# Complete Summary

## GUIDELINE TITLE

EFNS guideline on the treatment of cerebral venous and sinus thrombosis.

## BIBLIOGRAPHIC SOURCE(S)

Einhaupl K, Bousser MG, de Bruijn SF, Ferro JM, Martinelli I, Masuhr F, Stam J. EFNS guideline on the treatment of cerebral venous and sinus thrombosis. Eur J Neurol 2006 Jun;13(6):553-9. [30 references] PubMed

## GUIDELINE STATUS

This is the current release of the guideline.

## ** REGULATORY ALERT **

## FDA WARNING/REGULATORY ALERT

**Note from the National Guideline Clearinghouse**: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- February 28, 2008, Heparin Sodium Injection: The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.

## COMPLETE SUMMARY CONTENT

## SCOPE

### DISEASE/CONDITION(S)

Cerebral venous and sinus thrombosis (CVST)

### GUIDELINE CATEGORY

Management
Treatment

### CLINICAL SPECIALTY

Family Practice
Internal Medicine
Neurology

### INTENDED USERS

Physicians

### GUIDELINE OBJECTIVE(S)

To review the strength of evidence for the treatment of cerebral venous and sinus thrombosis (CVST) and provide recommendations on the therapy of CVST based on the best available evidence

### TARGET POPULATION

Patients with cerebral venous and sinus thrombosis (CVST)

### INTERVENTIONS AND PRACTICES CONSIDERED

#### Management/Treatment

Anticoagulation (dose-adjusted intravenous unfractionated heparin or body weight-adjusted subcutaneous low-molecular-weight heparin [LMWH])

**Note**: The following may be therapeutic options in select cases, but lack sufficient data to recommend:

- Thrombolysis (urokinase or recombinant tissue plasminogen activator [rtPA])
- Oral anticoagulation
- Prophylactic antiepileptic therapy
- Lumbar punctures, acetazolamide, or cerebrospinal fluid [CSF]-shunting procedures

## MAJOR OUTCOMES CONSIDERED

- Effectiveness of treatment in improving headache, focal signs, and level of consciousness and absolute risk reduction in death
- Predictors of late seizures
- Adverse effects of therapy
- Risk of recurrence

# 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

MEDLINE 1966 to 2004 and EMBASE 1966 to 2004 were examined with appropriate MESH and free subject terms: 1, cerebral venous and sinus thrombosis; 2, cerebral venous thrombosis; 3, cortical vein thrombosis; 4, intracranial thrombosis. 1–4 was combined with the terms: 7, treatment; 8, medication; 9, therapy; 10, controlled clinical trial; 11, randomized controlled trial; 12, multicentre study; 13, meta analysis; 14, anticoagulation; 15, thrombolysis; 16, local thrombolysis; 17, antiepileptic therapy; 18, intracranial pressure; 19, steroids; 20, hyperventilation; 21, osmotic diuretics; 22, craniectomy; 23, decompressive surgery.

The Cochrane Central Register of Controlled Trials (CENTRAL) and the Cochrane Library and references of selected articles were also searched. Review articles and book chapters were also included if they were considered to provide comprehensive reviews of the topic. The search included reports of research in human beings only and in English language. The literature search was performed by two Task Force members who also prepared a first draft of the manuscript.

## 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

### Evidence Classification Scheme for a Therapeutic Intervention

**Class I**: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately

powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

**Class II**: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

**Class III**: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

**Class IV**: Evidence from uncontrolled studies, case series, case reports, or expert opinion

## METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The classification for evidence levels for therapeutic interventions were made according to the guidance for the preparation of neurological management guidelines by European Federation of Neurological Societies (EFNS) scientific task forces (see the "Rating Scheme for the Strength of the Evidence" field and "Availability of Companion Documents" field in this summary).

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The first draft of the manuscript was sent via e-mail and was reviewed by all members of the Task Force and suggestions and corrections were incorporated. Recommendations were reached by consensus of all Task Force members and were also based on their own awareness and clinical experience. Where there was a lack of evidence but consensus was clear the Task Force members stated their opinion as good practice points. The final draft of the manuscript was approved by all members of the Task Force.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

### Rating of Recommendations

**Level A rating** (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

**Level B rating** (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

**Level C rating** (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

**Good practice point (GPP)** Where there was lack of evidence but consensus was clear the Task Force members have stated their opinion as good practice points.

## 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

The guidelines were validated according to the European Federation of Neurological Societies (EFNS) criteria (See "Availability of Companion Documents" field in this summary)

# RECOMMENDATIONS

## MAJOR RECOMMENDATIONS

The levels of evidence (class I-IV) supporting the recommendations and ratings of recommendations (A-C, Good practice point [GPP]) are defined at the end of the "Major Recommendations" field.

### Heparin Therapy

Current evidence shows that patients with cerebral venous and sinus thrombosis (CVST) without contraindications for anticoagulation (AC) should be treated either with body weight-adjusted subcutaneous low-molecular-weight heparin (LMWH) (180 anti-factor Xa U/kg/24 hour administered by two subcutaneous injections daily) or dose-adjusted intravenous heparin with an at least doubled activated partial thromboplastin time. Concomitant intracranial haemorrhage (ICH) related to CVST is not a contraindication for heparin therapy. For the reasons mentioned

above, LMWH should be preferred in uncomplicated CVST cases. **(Good practice point [GPP])**

### Thrombolysis

There is insufficient evidence to support the use of either systemic or local thrombolysis in patients with CVST. If patients deteriorate despite adequate AC and other causes of deterioration have been ruled out, thrombolysis may be a therapeutic option in selected cases, possibly in those without intracranial haemorrhage (ICH). The optimal substance (urokinase or recombinant tissue plasminogen activator [rtPA]), dosage, route (systemic or local), or method of administration (repeated bolus or bolus plus infusion) are not known **(GPP)**.

### Oral Anticoagulation

There are insufficient data about the optimal duration of oral AC in patients with CVST. Analogous to patients with a first episode of extracerebral venous thrombosis, oral AC may be given for 3 months if CVST was secondary to a transient risk factor, for 6 to 12 months in patients with idiopathic CVST and in those with "mild" hereditary thrombophilia. Indefinite AC should be considered in patients with two or more episodes of CVST and in those with one episode of CVST and "severe" hereditary thrombophilia **(GPP)**.

### Symptomatic Treatment

*Control of Seizures*

Prophylactic antiepileptic therapy may be a therapeutic option in patients with focal neurological deficits and focal parenchymal lesions on admission computed tomography/magnetic resonance imaging (CT/MRI). The optimal duration of treatment for patients with seizures is unclear **(GPP)**.

*Treatment of Elevated Intracranial Pressure*

In patients with isolated intracranial hypertension (IIH) and threatened vision, possible therapeutic measures may include one or more lumbar punctures, acetazolamide and incidentally CSF-shunting procedures. There are no controlled data about the risks and benefits of certain therapeutic measures (e.g. steroids and decompressive surgery) to reduce an elevated intracranial pressure (with brain displacement) in patients with CVST. Antioedema treatment should be carried out according to general principles of therapy of raised intracranial pressure. In a very small subgroup of patients who deteriorate especially in the presence of large intracerebral haemorrhages, decompressive craniectomy might be an alternative treatment option in the future. Now, this therapy needs further investigation and should be regarded as experimental **(GPP)**.

## Definitions

### Evidence Classification Scheme for a Therapeutic Intervention

**Class I**: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
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**Class III**: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

**Class IV**: Evidence from uncontrolled studies, case series, case reports, or expert opinion

**Rating of Recommendations**

**Level A rating** (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

**Level B rating** (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

**Level C rating** (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

**Good practice point (GPP)** Where there was lack of evidence but consensus was clear the Task Force members have stated their opinion as good practice points.

### CLINICAL ALGORITHM(S)

None provided

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for selected recommendations (see "Major Recommendations").

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

Appropriate treatment of cerebral venous and sinus thrombosis (CVST)

### POTENTIAL HARMS

Treatment of cerebral venous and sinus thrombosis (CVST) carries the risk of bleeding particularly in patients with concomitant intracranial hemorrhage

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

This guideline provides the view of an expert task force appointed by the Scientific Committee of the European Federation of Neurological Societies (EFNS). It represents a peer-reviewed statement of minimum desirable standards for the guidance of practice based on the best available evidence. It is not intended to have legally binding implications in individual cases.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

The European Federation of Neurological Societies has a mailing list and all guideline papers go to national societies, national ministries of health, World Health Organisation, European Union, and a number of other destinations. Corporate support is recruited to buy large numbers of reprints of the guideline papers and permission is given to sponsoring companies to distribute the guideline papers from their commercial channels, provided there is no advertising attached.

### IMPLEMENTATION TOOLS

Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better

## IOM DOMAIN

Effectiveness

# IDENTIFYING INFORMATION AND AVAILABILITY

## BIBLIOGRAPHIC SOURCE(S)

Einhaupl K, Bousser MG, de Bruijn SF, Ferro JM, Martinelli I, Masuhr F, Stam J. EFNS guideline on the treatment of cerebral venous and sinus thrombosis. Eur J Neurol 2006 Jun;13(6):553-9. [30 references] PubMed

## ADAPTATION

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

## DATE RELEASED

2006 Jun

## GUIDELINE DEVELOPER(S)

European Federation of Neurological Societies - Medical Specialty Society

## SOURCE(S) OF FUNDING

European Federation of Neurological Societies

## GUIDELINE COMMITTEE

European Federation of Neurological Societies Task Force on the Treatment of Cerebral Venous and Sinus Thrombosis

## COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

None declared

## GUIDELINE STATUS

This is the current release of the guideline.

## GUIDELINE AVAILABILITY

Electronic copies: Available to registered users from the European Federation of Neurological Societies Web site.

Print copies: Available from Karl Einhäupl, Department of Neurology, Charité Medical School, Humboldt-University, Schumann Strasse 20-21, 10117 Berlin, Germany; Phone: 0049-30-450-560102; Fax: 0049-30-450-560932; E-mail: karl.einhaeupl@charite.de

## AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Brainin M, Barnes M, Baron JC, Gilhus NE, Hughes R, Selmaj K, Waldemar G; Guideline Standards Subcommittee of the EFNS Scientific Committee. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces – revised recommendations 2004. Eur J Neurol. 2004 Sep;11(9):577-81. Electronic copies: Available in Portable Document Format (PDF) from the European Federation of Neurological Societies Web site.
- Guideline papers. European Federation of Neurological Societies. Electronic copies: Available from the European Federation of Neurological Societies Web site.
- Continuing Medical Education questions available from the European Journal of Neurology Web site.

## PATIENT RESOURCES

None available

## NGC STATUS

This NGC summary was completed by ECRI on March 27, 2007. The information was verified by the guideline developer on September 18, 2007. This summary was updated by ECRI Institute on March 14, 2008 following the updated FDA advisory on heparin sodium injection.

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