

Athletes and Their Rheumatic Diseases

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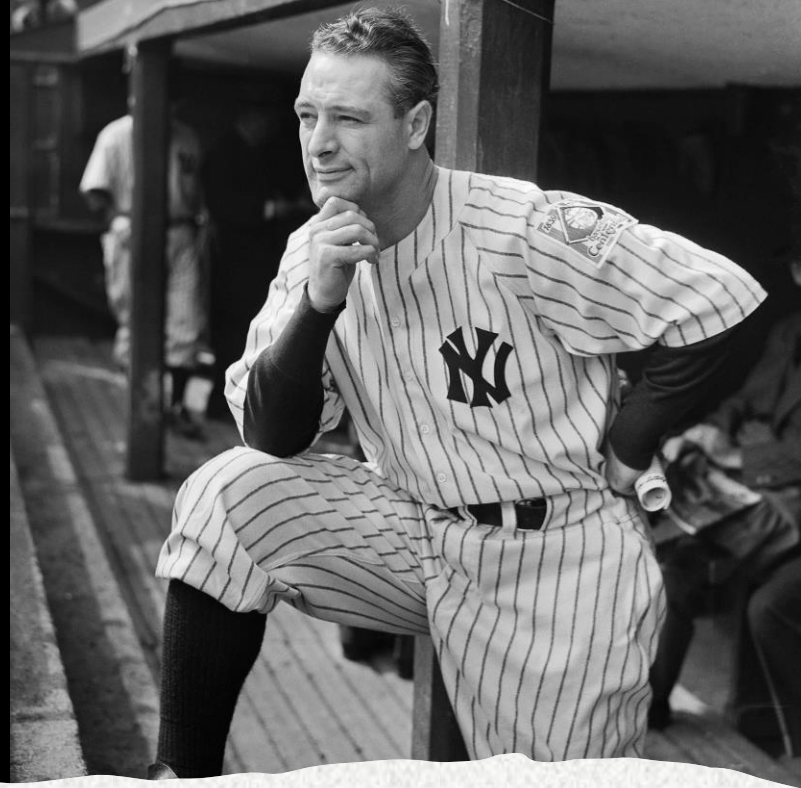
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November 2, 2022

Disclosures

- Clinical Research Funding:
 - Amgen
 - Novartis
 - Roche
- Speaker:
 - Novartis



Junior Seau

Lou Gehrig

Magic Johnson

CROSS-COUNTRY SKIING

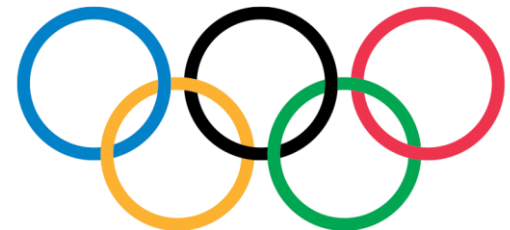
Finnish Cross-Country Skier Suffers Frozen Penis at 2022 Winter Olympics

This is not the first time Remi Lindholm has encountered this during a race

By Max Molski • Published February 22, 2022



BEIJING 2022™



Athletes and their Rheumatic Diseases: Introduction

- Young MLB player develops chronic LBP
- PGA star has severe back pain and rashes
- NFL running back develops periodic swollen joints
- NFL quarterback develops swollen hand joints
- Young WTA star develops stiff and aching hands that limits play
- Another WTA star develops fatigue and needs to be off tour for a year
- NFL lineman succumbs to progressive dyspnea and inflammation
- 1976 Heisman runner up develops muscle weakness and lung inflammation
- Young track athlete admitted for severe muscle pain with elevated CPK

Case 1



“Philip” was a 40 year old athlete with the following story:

“In the months leading up to ... 2010 ... I developed pain near my ankle that made it difficult to walk, and my left index finger and right wrist felt as if they were sprained. At first, I thought these aches could be caused by years of practicing... and that they would eventually pass. Then, after two days of preparing I awoke and the pain in my joints was so intense I could hardly get out of bed.”

Who is this person?

Philip Rivers

Phil Mickelson

Phil Nevin

Phil Collins



What is the diagnosis?

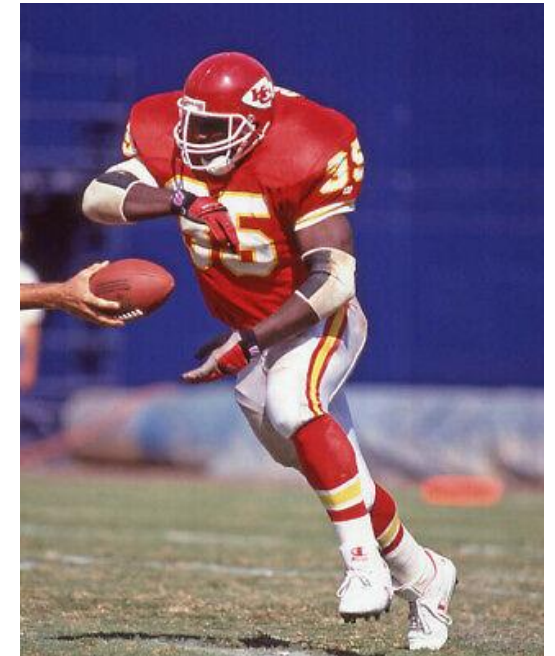
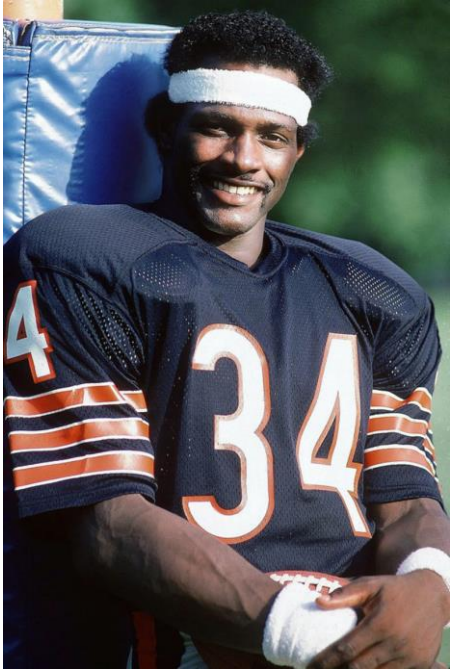
- Tendonitis
- Fibromyalgia
- Lumbar radiculopathy
- Spondylolisthesis
- ✓ • Psoriatic arthritis



Case 2

- This record setting running back was told he had abnormal blood test results in his early 30's while asymptomatic but later developed swollen toes at approximately age 42 and has battled this condition since then:

- Walter Payton
- Barry Sanders
- Christian Okoye
- Emmitt Smith
- Franco Harris



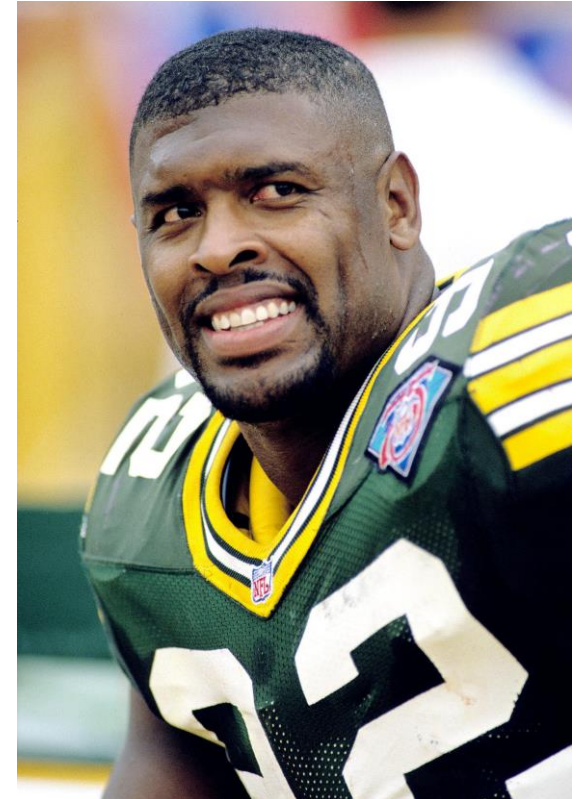
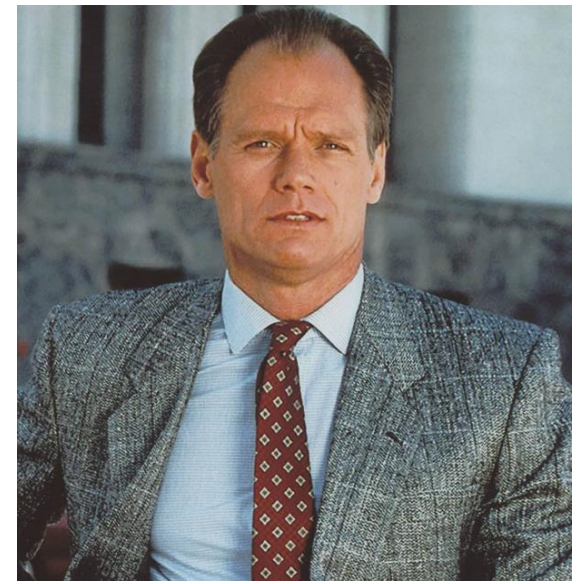
What is the diagnosis?

- Calcium pyrophosphate deposition (CPPD)
- ✓ • Gout
- Turf toe
- Dactylitis
- Hydroxyapatite crystal arthritis

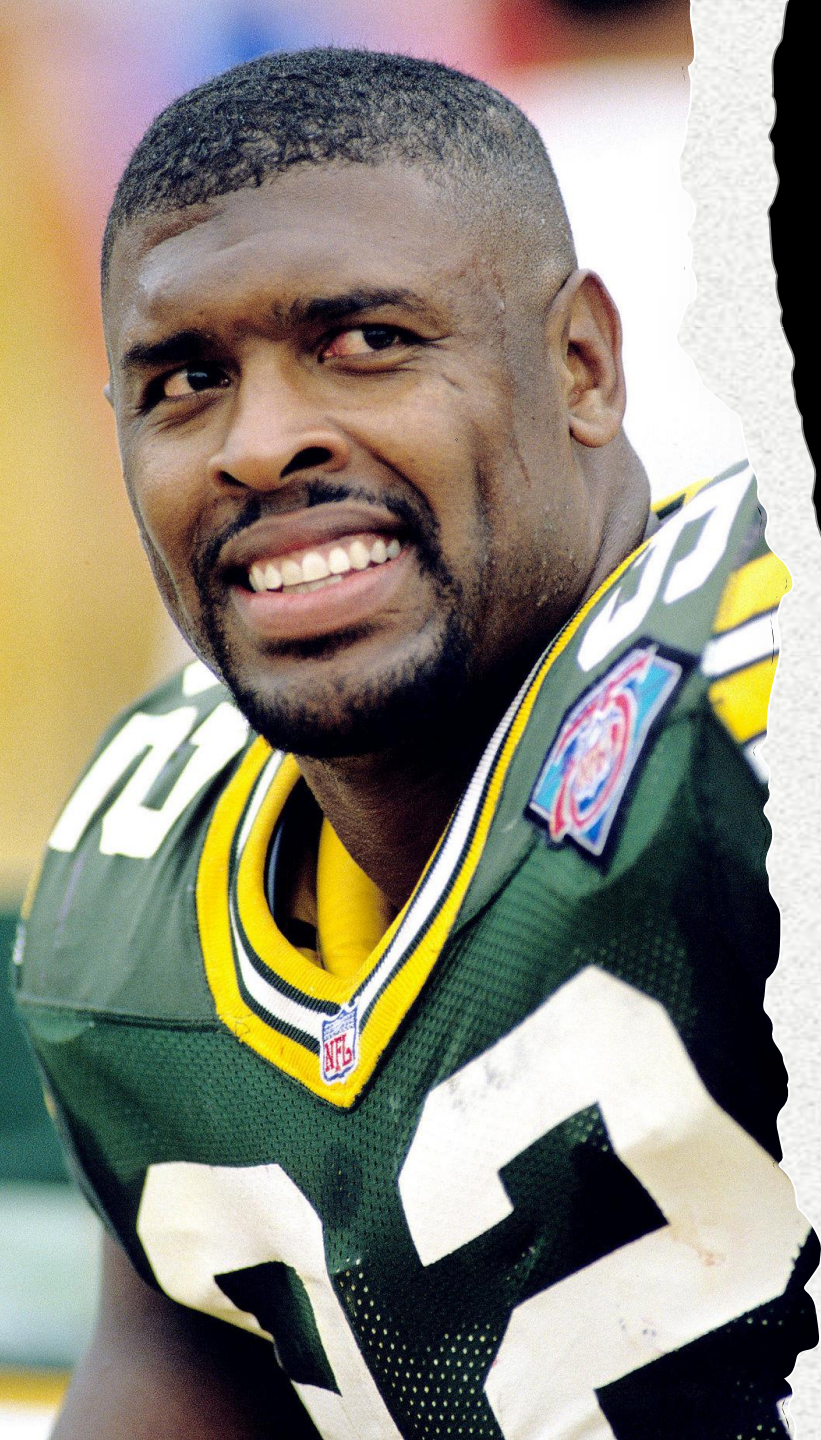


Case 3

- This football player menaced quarterbacks and running backs alike in the USFL and NFL, setting records for sacks per season but had severe complications in 2004 at age 43 from an inflammatory condition in his lungs
- Lawrence Taylor
- Fred Dryer
- 'mean' Joe Greene
- Reggie White



What is this multi-system inflammatory condition?



In Loving Memory...

REGGIE WHITE
1961 - 2004



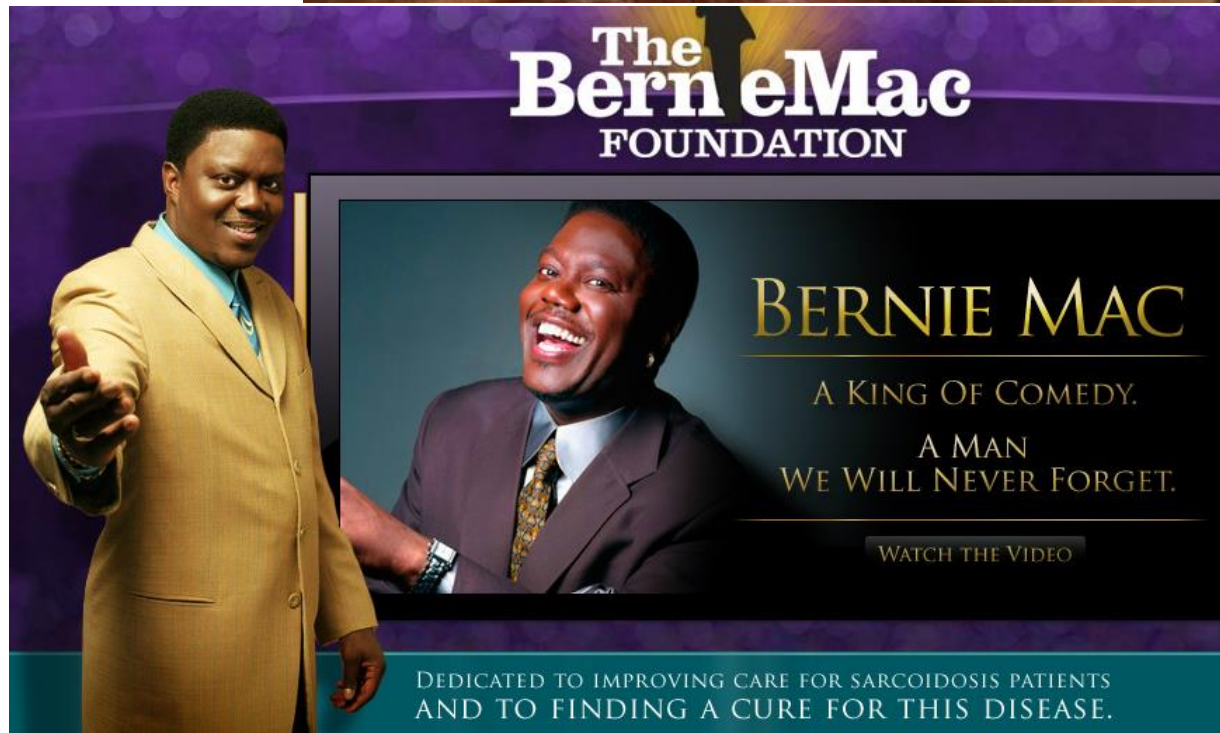
- Amyloidosis
- Asthma
- ✓ • Sarcoidosis
- Granulomatosis with polyangiitis
- Idiopathic pulmonary fibrosis

Sarcoidosis Key Points

- General:
 - Heterogeneous, Idiopathic
 - Non-caseating granulomas
- Clinically
 - 90% with lung domain
 - Eyes, liver, skin, CNS
 - Ca, ACE often ↑; nonspecific

Preliminary Report: White Died From Lung Ailment

Dec 26, 2004 at 06:00 PM



Ex: Sep 12 2008

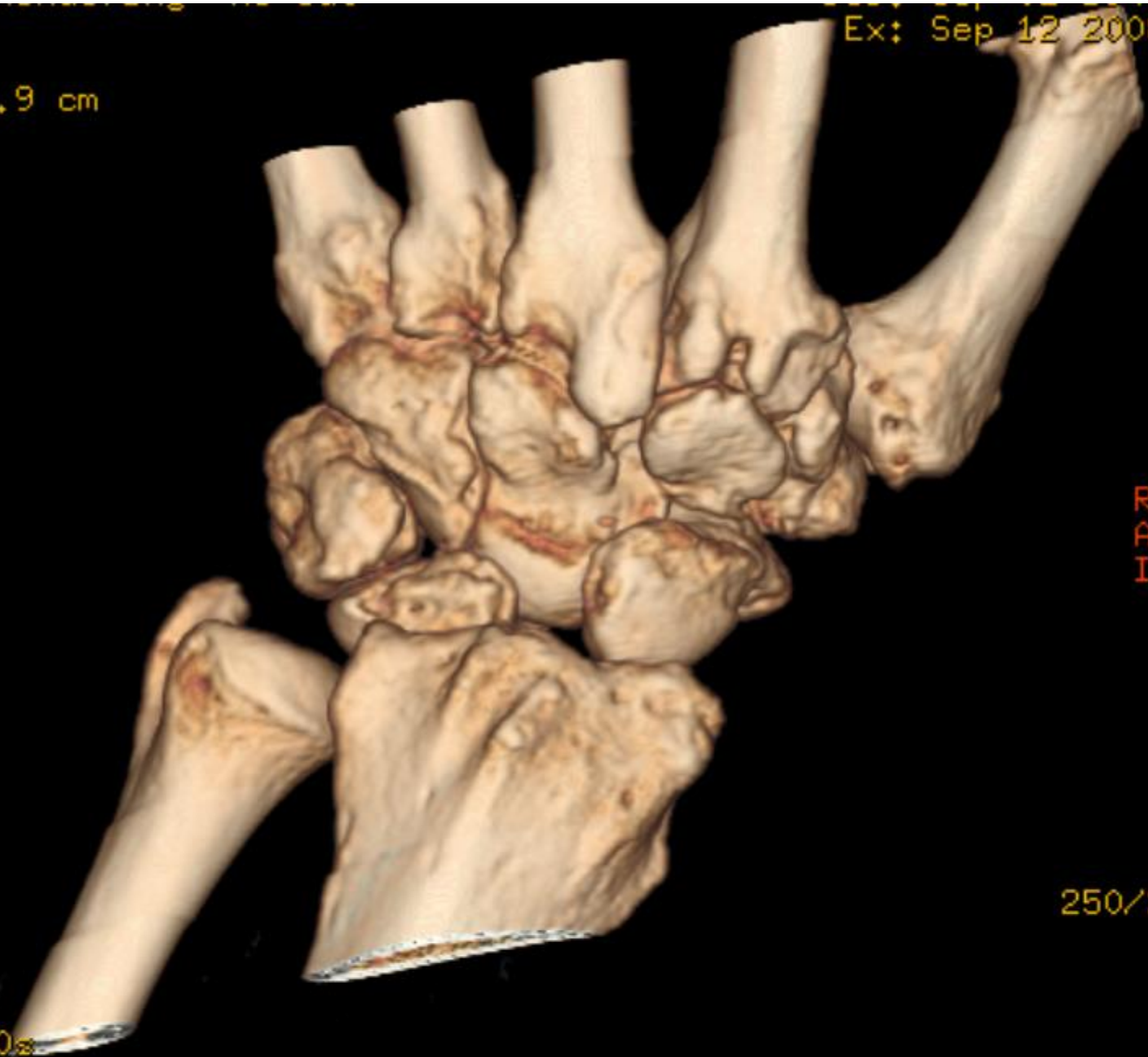
DFOV 12.9 cm
DETAIL

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No VOI
kv 120
mA 300
Rot 1.00s
0.6mm / 0.6sp
Tilt: 0.0

250/2



Ex: Sep 12 2008

DFOV 12.9 cm
DETAIL

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No VOI
kv 120
mA 300
Rot 1.00s
0.6mm / 0.6sp
Tilt: 0.0

250/3



Ex: Sep 12 2008

DFOV 12.9 cm
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No VOI
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mA 300
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Tilt: 0.0

250/4



Ex: 5 Sep 12 2008

DFOV 12.9 cm
DETAIL

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No VOI
kv 120
mA 300
Rot 1.00s
0.6mm / 0.6sp
Tilt: 0.0

250/5



Ex: Sep 12 2008

DFOV 12.9 cm
DETAIL

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No VOI
kv 120
mA 300
Rot 1.00s
0.6mm /0.6sp
Tilt: 0.0

250/6



Ex: Sep 12 2008

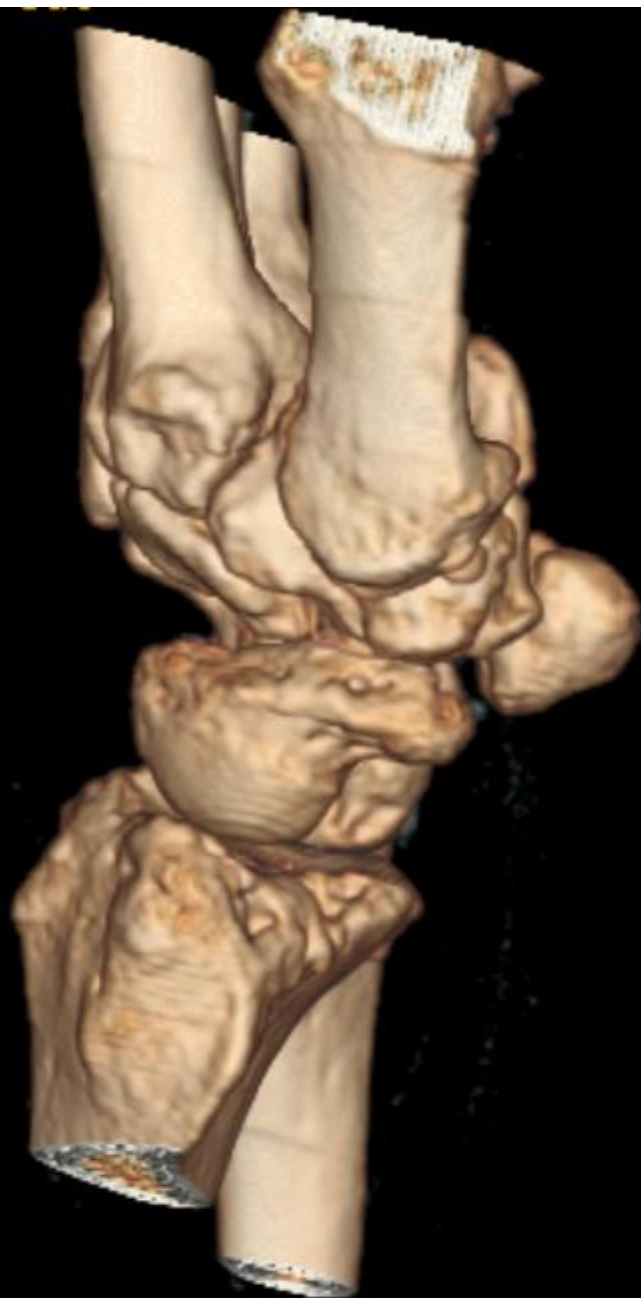
DFOV 12.9 cm
DETAIL

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No VOI
kv 120
mA 300
Rot 1.00s
0.6mm /0.6sp
Tilt: 0.0

250/7



Ex: Sep 12 2008

DFOV 12.9 cm
DETAIL

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No VOI
kv 120
mA 300
Rot 1.00s
0.6mm /0.6sp
Tilt: 0.0

250/8



Ex: Sep 12 2008

DFOV 12.9 cm
DETAIL

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No VOI
kv 120
mA 300
Rot 1.00s
0.6mm /0.6sp
Tilt: 0.0

250/9



Ex: Sep 12 2008

DFOV 12.9 cm
DETAIL

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S
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No VOI
kv 120
mA 300
Rot 1.00s
0.6mm /0.6sp
Tilt: 0.0

250/10



Ex: Sep 12 2008

DFOW 12.9 cm
DETAIL

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No VOI
kv 120
mA 300
Rot 1.00s
0.6mm /0.6sp
Tilt: 0.0

250/11



Ex: Sep 12 2008

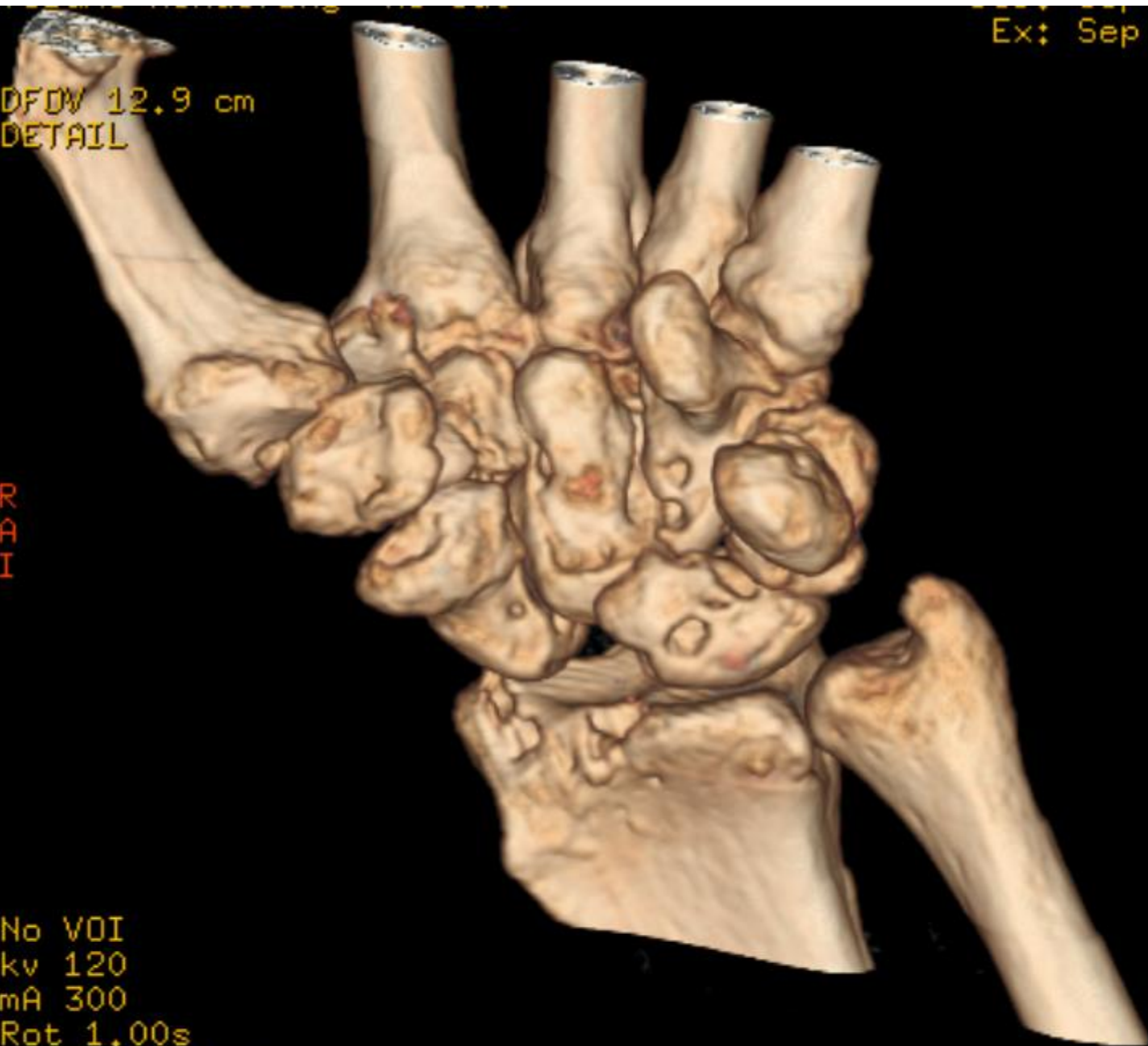
DFDW 12.9 cm
DETAIL

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No VOI
kv 120
mA 300
Rot 1.00s
0.6mm /0.6sp
Tilt: 0.0

250/12



Ex: Sep 12 2008

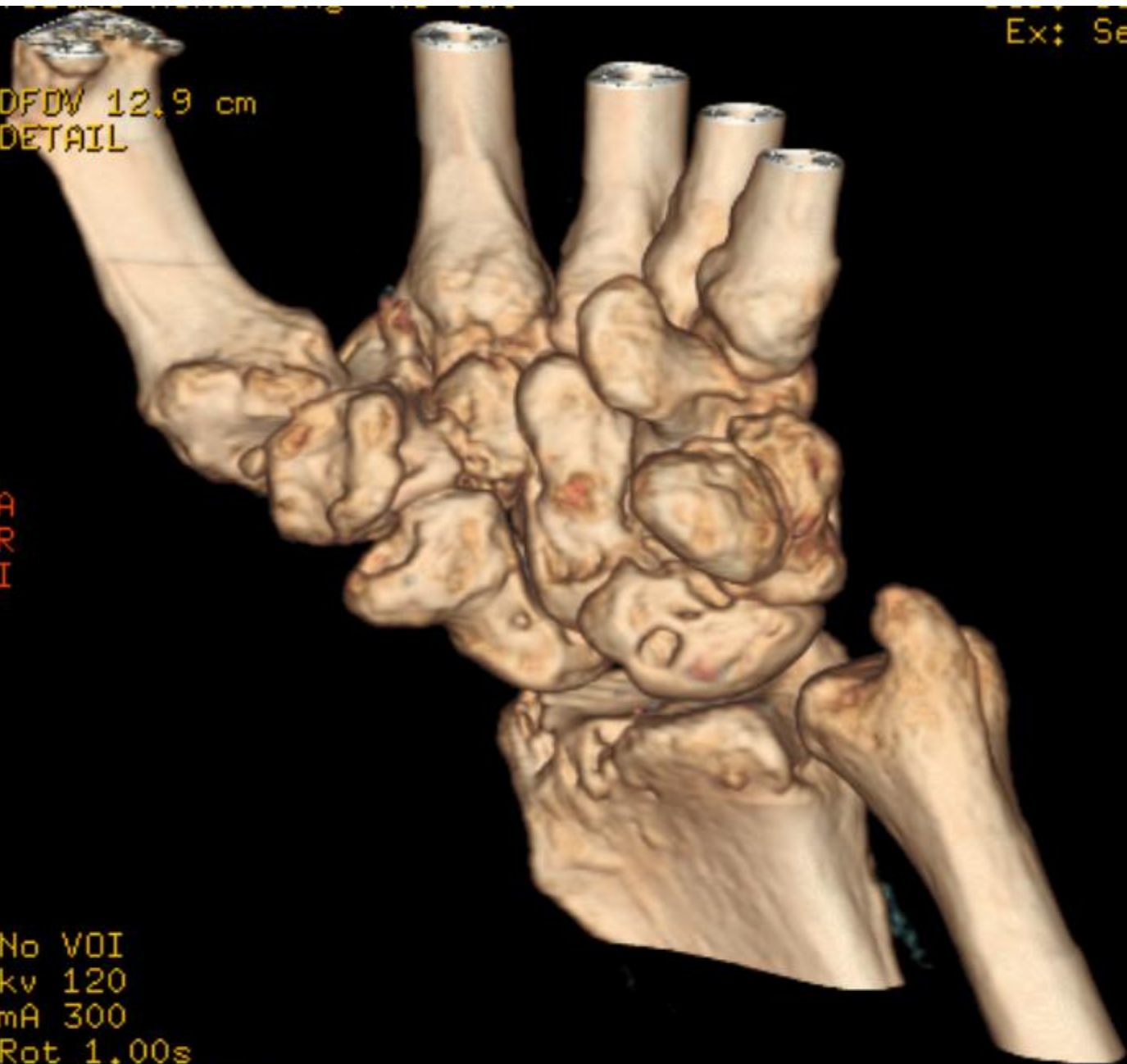
DFDW 12.9 cm
DETAIL

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No VOI
kv 120
mA 300
Rot 1.00s
0.6mm /0.6sp
Tilt: 0.0

250/13



Ex: Sep 12 2008

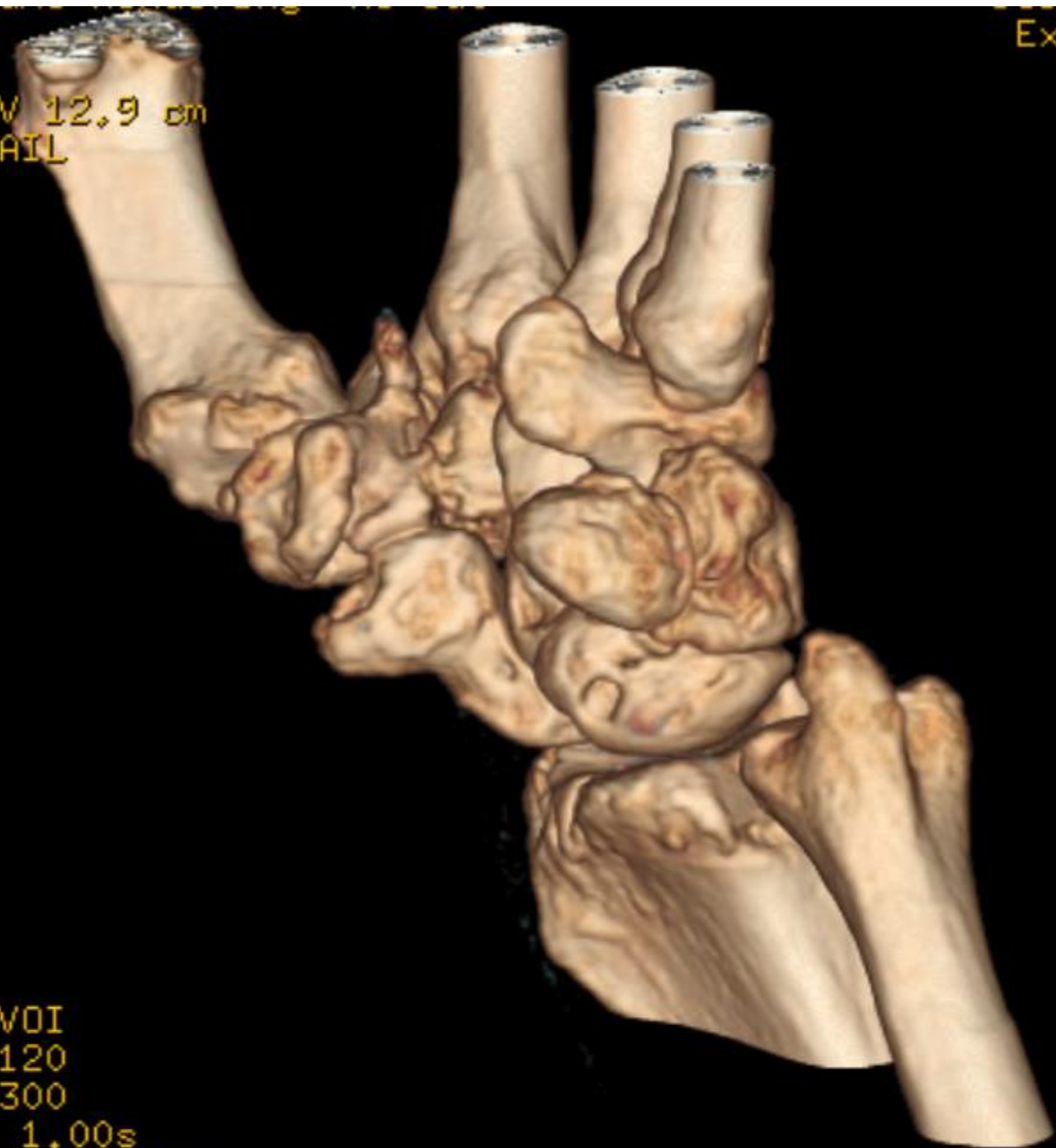
DFOV 12.9 cm
DETAIL

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No VOI
kv 120
mA 300
Rot 1.00s
0.6mm /0.6sp
Tilt: 0.0

250/14



Ex: Sep 12 2008

DFOV 12.9 cm
DETAIL

A
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S

P
L
I

No VOI
kv 120
mA 300
Rot 1.00s
0.6mm /0.6sp
Tilt: 0.0

250/15



Ex: Sep 12 2008

DFOV 12.9 cm
DETAIL

A
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L

P
I
R

No VOI
kv 120
mA 300
Rot 1.00s
0.6mm /0.6sp
Tilt: 0.0

250/16



Ex: Sep 12 2008

DFOV 12.9 cm
DETAIL

A
L
S

P
R
I



No VOI
kv 120
mA 300
Rot 1.00s
0.6mm /0.6sp
Tilt: 0.0

250/17

Ex: Sep 12 2008

DFOV 12.9 cm
DETAIL

L
A
S

R
P
I



No VOI
kv 120
mA 300
Rot 1.00s
0.6mm / 0.6sp
Tilt: 0.0

250/18

Ex: Sep 12 2008

DFOV 12.9 cm
DETAIL

L
A
S

R
P
I

No VOI
kv 120
mA 300
Rot 1.00s
0.6mm /0.6sp
Tilt: 0.0

250/19



Sarcoidosis Pearls

- LÖFGREN'S syndrome
 - Hilar Lymphadenopathy
 - Erythema Nodosum
 - Arthritis



- LUPUS PERNIO
 - Misnomer
- Sarcoid arthritis
 - RA mimic
 - Erosive granulomas
- Treatments
 - Corticosteroids
 - Methotrexate
 - TNF α inhibitors
 - infliximab



Case 4

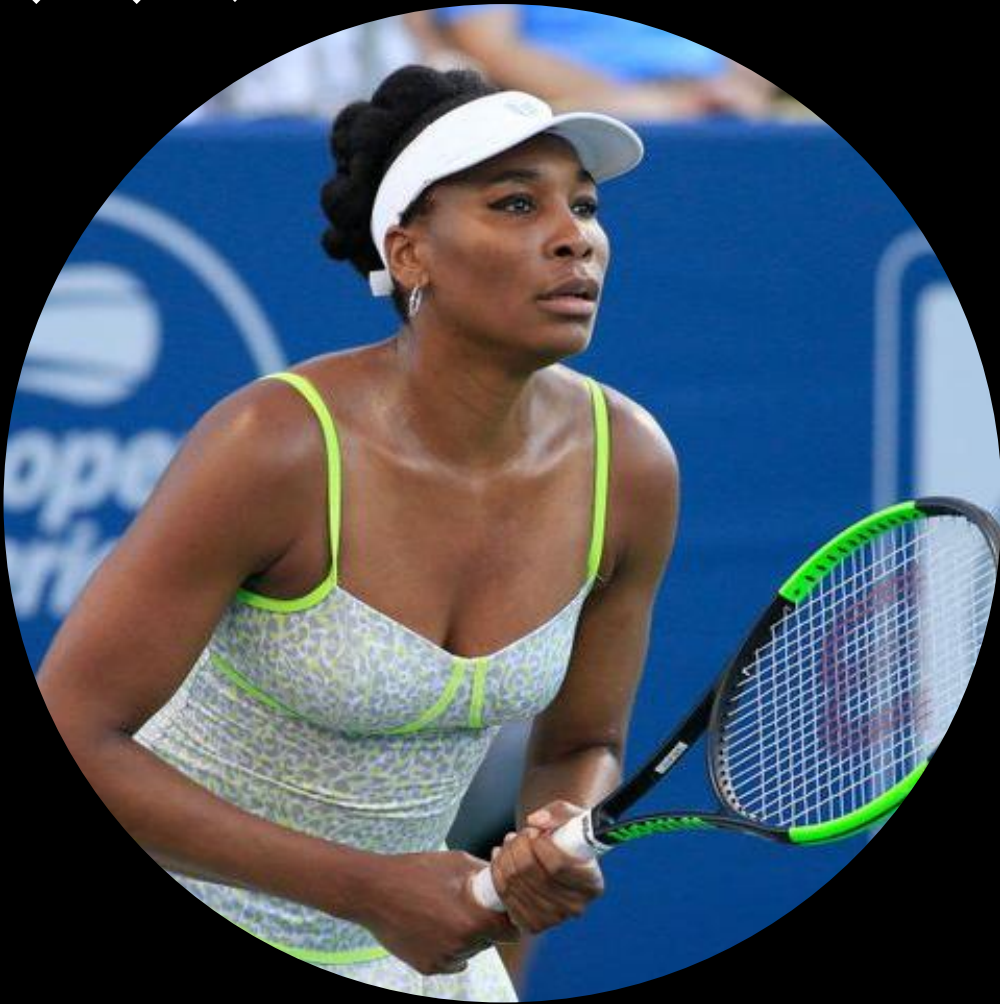
This female athlete played tennis at some of the highest levels until having to sit out a year of the ATP tour from fatigue and arthralgias. The condition does not typically cause swollen joints but does feature mucocutaneous dryness. Eventually though with education and management, she successfully returned to the tour.



Who is this woman?

- Caroline Wozniacki
- Monica Seles
- Venus Williams
- Martina Navratilova





What is the diagnosis?

- Lyme disease
- Chronic Epstein Barr
- IgG4 related disease
- ✓ • Sjogren's syndrome
- Myalgic encephalomyelitis



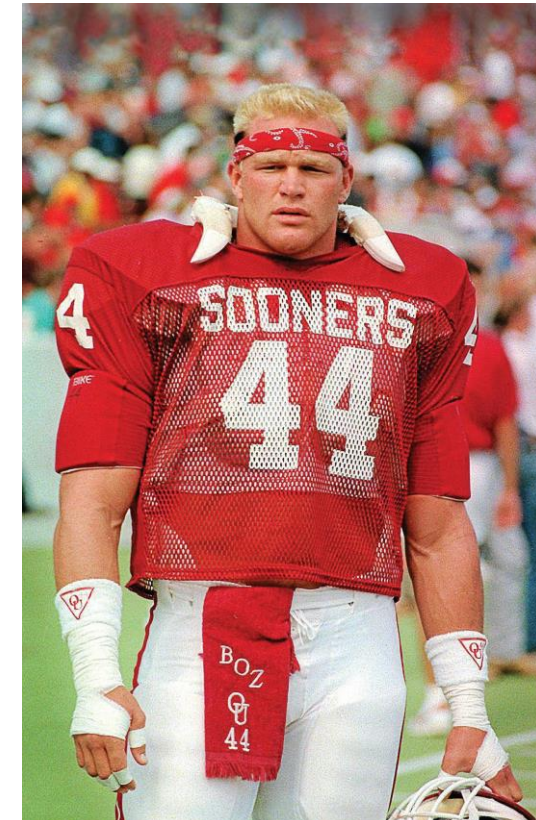
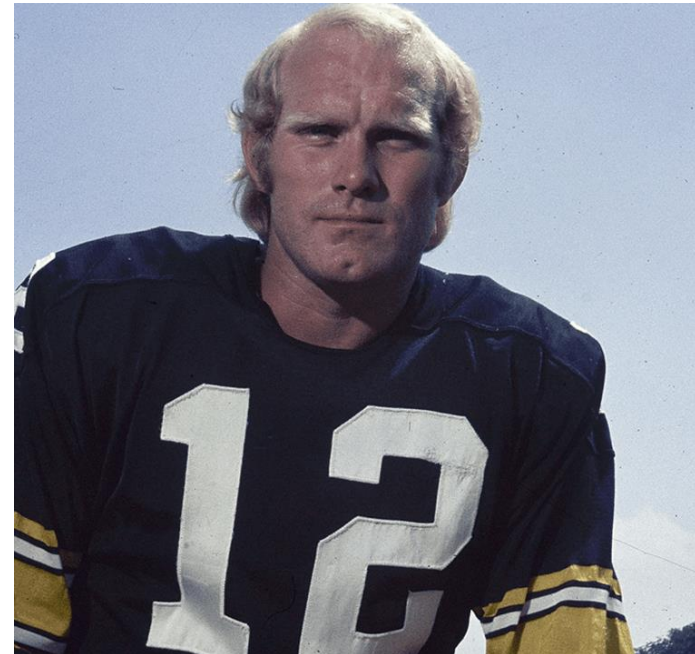


Case 5

- This former NFL star entered the broadcaster's booth soon after his playing days and remains an influential media voice but also serves as a patient and spokesman for the American College of Rheumatology after his inflammatory diagnosis:

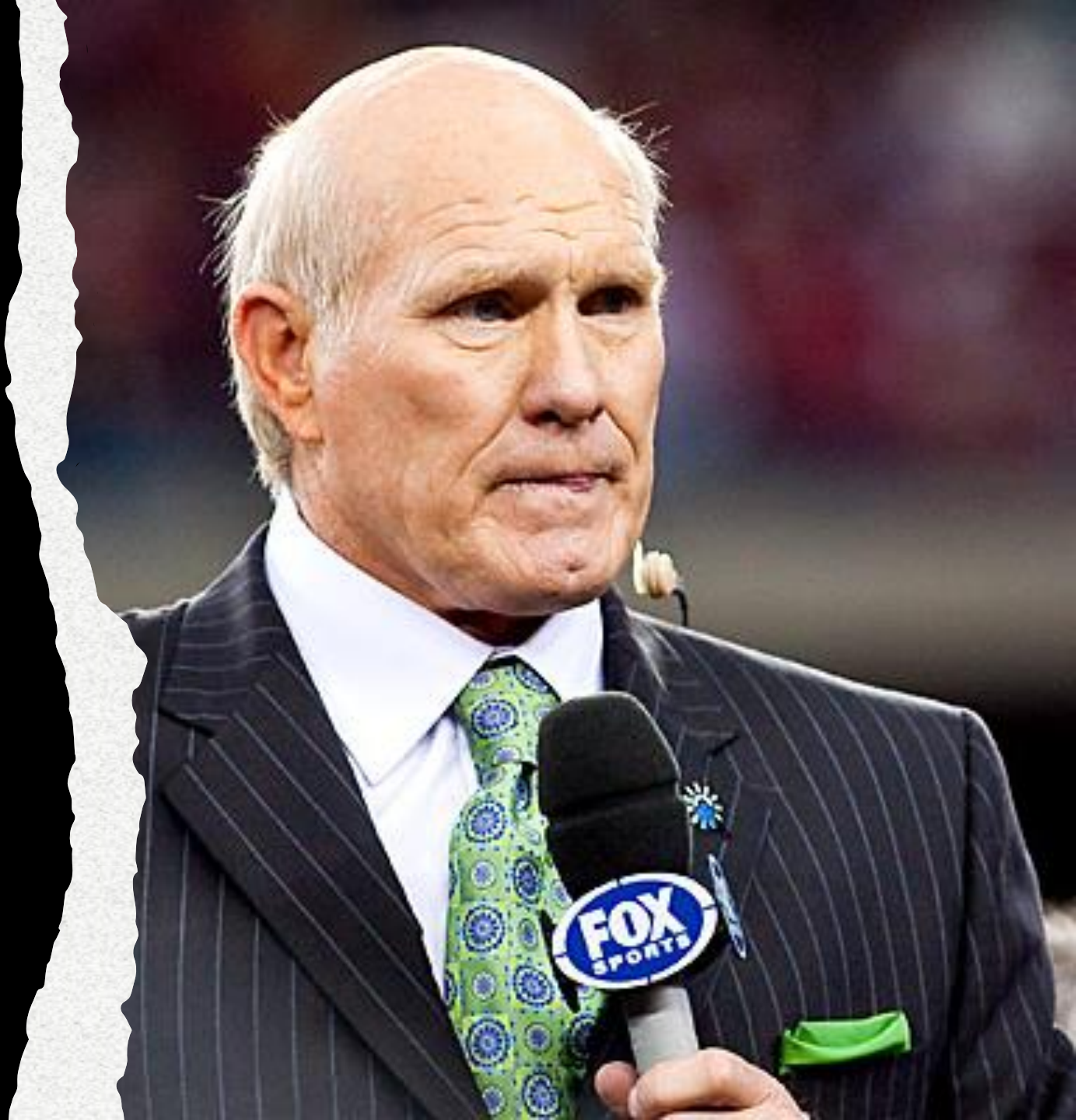


- Boomer Esiason
- Terry Bradshaw
- Cris Collinsworth
- Phil Simms
- Brian Bosworth



Diagnosis?

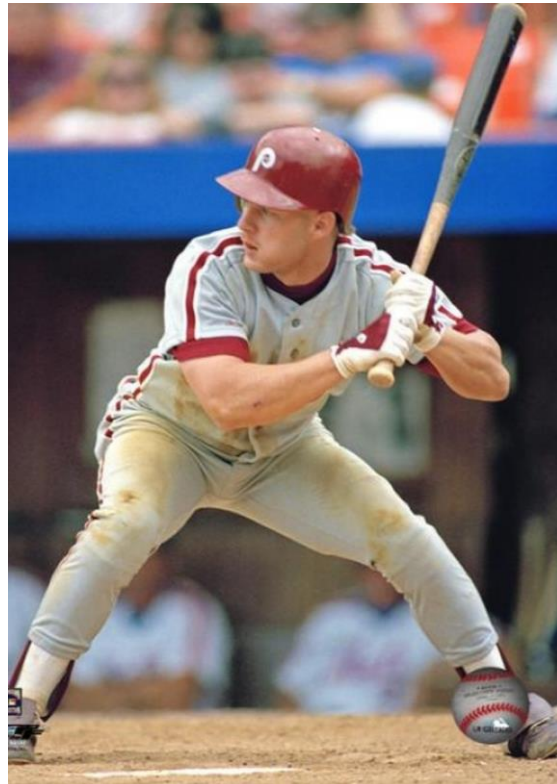
- ✓ • Rheumatoid arthritis
- Polymyalgia rheumatica
- Alopecia areata
- Familial Mediterranean fever
- Acromegaly



Case 6

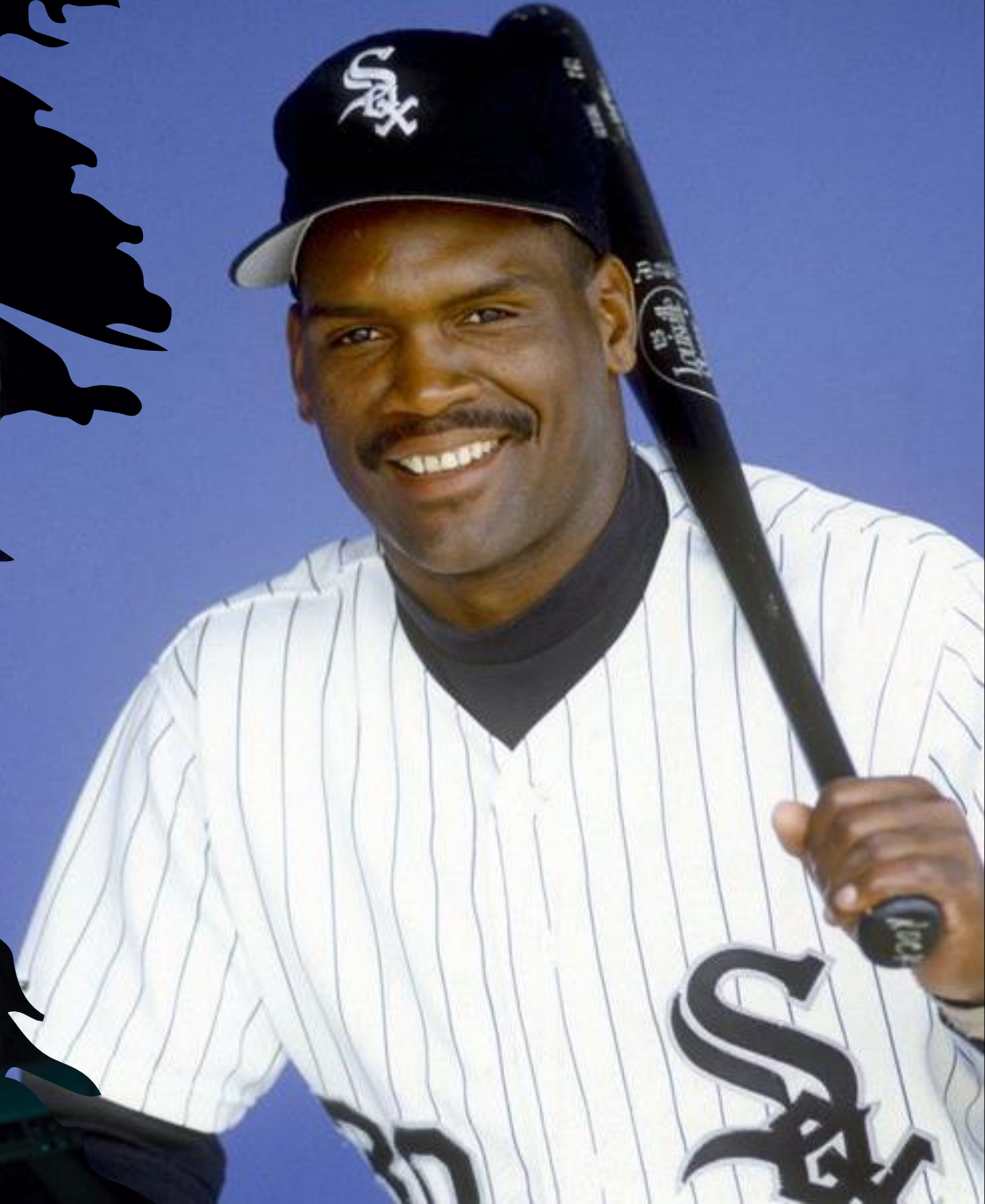
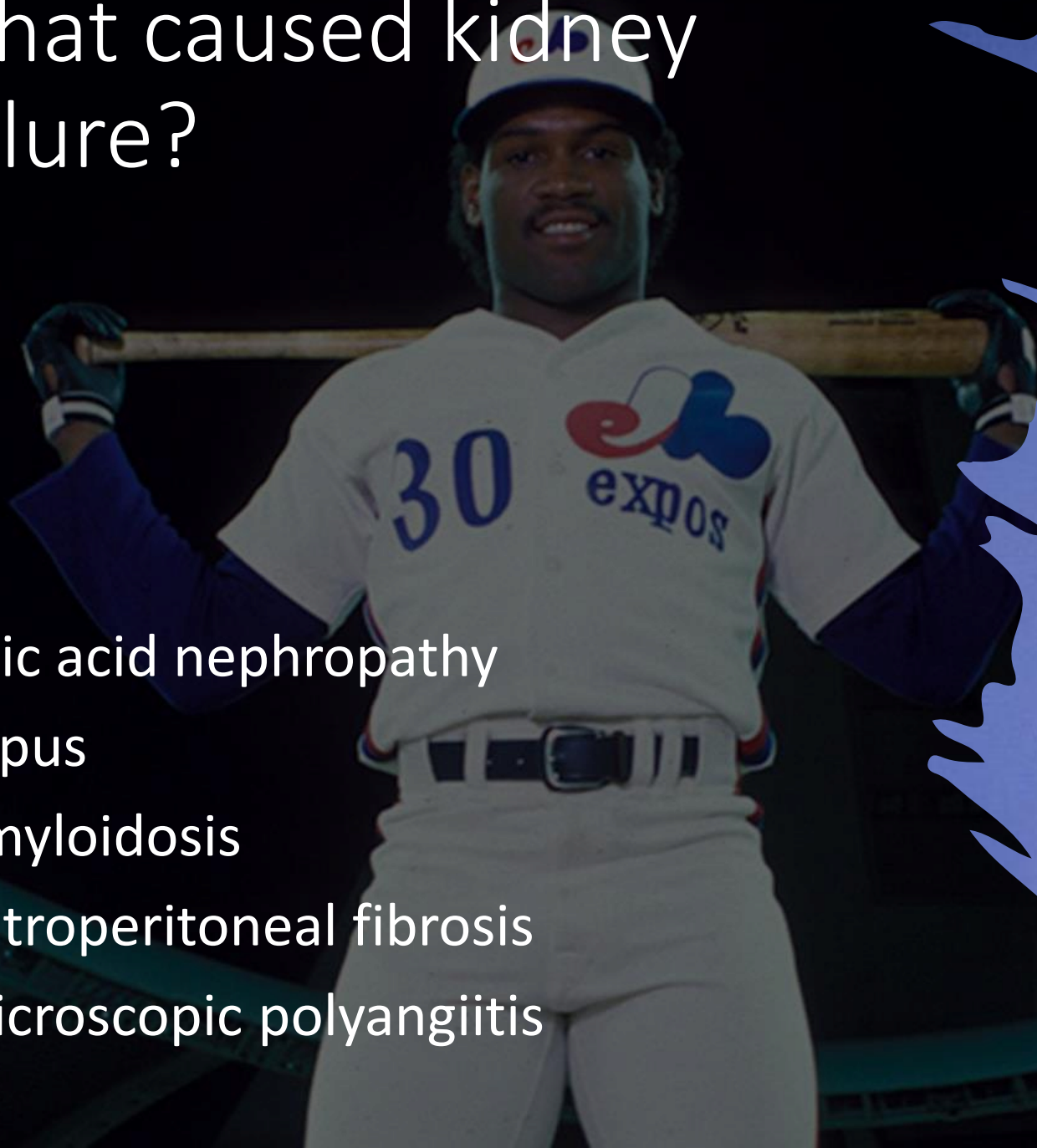
This feared leadoff hitter in MLB holds the distinction of playing in 4 decades and only after developing kidney failure from an autoimmune disease, did he eventually have to retire, only to be inducted into the HOF in 2017:

- Ricky Henderson
- Lenny Dykstra
- Vince Coleman
- Derek Jeter
- Tim Lincecum



What caused kidney failure?

- Uric acid nephropathy
- ✓ • Lupus
- Amyloidosis
- Retroperitoneal fibrosis
- Microscopic polyangiitis

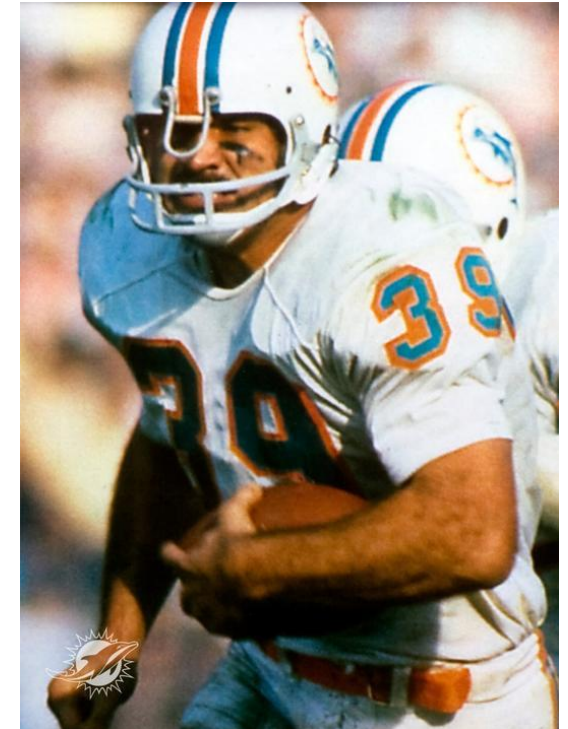
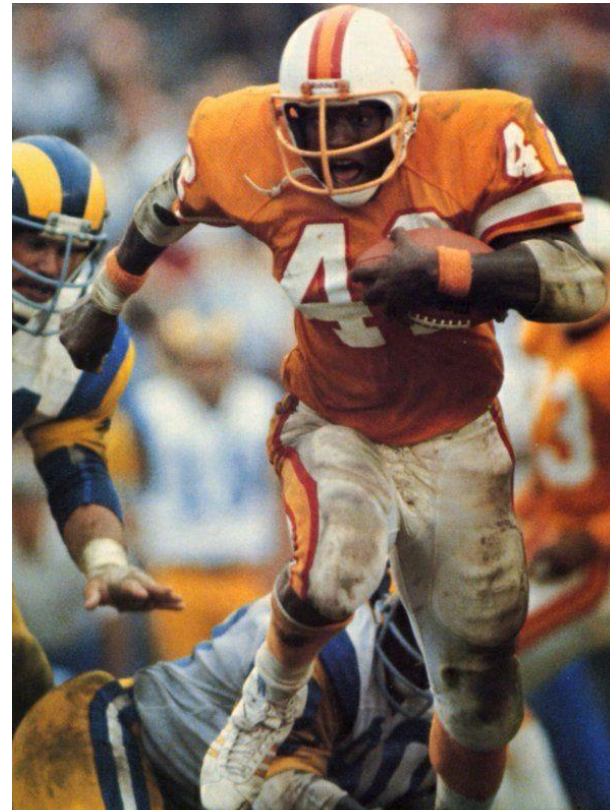


Case 7



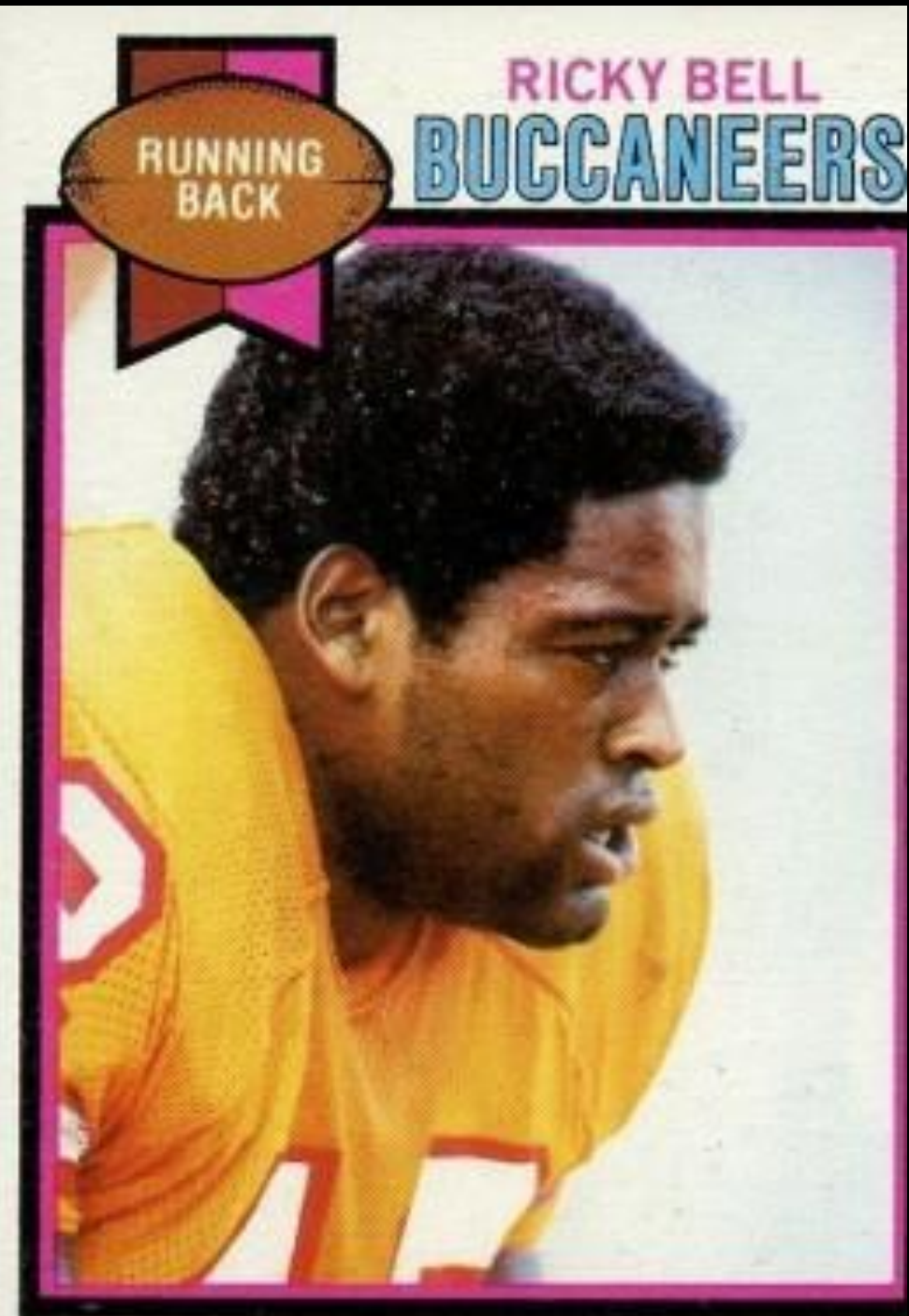
- This former Heisman Trophy runner up and 1st overall pick in the 1977 NFL draft had several successful years and was one win from a superbowl but in his 5th year developed weight loss, chronic muscle weakness and rashes and eventually led to his early retirement

- Marcus Allen
- Tony Dorsett
- Larry Csonka
- Ricky Bell
- Eric Dickerson



Diagnosis?

- Polyarteritis nodosa
- Mixed connective tissue disease
- Celiac disease
- ✓ • Dermatomyositis
- Scleroderma



47 yo lady with gradual onset of fatigue and itchy scaly rash on hands over the past month. What test is most helpful in diagnosis?

1. anti-double stranded DNA
2. hepatitis C antibody
3. angiotensin converting enzyme
4. anti-nuclear antibody
- ✓ 5. creatine phosphokinase



Idiopathic Inflammatory Myopathy

- Uncommon idiopathic heterogeneous inflammatory muscle disorders featuring **proximal** muscle weakness
 - Adult **Polymyositis**
 - Adult **Dermatomyositis**
 - Childhood DM
 - PM/DM associated with other CTD

Epidemiology

- Rare: incidence from 2-10 new cases/ million persons (underestimate?)
- Bimodal: 10-15 yrs, 45-55 yrs
- 3-4:1 African-American to White
- F:M 2-3:1
- Overlap syndromes (scleroderma, lupus, MCTD)

Pathophysiology

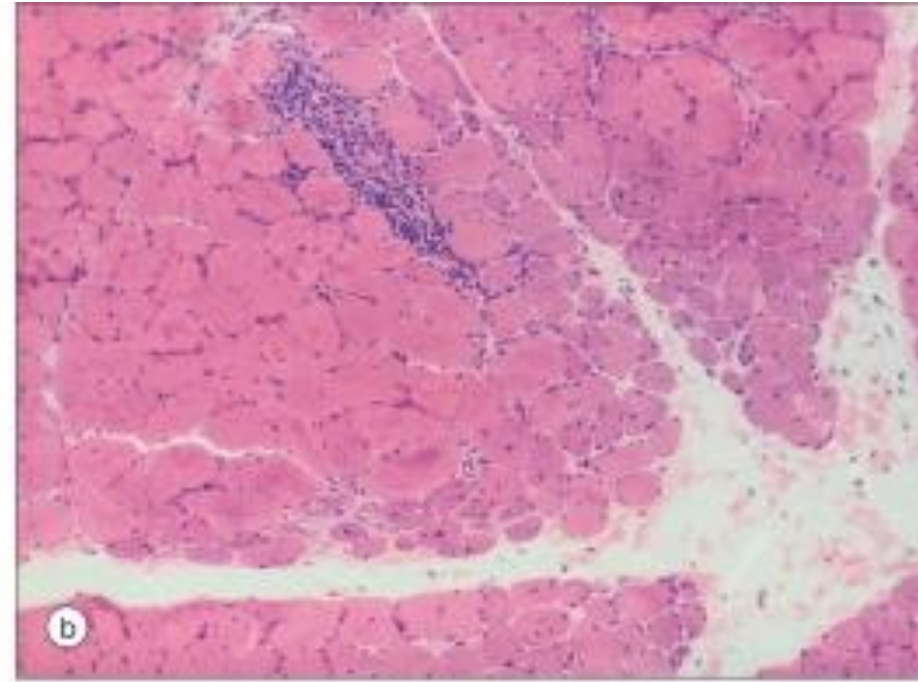
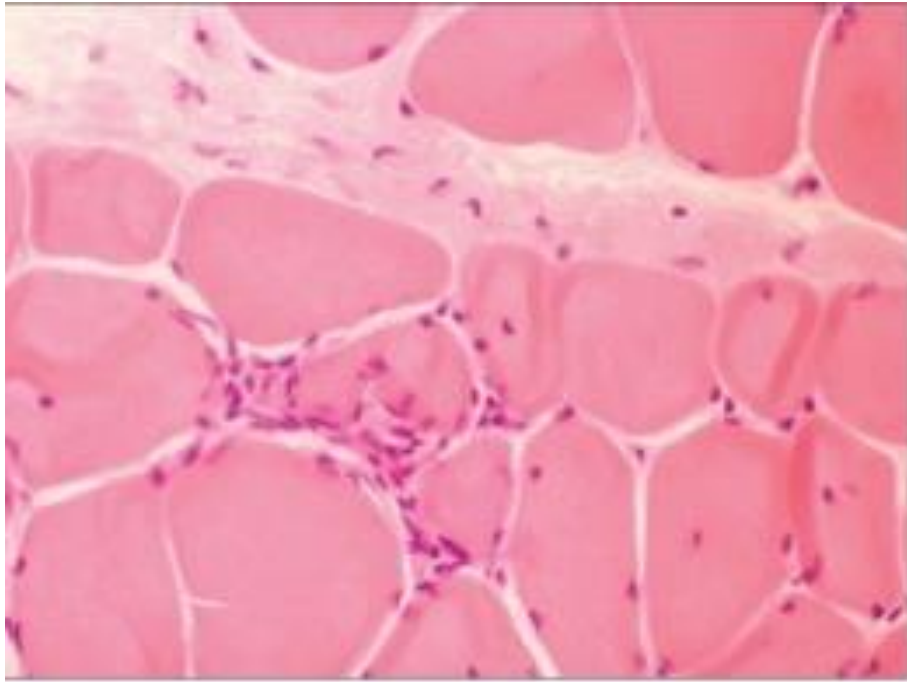
- B lymphocytes (myositis specific auto-Ab)
- Pro-inflammatory cascade:
 - chemokines
 - complement activation
 - IL-1 and TNF
 - focal inflammation, death, repair

- **Polymyositis**

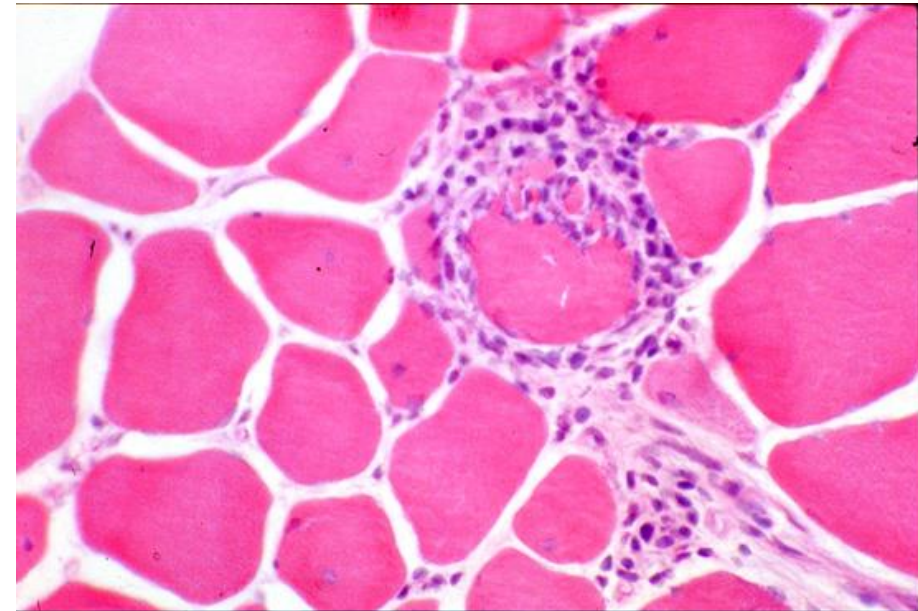
- Inflammatory infiltrate within **fascicle**.
- Cytotoxic **CD8**+T cells
- Scattered or isolated necrotic fibers.
- Target= **myofiber**.

- **Dermatomyositis**

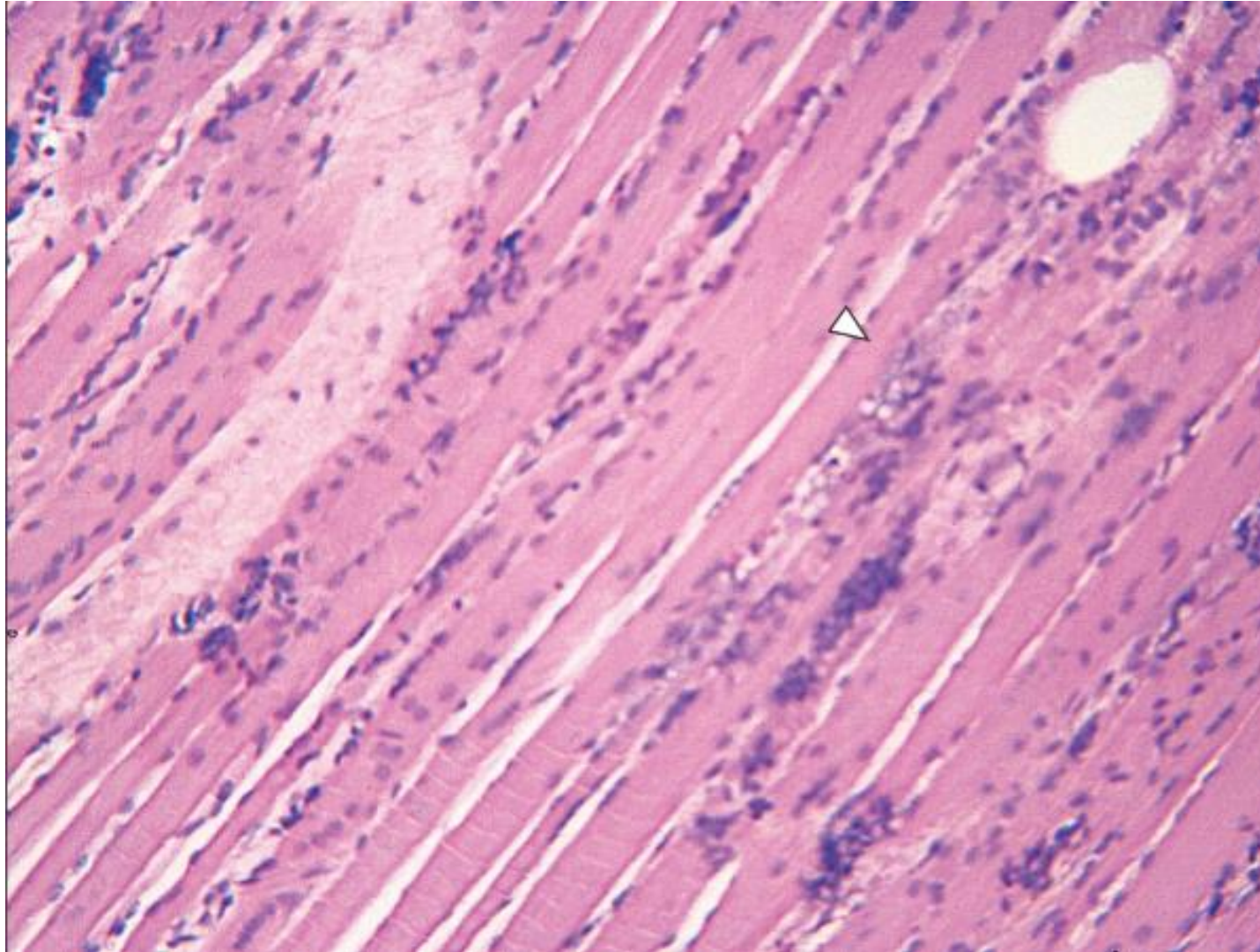
- **Perivascular** infiltrate around fascicles.
- **CD4**+T cells
- Necrotic fibers in group.
- Target= **blood vessels**.



- **Hematoxylin and Eosin cross-section of polymyositis:**
 - **necrosis, regeneration and inflammation**
 - **lymphocytic infiltration**



Polymyositis: longitudinal



myofiber destruction; areas of degeneration and necrosis of myofibers in association with interstitial lymphocytic infiltration

Bohan and Peter Classification (1975)

1. Symmetrical proximal muscle weakness

insidious and proximal muscles

2. Muscle biopsy evidence of myositis

necrosis, phagocytosis, regeneration, atrophy, perivasc infiltrate

3. Increase in serum skeletal muscle enzymes

CPK, aldolase, LDH, AST, ALT

4. Characteristic electromyographic pattern

short polyphasic motor units, fibrillations, irritability and repetitive dc's

5. Typical rash of dermatomyositis

heliotrope, gottrons, shawl, v neck

Polymyositis:

Definite: all of 1-4

Probable: any 3 of 1-4

Possible: any 2 of 1-4

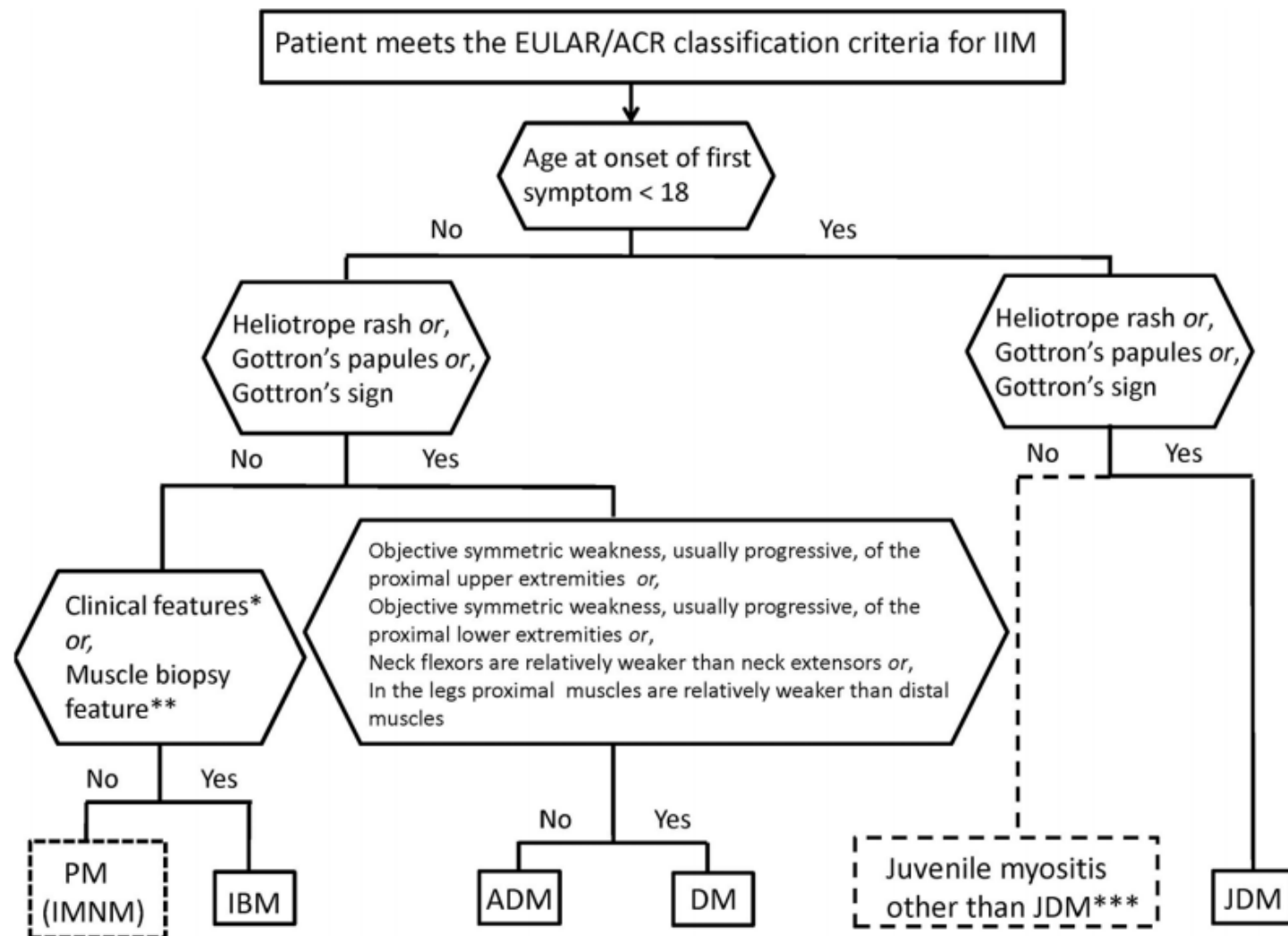
Dermatomyositis:

Definite: 5 plus any 3 of 1-4

Probable: 5 plus any 2 of 1-4

Possible: 5 plus any 1 of 1-4

2017 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies and Their Major Subgroups



Diagnosis: Muscle Enzymes

- Diagnosis; monitoring
 - Enzymes leak
- Sensitivity:
 - CPK>aldolase>ALT/AST>LDH
- Lack of specificity
 - Trauma
 - Benign hyper-ck-emia
 - African American
 - Exercise



Diagnosis: Muscle Biopsy

- Gold standard for confirmation
- Pitfalls:
 - patchy disease and sampling error
 - Most myopathic muscle has highest yield
 - Biopsy the contralateral muscle to EMG
- Role of MRI mapping?

Clinical Features - Muscle

- Nonspecific fatigue, fevers, weight loss
 - constitutional vs malignancy
- Usually painless symmetrical muscle weakness:
 - proximal>distal
 - stairs, toileting, abduction, neck flexion
 - gait abnormalities
- Dysphagia
- Hoarseness

Clinical Features - Skin

- May precede, develop simultaneously or subsequently
- Heliotrope rash
- Shawl sign
- V neck sign
- Gottron's papules
 - scaly, erythematous/violaceous
 - papules and plaques
 - metacarpophalangeal and interphalangeal joints



Heliotrope rash

Erythematous/violaceous rash over the eyelids,
face with/without perioribital edema

Clinical Features: shawl and v neck signs





Gottron's papules
dilated capillary nailfold loops
Samitz sign

Treatment: Medications

- Glucocorticoids:
 - high dose prednisone 1 mg/kg/day
 - taper gradually after 4 weeks
- Immunosuppressants:
 - azathioprine
 - methotrexate (unless ILD)
 - cyclophosphamide
 - mycophenolate mofetil
 - tacrolimus
- IVIg – monthly (especially for anti-HMG-coA reductase)
- B cell depletion:
 - rituximab

Prognosis

- Rehabilitation: muscle reserves
 - passive/active assisted ROM exercises
 - strengthening/hypertrophy of reserves
- Mortality:
 - pulmonary or systemic complications
 - malignancy
 - medications, infections
- Poor markers:
 - older age at diagnosis
 - delayed treatment
 - cardiac and pulmonary involvement

Component	CK	REPORT	LDH
Latest Ref <u>Rng</u>	15 - 170 IU/L	< OR = 8.1	91 - 180 IU/L
10/15/2009	6902 (H)	<u>Aldolase</u> : 75.2 (H)	1340 (H)

Component	CK	REPORT	LDH
Latest Ref <u>Rng</u>	15 - 170 IU/L	< OR = 8.1	91 - 180 IU/L
10/15/2009	6902 (H)	<u>Aldolase</u> : 75.2 (H)	1340 (H)
10/23/2009			
10/30/2009	5370 (H)		1319 (H)
11/2/2009			
11/6/2009	7420 (H)	<u>Aldolase</u> : 101.1 (H)	1449 (H)
11/7/2009			
11/30/2009	4024 (H)	<u>Aldolase</u> : 82.6 (H)	1053 (H)
12/11/2009	3314 (H)	<u>Aldolase</u> : 67.8 (H)	772 (H)
1/5/2010	2418 (H)	<u>Aldolase</u> : 50.4 (H)	664 (H)
1/22/2010	251 (H)		459 (H)
2/17/2010	2459 (H)		519 (H)
3/18/2010	913 (H)	<u>Aldolase</u> : 17.8 (H)	345 (H)
4/27/2010	571 (H)	<u>Aldolase</u> : 10.0 (H)	249 (H)
6/3/2010	252 (H)	<u>Aldolase</u> : 4.5	183 (H)
8/11/2010	150	<u>Aldolase</u> : 4.0	175

Case 1 – severe exercise intolerance.....

- 24 year old college student notes significant myalgias after track and field practice and feels like he is even dragging his feet.

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Component	CK
Latest Ref R	<=398 U/L

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Component	CK
Latest Ref R	<=398 U/L
2/12/2013	498651 (H)

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- Treatment

Component	CK
Latest Ref R	<=398 U/L
2/12/2013	498651 (H)

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Component	CK
Latest Ref R	<=398 U/L
2/12/2013	498651 (H)
2/13/2013	368800 (H)
2/19/2015	31,161 (H)
4/22/2015	301

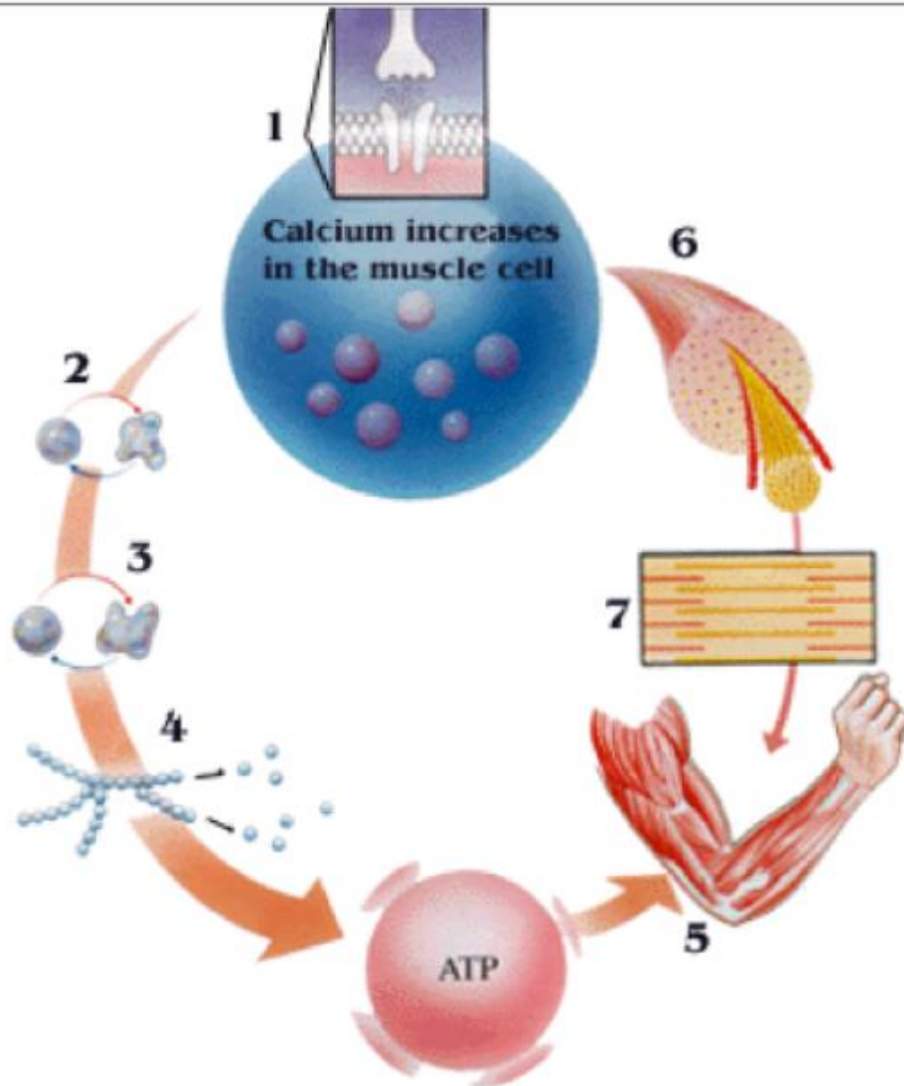
What is this condition?

- Muscle infarction
- ✓ • Metabolic myopathy
- Polymyositis
- Muscular dystrophy

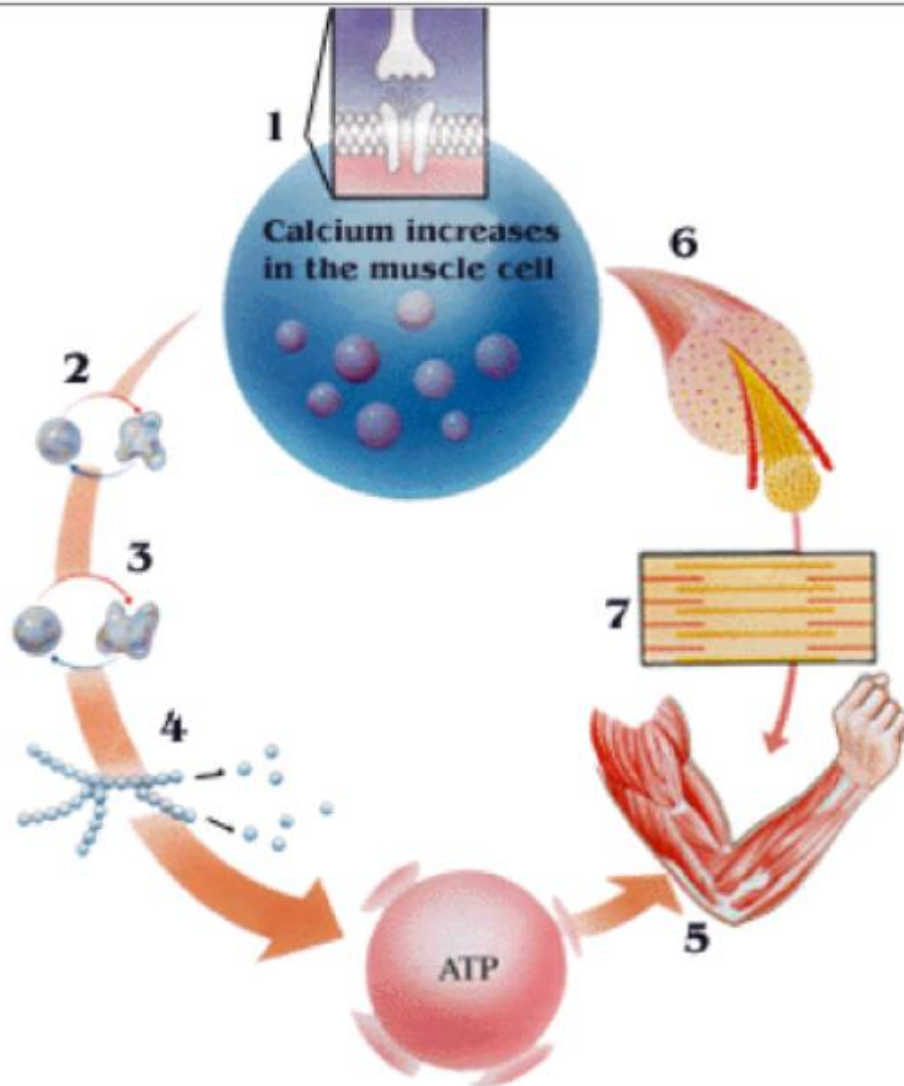
What was the treatment?

- glucocorticoids
- hemodialysis
- infliximab
- plasmapheresis
- ✓ • cautious monitoring and diet and exercise counseling

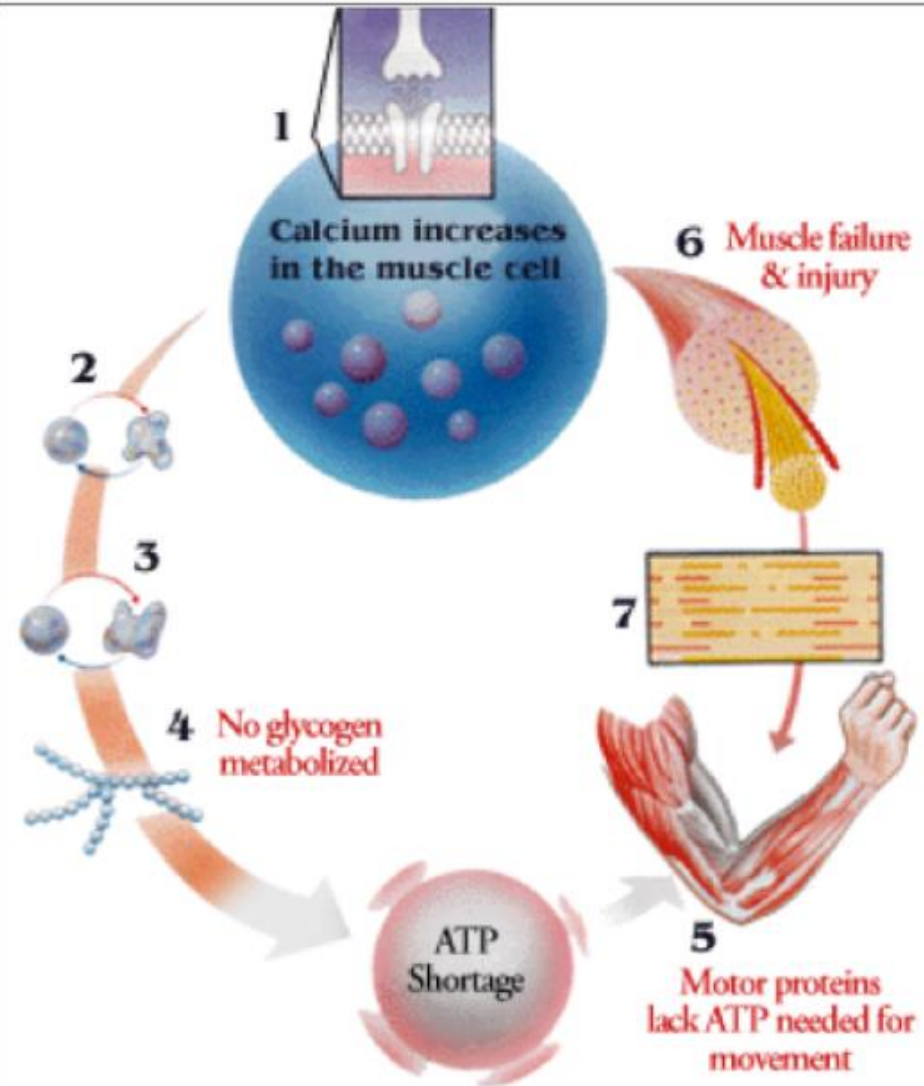
Normal Skeletal Muscle Contraction



Normal Skeletal Muscle Contraction



McArdle's Disease Muscle Contraction



Case 2: high cholesterol and muscle weakness

- 68 year old woman with hyperlipidemia and hypertension is unsuccessful controlling each with diet. She added red yeast rice. She started a gradual weight training program and stationary bicycling.
- Lisinopril/hydrochlorothiazide 10/25 mg & atorvastatin 10 mg daily added.
- Gradually she develops significant muscle weakness in thighs and shoulders.

Component	CK	ALDOLASE
Latest Ref R	<=234 U/L	< OR = 8.1 U/L
12/7/2017	6,058 (H)	64.1 (H)

What is the cause of these symptoms?

- ✓ Polymyositis
- ✓ Anti-HMG coA reductase associated myopathy
- Exercise induced hyper-ck-emia
- Hctz induced myopathy
- Red yeast rice side effect

Case 2: high cholesterol and muscle weakness

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- Gradually she develops significant muscle weakness in thighs and shoulders.
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REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Statin-Associated Autoimmune Myopathy

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STATINS SIGNIFICANTLY REDUCE THE INCIDENCE OF CARDIOVASCULAR disease, are generally safe, and have an acceptable side-effect profile. Indeed, a recent meta-analysis confirmed that mild musculoskeletal problems, such as myalgia, occur in approximately equal numbers of persons treated with statins and those given placebo.¹ Only in rare cases, in approximately 1 of 10,000 treated persons per year,² do statins cause serious muscle damage, with weakness and elevated levels of creatine kinase. In the majority of such cases, the patients recover spontaneously after the statin treatment is discontinued.^{3,4} It is now recognized, however, that in very rare cases, an autoimmune myopathy develops in patients treated with statins; this disorder is characterized by muscle weakness, evidence of muscle-cell necrosis on biopsy, and the presence of autoantibodies against 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase.⁵⁻¹⁶ In contrast to most patients who have side effects from statin therapy, those with statin-associated autoimmune myopathy may have progressive weakness that must be controlled with immunosuppressive therapy. This review describes the clinical characteristics, diagnosis, proposed pathologic mechanisms, and treatment of statin-associated autoimmune myopathy.

REMARKS	REFERRING PHYSICIAN	REPORTED 10/26/2017	11:53
	LEE	STATUS	FINAL

TEST	RESULT (* = OUT OF RANGE)	UNITS	REFERENCE RANGE
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TEST NAME: SEE BELOW

ANTI-HMGCR AB, (EIA)

RESULT: SEE BELOW

>200* Units

NORMAL RANGE: <20

NEGATIVE. <20
 WEAK POSITIVE. 20-39
 MODERATE POSITIVE. 40-59
 STRONG POSITIVE. ≥60

ANTI-HMGCR ANTIBODIES ARE USUALLY FOUND IN ASSOCIATION WITH NECROTIZING MYOPATHY RELATED TO STATIN THERAPY. HOWEVER, ABOUT 30% OF ANTI-HMGCR ANTIBODY POSITIVE PATIENTS WITH NECROTIZING MYOPATHY HAVE NEVER BEEN EXPOSED TO STATINS. THE LITERATURE SUGGESTS THAT FALSE POSITIVES ARE EXTREMELY RARE.

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10/15/2018	1,266 (H)	19.8 (H)
12/7/2018	371 (H)	10.3 (H)
12/27/2018	306 (H)	
1/28/2019	86	
4/9/2019	48	
5/7/2019	44	3.2
8/5/2019	55	
10/15/2019	114	

- IVIG started

Elevated creatine phosphokinase

General type

Denervating conditions
Sarcoidosis
Neuromuscular disorders
Genetic muscular dystrophies

Glycogen storage diseases
Lipid storage myopathies
Periodic paralyses
Endocrine myopathies

Metabolic myopathies
Toxic myopathies

Nutritional myopathies
Acute rhabdomyolysis
Proximal neuropathies

Subtypes/examples

Spinal muscular atrophies, amyotrophic lateral sclerosis

Eaton–Lambert syndrome, myasthenia gravis

Duchenne's facioscapulohumeral, limb girdle, Becker's, Emery–Dreifuss type, distal, ocular

Adult-onset acid maltase deficiency, McArdle's disease

Carnitine deficiency, carnitine palmityltransferase deficiency

Hypothyroidism, hyperthyroidism, acromegaly, Cushing's disease, Addison's disease, hyperparathyroidism, hypoparathyroidism, vitamin D deficiency myopathy, hypokalemia, hypocalcemia

Uremia, hepatic failure

Acute and chronic alcoholism, drugs including penicillamine, clofibrate, chloroquine, emetine, statins, niacin, colchicine

Vitamin E deficiency, malabsorption

Guillain–Barré syndrome, acute intermittent porphyria, diabetic lower-limb chronic plexopathies, chronic autoimmune polyneuropathy

In Summary

- Differentiate 'tiredness' vs 'fatigue' vs 'low energy'
- Recognize skin and biochemical changes of IIM
- CPK levels are nonspecific
 - proximal muscle weakness is key
- Recognize McArdle's in athletes
- Medications and drugs
 - Statins (anti-HMG coA reductase induced necrotizing myopathy)



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