Report

Outcome measures and classification criteria for the rheumatic diseases. A compilation of data from OMERACT (Outcome Measures for Arthritis Clinical Trials), ILAR (International League of Associations for Rheumatology), regional leagues and other groups

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The International League of Associations for Rheumatology (ILAR) has been meeting with the World Health Organization (WHO) on a regular basis to discuss issues of mutual interest. Over the last few years these meetings have focused on the development of outcome measures in the rheumatic diseases, principally driven through OMERACT (Outcome Measures for Arthritis Clinical Trials). OMERACT has now held five meetings addressing a number of important areas in rheumatology, including clinical and imaging outcome measures, health economics and drug safety. The advantage of the WHO/ILAR Task Force Meeting has been to ratify these measures and allow them to be promulgated widely around the world.

This paper summarizes discussions which took place at the Sixth Joint WHO/ILAR Task Force Meeting on Rheumatic Diseases which was held in Geneva on 16 January 2000. This meeting reviewed a number of outcome measures for rheumatic diseases that had been developed over the past few years under the aegis of OMERACT. The WHO/ILAR meeting formally endorsed these outcome measures and acknowledged them as the gold standard for outcome measures in these conditions.

At the same meeting, a series of criteria for the classification of rheumatic diseases was also reviewed. These criteria have also been established through discussion by a number of different organizations, including ILAR, the American College of Rheumatology and EULAR (the European League of Associations for Rheumatology). These classification criteria have been put together by experts and have been adopted widely throughout the world. The meeting recommended that WHO/ILAR adopt these well-recognized classification criteria and encourage their use in clinical and epidemiological studies. It should be noted that classification criteria should not be used as diagnostic criteria but for the purposes of classifying patients in studies. An understanding of this concept will help in the interpretation of many clinical studies.

Outcome measures for rheumatoid arthritis

The outcome measures for rheumatoid arthritis clinical trials were developed at OMERACT 1 [1] and are very similar to those developed by the ACR [2]. The recommendations for the preliminary core set were:

- acute-phase reactants
- disability
- joint pain/tenderness
- joint swelling
- pain
- patient global assessment
- physician global assessment
- radiographs for studies of 1 yr or longer.

Outcome measures for osteoarthritis

These outcome measures for future phase III clinical studies in hip, knee and hand osteoarthritis were developed at OMERACT 3 and were published in the Journal of Rheumatology [3]. The core set of outcome measures in osteoarthritis should be:

- pain
- physical function
- patient global assessment

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joint imaging (using standardized methods for taking
and rating radiographs, or any demonstrably superior
imaging technique) for studies of 1 yr or longer.

Quality of life and/or utility measures are also strongly
recommended, but further work should be carried out to
assess the usefulness of biological markers, stiffness,
measures of inflammation and other assessments such as
performance-based measures, time to surgery, flares or
analgesic consumption before they are accepted as core
measures.

Outcome measures for ankylosing spondylitis

This core set of endpoints in ankylosing spondylitis
clinical trials was developed at OMERACT 4 and
published in the Journal of Rheumatology [4]. Defined
core sets have been developed for use in four settings:
disease-controlling anti-rheumatic therapy (DC-ART),
symptom-modifying anti-rheumatic drugs (SM-ARD)
and physical therapy, and for clinical record keeping.
These are as follows:

- SM-ARD and physical therapy
  - physical function
  - spinal stiffness
  - patient global assessment
  - spinal mobility and pain

- Clinical record keeping
  - add acute-phase reactants and peripheral joints/
  - entheses

- DC-ART
  - add fatigue
  - hip radiograph
  - spine radiograph.

Outcomes measures for systemic lupus
erythematousus

A core set of outcome measures and response criteria
were developed during OMERACT 4 and published in
the Journal of Rheumatology [5, 6].

The core outcome domains to be measured in both
randomized clinical trials and longitudinal observation
studies in systemic lupus erythematosus are:

- disease activity
- health-related quality of life
- damage
- toxicity/adverse events.

Outcome measures for osteoporosis

The core endpoints for osteoporosis trials were dis-
cussed at OMERACT 3 and subsequently published in
the Journal of Rheumatology [7].

The outcome measures for osteoporosis trials were
discussed according to two broad groupings of trials:
randomized trials where prevention of rapid bone loss
was the primary aim and randomized trials where
prevention of fractures may be a feasible outcome
because patients were already at high risk of osteopo-
tic fractures either on the basis of low bone mass or
previous osteoporotic fracture.

Randomized trials where prevention of rapid bone loss
was the primary aim

Two core outcome measures of clinical benefit were
considered appropriate:

- (a) bone minimum density (measured at two sites:
  the lumbar spine and proximal femur);
- (b) biochemical markers which should include at
  least one resorption marker (which should be
  based on a urinary cross-linked excretion) and at
  least one formation marker.

Non-core outcome measures of clinical benefit were
considered to be:

- (a) fractures;
- (b) quality of life;
- (c) change in height (measured in a standardized
  manner).

Randomized trials of fracture prevention in
high-risk populations

The core outcome measures of benefit were:

- (a) fracture;
- (b) hip and spine bone mineral density;
- (c) biochemical markers;
- (d) change in height.

The non-core outcome measures of benefit in these
studies would include:

- (a) quality of life instrument;
- (b) back pain measure;
- (c) economic evaluation, including health service
  utilization such as hospitalization, cotherapy,
  etc.;
- (d) measure of incident falls.

It was recommended that these studies should be of
3–5 yr duration.

Criteria for the classification of rheumatic
diseases

Ankylosing spondylitis

The 1961 Rome criteria for ankylosing spondylitis [8]

Low back pain and stiffness for more than 3 months
not relieved by rest;
- Pain and stiffness of the thoracic region;
Limited motion in lumbar spine;
Limited chest expansion;
Evidence or history of iritis or its sequelae.

Requirements: either positive radiographs (bilateral SI) and one or more clinical criteria, or four out of five clinical criteria.

The 1966 New York criteria for ankylosing spondylitis [9]

(1) Presence of history of pain at dorsolumbar junction or in lumbar spine;
(2) Limitation of motion in anterior flexion, lateral flexion and extension;
(3) Limitation of chest expansion to 1 inch (2.5 cm) or less at the fourth intercostal space.

Requirements: either positive radiographs (grade 3–4 bilateral sacroiliac) and one or more clinical criteria, or grade 3–4 unilateral or grade 2 bilateral SI with clinical criterion (2) or with clinical criteria (1) and (3).

The European Spondyloarthropathy Study Group classification for spondyloarthropathy [10]

Inflammatory spinal pain
or
synovitis
asymmetric
predominantly in the lower limbs
and one or more of the following:
alternate buttock pain;
sacroilitis;
enthesopathy;
positive family history;
psoriasis;
inflammatory bowel disease;
sacroilitis or cervicitis or acute diarrhoea occurring within 1 month before arthritis.

Domains of the core sets for SM-ARD/physical therapy, clinical record keeping and DC-ART as endorsed by Assessment in Ankylosing Spondylitis Working Group/OMERACT/ILAR [11]

Level 1, SM-ARD/physical therapy:
physical function;
pain;
spinal mobility;
spinal stiffness;
patient global assessment.

Level 2, Clinical record keeping:
acute-phase reactants;
peripheral joints/entheses.

Level 3, DC-ART:
spine radiograph;
hip radiograph;
fatigue.

Behçet’s disease [12]

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent oral ulceration</td>
<td>Minor aphtous, major aphtous, or herpetiform ulceration observed by physician or patient, which recurred at least three times in one 12-month period</td>
</tr>
<tr>
<td>Plus two of:</td>
<td></td>
</tr>
<tr>
<td>Recurrent genital ulceration</td>
<td>Aphthous ulceration or scarring, observed by physician or patient</td>
</tr>
<tr>
<td>Eye lesions</td>
<td>Anterior uveitis, posterior uveitis, or cells in vitreous on slit lamp examination; or retinal vasculitis observed by ophthalmologist</td>
</tr>
<tr>
<td>Skin lesions</td>
<td>Erythema nodosum observed by physician or patient, pseudofolliculitis, or papulopustular lesions; or acneiform nodules observed by physician in post-adolescent patients not on corticosteroid treatment</td>
</tr>
<tr>
<td>Positive pathergy test</td>
<td>Read by physician at 24–48 h</td>
</tr>
</tbody>
</table>

Findings applicable only in the absence of other clinical explanations.

Churg–Strauss syndrome [13]

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>History of wheezing or diffuse high-pitched rales on expiration</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>Eosinophilia &gt;10% on white blood cell differential count</td>
</tr>
<tr>
<td>History of allergy</td>
<td>History of seasonal allergy (e.g. allergic rhinitis) or other documented allergies, including food, contactants, and other, except drug allergy</td>
</tr>
<tr>
<td>Mononeuropathy or polyneuropathy</td>
<td>Development of mononeuropathy, multiple mononeuropathies, or polyneuropathy (i.e. glove/stocking distribution) attributable to a systemic vasculitis</td>
</tr>
<tr>
<td>Pulmonary infiltrates, non-fixed</td>
<td>Migratory or transitory pulmonary infiltrates on radiographs (not including fixed infiltrates), attributable to a systemic vasculitis</td>
</tr>
<tr>
<td>Paranasal sinus abnormality</td>
<td>History of acute or chronic paranasal sinus pain or tenderness or radiographic opacification of the paranasal sinuses</td>
</tr>
<tr>
<td>Extravascular eosinophils</td>
<td>Biopsy including artery, arteriole, or venule, showing accumulations of eosinophils in extravascular areas</td>
</tr>
</tbody>
</table>

*History of allergy, other than asthma or drug-related, is included only in the tree classification criteria set and not in the traditional format criteria set, which requires four or more of the six other items listed here.

Fibromyalgia [14]

History of widespread pain
Definition: Pain is considered widespread when all of the following are present: pain in the left side of the
body, pain in the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present. In this definition, shoulder and buttock pain is considered as pain for each involved. ‘Low back’ pain is considered lower segment pain.

Pain in 11 of 18 tender point sites on digital palpation

Definition: Pain, on digital palpation, must be present in at least 11 of the following 18 tender point sites:

1. **Occiput—bilateral**, at the suboccipital muscle insertions;
2. **Low cervical—bilateral**, at the anterior aspects of the intertransverse spaces at C5–C7;
3. **Trapezius—bilateral**, at the midpoint of the upper border;
4. **Supraspinatus—bilateral**, at origins, above the scapula spine near the medial border;
5. **Second rib—bilateral**, at the second costochondral junctions, just lateral to the junctions on upper surfaces;
6. **Lateral epicondyle—bilateral**, 2 cm distal to the epicondyles;
7. **Gluteal—bilateral**, in upper outer quadrants of buttocks in anterior fold of muscle;
8. **Knee—bilateral**, at the medial fat pad proximal to the joint line.

Digital palpation should be performed with an approximate force of 4 kg. For a tender point to be considered ‘positive’ the subject must state that the palpation was painful. ‘Tender’ is not to be considered ‘painful’. For classification purposes, patients will be said to have fibromyalgia if both criteria are satisfied. Widespread pain must have been present for at least 3 months. The presence of a second clinical disorder does not exclude the diagnosis of fibromyalgia.

Giant cell arteritis [15]

The 1990 criteria for the classification of giant cell (temporal) arteritis (traditional format)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Age at disease onset ( \geq 50 ) yr</td>
<td>Development of symptoms or findings beginning at age 50 yr or older</td>
</tr>
<tr>
<td>(2) New headache</td>
<td>New onset of or new type of localized pain in the head</td>
</tr>
<tr>
<td>(3) Temporal artery abnormality</td>
<td>Temporal artery tenderness to palpation or decreased pulsation, unrelated to arteriosclerosis of cervical arteries</td>
</tr>
<tr>
<td>(4) Elevated erythrocyte sedimentation rate</td>
<td>Erythrocyte sedimentation rate ( \geq 50 ) mm/h by the Westergren method</td>
</tr>
<tr>
<td>(5) Abnormal artery biopsy</td>
<td>Biopsy specimen with artery showing vasculitis characterized by a predominance of mononuclear cell infiltration or granulomatous inflammation, usually with multinucleated giant cells</td>
</tr>
</tbody>
</table>

For the purposes of classification, a patient shall be said to have giant cell (temporal) arteritis if at least three of these five criteria are present. The presence of any three or more criteria yields a sensitivity of 93.5% and a specificity of 91.2%.

Gout [16]

(a) The presence of characteristic urate crystals in the joint fluid, and/or
(b) A tophus proved to contain urate crystals by chemical or polarized light microscopic means, and/or
(c) The presence of six of the 12 clinical, laboratory, and X-ray phenomena listed below:

- Maximum inflammation in 1 day;
- More than one attack;
- Monoarticular arthritis;
- Redness;
- First metatarsophalangeal joint (MTP) pain or swelling;
- Unilateral first MTP;
- Unilateral tarsal;
- Suspected tophus;
- Hyperuricemia;
- Asymmetric swelling;
- Subcortical cysts, no erosions;
- Negative organisms on culture.

**Criteria and definitions used for the classification of giant cell (temporal) arteritis (tree format)**

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>(1) Age at disease onset ( \geq 50 ) yr</td>
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<tr>
<td>(2) New headache</td>
<td>New onset of or new type of localized pain in the head</td>
</tr>
<tr>
<td>(3) Claudication of jaw, tongue, or on deglutition</td>
<td>Development or worsening of fatigue or discomfort in the muscles of mastication, tongue, or swallowing muscles while eating</td>
</tr>
<tr>
<td>(4) Temporal artery abnormality</td>
<td>Temporal artery tenderness to palpation or decreased pulsation, unrelated to arteriosclerosis of cervical arteries</td>
</tr>
<tr>
<td>(5) Scalp tenderness or nodules*</td>
<td>Development of tender areas or nodules over the scalp, away from the temporal artery or other cranial arteries</td>
</tr>
<tr>
<td>(6) Abnormal artery biopsy</td>
<td>Biopsy specimen with artery showing vasculitis characterized by a predominance of mononuclear cell infiltration or granulomatous inflammation, usually with multinucleated giant cells</td>
</tr>
</tbody>
</table>

*Used as a surrogate if artery biopsy is not available [criterion (2)] or if temporal artery abnormality is not present [criterion (5)].
Henoch–Schönlein purpura [17]

The 1990 criteria for the classification of Henoch–Schönlein purpura (traditional format)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpable purpura</td>
<td>Slightly raised 'palpable' haemorrhagic skin lesions, not related to thrombocytopenia</td>
</tr>
<tr>
<td>Age ≤ 20 yr at disease onset</td>
<td>Patient 20 yr or younger at onset of first symptoms</td>
</tr>
<tr>
<td>Bowel angina</td>
<td>Diffuse abdominal pain, worse after meals, or the diagnosis of bowel ischaemia, usually including bloody diarrhoea</td>
</tr>
<tr>
<td>Wall granulocytes on biopsy</td>
<td>Histological changes showing granulocytes in the walls of arterioles or venules</td>
</tr>
</tbody>
</table>

For the purposes of classification, a patient shall be said to have Henoch–Schönlein purpura if at least two of these four criteria are present. The presence of any two or more criteria yields a sensitivity of 87.1% and a specificity of 87.7%.

Criteria and definitions used for the classification of Henoch–Schönlein purpura (tree format)

<table>
<thead>
<tr>
<th>Criteria</th>
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</tr>
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<tbody>
<tr>
<td>Palpable purpura</td>
<td>Slightly elevated purpuric rash over one or more areas of the skin; does not blanch with pressure and is not related to thrombocytopenia</td>
</tr>
<tr>
<td>Maculopapular rash</td>
<td>Flat and raised lesions of various sizes over one or more areas of the skin</td>
</tr>
<tr>
<td>Polymorphonuclear neutrophils in vessel wall</td>
<td>Biopsy demonstrating granulocytes in the wall of a venule or arteriole</td>
</tr>
<tr>
<td>Eosinophils in biopsy</td>
<td>Biopsy demonstrating eosinophils in a venule or arteriole at any location</td>
</tr>
</tbody>
</table>

Hypersensitivity vasculitis [18]

The 1990 criteria for the classification of hypersensitivity vasculitis (traditional format)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at disease onset &gt; 16 yr</td>
<td>Development of symptoms after age 16 yr</td>
</tr>
<tr>
<td>Medication at disease onset</td>
<td>Medication was taken at the onset of symptoms that may have been a precipitating factor</td>
</tr>
<tr>
<td>Palpable purpura</td>
<td>Slightly elevated purpuric rash over one or more areas of the skin; does not blanch with pressure and is not related to thrombocytopenia</td>
</tr>
<tr>
<td>Maculopapular rash</td>
<td>Flat and raised lesions of various sizes over one or more areas of the skin</td>
</tr>
<tr>
<td>Biopsy including arteriole and venule</td>
<td>Histological changes showing granulocytes in a perivascular or extravascular location</td>
</tr>
</tbody>
</table>

For the purposes of classification, a patient shall be said to have hypersensitivity vasculitis if at least three of these five criteria are present. The presence of any three or more criteria yields a sensitivity of 71.0% and a specificity of 83.9%.

Criteria and definitions used for the classification of hypersensitivity vasculitis (tree format)

<table>
<thead>
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<tr>
<td>Eosinophils in biopsy</td>
<td>Biopsy demonstrating eosinophils in a venule or arteriole at any location</td>
</tr>
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</table>

Kawasaki syndrome [19]

Principal symptoms

Fever lasting from 1 to 2 weeks and not responding to antibiotics

Bilateral congestion of ocular conjunctivae

Changes in lips and oral cavity:

- dryness, redness and fissuring of lips;
- protuberance of tongue papillae (strawberry tongue);
- diffuse reddening of oral and pharyngeal mucosa.

Changes in peripheral extremities:

- reddening of palms and soles (initial stage);
- indurative oedema (initial stage);
- membranous desquamation from fingertips (convalescent stage).

Polymorphous exanthema of body trunk without vesicles or crusts

Acute non-purulent swelling of cervical lymph nodes of 1.5 cm or more in diameter

Other significant symptoms or findings

Carditis, especially myocarditis and pericarditis

Diarrhoea

Arthralgia or arthritis

Proteinuria and increase of leucocytes in urine sediment

Changes in blood tests:

- leucocytosis with shift to the left;
- slight decrease in erythrocyte and haemoglobin levels;
increased erythrocyte sedimentation rate; positive C-reactive protein; increased α2-globulin; negative anti streptolysin-O titre

Changes occasionally observed:
aseptic meningitis; mild jaundice or slight increase in serum transaminase

Osteoarthritis of the hand [20]

Classification criteria for osteoarthritis of the hand (traditional format)
Hand pain, aching, or stiffness and three or four of the following features:

- hard tissue enlargement of two or more of 10 selected joints;
- hard tissue enlargement of two or more distal interphalangeal joints;
- fewer than three swollen metacarpophalangeal (MCP) joints;
- deformity of at least one of 10 selected joints.

The 10 selected joints are the second and third distal interphalangeal joints, the second and third proximal interphalangeal (PIP), and the first carpometacarpal joints of both hands. This classification method yields a sensitivity of 94% and a specificity of 87%.

Osteoarthritis of the hip [21]

Classification criteria for osteoarthritis of the hip (traditional format)
Hip pain and at least two of the following three features:

- erythrocyte sedimentation rate < 20 mm/h; radiographic femoral or acetabular osteophytes; radiographic joint space narrowing (superior, axial, and/or medial).

This classification method yields a sensitivity of 89% and a specificity of 91%.

Combined clinical (history, physical examination, laboratory) and radiographic classification criteria for osteoarthritis of the hip (classification tree format)

Hip pain and
Femoral and/or acetabular osteophytes on radiograph or Erythrocyte sedimentation rate ≤ 20 mm/h and Axial joint space narrowing on radiograph

This classification method yields a sensitivity of 91% and a specificity of 89%.

Osteoarthritis of the knee [22]

Criteria for the classification of idiopathic osteoarthritis of the knee

<table>
<thead>
<tr>
<th>Clinical and laboratory</th>
<th>Clinical and radiographic</th>
<th>Clinical*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee pain + at least five of nine:</td>
<td>Knee pain + at least one of three:</td>
<td>Knee pain + at least three of six:</td>
</tr>
<tr>
<td>age &gt; 50 yr</td>
<td>age &gt; 50 yr</td>
<td>age &gt; 50 yr</td>
</tr>
<tr>
<td>stiffness &lt; 30 min</td>
<td>stiffness &lt; 30 min</td>
<td>stiffness &lt; 30 min</td>
</tr>
<tr>
<td>crepitus</td>
<td>crepitus + osteophytes</td>
<td>crepitus</td>
</tr>
<tr>
<td>bony tenderness</td>
<td>bony tenderness</td>
<td>bony tenderness</td>
</tr>
<tr>
<td>no palpable warmth</td>
<td>no palpable warmth</td>
<td></td>
</tr>
<tr>
<td>ESR &lt; 40 mm/h</td>
<td>SF OA</td>
<td></td>
</tr>
<tr>
<td>RF &lt; 1:40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>92% sensitive</td>
<td>91% sensitive</td>
<td>95% sensitive</td>
</tr>
<tr>
<td>75% specific</td>
<td>86% specific</td>
<td>69% specific</td>
</tr>
</tbody>
</table>

ESR, erythrocyte sedimentation rate (Westergren); RF, rheumatoid factor; SF OA, synovial fluid signs of osteoarthritis (clear, viscous, or white blood cell count < 2000/mm³).

*An alternative for the clinical category would be four of six, which is 85% sensitive and 89% specific.

Polyarteritis nodosa [23]

The 1990 criteria for the classification of polyarteritis nodosa (traditional format)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss ≥ 4 kg</td>
<td>Loss of 4 kg or more of body weight since illness began, not due to dieting or other factors</td>
</tr>
<tr>
<td>Livedo reticularis</td>
<td>Mottled reticular pattern over the skin of portions of the extremities or torso</td>
</tr>
<tr>
<td>Testicular pain or tenderness</td>
<td>Pain or tenderness of the testicles, not due to infection, trauma, or other causes</td>
</tr>
<tr>
<td>Myalgias, weakness, or leg tenderness</td>
<td>Diffuse myalgias (excluding shoulder and hip girdle) or weakness of muscles or tenderness of leg muscles</td>
</tr>
<tr>
<td>Mononeuropathy or polyneuropathy</td>
<td>Development of mononeuropathy, multiple mononeuropathies, or polyneuropathy</td>
</tr>
<tr>
<td>Diastolic blood pressure &gt; 90 mmHg</td>
<td>Development of hypertension with diastolic blood pressure higher than 90 mmHg</td>
</tr>
<tr>
<td>Elevated BUN or creatinine &gt; 1.5 mg/dl</td>
<td>Elevation of BUN &gt; 40 mg/dl or creatinine &gt; 1.5 mg/dl, not due to dehydration or obstruction</td>
</tr>
<tr>
<td>Hepatitis B virus</td>
<td>Presence of hepatitis B surface antigen or antibody in serum</td>
</tr>
<tr>
<td>Arteriographic abnormality</td>
<td>Arteriogram showing aneurysms or occlusions of the visceral arteries, not due to arteriosclerosis, fibromuscular dysplasia, or other non-inflammatory causes</td>
</tr>
<tr>
<td>Biopsy of small or medium-sized artery containing PMN</td>
<td>Histological changes showing the presence of granulocytes or granulocytes and mononuclear leukocytes in the artery wall</td>
</tr>
</tbody>
</table>

BUN, blood urea nitrogen; PMN, polymorphonuclear neutrophils.
For classification purposes, a patient shall be said to have polyarteritis nodosa if at least three of these 10 criteria are present. The presence of any three or more criteria yields a sensitivity of 82.2% and a specificity of 86.6%.

**Polymyalgia rheumatica** [24]

*Characteristics*
- Shoulder pain and/or stiffness bilaterally
- Onset of illness of < 2 weeks’ duration (refers to time taken for symptoms to reach their full-blown picture)
- Initial erythrocyte sedimentation rate $\geq 40$ mm/h
- Morning stiffness duration $> 1$ h
- Age $> 65$ yr
- Depression and/or loss of weight
- Upper arm tenderness bilaterally

**Polymyositis and dermatomyositis** [25]

*Criteria*
1. Skin lesions:
   - (a) heliotrope rash (red purple erythema on the upper palpebra);
   - (b) Gottron’s sign (red purple keratotic, atrophic erythema, or macules on the extensor surface of finger joints);
   - (c) erythema on the extensor surface of extremity joints: slightly raised red purple erythema over elbows or knees.
2. Proximal muscle weakness (upper or lower extremity and trunk).
3. Elevated serum creatine kinase or aldolase level.
4. Muscle pain on grasping or spontaneous pain.
5. Myogenic changes on EMG (short duration, polyphasic motor unit potentials with spontaneous fibrillation potentials).
6. Positive anti-Jo-1 (histadyl tRNA synthetase) antibody.
7. Non-destructive arthritis or arthralgias.
8. Systemic inflammatory signs (fever: more than 37°C at axilla, elevated serum C-reactive protein level or accelerated erythrocyte sedimentation rate of more than 20 mm/h by the Westergren method).
9. Pathological findings compatible with inflammatory myositis (inflammatory infiltration of skeletal muscle with degeneration or necrosis of muscle fibres; active phagocytosis, central nuclei, or evidence of active regeneration may be seen).

A patient is said to have dermatomyositis if at least one item from (1) and at least four items from (2) to (9) are present. The sensitivity is 94.1% (127/135), and the specificity of skin lesions against systemic lupus erythematosus and systemic sclerosis is 90.3% (214/237). A patient is said to have polymyositis if at least four items from (2) to (9) are present. The sensitivity is 98.9% (180/182) and the specificity of polymyositis and dermatomyositis against all control diseases combined is 95.2% (373/392).

**Reiter’s syndrome** [26]

*Percentage sensitivity and specificity of various criteria for typical Reiter’s syndrome (initial episode)*

<table>
<thead>
<tr>
<th>Method of classification</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episode of arthritis of more than 1 month with urethritis and/or cervicitis</td>
<td>84.3% (70/83)</td>
<td>98.2% (163/166)</td>
</tr>
<tr>
<td>Episode of arthritis of more than 1 month and either urethritis or cervicitis, or bilateral conjunctivitis</td>
<td>85.5% (71/83)</td>
<td>96.4% (160/166)</td>
</tr>
<tr>
<td>Episode of arthritis, conjunctivitis, and urethritis</td>
<td>50.6% (42/83)</td>
<td>98.8% (164/166)</td>
</tr>
<tr>
<td>Episode of arthritis of more than 1 month, conjunctivitis, and urethritis</td>
<td>48.2% (40/83)</td>
<td>98.8% (164/166)</td>
</tr>
</tbody>
</table>

The numbers in parentheses indicate the number of patients correctly classified/the number tested.

**Rheumatic fever** [27]

*Guidelines for the diagnosis of an initial attack of rheumatic fever (Jones criteria, 1992 update)*

**Major manifestations**
- Carditis
- Polyarthritis
- Chorea
- Erythema marginatum
- Subcutaneous nodules

**Minor manifestations**

*Clinical findings:*
- arthralgia;
- fever.

*Laboratory findings:*
- elevated acute-phase reactants
- erythrocyte sedimentation rate
- C-reactive protein
- prolonged PR interval

Supporting evidence of antecedent group A streptococcal infections
- Positive throat culture or rapid streptococcal antigen test
- Elevated or rising streptococcal antibody titre

If supported by evidence of preceding group A streptococcal infection, the presence of two major manifestations or of one major and two minor manifestations indicates a high probability of acute rheumatic fever.
Rheumatoid arthritis [28]

The 1987 revised criteria for the classification of rheumatoid arthritis (traditional format)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Morning stiffness</td>
<td>Morning stiffness in and around the joints, lasting at least 1 h before maximal improvement</td>
</tr>
<tr>
<td>(2) Arthritis of three or more joint areas</td>
<td>At least three joint areas simultaneously have had soft tissue swelling or fluid (not bony overgrowth alone) observed by a physician. The 14 possible areas are right or left proximal interphalangeal (PIP), MCP, wrist, elbow, knee, ankle, and MTP joints</td>
</tr>
<tr>
<td>(3) Arthritis of hand joints</td>
<td>At least one area swollen (as defined above) in a wrist, MCP, or PIP joint</td>
</tr>
<tr>
<td>(4) Symmetric arthritis</td>
<td>Simultaneous involvement of the same joint areas as defined in (2) on both sides of the body (bilateral involvement of PIPs, MCPs, or MTPs is acceptable without absolute symmetry)</td>
</tr>
<tr>
<td>(5) Rheumatoid nodules</td>
<td>Subcutaneous nodules, over bony prominences, or extensor surfaces, or in juxta-articular regions, observed by a physician</td>
</tr>
<tr>
<td>(6) Serum rheumatoid factor</td>
<td>Demonstration of abnormal amounts of serum rheumatoid factor by any method for which the result has been positive in &lt; 5% of normal control subjects</td>
</tr>
<tr>
<td>(7) Radiographic changes</td>
<td>Radiographic changes typical of rheumatoid arthritis on posteroanterior hand and wrist radiographs, which must include erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joints (osteoarthritis changes alone do not qualify)</td>
</tr>
</tbody>
</table>

For classification purposes, a patient shall be said to have rheumatoid arthritis if he/she has satisfied at least four of these seven criteria. Criteria (1)–(4) must have been present for at least 6 weeks. Patients with two clinical diagnoses are not excluded. Designation as classic, definite, or probable rheumatoid arthritis is not to be made.

Ocular symptoms
Definition: a positive response to at least one of the following three questions:
(a) Have you had a daily feeling of dry mouth for more than 3 months?
(b) Have you had recurrent or persistently swollen salivary glands as an adult?
(c) Do you frequently drink liquids to aid in swallowing dry foods?

Sjögren’s syndrome [29]

Preliminary criteria for the classification of Sjögren’s syndrome

Ocular symptoms
Definition: a positive response to at least one of the following three questions:
(a) Have you had daily, persistent, troublesome dry eyes for more than 3 months?
(b) Do you have a recurrent sensation of sand or gravel in the eyes?
(c) Do you use tear substitutes more than three times a day?

Oral symptoms
Definition: objective evidence of ocular involvement, determined on the basis of a positive result on at least one of the following two tests:
(a) Schirmer-1 test (< 5 mm in 5 min);
(b) Rose Bengal score (> 4, according to the van Bijsterveld scoring system).

Histopathological features
Definition: focus score ≥ 1 on minor salivary gland biopsy (focus defined as an agglomeration of at least 50 mononuclear cells; focus score defined as the number of foci in 4 mm² of glandular tissue).

Salivary gland involvement
Definition: objective evidence of salivary gland involvement, determined on the basis of a positive result on at least one of the following three tests:
(a) Salivary scintigraphy;
(b) Parotid sialography;
(c) Unstimulated salivary flow (< 1.5 ml in 15 min).

Autoantibodies
Definition: presence of at least one of the following serum autoantibodies:
(a) Antibodies to Ro/SS-A or La/SS-B antigens;
(b) Antinuclear antibodies;
(c) Rheumatoid factor.

Exclusion criteria: pre-existing lymphoma, acquired immunodeficiency syndrome, sarcoidosis, or graft-vs-host disease.

Spondyloarthropathies [30]

Inflammatory spinal pain or synovitis asymmetrical or predominantly in the lower limbs

and one or more of the following:

- positive family history;
- psoriasis;
- inflammatory bowel disease;
- urethritis, cervicitis, or acute diarrhoea within 1 month before arthritis;
- buttock pain alternating between right and left gluteal areas;
- enthesopathy;
- sacroiliitis.
Systemic lupus erythematosus [31, 32]

The 1982 revised criteria for the classification of systemic lupus erythematosus

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malar rash</td>
<td>Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds</td>
</tr>
<tr>
<td>Discoid rash</td>
<td>Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation</td>
</tr>
<tr>
<td>Oral ulcers</td>
<td>Oral or nasopharyngeal ulceration, usually painless, observed by a physician</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Non-erosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling, or effusion</td>
</tr>
<tr>
<td>Serositis</td>
<td>(a) Pleuritis: convincing history of pleuritic pain or rub head by a physician or evidence of pleural effusion; or (b) Pericarditis: documented by ECG or rub or evidence of pericardial effusion</td>
</tr>
<tr>
<td>Renal disorder</td>
<td>(a) Persistent proteinuria greater than 0.5 g/day or greater than 3 + if quantitation not performed; or (b) Cellular casts: may be red cell, haemoglobin, granular, tubular, or mixed</td>
</tr>
<tr>
<td>Neurological disorder</td>
<td>(a) Seizures: in the absence of offending drugs or known metabolic derangements; e.g. uraemia, ketoacidosis, or electrolyte imbalance; or (b) Psychosis: in the absence of offending drugs or known metabolic derangements, e.g. uraemia, ketoacidosis, or electrolyte imbalance</td>
</tr>
<tr>
<td>Haematological disorder</td>
<td>(a) Haemolytic anaemia with reticulocytosis; or (b) Leucopenia: less than 4.00/mm³ total on two or more occasions; or (c) Lymphopenia: less than 1.55/mm³ on two or more occasions; or (d) Thrombocytopenia: less than 100 000/mm³ in the absence of offending drugs</td>
</tr>
<tr>
<td>Immunological disorder (modified 1997)</td>
<td>(a) Anti-DNA: antibody to native DNA in abnormal titre; or (b) Anti-Sm: presence of antibody to Sm nuclear antigen; or (c) Positive finding of antiphospholipid antibodies based on: (1) an abnormal serum level of IgG or IgM antiphospholipid antibodies; (2) a positive test result for lupus anticoagulant using a standard method; or (3) a false-positive serological test for syphilis known to be positive for at least 6 months and confirmed by Treponema pallidum immobilization or fluorescent treponemal antibody absorption test</td>
</tr>
<tr>
<td>Antinuclear antibody</td>
<td>An abnormal titre of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time and in the absence of drugs known to be associated with 'drug-induced lupus' syndrome</td>
</tr>
</tbody>
</table>

The proposed classification is based on 11 criteria. For the purpose of identifying patients in clinical studies, a person shall be said to have systemic lupus erythematosus if any four or more of the 11 criteria are present, serially or simultaneously, during any interval of observation.

Systemic sclerosis [33]

American Rheumatism Association Scleroderma Criteria

Cooperative Study (SCCS): preliminary clinical criteria for systemic sclerosis (excludes localized scleroderma and pseudosclerodermatous disorders)

Proximal scleroderma is the single major criterion; sensitivity was 91% and specificity was over 99%.

Sclerodactyly, digital pitting scars of fingertips or loss of substance of the distal finger pad, and bibasilar pulmonary fibrosis contributed further as minor criteria in the absence of proximal scleroderma.

One major or two or more minor criteria were found in 97% of definite systemic sclerosis patients, but only in 2% of the comparison patients with systemic lupus erythematosus, polymyositis/dermatomyositis, or Raynaud’s phenomenon.

Takayasu’s arteritis [34]

The 1990 criteria for the classification of Takayasu’s arteritis (traditional format)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at disease onset ≤40 yr</td>
<td>Development of symptoms or findings related to Takayasu’s arteritis at age ≤40 yr</td>
</tr>
<tr>
<td>Claudication of extremities</td>
<td>Development and worsening of fatigue and discomfort in muscles of one or more extremity while in use, especially the upper extremities</td>
</tr>
<tr>
<td>Decreased brachial artery pulse</td>
<td>Decreased pulsation of one or both brachial arteries</td>
</tr>
<tr>
<td>Blood pressure difference &gt;10 mmHg</td>
<td>Difference of &gt;10 mmHg in systolic blood pressure between arms</td>
</tr>
<tr>
<td>Bruit over subclavian arteries or aorta</td>
<td>Bruit audible on auscultation over one or both subclavian arteries or abdominal aorta</td>
</tr>
<tr>
<td>Arteriogram abnormality</td>
<td>Arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities, not due to arteriosclerosis, fibromuscular dysplasia, or similar causes: changes usually focal or segmental</td>
</tr>
</tbody>
</table>

For the purposes of classification, a patient shall be said to have Takayasu’s arteritis if at least three of these six criteria are present. The presence of any three or more criteria yields a sensitivity of 90.5% and a specificity of 97.8%.
Wegener’s granulomatosis [35]

**The 1990 criteria for the classification of Wegener’s granulomatosis (traditional format)**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal or oral inflammation</td>
<td>Development of painful or painless oral ulcers or purulent or bloody nasal discharge</td>
</tr>
<tr>
<td>Abnormal chest radiograph</td>
<td>Chest radiograph showing the presence of nodules, fixed infiltrates, or cavities</td>
</tr>
<tr>
<td>Urinary sediment</td>
<td>Microhaematuria (&gt;5 red blood cells per high power field) or red cell casts in urine sediment</td>
</tr>
<tr>
<td>Granulomatous inflammation on biopsy</td>
<td>Histological changes showing granulomatous inflammation within the wall of an artery or in the perivascular or extravascular area (artery or arteriole)</td>
</tr>
</tbody>
</table>

For the purposes of classification, a patient shall be said to have Wegener’s granulomatosis if at least two of these four criteria are present. The presence of any two or more criteria yields a sensitivity of 88.2% and a specificity of 92.0%.

**Criteria and definitions used for the classification of Wegener’s granulomatosis (tree format)**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal or oral inflammation</td>
<td>Development of painful or painless oral ulcers or purulent or bloody nasal discharge</td>
</tr>
<tr>
<td>Haemoptysis*</td>
<td>Haemoptysis during illness</td>
</tr>
<tr>
<td>Abnormal chest radiograph</td>
<td>Chest radiograph showing the presence of nodules, fixed infiltrates, or cavities</td>
</tr>
<tr>
<td>Urinary sediment</td>
<td>Microhaematuria (&gt;5 red blood cells per high power field) or red cell casts in urine sediment</td>
</tr>
<tr>
<td>Granulomatous inflammation on biopsy</td>
<td>Histological changes showing granulomatous inflammation within the wall of an artery or in the perivascular or extravascular area (artery or arteriole)</td>
</tr>
</tbody>
</table>

*Used as a surrogate if biopsy data are not available.

**Polyarthritides (rheumatoid factor negative)**
- Polyarthritis
- Psoriatic arthritis
- Enthesitis-related arthritis
- Other arthritis:
  - fits no other category
  - fits more than one category

**References**

15. Hunder GG, Bloch DA, Michel BA et al. The American College of Rheumatology 1990 criteria for the...