other neuroprotective drugs, for every one given thrombolysis.

We agree with the need to discover if aspirin, heparin, or both, improve outcome after stroke and we have placed suitable patients in the pilot and main phases of IST at random. In practice, however, it is only patients in whom the benefits of aspirin/heparin are uncertain who are eligible for this trial. These are treatments for secondary prevention and for the avoidance of deep venous thrombosis, etc, not acute interventions. It has been predicted that 20 000 patients may be required for a clear result with this trial design; factorial randomisation within MAST would be an unnecessary complication to the design, and many clinicians are unhappy about withholding aspirin from a patient who recovers from a proven ischaemic stroke.

It is counterproductive to argue over the detail of the various trials that are in progress. Meta-analysis has already been agreed among the coordinators of the major randomised thrombolytic stroke trials. We should concentrate our efforts on increasing the proportion of stroke patients who are adequately assessed, investigated by CT scan and offered rational treatment.

K R LEES
A D MORRIS
I B SQUIRE
D G GROSSET
J L REID
Acute Stroke Unit, University Department of Medicine and Therapeutics, Western Infirmary, Glasgow G11 6NT, UK
I BONE
Department of Neurology, Institute of Neurological Sciences, Southern General Hospital, Glasgow G53, UK

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NOTICE

Guillain-Barré syndrome: the evolution of therapy.

In 1980, a new era in Guillain-Barré syndrome (GBS) research began. Before that year, most studies of GBS had been single-centre studies of various clinical, immunological, pathologic, or epidemiological aspects of the disease. Descriptions of the response to treatment also fell into that category, and no clearly proven treatments were available. Following a series of presentations at the annual meeting of the American Academy of Neurology on the use of plasma exchange in GBS, a distinguished group of senior investigators organised a multicentre, two-country study of plasma exchange in GBS.[1] At the same time, a four-centre Swedish study[2] and a multicentre French study[3] began. All three reached the same conclusion as regards the efficacy of plasma exchange in GBS—outcome improved more with plasma exchange than with no treatment.[2-4] In the meantime, the Dutch GBS Study Group compared plasma exchange and human immune globulin, determining that the two treatments were at least equally efficacious and possibly that human immune globulin was even better than plasma exchange.[5] A large multicentre European trial has suggested that a five-day course of intravenous methylprednisolone, when used alone or added to plasma exchange in the treatment of GBS, does not produce significant benefit.[6]

Where do we stand now? Both plasma exchange and human immune globulin have been proven to be effective in GBS, and one should be used in those individuals with clear diagnoses who are unable to walk. Both treatments require expertise in delivering them, due to known side effects. Despite these findings, many questions still remain. Should treatment be given to those with GBS still able to walk? How can clinically significant relapses, which occur following both treatments best be handled? Moreover, neither is perfect: a significant number of patients apparently do not respond at all, most still have prolonged disability, and some are left with significant permanent deficits.

These issues lead to the most important question: are there other treatments that might be better than plasma exchange and human immune globulin? In order to provide at least one answer to this question, an international group of investigators has met and designed a three-armed trial comparing plasma exchange, human immune globulin, and plasma exchange followed by human immune globulin in patients with GBS who are less than 14 days from onset of neuropathic symptoms. This trial is designed to confirm the results of the Dutch study showing equal efficacy of plasma exchange and human immune globulin and to discover whether plasma exchange followed by human immune globulin is even more effective. The study is currently underway in 41 centres in 10 countries, and plans to enroll 390 patients. The costs are being partly underwritten by Sandoz AG, and all subjects randomized to human immune globulin or plasma exchange plus human immune globulin receive Sandoglobulin at no cost. We are actively seeking patients for this study and would welcome referrals. The study centres and principal investigators are listed below. Another answer to the same question is being sought by the Dutch GBS Study Group, whose preliminary studies using historical controls suggest that human immune globulin plus steroids is better than human immune globulin alone for the treatment of GBS (F van der Meché, personal communication). A randomised controlled trial is planned. The results of both these trials will be eagerly awaited.

Centre	*Principal Investigator*
Australia	
Sydney	J McLeod
Westmead	J Morris
Belgium	
Antwerp	P P De Deyn
Brugge	I Dehaene
Brussels	P De Keyser
	C J M Sindic
Liege	G Franck
Leuven	W Robberecht
Centre	*Principal Investigator*
Canada	
Calgary	T Feasby
London, Ontario	A Hahn
Montreal	C Chalk
Montreal Neuro Institute	J Stewart
Toronto, Ontario	V Bril
Germany	
Düsseldorf	G Stoll
Erlangen	B Neundörfer
Heidelberg	W Hacke
Homburg/Saar	G Hamann
Munich	R Hohlfeld
Würzburg	K Toyka
Israel	
Jerusalem	T Ben-Hur
Italy	
Monza, Milan	G Cavaletti
Norway	
Trondheim	J Aasly
Portugal	
Lisbon	M L Sales Luis
Switzerland	
Basel/Bern	A Steck, C Hess
United Kingdom	
Birmingham	J B Winer
Bristol	I Ferguson
Cardiff	C M Wiles
Edinburgh	R G Will
Glasgow	H Willison
Leicester	I Pye
Liverpool	B R F Lecky
London, Guy's	R A C Hughes
London National	D H Miller
Middlesbrough	P Newman
Oxford	M Donaghy
Southampton	H Katifi
United States	
Baltimore, MD	D Cornblath
Boston, MA	A H Ropper
Milwaukee, WI	B Khatri
Peoria, IL	S Sundrani
New Haven, CT	J Goldstein

DAVID R CORNBLATH
Deartment of Neurology, Johns Hopkins University School of Medicine, 600 North Wolfe Street, Baltimore, MD 21205, USA
RICHARD A C HUGHES
Department of Neurology, United Medical and Dental School, Guy's Campus, London, UK

On behalf of the Plasma-Exchange/Sandoglobulin/Guillain-Barré Syndrome (PSGBS) Trial Group.

Correspondence to: Dr Cornblath.

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