Complete Summary

GUIDELINE TITLE

Systemic lupus erythematosus (SLE).

BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Systemic lupus erythematosus (SLE). In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2007 Feb 20 [Various].

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Gripenberg-Gahmberg M. Systemic lupus erythematosus (SLE). In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2006 May 24 [various].

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references drugs for which important revised regulatory information has been released.

- June 30, 2008, CellCept (mycophenolate mofetil) and Myfortic (mycophenolate acid): Novartis and Roche have agreed to include additional labeling revisions to the WARNINGS and ADVERSE REACTIONS sections of the Myfortic and CellCept prescribing information, based on post-marketing data regarding cases of Progressive Multifocal Leukoencephalopathy (PML) in patients treated with these drugs.
- October 29, 2007, CellCept (mycophenolate mofetil): Roche has agreed to include additional labeling revisions to the BOXED WARNING, WARNINGS/Pregnancy and Pregnancy Exposure Prevention, PRECAUTIONS/Information for Patients, and ADVERSE REACTIONS/Postmarketing Experience sections.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Systemic lupus erythematosus (SLE)

GUIDELINE CATEGORY

Diagnosis
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Rheumatology

INTENDED USERS

Health Care Providers
Physicians

GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collects, summarizes, and updates the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

TARGET POPULATION

Patients with or suspected to have systemic lupus erythematosus (SLE)

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Assessment of clinical features
2. Laboratory evaluation (blood count, platelets, sedimentation rate, anti-nuclear antibodies, dipstick test of the urine and urinalysis)
3. American Rheumatism Association (ARA) classification
4. Referral to a specialist, as indicated, for evaluation

Treatment

1. Individualized treatment depending on the manifestations and activity of the disease
2. Patient education: avoidance of sunbathing, use of sunscreens
3. Pharmacologic therapy (nonsteroidal anti-inflammatory drugs, hydroxychloroquine, corticosteroids, immunosuppressive drugs [e.g. azathioprine, cyclophosphamide, methotrexate, mycophenolate])
4. Other drugs as indicated, such as antihypertensive treatment
5. Referral to nephrologist for signs of renal manifestations

MAJOR OUTCOMES CONSIDERED

- Risk of relapse
- Risk for mortality
- Risk for end-stage renal disease
- Degree of clearing/improvement of discoid lupus
- Lupus signs and symptoms

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

A. **Quality of Evidence: High**

   Further research is very unlikely to change confidence in the estimate of effect

- Several high-quality studies with consistent results
- In special cases: one large, high-quality multi-centre trial

B. **Quality of Evidence: Moderate**

Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.

- One high-quality study
- Several studies with some limitations

C. **Quality of Evidence: Low**

Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.

- One or more studies with severe limitations

D. **Quality of Evidence: Very Low**

Any estimate of effect is very uncertain.

- Expert opinion
- No direct research evidence
- One or more studies with very severe limitations

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

Definition

- Systemic lupus erythematosus (SLE) is a syndrome characterized by clinical diversity, changes in the disease activity over time, and by aberrant immunological findings and especially the presence of antinuclear antibodies.

Epidemiology

- The prevalence of SLE worldwide is 4 to 250 per 100,000. About 90% of the patients are female. The incidence is most frequent in women aged 15 to 25 years.

Clinical Presentation

- The clinical presentation varies between different patients, and in a single patient the disease activity varies over time.
- General symptoms such as fatigue and fever are common.
- A vast majority of the patients have arthralgia, mostly of the hands.
- About one-half of the patients have cutaneous features, such as butterfly rash and discoid lupus (see Pictures 1 and 2 in the original guideline document) as well as photosensitivity.
- About one-third of the patients have oral ulcerations.
- About 50% of the patients have nephropathy, which varies from mild proteinuria and microscopical hematuria to end-stage renal failure.
- About 20 to 40% of the patients have pleurisy. Acute pneumonitis and chronic fibrotising alveolitis are relatively rare.
- Pericarditis is somewhat more uncommon than pleuritis. T-wave changes in the electrocardiogram (ECG) are usual.
- Depression and headache are the most common of the neuropsychiatric symptoms. Generalized tonic-clonic seizures and organic psychoses are rare. Peripheral neuropathy is observed in about 10% of the patients and as many patients get a thromboembolic or haemorrhagic complication of the brain.
- The lymph nodes may enlarge especially when the disease is active.
- There is a risk of first and second trimester foetal losses and of premature birth.

Laboratory Findings

- Laboratory findings are diverse.
- Erythrocyte sedimentation rate (ESR) is usually elevated; the C-reactive protein (CRP) value is often normal.
- Mild or moderate anaemia is common. A clear-cut haemolytic anaemia is seen in less than 10% of the patients.
- Leucocytopenia (lymphocytopenia)
- Mild thrombocytopenia
- Antinuclear antibodies are found in over 90% of the patients.
- Anti-deoxyribonucleic acid (DNA) antibodies (in 50 to 90% of the patients)
- Polyclonal hypergammaglobulinaemia
- Decreased complement values (C3 and C4)
- Antiphospholipid antibodies
- Proteinuria, microscopic hematuria, decreased creatinine clearance

Diagnosis

- There is no single symptom or finding that is sufficient in itself for making the diagnosis.
- When SLE is suspected the basic laboratory investigations are:
    - Blood count
    - Platelets
    - Erythrocyte sedimentation rate
    - Anti-nuclear antibodies
    - Dipstick test of the urine and urinalysis
- The diagnosis is based on the clinical symptoms and the laboratory findings and on the American Rheumatism Association (ARA) classification criteria (1982).
- The patient should be referred to a specialist for confirmation of the diagnosis.

Treatment

- The treatment is always individual and depends on the manifestations and activity of the disease. There is no need for treatment solely on the basis of the immunological findings.
- The patients should be encouraged to restrain from sunbathing and to use sunscreens.
- The most important drugs are:
    - Nonsteroidal anti-inflammatory drugs
    - Hydroxychloroquine ("A randomized study of the effect," 1991; Wallace, 1994) [**C**]
    - Corticosteroids
    - Immunosuppressive drugs (e.g., azathioprine, cyclophosphamide, methotrexate, mycophenolate)
- Hydroxychloroquine and nonsteroidal anti-inflammatory drugs are used in the treatment of mild symptoms such as cutaneous manifestations and arthralgia. When the response is insufficient or when the patient has fatigue or fever, a low dose of corticosteroids (prednisolone 5 to 7.5 mg/day) can be added.
- In the treatment of pleuritis or pericarditis, larger amounts of corticosteroids (about 30 mg prednisolone per day) are used.
- In the treatment of severe central nervous system (CNS) symptoms and of severe glomerulonephritis, thrombocytopenia, and haemolytic anaemia, large

corticosteroid doses and other immunosuppressive drugs are used (Bansal & Beto, 1997; Flanc et al.,2004) [**A**].
- The differential diagnosis between an infection and a flare of the SLE is of utmost importance.
- Other drugs that the patient might need, such as antihypertensive treatment, should be remembered.
- If there are signs of renal manifestations, the patient should be referred to a nephrologist for a renal biopsy.
- The patients are often allergic to a variety of antibiotics, especially sulfonamides.

Primary Antiphospholipid Syndrome

- A syndrome manifesting as recurrent venous or arterial thrombotic events, recurrent miscarriages, thrombocytopenia, and antiphospholipid antibodies, but without other features of SLE

Related Resources

Evidence Summaries

- Discontinuing hydroxychloroquine medication in stabile systemic lupus erythematosus may increase the risk of relapse (("A randomized study of the effect," 1991; Wallace, 1994) [**C**].

Refer to the original guideline document for related literature.

Definitions:

Levels of Evidence

A. **Quality of Evidence: High**

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D. **Quality of Evidence: Very Low**

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- Expert opinion
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CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Effective and safe treatment of systemic lupus erythematosus (SLE)
- Appropriate specialist referral

POTENTIAL HARMS

Not stated

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Apr 30 (revised 2007 Feb 20)

GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Marianne Gripenberg-Gahmberg

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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This guideline updates a previous version: Gripenberg-Gahmberg M. Systemic lupus erythematosus (SLE). In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2006 May 24 [various].

GUIDELINE AVAILABILITY

This guideline is included in a CD-ROM titled "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: info@ebm-guidelines.com; Web site: www.ebm-guidelines.com.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on December 17, 2002. The information was verified by the guideline developer as of February 7, 2003. This NGC summary was updated by ECRI on October 4, 2004. This summary was updated on May 3, 2005 following the withdrawal of Bextra (valdecoxib) from the market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs). This NGC summary was updated by ECRI on August 7, 2006, and again on January 7, 2008. This summary was updated by ECRI Institute on July 8, 2008, following the U.S. Food and Drug Administration (FDA) advisory on CellCept (mycophenolate mofetil) and Myfortic (mycophenolate acid).

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