Report of the 18th European Stroke Conference, Stockholm, May 26–29, 2009

J.P. Mohr

Neurological Institute, Columbia University College of Physicians and Surgeons, New York, N.Y., USA

The 18th European Stroke Conference was held on 26–29 May in Stockholm, the second occasion for the meeting and the first city to be a repeat host. In the 15 years since the last meeting in Stockholm, the venue has changed to a modern large congress facility, suitable for the attendance expansion in the last decade and a half.

Although the attendance for the 18th Conference, at approximately 3,000 registrants from 86 countries, was a bit lower than that in Nice, mainly a sign of the worldwide economic downturn, the scope of the meeting continues to grow and the number of abstracts submitted (>1,100) and scientific contributions presented was the largest ever. One clear indication of growth was the daunting 256-page special publication containing the abstracts for the Conference in the leading European journal *Cerebrovascular Diseases*.

As has become a custom, the first day, Tuesday, 26 May, was devoted to a range of 10 teaching courses occupying the entire afternoon. Subjects spanned the range from basic research through clinical presentation, risk factors, stroke related to differing organ systems, and management decision-making. Fully 45 speakers made presentations. In addition the 3rd Stroke Meeting for Nurses, Physiotherapists, Speech and Occupational Therapists and Study/Monitoring Assistants covered a full day program with lectures, workshops and poster presentations on rehabilitation and nursing.

Opening day, 27 May, had participants fully occupied from 8.30 to 19.30 h, using all 6 major rooms and lecture halls including plenary sessions in the Victoria Hall.

The early morning started with a symposium on *small-vessel disease* (H. Chabriat, M. Dichgans, chairs). Individual sessions in parallel covered oral presentations on acute events (TIA included), patterns and treatment of acute stroke, and a full session on vascular, neurointerventional, neurosurgical and neuroradiological management for stroke, this last yet another sign of the expanding scope and participation for subspecialties in the Conference. As has been the custom in this report, for reasons of brevity some of the findings are cited without the full list of authors or even abstract title – apologies to any who might take offense. *Time trends in patient behavior immediately after TIA or minor stroke* showed the reassuring finding that those familiar with the symptoms and signs reported for medical management earlier. The *ABCD2 score* proved a surprise by predicting the severity, if not the risk of recurrent event but, as hoped, had significant associations with *DWI+* findings. *Aspirin and clopidogrel in aspirin-naïve patients had the puzzling finding of a higher risk of bleeding, including life-threatening bleeds, compared with those for whom clopidogrel was added to aspirin* ($p < 0.004$). *Baseline NIHSS <10 and absence of carotid disease* best predicted short- and long-term outcome in acute stroke patients without intracra-

nial occlusions on imaging. *Striatocapsular infarcts at 24 h (odds ratio, OR, 4.6) were more frequently identified by CT compared with cortical infarcts (OR 6.9) with initial high middle cerebral sign and its disappearance after thrombolysis, a possible indication that the initial occlusion was presumably already associated with image-invisible infarction. Isolated ischemic lesions in the foot motor area mimicking lower limb ischemia were detectable by DWI+, another pseudoneuropathic sign important to consider in daily practice. The risks of carotid angioplasty proved predictable by a set of risk factors.* 117 patients followed for a mean of 7.5 years after TIA or minor stroke (symptomatic internal carotid occlusion) had a 2.6% annual rate of stroke, cited as 'relatively low risk'.

In the Victoria Hall, after the Johann Jacob Wepfer Award lecture (J.P. Mohr), a session on large clinical trials covered 6 subjects, for each the findings and interpretation being rather straightforward: *Dronedarone and atrial fibrillation*, presented by C. Torp-Pedersen, cited the Athena trial involving 4,500 patients, showing a 40% reduction in stroke ($p = 0.027$), this with the agent atop standard antithrombotic therapy. The more risk factors, the better the effect was seen by use of the drug. The authors claimed that no previous antiarrhythmic therapy had been shown to reduce stroke. Martin Brown discussed the safety results in the *International Carotid Stenting Study (ICSS)* for early outcomes of stenting versus endarterectomy for symptomatic carotid stenosis ($>50\%$, excluding those with string sign), the findings a disappointment to those favoring stenting. The stent device chosen was recommended at the discretion of the interventionalist. The initial stroke rate was higher in the stent group (65 vs. 34, hazard rate 1.73, 3-month difference 3.4% and $p = 0.003$). 80% of the stented cases were treated with the 'embolic protection' device but analysis of outcomes with and without the device are not yet available. Center size did not impact on the outcomes ($p = 0.123$). M. Brown was followed by J. Ederle for the ICSS investigators, who discussed the *economic impact on health resources for the two treatments* and the impact of white matter changes on outcomes. The increased risk for stenting was greater regardless of the presence and scoring for white matter disease. *TOSS-2* was presented by S.U. Kwon. This study followed the progression of symptomatic intracranial stenosis comparing cilostazol and clopidogrel. Participants were in Korea, the Philippines, Thailand and Hong Kong. Cilostazol was given at 100 mg b.i.d. and clopidogrel at 75 mg q.d. Many patients were also on aspirin. Worsening of intracranial stenosis by 1 or more grades of severity was seen in the combined cilostazol and clopidogrel group in

202 patients and in the clopidogrel alone group in 207 patients, the latter group showing fewer asymptomatic new lesions. The *CLOTS1 trial*, discussed by M. Dennis, assessed the value of full-length compression stockings in the prevention of deep leg vein thrombosis. Patients were randomized to routine care versus thigh length stockings, duplex sonography done in both legs at 7–10 days and again at 25–30 days. No difference was found between the two groups, arguing against the value of thigh length stockings as a means to decrease deep vein thrombosis after stroke, a keen disappointment to manufacturers represented in the large exhibitors' hall. A new trial is being organized (CLOTS3), comparing full thigh length stockings against below-the-knee stockings and intermittent pneumatic compression.

The lunch hour started the poster session, with no less than 294 posters: 52 on acute stroke, 20 on acute clinical features including nursing aspects, 57 on epidemiology, 46 on experimental stroke, 11 on genetic studies, 62 presenting interesting cases, 10 'challenging cases' (as if interesting and challenging are different categories, surely an overlap), 9 stroke and metabolic syndrome, 18 vascular surgery and 9 large clinical trials (more than enough to test the indefatigable). At the same time, a satellite symposium sponsored by Boehringer Ingelheim was presented on the *evidence-based management of acute ischemic stroke and prevention of recurrence* (chaired by V. Hachinski and B. Norrving), with a wide-ranging discussion of the implications of recent trials, ECASS and SITS-ISTR recurrence prevention, new analysis of antiplatelet therapy and a plan for the World Stroke Academy. In the afternoon, two educational symposia covered important *aspects of stroke prevention and acute treatment*: one, an update on carotid disease, symptomatic and asymptomatic, chaired by M.G. Hennerici and J.-L. Mas, featured a discussion of best medical treatment versus stenting and endarterectomy that was a lively continuation of the Victoria Hall presentation; the other was an *update on recanalization therapies beyond 3 h* including the results of ECASS3 (D. Toni) and the present state of IST3 (P. Sandercock).

Afternoon oral presentation sessions ranged over epidemiology, acute stroke treatment, experimental studies and genetic disorders, ending in 2 satellite symposia: one, sponsored by Sanofi/Aventis/BMS (M. Alberts and P. Rothwell presiding), discussed individualizing treatment; the other, sponsored by the Ferrer Group (E. Diez Tejedor and A. Massaro presiding), discussed stroke management in developing countries.

Your correspondent was unable to attend all parallel sessions so confines comments to a few presentations heard while attempting to attend many in differing rooms. The *Interact trial*, which studied 404 patients with acute brain hematoma, found blood pressure lowering feasible, safe and associated with a 'modest' reduction in hematoma growth. The target reduction for blood pressure was to a value of 140 mm Hg systolic within 1 h, maintained for 24 h, versus standard hypotensive therapy of the admission blood pressure >180 mm Hg. Treatment within <3 h of onset reduced the hematoma by some 6.5 mm ($p = 0.1$), with less effect for hours 2.9–3.6, and least for hours 3.7–4.8. The investigators are planning *Interact 2*, by adding centers to the investigation group. The *Safety of Intravenous Thrombolysis in Patients on Antiplatelet* study reviewed the outcomes for 11,865 patients during the years 2002–2007. The incidence of symptomatic intracranial hematoma for those on no antiplatelet drug was 1.0%, and for those on antiplatelet drugs it was 2.5%. The effects for those on aspirin alone, aspirin with clopidogrel and aspirin with long-acting dipyridamole were similar, arguing that thrombolysis for those on antiplatelet drugs is not a contraindication. The *effects of prior medical treatments on ischemic stroke severity and outcome* summarized outcomes from 118 Italian centers in 2005 and found that prestroke therapy with statins did not influence stroke severity but had a better functional outcome by modified Rankin Scale (mRS) status at discharge. Antiplatelet agents or antihypertensives had no such effects. *Recent silent MR infarct and thrombolysis* was a 2-year study encompassing 86 consecutive French patients, 66% undergoing thrombolysis, 10 (12%) having had a prior recent small stroke. No hemorrhagic transformation occurred in the area of the prior recent small infarction.

Perfusion CT > aspects mismatch was a novel parameter-specific algorithm for perfusion CT assessment to demonstrate a 'tissue at risk' area by the 'Kalk' method. Kalk has narrower confidence intervals compared with the aspects ratio. Mismatch did not help predict discharge status.

Thursday, 28 May, offered another dawn-to-dusk array of presentations.

Starting off with a short symposium on cognitive impairment after stroke (D. Leys and L. Pantoni, chairs), the many conference rooms were filled with parallel sessions on risk factors, meta-analyses, emergency management of acute stroke, intracerebral imaging, cerebral reorganization and rehabilitation. No matter how enthusiastic, no participant could attend all the sessions of interest. What

follows are summaries of those presentations attended by your correspondent: *Perfusion MRI which identifies persistent vasculopathy pathology in acute pontine stroke* was an effort to identify paramedian basilar branch versus lacunar infarcts. Those with persistent hypoperfusion (on apparent diffusion coefficient maps) had more frequently large-artery disease ($p = 0.001$), and those who were deemed hypoperfused had worse clinical outcomes. The initial clinical syndromes did not predict those with and without perfusion impairment. *Contrast extravasation in primary brain hematoma* was shown in 4 patterns: central and outside rim, central dot + ring, and a total even signal. Studied within 12 h after onset and then at follow-up, 58% of cases showed contrast extravasation. Those with the contrast dot + ring had a higher mortality than those with the central pattern alone. *Predictors of disability after arteriovenous malformation rupture* was a review of 200 cases, where parenchymal arteriovenous malformation hematoma was more associated with mRS >2 than was subarachnoid bleeding. By comparison, there were no distinctive effects for lobar location or for functionally important location. 'Clinical correlates of nonhemorrhagic lesions with cerebral venous thrombosis' was a report from 624 cases in a worldwide database. Those with nonhemorrhagic lesions were more often younger, had aphasia, mental status abnormalities, seizures or motor deficits. The straight sinus and deep venous systems were more frequently affected. Discharge status was best for those with no lesion.

After a short break, the first symposium – video transmitted in a second auditorium for an unexpectedly large audience of >800 participants – reflected current activities from the *European Stroke Research Network*, supported with 20 million EUR from the European Union. The main focus was on *experimental models and neurobiological aspects of regeneration and repair after stroke* (e.g. brain inflammation and neurogenesis, presented by O. Lindvall, and advances in MRI of brain reorganization after stroke, by R. Dijkhuizen).

The second poster session proved another feast; this time there were no less than 306, covering risk factors (53), vascular imaging (32), meta-analyses (8), emergency therapy (30), intracranial hematoma, subarachnoid hemorrhage and venous occlusive disease (26), vascular biology (15), imaging (24), small-vessel disease (16), heart and brain (14), cerebral reorganization (16), rehabilitation (23), vascular dementia (13), 'very old' patients >80 years (8 posters, the definition of 'very old' being subject of dispute among some of those >80), etiology of stroke (23), region issues of stroke outside the European Union (15),

and management and economic issues (17 posters). 'New concepts in stroke prevention' was the topic of the second satellite lunch symposium sponsored by Servier (M.-G. Bousser and M.G. Hennerici, chairs) introducing the clinical and theoretical background of the PERFORM trial, currently the largest ongoing secondary prevention trial worldwide.

In the afternoon, two other minisymposia gained large interest: one dealt with alternative treatment strategies (M. Fisher and W.D. Heiss presiding); A. Alexandrov described the use of *sonothrombolysis*, 2-MHz transcranial Doppler ultrasound, citing reversible changes in fibrin structure, plasma streaming through the thrombus, vasodilation of NO release and tissue plasminogen activator delivered to binding sites. Compared with tissue plasminogen activator alone, pulsed transcranial Doppler ultrasound + low-frequency microbubbles had improved recanalization rates (19 vs. 42%) but also high symptomatic hemorrhage rates (3.5 vs. 9.7%). $p = 0.021$ and relative risk = 1.45 (95% confidence interval = 0.84–2.51) for mRS made a favorable outcome according to the small pilot Tucson study. Microbubble destruction can open the bubble and possibly deliver medication but, by oscillating and transmitting energy, activate the clot and may contribute to recanalization. Other concepts are currently under investigation, e.g. flow augmentation in the *SENTIS trial* (W.D. Heiss), *oxygen therapy in acute stroke treatment* (M. Fisher) and *neuroprotection by hypothermia* (P. Schellinger). The other minisymposium covered controversial aspects in *intracerebral hemorrhages* (R. Al-Shahi Salman and T. Steiner, chairs).

Among the oral communications presented in the individual conference rooms were: the *North Dublin Atrial Fib Warfarin Study*, which demonstrated that the therapeutic INR predicts improved early recovery in anticoagulated patients. The mRS on days 7, 28 and 90 were better for those whose prestroke INR ≥ 2 . The admission INR inversely correlated with mRS 90d $\geq$. The *Glasgow group discussed the important issues of aspirin 'resistance'*. Despite the literature citing resistance in 28% of the population and a higher risk of cerebrovascular disease (OR = 3.85 for all vascular events), the authors discovered that for those whose tests argued for resistance, among patients who said they were compliant, as many as half of the cases really had not actually been taking the drug! *Histological correlates of a systematic predisposition to plaque instability* described the features of 526 carotid plaques, discovering that those ulcerated exceeded all other features for plaque instability. Among the large range of findings, OR >1.0 included large lipid core (1.79)

and plaque hematoma (1.09) but plaque inflammatory markers were not major markers for risk. The UK authors concluded that ultrasound or MRI of the lipid core were potentially more useful markers of vulnerable plaque than imaging of plaque inflammation. *Measuring the degree of carotid stenosis* was a welcome return to decades past, arguing that the important measurement is residual diameter of <2.2 – 2.4 mm. *Carotid atheroma plaque echogenicity in acute stroke risk* noted that unstable plaques have more echogenicity, which might contribute to the increased risk. The 51 patients with carotid territory stroke within the prior week allowed study of 120 plaques. Echogenicity related to cholesterol low-density lipoprotein levels >130 mg/dl and to antihypertensive therapy, but not to any other risk factor. Note was made that statin therapy was associated with a trend to higher echogenicity. *Plaque MRI to identify high-risk patients of ICA stenosis* studied 78 pre-endarterectomy by plaque MRI and brain DWI, before and after stenting (10 cases) or endarterectomy (64 cases). New brain DWI lesions, many symptomatic, were seen more often with the 38 unstable plaques. *Leptomeningeal collaterals predicted clinical and imaging outcomes in M1 occlusion ischemic stroke*, a scale for detection of the presence of a sylvian vessel on the CT angiogram, inferring a collateral over the convexity. Scored as excellent, good or poor, the difference in mRS >2 between the groups was successful at $p = 0.002$. The *Dutch COMET study* compared MR angiography versus digital subtraction angiography for follow-up of coiled aneurysms. Among 381 seeking residual aneurysm, MR angiography proved to have a high negative predictive value in 95, the cost and effect on quality-adjusted life years about the same between the two techniques.

The full day was closed by 3 major satellite symposia, conducted in parallel, one on *prevention of atrial-fibrillation-related stroke* (B. Norrving and R.L. Sacco, chairs, sponsored by Sanofi-Aventis), which emphasized the underestimation of atrial fibrillation in stroke, new antiarrhythmics and a review of ongoing antithrombotic trials which may yield new therapies. The other two, which your correspondent was not able to attend, reviewed the *antithrombotic strategy with cilostazol* (J. Kim and S. Uchiyama presiding, sponsored by Otsuka Pharmaceutical) and cited results from the CAIST and TOSS-2 trials and a meta-analysis of randomized controlled trials with cilostazol. The third was a symposium sponsored by the Ferrer Group on *methodological issues for new neuroprotective trials* (A. Davalos and P. Ringleb, chairs).

Friday, 29 May, the last day, found your correspondent forced by needs to return to New York City, which pre-

vented him from attending the closing sessions, one on challenging cases in Victoria Hall in which he had expected to present an interesting case for discussion. Regrets to all for the inability to be on hand for what must have been an interesting discussion of other cases. M.G. Hennerici told me, however, that two other symposia were also well attended despite the full program of this year's meeting: the first joint meeting organized by the *European Society of Hypertension* (ESH) represented by its current President S. Laurent in cooperation with the European Stroke Conference (ESC) with M.G. Hennerici, Chair of the Program Committee, provided new knowledge about recent aspects of blood pressure measurement strategies – supposed to be straightforward but surprisingly complex if assumed to be valid for treatment recommendations (P. Rothwell), *epidemiology of hypertension and stroke* (R. Cifkova) and finally excellent take-home messages from the guidelines on *blood pressure management* supplied by the ESH (J. Redon). The other minisym-

posium covered major aspects of *aneurysmal subarachnoid hemorrhage* (A. Molyneux and H. Steinmetz, chairs) and an update on diagnosis, management and treatment strategies. Oral presentations in 3 halls concentrated on *etiologies of stroke, regional/national stroke aspects and management/economics*. After a last break, G.L. Lenzi presented *awards for 12 young investigators* and their research groups nominated according to the anonymous abstract rating process of the ESC's Scientific Committee members, who this year managed an enormous task to review, rate and select among the huge number of so many excellent scientific contributions from a truly international rather than European origin. Before closure V. Hachinski gave the traditional special lecture of the ESC on *vascular cognitive impairment* and met all expectations of the audience who, as usual, much applauded his masterly presentation.

And on to Barcelona, site for the 2010 conference!