LUTON & DUNSTABLE UNIVERSITY HOSPITAL

UCL Medical School Clinical Teaching Hospital

Random stuff!

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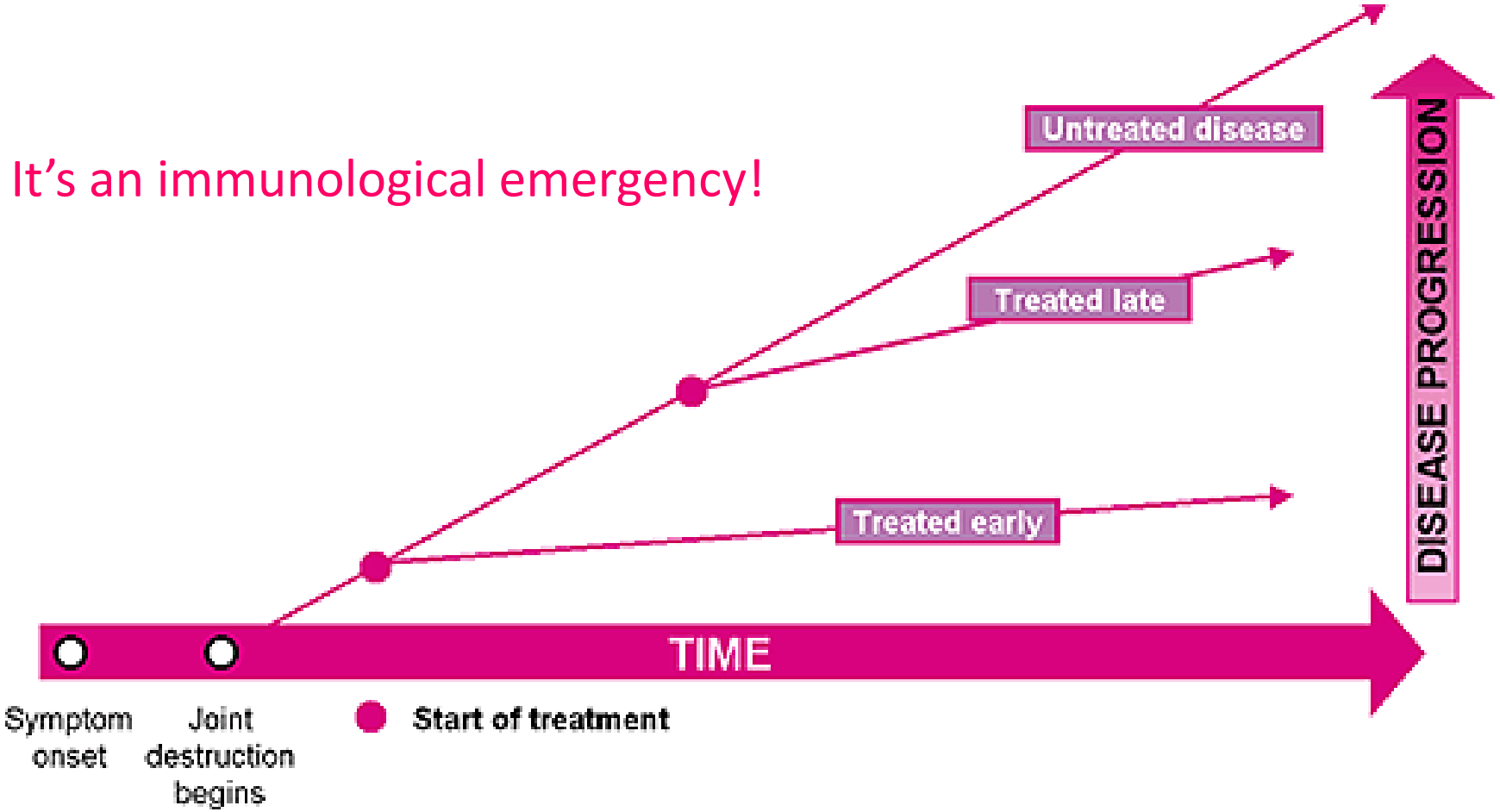
Luton & Dunstable University Hospital NHSFT

Early diagnosis and treatment essential

It’s an immunological emergency!



EIA proforma

Referral Proforma: **Early Inflammatory Arthritis Clinic (EIAC)**

This is a rapid access clinic (max 4 weeks); please assess the patient's suitability for this clinic by completing the referral criteria below

Refer via Choose and Book or fax: 01582 497902

☐ I am sending an accompanying letter

Patient's details:

Surname: ..... NHS No: .....

Forename: ..... Hosp No: .....

Address: ..... Date of birth: .....

..... Daytime Tel: .....

..... Evening Tel: .....

..... Mobile Tel: .....

Postcode: ..... Language of choice: .....

☐ Communication/understanding difficulties

.....

Referring GP's details (please print or stamp):

Name: .....

Surgery address: .....

Referral date: ..... Surgery Fax: .....

Referral Criteria:

In order for the patient to be eligible for referral:

1) **The patient must have had symptoms for ≤ 12 months or this is the first presentation of established RA**

Plus

2) **≥ 2 of the following symptoms:**

- ☐ Swelling of ≥2 joints
- ☐ Positive MTP/MCP joint 'squeeze test'
- ☐ Early morning stiffness ≥30 minutes

Please request: FBC, ESR, LFT, CRP, Rh F, U&E and urinalysis:

Date requested ..... (Patient may be referred with these test results pending)

Note: normal ESR/CRP and Rh F does not exclude a diagnosis of Inflammatory Arthritis

Allergies: .....

GP signature: ..... **Date:** .....

Date: 10/12/2012 One-page form
File: In correspondence section of Medical Records

Classification criteria

TABLE 1: 1987 ACR Classification Criteria For RA

	1987 Classification Criteria
Criteria	1. Morning stiffness (at least one hour) 2. Arthritis in three or more joint areas 3. Arthritis of hand joints (≥1 swollen joints) 4. Symmetric arthritis 5. Rheumatoid nodules 6. Serum RF 7. Radiographic changes (erosions) on X-rays of hands
Applicable for	All arthritis patients
Results in	Classification of RA (yes/no)
Positive in case	Four of the seven criteria must be present. Criteria one through four must have been present for at least six weeks.
Test characteristics	Sensitivity of 79%–80% and specificity of 90%–93% for established RA. Sensitivity of 77%–80% and specificity of 33%–77% for early RA.

Table. The ACR/EULAR 2010 classification criteria for RA[a]

Criteria	Score
A. Joint involvement	
1 large joint	0
2–10 large joints[b]	1
1–3 small joints (with or without involvement of large joints)	2
4–10 small joints[c] (with or without involvement of large joints)	3
> 10 joints (at least 1 small joint)	5
B. Serology (at least one test result is needed for classification):	
Negative RF and negative anti-CCP antibodies	0
Low-positive RF or low-positive anti-CCP antibodies[d]	2
High-positive RF or high-positive anti-CCP antibodies[e]	3
C. Acute phase reactants:	
Normal CRP level and normal ESR	0
Abnormal CRP level or abnormal ESR	1
D. Duration of symptoms:	
< 6 weeks	0
≥ 6 weeks	1

ACR = American College of Rheumatology; EULAR = European League Against Rheumatism; RA = rheumatoid arthritis; DIP = distal interphalangeal; MTP = metatarsophalangeal; CMC = carpometacarpal; MCP = metacarpophalangeal; PIP = proximal interphalangeal; IP = interphalangeal; RF = rheumatoid factor; anti-CCP = anti–cyclic citrullinated protein; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.

[a]To be applied to patients: (1) who have ≥ 1 joint with definite synovitis, excluding the DIP joints, first MTP joints, and first CMC joints, and (2) in whom the synovitis cannot be explained by another disease.

[b]Large joints = shoulders, elbows, hips, knees, ankles.

[c]Small joints = MCPs, PIPs, second to fifth MTPs, thumb IPs, wrists.

[d]Low-positive is ≤ 3 times the upper limit of normal.

[e]High-positive is > 3 times the upper limit of normal.

Aletaha D et al. Ann Rheum Dis 2010;69:1580-1588

Referral for Specialist opinion 2009 NICE RA guidelines

Refer for specialist opinion any person with suspected persistent synovitis of undetermined cause

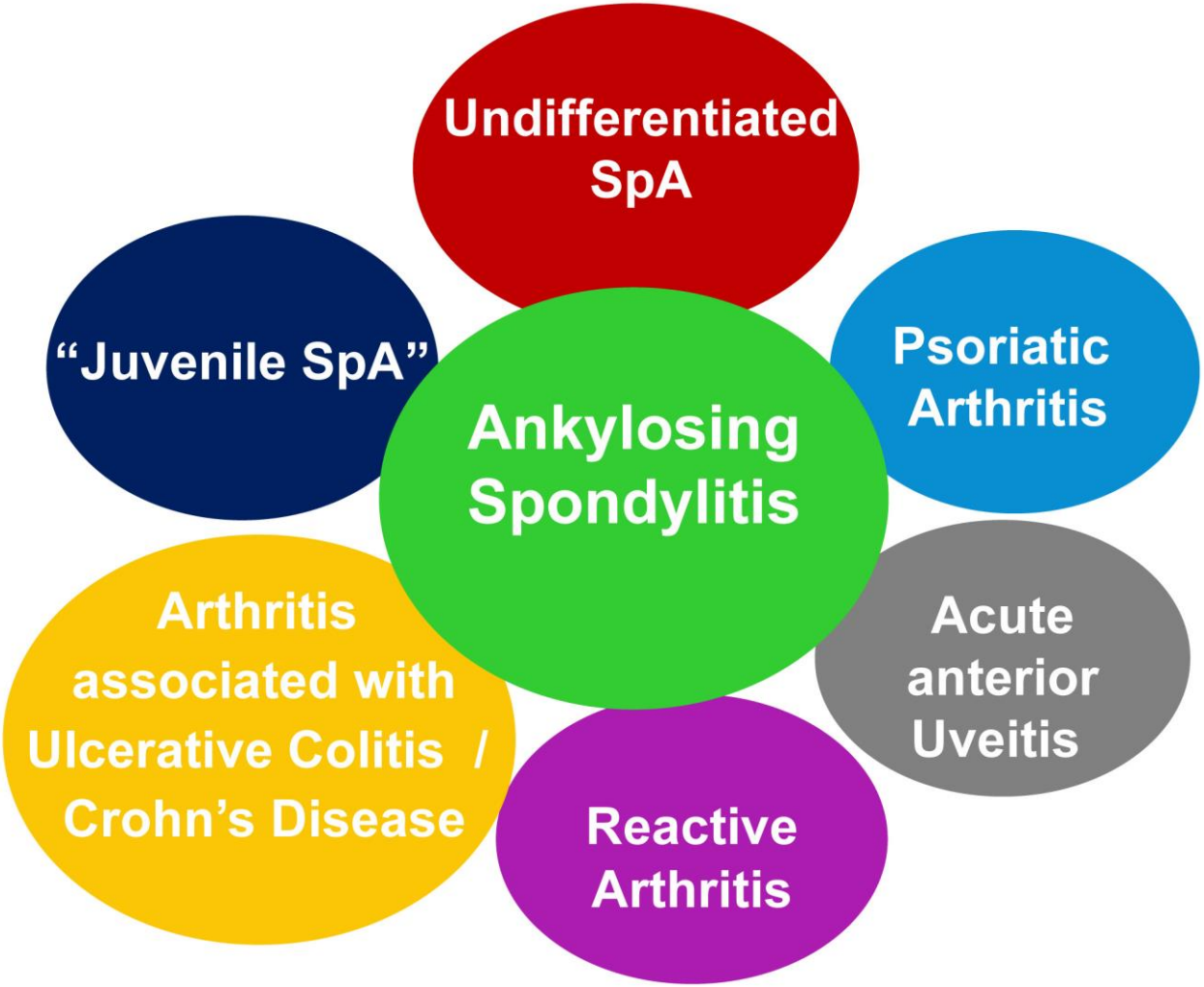
Refer urgently if any of the following apply:

– the small joints of the hands or feet are affected

– > 1 joint is affected

– there has been a delay of > 3 months between onset of symptoms and seeking medical advice

Concept of Spondyloarthritis (SpA)



Concept of Spondyloarthritides (SpA)

Non-radiographic axial SpA

Ankylosing Spondylitis

Predominantly Axial SpA

Reactive arthritis

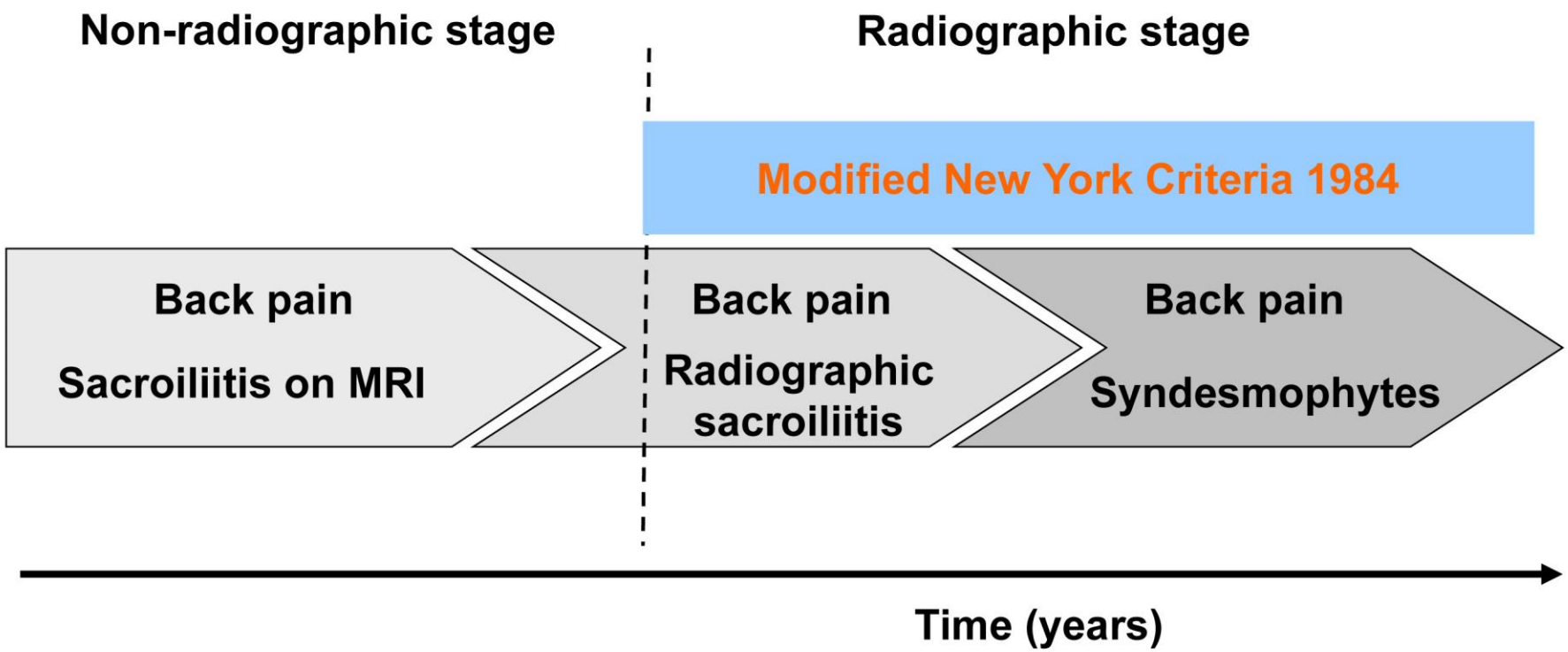
Psoriatic Arthritis

Arthritis with inflammatory bowel disease

Undifferentiated SpA

Predominantly Peripheral SpA

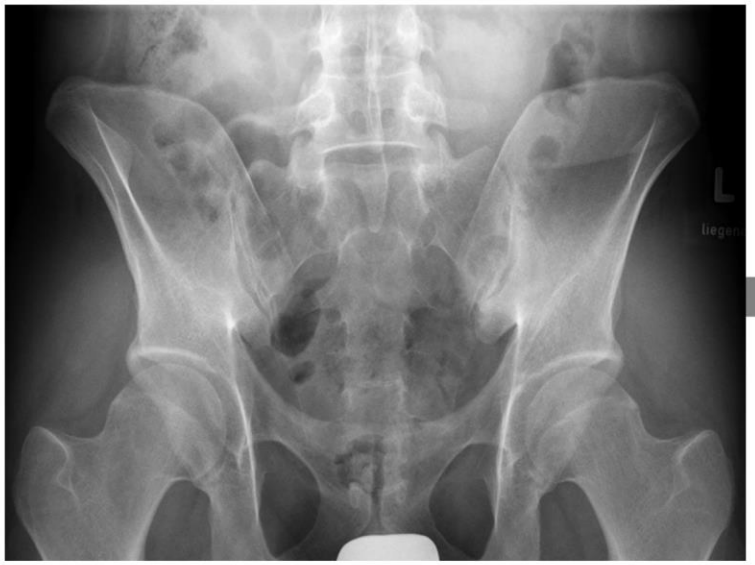
Axial Spondyloarthritis



Rudwaleit M et al. Arthritis Rheum 2005;52:1000-8 (with permission)

Progression of Non-radiographic Axial SpA to AS: Data from GESPIC*

Non-radiographic axial SpA

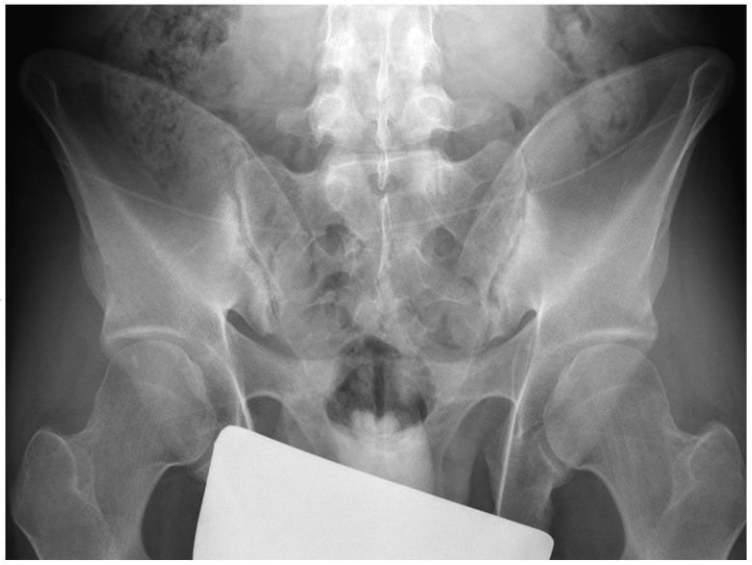


no definite radiographic sacroiliitis (grade 0 at the right side, grade 1 – possible subchondral sclerosis – at the left side)

12%
in 2 years

Main predictor:
elevated CRP**

Ankylosing spondylitis



definite radiographic sacroiliitis (grade 2 bilaterally) fulfilling the radiographic criterion of the modified New York criteria

*GESPIC = GErman Spondyloarthritis Inception Cohort

**Odds ratio for progression in patients with elevated serum C-reactive protein level (>6 mg/l) was: 4.11 (95% CI 1.13-14.95).

Poddubnyy D et al. Ann Rheum Dis 2011;70:1369-74

ASAS

ASAS Classification Criteria for Peripheral Spondyloarthritis (SpA)

Arthritis or enthesitis or dactylitis

plus

≥ 1 SpA feature
- uveitis
- psoriasis
- Crohn's/colitis
- preceding infection
- HLA-B27
- sacroiliitis on imaging

OR

≥ 2 other SpA features
- arthritis
- enthesitis
- dactylitis
- inflammatory back pain (ever)
- family history for SpA

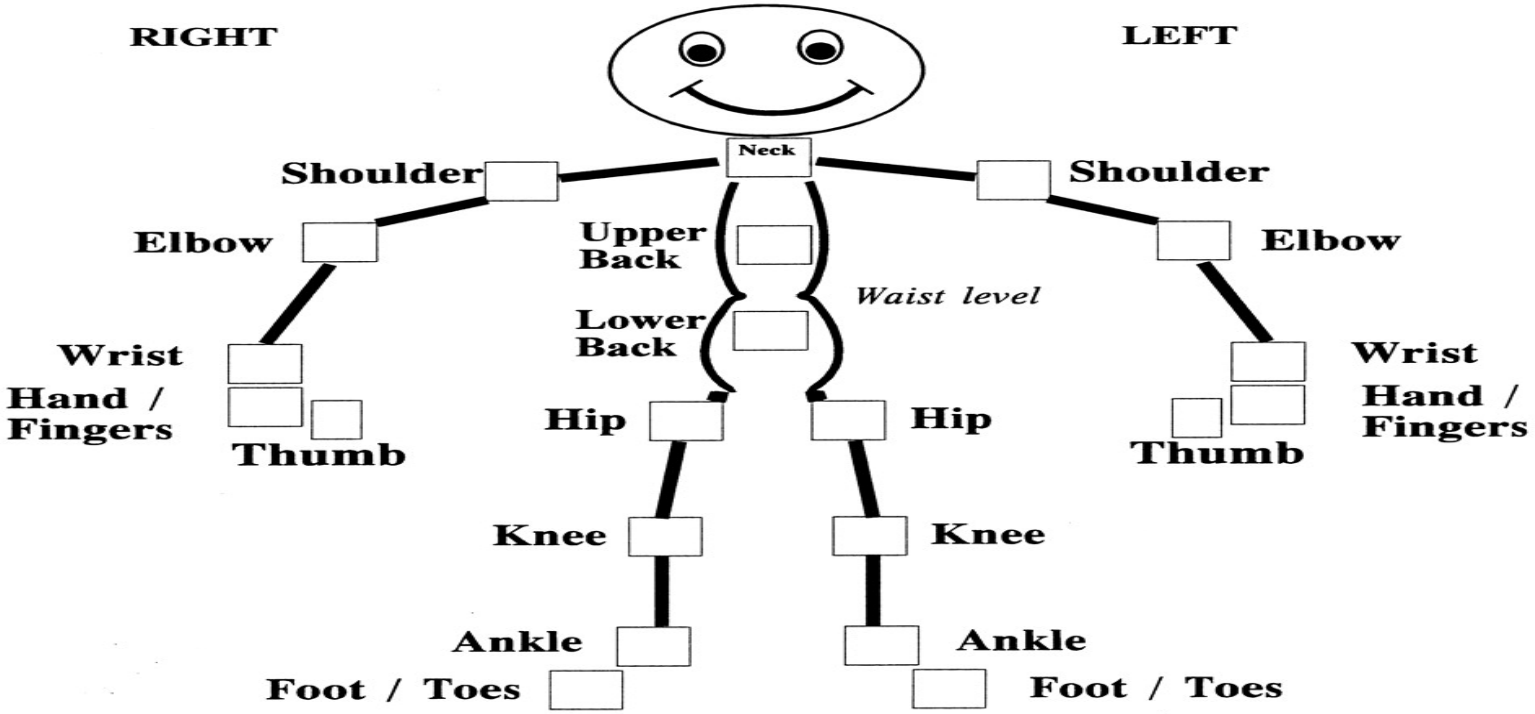
Sensitivity: 77.8%, Specificity: 82.2%; n=266

Rudwaleit M et al. Ann Rheum Dis 2011;70:25-31 (with permission)

PEST questionnaire

	NO	YES
Have you ever had a swollen joint (or joints)?		
Has a doctor ever told you that you have arthritis?		
Do your finger nails or toe nails have holes or pits?		
Have you had pain in your heel?		
Have you had a finger or toe that was completely swollen and painful for no apparent reason?		

In the drawing below, please tick the joints that have caused you discomfort (i.e., stiff, swollen, or painful joints).



Sensitivity 92%, Specificity 78%

Helliwell P. J Rheum.2011:38:551-2

ASAS Classification Criteria for Axial Spondyloarthritis (SpA)

In patients with ≥3 months back pain and age at onset <45 years

Sacroiliitis on imaging*

plus

≥1 SpA feature#

OR

HLA-B27

plus

≥2 other SpA features#

#SpA features

- inflammatory back pain
- arthritis
- enthesitis (heel)
- uveitis
- dactylitis
- psoriasis
- Crohn's/colitis
- good response to NSAIDs
- family history for SpA
- HLA-B27
- elevated CRP

*Sacroiliitis on imaging

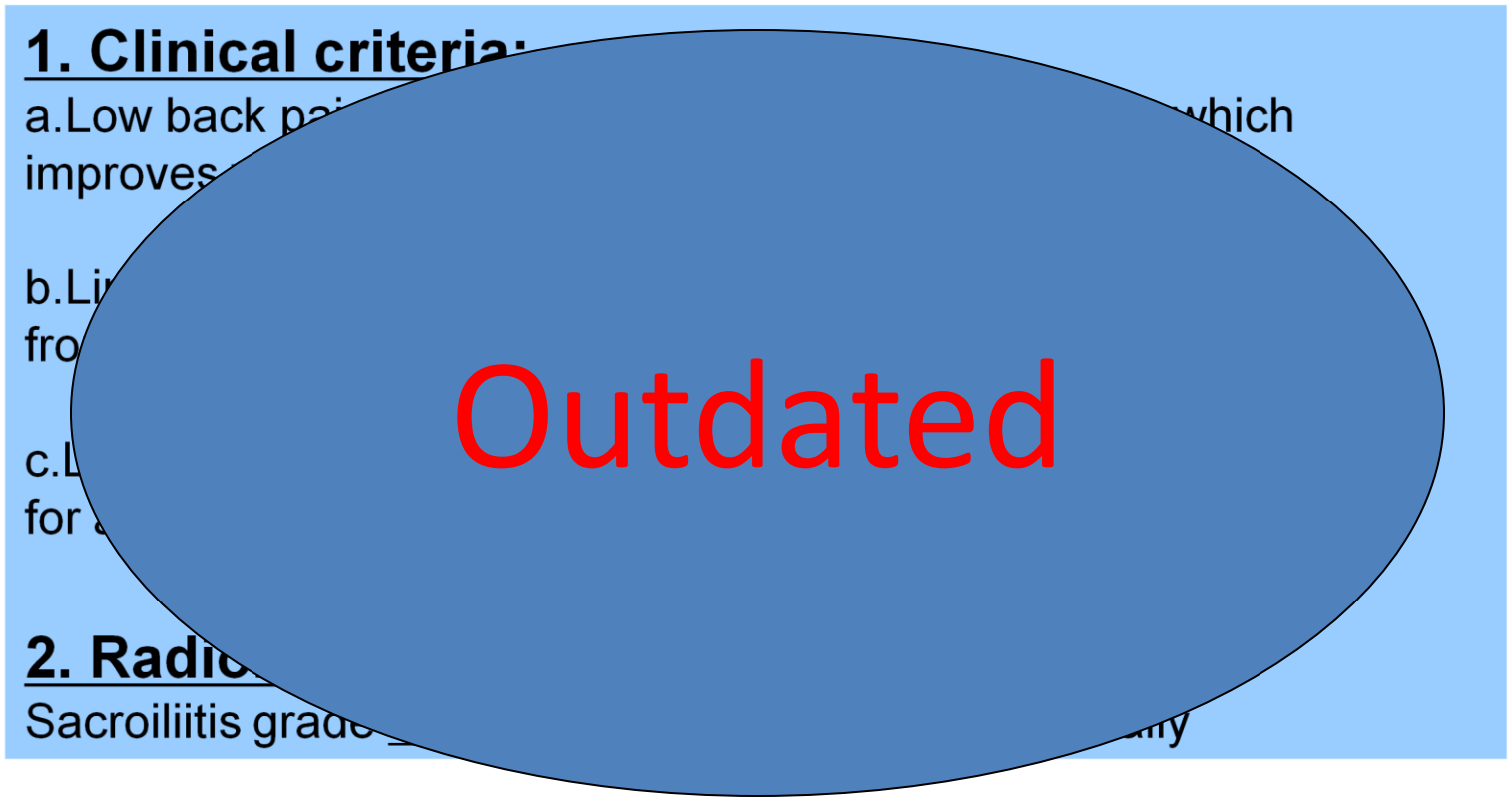
- active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
- definite radiographic sacroiliitis according to mod NY criteria

n=649 patients with back pain;
Sensitivity: 82.9%, Specificity: 84.4%
Imaging alone: Sensitivity: 66.2%, Specificity: 97.3%

Rudwaleit M et al. Ann Rheum Dis 2009;68:777-783 (with permission)

ASAS

Modified New York Criteria for Ankylosing Spondylitis (1984)

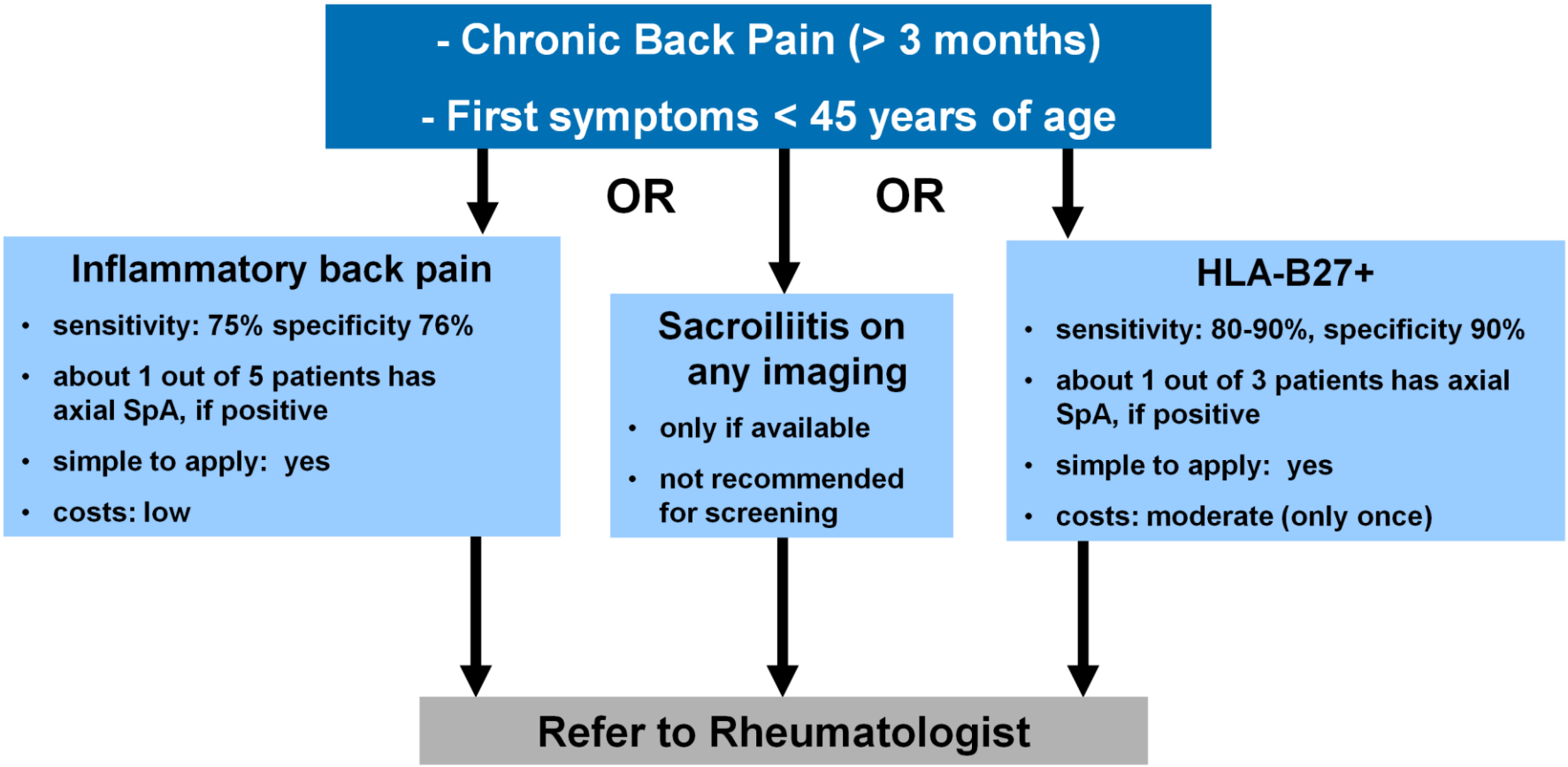


Definite ankylosing spondylitis if the radiological criterion is associated with at least 1 clinical criterion.

van der Linden S et al. Arthritis Rheum 1984;27:361

ASAS

Possible Screening Approach for Axial SpA Among Patients with Chronic Low Back Pain



Adapted from Sieper J et al. Ann Rheum Dis 2005;64:659-63

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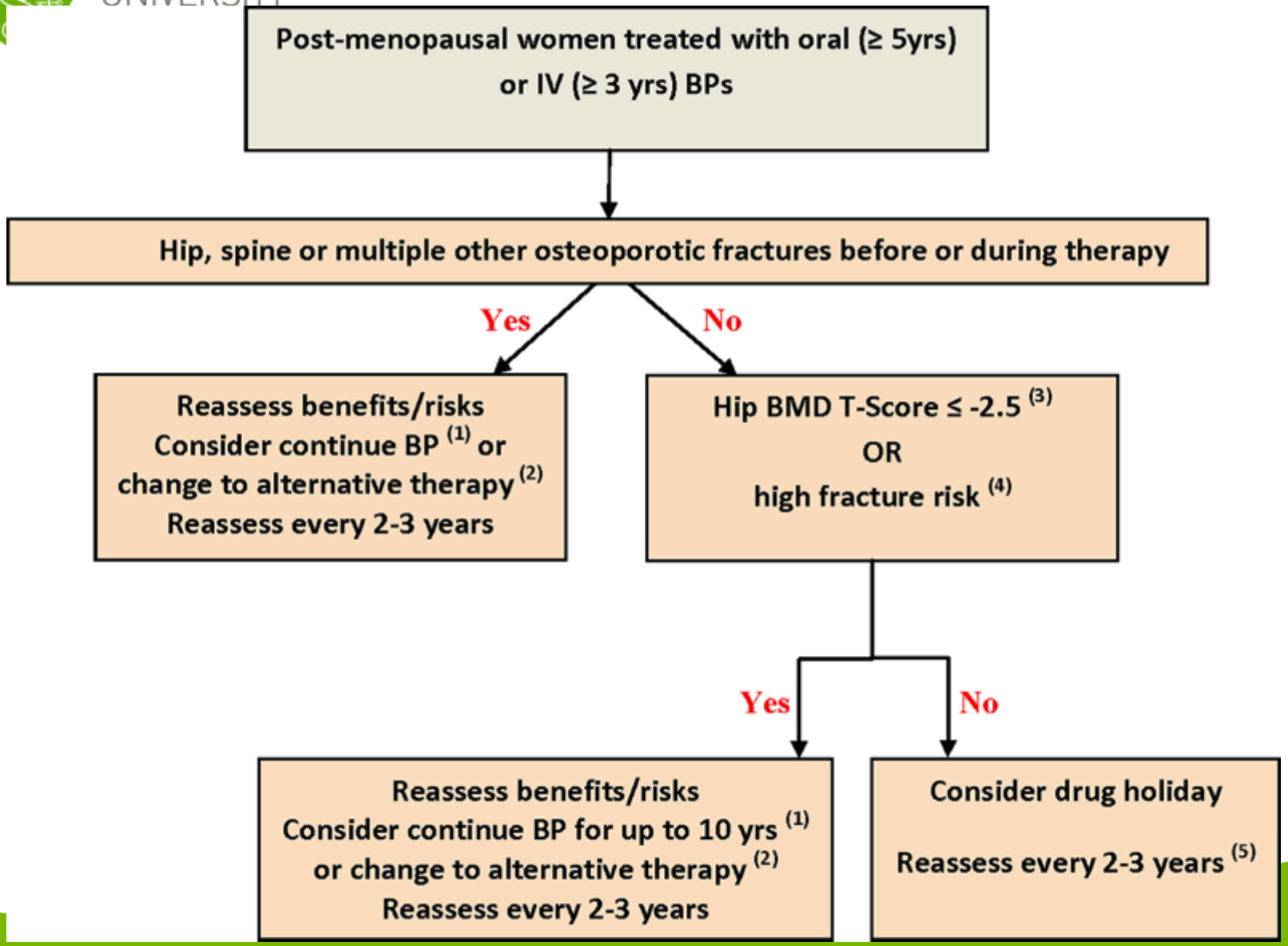
Drug Holiday



JBMR 2016;31:16-35

What are EDS and HSD?

Ehlers-Danlos syndromes (EDS)

Group of connective tissue disorders that can be inherited:

- Varied in how they affect the body and in their genetic causes;
- Characterized by joint hypermobility, skin hyper-extensibility, and tissue fragility;
- Can cause symptoms throughout the body, requiring medical attention and validation.

Hypermobility spectrum disorders (HSD)

Group of conditions involving joint hypermobility:

- Can cause symptoms throughout the body, requiring medical attention and validation;
- Diagnosed after all other conditions that cause joint hypermobility, including all EDS types, have been excluded.

Hypermobile EDS (hEDS)

- Believed to be the most common genetic connective tissue disorder.
- Can experience:
  - Joint hypermobility with subluxations and dislocations;
  - Skin issues;
  - Other symptoms.
- Some of the possible associated features include:
  - Chronic pain and fatigue;
  - Dysautonomia;
  - Gastrointestinal issues;
  - TMJ and dental problems
  - Spine problems;
  - Mast cell activation disorder.

For more information:

"Hypermobile Ehlers-Danlos Syndrome"

http://bit.ly/EDS2017papers

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The Hypermobility Spectrum Disorders

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Hypermobility spectrum disorders (HSD)

- Diagnosis of exclusion, made after all other possible conditions resulting in joint hypermobility (JH) are considered;
- JH can be localized or affect all joints;
- HSD range from
  - JH with no other symptoms to
  - Complex HSD that can have the same life-altering symptoms as hEDS;
- Treatment for symptoms is the same as treatment for hEDS.

For more information:

"A framework for the classification of joint hypermobility and related conditions"

http://bit.ly/EDS2017papers

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Joint hypermobility (JH)

Is the capability of joints to move beyond normal limits:

- JH in fewer than five joints is localized joint hypermobility (LJH);
- JH in five or more joints is generalized joint hypermobility (GJH);
  - possibly inherited
  - acquired forms of GJH exist (training, inflammatory or degenerative diseases, hypothyroidism and other endocrine disorders).
- Peripheral joint hypermobility (PJH) affects the hands and/or feet only;
- Historical joint hypermobility is found in older adults who have progressively lost JH.

For more information:

"A framework for the classification of joint hypermobility and related conditions"

http://bit.ly/EDS2017papers

Types of hypermobility spectrum disorders

NAME OF HSD	BEIGHTON SCORE	MUSCULOSKELETAL INVOLVEMENT
Asymptomatic GJH	Positive	Absent
Asymptomatic PJH	Usually negative	Absent
Asymptomatic LJH	Negative	Absent
Generalized-HSD	Positive	Present
Peripheral-HSD	Usually negative	Present
Localized-HSD	Negative	Present
Historical-HSD	Negative*	Present
hEDS	Positive	Possible

* Historical presence of joint hypermobility (*e.g.*, positive 5-point questionnaire)

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Secondary musculoskeletal manifestations

- Trauma:
  - Macrotrauma includes dislocation, subluxations, and connected soft tissue damage (ligaments, tendons, muscles);
  - Microtrauma are injuries too small for them to be noticed as they happen.
- Chronic pain:
  - Occasional, recurring pain is a natural result of the trauma;
  - Chronic pain can develop from sensitivity to pain, impaired connective tissue.
- Disturbed proprioception – the sense of the relative position of parts of the body and how much effort is needed for movement – can be reduced.
- Other musculoskeletal traits:
  - Flat feet (flexible type);
  - Misaligned bones in elbow and big toes;
  - Mild to moderate scoliosis, kyphosis of upper spine, lordosis of the lower spine;
  - Indirect association with mild reduced bone mass as a result of many factors.
  - .

Associated problems not based in the musculoskeletal system

Issues not the direct result of the mechanics of JH:

- Very real;
- Seriously affect quality of life;
- Must be managed as part of treatment.

The strongest (but not only) associations:

- Anxiety disorders;
- Orthostatic tachycardia;
- Variety of functional gastrointestinal disorders;
- Pelvic and bladder dysfunction.

These additional problems need to be evaluated and treated when an HSD is diagnosed.

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Associated Conditions and Disorders

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Physical therapy guidelines

Important treatment for those with hypermobility-related conditions:

- Individualized for each patient;
- Useful to address
  - Pain,
  - Proprioception,
  - Balance,
  - Muscle tone, and
  - Overall physical fitness.

For more information:

"The evidence-based rationale for physical therapy treatment of children, adolescents, and adults diagnosed with joint hypermobility syndrome/ hypermobile Ehlers-Danlos syndrome"

http://bit.ly/EDS2017papers

Autonomic dysfunction guidelines

- Common in hypermobility-related disorders and includes:
  - Postural orthostatic tachycardia syndrome;
  - Orthostatic intolerance;
  - Neurally mediated hypotension.
- May cause:
  - Tachycardia;
  - Low blood pressure;
  - Gastrointestinal problems;
  - Bladder issues;
  - Sweating too much or too little.
- Conservative treatment includes:
  - Increased fluids and salt;
  - Compression wear;
  - Increased physical activity.

For more information and management:

"Cardiovascular autonomic dysfunction in Ehlers-Danlos syndrome–Hypermobile typeEhlers Danlos syndrome"

http://bit.ly/EDS2017papers

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Chronic fatigue

Common in hypermobility conditions:

- Symptoms overlap chronic fatigue syndrome;
- Problems that worsen fatigue:
  - Sleep disorders;
  - Autonomic dysfunction;
  - Chronic and acute pain;
  - Deconditioning;
  - Psychological issues;
  - Nutritional deficiencies.

For more information:

"Chronic fatigue in Ehlers-Danlos syndrome–Hypermobile type"

http://bit.ly/EDS2017papers

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Gastrointestinal disorders

Common in hypermobility conditions:

- Structural (such as hiatal hernias, rectal prolapse);
- Functional (such as irritable bowel syndrome, gastroparesis);
- Treat based on symptoms;
- Added precautions for GI procedures may be needed depending on EDS type and individual.

For more information on symptom management and procedure precautions:

"Gastrointestinal involvement in the Ehlers-Danlos syndromes"

http://bit.ly/EDS2017papers

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Orthopedic management

EDS can cause early damage to joints and joint instability.

Benefit from working with:

- Physical therapists;
- Orthopedic surgeons with EDS experience, who have an excellent understanding of human anatomy and physiology.

For more information about how EDS can affect individual joints and about available treatment :

"Orthopaedic management of the Ehlers-Danlos syndromes"

http://bit.ly/EDS2017papers

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Neurological and spine issues

Laxity in ligaments caused by EDS results in most of these problems:

- Craniocervical instability;
- Chiari malformation;
- Tethered cord syndrome;
- Early disc damage;
- Muscle weakness; and
- Migraine.
- Also seen:
  - Kyphosis ("hunchback");
  - Motor delay; and
  - Unstable vertebrae.

- Physical therapy and bracing may help;
- Surgery may be needed.

For more information:

"Neurological and spinal manifestations of the Ehlers-Danlos syndromes"

http://bit.ly/EDS2017papers

Pain management

Chronic and acute pain are common:

- Joints;
- Gastrointestinal system;
- Temporomandibular joint (TMJ);
- Headaches and migraines;
- Pelvic organs;
- Other systems and locations.
- Management includes:
  - Treating the cause;
  - Physical therapy;
  - Medications;
  - Braces and cushions;
  - Compression wear.

For more information:

"Pain management in the Ehlers–Danlos syndromes"

http://bit.ly/EDS2017papers

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Mouth and TMJ issues

Those with EDS may have issues with their teeth, TMJ, facial tissue, and headaches:

- Soft tissue, such as gum disease;
- Teeth, such as dental fractures;
- Temporomandibular joint dysfunction.
- Treatment options depend upon the type of EDS and the specific oral or TMJ problem.

For more information:

"Oral and mandibular manifestations in the Ehlers-Danlos syndromes"

http://bit.ly/EDS2017papers

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Mast cell disorders

- Mast cell activation syndrome (MCAS) is commonly seen in those with EDS.
- Management includes
  - Identifying and avoiding triggers;
  - Using medications to manage mast cells.

For more information:

"Mast cell disorders in Ehlers-Danlos syndrome"

http://bit.ly/EDS2017papers

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Psychiatric and psychological symptoms

Growing evidence shows an association with EDS of:

- Anxiety;
- Depression;
- Neurodevelopmental disorders
  - Attention deficit/hyperactivity disorder (ADHD)
  - Autism spectrum disorders (ASD).
- People with EDS may benefit from:
  - Proper medication;
  - Psychotherapy;
  - Physical therapy and other treatment of physical symptoms.

These symptoms are the result of having an EDS; EDS are not the result of any of these conditions and EDS are not "all in the patient's head."

For more information:

"Psychiatric and psychological aspects in the Ehlers–Danlos syndromes"

http://bit.ly/EDS2017papers