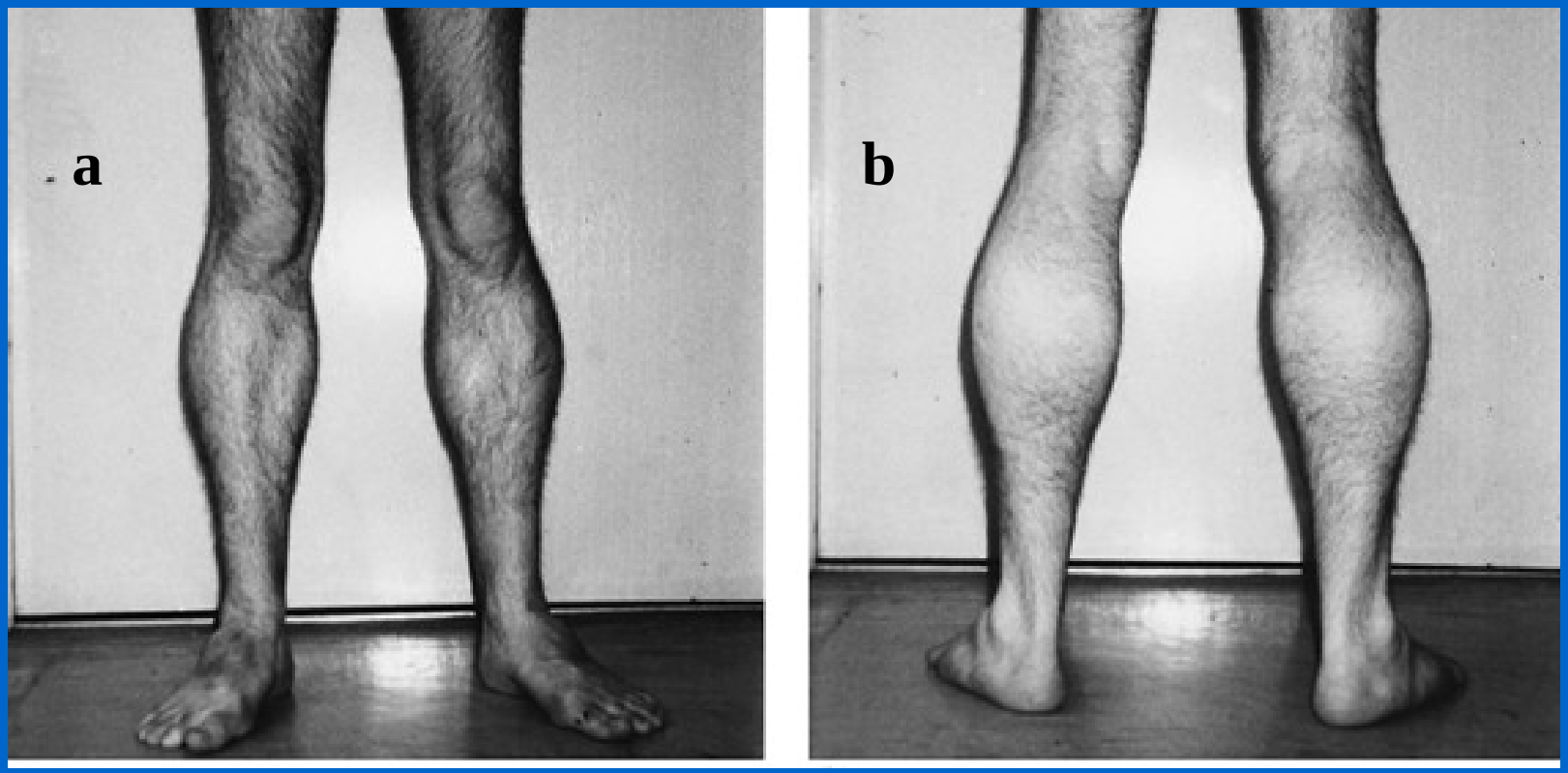
Duchenne muscular dystrophy



Gower’s sign

Becker’s muscular dystrophy

- Onset at 5-20 years
- Initial symptoms: exercise induced pain and cramps, decrease sport success, calf hypertrophy.
- Later: proximal weakness, waddling gait
- Weakness most pronounced in limb-girdle muscles, trunk erectors; **craniobulbar muscles are spared**
- Cardiac.



Becker muscular dystrophy. Note the quadriceps wasting (a) and asymmetrically enlarged calves, so-called pseudohypertrophy (b).

Limb-girdle MD

- AR in 90% and AD in 10%.
- Proximal ULs and LLs affection.
- No facial weakness.
- Contractures and cardiomyopathy are rare.
- Normal or mild elevated CK.

Facioscapulohumeral dystrophy

- Prevalence: 1 in 20,000
- Autosomal dominant
- Age of onset: infancy to middle age
- Progressive muscular weakness and atrophy involving the face, scapular, proximal arm and peroneal muscles → myopathic face, winging of the scapula, inability to raise the arms, foot drop
- Life span is not significantly affected

Treatment of MD

A. Traditional

- Drugs (steroids, L.carnitine, Vit.E).
- Physiotherapy.
- Genetic counseling.
- Surgical.
- Ventilatory support.
- Cardiac ttt.

B. Non-traditional

- Stem cell
- Gene therapy

Myotonic dystrophy 1

- Prevalence: 1 in 8000
- Cause: CTG repeat expansion in a gene on chr. 19
- Autosomal dominant inheritance, with anticipation
- Multisystemic disease:

A. Neurological

  - Myotonia: hyperexcitability of muscle membrane → inability of quick muscle relaxation
  - Progressive muscular weakness and wasting, most prominent in **cranial and distal muscles**
  - Muscle pain
  - CNS: EDS, mental subnormality

Myotonic dystrophy 1

- **B. non-neurological:**
  - **Respiratory**
  - **Cardiac abnormalities** (HB, arrhythmias, sudden death).
  - **Eye:** Cataracts, retinal degeneration
  - **Face:** frontal premature balding
  - **Endocrinal:** testicular atrophy, DM

Myotonic dystrophy 1

Myotonia congenita

- Mutation in the muscle **Cl^- gene**
- autosomal dominant form: **Thomsen**
  autosomal recessive form: **Becker**
- Symptoms:
  - **Myotonia** (hyperexcitability of the muscle membrane): muscle stiffness and abnormal muscle relaxation, warm-up phenomenon
  - Hypertrophied muscles
  - No permanent weakness
- Therapy: phenytoin, mexiletin

Inflammatory muscle diseases

- Dermatomyositis
- Polymyositis
- Inclusion body myositis
- Other systemic autoimmun diseases (SLE, Sjögren sy. etc.)

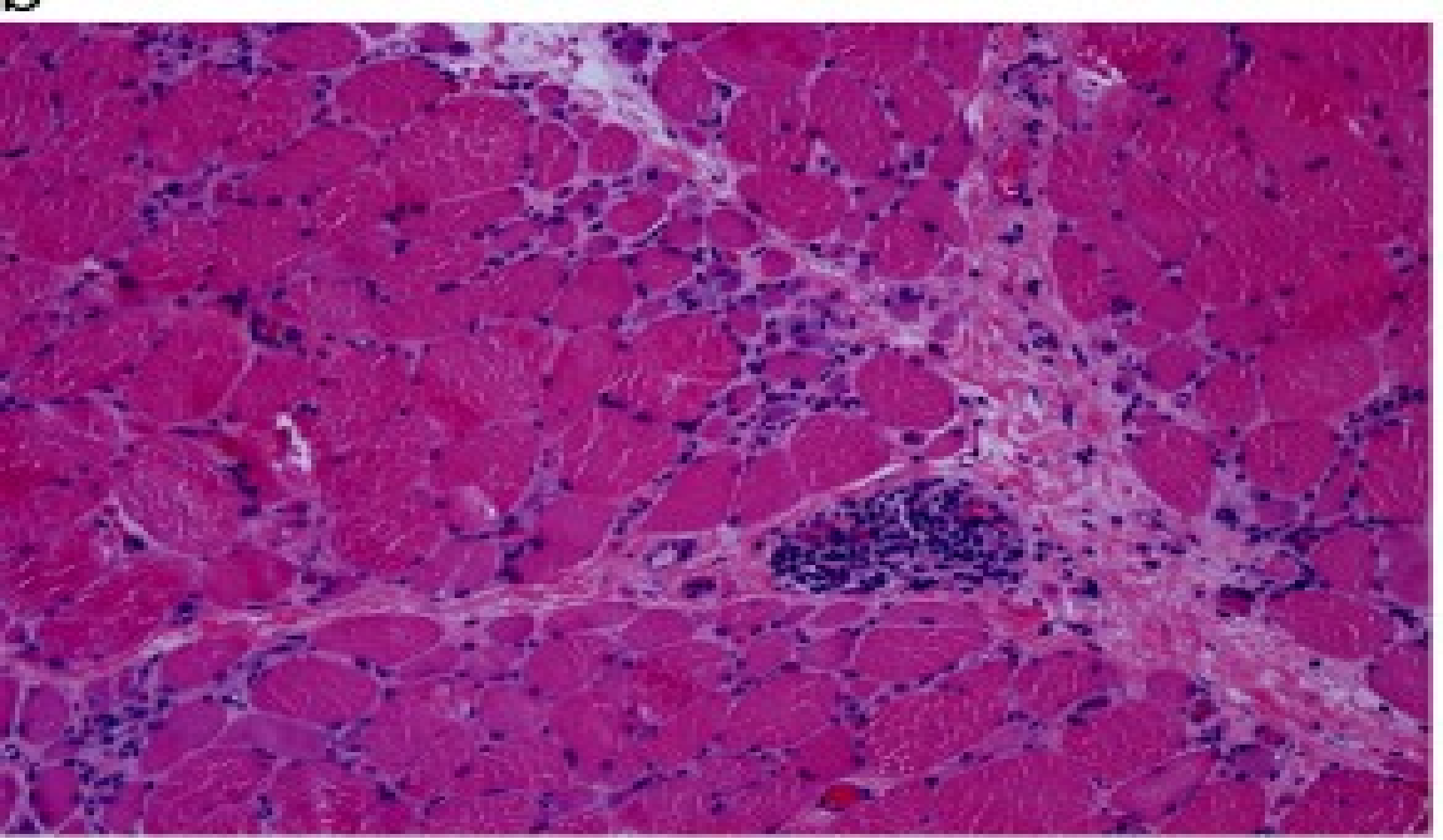
Epidemiology of IIM

- **Incidence** (1 for 100,000)
- **Age** (adults, IBM in elderly)
- **Sex** (more in females except IBM)

Immunopathogenesis

:Dermatomyositis

- ***Is a humorally mediated autoimmune disorder***.
- Target antigen.
- Complement-dependent attack with formation of **C5b-9 (MAC)**→Microangiopathy of ***muscle*** and ***skin***.
- Characteristic pathological features of ***infarction*** and ***perifascicular atrophy***.
- Cytokines release →***perivascular*** Inflammatory

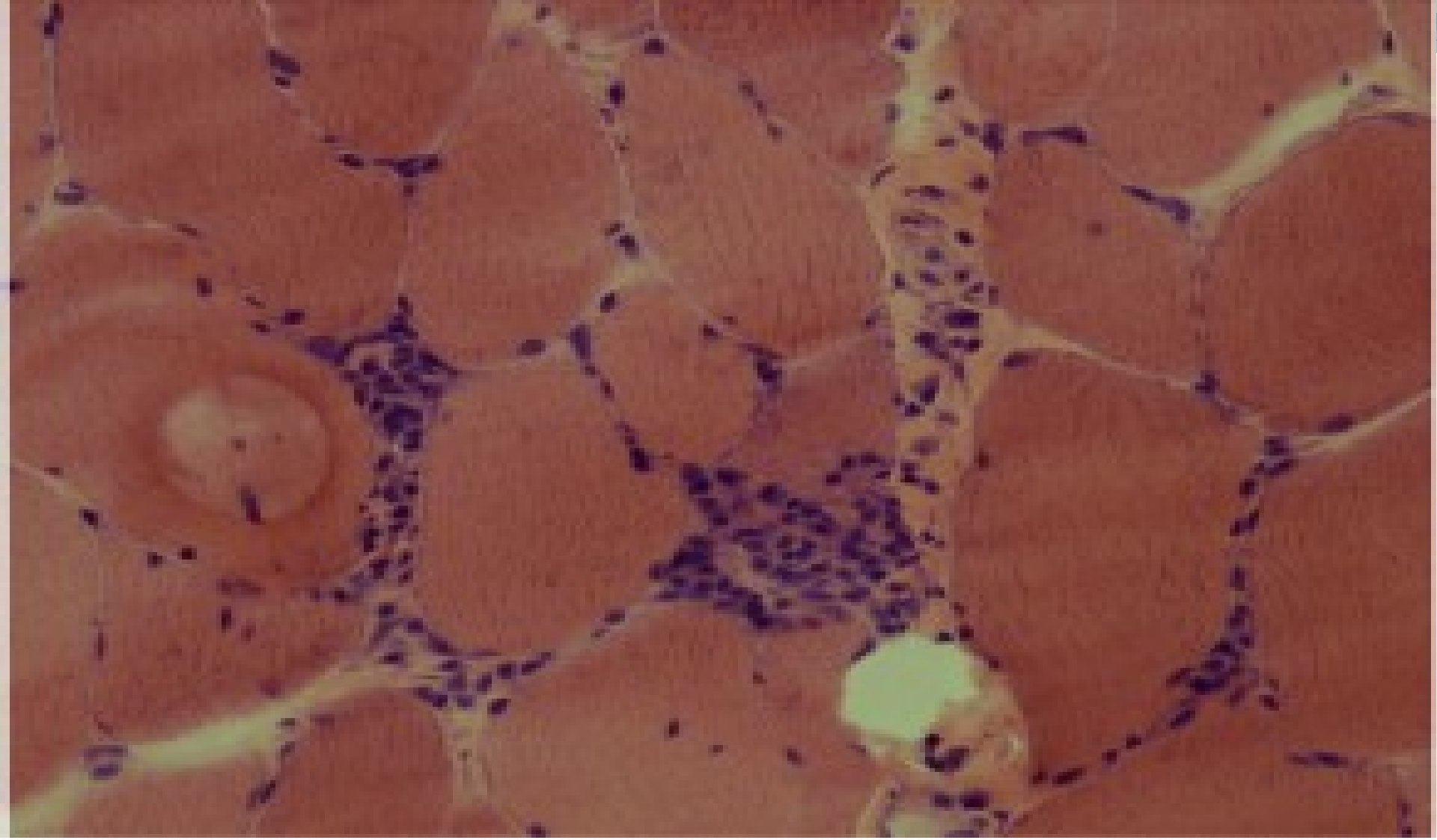


DM: perimysial inflammation — hematoxylin and eosin

Immunopathogenesis

:Polymyositis

- **Cell-mediated immunity.**
- ***Partial invasion of non-necrotic muscle fibres*** by ***CD8+ cytotoxic T cells***.
- Inflammatory infiltrates tend to be ***within fascicles*** and ***T cells predominate over B cells.***
- Invaded and non-invaded fibres show major histocompatability complex (***MHC) class I expression.***
- ***Formation of immunological synapses.***



PM: inflammatory infiltrates surrounding and invading non-necrotic fibers — hematoxylin and eosin

Clinical picture

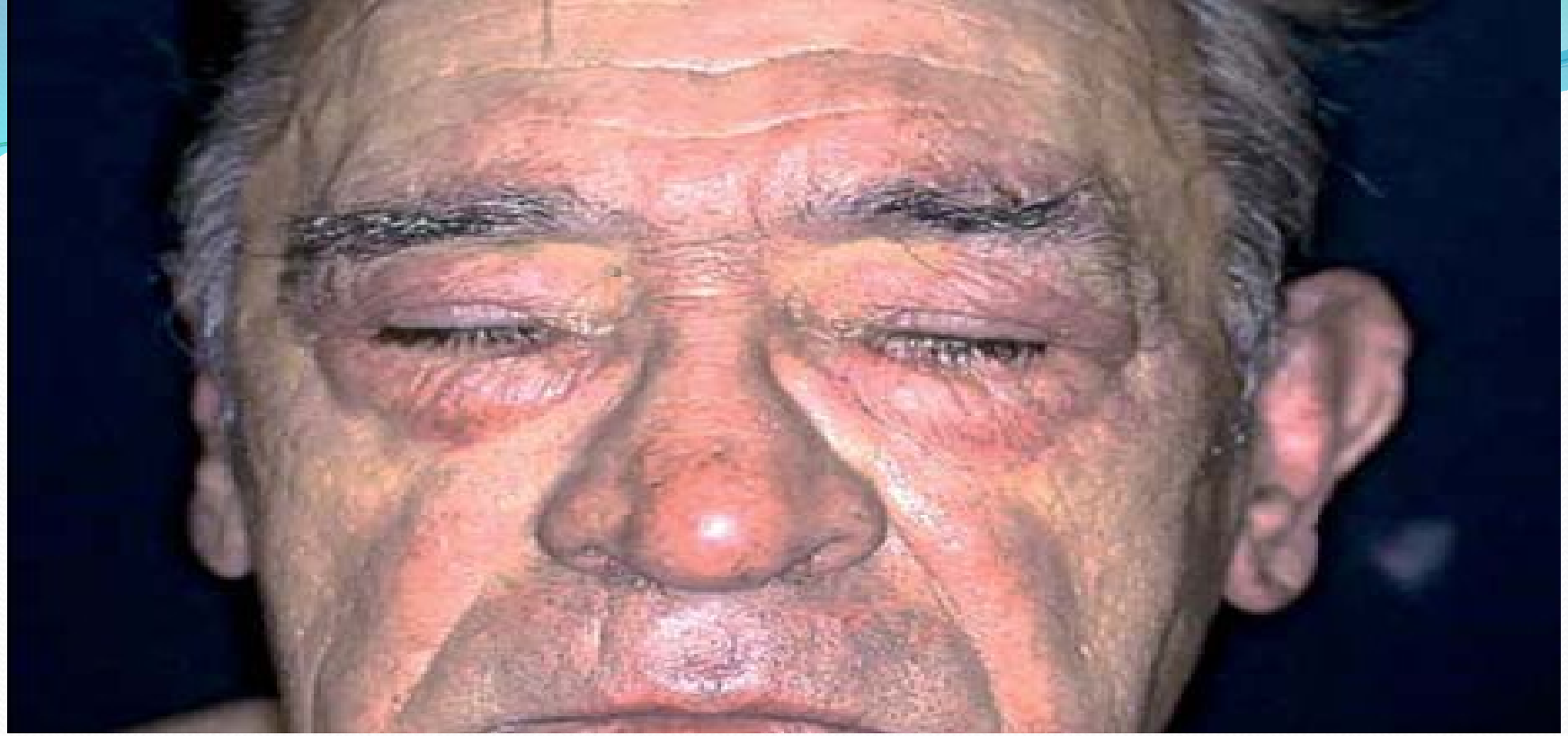
A) **Neurological:**

- **Weakness.**
- **Dysphagia** (affection of striatal muscle of oroparynx).
- **Pain.**
- **Sleep apnea** (upper airway collapse due to oropharyngeal weakness).
- **Sparing of EOMs, sensory system and deep reflexes.**

Clinical picture

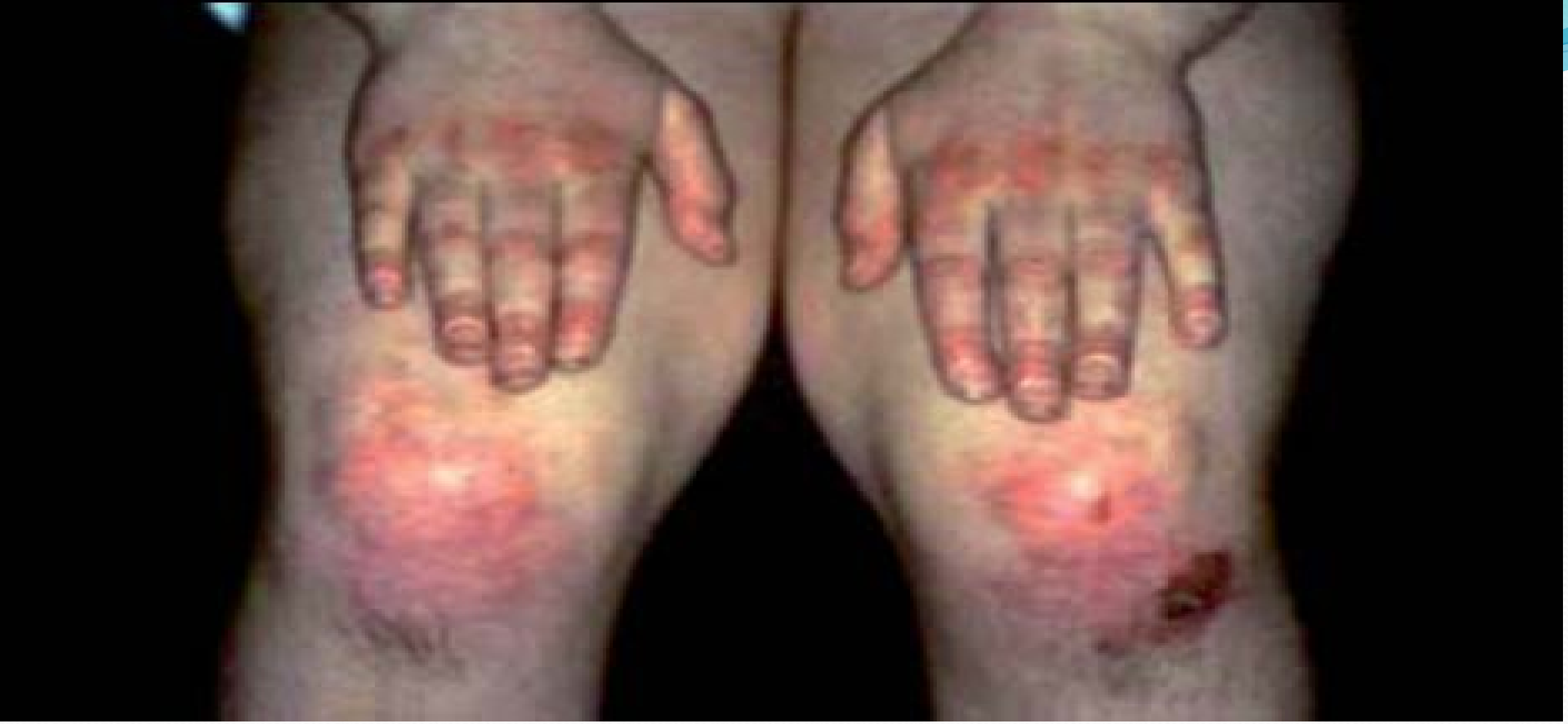
B. **Non-Neurological:**

- **Skin and subcutaneous tissues.**



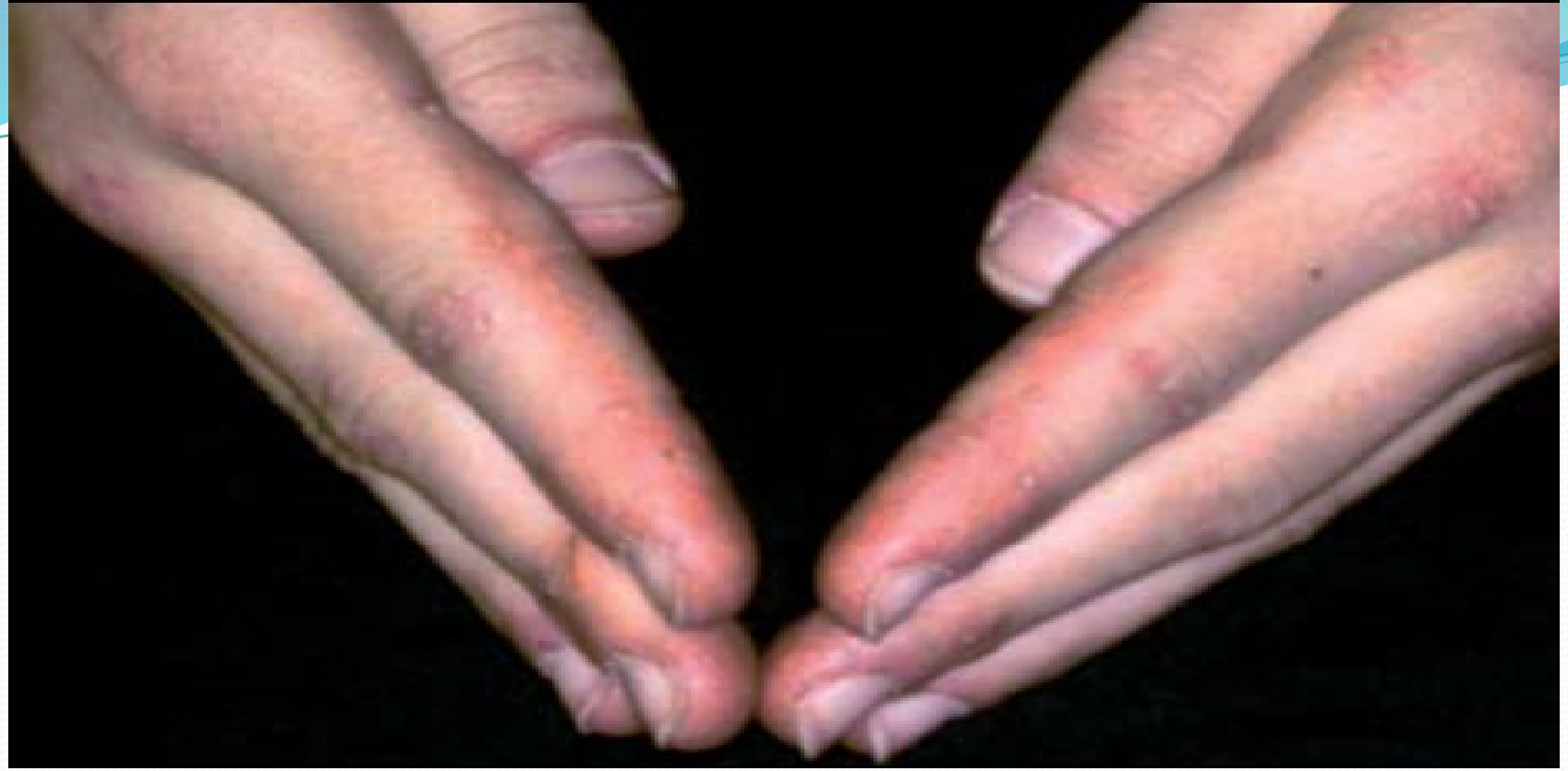
Heliotrope erythema

Typical purplish discoloration of the eyelids often associated with periorbital oedema.



Gottron's sign

Erythematous papular scaly rash, appear on the extensor surface of the hands, fingers, elbows, knees and also in the intersection of the hairline and the back of the neck.



Mechanic's hands

Thickened cracked skin on the dorsal and ventral surfaces of the hands, lateral area of the fingers is encountered in patients with the antisynthetase syndrome.

Diagnosis / therapy of DM, PM

- Blood CK levels are elevated
- EMG: myogenic findings
- Muscle biopsy: inflammation
  - DM: perivascular infiltration, mainly in the perimysium
  - PM: endomysial inflammation
- Therapy: immunosuppression, long-term treatment with corticosteroids (1 mg/kg/day)

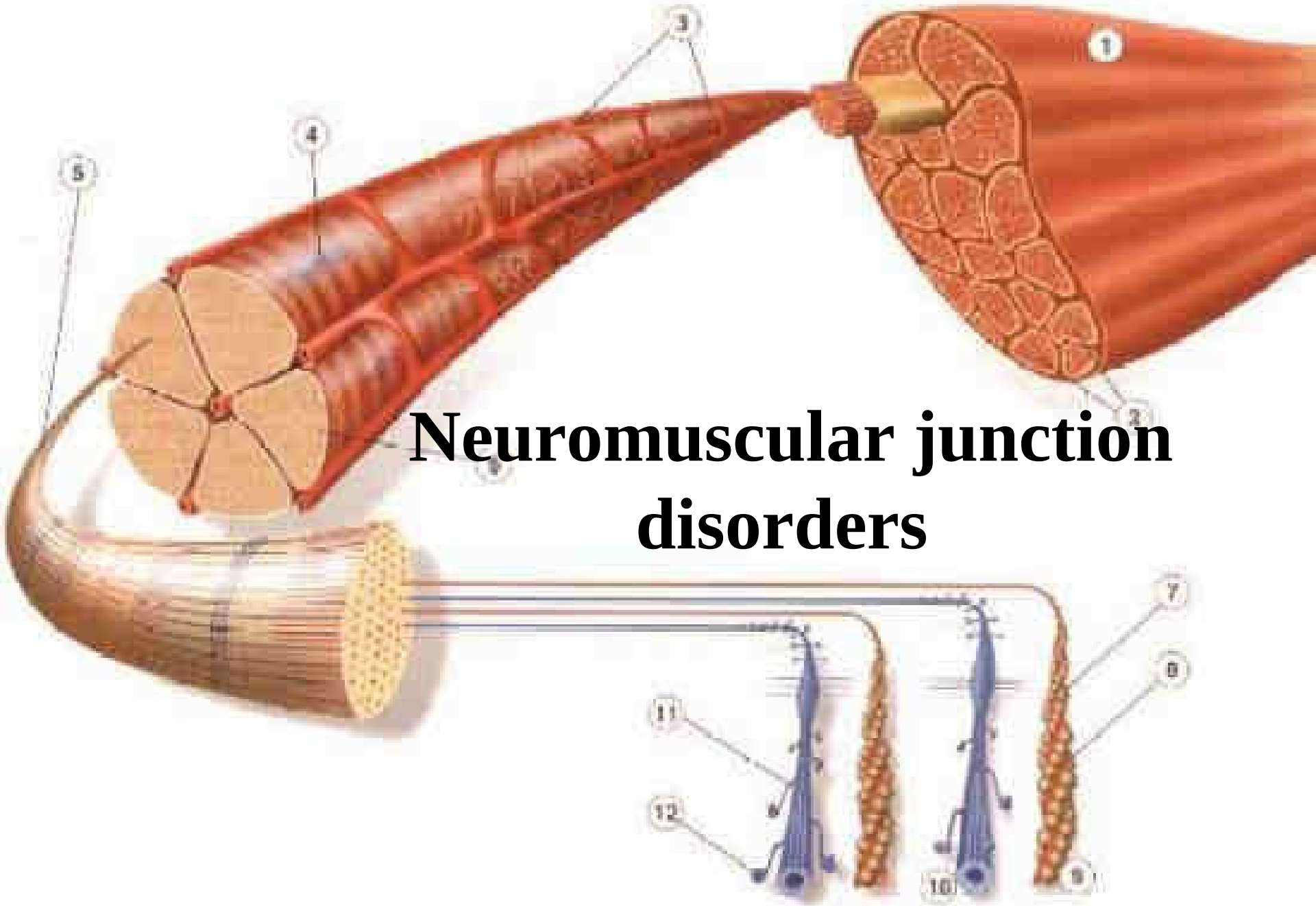
Endocrine and toxic myopathies

- Toxic myopathies:
  - Drugs aimed at reducing blood lipid levels: **statins**, clofibrate
  - **Corticosteroids – steroid myopathy**
  - **B-blockers and amiodarone**
  - Alcohol in a couple of days
  - Heroin, cocaine and amphetamines.

Endocrine and toxic myopathies

- Endocrine myopathies
  - Thyrotoxic myopathy
  - Hypothyrodism
  - Hyperparathyrodism
  - Adrenal insufficiency
  - Hypokalemia
  - Renal failure
  - osteomalacia

Neuromuscular junction disorders



Disorders of the Neuromuscular Junction

Myasthenia gravis

Definition

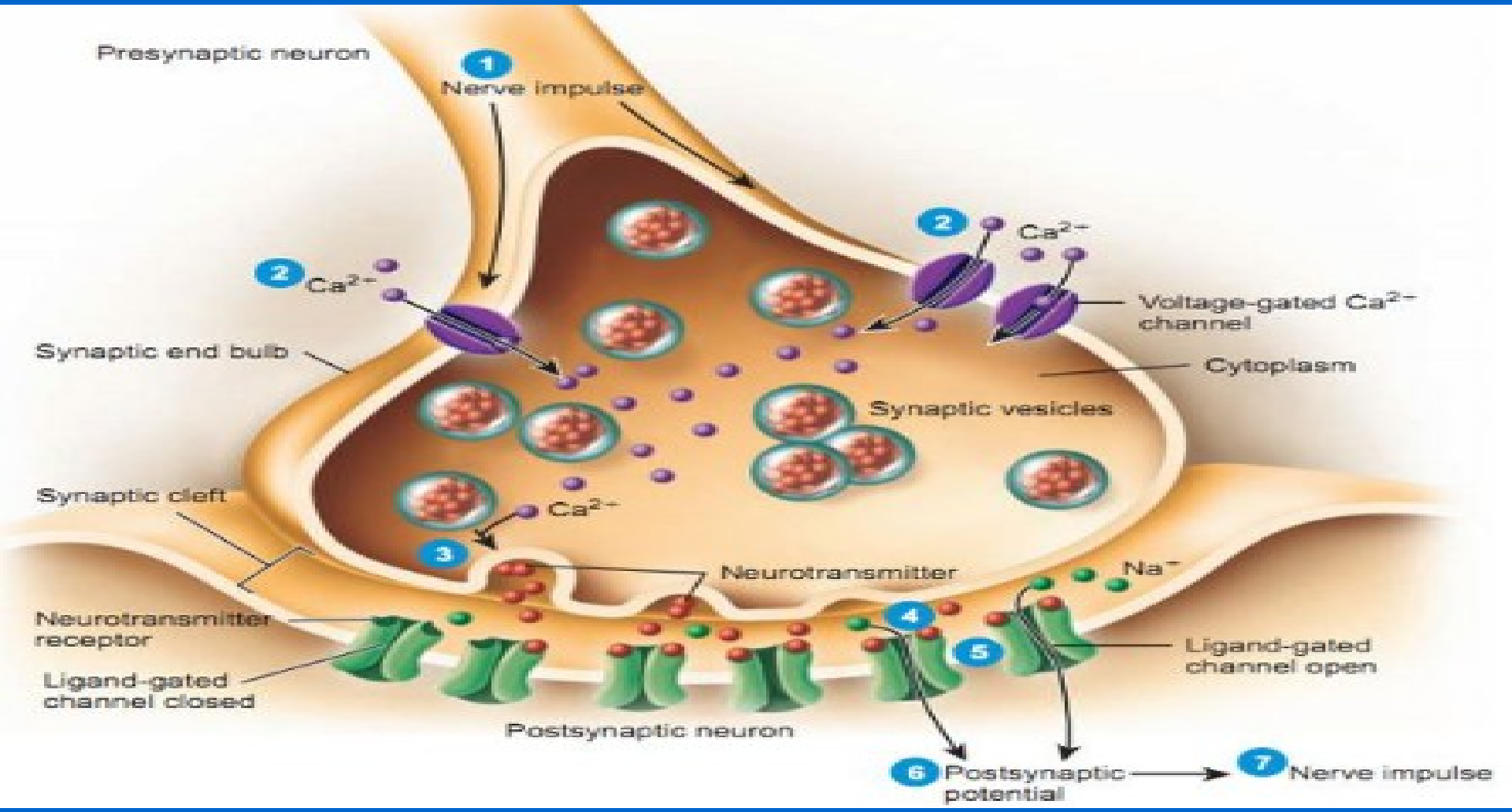
- An autoimmune disease due to an antibody mediated attack directed against nicotinic AchR at neuromuscular junction

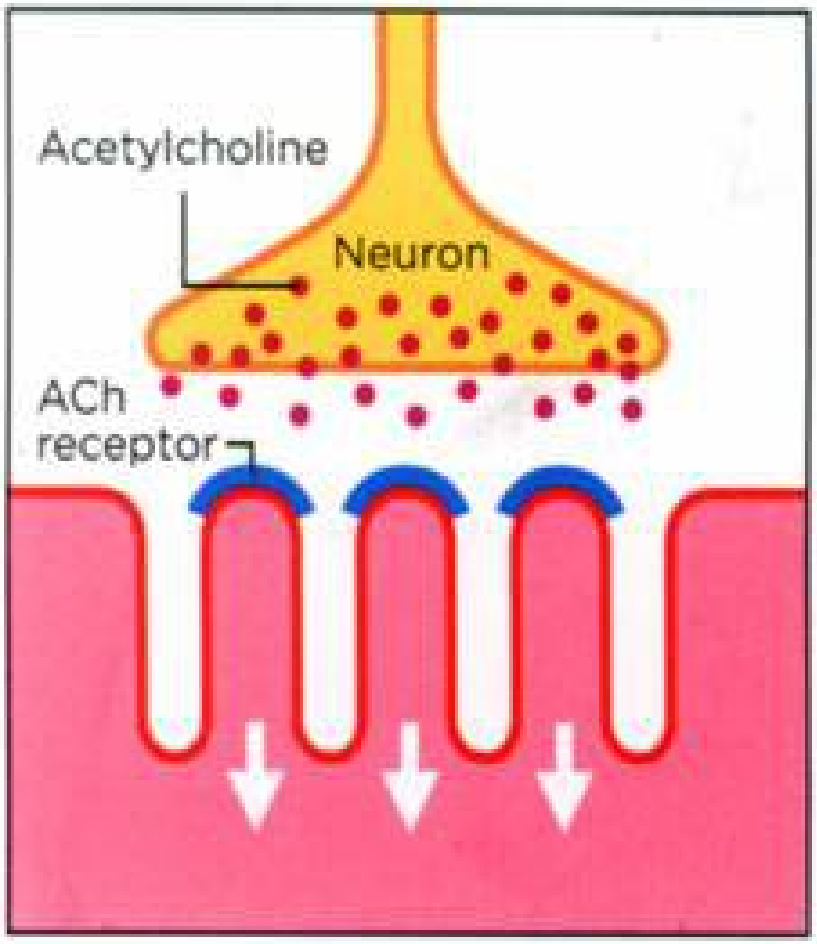
- **10% have thymoma**
- **70% have thymic hyperplasia**

Epidemiology

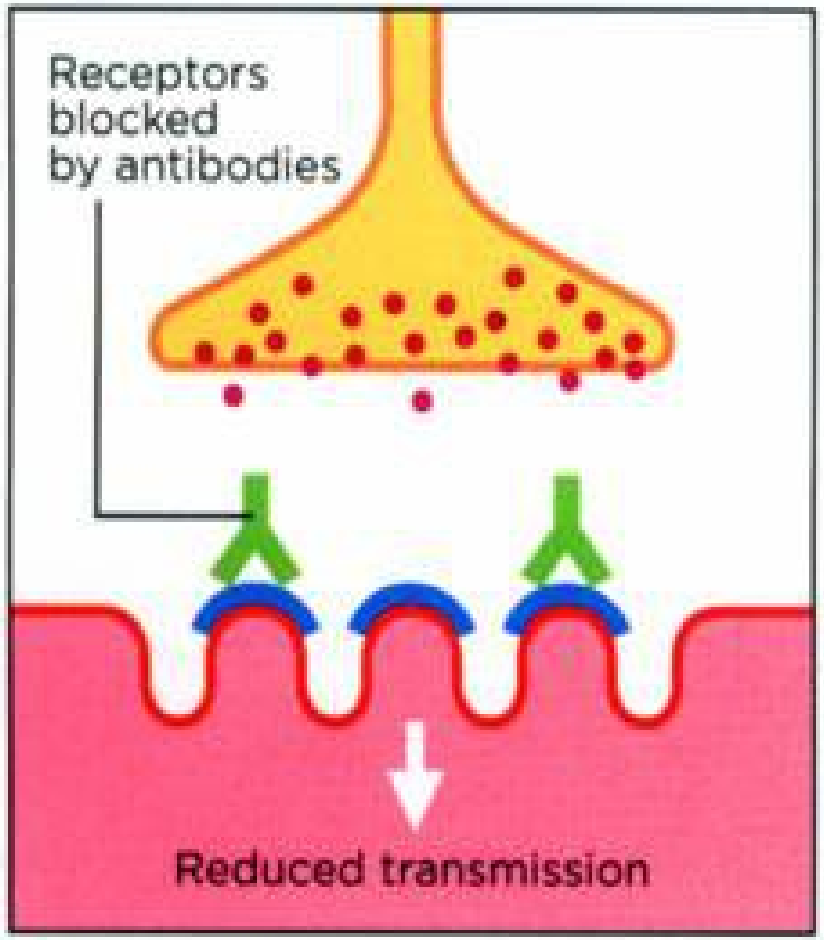
- Incidence 5-10 : 100,000.

- Women slightly higher incidence 3 : 2
- **Majority of the MG are young women in the third decade and middle aged men in 5th and 6th decade**
- Comorbidities: 5% autoimmune diseases, 10% thyroid.


Presynaptic neuron
1
Nerve impulse
2
Ca^{2+}
2
Ca^{2+}
Voltage-gated Ca^{2+} channel
Synaptic end bulb
Cytoplasm
Synaptic vesicles
Synaptic cleft
Ca^{2+}
3
Neurotransmitter
Na^{+}
Neurotransmitter receptor
4
5
Ligand-gated channel open
Ligand-gated channel closed
Postsynaptic neuron
6
Postsynaptic potential
7
Nerve impulse



Normal neuromuscular junction



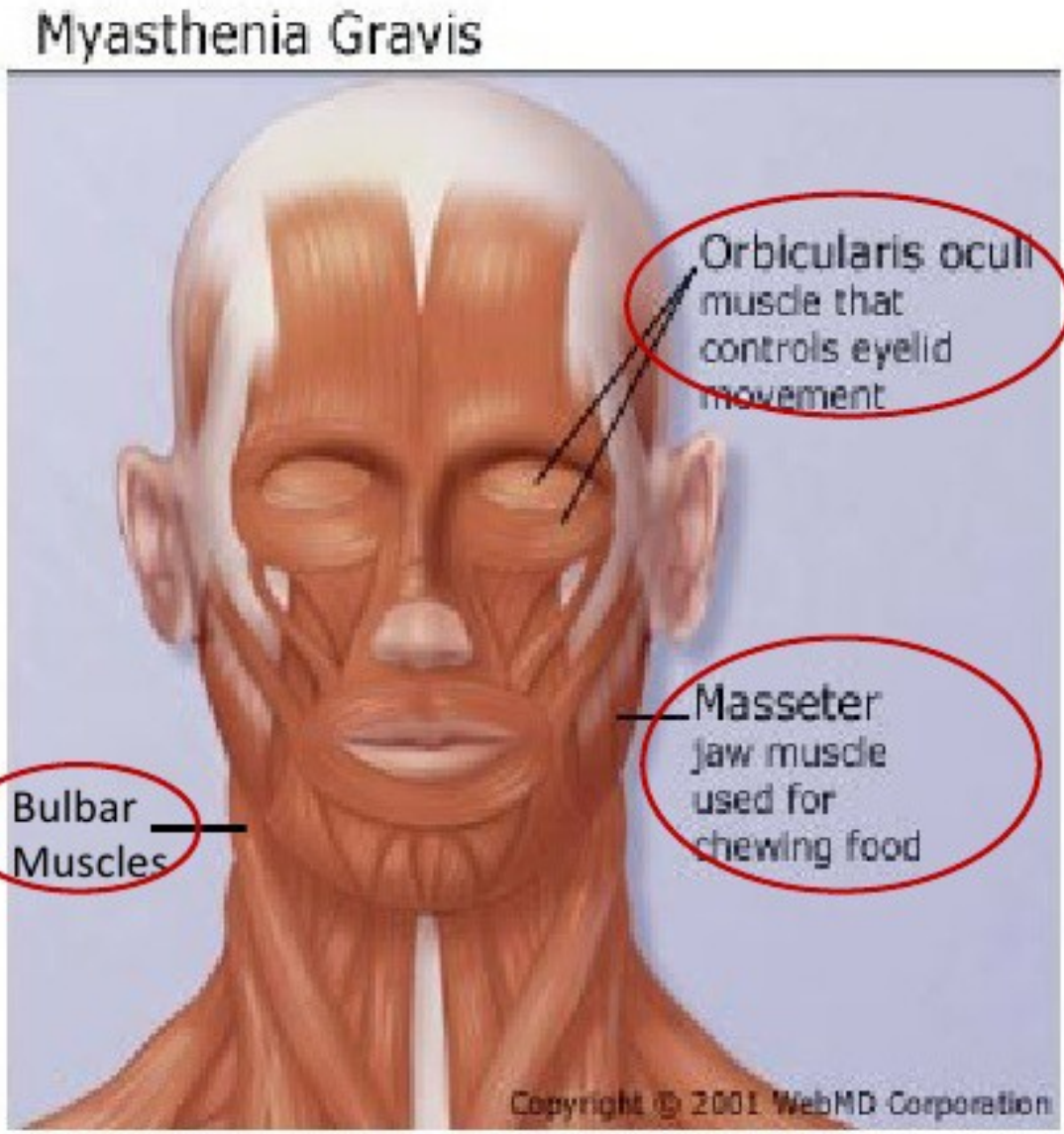
Neuromuscular junction in myasthenia gravis

CLINICAL PRESENTATION

MUSCLE STRENGTH

- Ocular muscle weakness
- Facial muscle weakness
- Bulbar muscle weakness
- Limb muscle weakness
- Respiratory weakness

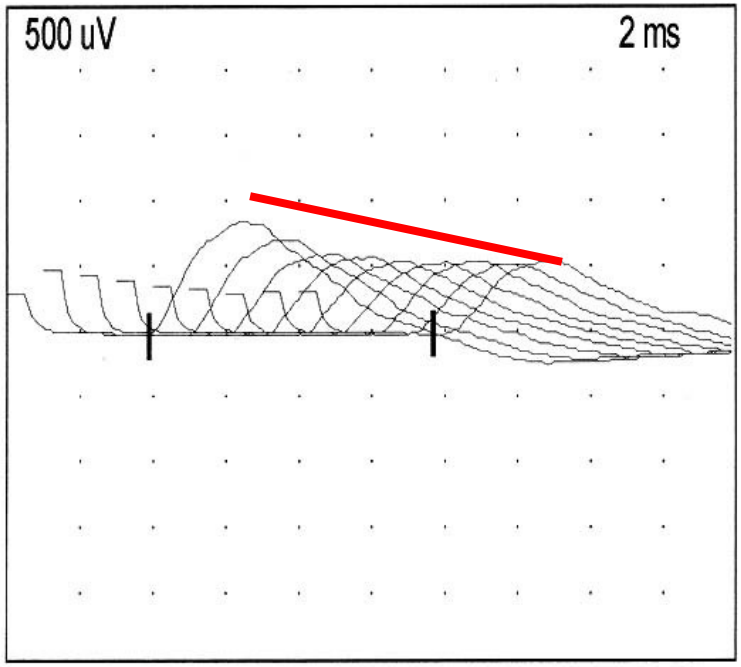
- Diurnal variation
-↑ by heat, stress, menses and infection



Diagnostic algorhitm

- Repetitive nerve stimulation
- Tensilon test
- Anti AChR antibodies
- MR of mediastinum – thymomas, hyperplasia

Low frequency stimulation - decrement



Stim.Mode: **Train** / Single

Stim Freq:	3 Hz	No. in Train:	10
Stim Dur:	0.3 ms	Stim Rjct:	0.5 ms
Time:	13:28:22		
Comment:			

Pot No.	P-P Amp mV	Amp. Decr %	Area mVms	Area Decr %	Stim. Level
1	0.88	0	3.42	0	51.8mA
2	0.75	15	2.86	16	51.8mA
3	0.64	27	2.52	26	51.8mA
4	0.61	31	2.37	31	51.8mA
5	0.57	35	2.26	34	51.8mA
6	0.56	36	2.23	35	51.8mA
7	0.58	34	2.26	34	51.8mA
8	0.55	37	2.23	35	51.8mA
9	0.57	35	2.31	32	51.8mA
10					

Treatment

- Thymectomy
- Plasma exchange in myasthenic crisis (TPE)
- Human immune globuline (IvIg)
- Corticosteroids + cytostatics
- AChE inhibitors (pyridostigmine, distigmine)

Myasthenic crisis

Respiratory insuficiency – paralysis of respiratory muscles. Affect 15-20% myasthenic patients

Clinical features

- **Respiratory failure 99%**
- **Oropharyngeal or ocular weakness 86%**
- **Respiratory tract infection, pneumonia (38%)**
- **Arms and legs weakness 76%**

Assisted ventilation required