Patient with Musculo-skeletal Complaints - Summary

1. Soft Tissue Rheumatism or Arthritis
2. Arthritis –
   - Monoarticular - Crystals, Gout
     - Infective – acute – G+ve – ve
     - Chronic – Koch's
   - Polyarticular - :
     (Asymmetrical) SSA - Reiter's, Reactive
     AS Psoriasis
     (Symetrical) :- RA, SLE, DM, PM,
     Scleroderma APS, Vasculitis
3. Extrarticular features…
4. Laboratory, Imaging workup : DIAGNOSIS
Patient with Musculoskeletal Pain

Arthritis

- Inflammatory arthritis
  - Monoarticular
  - Polyarticular

Non-articular rheumatism and trauma

Non-inflammatory arthritis

- Monoarticular
- Polyarticular

Step 1:

Step 2:

Step 3:

Step 4:
Look for extra-articular findings

Step 5:
Laboratory tests & special procedures
Diagnosis
## Differences between arthritis and soft tissue rheumatism (STR)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Arthritis</th>
<th>STR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Deep, diffuse &amp; circumferential</td>
<td>Superficial &amp; sharply localised</td>
</tr>
<tr>
<td>Tenderness</td>
<td>Circumferential around the joint</td>
<td>Localised over the affected structure</td>
</tr>
<tr>
<td>Pain on active range of motion (ROM)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pain on passive ROM</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Clinical synovitis/effusion</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Crepitus, instability, deformity</td>
<td>Often yes</td>
<td>No</td>
</tr>
</tbody>
</table>
Differential Diagnosis of Monoarthritis

1. **Step 1:**
   - **Arthritis**
   - **Non-articular rheumatism**
   - **Further appropriate work up**

2. **Step 2:**
   - **Monoarthritis**
   - **Polyarthritis**
   - **Further appropriate work up**

3. **Step 3:**
   - **Extraarticular features**

4. **Step 4:**
   - **Synovial fluid analysis**
   - **Specific Microscopic findings**
   - **Diagnosis**
     - *Gout* – monosodium urate crystals
     - *Pseudogout* – calcium pyrophosphate crystals
     - Infections arthritis – positive Gram stain for bacteria
     - *Trauma* – grossly bloody fluid & positive history
   - **No specific microscopic findings**
Monoarticular – Extraarticular Features

- Iritis conjunctivitis
- Nodules
- Ulcers, pharyngitis
- Splenomegaly
- Papules

Gout, JRA, Reiter's, Gonococcal
Monoarticular – Extraarticular Features

Gout
JRA
Reiter's
Gonococcal
Balanitis urethritis
Dermatides

Keratodermia blennorrhagica
Polyarticular Asymmetrical: Extraarticular Features

- Rash
- Iritis, conjunctivitis
- Ulcers, pharyngitis
- Aortic insufficiency

Conditions:
- Ankylosing spondylitis
- Reiter's
- Inflammatory bowel disease
- Psoriatic arthritis
Polyarticular Asymmetrical: Extraarticular Features

- Prostatitis
- Balanitis urethritis
- Onycholysis nail pitting
- Pyoderma gangrenosum
- Keratodermia blennorrhagica
Polyarticular Symmetrical: Extraarticular Features

- SLE
- Dermatomyositis
- Scleoderma
- Sjogren's
- Felty's

- Alopecia, rash
- Heliotrope, scleritis, sicca
- Rash, telangiectasia, parotitis
- Sicca, ulcers
- Pleuritis, pericarditis
- Splenomegaly
- Nodules
Polyarticular Symmetrical Extraarticular Features:

- Carpal tunnel
- Papular lesions (Gottron's)
- Raynaud's, sclerodactylyia, pitting
- Popliteal cyst
- Ulcers
- Neuropathy
EXTENSOR TENDON RUPTURE IN RHEUMATOID ARTHRITIS
DERMATOMYOSITIS
CREST SYNDROME.

C = CALCINOSIS.

R = RAUNAUDE'S PHENOMENON.

E = ESOPHAGEAL DYSFUNCTION.

S = SCLERODACTYLE.

T = TELANGIACTESIS.
Anti Phospholipid : Hughes Syndrome

"Sticky Blood" : the Disease Is Common
“There are two major ‘new’ diseases of the late 20th century - AIDS and APS”

Vilardell
Barcelona, 2002
Thrombosis, abortion, cerebral disease, and the lupus anticoagulant

Systemic lupus erythematosus, with its broad range of clinical and immunological abnormalities, continues to provide lessons relevant to research in a wider variety of disciplines and diseases. In some patients three apparently unrelated clinical features of systemic lupus erythematosus—recurrent venous thrombosis, central nervous system disease (including myelitis), and recurrent abortions—may, it seems, have common pathogenic mechanisms. Clinicians have suspected as much for some time—those dealing with many patients with systemic lupus erythematosus recognise a group of women who have as features of their disease multiple (even a dozen or more) spontaneous abortions, multiple deep vein and other thromboses, and neurological abnormalities including either putative cerebral thrombosis or myelitis or both. Interestingly, some of these patients have negative test results for antinuclear antibody.\(^1\)

The serological abnormality common to some (but not all) of these patients is a circulating anticardiolipin antibody responsible for the positive Wassermann reaction or so-called false positive serological test for syphilis. Over 25 years ago Laurell and Nilsson\(^2\) recognised that patients with systemic lupus erythematosus with biological false positive Wassermann reactions also had a high incidence of another "antilipid" antibody—the so-called "lupus anticoagulant." This antibody, now known to be present in conditions other than systemic lupus erythematosus, appears to act by interfering with the binding of phospholipid to form prothrombin activator, thereby affecting both the intrinsic and extrinsic clotting pathways.\(^3\) Though in laboratory tests the lupus anticoagulant slightly prolongs the partial thromboplastin time, the seeming paradox in this respect is not that surprising.
... and epilepsy

ASSOCIATION BETWEEN ANTIPHOSPHOLIPID ANTIBODIES AND EPILEPSY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

M. YERES HERNÁNDEZ, MILLER BROWN, MONTHER A. KRAMMER, ELIA G. BLANCO, AND LEWIS J. R. KENNEDY

Objective. To determine whether the presence of antiphospholipid antibodies (APA) is associated with the development of epilepsy in SLE patients.

The study included 222 consecutive patients with SLE. Of these, 30 patients with epilepsy and 192 without epilepsy were evaluated.

Methods. A clinical evaluation was performed, and APA were tested in all patients using the enzyme-linked immunosorbent assay method.

Results. The prevalence of APA in patients with epilepsy was significantly higher than in patients without epilepsy (P < 0.05).

Conclusions. The presence of APA in patients with epilepsy is associated with an increased risk of developing epilepsy in SLE patients.

... and low platelet counts

... and liver thrombosis

as well as a potentially treatable cause of some cases of:
- V.S.
- Alzheimer's
- Migraine
- Heart Attack

THE LANCET

... and heart valve disease

... early laboratory studies
Hughes Syndrome
Main Clinical Features

- Headaches
- Memory loss
- Internal organ thrombosis
- Recurrent pregnancy loss
- Deep vein thrombosis ‘DVT’
APS: Clinical Impact

- Migraine
- Memory Loss
- Multiple Sclerosis
- Infertility
- Strokes
- Leg Ulcers
- DVT
- Recurrent Pregnancy Loss
# Hughes' syndrome: Major clinical features

<table>
<thead>
<tr>
<th>Major Clinical Features</th>
<th>Details</th>
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</table>
| **Pregnancy Loss**      | • Early in pregnancy (miscarriage) or late (fetal death)  
                         • Recurrent very early miscarriage may give rise to diagnosis of infertility |
| **Vein thrombosis**    | • Deep vein thrombosis (DVT) e.g. arm or leg  
                         • Thrombosis in internal organs, e.g. kidney, liver, lung, brain, eye  
                         • Thrombosis of skin vessels – skin ulcers "Livedo" (blotchiness) |
| **Artery thrombosis**  | • Brain – headaches, weakness, slurred speech (transient ischaemic attacks – TIA's), strokes, seizures, memory loss  
                         • Limb – pain, circulation problems, other organs – heart, kidney, adrenal |
| **Low platelet count** | • Bruising (5-20%) |
# Diagnostic criteria: Hughes Syndrome

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Laboratory</th>
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<tbody>
<tr>
<td>• Venous thrombosis</td>
<td>• IgG aCL in moderate/high levels</td>
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<tr>
<td>• Arterial thrombosis</td>
<td>• IgM aCL in moderate/high levels</td>
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<tr>
<td>• Fetal loss</td>
<td>• Positive lupus anticoagulant test</td>
</tr>
<tr>
<td>• Thrombocytopenia</td>
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</table>
The 3 Tests

- aCL
- LA
- VDRL (WR)
APS : APLA

- **aCL**
  - <5 : negative
  - 5-20 : low positive
  - 20-60 : moderate positive
  - >60 : high positive

- **LAC**
  - <.17 : negative
  - .17-.29 : low positive
  - .3-.69 : medium positive
  - >.7 : high positive

- **VDRL**
  - False positive for syphilis

- **MISC**
  - ANA, Coagulation & Organ profile
1960 – “sero-negative RA”

1970 – “sero-negative SLE”

2000 – “sero-negative APS”
Blood Thickness

‘INR’

- Normal blood (INR = 1)
- ‘Half-Thick’ blood (INR = 2)
- ‘One Third Thick’ blood (INR = 3)
Triggers for Thrombosis

- Smoking
- Oral contraceptive pill
- Dehydration
- Pregnancy
APS  Pregnancy Loss

Weeks

1–20  20–40

Abortion  Fetal Loss
MEETING PAPERS

Multiorgan failure due to rapid occlusive vascular disease in antiphospholipid syndrome: the ‘catastrophic’ antiphospholipid syndrome

Ricard CERVERA¹ and Ronald A. ASHERSON²

MEETING PAPERS

Pregnancy in systemic lupus erythematosus and antiphospholipid syndrome

Ricard CERVERA,¹ Josep FONT,¹ Francisco CARMONA² and Juan BALASCH²

¹Department of Autoimmune Diseases, Institut Clinic of Medicine and Dentistry and Neonatology, Hospital Clínic, Barcelona, Catalonia, Spain
ANTIPHOSPHOLIPID SYNDROME
The Hospital Clínica of Barcelona Experience

Before treatment

n: 137 (78%)
ABORTION/FETAL DEATH
n = 39 (22%)

After treatment

n = 63 (81%)
LIVEBORN
n = 14 (19%)
# Monitoring of SLE Pregnancy

The Hospital Clínica of Barcelona Experience

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<th>Week</th>
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<th>16</th>
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ANA/Com + + + + + + + + + + +
APS and the Brain

- Visual symptoms
- Memory loss
- Headache
- Stroke
- Movement disorder
- Paralysis
- Seizure
aPL and white matter hyperintensity lesions - “small vessel disease”? 
What proportion of ‘idiopathic’ strokes have this aetiology?

Primary Stroke and aPL
APASS Study 2004

- 1770 subjects with ischaemic stroke
- 740 (41%) aPL positive

Levine et al
JAMA 2004
Cognitive dysfunction in APS

Verbal memory  )
Working memory  )
Verbal fluency  ) all decreased
Psychomotor speed  )
Cognitive flexibility  )
Darts champion
ALZHEIMER’S

Are some cases APS?

‘I thought I was developing Alzheimer’s’
Headache/migraine

- A major feature of APS
- Teenage / later
- Often familial
- May respond to anticoagulation
DVT and Hughes’ syndrome

Up to 30% of DVT’s have aPL
• Coronary artery stenosis…
• Carotid/cerebral stenosis…
• Renal artery stenosis...
• Coeliac artery stenosis?
Kidney & APS
... coeliac artery stenosis in APS

... 27 cases

Sangle et al
Lupus Unit, 2004
aPL-negative APS

- Significance of livedo?

- 56 livedo patients aPL -ve
- 66% pregnancy-related morbidity

Sangle et al
Lupus Unit, 2004
Antiphospholipid antibodies, systemic lupus erythematosus, and non-traumatic metatarsal fractures

S Sangle, D P D'Cruz, M A Khamashta, G R V Hughes

19 spontaneous MT fractures in APS

Sangle et al, 2004
Ann Rheum Dis
LETTERS

Hug(h)e(s’) ears: an unusual presentation of antiphospholipid syndrome
Benign Intracranial Hypertension  
Teenage Migraine  
"Atypical" M.S.  
Skin Necrosis  
Avascular necrosis  
Memory Loss  
Accelerated Atheroma  
Impotence  
Mitral Valve disease  
Monocular Visual Loss  

TEN “small print” clinical features
Aspirin.

Der in manchen Fällen recht unangenehmen Nebenwirkungen, welche die Salicylsäure und deren Salze zeigen, haben schon lange das Bedürfnis nach geeigneten Ersatzmitteln, die frei von diesen Nebenwirkungen sind, gezeigt. Die Verwendung eines heute bewährten Präparates, welches wir als „Aspirin“ bezeichnen, in der Therapie einzuweihen.

Das Aspirin ist der Hauptrepräsentant der Salicylsäure und bildet ein weisses kristallinisches Pulver vom Schmelzpunkt 135° im Wasser schwer, in Wasser leicht löslich. Der Hauptvorteil des Aspirines vor der Salicylsäure und ihren Salzen ist vor allem der, dass damals die Schleimhaut des Magens nicht reizt, ferner infolge seiner langsamen Spaltbarkeit den Magen unzersetzend passiert und erst im Darm gespalten wird.


Nach den bislang vorliegenden klinischen Erfahrungen (Dr. Kurt Wittbauer: „Die Heilkunde. Aprilheft) bildet das Aspirin einen vollkommenen Ersatz für Salicylsäure und deren Salze und wird als angenehme Form der Darreichung einer Mischung von 3 g Aspirin mit 3–4 g Zucker und 15 g Wasser empfohlen.

Wir bitten Sie, dem Aspirin, welches sich zweifellos einen hervorragenden Platz in der Arzneimittelwelt erworben hat, Ihre Aufmerksamkeit zu schenken und empfehlen Ihnen hochachtungsvoll!

APL : Rx

- Aspirin
- Anticoagulation
- Steroids
- Systemic management
CNS and anticoagulation

Headaches, dysarthria

INR

Months
Global impact of APS

“1 in 5”

- 1 in 5 young strokes
- 1 in 5 DVT
- 1 in 5 recurrent miscarriages
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4. Laboratory, Imaging workup : DIAGNOSIS
DIAGNOSIS