

Enfermedades autoinmunes del sistema nervioso periférico

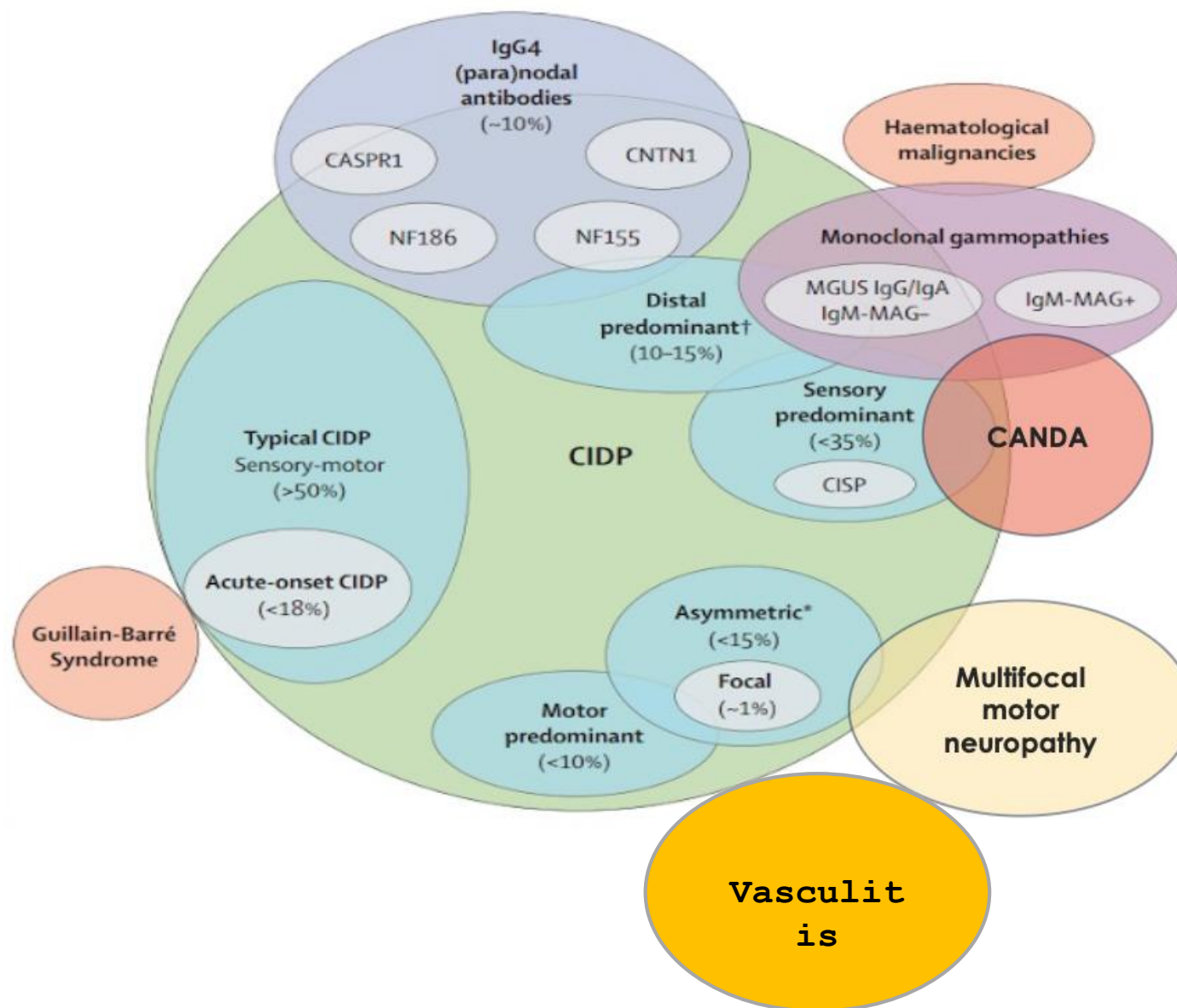
José M. Pastor Rueda - Neurología
Sección de Enfermedades Neuromusculares
Departamento de Neurología - FLENI

Neuropatías inmunomediadas

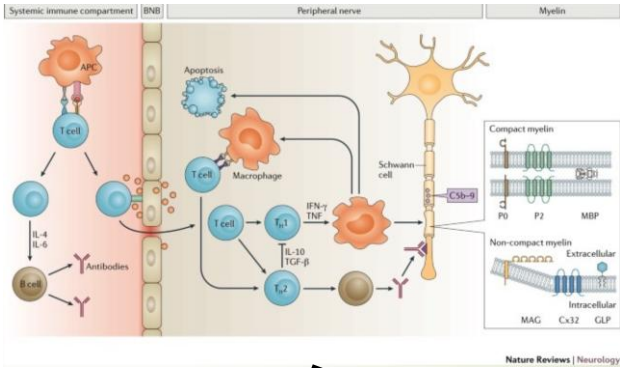
Enfermedades autoinmunes del sistema nerviosos periférico

Definición

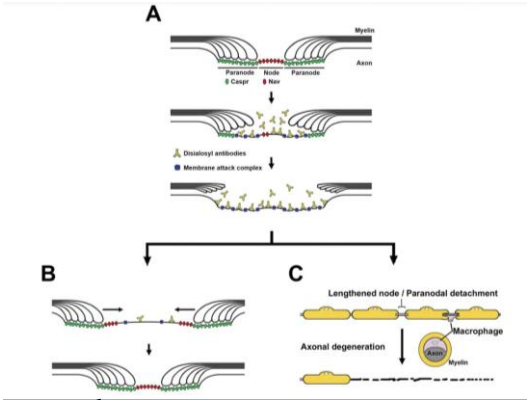
“Trastornos heterogéneos causados por una respuesta inmune dirigida contra componentes del sistema nervioso periférico, que produce daño y disfunción del nervio”.



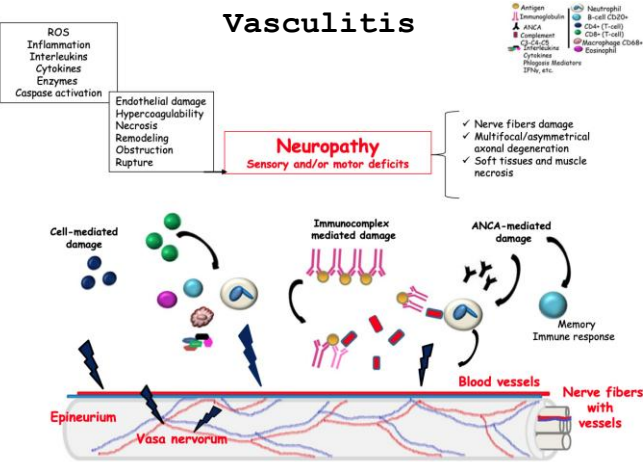
CIDP



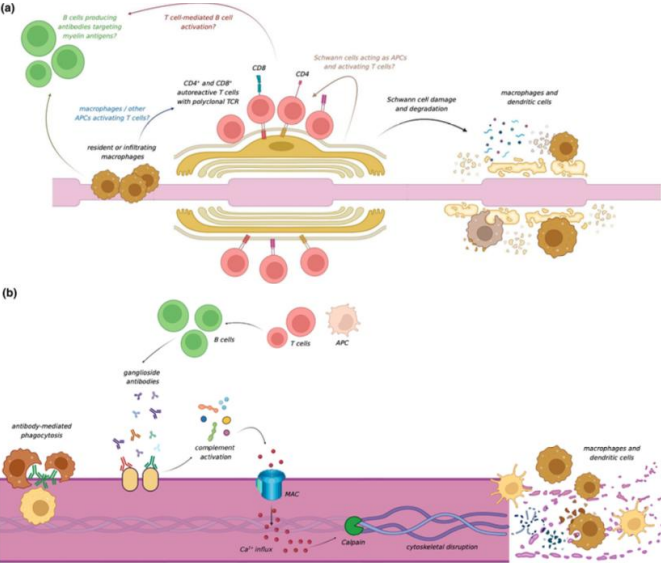
CANDA/CANOMAD



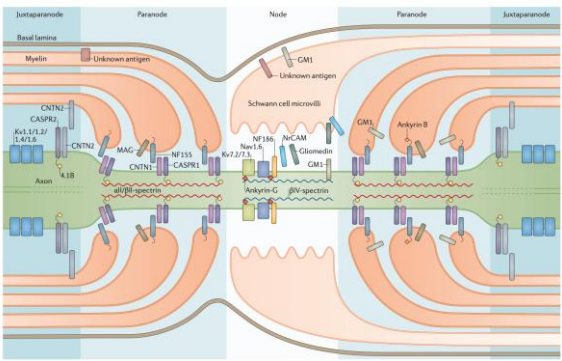
Vasculitis



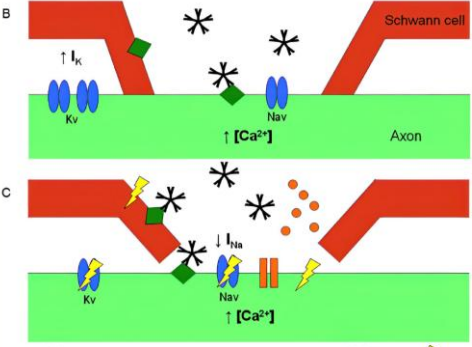
GBS

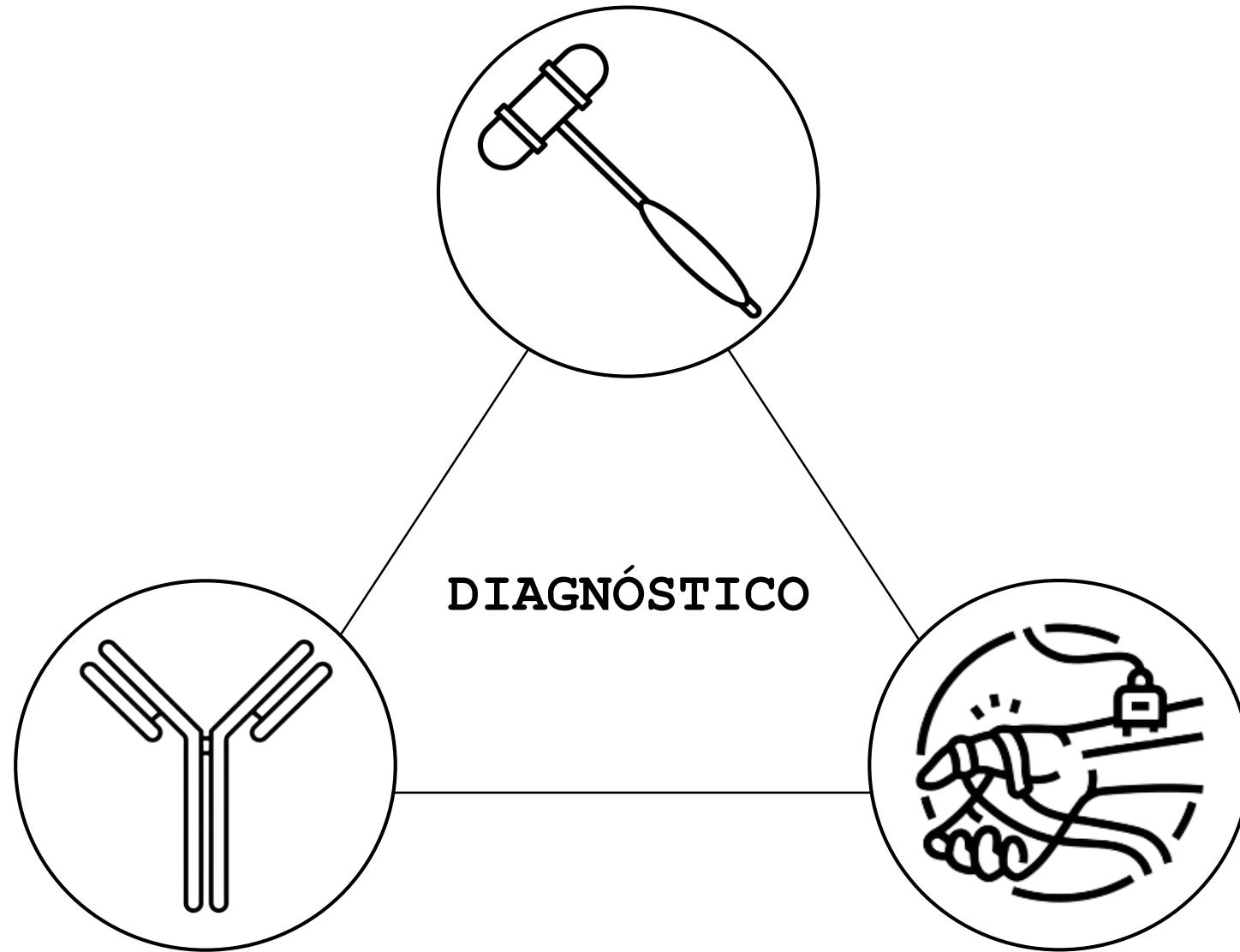


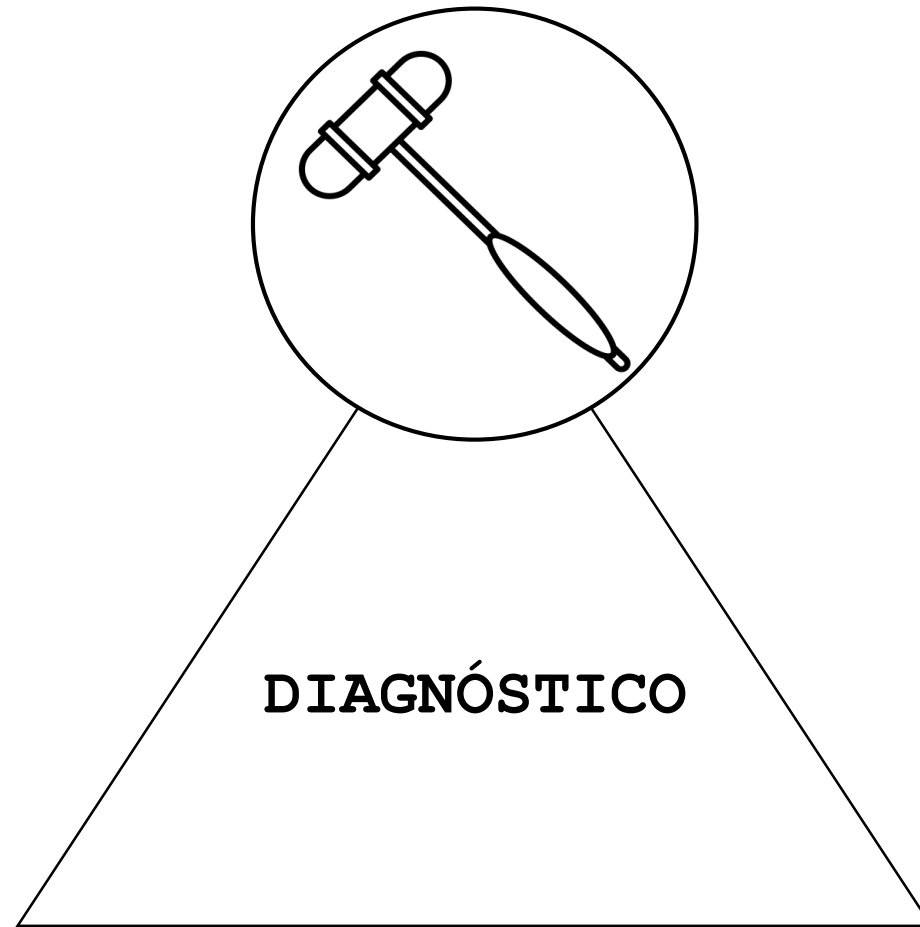
Nodopatías

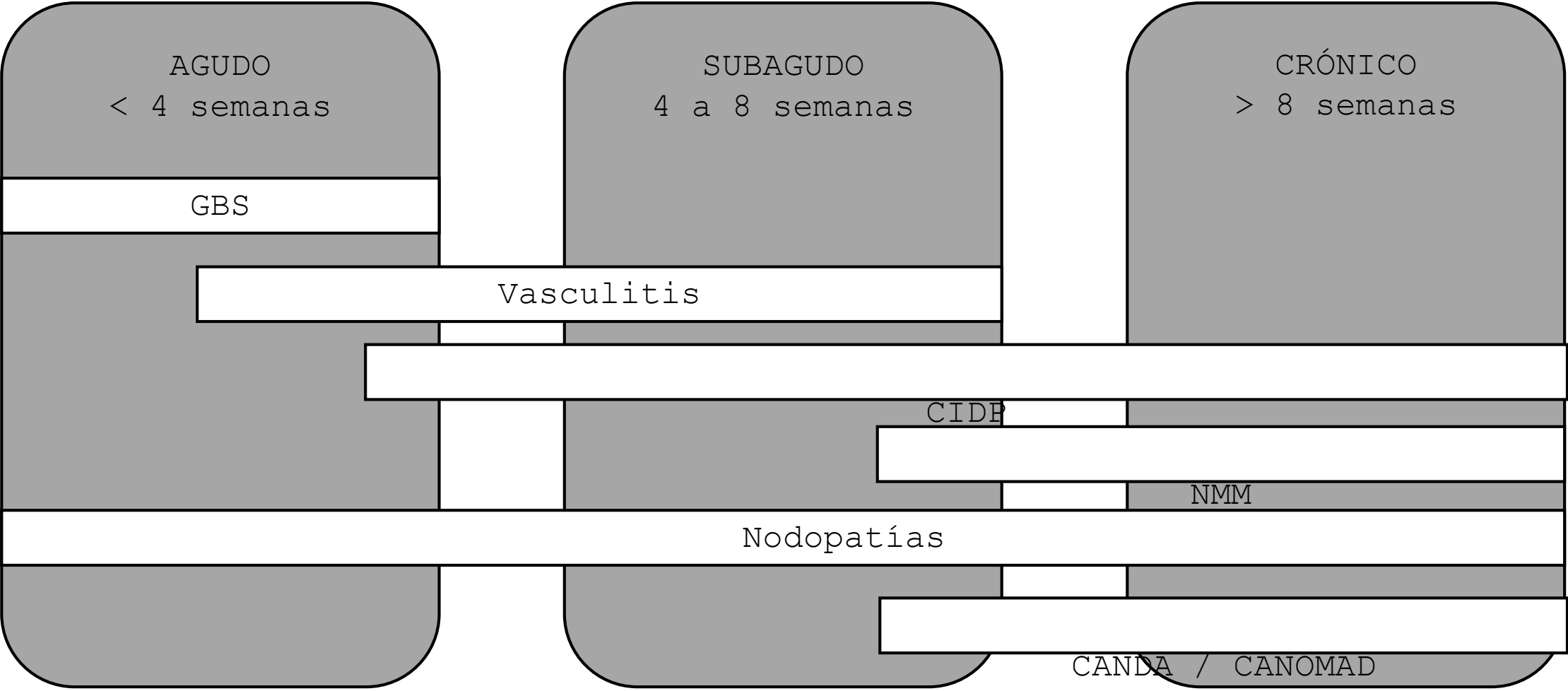


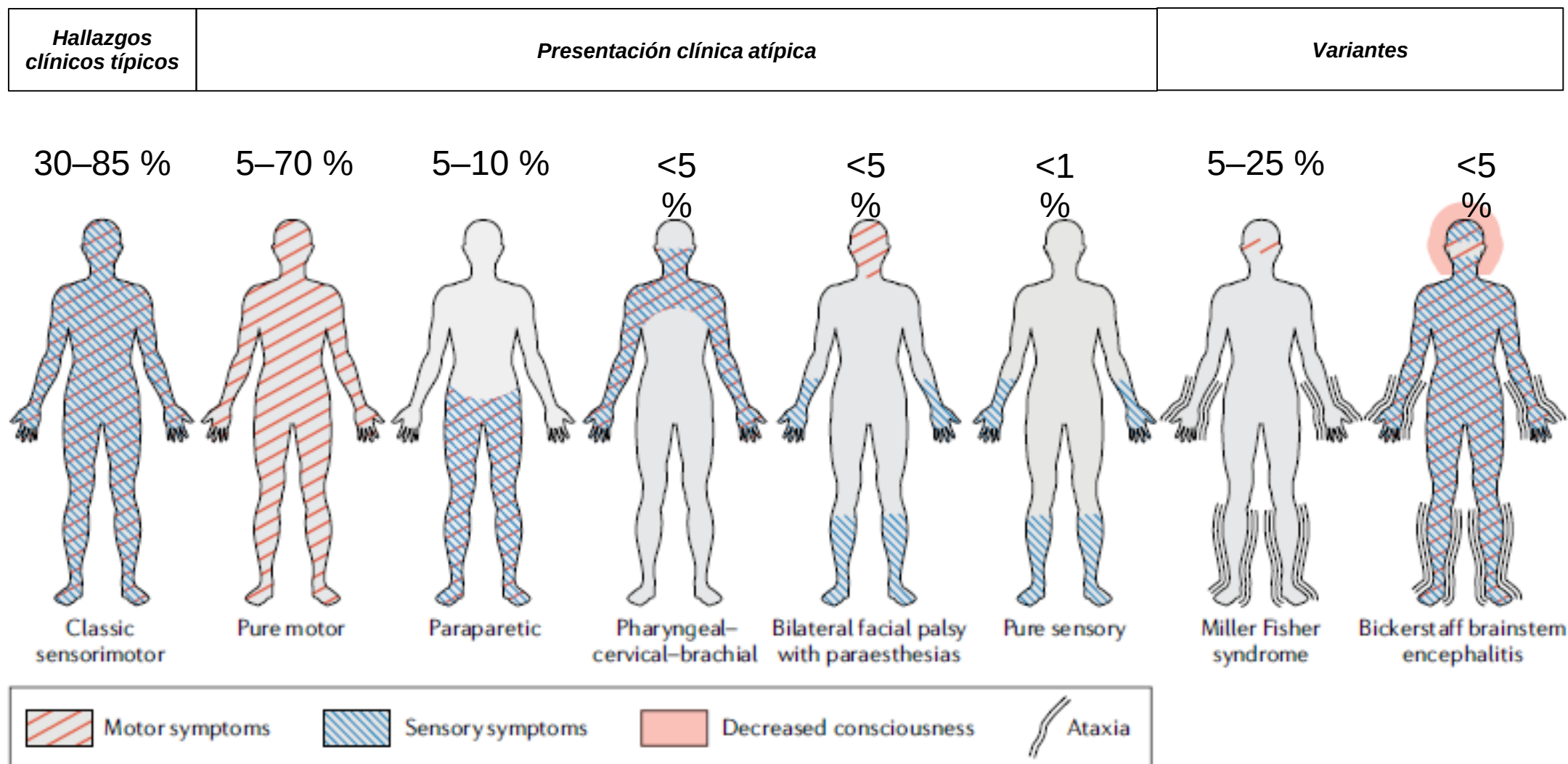
Neuropatía motora multifocal

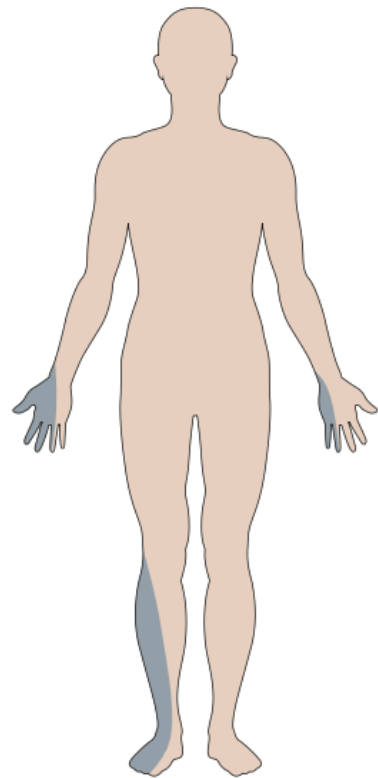




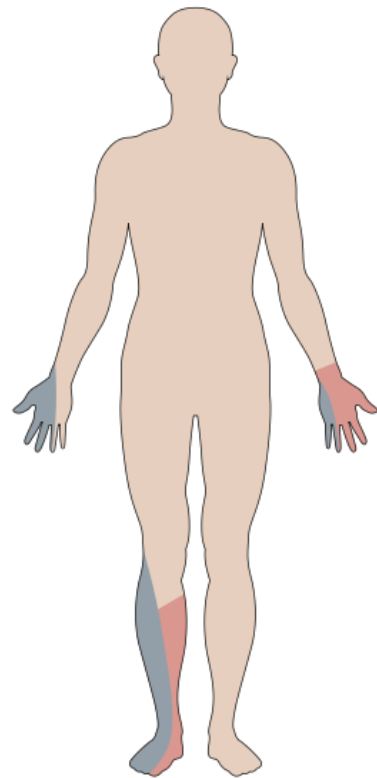




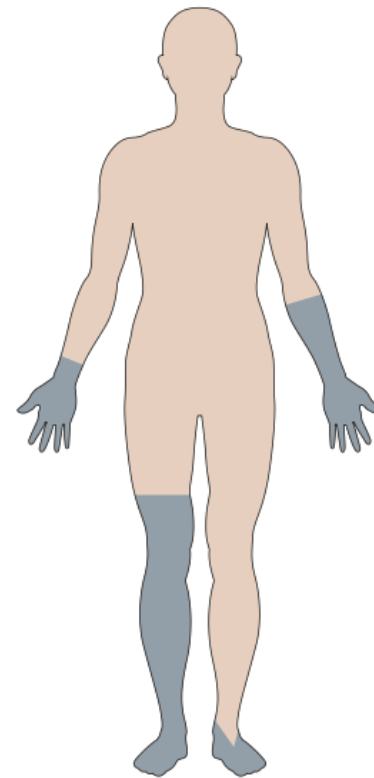




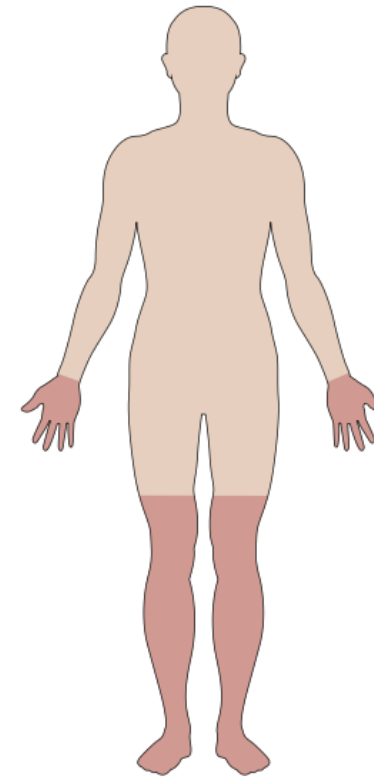
Mutifocal neuropathy



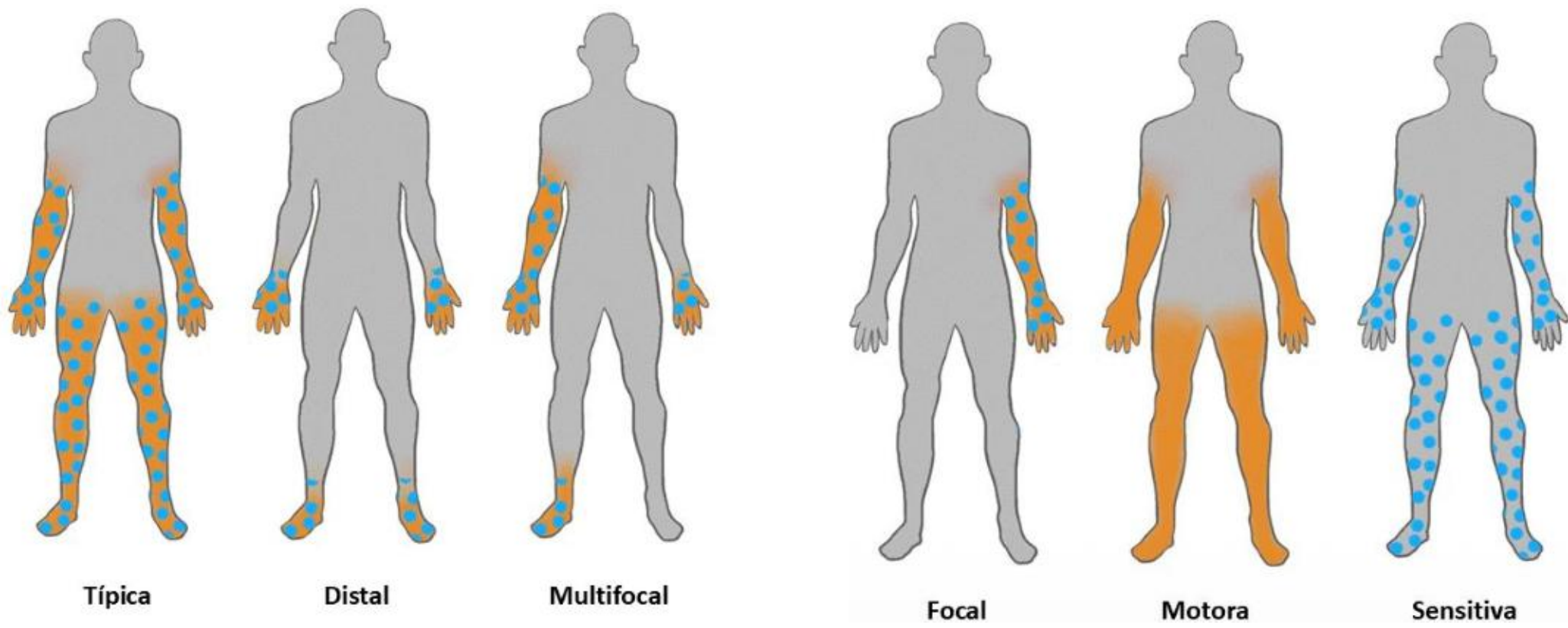
Early overlapping
mutifocal neuropathy



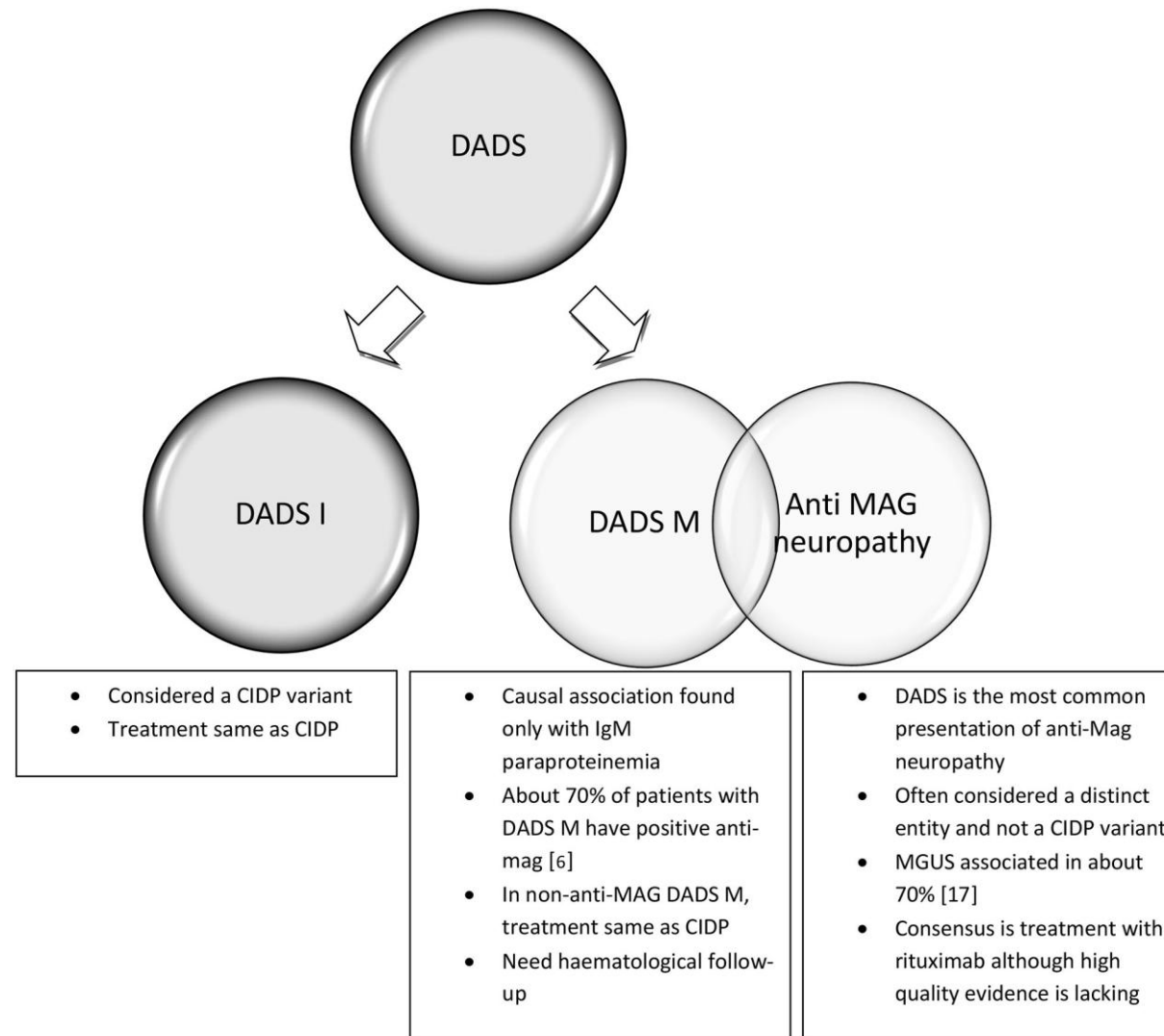
Late overlapping multifocal
neuropathy (asymmetric
polyneuropathy)



Distal symmetric
polyneuropathy



Distal acquired demyelinating sensory neuropathy (DADS)





Autoimmune nodopathies

- Sensory-motor +/- cranial
- "Demyelinating" physiology

- Nerve biopsy: Axonal
- MRI: Roots enhancement
- CSF: High protein levels

- IVIG: Poor response
- Steroids: Partial/good response
- Rituximab: Good response

CNTN1 IgG4/IgG3*

- Subacute onset
- Tetraparesis
- Early denervation
- Ataxia
- Cranial nerves
- Nephrotic syndrome
- *IgG3 in the early phase

Caspr1 IgG4/IgG3

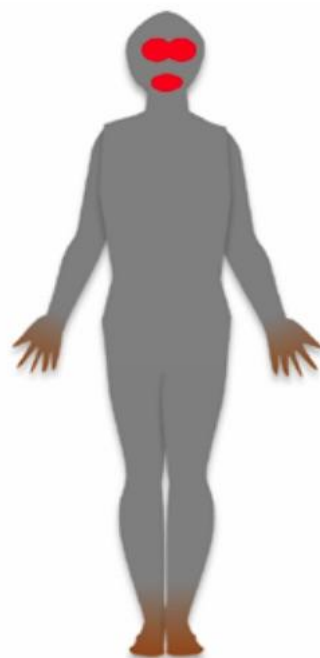
- Acute/subacute onset
- Tetraparesis
- Sensory ataxia and tremor
- Cranial nerves
- Respiratory pain (50%)

NF155 IgG4

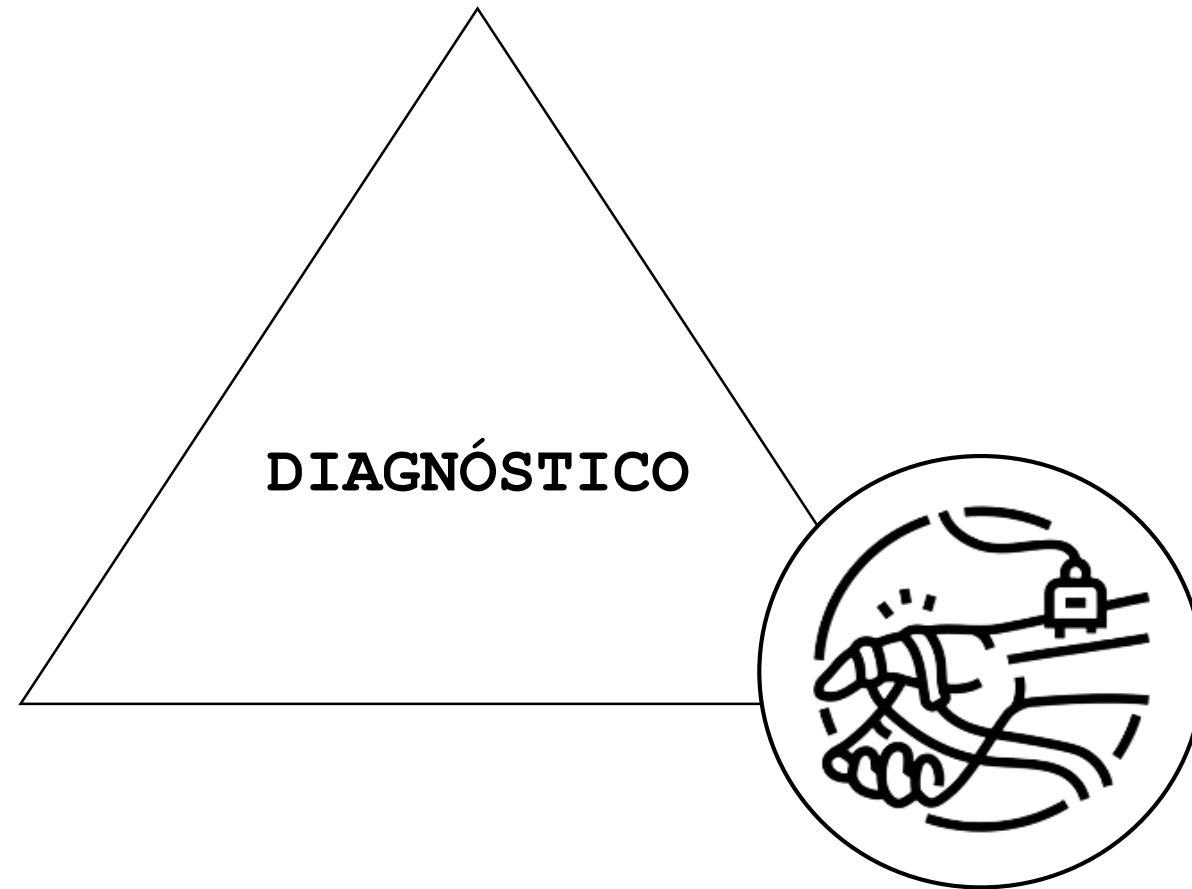
- Chronic onset
- Young male
- Distal weakness
- Cerebellar ataxia and tremor
- **HLA DRB1*15**

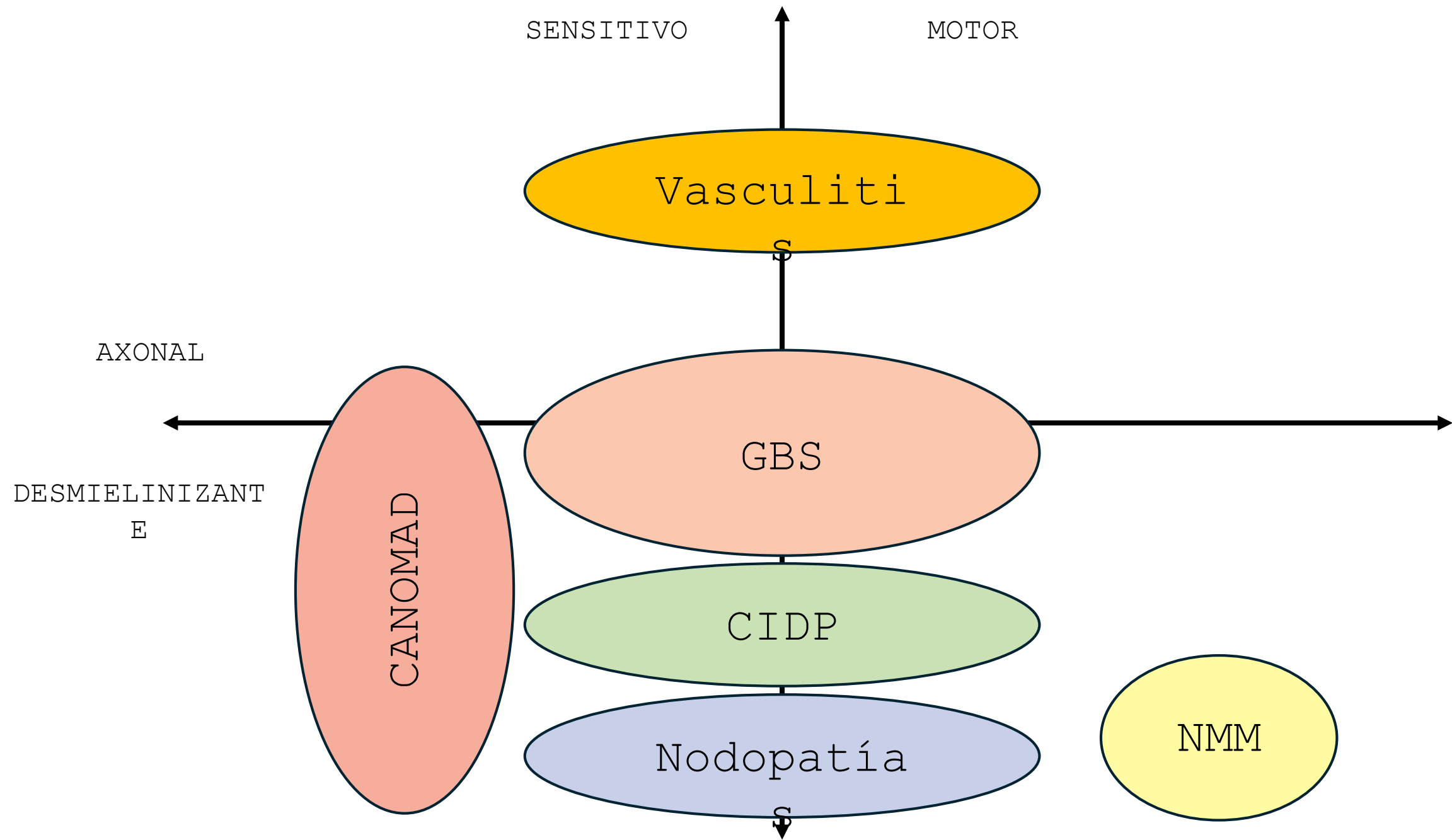
Pan-NF IgG1/IgG3/IgG4

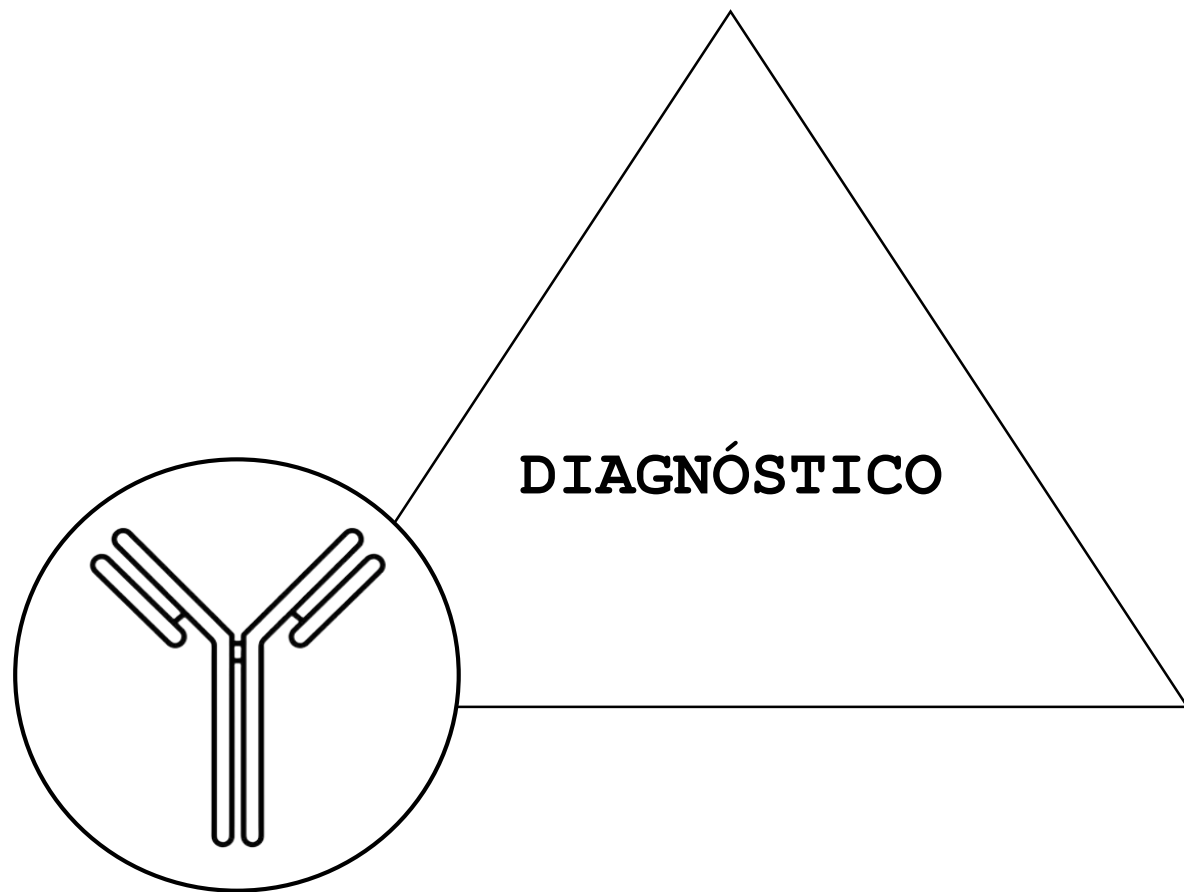
- Acute/subacute onset
- Severe monophasic course
- Initial IVIG response
- Cranial nerve
- Respiratory involvement
- Autonomic dysfunction
- Nephrotic syndrome
- Reversible conduction failure



Demyelinating polyneuropathy 48%	Demyelinating polyneuropathy with ocular and/or bulbar involvement 16%	CANOMAD syndrome 20%	Axonal sensory polyneuropathy 16%
--	--	--------------------------------	---







Onset	Syndrome	Category	Antibody	Clinical use	Pathogenicity	Diagnostic tests
Acute	Sensory-ataxic	ASAN	Disialosyl IgG	Diagnostic	Likely pathogenic	ELISA/TLC
	Pure motor	AMAN/AMSAN	GM1/GD1a – GalGalNAc IgG	Diagnostic	Likely pathogenic	ELISA/TLC
	Sensory-motor	AIDP	GalGalNAc IgG	Diagnostic	Likely pathogenic	ELISA/TLC
		Acute onset nodopathies	Pan-NF, Caspr1, CNTN1, NF155	Diagnostic, monitoring	Pan-NF, Caspr1 → Likely pathogenic CNTN1, NF155 → Pathogenic	CBA, ELISA, teased nerve fibers IF
	Pharyngo-cervical	PCB palsy	GT1a IgG	Diagnostic	Likely pathogenic	ELISA/TLC
	Ataxia ophthalmoparesis	MFS spectrum	GQ1b-GT1a IgG	Diagnostic	Likely pathogenic	ELISA/TLC
Subacute/chronic	Sensory-ataxic	IgM MGUSP	MAG IgM, sulfatides IgM	Diagnostic, monitoring?	MAG → Pathogenic Sulfatides → Unknown	ELISA, nerve IF, HNK-1 CBA
		CANOMAD	Disialosyl IgM	Diagnostic	Likely pathogenic	ELISA/TLC
		Sensory neuronopathy	Para-neoplastic	Diagnostic	Not pathogenic	Brain IF, blot
			Hu IgG, amphiphysin IgG			
			Sjögren	Diagnostic	Not pathogenic	EIA
			Ro, La IgG			
	Pure motor	MMN	GM1/GalGalNAc IgM	Diagnostic	Likely pathogenic	ELISA/TLC
	Sensory-motor asymmetric	Multifocal CIDP	?	Diagnostic, monitoring	MPO → Pathogenic; PR3 → Unknown Cryoglobulins → Unknown	ANCA → IF; MPO, PR3 → EIA Cryoglobulins → Cryoprecipitate quantification and immunofixation
		Mononeuritis multiplex	ANCA (MPO, PR3), cryoglobulins			
	Sensory-motor symmetric	CIDP	Typical	Diagnostic, monitoring	Pathogenic	ELISA, nerve IF, HNK-1 CBA
			Distal			
		Autoimmune nodopathies	NF155, CNTN1 Caspr1, Pan-NF	Diagnostic, monitoring	NF155, CNTN1 → Pathogenic Caspr1, Pan-NF → Likely pathogenic	CBA, ELISA, teased nerve fibers IF
		Paraneoplastic	CRMP5, amphiphysin IgG	Diagnostic	Not pathogenic	Brain IF, blot

Estudios complementarios

- Análisis de laboratorio: estudios hematológicos, autoinmunidad en sospecha de vasculitis, otras causas de neuropatía.
- Análisis de LCR: disociación albúmino-citológica.
- RMN de plexos: engrosamiento y realce de nervios.
- Biopsia de nervio: casos seleccionados (vasculitis).

Tratamiento

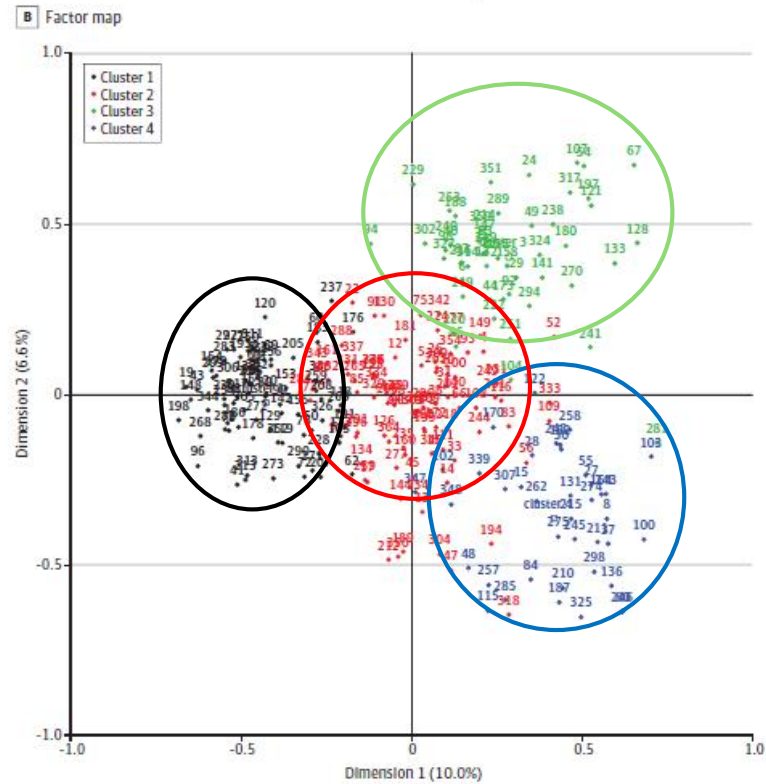
Entidad	Tratamiento de elección	Si respuesta insuficiente / refractaria	Referencias
GBS	IgIV o plasmaféresis	Soporte intensivo + tratamiento de complicaciones. No corticoides	Leonhard SE, et al. <i>Eur J Neurol</i> . 2023;30:3646-3674.
CIDP	IgIV o corticoides	Plasmaféresis → inmunoterapia ahorradora / rituximab en casos seleccionados	Van den Bergh PYK, et al. <i>J Peripher Nerv Syst</i> . 2021;26:242-268.
MMN	IgIV (± IgSC de mantenimiento)	Rituximab / ciclofosfamida en casos seleccionados. No corticoides ni plasmaféresis	Van Schaik IN, et al. <i>Eur J Neurol</i> . 2006;13:802-808.
Nodopatías	Rituximab ; corticoides pueden ser útiles en algunos subgrupos	Plasmaféresis en casos graves/refractarios; IgIV suele tener respuesta limitada	Querol L, et al. <i>Neurol Neuroimmunol Neuroinflamm</i> . 2024.
CANDA / CANOMAD	IgIV	Rituximab como segunda línea; tratar la gammapatía/hemopatía asociada	Pujol C, et al. <i>Blood</i> . 2020;136:1090-1099.
Vasculitis	Corticoides + inmunosupresor (habitualmente ciclofosfamida)	Rituximab u otros inmunosupresores según etiología; tratar enfermedad sistémica	Collins MP, et al. <i>Neurol Clin</i> . 2013;31:557-595.

Miopatías inmunomediadas

Enfermedades autoinmunes del sistema nerviosos periférico

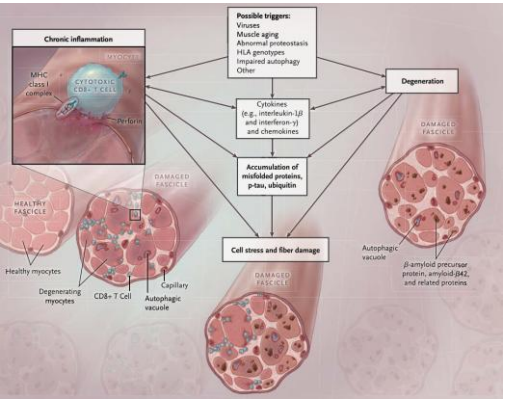
Definición

“Grupo heterogéneo de enfermedades autoinmunes que afectan principalmente al músculo esquelético y pueden presentar manifestaciones extramusculares (piel, pulmón, articulaciones y corazón), con distintos fenotipos clínicos y serológicos”.



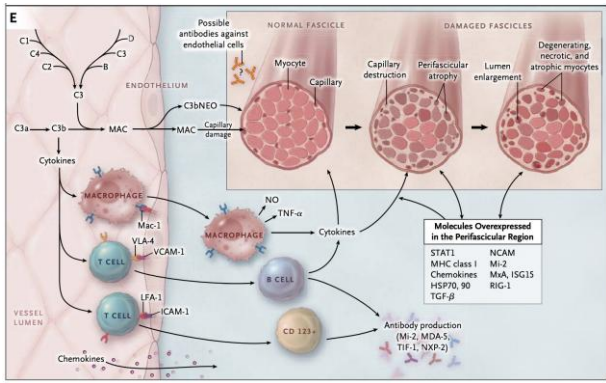
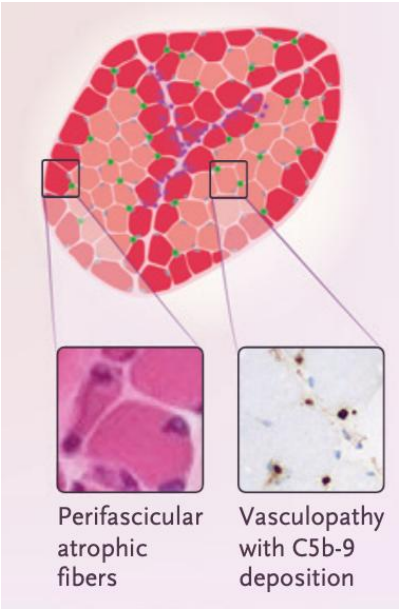
1. Miositis por Cuerpos de Inclusión (sIBM)
2. Miositis Necrotizante Auto-Inmune (IM-NM)
3. Dermatomiositis (DM)
4. Miositis por Superposición - Síndrome Anti-Sintetasa (OM - ASS)
5. Polimiositis (PM) ... (?)

sIBM



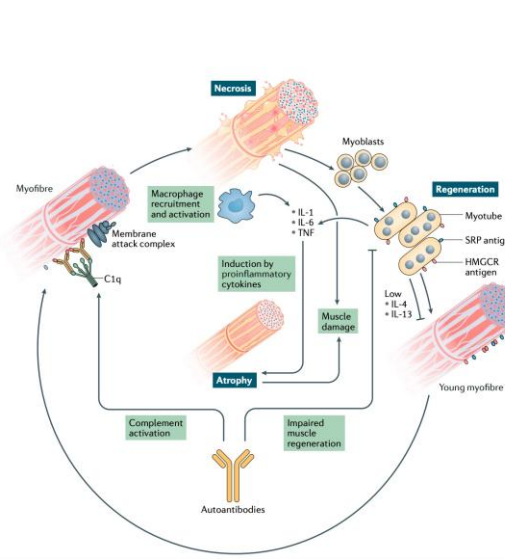
N Engl J Med. 2015;372:1734-1747.

DM



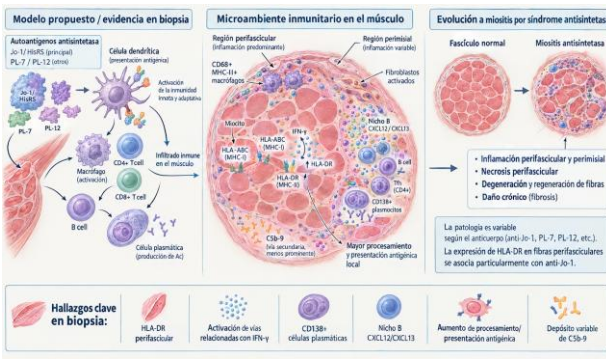
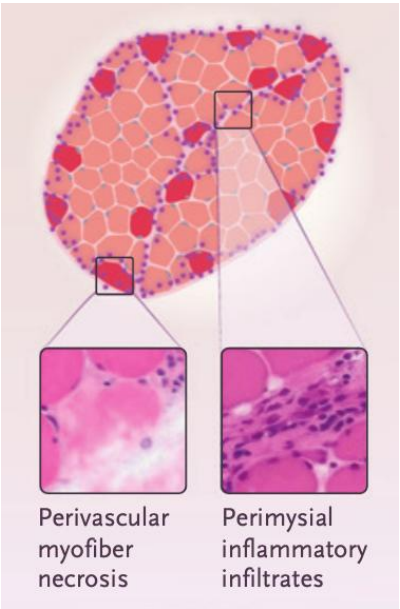
N Engl J Med. 2015;372:1734-1747.

IM-NM

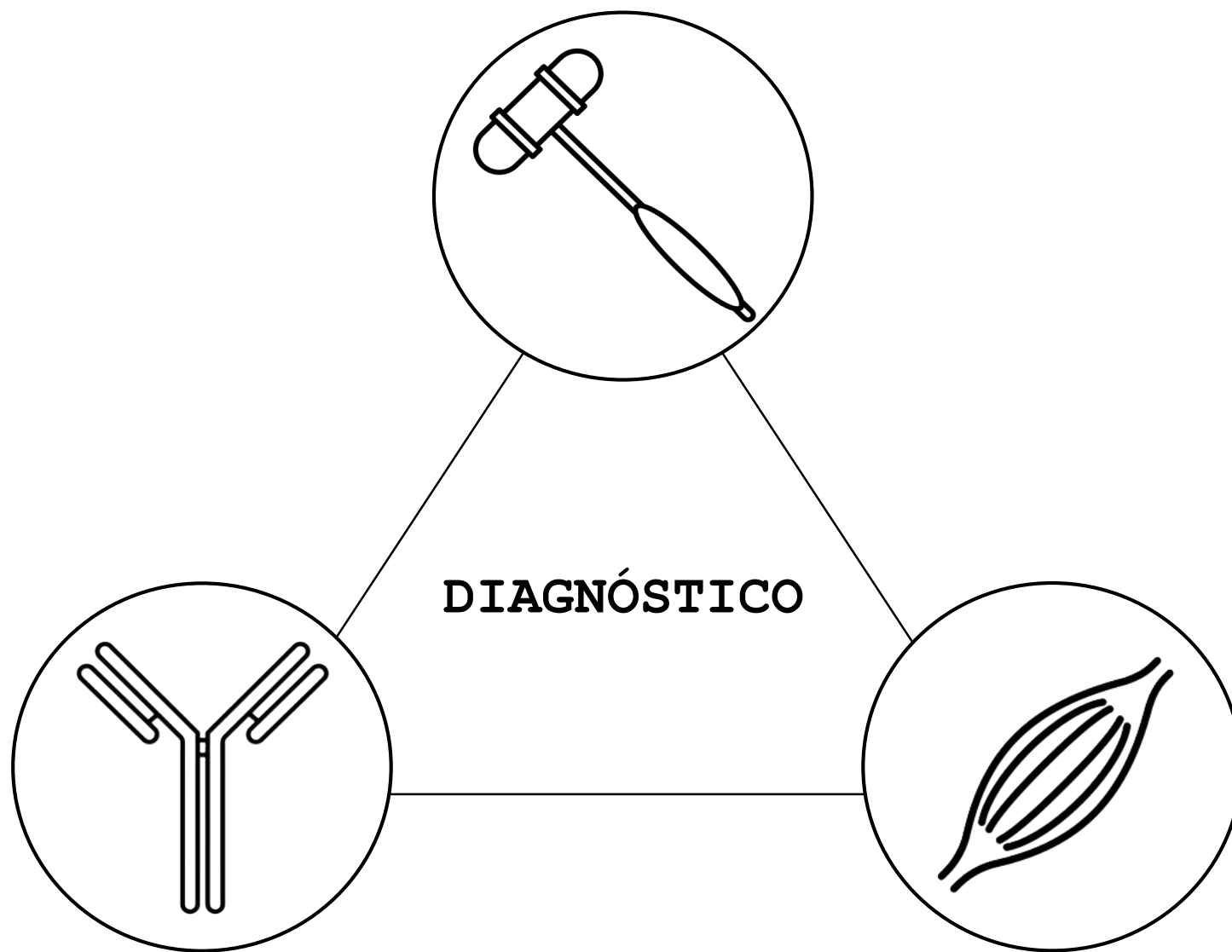


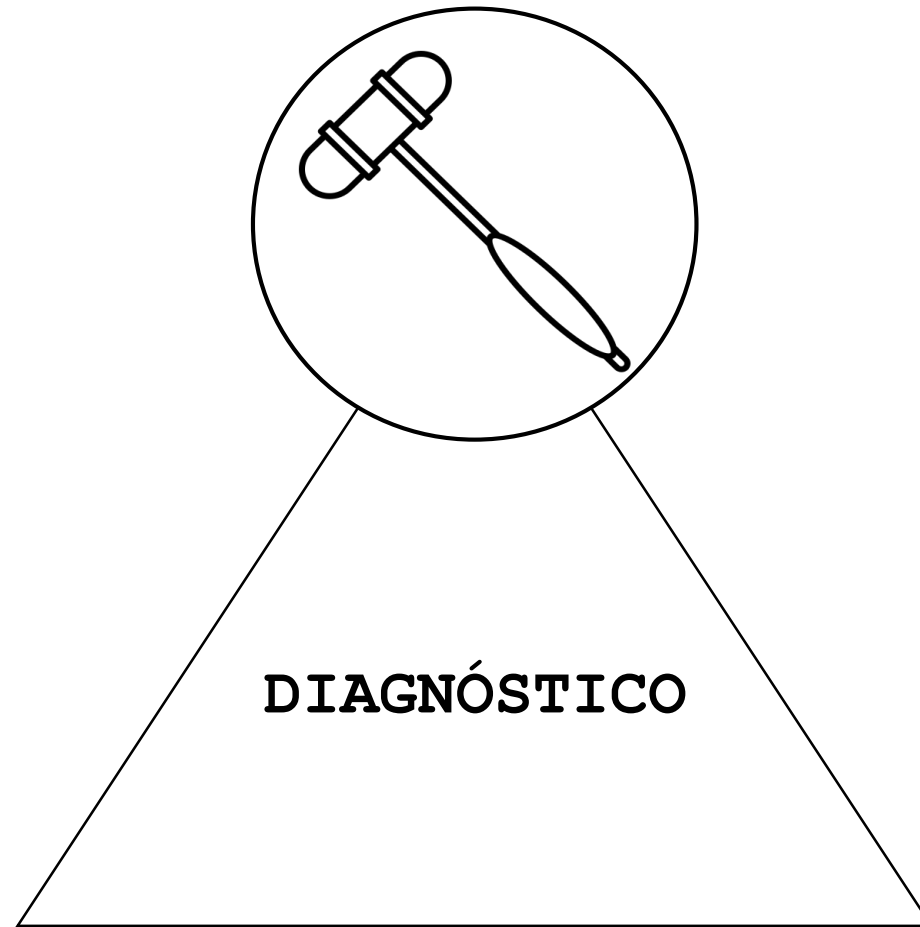
Nat Rev Rheumatol. 2020 Dec;16(12):689-701.

ASS



Acta Neuropathologica. 2022;144(2):353-372.

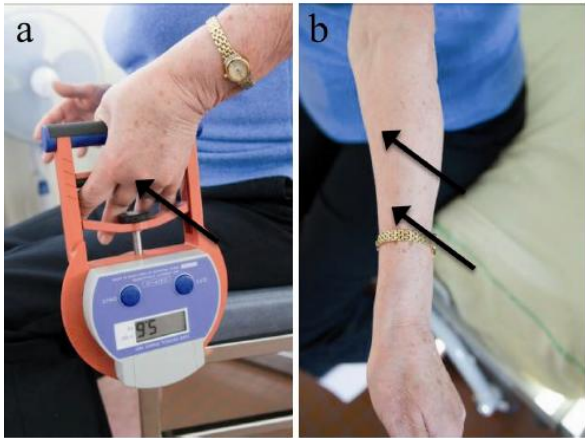




sIBM

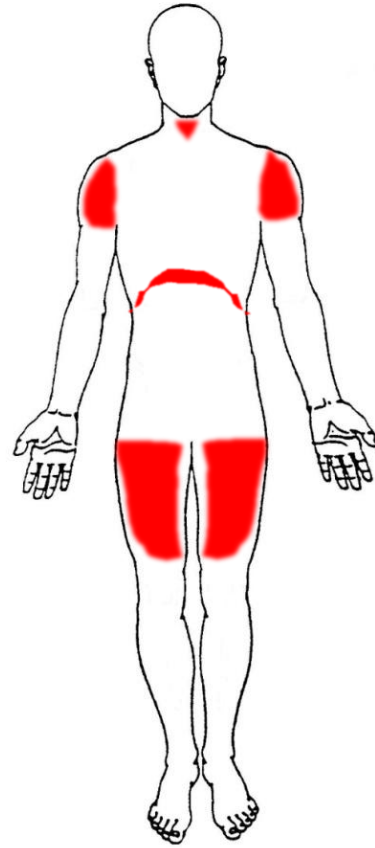


[La Revue de médecine interne 35 \(2014\) 472–479](#)

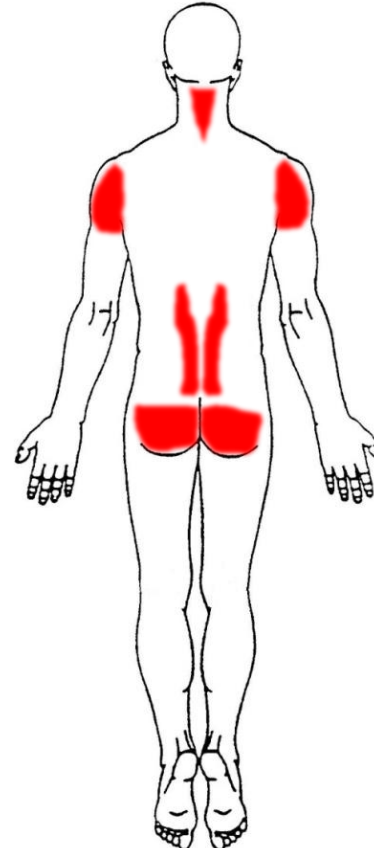


[Acta Neuropathol \(2015\) 129:611–624](#)

DM



ASS – OM



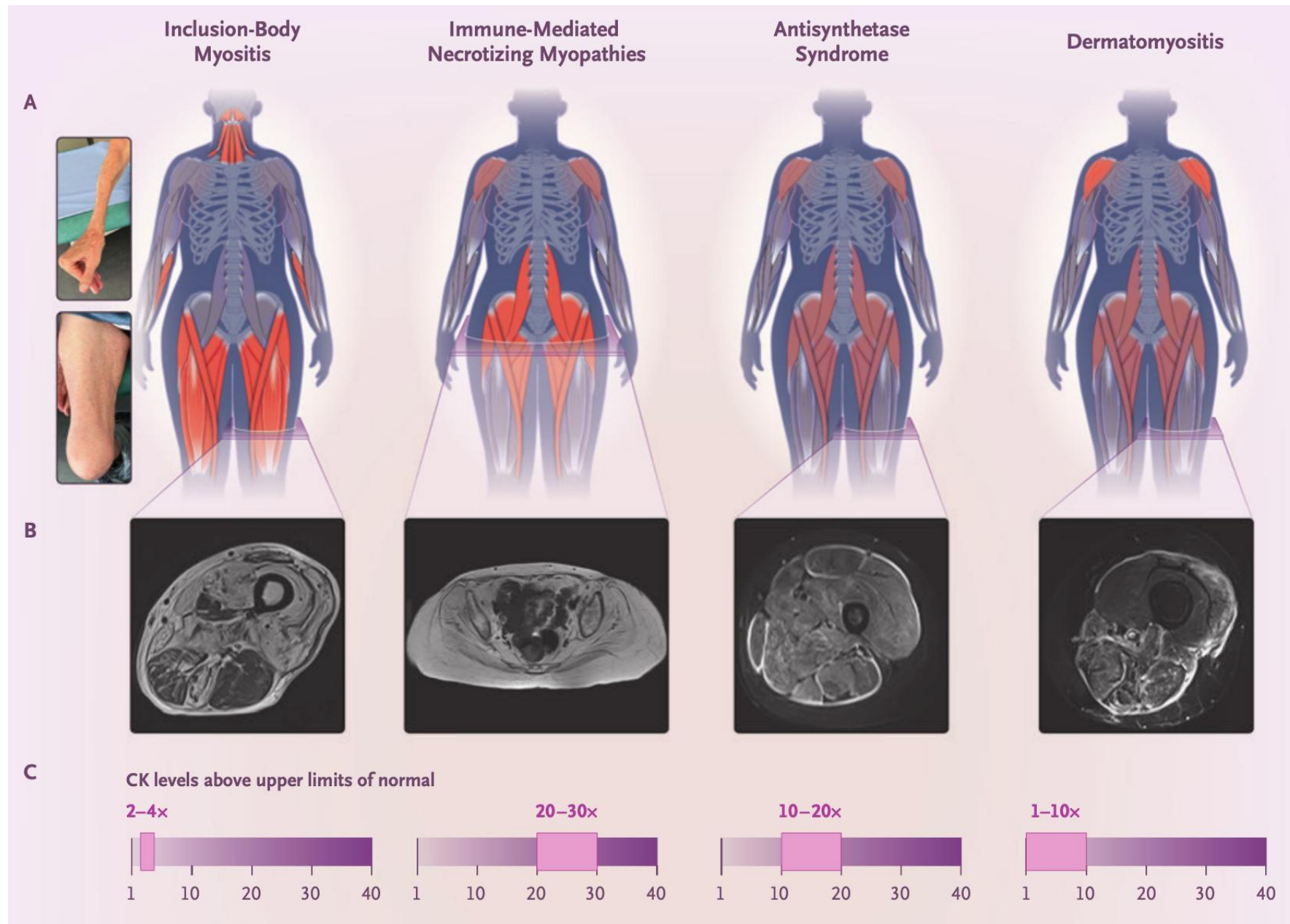
IMNM



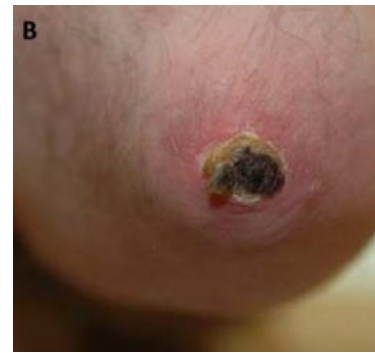
[Clin Med Res. 2016 Dec; 14\(3-4\): 145–150.](#)



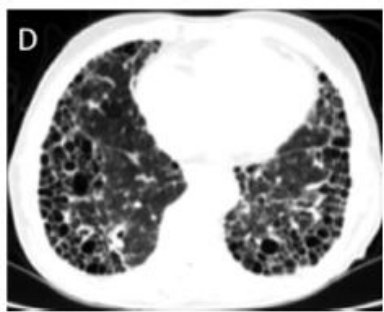
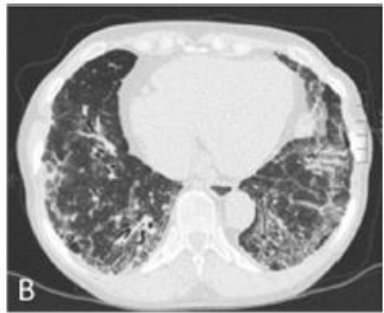
[Autoimmun Rev. 2019 Mar;18\(3\):223–230.](#)



DM



aDM



ASS

Am Acad Dermatol 2015;72:449-55.

Rheumatology 2017;0:1

J Am Acad Dermatol 2011;65:25-34.

Rev Med Interne. 2014 Jul;35(7):453-60.

Rietveld A, et al. Pract Neurol 2019;19:284-294.

40% Dermatologic



Heliotrope rash



Gottron's sign



Shawl sign



Calcinosis



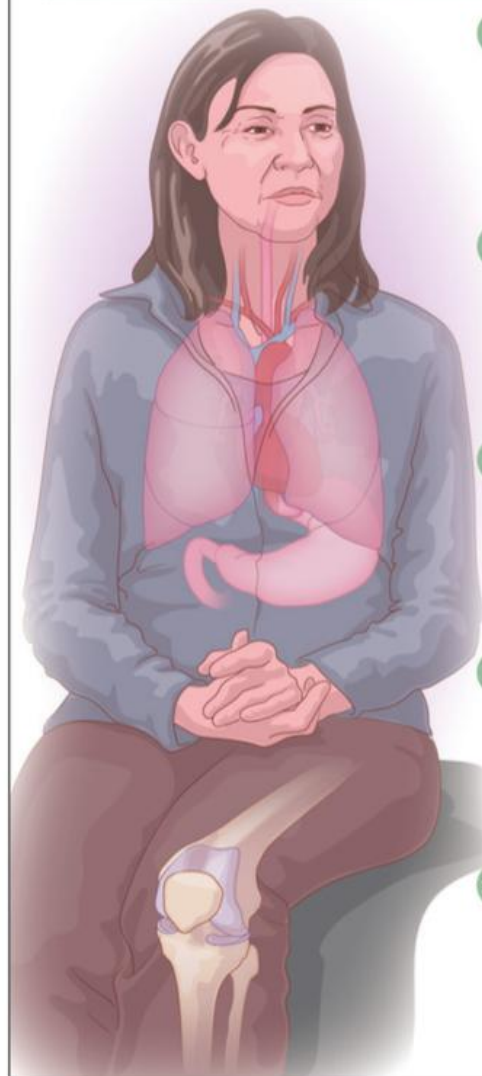
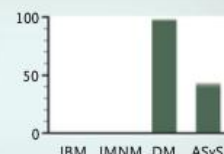
Holster sign



Raynaud's phenomenon

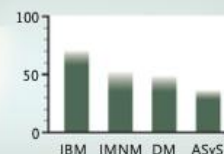


Mechanic's hands



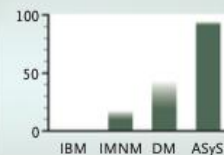
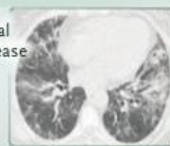
30% Digestive

Swallowing problems



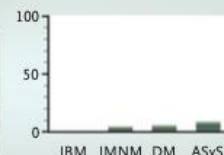
40% Respiratory

Interstitial lung disease

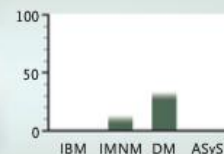
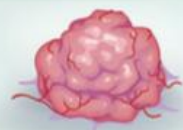


5% Cardiac

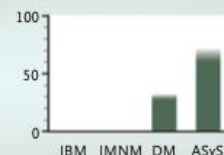
Myocarditis

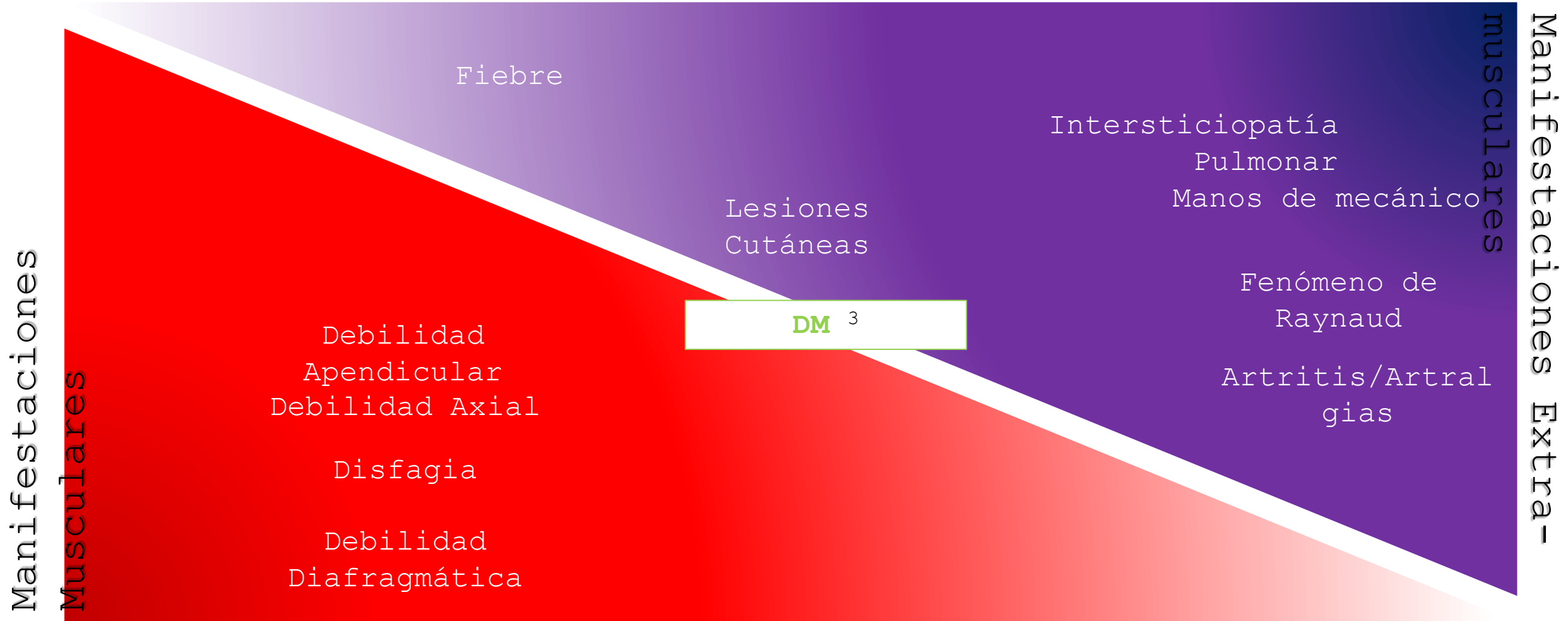


15% Oncologic



20% Joint





1. Rev. Médecine Interne 35 (2014) 472-479
2. [Autoimmun Rev.](#) 2019 Mar;18(3):223-230.
3. [Rietveld A, et al. Pract Neurol 2019;0:1-11.](#)
4. [Rev Med Interne.](#) 2014 Jul;35(7):453-60.

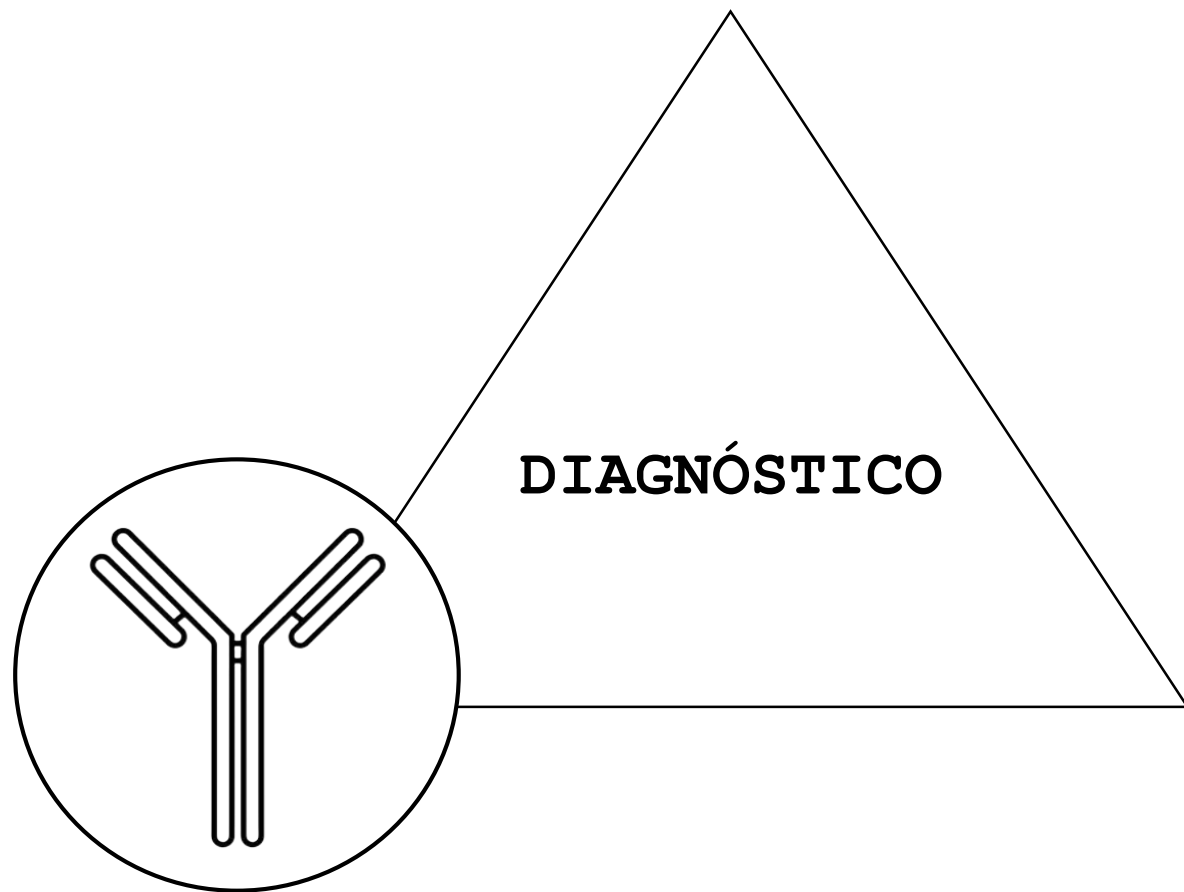
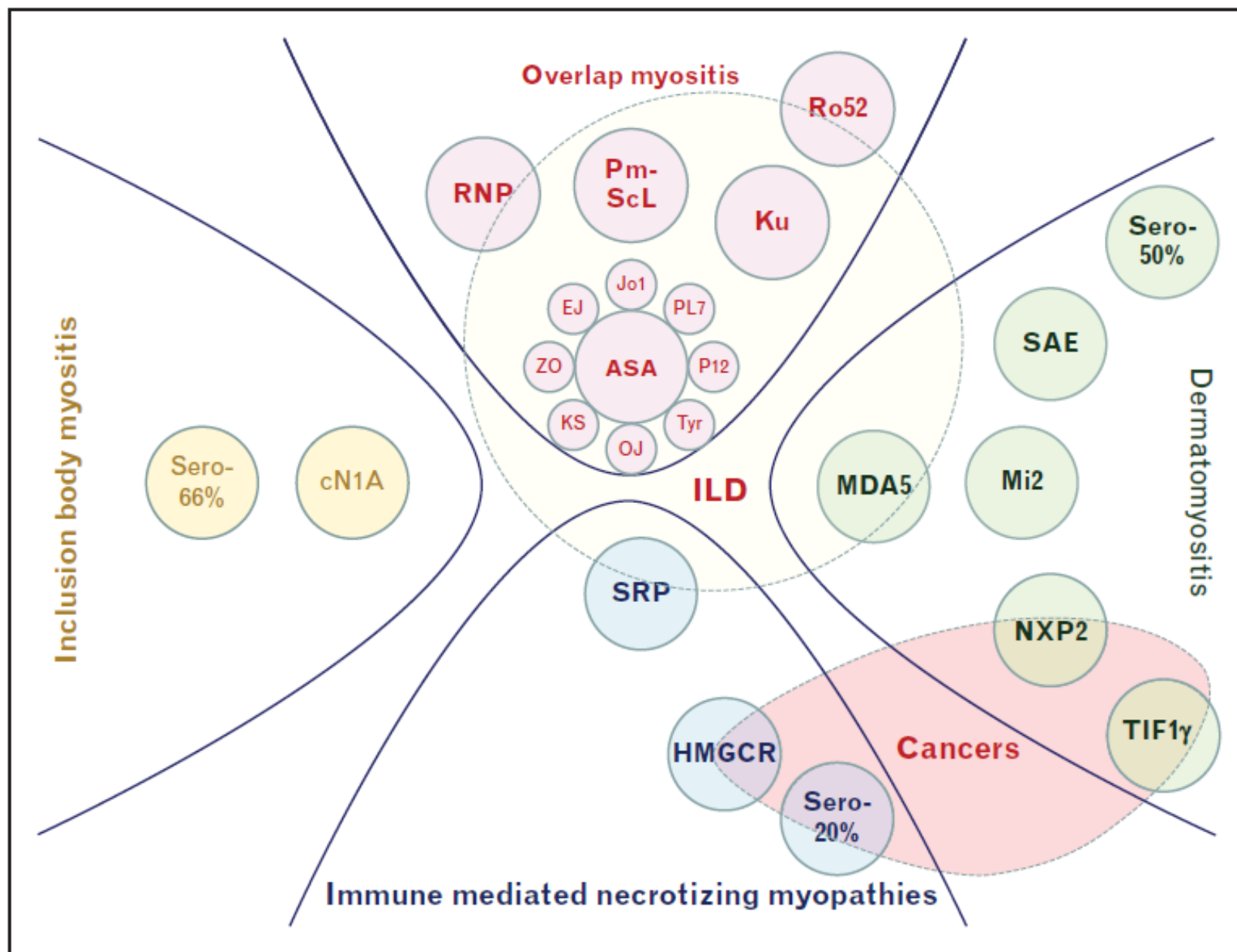
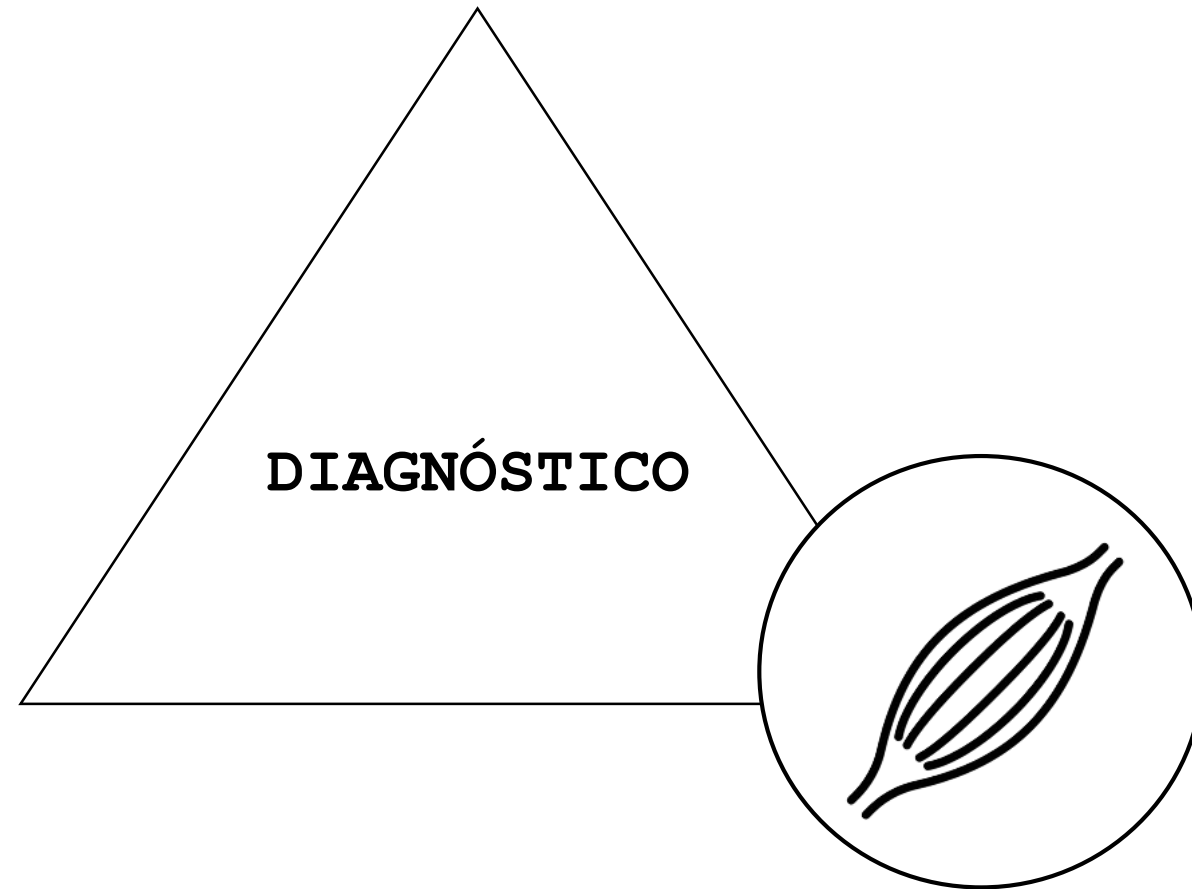


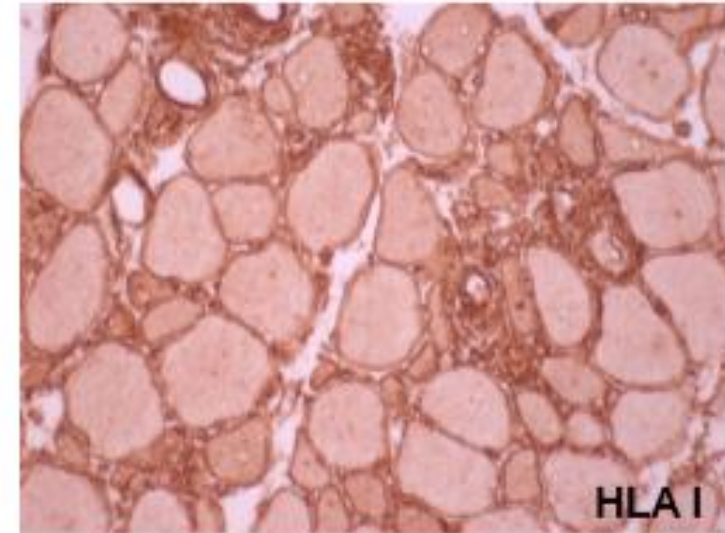
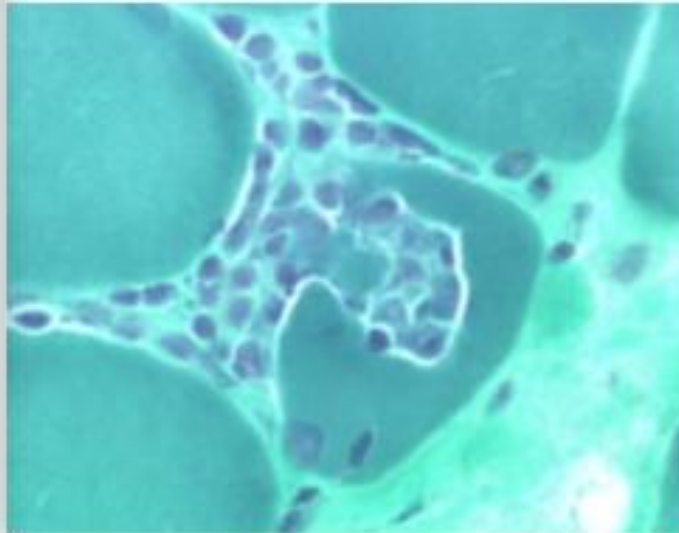
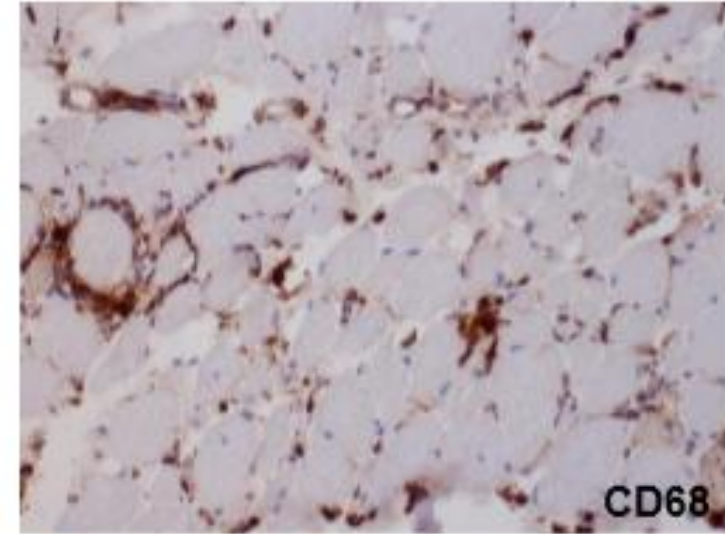
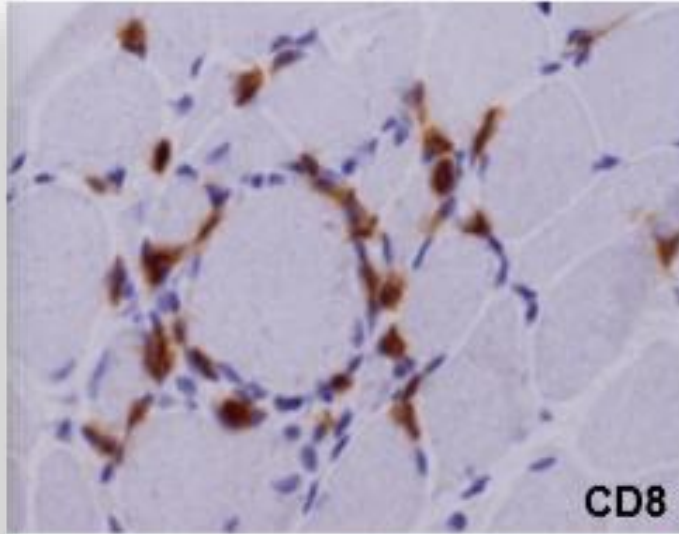
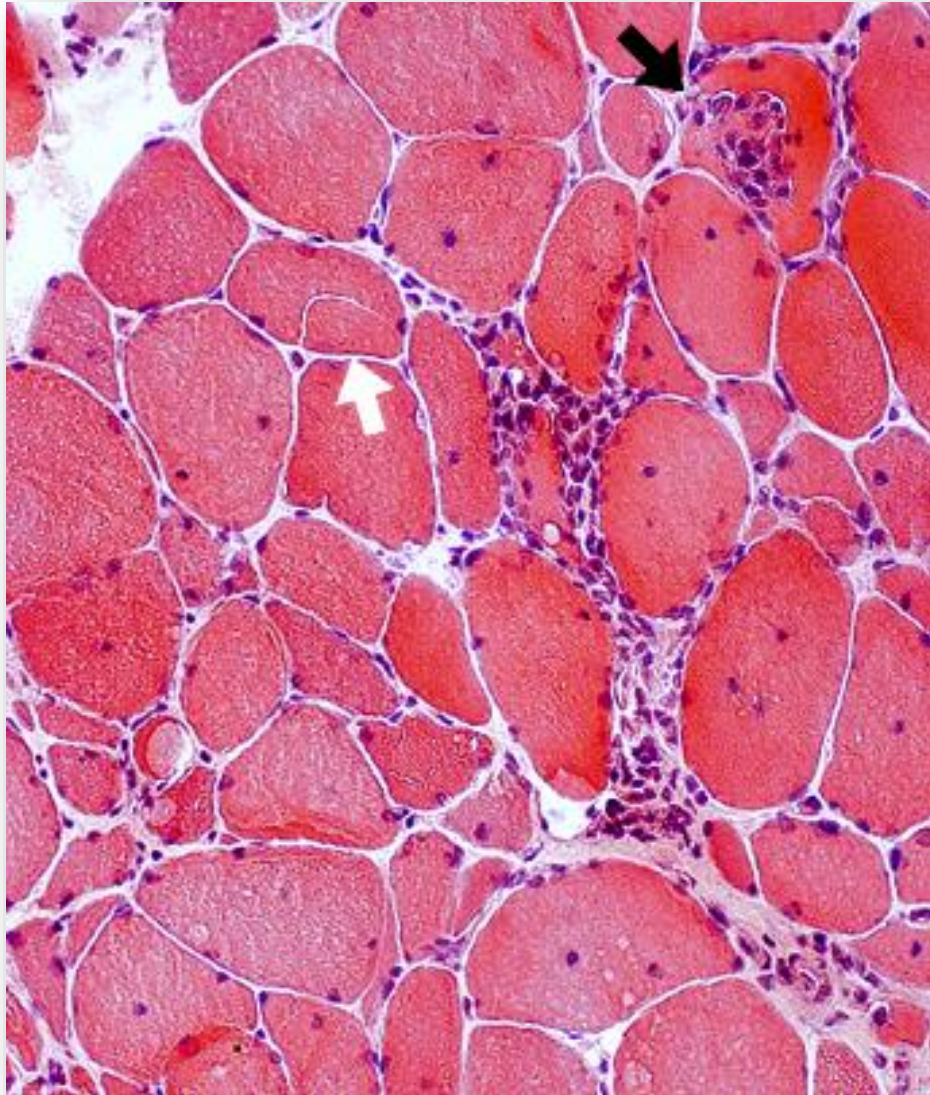
Table 1. Myositis-Specific and Myositis-Associated Autoantibody Features.*				
IIM Subtype and Autoantibody	Immunoassay Available?	Assessment of Immunoassay Quality†	Clinical Features or Prognosis	Cancer Risk ²⁶
Inclusion-body myositis				
Seronegative				Low
Anti-cN1A	Yes	Awareness of limitations indicated	Worse prognosis than seronegative IBM	Low
Immune-mediated necrotizing myopathy				
Seronegative				High
Anti-HMGCR	Yes	Acceptable	Better muscle function prognosis in patients who have received statins than in those who have not	Intermediate
Anti-SRP	Yes	Acceptable	Severe weakness, frequent mild ILD	Low
Antisynthetase syndrome				
Anti-Jo-1	Yes	Acceptable	Most frequent, classic phenotype (myositis, arthritis, ILD)	Low
Anti-PL-7	Yes	Acceptable	Worse prognosis owing to more severe ILD	Low
Anti-PL-12	Yes	Acceptable	Worse prognosis owing to more severe ILD	Low
Anti-EJ	Yes	Awareness of limitations indicated	Constant ILD	Low
Anti-OJ	Yes	Serious concerns	Frequent ILD, arthritis and fever	High ²⁷
Anti-KS	Yes	Acceptable	Frequent amyopathy, sicca syndrome	Low
Anti-Zo	Yes	Awareness of limitations indicated	Classic phenotype (myositis, arthritis, ILD)	Low
Anti-Ha	Yes	Awareness of limitations indicated	Predominant muscle involvement, frequent skin lesions, infrequent ILD	Low
Other‡	No	Immunoassays not yet available for routine detection		Low

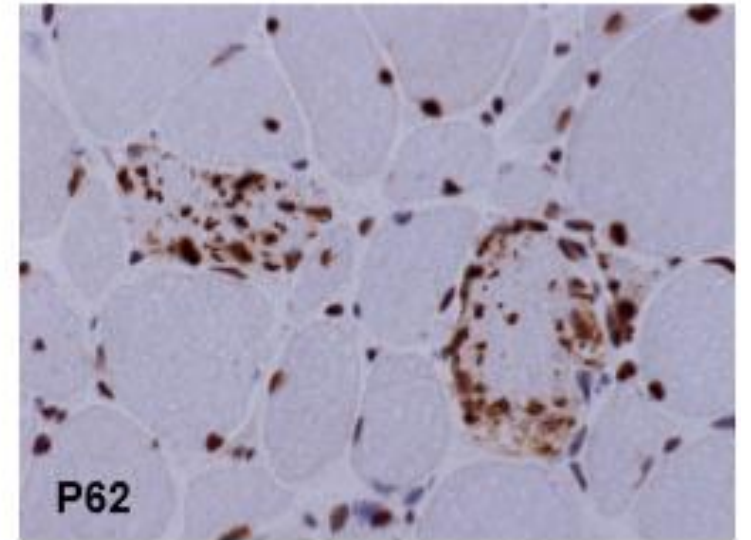
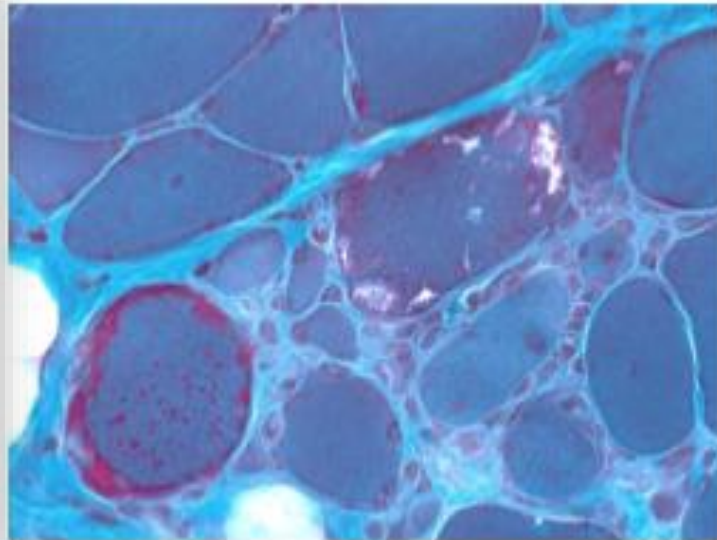
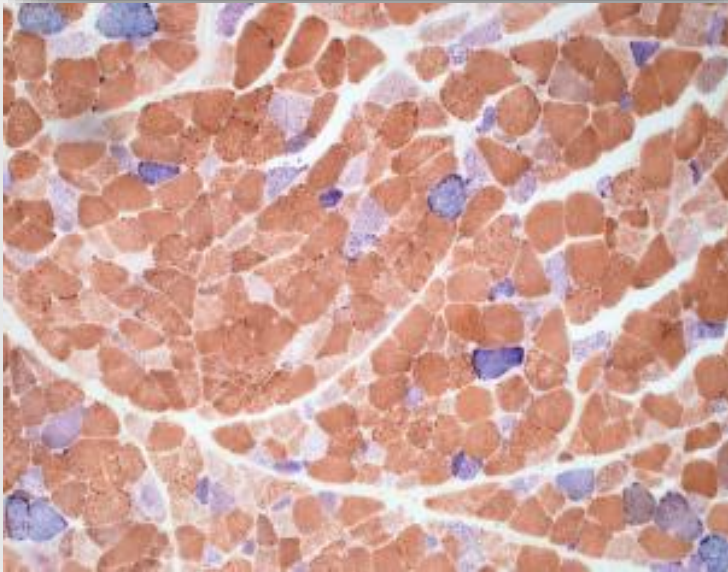
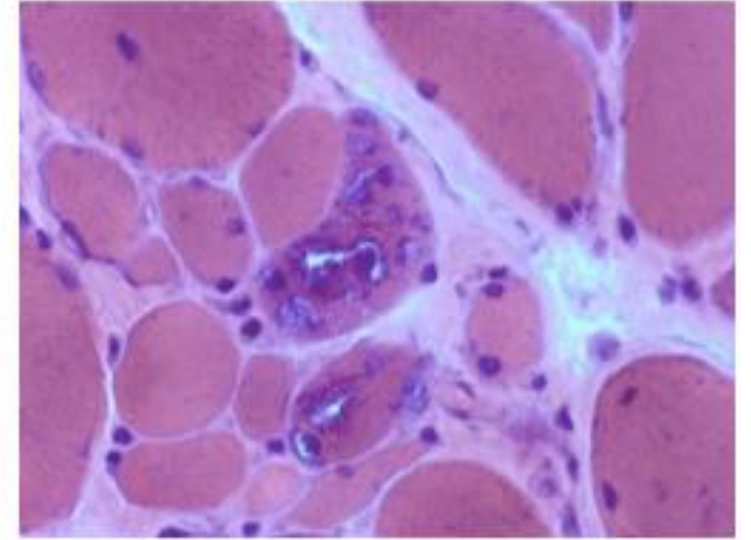
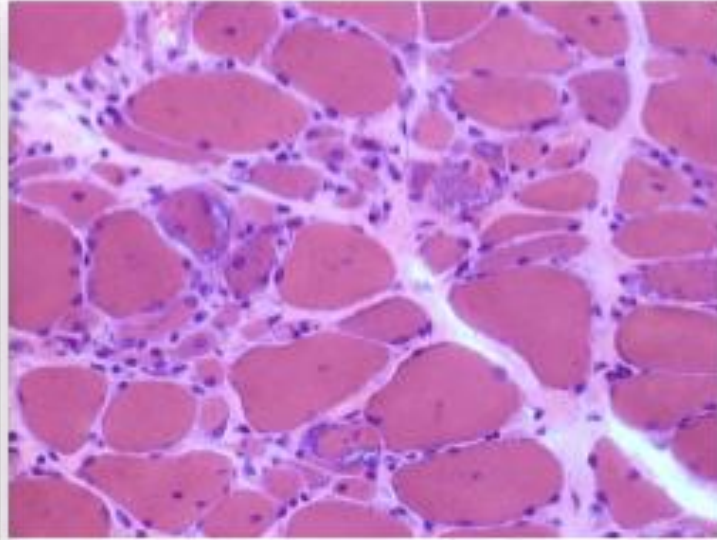
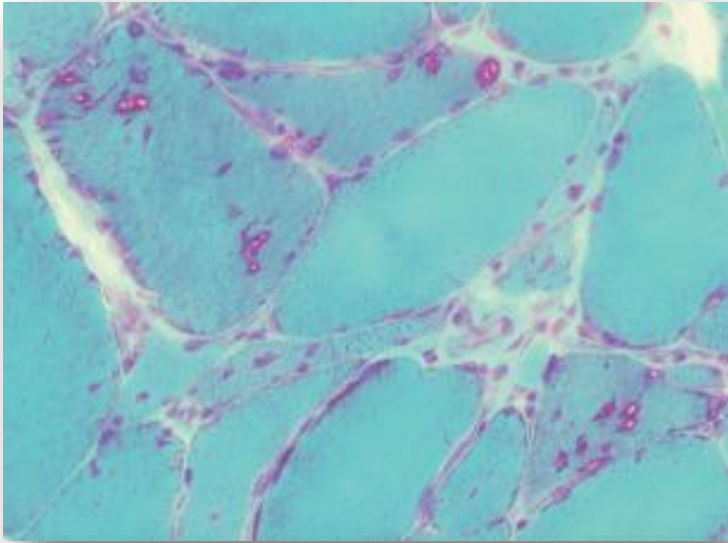
Dermatomyositis				
Seronegative				High if age >40 yr at onset
Anti-TIF-1γ	Yes	Awareness of limitations indicated	Psoriasis-like, poikiloderma, ovoid palatal patch	High
Anti-NXP2	Yes	Acceptable	Intestinal vasculopathy, skin edema, calcinosis	High
Anti-Mi-2	Yes	Acceptable	High creatine kinase level, photodistributed rash	Intermediate
Anti-MDA5	Yes	Acceptable	Severe ILD, amyopathic, arthritis, cutaneous ulcers	Intermediate
Anti-SAE	Yes	Awareness of limitations indicated	OP ILD pattern, “angel wing” rash on back	Intermediate

Table 1. (Continued.)				
IIM Subtype and Autoantibody	Immunoassay Available?	Assessment of Immunoassay Quality†	Clinical Features or Prognosis	Cancer Risk ²⁶
Overlap myositis				
Seronegative				Low
Anti-PM/ScL	Yes	Acceptable	NSIP or OP ILD pattern, skin thickening, sclerodactyly	Low
Anti-Ku	Yes	Acceptable	Arthralgia, ILD, glomerulonephritis, sclerodactyly	Low
Anti-RNP	Yes	Acceptable	ILD, arthralgia, sclerodactyly	Low



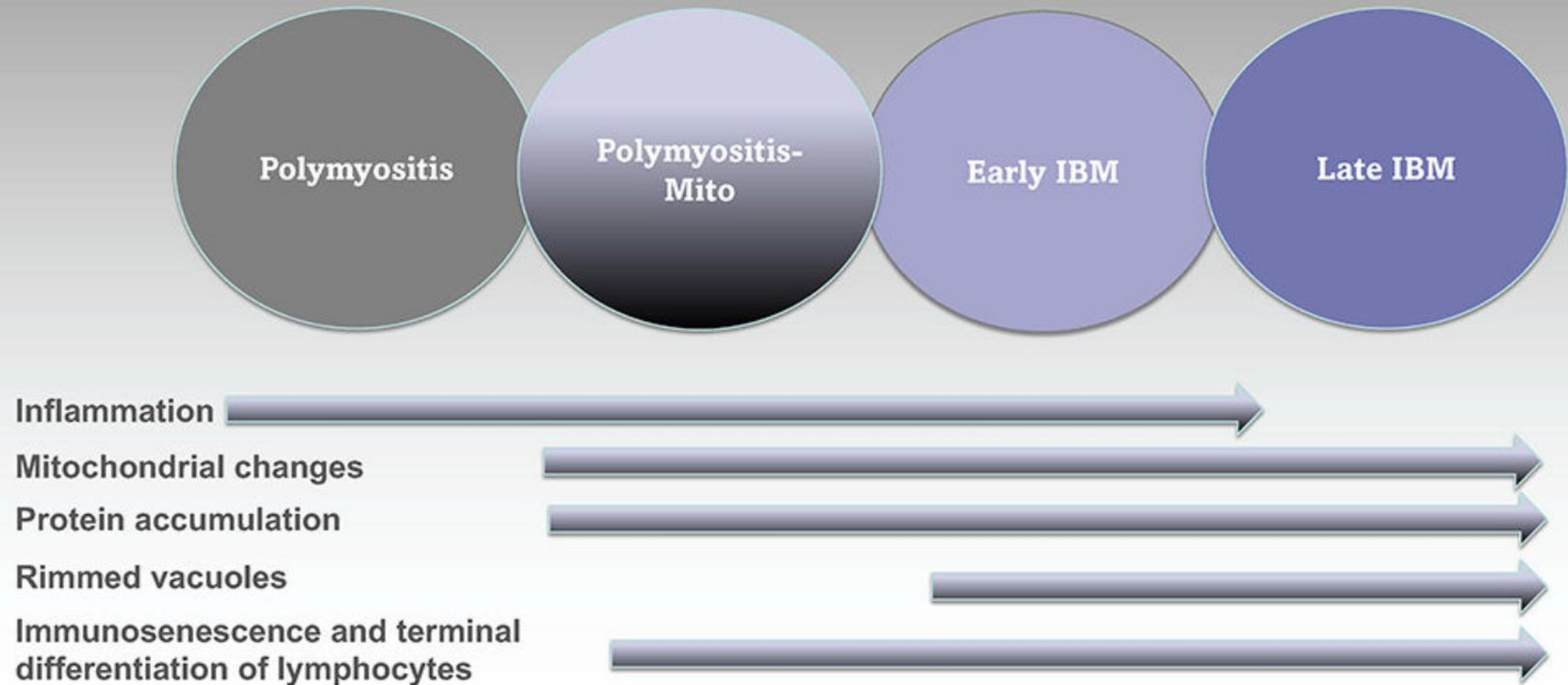






P62

Inclusion Body Myositis as a Spectrum Disorder



Box 1 | Myopathological features for the diagnosis of IMNM^a

Required features

- Individualized necrotic myofibres scattered throughout the muscle biopsy
- Different stages of necrosis, myophagocytosis and regeneration
- Paucilymphocytic infiltrates composed predominantly of macrophages

Consistent features

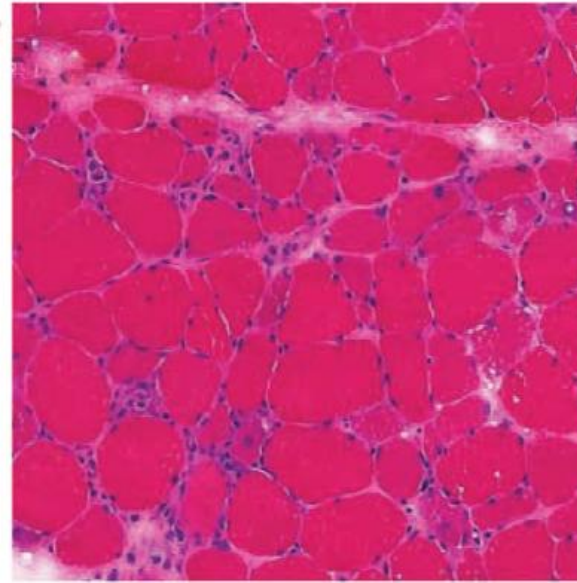
- MHC class I on the sarcolemma of non-necrotic muscle fibres with regional focal differences in intensity
- Deposition of complement (C5b–9) on the sarcolemma
- Atrophic myofibres (long-standing processes) with signs of fibrosis and fatty tissue replacement
- Homogeneous, fine-granular sarcoplasmic staining for p62
- Coarse staining of many fibres in the sarcolemma with NADH-tetrazolium reductase stains
- Enlarged vessel walls

Unusual or inconsistent features

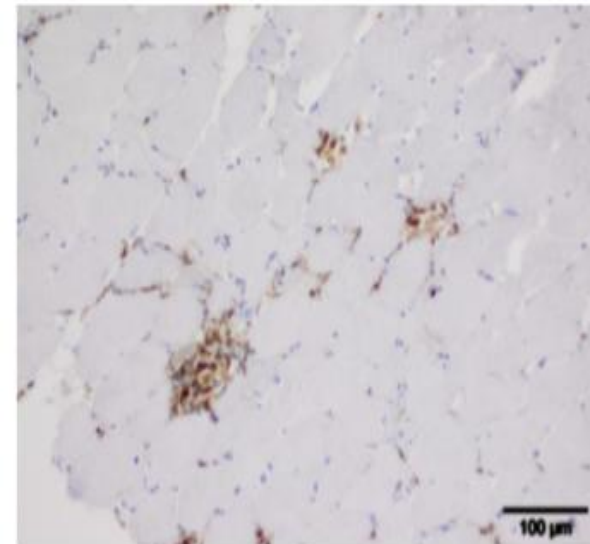
- Coarse plaque-like staining for p62
- Large, rimmed vacuoles
- Mitochondrial abnormalities unrelated to ageing
- Interferon-signature gene markers such as *ISG15*, *MX1* or *SIGLEC1*
- MHC class II on the sarcolemma
- B cells and plasma cells
- Complement deposits on vessels

^aBased on the information in Allenbach et al.¹⁷.

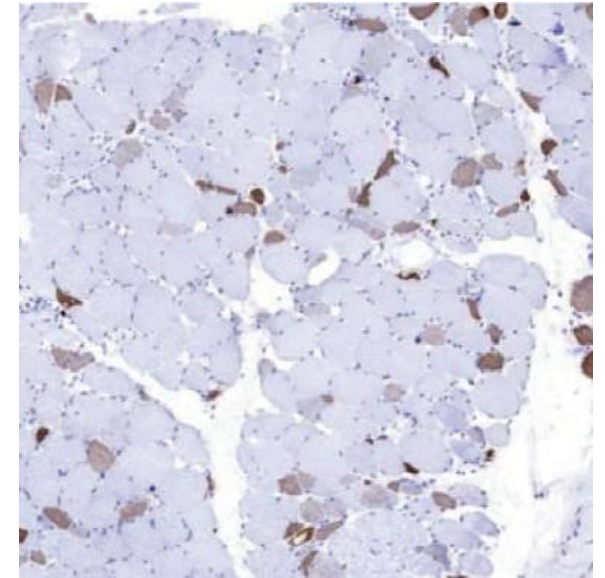
HE



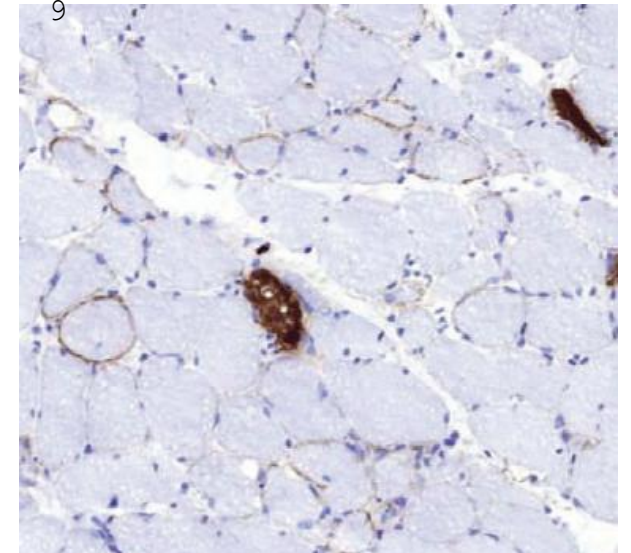
CD68



Myo



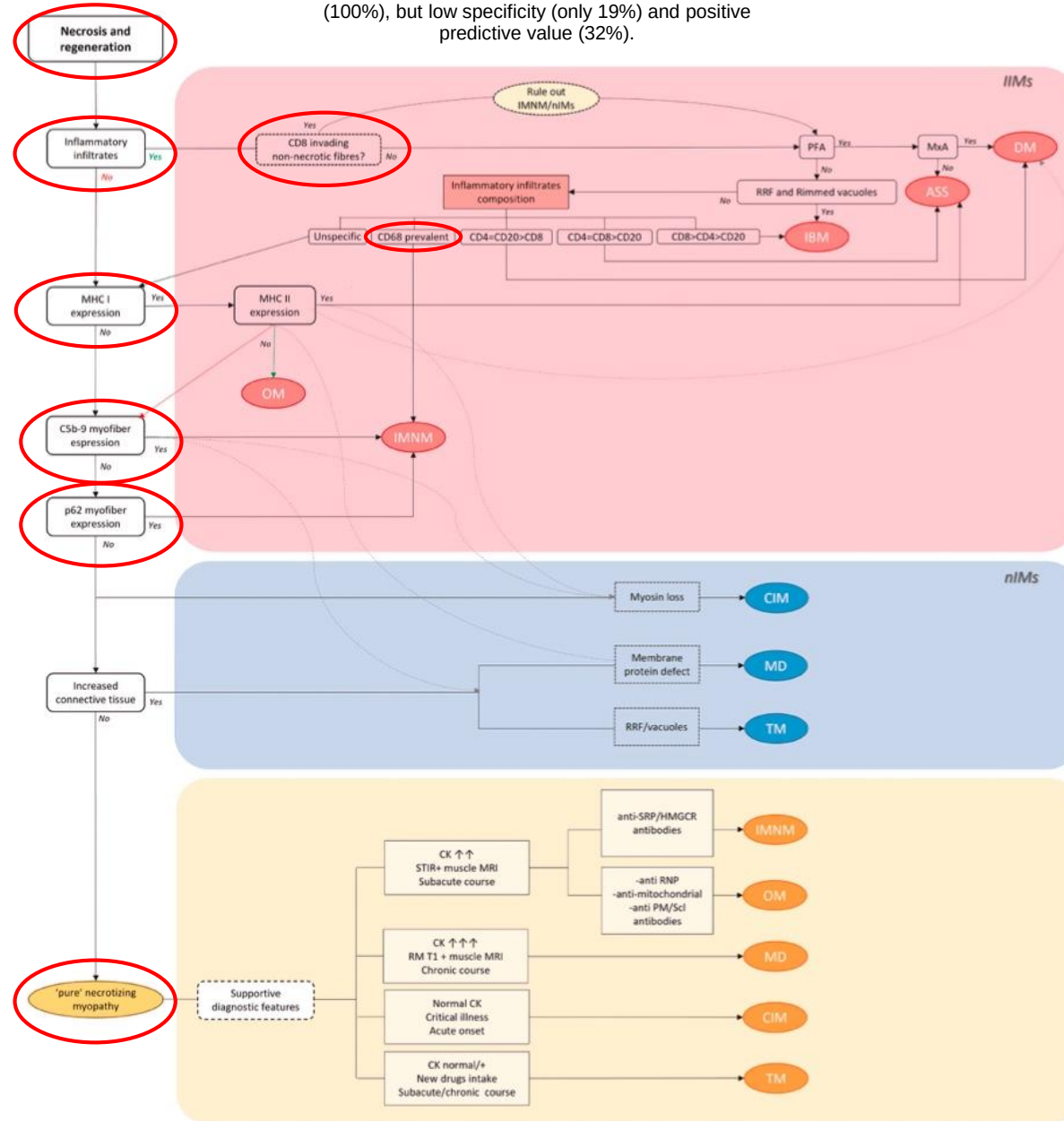
C5b–
9



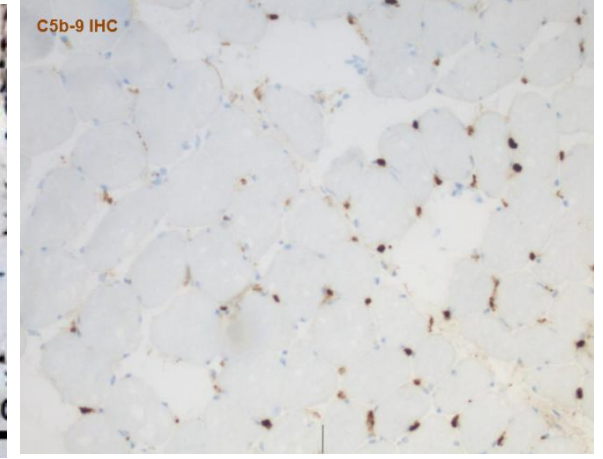
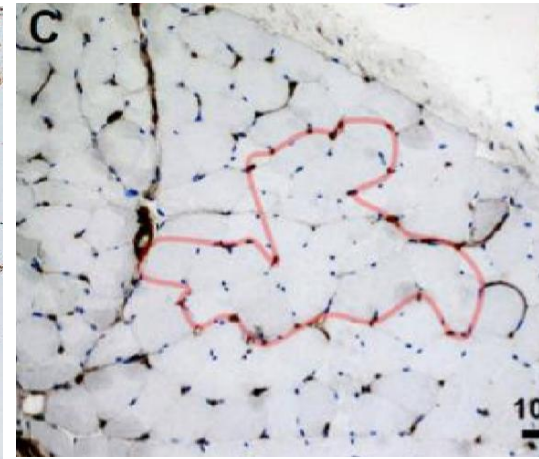
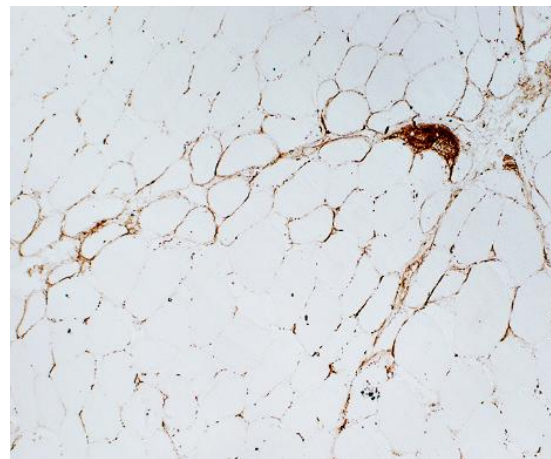
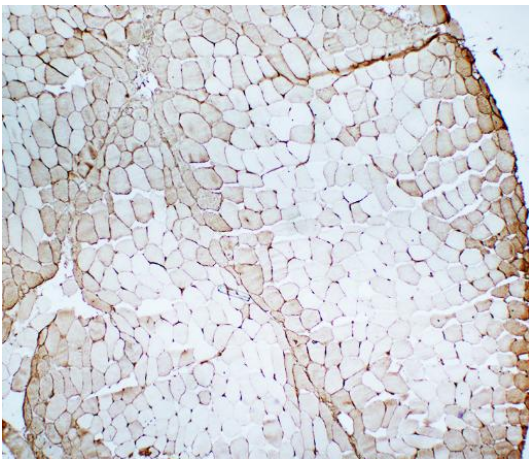
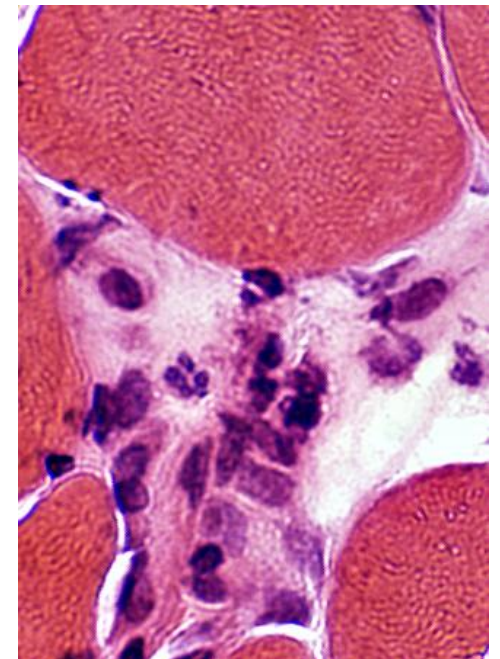
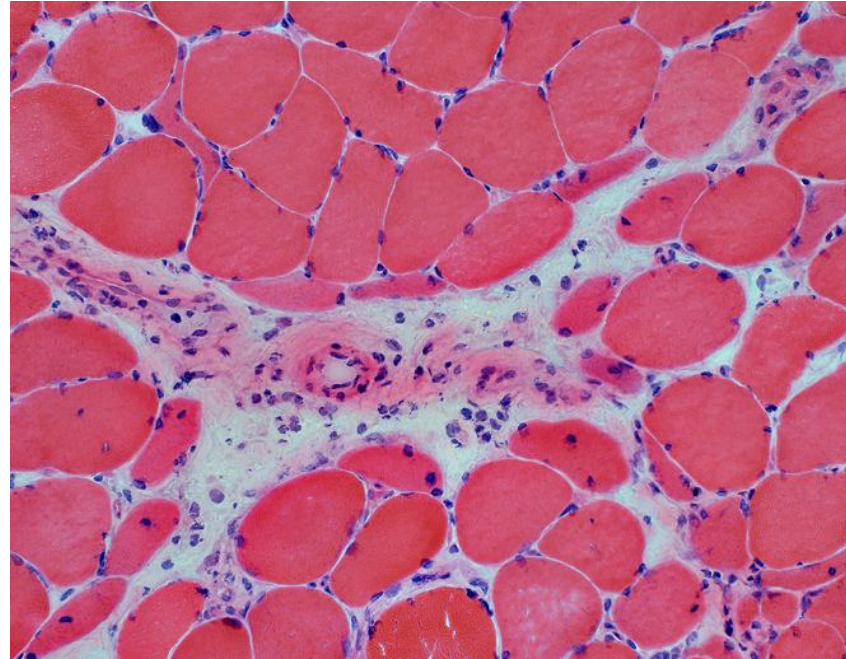
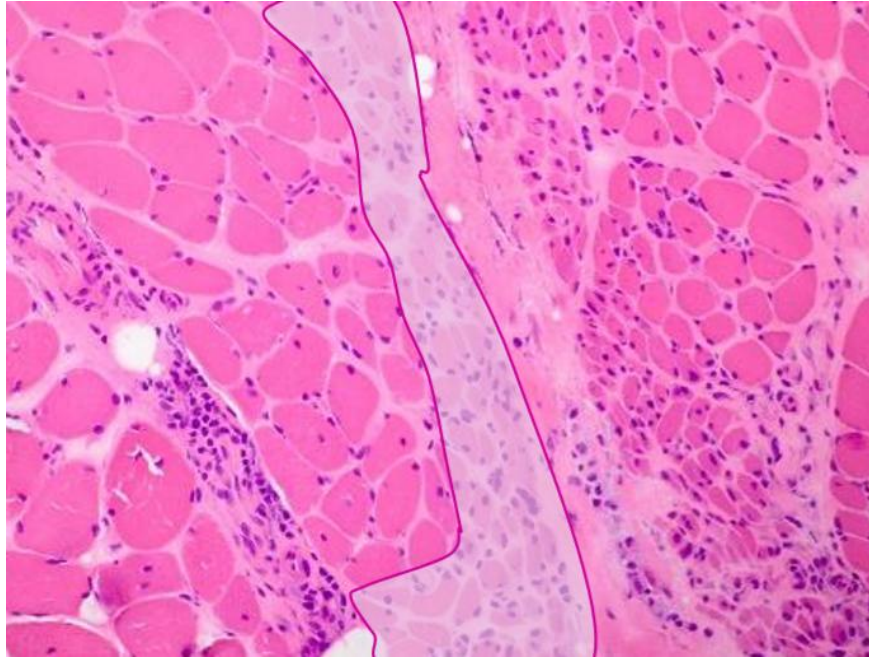
High sensitivity (93%) and negative predictive value (NPV = 92%), but low specificity (57%) and positive predictive value (PPV = 60%)

High sensitivity (100%) and negative predictive value (100%), but low specificity (only 19%) and positive predictive value (32%).

sensitivity 44%; specificity 85%;
positive predictive value 46%;
negative predictive value 84%



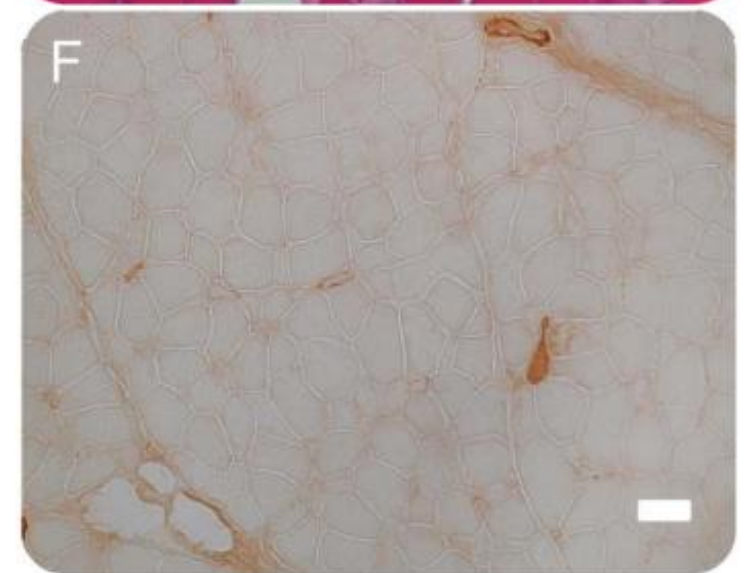
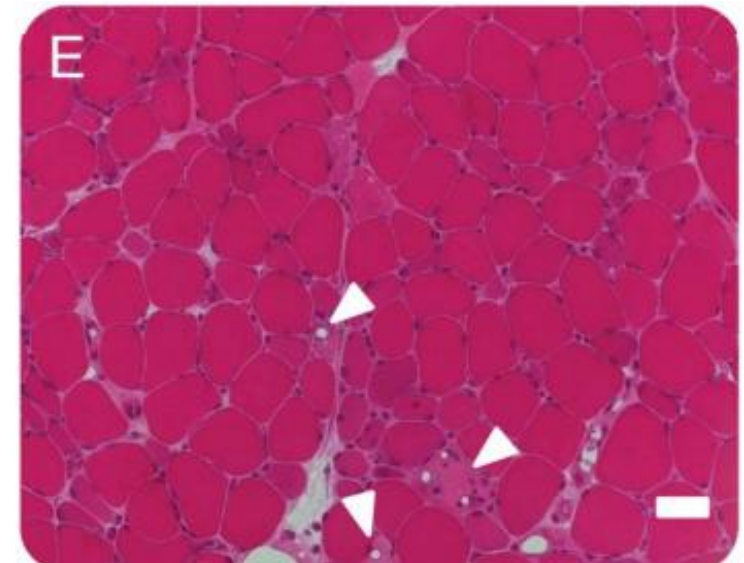
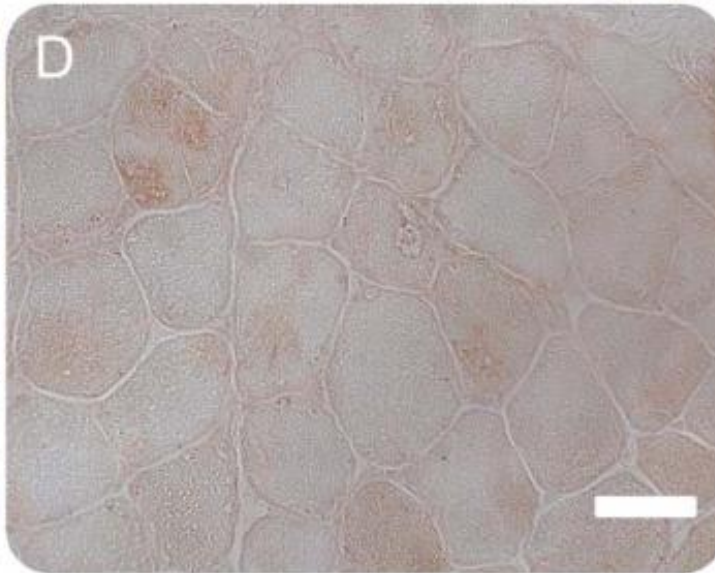
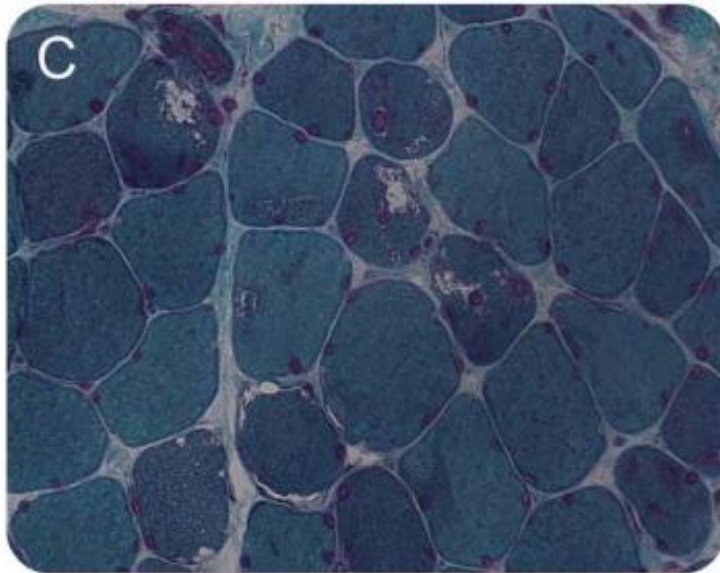
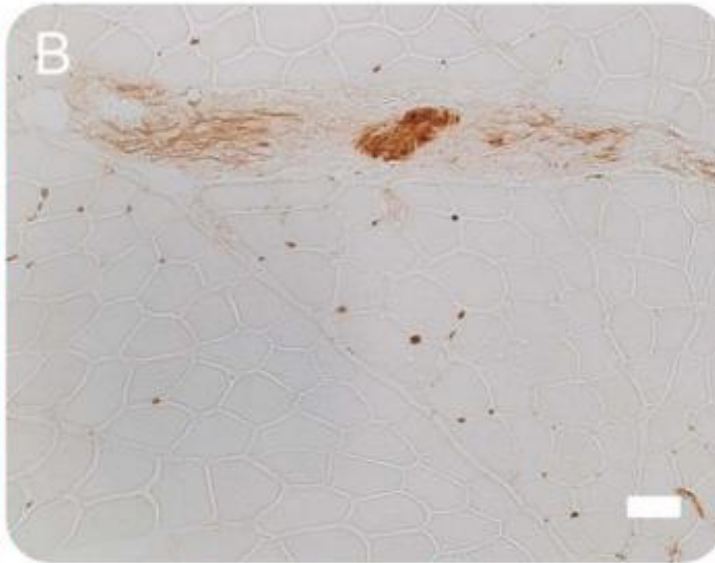
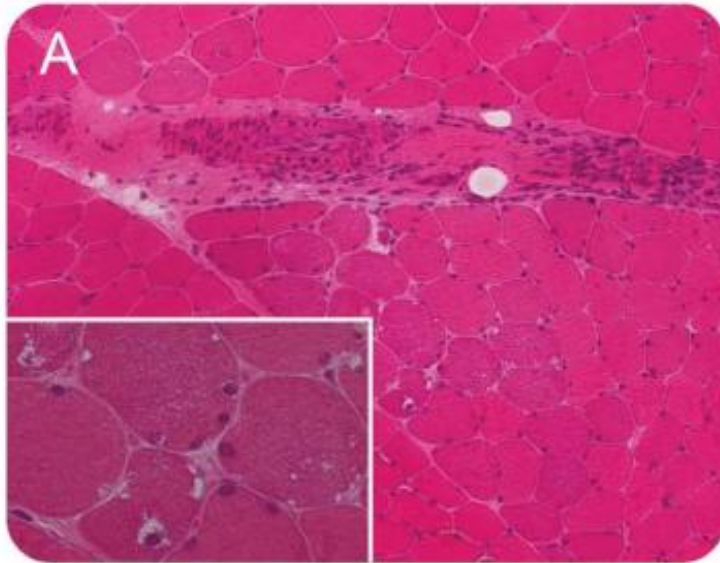
...even if muscle biopsy represents the gold standard for the diagnosis of IMNMs..., only a complete evaluation that, in addition to histological examination (medical history, clinical examination, laboratory and serological tests, as well as muscle imaging data), can correctly address the final diagnosis..

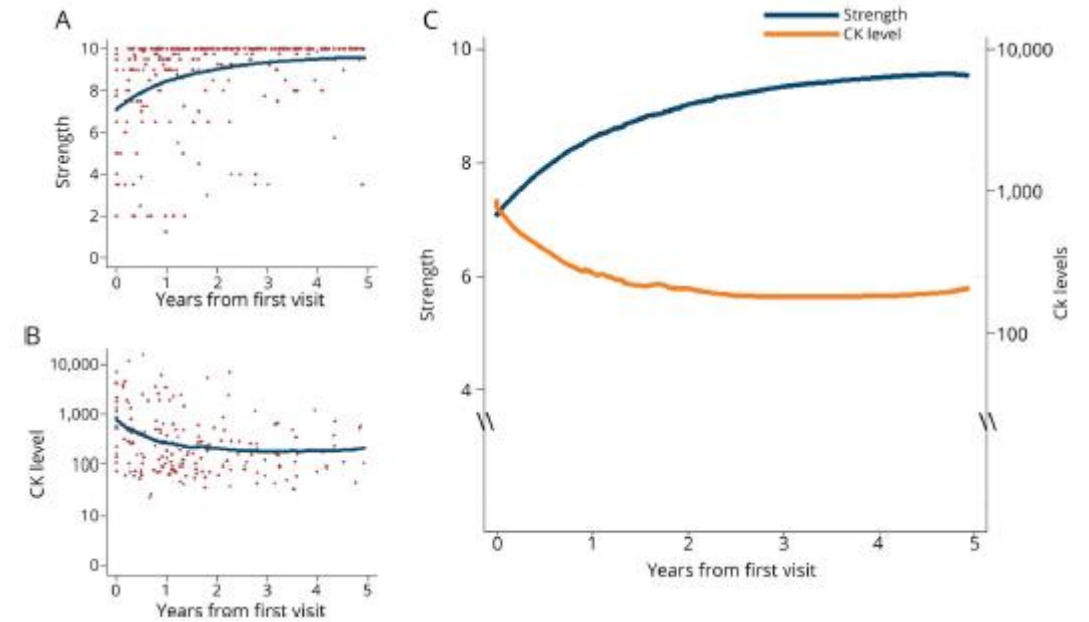
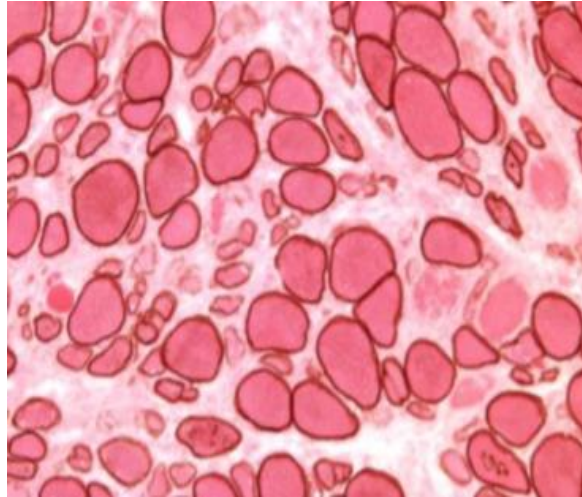
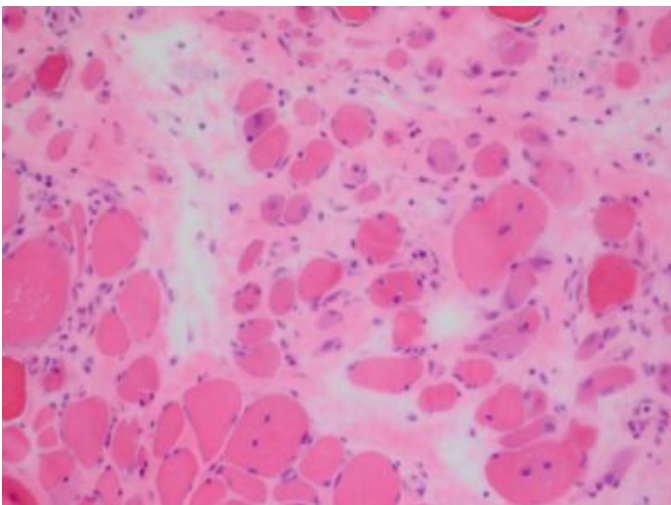
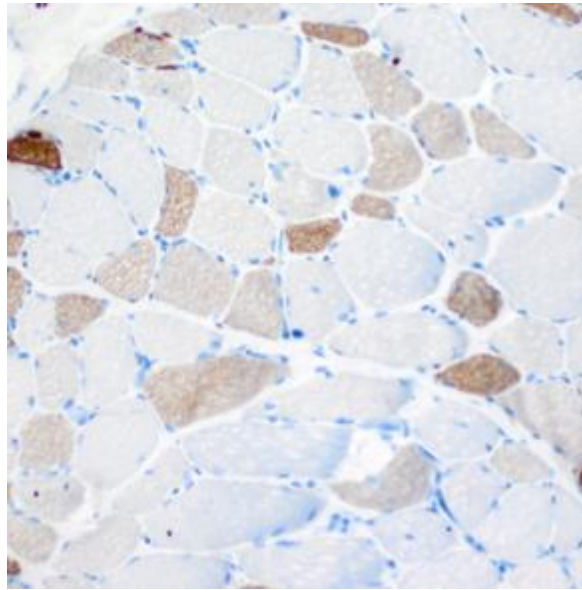
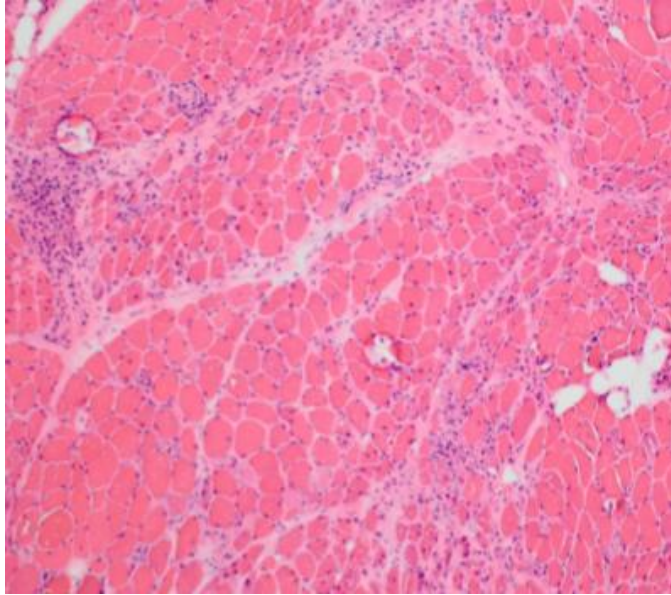


DM

TIF-
1g

Fibras vacuoladas no
necróticas.



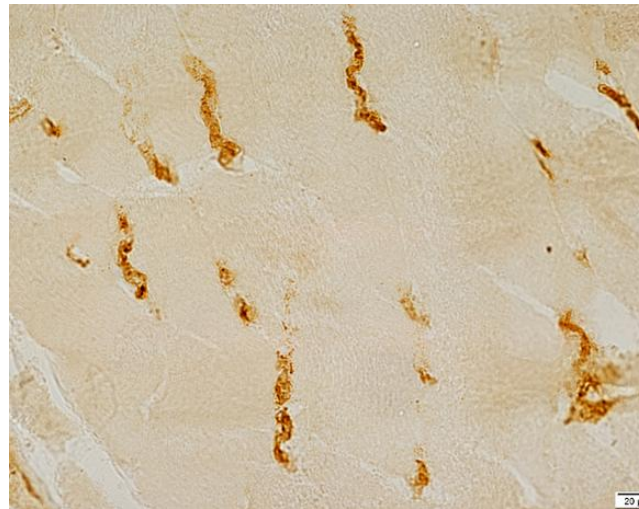
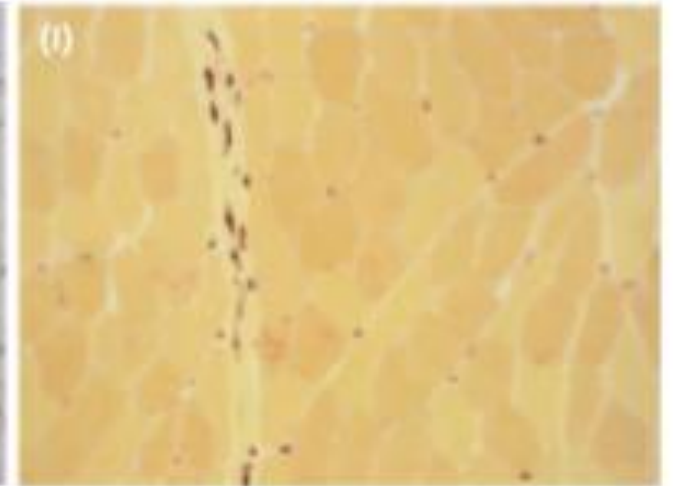
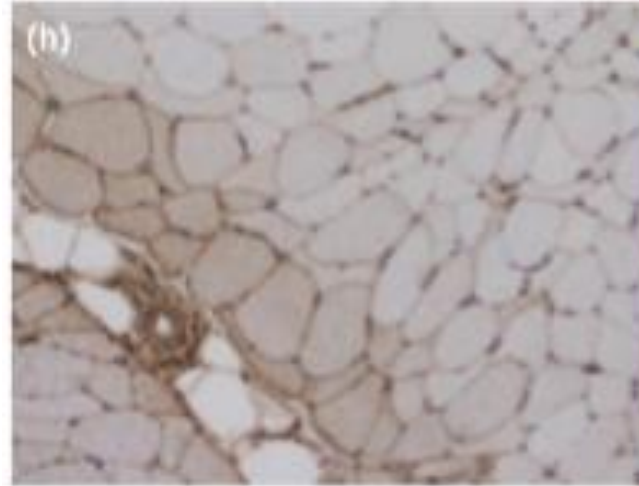
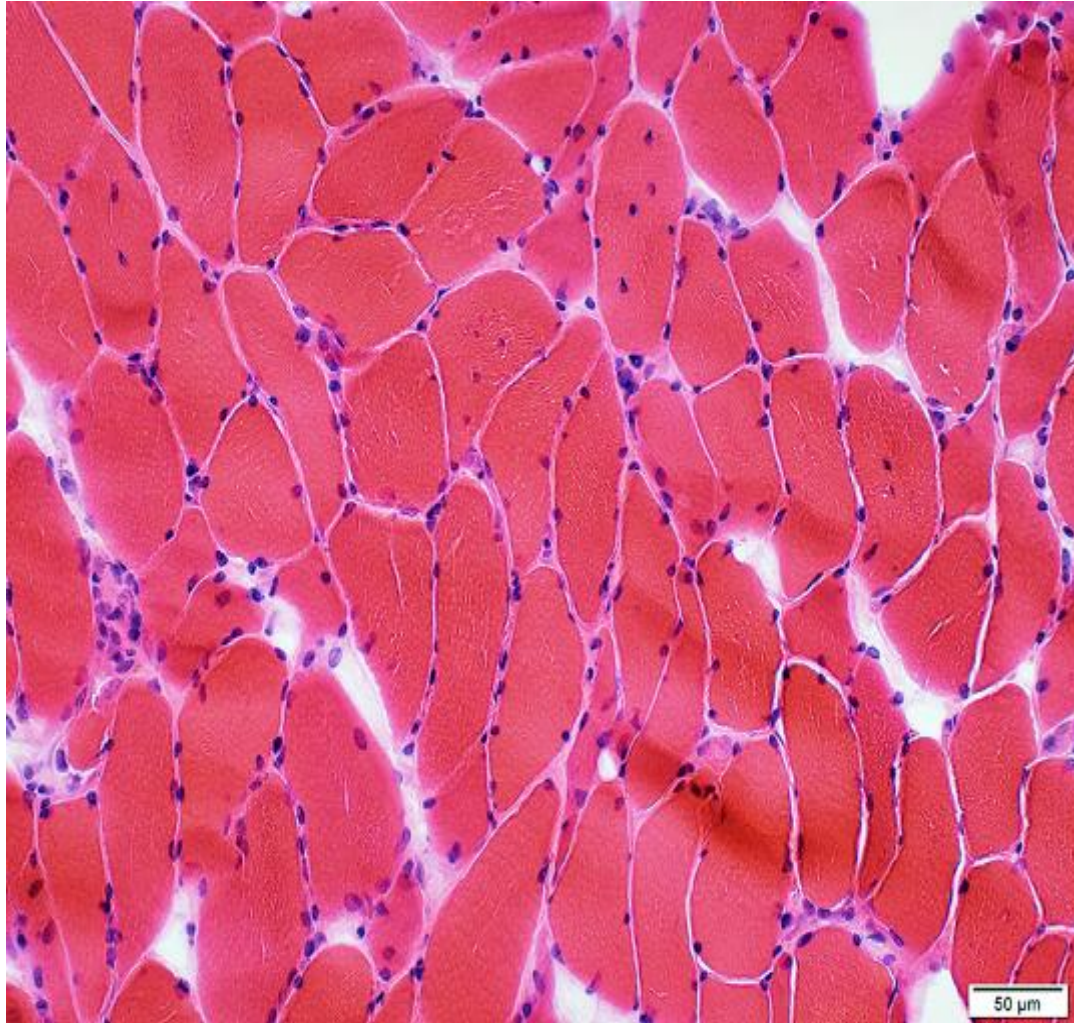


Los niveles de CK se asocian de manera inversa a la fuerza.

DM

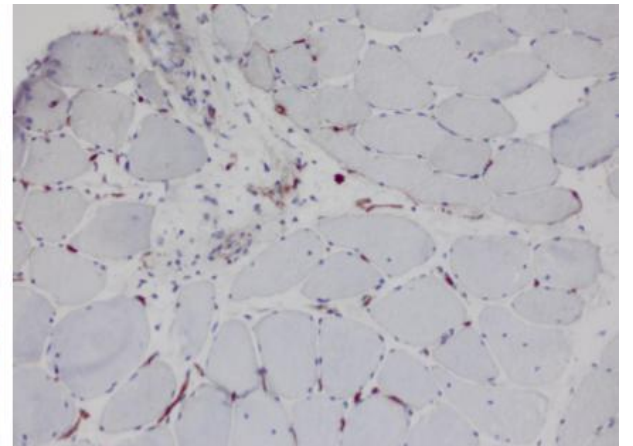
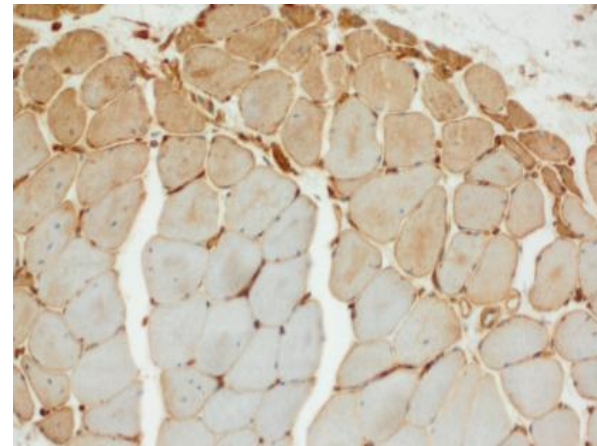
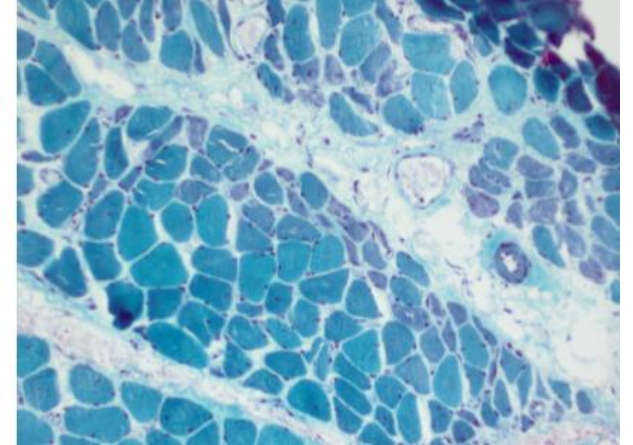
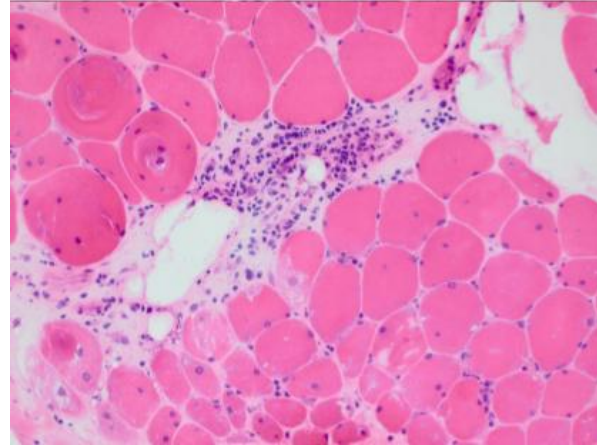
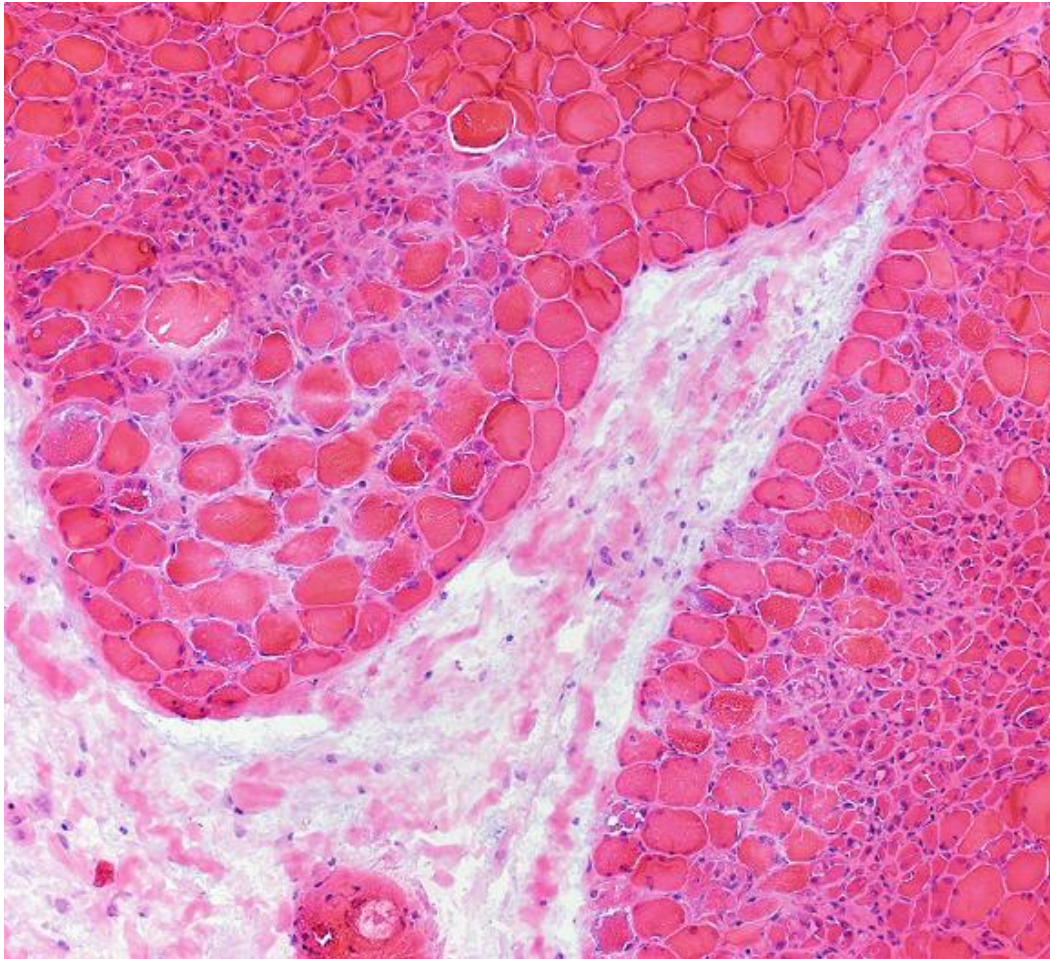
MDA5

Puede tener alteraciones leves o ser normal.



Capilares: en forma de sacacorchos

Cantidad normal o levemente reducida



Necrosis/Regeneración perifascicular.

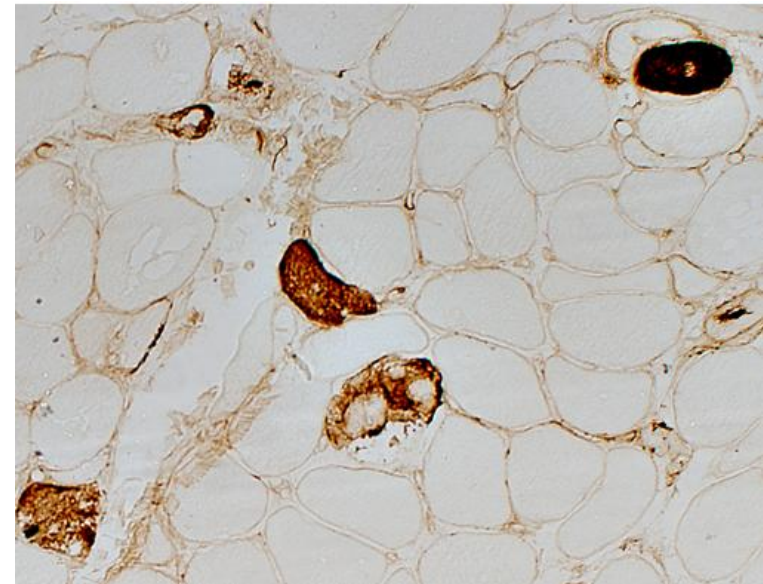
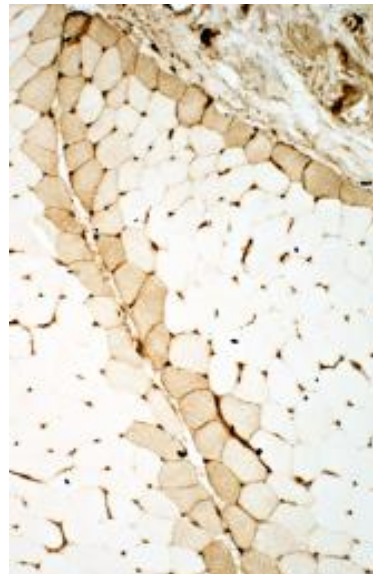
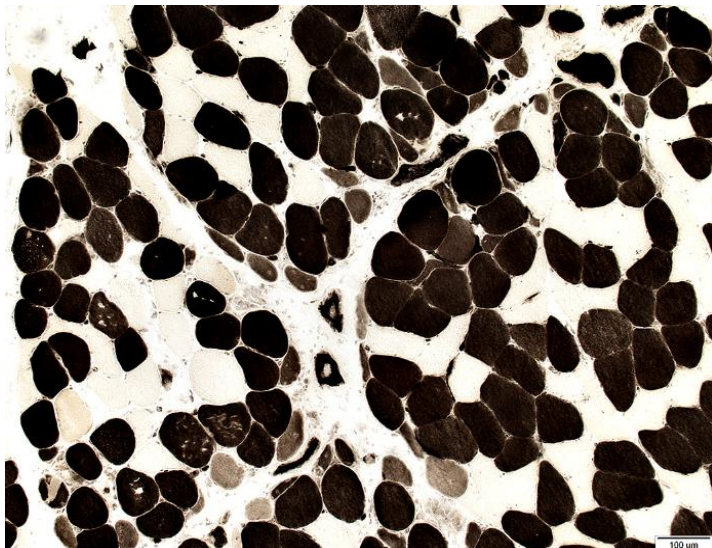
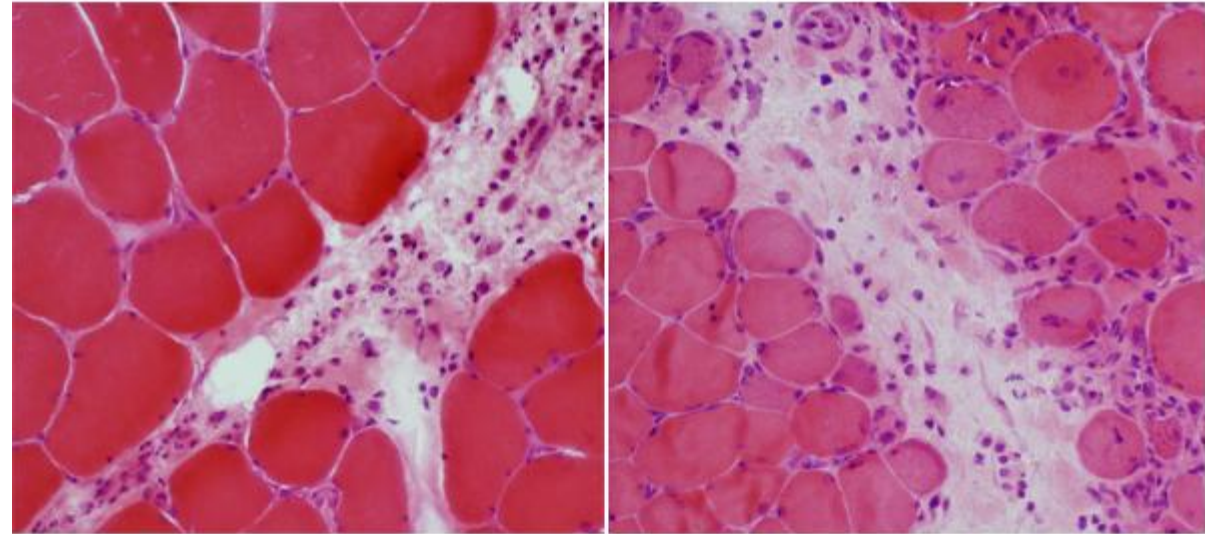
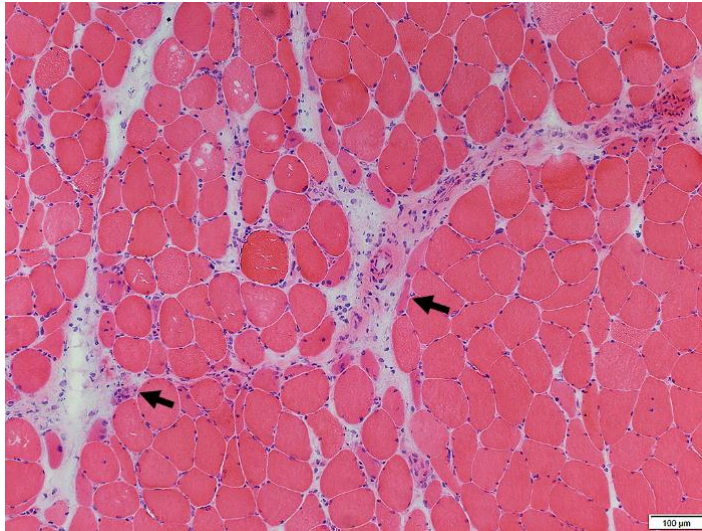
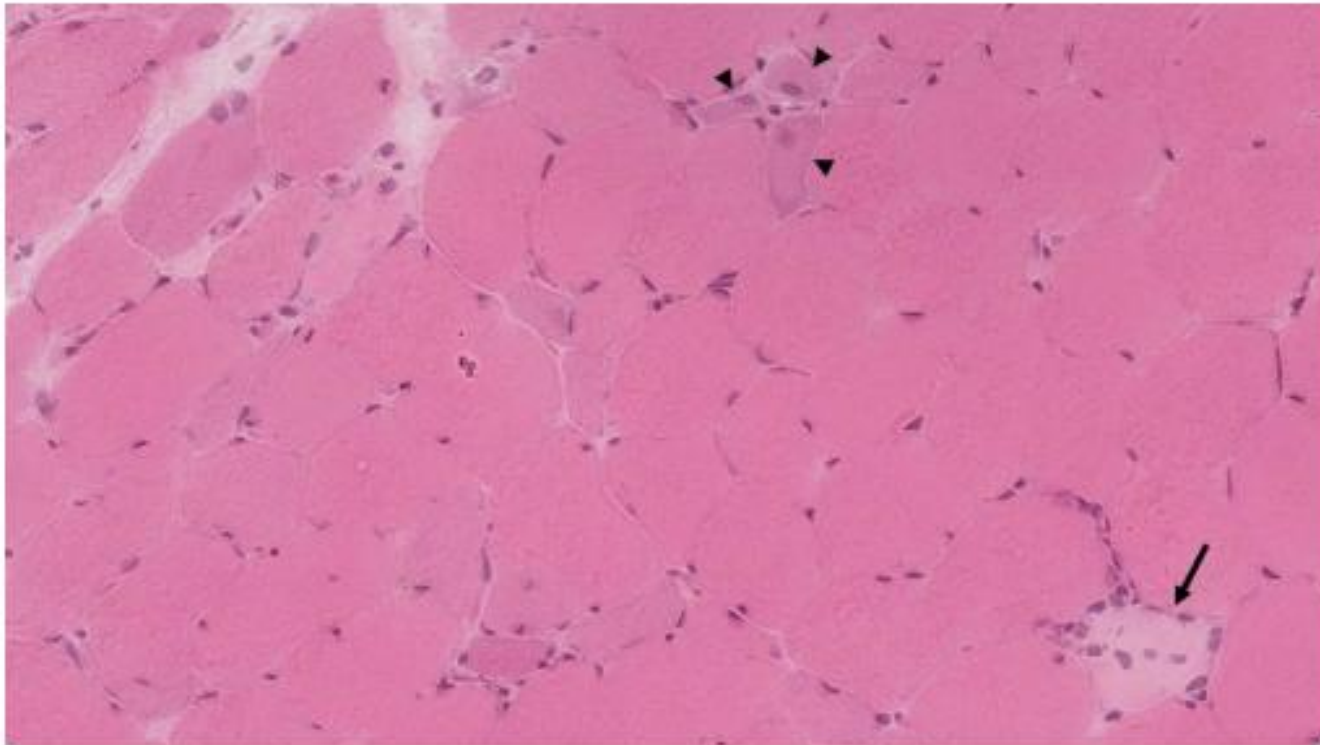
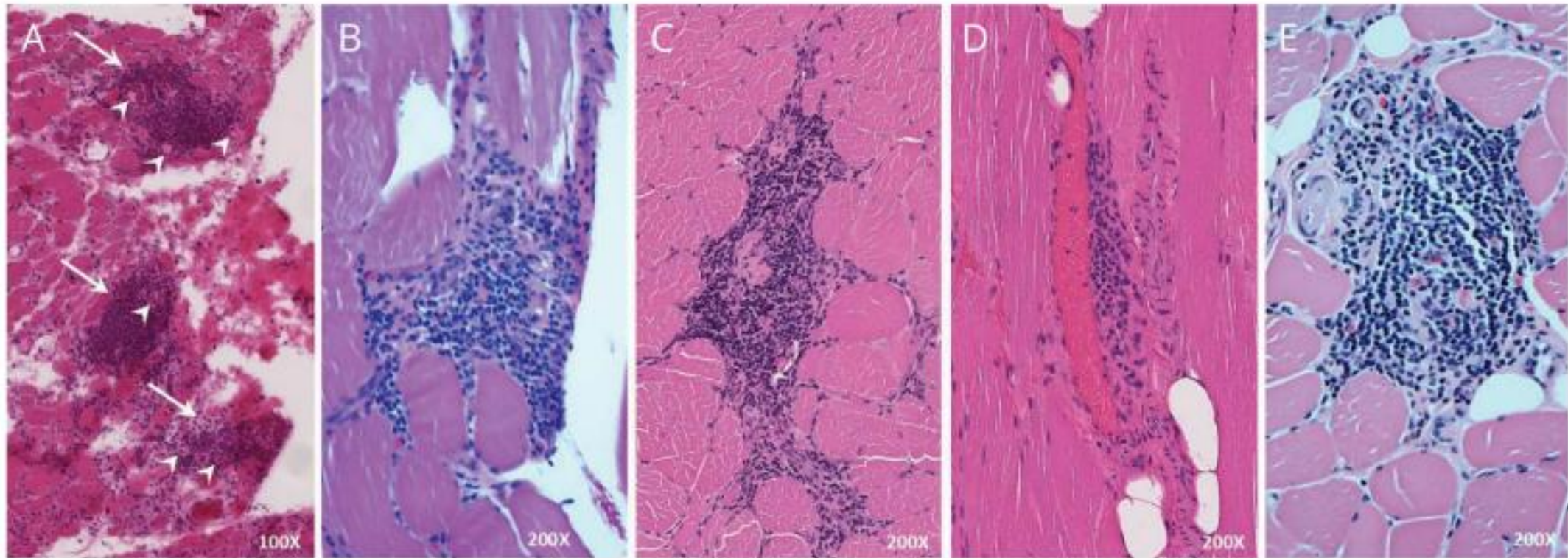


Figure Muscle biopsy from an anti-U1-ribonucleoprotein-positive patient (hematoxylin & eosin)



The arrow shows a necrotic cell undergoing early-stage myophagocytosis. Regenerating myofibers, characterized by basophilic cytoplasm and enlarged nuclei, are indicated by the arrowheads (×200 magnification).

Figure 1 Muscle biopsies from patients positive for anti-PM/Scl autoantibodies show intense perivascular inflammation



(A) The arrows indicate perivascular collections of inflammatory cells, and vessels are marked by the arrowheads. (A-E) Each panel shows an example of perivascular inflammation from a different patient. Hematoxylin & eosin staining.

Estudios complementarios

- Análisis de laboratorio: dosaje de CK (principal marcador de lesión muscular).
- Electromiografía: confirma miopatía y descarta otras causas de debilidad.
- RMN muscular: detecta actividad inflamatoria, define la distribución del compromiso, guía la biopsia y evidencia atrofia y reemplazo graso.

Tratamiento

Entidad	Tratamiento inicial	Refractaria / grave	Serología: ¿modifica la conducta?	Referencia
sIBM	Ejercicio + rehabilitación. Manejo de disfagia y complicaciones.	IVIG: considerar en disfagia . Inmunosupresión: beneficio limitado.	No. Anti-cN1A no modifica el tratamiento.	<i>Santos et al., 2025</i> (PubMed)
IMNM	Corticoides + inmunosupresor ± IVIG.	IVIG / rituximab; combinación en casos graves.	Sí. HMGCR → IVIG; SRP → considerar rituximab precoz.	<i>Suh & Amato, 2024; Mammen, 2018</i> (PubMed)
DM	Corticoides + ahorrador (MTX, AZA, MMF). IVIG en enfermedad activa/grave.	IVIG / rituximab / JAK-i según fenotipo.	Sí. MDA5 → EPI rápidamente progresiva; TIF1γ/NXP2 → riesgo de cáncer.	<i>Moghadam-Kia et al., 2017; Fuzzi et al., 2022</i> (PubMed)
AAS	Corticoides + inmunosupresor precoz (MMF, AZA, tacrolimus).	Rituximab / ciclofosfamida en EPI grave; antifibrótico si EPI progresiva.	Sí. El anticuerpo ayuda a definir el fenotipo pulmonar y la gravedad.	<i>Nakashima, 2024</i> (PubMed)
OM	Corticoides + inmunosupresor, según enfermedad asociada.	Rituximab / IVIG / ciclofosfamida según órgano.	Sí. PM/Scl, Ku, U1-RNP → orientan el fenotipo de superposición.	<i>Gonçalves Júnior et al., 2022</i> (PubMed)



¡Muchas Gracias!

www.fleni.org.ar



@FleniOficial