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**To:** aspewise.ASPEPO(COI)  
**Date:** Mon, Jul 17, 2000 4:36 PM  
**Subject:** Financial conflict of interest conference

Stuart Nightingale, M.D.  
Office of the Assistant Secretary for Planning and Evaluation  
Hubert H. Humphrey Bldg., Room 447D  
200 Independence Ave., S.W.  
Washington, D.C. 20201

Re: Human Subject Protection and Financial Conflicts of Interest conference sponsored by the NIH August 15-16, 2000.

Dear Dr. Nightingale,

Enclosed is the title page and summary of an article titled, "Anticoagulation Therapy for Venous Thromboembolism (VTE) - The Emperor Has No Clothes." I am interested in presenting it in the upcoming financial conflict of interest conference by the NIH.

Canadian investigators dominate the field of research involving anticoagulants for VTE. Canadians and other researchers throughout the world are funded directly or indirectly by pharmaceutical companies for their studies. My two-year investigation into this topic revealed that research studies and literature reviews of the topic are biased toward the efficacy of these drugs. Literature questioning the efficacy is ignored and other literature misrepresented.

From an internet search, I found that the large group of venous thromboembolic disease (VTE) investigators from McMaster University are funded primarily by the Heart and Stroke Foundation of Ontario. The 1999 annual report of the Heart and Stroke Foundation of Ontario documents eight grants, totaling \$835,000. Drug companies can and do target their donations to specific projects of specific investigators.

Pharmaceutical companies that are major contributors to the Heart and Stroke Foundation of Ontario include Astra Zeneca (streptokinase), Boehringer Ingelheim (Canada) Ltd (Actilyse® (rt-PA)), Eli Lilly Canada Inc (heparin), and Wyeth-Ayerst (Normiflo, a low molecular weight heparin and heparin).

Dr. Jeffery Ginsburg, a member of the McMaster VTE research team who reviewed the management of VTE for the NEJM in 1996, (1) is the recipient of a research scholarship from the Heart and Stroke Foundation of Canada. He also administers several research grants funded by the Heart and Stroke Foundation of Canada and Heart and Stroke Foundation of Ontario. AstraZeneca (streptokinase). targeted \$500,000 over two years to the Heart and Stroke Foundation of Canada for a "research-based pharmaceutical companies research fellowship program." Another major pharmaceutical company supporters of the Heart and Stroke Foundation of Canada is Hoffmann-La Roche Limited (alteplase).

Dr. Ginsburg was on the writing team for the Columbus Investigators reporting on a low molecular weight heparin (Reviparin, Knoll AG, Ludwigshafen, Germany). (2) He has published numerous articles with the various ACCP

Consensus Conferences on Antithrombotic Therapy. (3-10) DuPont Pharmaceuticals, makers of Coumadin, provide the educational grants to support these conferences.

Jack Hirsh, MD, who reviewed heparin for the NEJM in 1991, 11 is a career investigator with the Heart and Stroke Foundations of Ontario and Canada. He has also published numerous articles related to ACCP Consensus Conferences of Antithrombotic Therapy. (3, 7-9, 12-20)

If you are interested, I can send you the full article for consideration for presentation at the conference on Human Subject Protection and Financial Conflicts of Interest sponsored by the NIH August 15-16, 2000.

Thank you for your consideration.

Sincerely,

David K. Cundiff, MD  
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Anticoagulation Therapy for Venous Thromboembolism

The Emperor Has No Clothes

Review Article

Drug Therapy

By David K. Cundiff, MD

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Reprints not available.

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### Summary

(Pulmonary emboli) PE occur frequently in healthy people and much more commonly in people with medical or surgical risk factors. In people with adequate cardiovascular reserve, natural fibrinolytic mechanisms clear thrombi that migrate to the pulmonary artery within two weeks.(21) Fatal PE occur primarily as an agonal event of terminally ill people.

While heparoids and vitamin K antagonists have a theoretic rationale regarding prevention of death from PE, the medical scientific basis for the widespread use of anticoagulants in VTE is flawed. The only placebo-controlled trial of anticoagulants in PE (22) provides no scientific evidence of the efficacy. The only randomized trial of anticoagulants versus no anticoagulants in deep venous thrombosis (DVT) showed no benefit with heparin and phenprocoumon. (23, 24)  
No placebo-controlled trials of low molecular weight heparins or thrombolytic drugs have been done, so their efficacy depends entirely on Barritt and Jordan's flawed study. (22) They have not been proven safer or more

efficacious than unfractionated heparin. (2, 25-28) Thrombolysis causes more major and fatal bleeds than heparin (29, 30) and is no more effective in preventing PE. (31)

The previous practice of prolonging bed rest in medical, surgical, and obstetrical patients probably increased the morbidity and mortality of venous thromboembolic disease (VTE). A plant-based diet and more aerobic exercise (i.e., the civilian lifestyle during world wars) may significantly reduce the morbidity and mortality of VTE. (32, 33)

Diagnosing and treating 157,000 - 607,000 VTE Americans with anticoagulants costs \$3.2 - 15.5 billion per year (1992 dollars). Bleeding and complications of angiography cost 1017 - 3525 lives. Diagnosing and anticoagulating all of the estimated people with VTE in the U. S. would astronomically increase the costs in lives and money.

Anticoagulants have not been proven efficacious or safe in VTE. The bleeding risks and other complications of anticoagulation are unacceptably high without proof that anticoagulants reduce the overall morbidity and mortality of VTE. The use of anticoagulants for patients with VTE should be reconsidered.

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