Antithrombotic and Thrombolytic Therapy*: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition)

Jack Hirsh, Gordon Guyatt, Gregory W. Albers, Robert Harrington and Holger J. Schünemann

Chest 2008;133;110S-112S
DOI 10.1378/chest.08-0652

The online version of this article, along with updated information and services can be found online on the World Wide Web at:
http://chestjournal.chestpubs.org/content/133/6_suppl/110S.full.html

Supplemental material related to this article is available at:
http://chestjournal.chestpubs.org/content/suppl/2008/06/23/133.6_suppl.110S.DC1.html
http://chestjournal.chestpubs.org/content/suppl/2008/06/25/133.6_suppl.110S.DC2.html

Chest is the official journal of the American College of Chest Physicians. It has been published monthly since 1935. Copyright 2008 by the American College of Chest Physicians, 3300 Dundee Road, Northbrook, IL 60062. All rights reserved. No part of this article or PDF may be reproduced or distributed without the prior written permission of the copyright holder.
(http://chestjournal.chestpubs.org/site/misc/reprints.xhtml)
ISSN:0012-3692
Since publication of the seventh American College of Chest Physicians (ACCP) supplement on antithrombotic and thrombolytic therapy, the results of clinical trials have provided important new information on the management of thromboembolic disorders, and the science of developing recommendations has advanced. In the accompanying supplement, we provide the new and updated recommendations and review several important changes that we have made in our guideline development process.

We again made a conscious effort to increase the participation of female authors and contributors from outside North America, the latter reflecting the widespread use and dissemination of these guidelines internationally. The grading system for the recommendations was adopted in 2006 by the ACCP for all its guidelines, is similar to the increasingly widely used Grades of Recommendation, Assessment, Development, and Evaluation approach, and is described in detail in one of the introductory chapters.

While most of the evidence on which recommendations are made remains low quality in fields of pediatric thrombosis, thrombosis in pregnancy, and thrombosis in valvular heart disease, rigorous studies in other fields have resulted in new and strong evidence-based recommendations for many indications.

*From Hamilton Civic Hospitals (Dr. Hirsh), Henderson Research Centre, Hamilton, ON, Canada; McMaster University Medical Centre (Dr. Guyatt), Hamilton, ON, Canada; Stanford University Medical Center (Dr. Albers), Stanford Stroke Center, Palo Alto, CA; Duke Clinical Research Institute (Dr. Harrington), Duke University Medical Center, Durham, NC; and Department of Clinical Epidemiology/INFORMA (Dr. Schünemann), Istituto Regina Elena, Rome, Italy.

Manuscript accepted December 20, 2007.

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (www.chestjournal.org/misc/reprints.shtml).

Correspondence to: Gordon Guyatt, MD, FCCP, McMaster University Medical Centre, 2C12, 1200 Main St W, Hamilton, ON, LAN 3Z5, Canada; e-mail: guyatt@mcmaster.ca

DOI: 10.1378/chest.08-0652
comprehensive literature searches for evidence relevant to these specific questions or recommendations. Authors reviewed citations and applied the predefined criteria to ascertain whether studies contributed to the evidence that underlies the recommendations.

Once again to ensure transparency and explicitness among questions, evidence, and recommendations, we use a numbering scheme to ensure that the number associated with the explicitly defined questions presented in the summary table of each chapter corresponds to the number of the section laying out the evidence, as well as any corresponding recommendations. This scheme allows readers to quickly identify the underlying question associated with each recommendation, and the relevant evidence.

The grading system in the eighth edition of the ACCP guidelines now reflects the system adopted for all ACCP guidelines, and is similar to the Grades of Recommendation, Assessment, Development, and Evaluation system, which is being widely adopted by many guideline groups. As in the 2004 guidelines, if experts are very certain that benefits do or do not outweigh risks, burden, and costs, they will make a strong recommendation, in our formulation, Grade 1. If they are less certain of the magnitude of the benefits and risks, burden, and costs, and thus their relative impact, they make a weaker, Grade 2, recommendation.

The system also provides a rating of the quality of evidence (high quality, moderate quality, and low quality: “A,” “B,” and “C,” respectively). The important changes in quality rating from 2004 are more explicitness in the criteria for downgrading or upgrading evidence, and designating high-quality evidence from observational studies with large effects as “A” rather than “C+.” Randomized trials provide high-quality evidence unless they suffer from limitations in design and execution, imprecision, indirectness, inconsistency, or reporting bias. Observational studies provide weak evidence unless there are no obvious biases and the effects are very large and consistent.

While conference participants agreed that recommendations should reflect economic considerations, incorporating costs is fraught with difficult challenges. For most recommendations, formal economic analyses are unavailable. Even when analyses are available, they may be methodologically weak or biased. Furthermore, costs differ radically across jurisdictions, and even sometimes across hospitals within jurisdictions. Thus, we have omitted resource allocation considerations from all but a few recommendations in which these issues are particularly important, and in which informative evidence from economic analyses are available. For these recommendations, we obtained guidance from health economists whose observations are included in the relevant discussions.

As in the 2004 recommendations, we endeavored to stay alert to the patient and community values and preferences underlying our recommendations. Once again, when values and preferences were particularly salient, we identified the underlying values associated with particular recommendations. For the first time, three individuals with a special interest, knowledge, and perspective in how values and preferences influence recommendations provided input into the guidelines.

Although the rigor with which trials for many indications are evaluated has improved dramatically, the evidence remains weak in fields of pediatric thrombosis, thrombosis in pregnancy, and thrombosis in valvular heart disease. This deficiency needs to be addressed.

**CONFLICT OF INTEREST DISCLOSURES**

**Dr. Hirsh** discloses that he has received partial support for writing two books, one on Fondaparinux and one on low-molecular-weight heparin.

**Dr. Albers** discloses that he has received grant monies from the National Institutes of Health, Astra, Genentech, Bristol-Myers Squibb, Sanofi, Boehringer Ingelheim, NMT Medical, and Aventis. He is also on the speakers bureau for Boehringer Ingelheim, and advisory committees for Astra, Aventis, Boehringer Ingelheim, NMT Medical, Bristol-Myers Squibb, and Sanofi.

**Dr. Guyatt** reveals no real or potential conflicts of interest or commitment.

**Dr. Harrington** discloses that he holds a fiduciary position as Director of the Duke Clinical Research Institute (DCRI). Either he or the DCRI have received grant monies from the following: Abbott Laboratories; Abbott Vascular Business; Acorn Cardiovascular; Actelion, Ltd; Acusphere, Inc; Adolor Corporation; Advanced Cardiovascular Systems, Inc; Air Products; PLC; Ajinomoto; Alexion, Inc; Allergan, Inc; Alkion Corporation; Amgen, Inc; Amylin Pharmaceuticals; Anadys; Angi Medical Systems, Inc; AnGes MG Inc; Angiome, Inc; ArgNox Pharmaceuticals; Ark Therapeutics; Astellas Pharma US; Astra Hassle; AstraZeneca; Attotech; Aventis; BARRX Medical, Inc; Baxter; Bayer AG; Bayer Corporation US; Berlex, Inc; Bioheart; Biologic Therapeutics; Biosense Webster, Inc; Biosite, Inc (also Biosite Diagnostics); Biosynex; Boehringer Ingelheim; Boston MedTech Advisors; Bristol Scientific Corporation; Bristol-Myers Squibb; CanAm Bioresearch; Cardio Thoracic Systems; CardioDynamics International; CardioKinetics; CardioOptics; Celgene Corporation; Celsion Corporation; Centocor; Cerexa; Inc; Chase Medical; Chugai Pharmaceutical; Cierra Inc; Coley Pharmaceutical Group; Conor Medsystems; Corantus Genetics; Cordis; Critical Therapeutics; Cubist Pharmaceuticals; CV Therapeutics; CytoGenetics; Daiichi Sankyo; deCode Genetics; Dyas; Echogen, Inc; Eclipse Surgical Technologies; Edwards Lifesciences; Eli Lilly & Company; Enteromedics; Enzon Pharmaceutical; EOS Electro Optical Systems; EPI-2Q, Inc; ev3; Inc; Evolve; Inc; Flow Care Inc; Fox Hollow Pharmaceuticals; Fujisawa; Genentech; General Electric Company; General Electric Healthcare; General Electric Medical Systems; Genzyme Corporation; Getz Bros & Co;
Dr. Schünemann reports no personal payments from for-profit organizations, but he has received research grants and/or honoraria that were deposited into research accounts or received by a research group that he belongs to from AstraZeneca (research grant, honoraria), Amgen (research grant), Barilla (research grant), Chiesi Foundation (honorarium), Lily (honorarium), Pfizer (research grant, honorarium), Roche (honorarium), and UnitedBioSource (honorarium) for development or consulting regarding quality-of-life instruments for chronic respiratory diseases and as lecture fees related to the methodology of evidence-based practice guideline development and/or research methodology. He is a documents editor for the American Thoracic Society and senior editor of the American College of Chest Physicians Antithrombotic and Thrombolytic Therapy Guidelines, and both organizations receive funding from for-profit organizations. Other institutions or organizations that he is affiliated with likely receive funding from for-profit sponsors that are supporting infrastructure and research that may serve his work.

REFERENCES
