thrombosis. It is surely in younger subjects, where the confounding presence of other risk factors is less likely, that the significance of the finding of APA is likely to be revealed. In a UK survey of results of screening for APA, 109 subjects with detectable APA have been registered in an unselected group. An outstanding feature is a cohort of young women (n = 18, mean age 32 years) with thrombotic cerebrovascular events. Muir, Alwan, and Squire will no doubt be aware of the large, multicentre, case-control study performed by the Antiphospholipid Antibodies in Stroke Study Group (APASS); the authors concluded that the results "provide the strongest evidence to date that antiphos- 
pholipid antibodies are an independent risk factor for stroke." Although accepting that there have been few, rigorously designed, epidemiological studies, Kitner and Garellick have concluded that the stroke risk associated with antiphospholipid anti-
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M GREAVES
Department of Haematology,
Royal Hallamshire Hospital,
Glossop Road,
Sheffield S10 2JF, UK


4 McNeil HP, Simpson RJ, Chesterman CN, Krisa SA. Anti-phospholipid antibodies are directed against a complex antigen that includes a lipid binding inhibitor of coagula-


6 Lindsay N, Henderson FL, Malia R, Milford-


7 Greaves M. Clinical associations and prognostic significance of antibodies to phospho-

8 Antiphospholipid Antibodies in Stroke Study Group (APASS). The association of antiphos-


Antithrombotic therapy in acute ischaemic stroke: an overview of the completed randomised trials

The primary goal of these studies was to assess the efficacy and safety of antithrombotic
drugs for prevention of deep venous thrombosis (DVT). We therefore disagree with the authors, who extrapolated major conclusions on the effect of antithrombotic drugs on a secondary endpoint such as death. In addition, the incidence of pul-
monary embolism as a study end-point probably did not reflect reality because, in the trial setting, the method of diagnosing DVT allowed very early detection and sub-
sequent aggressive treatment.1 This probably resulted in the incidence of pulmonary embolism, diagnosed on the basis of clinical suspicion and death, com-
pared with the routine, clinical situation.2

Furthermore it is unclear why the authors concluded that "whilst heparin is promis-

ing, aspirin is equally, or perhaps even more promising as an antithrombotic regime" because, of the six trials of antiplatelet therapy described, the three largest have not been completed, two did not provide data on clinical events, and the third was too small to be informative.

We would also like to correct some misconceptions about Org 10172 (Orgaran).

Firstly, it is a low molecular weight heparin not a low molecular weight heparin. It contains no heparin or heparin derivatives.

Secondly, in table 1 the following cita-
tions to Orgaran are incorrect. (1) It should not be included under low molecular weight heparin trials. (2) The study published by Turpie4 is an Orgaran trial. (3) TOAST is a continuing Orgaran trial. The administra-
tion route is intravenous and the drug is administered for seven days by continuous infusion. (4) UK Org 10172 is the research code for the heparinoid marketed as Orgaran.

Thirdly, as Orgaran is superior to heparin for DVT prophylaxis in a patellar compression stroke, it is unfair to compare it with heparin and the low molecular weight heparin.4

Indeed because of their different haemosta-
tic activities it is confusing to combine under "All trials" the effects of these three types of anticoagulant.

Finally, Sandercord et al emphasise in their abstract the difference in haemor-
rhagic transformations in TOAST 7/102 and 8/106 as a "non-significant 12% increase"! Surely, such a conclusion is totally unjusti-

fied in a scientific journal.

If such overviews are to have any value, then the authors should apply with the same rigor to conclusions that, overall, in patients with

about the effect of fruit. Had James Lind done the same he would not have found a cure for scurvy.

HN MAGNANI
AHC RUYS
Organisation Internationale de
Scientific Development Group,
PO Box 20, 3400 BL Nijmegen,
The Netherlands


3 Turpie AG, Levine MN, Hirsh J, et al. Double-blind randomised trial of Org 10172 low molecular weight heparinoid in preven-

4 Ruys CM, de Groot RJ, et al. A low mol-

Matters arising

We feel that Magnani and Ruys have missed the point of our overview.1 Although eight of the 11 trials included were originally designed to assess the effect of early anti-
coagulant therapy on deep venous thrombosis (DVT), we felt that any assess-
ment of safety must include an analysis of the effect of treatment on deaths and other haemorrhagic transformation of cerebral infarction,2 as these are not "secondary end-
points" of trivial importance, but major deaths. Events and haemorrhagic transfor-
mations are—fortunately—infrequent. Individual trials lacked sufficient power to provide reliable evidence on whether or not their occurrence was influenced by the use of anticoagulants.3,4 Even with using all the available data, however, still did not provide clear answers to the following important questions. (1) Does early anti-
coagulant treatment reduce (or increase) morality? (2) Does routine anticoagulant therapy increase the risk of haemorrhagic transformation moderately, substantially (or not at all)?

We accept Drs Magnani and Ruys’ comments on the nomenclature of the low molecular weight heparinoid (Orgaran). We agree that Turpie’s relatively small study suggested that Orgaran reduced the risk of DVT, compared with low-dose heparin.5

In this study, however, four patients (8.9%) in the Orgaran group and two patients (4.8%) in the standard heparin group developed haemorrhagic transforma-
tion of cerebral infarction (odds ratio 1.95: 95% confidence interval 0.34 to 11.3) and this observed excess of haemorrhagic transforma-
tion of cerebral infarction with Orgaran compared with low-dose heparin is consistent with the hypothesis that Orgaran is indeed a more potent antithrombotic agent. Only nine patients in each group died (9/45 Orgaran versus 9/42 heparin: odds ratio 0.92, 95% CI 0.3 to 2.6). Thus, although benefit for DVT may be greater with Orgaran compared with low-dose heparin, the data on safety are insufficient to exclude a moderate risk of haemorrhagic transformations or death, or both, with Orgaran. As the data are so limited, we feel it is premature (taking important events such as death and hae-
morrhagic transformation) to conclude that, overall, in patients with

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H N Magnani and A H Ruys

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