

aetiological factors of this problem to identify pregnancies at risk must remain a prerequisite for any selective strategy to prevent these deaths.

Contributors: CSC refined the methodology, collected and analysed the data, and drafted the paper. SP-B contributed to the study design, analysis, and paper drafts. NMF had the original idea for the study and contributed to drafting and revising the paper. CSC is guarantor for the study.

Funding: None.

Competing interests: None declared.

- 1 Confidential Enquiry into Stillbirths and Deaths in Infancy. *Fourth and fifth annual reports*. London: Stationery Office, 1996 and 1998.
- 2 Yudkin PL, Wood L, Redman CWG. Risk of unexplained stillbirth at different gestational ages. *Lancet* 1987;i:1192-4.
- 3 Feldman G. Prospective risk of stillbirth. *Obstet Gynecol* 1992;79:547-52.
- 4 Hilder L, Costeloe K, Thilaganathan B. Prolonged pregnancy: evaluating gestation-specific risks of fetal and infant mortality. *Br J Obstet Gynaecol* 1998;105:169-73.
- 5 Thornton J, Lilford R. The caesarean section decision: patients' choices are not determined by immediate emotional reactions. *J Obstet Gynaecol* 1989;9:283-8.

(Accepted 25 February 1999)

Predicted impact of intravenous thrombolysis on prognosis of general population of stroke patients: simulation model

Henrik Stig Jørgensen, Hirofumi Nakayama, Lars Peter Kammersgaard, Hans Otto Raaschou, Tom Skyhøj Olsen

Department of Neurology, Bispebjerg Hospital, Bispebjerg bakke 23, DK-2400 Copenhagen NV, Denmark
Henrik Stig Jørgensen
consultant
Hirofumi Nakayama
senior registrar
Lars Peter Kammersgaard
senior registrar
Hans Otto Raaschou
consultant

Department of Neurology, Gentofte Hospital, Copenhagen, Denmark
Tom Skyhøj Olsen
associate professor

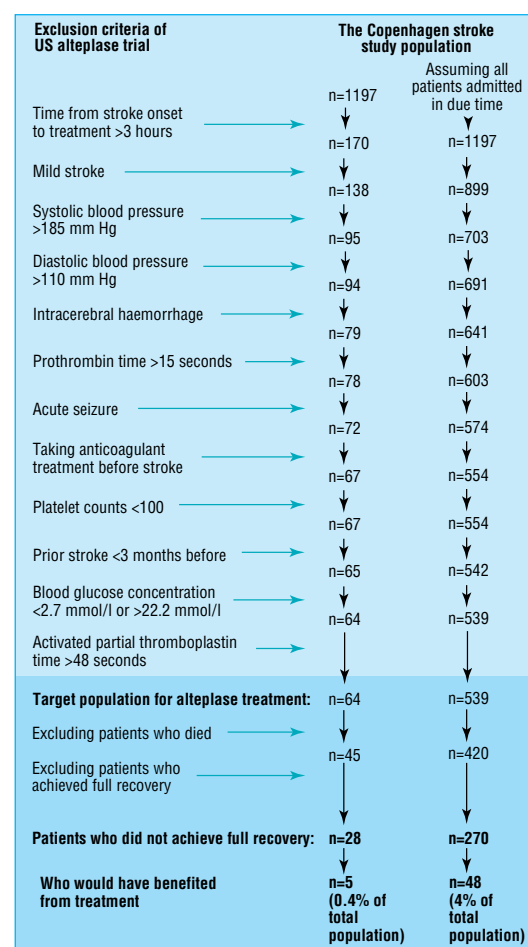
Correspondence to: H S Jørgensen
hsj@dadlnet.dk

BMJ 1999;319:288-9

Alteplase (recombinant tissue plasminogen activator) can be used to dissolve blood clots and achieve reperfusion in some stroke patients. Three randomised controlled trials have studied its clinical effect.¹⁻³ A US trial studied patients who were treated within three hours of onset of stroke and reported a 32% (95% confidence interval 1% to 70%) relative increase in the proportion of patients with full recovery but no effect on overall mortality.¹ This led to approval of alteplase for stroke patients in the United States. A European trial of patients treated within six hours of stroke onset was negative,² and a second trial, published recently, reported no significant positive effect.³ An application for European approval of alteplase treatment within three hours of stroke onset is being considered. Alteplase often leads to bleeding and should be given only by specialised teams.³ Reorganisation of stroke treatment is therefore necessary if alteplase is approved. The trials were performed in highly selected patients.¹⁻³ To elucidate the effect of alteplase on the general stroke population we conducted a retrospective analysis, applying the exclusion criteria and treatment effect reported in the US trial¹ to the unselected stroke population of the Copenhagen stroke study (COST).⁴

Subjects, methods, and results

COST comprised 1197 patients with acute stroke recruited during 1991-3 from an area of Copenhagen.⁴ These patients constituted 88% of stroke patients in the area: the remaining 12% were not admitted because they had very mild stroke or died before reaching hospital; none would have qualified for alteplase treatment. The figure shows the impact of each exclusion criterion from the US trial¹ on the COST population. Only 64 (5%) of the patients fulfilled all criteria. Nineteen of these patients died, and 17 had full recovery (defined as 95 or 100 points on the Barthel index at discharge¹). These patients would therefore not have benefited from alteplase treatment. The 28 patients who survived but did not achieve full recovery could have benefited from treatment. With a 32% relative increase in patients with full recovery, five



Flowchart showing impact of exclusion criteria of US alteplase trial¹ on population from Copenhagen stroke study and estimate of number of patients who would have benefited from alteplase treatment

patients ($17 \times 0.32 = 5$ (95% confidence interval 1 to 12)) or 0.4% (0.1% to 1.0%) of the stroke population would have benefited if alteplase had been available.

Time was the most critical criterion; only 14% of the patients were admitted in due time. However, this percentage would probably increase if alteplase were approved, so we also estimated treatment effect assuming the ideal—all patients admitted in due time. In this case 539 patients (45%) would have been eligible (figure). Of these patients, 119 died and 150 had full recovery, leaving 270 patients who survived but did not achieve full recovery who could have benefited from treatment. An estimated 48 patients ($150 \times 0.32 = 48$ (1 to 105)), or 4% (0.1% to 8%) of the stroke population, would have benefited from treatment.

Comment

Combining data from the US alteplase trial¹ and the Copenhagen stroke study, we estimated that 0.4% of unselected stroke patients would benefit from alteplase treatment. With no time constraints for treatment, still only 4% would benefit. These estimates may be too generous, as we could not exclude patients with rapidly improving symptoms, a criterion excluding 10% in the US trial. In conclusion, treatment with alteplase may benefit single patients but will have no impact on the general prognosis of stroke. Because time is crucial and

because evaluation of patient and paraclinical data requires a specialist setting, treatment with alteplase will need large investments and reorganisation of the care for stroke patients. Before it is decided to offer this expensive, potentially harmful, and possibly only marginally effective treatment we suggest that another, much larger, European trial is needed to test the results of the US trial.

Contributors: HSJ was principal investigator of the Copenhagen stroke study. All the authors participated in designing the study, data collection, and writing this paper. HSJ and TSO analysed and interpreted data for this paper and are guarantors for the paper.

Funding: The study was supported by grants from The Danish Health Foundation and The Danish Heart Foundation.

Competing interests: None declared.

- 1 National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 1995;333:1581-7.
- 2 The ECASS Study Group. Intravenous thrombolysis with recombinant tissue plasminogen activator for acute hemispheric stroke. *JAMA* 1995;274:1017-25.
- 3 The ECASS II Study Group. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). *Lancet* 1998;352:1245-51.
- 4 Jørgensen HS, Nakayama H, Raaschou HO, Olsen TS. Effect of blood pressure and diabetes on stroke in progression. *Lancet* 1994;344:156-9. (Accepted 18 February 1999)

Near patient testing for respiratory syncytial virus in paediatric accident and emergency: prospective pilot study

Audrey Mackenzie, Nick Hallam, Elaine Mitchell, Tom Beattie

Respiratory syncytial virus is the most important respiratory pathogen in young children, causing bronchiolitis and pneumonia. Infection is especially serious for those who are immunocompromised and those with conditions such as bronchopulmonary dysplasia and congenital heart disease.¹ The virus is highly infectious, and annual outbreaks cause many hospital admissions, putting great strain on isolation facilities and infection control measures. Nosocomial transmission is well documented.² Rapid testing for the virus is well established³ and cost effective.⁴ Near patient testing has the added potential benefits of even faster diagnosis, further cost saving, and improved patient management and infection control. We describe a prospective pilot study of near patient testing for respiratory syncytial virus which was carried out in the accident and emergency department of the Royal Hospital for Sick Children, Edinburgh, between December 1997 and March 1998.

Patients, methods, and results

One hundred and three pairs of nasopharyngeal secretions were obtained from 98 children under 2 years of age presenting with respiratory symptoms (five children presented twice). The first specimen was sent for direct immunofluorescence testing at the Regional Clinical Virology Laboratory, City Hospital, Edinburgh (accredited by Clinical Pathology Accreditation (UK)) using the

Imagen respiratory syncytial virus reagent (Dako, Ely, United Kingdom). The second specimen (taken immediately afterwards but often smaller in volume) was tested by staff of the accident and emergency department using an enzyme immunoassay (Abbott TestPack RSV, Abbott Laboratories, North Chicago, IL).

This protocol was adopted to avoid compromising the results of direct immunofluorescence testing (our routine method) while the pilot study was in progress. Staff training and near patient testing were carried out in accordance with published guidelines.⁵ Patients with positive results by the near patient test were isolated or put with others with positive results; those with negative results were also isolated if possible while awaiting further results.

The table shows the results for 94 specimen pairs. Results for the other nine specimen pairs are not included (in two cases the results of the near patient test were void, in two cases direct immunofluorescence was unsatisfactory, and in five cases no specimen was

Royal Hospital for Sick Children, Edinburgh EH9 1LF

Audrey Mackenzie, clinical nurse specialist

Elaine Mitchell, staff nurse

Tom Beattie, consultant in paediatric accident and emergency medicine

Regional Clinical Virology Laboratory, City Hospital, Edinburgh EH10 5SB

Nick Hallam, consultant virologist

Correspondence to: Dr Hallam

BMJ 1999;319:289-90

Comparison of results of near patient and direct immunofluorescence testing

	Direct immunofluorescence	
	Positive	Negative
Near patient:		
Positive	50	1
Negative	13	30