Covid and Musculoskeletal problems

Dr Ali Ashraf

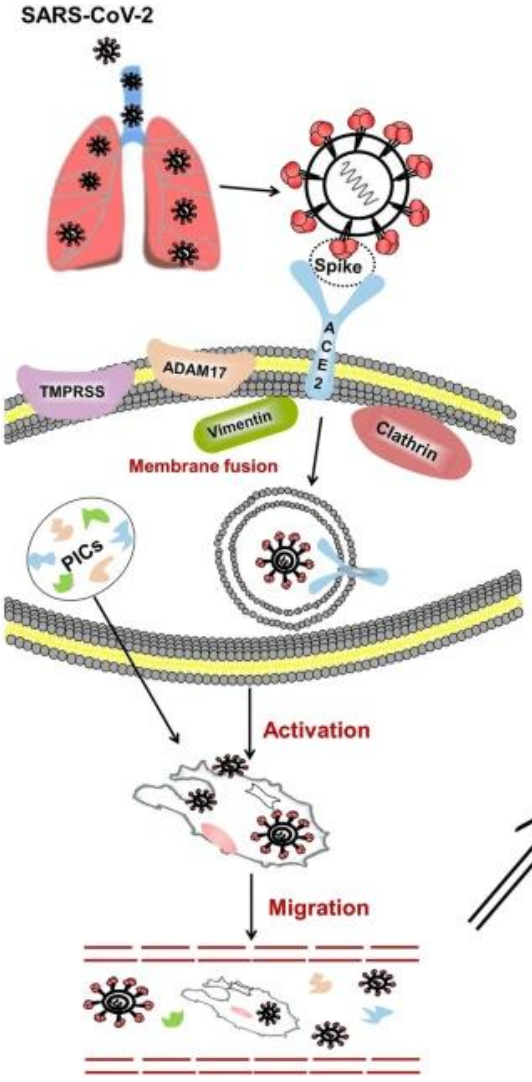
GUMS

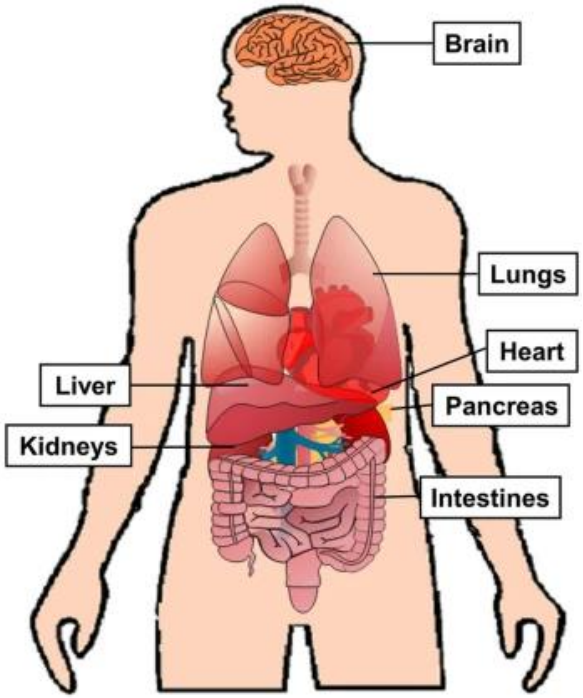
Intensive care unit

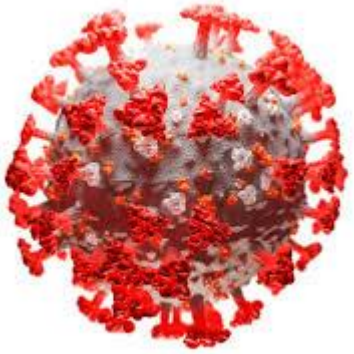
Avesina university hospital

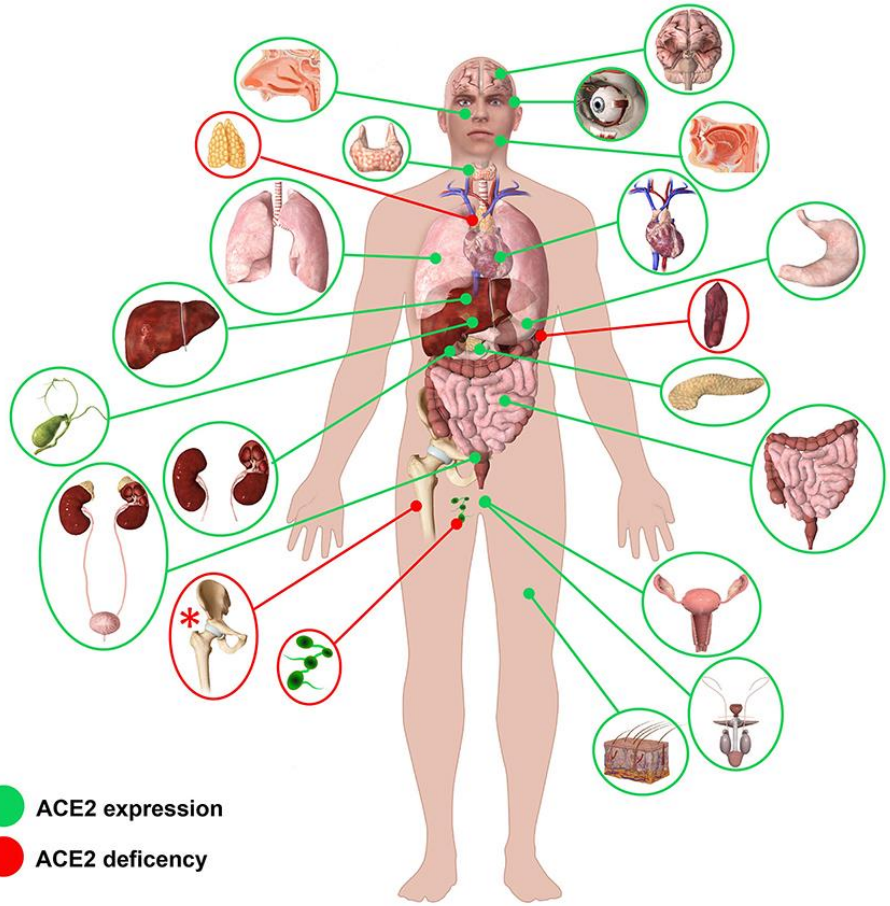
Symptoms of Covid 19

- spike (S) protein
- lung epithelial cells
- Heart
- Kidney
- Pancreas
- Spleen
- gastrointestinal system
- Bladder
- Cornea
- blood vessels
- central and peripheral nervous systems
- skeletal muscle
- cytokine storm multi-organ injury









Brain: nuclei involved in the central regulation of cardiovascular function (brainstem cardiorespiratory neurons), non-cardiovascular areas (motor cortex and raphe)

Eyes: luminal surface of epithelial cells, retinal and retinal pigment epithelium

Nasal cavity: mucosal surface of the airway, basal layer of the non-keratinizing squa mous epithelium

Oral cavity: basal layer of the non-keratinizing squamous epithelium, tongue, buccal mucosa, saliva, gingiva, lymphocytes within oral mucosa, and oral cavity

Thyroid: Glandular cells

Heart and blood vessels: Pericytes, endothelial and smooth muscle cells of intra-myocardial vessels, thoracic aorta, carotid arteries, and veins. Endothelial cells from small and large arteries and veins

Lungs: Type I and II alveolar epithelial cells, bronchiolar epithelial cells, endothelial cells and arterial smooth muscle cells

Liver: Epithelial cells of the bile duct, perinuclear hepatocytes, cholangiocytes

Gallbladder: Gallbladder epithelium

Kidneys and bladder: Proximal tubular brush border, proximal renal tubular epithelium, distal tubules, bladder urothelial cells, luminal surface of tubular epithelial cells, glomeruli

Stomach: Esophagus upper and stratified epithelial cells

Pancreas: Exocrine gland (duct cells and acinar cells), and pancreatic islets (alpha, beta, delta and PP cells)

Intestines: intestinal epithelial cells, enterocytes of the small intestine, duodenum, absorptive enterocytes from ileum and colon, rectum endothelial cells

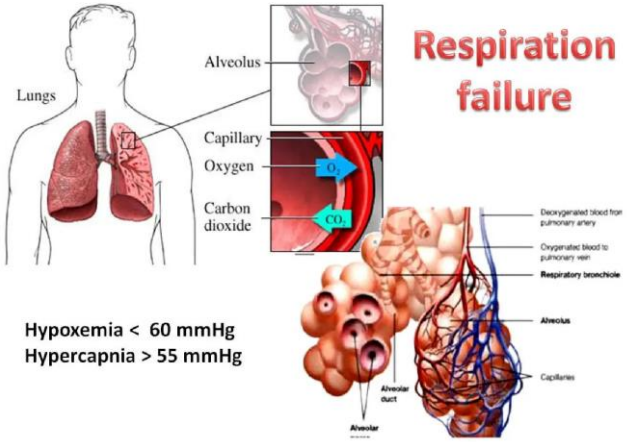
Reproductive system
Female: ovary, oocyte, uterus, vagina, placenta

Male: adult Leydig cells in the testis and in cells in the seminiferous ducts in testis

Skin: Basal epidermal layers and in sebaceous gland cells

Symptoms of Covid 19

- estimated 5% of COVID-19 patients have severe symptoms that require intensive care

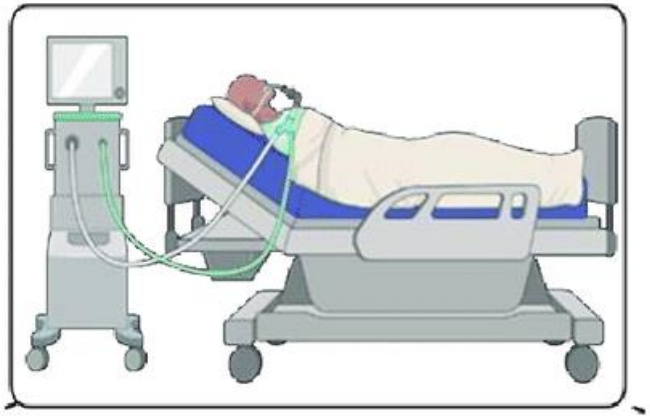


Covid morbidity

- Older age
- Comorbidities:
- cardiovascular disease
- diabetes mellitus
- obesity

Covid treatment

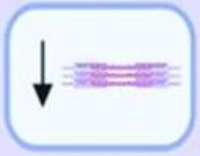
- supplemental oxygen & mechanical ventilation
- Corticosteroids
- thromboembolic prophylaxis
- Nutrition
- Antiviral therapy



Definitive Characteristics of CIM

Severe muscle atrophy; affecting both type I and II fibers

Preferential and significant loss of thick filament protein myosin



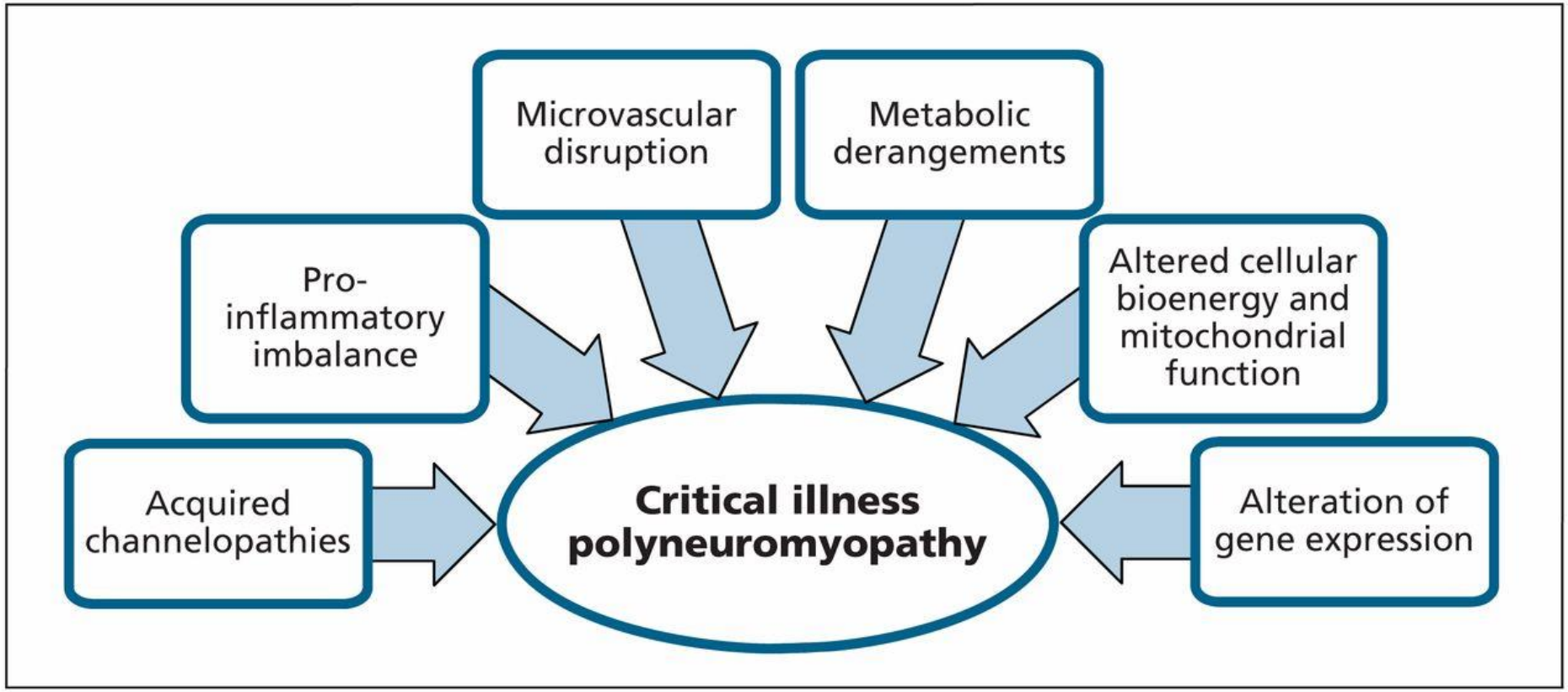
Eventual sarcomere disorganization

Electrical hypoexcitability of the muscle and poor excitation - contraction coupling

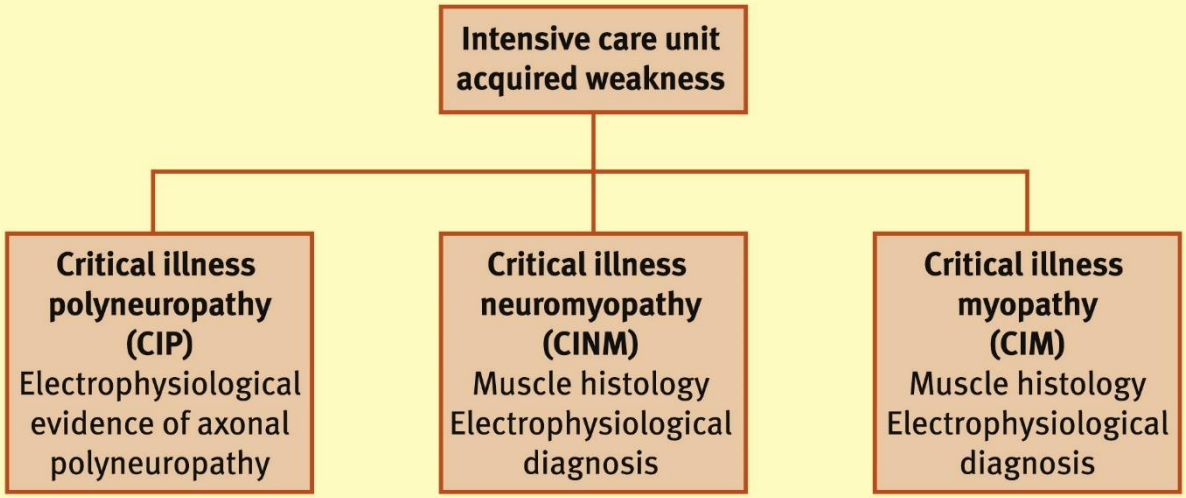
Critical illness polyneuropathy/myopathy

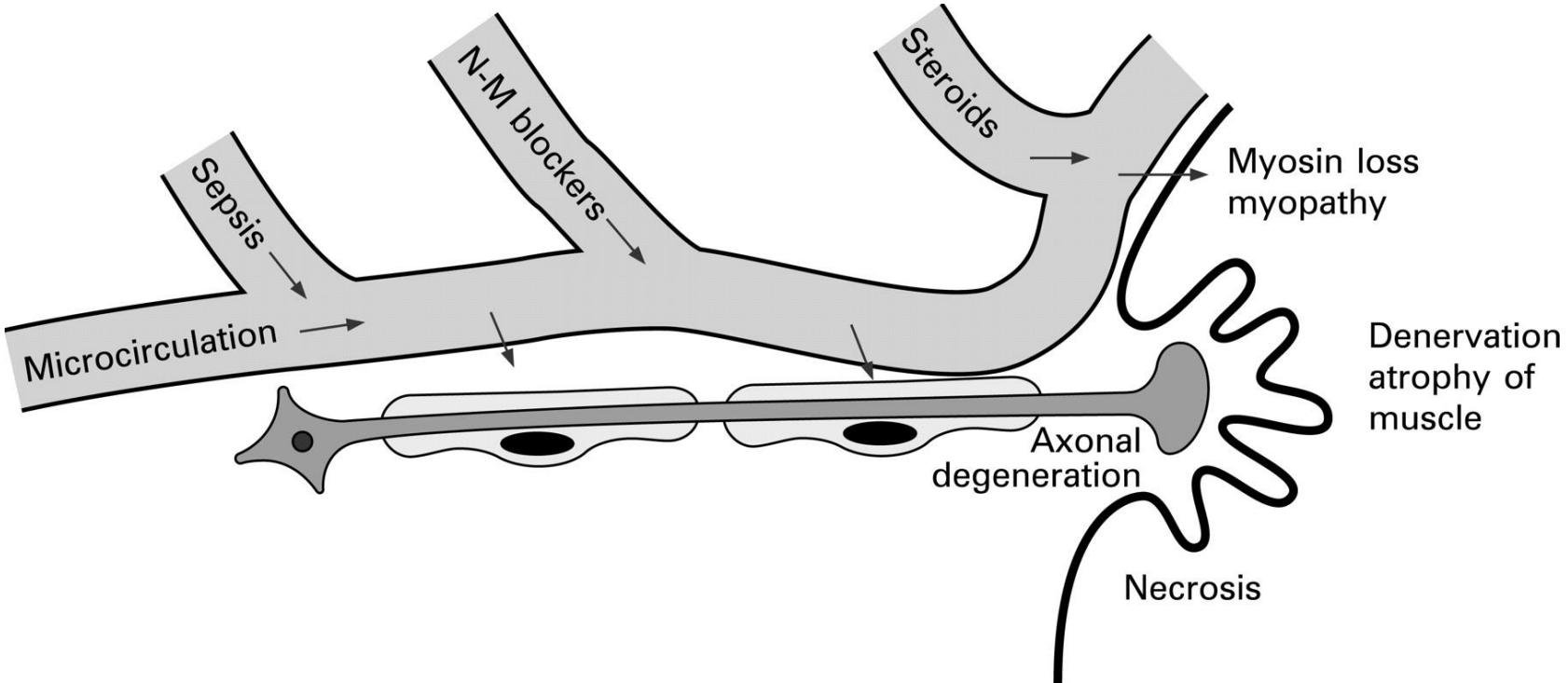
- Amyotrophic lateral sclerosis
- Poliomyelitis
- Guillain-Barre syndrome
- Heavy metal toxicity
- Vasculitis
- Sarcoidosis
- Mononeuritis multiplex
- Neuromuscular junction Myasthenia gravis
- Neuromuscular blockade
- Lambert-Eaton myasthenic syndrome
- Botulinum toxicity
- Organophosphate toxicity
- Tetrodotoxin toxicity
- Rhabdomyolysis
- Mitochondrial myopathy
- Muscular dystrophy (eg, Myotonic
- dystrophy)
- Critical illness myopathy
- Acid maltase deficiency

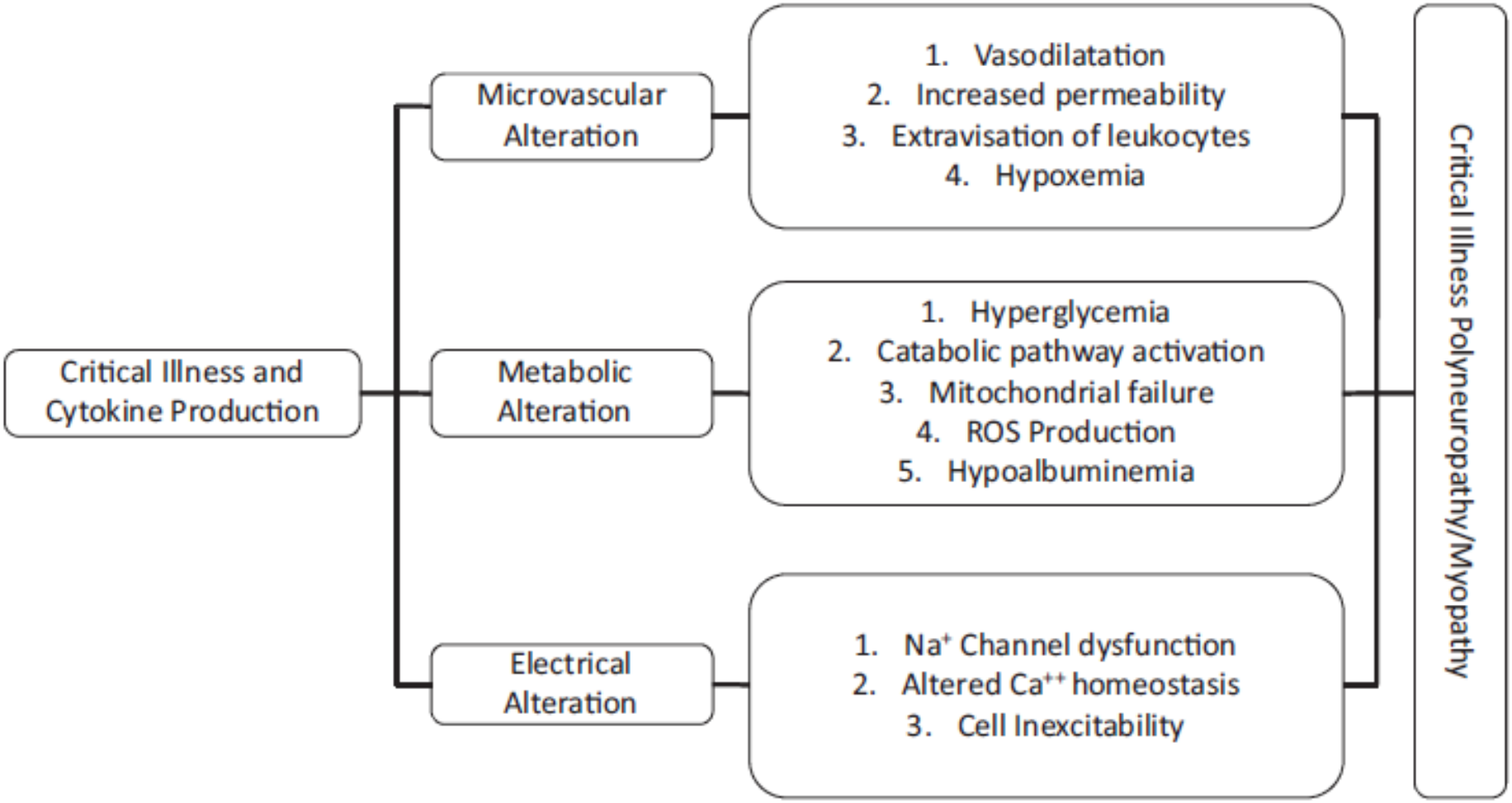
Critically illness polyneuro/myopathy



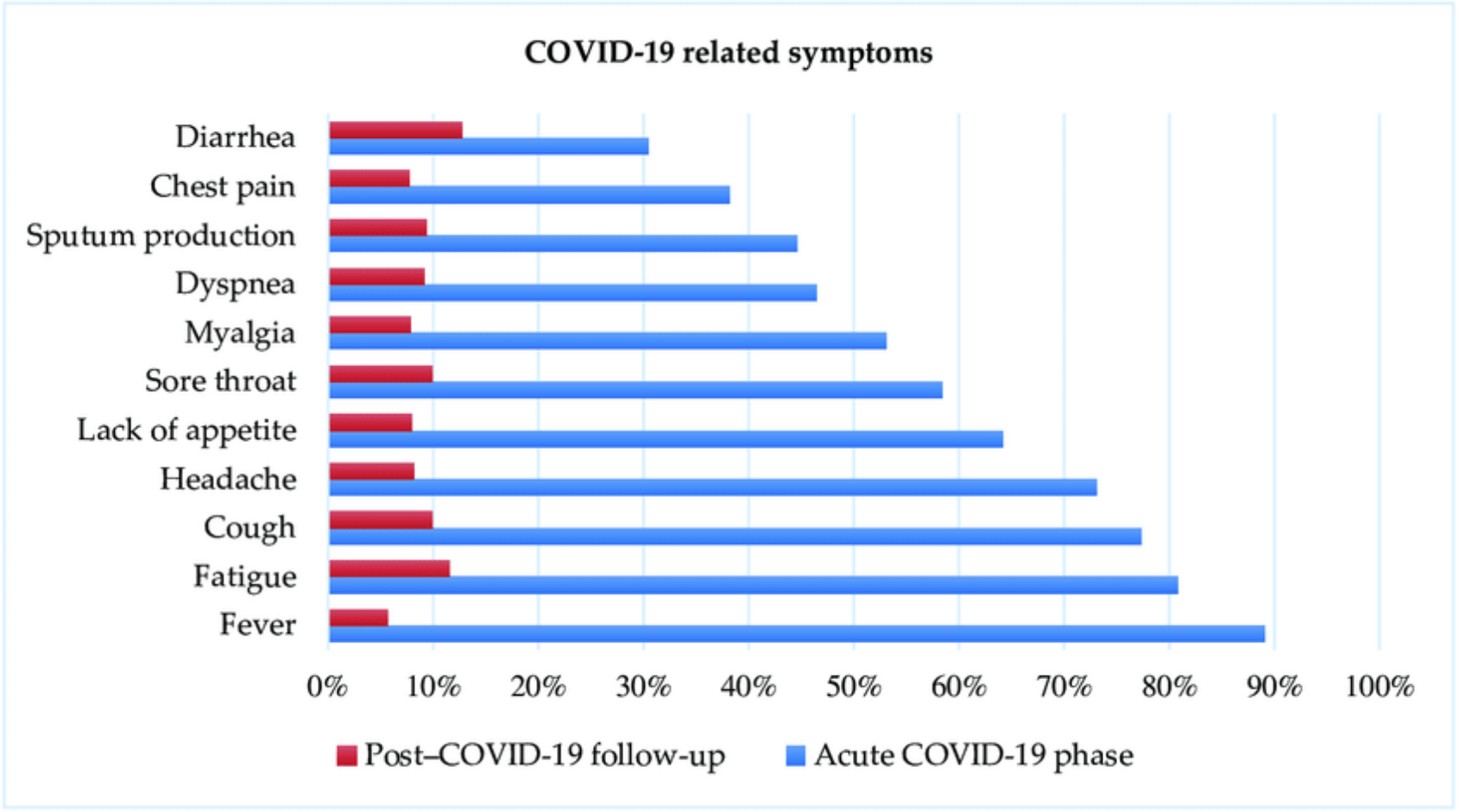
Classification of intensive care unit weakness

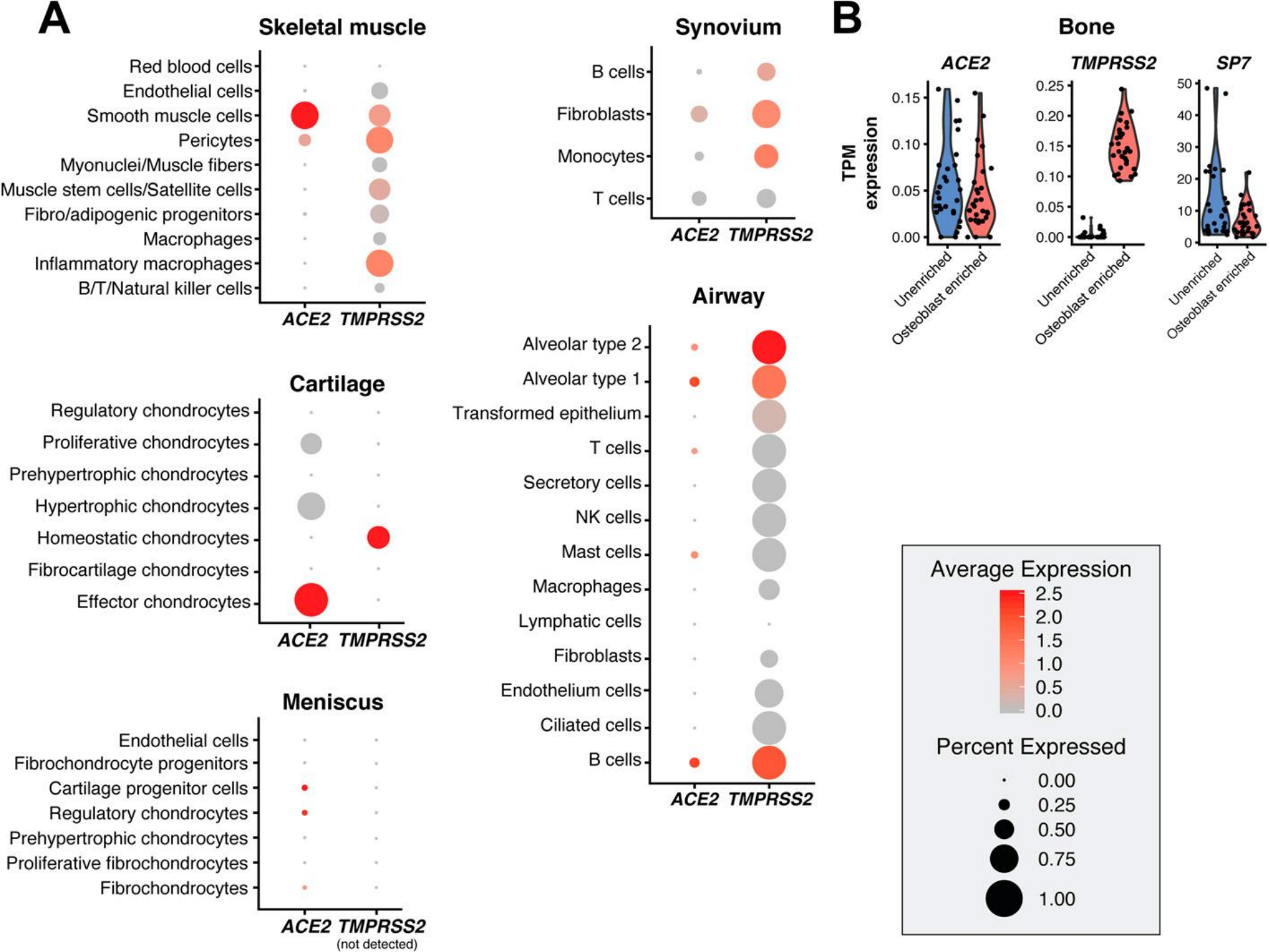


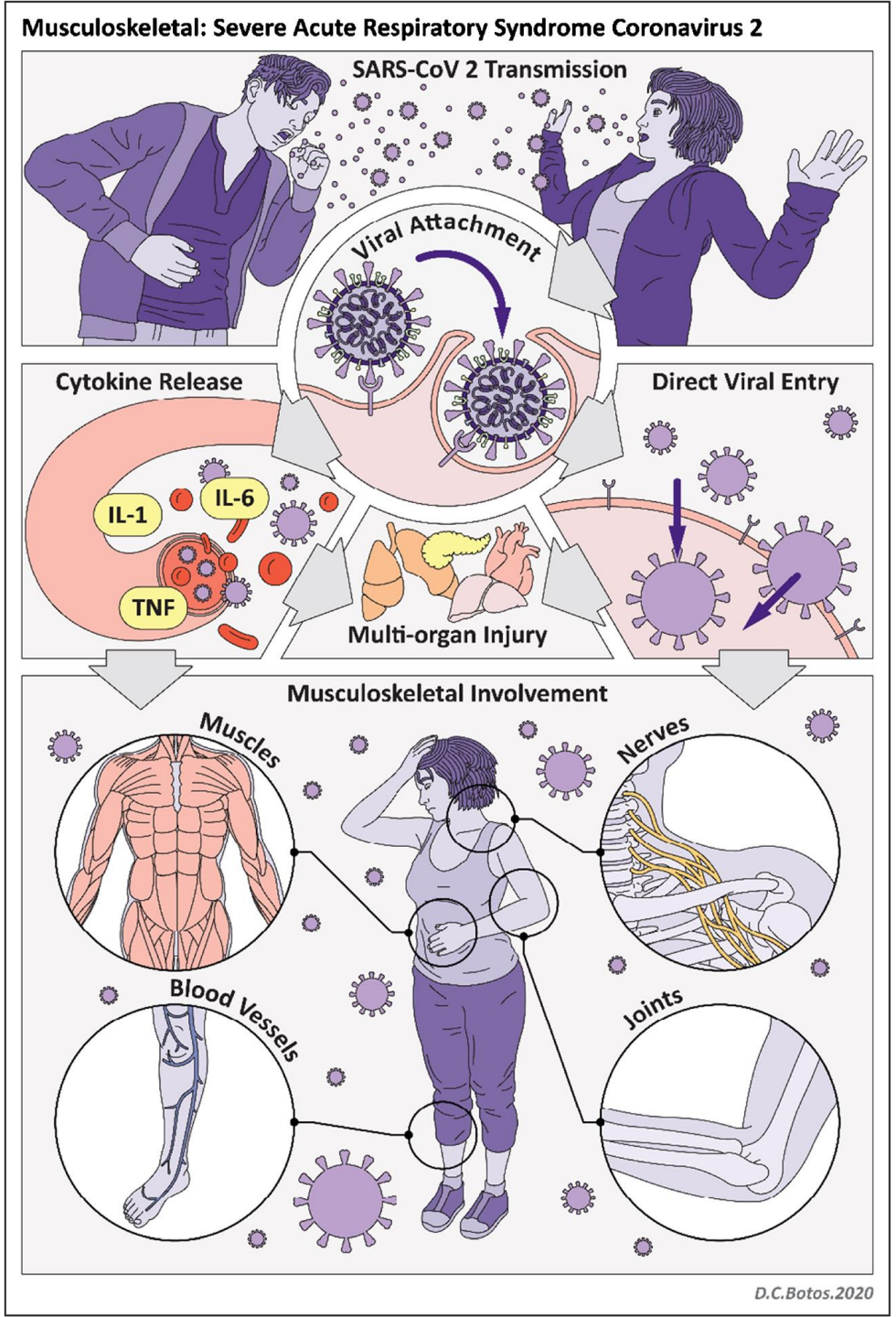



Critical Illness and Cytokine Production
Microvascular Alteration
Metabolic Alteration
Electrical Alteration
1. Vasodilatation
2. Increased permeability
3. Extravisation of leukocytes
4. Hypoxemia
1. Hyperglycemia
2. Catabolic pathway activation
3. Mitochondrial failure
4. ROS Production
5. Hypoalbuminemia
1. Na^{+} Channel dysfunction
2. Altered Ca^{++} homeostasis
3. Cell Inexcitability
Critical Illness Polyneuropathy/Myopathy

extrapulmonary COVID-19 manifestations




A
Skeletal muscle
Red blood cells
Endothelial cells
Smooth muscle cells
Pericytes
Myonuclei/Muscle fibers
Muscle stem cells/Satellite cells
Fibro/adipogenic progenitors
Macrophages
Inflammatory macrophages
B/T/Natural killer cells
ACE2 TMPRSS2
Synovium
B cells
Fibroblasts
Monocytes
T cells
ACE2 TMPRSS2
B
Bone
ACE2
TMPRSS2
SP7
TPM expression
0.15
0.10
0.05
0.00
0.25
0.20
0.15
0.10
0.05
0.00
50
40
30
20
10
0
Unenriched
Osteoblast enriched
Cartilage
Regulatory chondrocytes
Proliferative chondrocytes
Prehypertrophic chondrocytes
Hypertrophic chondrocytes
Homeostatic chondrocytes
Fibrocartilage chondrocytes
Effector chondrocytes
ACE2 TMPRSS2
Airway
Alveolar type 2
Alveolar type 1
Transformed epithelium
T cells
Secretory cells
NK cells
Mast cells
Macrophages
Lymphatic cells
Fibroblasts
Endothelium cells
Ciliated cells
B cells
ACE2 TMPRSS2
Meniscus
Endothelial cells
Fibrochondrocyte progenitors
Cartilage progenitor cells
Regulatory chondrocytes
Prehypertrophic chondrocytes
Proliferative fibrochondrocytes
Fibrochondrocytes
ACE2 TMPRSS2
(not detected)
Average Expression
2.5
2.0
1.5
1.0
0.5
0.0
Percent Expressed
0.00
0.25
0.50
0.75
1.00

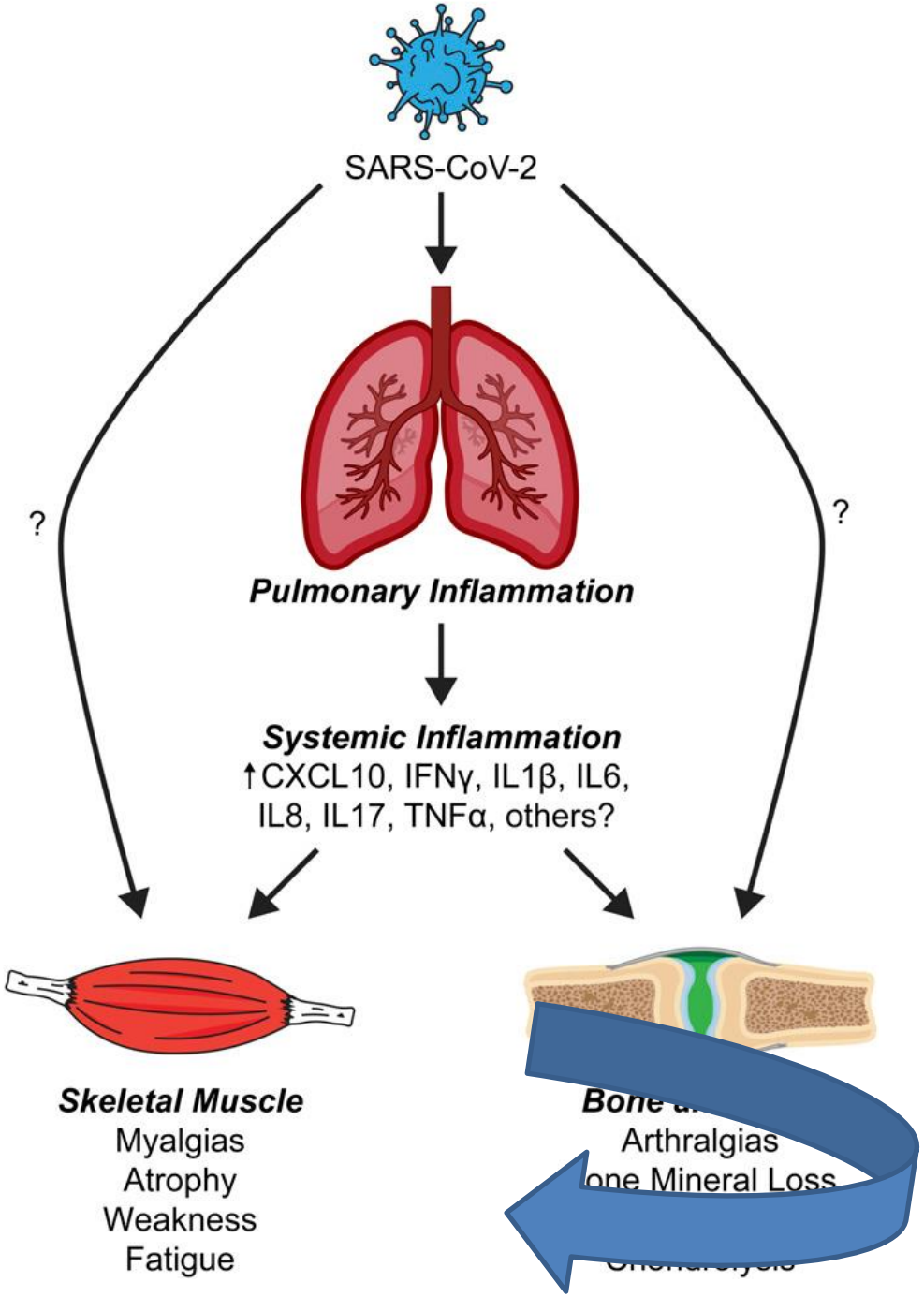

Musculoskeletal: Severe Acute Respiratory Syndrome Coronavirus 2
SARS-CoV 2 Transmission
Viral Attachment
Cytokine Release
IL-1
IL-6
TNF
Multi-organ Injury
Direct Viral Entry
Musculoskeletal Involvement
Muscles
Nerves
Blood Vessels
Joints
D.C.Botos.2020

Muscle

- Myalgia
- myositis
- rhabdomyolysis necrotizing autoimmune myositis

Mechanisms : ???

- Hematogenous spread and direct invasion of skeletal muscle
- Immune-mediated mechanisms
- inflammatory response with cytokine storming
- immune-mediated muscle damage
- immune complex deposition myotoxic cytokine release
- Homology between human muscle cells and viral antigens

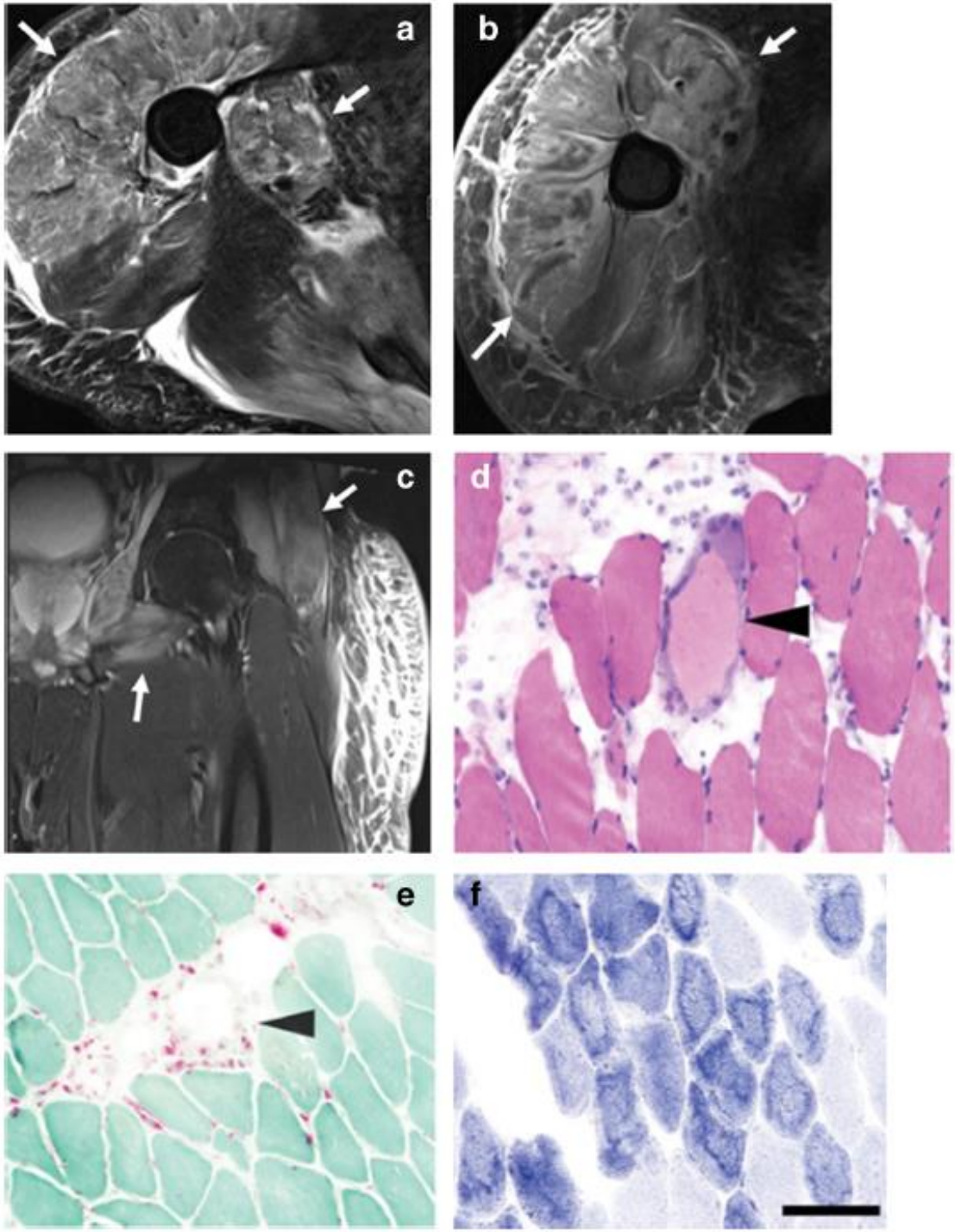

SARS-CoV-2
?
?
Pulmonary Inflammation
Systemic Inflammation
↑CXCL10, IFNγ, IL1β, IL6,
IL8, IL17, TNFα, others?
Skeletal Muscle
Myalgias
Atrophy
Weakness
Fatigue
Arthralgias

Myositis

- inflammation of muscles
- SARS-CoV-2
- viral infections: influenza A/B, hepatitis , HIV
- Rhabdomyolysis is a complication of myositis
- infarction of muscle (myonecrosis)
- Myoglobin in the blood (myoglobinemia)
    - kidney failure,
    - compartment syndrome
    - intravascular coagulation
- Clinical findings of myositis/rhabdomyolysis :
- myalgia/weakness
- elevated creatine phosphokinase
    - both reported in COVID-19
- electromyography (EMG)
- Imaging can support diagnosis
- Biopsy is the gold standard for diagnosis

MR imaging in myositis

- 1.5-T or 3.0-T
- Findings of myositis:
- muscle edema
- increased signal intensity on T2-weighted Patterns of disease include homogeneous hyperintense signal and enhancement (type 1)
- In severe disease, areas of necrosis or loss of normal muscle architecture may be seen.


a
b
c
d
e
f

Myonecrosis “stipple sign”

- foci of enhancement in a rim-enhancing area of non-enhancing muscle tissue
- Intramuscular hemorrhage
- hyperintense signal or blooming artifact

Differential diagnosis

- Critical illness myopathy
- a primary myopathy with non-specific imaging findings of multifocal muscle edema and atrophy
- Findings of necrosis are not present
- Clinical and imaging features of critical illness
- myopathy in COVID-19 are not distinctive from non- COVID-19 patients

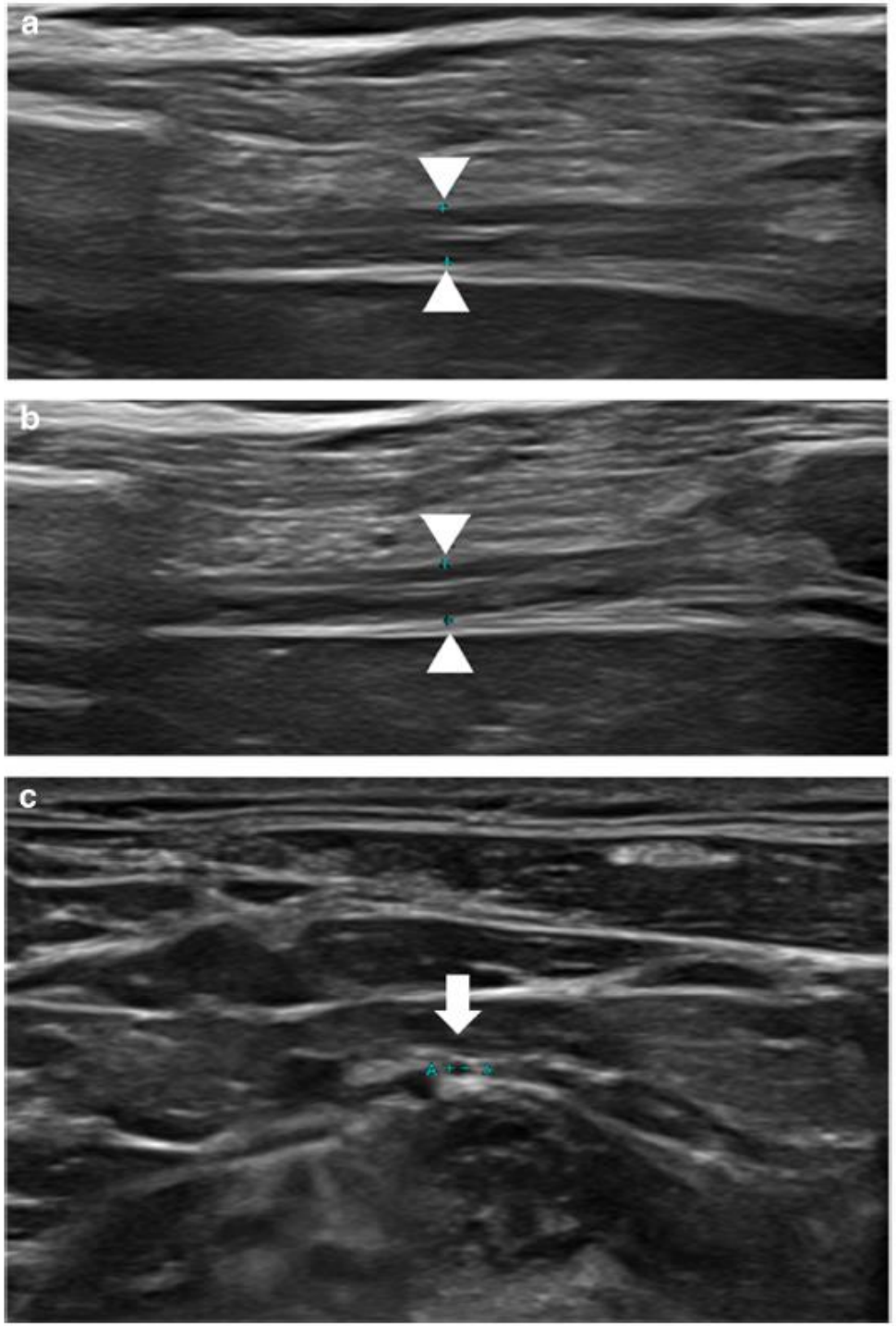
Diaphragm muscle dysfunction

- Critical illness myopathy
- Ventilator induced diaphragm dysfunction
- Phrenic nerve injury
- direct neuromuscular involvement of the SARS-CoV-2 virus
- Difficult weaning

Diaphragm muscle dysfunction

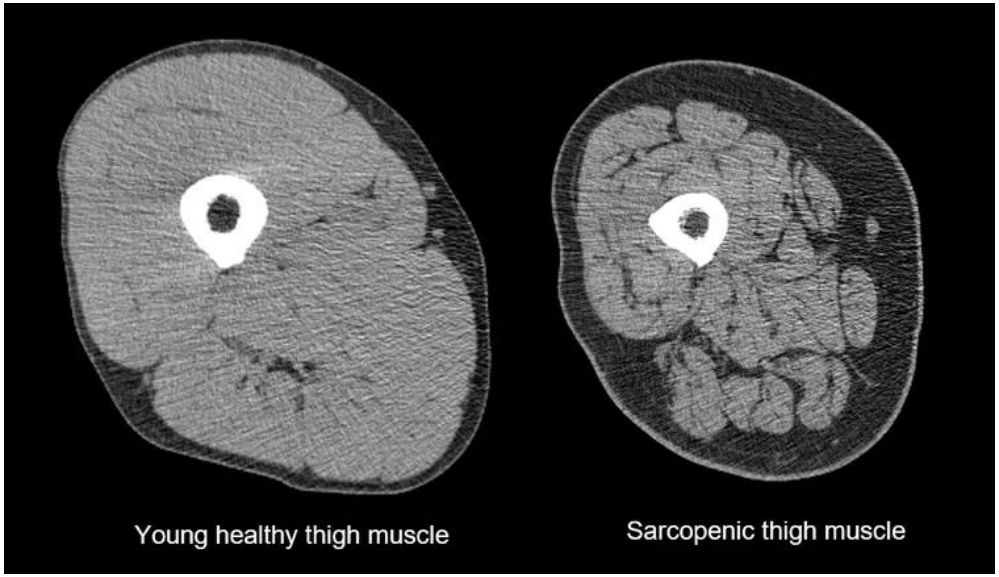
- Imaging is helpful
- The fluoroscopy sniff test offers a quick and real-time assessment of diaphragm excursion.
- Ultrasound :
  - diaphragm muscle atrophy
  - Calculation of the muscle thickening ratio with respiration
  - excursion with M mode imaging
  - High-resolution ultrasound for phrenic nerve in the region of the neck, which may aid in differentiation of neuropathic versus myopathic causes of diaphragm dysfunction

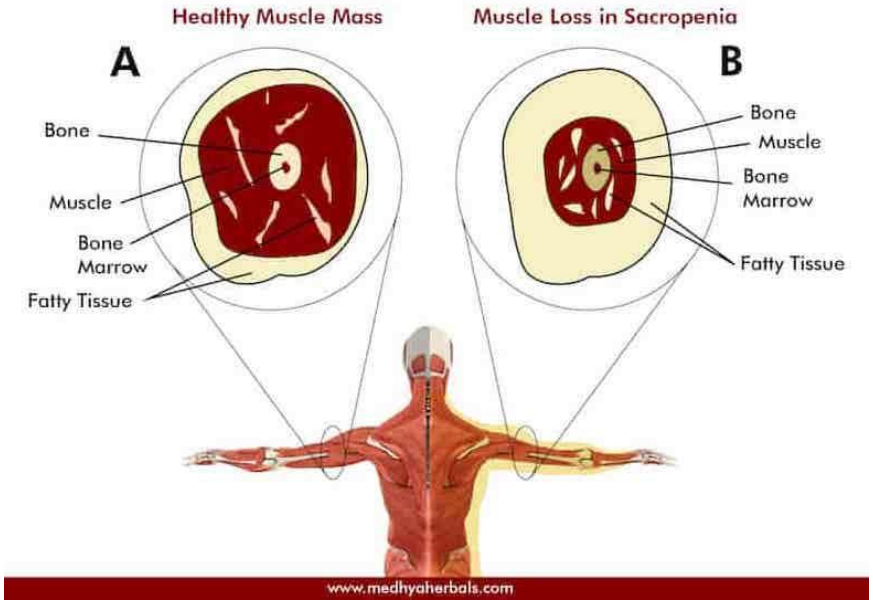
Ultrasound in Diaphragm muscle and phrenic nerve function study



Long-term muscular sequelae of COVID-19

- sarcopenia and cachexia





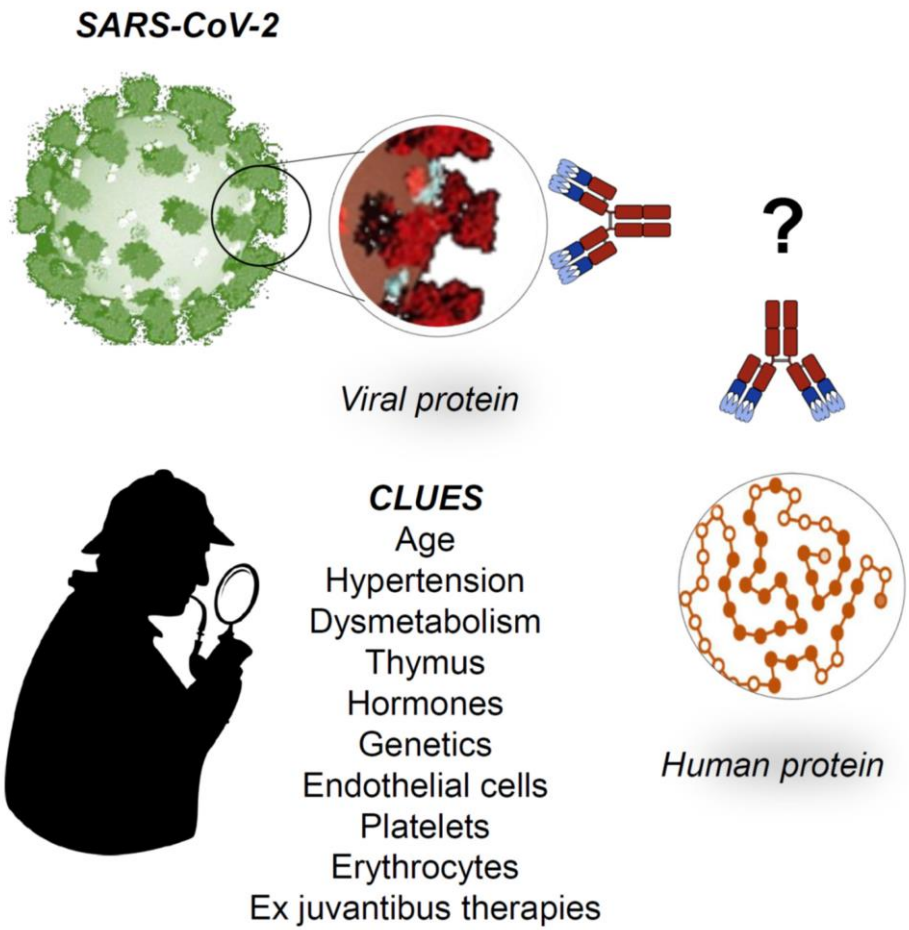
Peripheral neuropathy

1. “molecularmimicry”

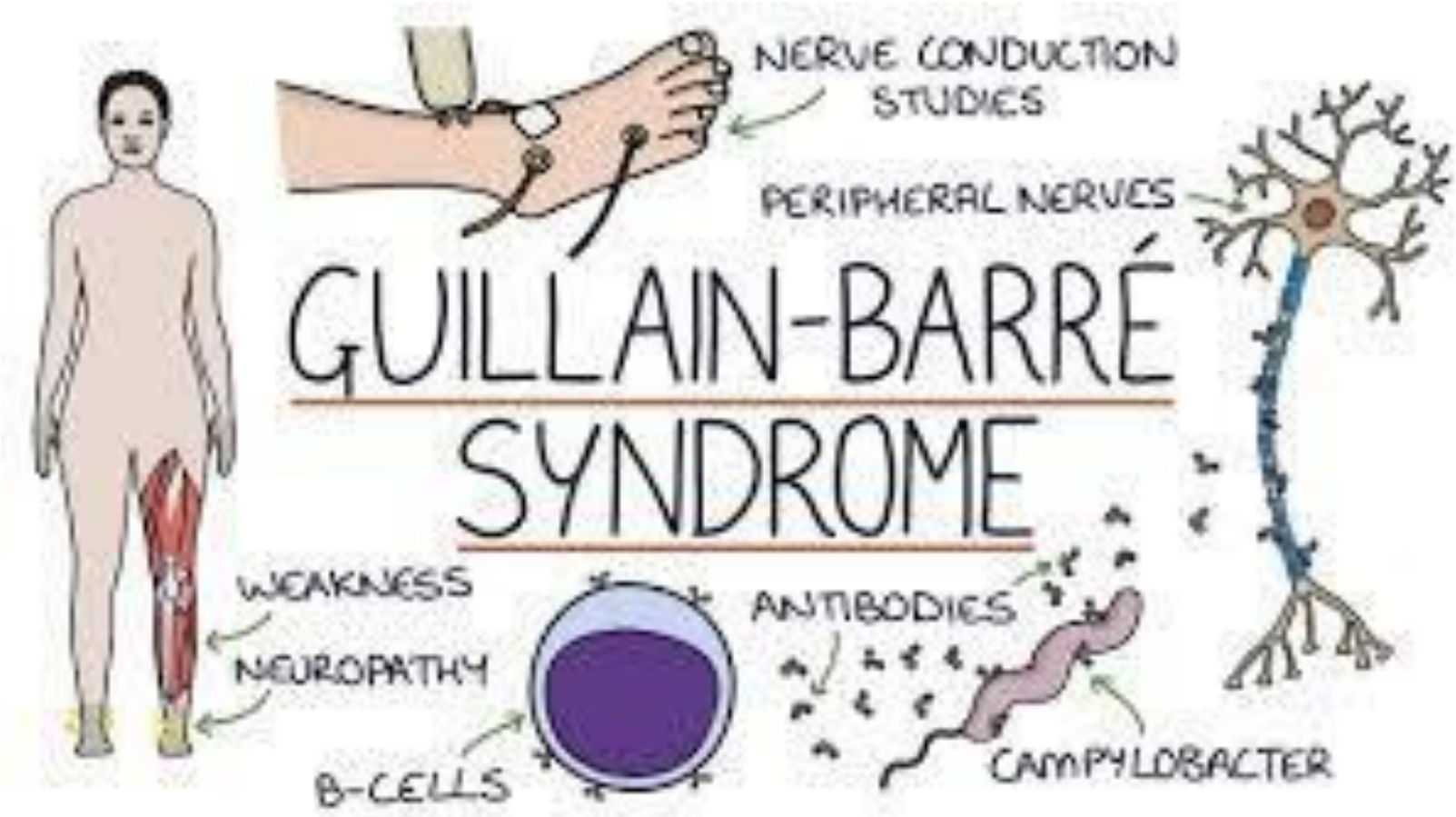
   similarities between SARS-CoV-2 surface glycoproteins and glycoconjugates in human nervous tissues

2. Direct cytotoxic effects of the virus on peripheral nerves

molecularmimicry



Guillain-Barre syndrome (GBS) secondary to COVID-19

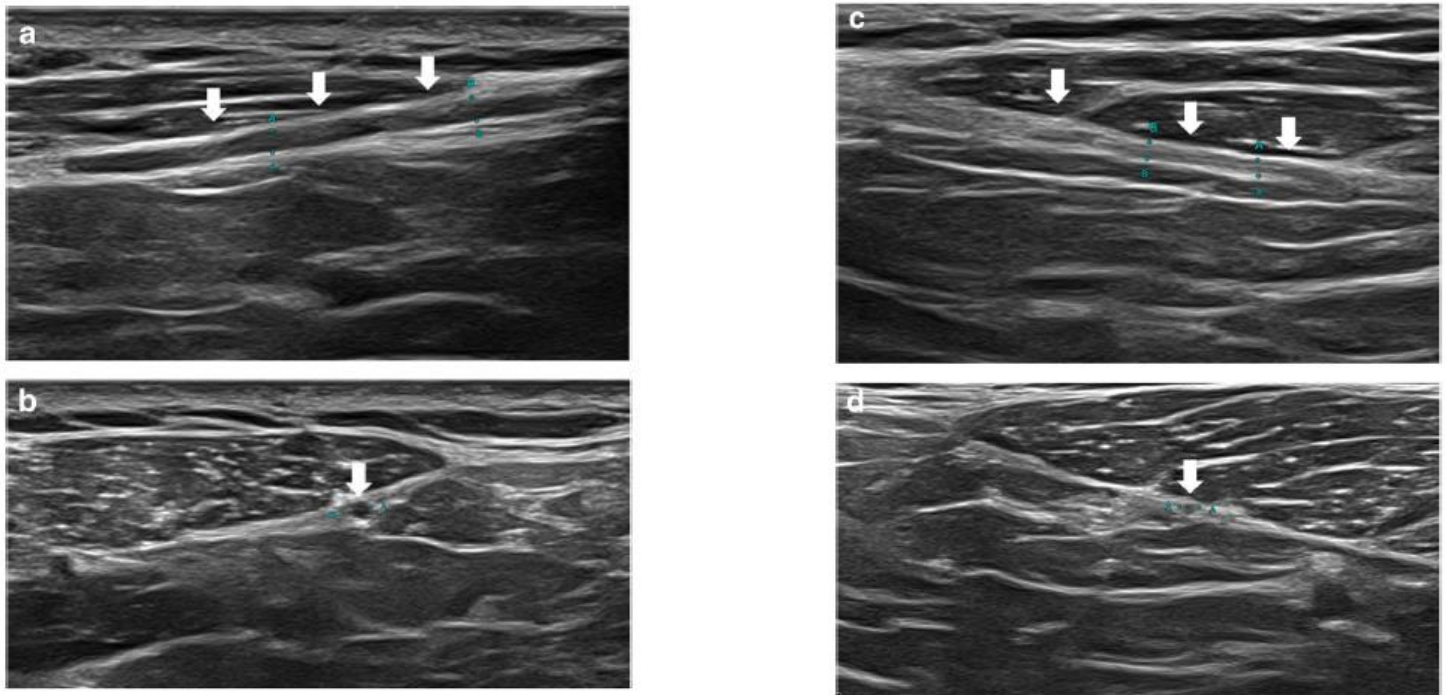


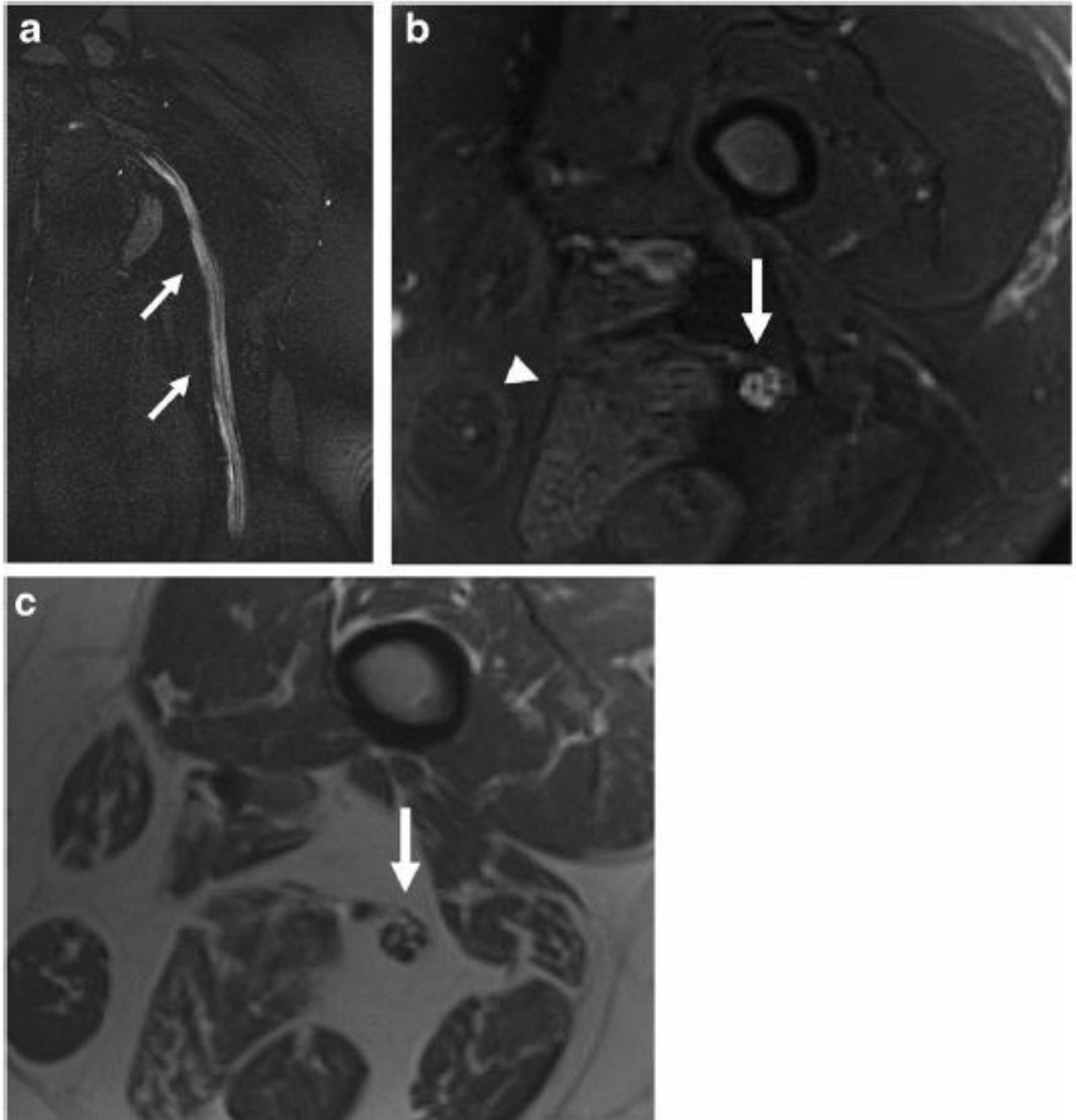
Iatrogenic peripheral neuropathy

- Hyperinflammation
- Comorbidities
- severe COVID-19 symptoms
- Prone positioning
- external compression
- internal compression from an intramuscular hematoma.
- Critical illness polyneuropathy

EMG and US

- Segmental nerve narrowing secondary to mass effect can be seen in hematoma-related compression neuropathy




a
b
c

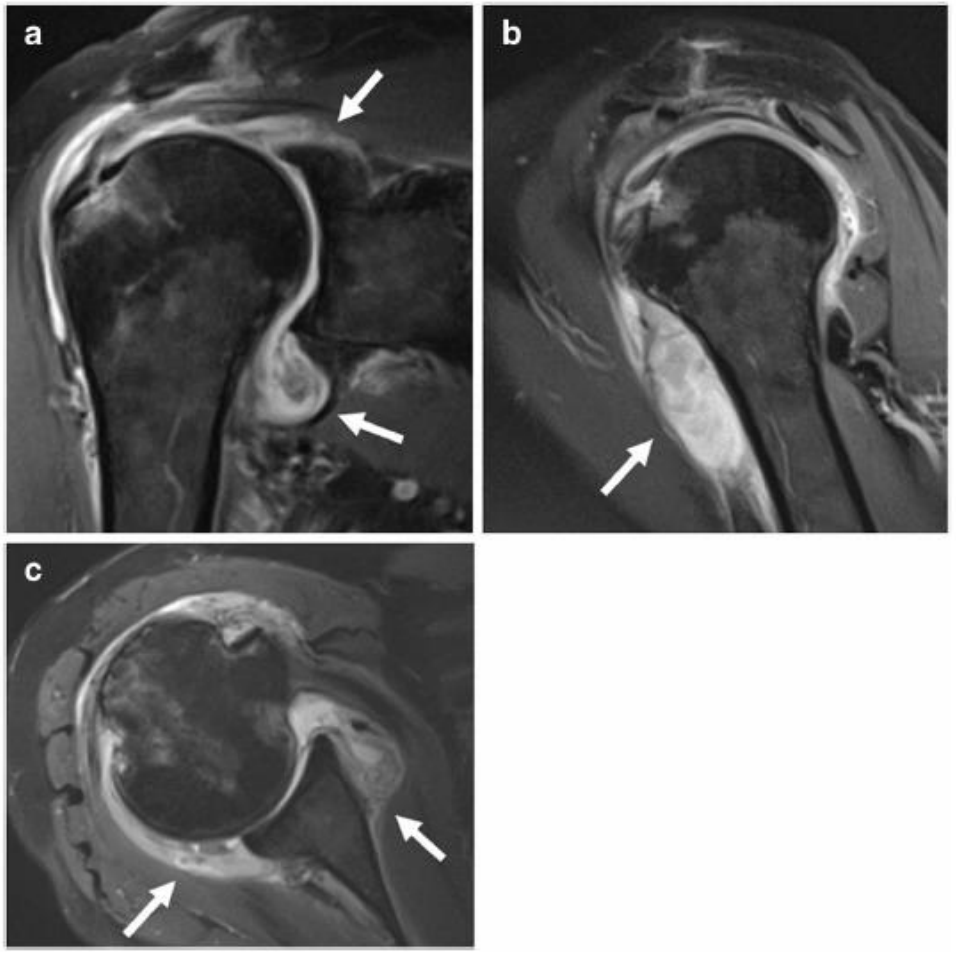
Joints

- Arthralgia in 2.5%
- several cases of acute clinical arthritis
- findings that suggest viral arthritis include
- onset of arthralgia within a few weeks following viral infection,
- a self-limiting course
- a good response to NSAIDs

Rheumatologic diseases triggered by SARS-CoV-2

- systemic lupus erythematosus
- Dermatomyositis
- Graves' disease
- Rheumatoid arthritis
- psoriatic spondyloarthritis
- Inflammatory arthropathies may be triggered by SARSCoV-
- COVID-19 patients with acute arthritis may benefit from rheumatologic consultation.

H.x of A.R in a 70 y.o male



Soft tissues

- COVID-19 coagulopathy
- thrombotic events
- vasopressor medications
- Distal extremities are more susceptible
  - Gangrene
  - underlying diabetes
  - peripheral vascular disease.
- Imaging features of gangrene include
  - skin ulcerations,
  - T2 signal hyperintensity of soft tissues
  - lack of enhancement

“COVID toes”

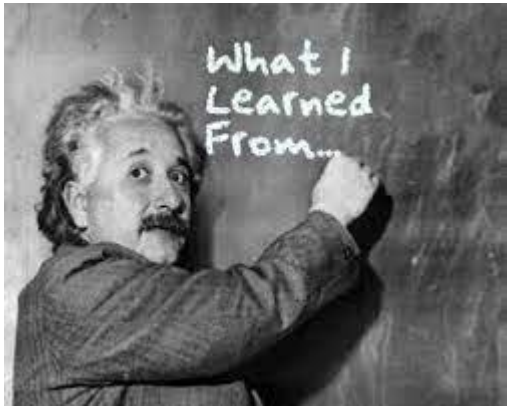
- a chilblain-like phenomenon
  - Erythema
  - vesicles or pustules
  - due to a microvascular occlusive mechanism

Bones

- There is little current information regarding osseous complications of COVID-19
- Critical illness
- corticosteroid treatment
- virus-induced coagulopathy
  - –osteoporosis
  - – osteonecrosis

Table 1 Imaging of musculoskeletal involvement in COVID-19

Organ system	Imaging modalities	Imaging findings
Muscle	MRI +/− contrast	Muscle edema, necrosis Muscle atrophy
	Ultrasound	Diaphragm dysfunction
Nerve	MR neurography	Nerve enlargement, signal hyperintensity, loss of fascicular architecture +/− muscle denervation
	High-resolution ultrasound	Nerve enlargement, hypoechogenicity, loss of fascicular architecture
Joints	MRI +/− contrast	Joint effusion with enhancement, +/− erosions
	Ultrasound with Doppler	Synovitis, hyperemia
Soft tissues	MRI, CT, ultrasound	Hematomas, gangrene, "COVID toes," atypical pressure ulcers from prone positioning
Bone	Radiography, CT, MRI	Osteoporosis, osteonecrosis



- Multimodality imaging
  can play an important role
  in diagnosis and evaluation of COVID-19-related musculoskeletal Pathology

- procedural guidance in case of sampling
- familiarity with incidence, etiology, and imaging findings of COVID-19-related musculoskeletal manifestations is important
- By considering these complications Short and long term consequences can be reduced .


Thanks For
Your
Time
And
Attention