Report of the 19th European Stroke Conference, Barcelona, May 25–28, 2010

J.P. Mohr

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

The 19th meeting of the European Stroke Conference (ESC) was held May 25–28, 2010, in beautiful Barcelona, under weather conditions sorely tempting the devotion of attendees to the content of the meeting. Despite the economic downturn, the meeting chaired by host *Angel Chamorro* was even better attended than in the past. In their opening remarks, conference chairs *J.M. Ferro* and *M.G. Hennerici* cited the 1,352 abstracts from 9,823 authors, which resulted in 289 oral presentations and even more posters covering over 20 subjects related to stroke.

The *Tuesday, 25 May sessions* were devoted to teaching, 10 of them to clinical features; an additional 2 were for nurses, including their special poster session, and there was a workshop for young stroke physicians. The evening welcome was held in the garden adjacent to the Palau de Congressos de Catalunya and the Hotel Rey Juan Carlos I, the suburban venue also an easy walk from the Camp Nou football stadium.

There were 24 *opening sessions on Wednesday, 26 May* from early morning into the evening: brain imaging; vascular surgery/neurosurgery/interventional neuroradiology; acute stroke – new treatments; interesting challenging cases, and a minisymposium on small vessel disease starting off the day. Even more than reported in prior years, your correspondent found himself not only unable to attend all parallel sessions, but increasingly frustrated by the rising number of memorable topics being discussed, some missed. Apologies to those not cited, the usual cause being difficulties leaving one session to attend another.

In the *vascular surgery session*, *R. Herzig* presented the results of 58 patients who underwent emergency carotid

endarterectomy, finding the favorable prognostic factors being younger age and smaller initial clinical deficit. Of interest, a strict time window did not appear as important for the outcomes. *D.A. Doig*, presenting for the ICSS (International Carotid Stenting Study), made an important observation that noted that cerebral protection devices did not prove helpful in the ICSS. Although the devices were recommended, mandatory use was not. Excluding those patients in whom intervention had been aborted before deployment of the stent, the rate of fatal or disabling strokes (modified Rankin Scale, mRS, score of ≥ 2) was 14 events with (2.4%) and 1 event without, for a risk ratio of 3.65, the risk ratios being based on 700 patients. *M. Rosenkranz* showed evidence for a relationship of carotid plaque surface irregular with solid cerebral emboli during stenting in a cohort of 87 patients. *O. Mansour* presented the a series of 18/35 severe ($>70\%$) restenoses occurring in the stent site.

In the *acute stroke – new treatment concepts session*, the room filled to the bursting point with listeners, *M. Rubiera* contributed to the controversy about bridging intravenous (IV)-intraarterial (IA) tissue plasminogen activator (tPA) rescue with results from 19 IV-IA versus 3 IV-only cases with an mRS score of 0 (final status), 15 versus 9 with an mRS score of 1, 4 versus 13 with an mRS score of 2, and 12 versus 20 with an mRS score of 3. These results argued for better results with bridging than with IV alone, claiming good outcome in patients who did not initially respond to IV tPA alone.

The main auditorium was used for the ESC opening and the Johann Jacob Wepfer Award. The recipient of the

Wepfer Award was *Jan van Gijn*, who needed no introduction. He was lauded in an introduction by *P. Sandercock*. Among the amusing anecdotes was his having found the awardee cited in Cochrane systematic reviews under 3 separate names: van Gin, Venin or Gijn. He then noted his remarkable 422 publications spanning the years 1969–2010, which have yielded over 18,000 citations by others. Dr. van Gijn's informative presentation appears in these pages separately.

The Wepfer Award was followed by the first *large clinical trials session* – a second session was scheduled for the last day of the conference, highlighting the final results of the CREST (Carotid Revascularization Endarterectomy versus Stenting Trial) published the same day in the *New England Journal of Medicine* and the ACES (Asymptomatic Carotid Emboli Study) simultaneously published in *Lancet*.

Australia's *G.J. Hankey* presented the VITATOPS (Vitamins to Prevent Stroke) trial. A total of 123 centers were involved in 23 countries across 4 continents. The agents used were folate, vitamin B₁₂ and vitamin B₆. The study was conducted in 8,164 patients with transient ischemic attack (TIA) or stroke ≤ 7 months prior to randomization. An absolute risk reduction of 1.57% was found, 616 stroke events in the treated groups (4.3% per year) against 678 (4.8% per year; risk reduction: 0.91; $p = 0.05$). He concluded the program was not statistically significant in reducing major vascular events, but might have a value in preventing 'lacunar' stroke.

S. Uchiyama, Tokyo, presented the CSPS II (Cilostazol Stroke Prevention Study II), a comparison of cilostazol (CIS) 200 mg with aspirin (ASA) 81 mg in 2,600 patients. All stroke (ischemic or hemorrhagic) was the primary endpoint, occurring in 82 subjects on CIS and 119 on ASA, the superiority significant at 0.036. The event rates per year favoring CIS resulted in an overall relative risk reduction of 25.7%, seen most often in those classified as 'atherosclerotic stroke'. The annual bleeding rates were higher for those on ASA (1.78) than on CIS (0.77).

L.H. Bonati represented the ICSS for a blinded comparison of new ischemic brain lesions after stenting or endarterectomy for symptomatic carotid stenosis randomized to the ICSS. Data from 377 patients were reviewed 1–7 days before, and 1–3 and 30+ days after the procedures. New diffusion-weighted imaging lesions were more frequent for stenting than for surgery ($p < 0.001$), but most of the lesions were small in stenting, larger in surgery, those symptomatic having the greater lesion volumes. New hemorrhages were rare (5 in each group).

A. Schwartz, Hannover, presented the results of the MRI substudy from the EARLY trial (early treatment with aspirin plus extended-release dipyridamole for TIA/ischemic stroke within 24 h of symptom onset). Baseline MRI identified a group of 51 cases at high risk for recurrent ischemic lesions, showing 'territorial' more than lacunar sites of infarction.

N. Wahlgren, Stockholm, presented the outcome of thrombolysis in the 3- to 4.5-hour time window for the 17 months after ECASS (European Cooperative Acute Stroke Study) III and SITS (Safe Implementations of Treatments in Stroke). The results clearly indicated these reports modified practice for use of thrombolysis. Not only were increasing numbers of patients treated in a comparable time period, but the increase did not come from stretching the time window for those usually treated within 3 h; the effect appeared to be almost entirely additive: the death rates were comparable for the 3- to 4.5-hour group (12) and the < 3 -hour group (12.3), for an odds ratio of 0.97 ($p = 0.4$). There was only a slight increase in the symptomatic hemorrhage rate.

N.K. Misha, Glasgow, presented an analysis of thrombolysis outcomes for those aged > 80 years, and for those with diabetes or previous stroke. Drawing on data from the available 29,500 cases, he found the outcomes for all 3 subsets favoring the use of alteplase over placebo.

Fully sated with these presentations, the participants had box lunches, followed by two educational symposia (*meet the professor* with *B. Norrving* and *K. Thygesen*, Sanofi-Aventis, sponsor) and contemporary achievements in the *treatment and prevention of ischemic stroke* presented by *P. Gorelick*, *K. Lees* and *W. Hacke* (Boehringer-Ingelheim, sponsor). Concurrently, *poster session red* was held.

The main auditorium was again the site of the *atrial fibrillation symposium*, chaired by *M.G. Hennerici* and *J.L. Mas*. Several major conclusions were forthcoming. *J.Y. le Heuzey* discussed *rhythm versus rate control* and deemed rhythm control the better choice for younger patients and symptomatic patients with few risk factors. Rate control was recommended for older patients, those asymptomatic or those with few symptoms. He discussed the risk of antiarrhythmic death risk reduction – citing sotalol, propafenone and flecainide as being superior to amiodarone, being itself superior to no therapy –, but noted these risks approach each other for all therapies over time. A new agent, dronedarone, structurally related to amiodarone, proved better than placebo and with better safety than amiodarone due to fewer gastrointestinal events; thus, it may replace amiodarone. Two important

quotes are: 'ablation is interesting but for only some patients, and complications can occur', and 'no antiarrhythmic therapies are clearly superior to any other'. Deleterious effects of antiarrhythmic drugs can offset the benefits of maintenance.

E.M. Aliot reviewed *interventional treatments*, recommending never to ablate a patient right after stroke, but to wait a few months. He also noted there is a risk of stroke during the procedure. He further commented that maintaining a sinus rhythm may slow down the progression of atrial fibrillation disease progression. Many start with paroxysmal atrial fibrillation, then progress to persistent and, finally, atrial fibrillation, which becomes permanent. For those considering ablation, the longer they wait before ablation, the less success they may have, and then the risk of the procedure increases. Addressing the question whether ablation is a first-line treatment, he cited a range of findings in the literature, leaving it unclear to this listener as to what the answer might be. What was clear were recent reports citing 53 deaths (0.9/1,000), including tamponade, atriophogal fistula, stroke and massive pneumonia – the latter severe in 5.6%. Complications were rising by age, especially in those aged >75 years. He closed by mentioning the WATCHMAN PROTECT trial, the results for noninferiority being 0.992, and for superiority 0.734. The Watchman device is not yet widely accepted and not yet available.

H.C. Diener discussed *the end of antivitamin K therapies*? His question went unanswered, but he discussed in detail the guidelines for warfarin therapy in atrial fibrillation, citing the usual warfarin, international normalized ratio (INR) 2–3, its reported use with an INR of 3–4.5, an INR of 1.3–1.8 + aspirin in different doses, clopidogrel and aspirin, and the *European Heart Journal* study from 2006 where the hemorrhage risk was related to a rising INR. He then turned to factor Xa inhibitors, noting idraparinux had a higher bleeding rate than warfarin. Apixaban and rivaroxaban were briefly mentioned, but his main focus was on dabigatran 100 mg bis in die versus 150 mg versus warfarin in the RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) study of 18,000 patients treated over 2 years. The dose of 100 mg dabigatran was as effective as warfarin; however, Diener was unable to explain how dabigatran 150 mg bis in die had the same efficacy as warfarin in the prevention of stroke events, but a hemorrhage rate reduced by 74% compared with warfarin, the mortality being the same. A warning was mentioned that, thus far, there is no antidote available to dabigatran; all patients have to be dialyzed.

During the same time period, the *RENEVAS (Red de Investigación Cooperativa Neurovascular)* symposium was held, featuring molecular imaging in stroke, organized by A. Davalos, P. Ramos-Cabrer and U. Dirnagl. At the same time there was a joint symposium by the ESC/World Federation of Neurorehabilitation on stroke rehabilitation, with presentations by G. Kwakkel, V. Sirtori, K. Müller and R.K. Seitz. An even longer session on neurosonology was organized as a joint workshop of the ESC and European Society of Neurosonology and Cerebral Hemodynamics, with presentations made by J. Molto, B. Ringelstein, E. Bartels, C. Molina and S. Meairs.

After a welcome coffee break and visit to the exhibition, the main auditorium was the site of a journal anniversary symposium sponsored by *Cerebrovascular Disease*, titled *stroke management and prevention*, introduced by M.G. Hennerici and featuring talks by D. Leys, K. Toyoda, S. Uschiyama, H.C. Diener and K. Minematsu.

Simultaneously, in other rooms, a second session on brain imaging included a presentation by O. Benavente on the MR findings of the first 900 cases by SPS-3. The cases were drawn from 62 centers, and their risk factors were hypertension (77%), diabetes (37%), and lower percentages for prior stroke and hyperlipidemia. The prevalence of MR+ infarcts were: corona radiata – 28%; thalamus – 26%; pons – 20%; basal ganglia internal capsule – 18%; centrum semiovale – 2%, and other sites – 2%. Their mean size was 1.4 cm (0.54), and there were multiple infarcts in 17% of the cases. Intracranial stenosis was found in 21%, and white matter (moderate-severe) in a total of 47%.

N. Perez de la Ossa found leukoaraiosis not to be a risk factor in intracerebral hemorrhage, but the cohort was small.

C. Xu presented the new method for imaging small vessels called 'vessel size imaging' in patients with acute ischemic stroke. This feasibility study involved 13 stroke patients and 11 studies, purporting to show an ischemic penumbra may be discoverable.

P.L. Clatworthy tried to show the relationship between optic radiation damage and visual field defects after middle cerebral artery (MCA) stroke in a probabilistic tractography study. His claim was that 2/3 of cases with large MCA stroke have a visual radiation damage, but that 50–60% improve. By dividing optic radiation into 4 segments based on the axial view, he argued that brain plasticity results in recovery despite persisting optic radiation damage. However, 7 patients were the subject of the study, 5 of whom had lower-division infarcts, and the others sylvian or upper convexity infarcts whose initial syndrome could well have been from hemineglect.

In the *acute stroke – new treatment concepts B sessions*, another standing-room-only, F.J.L. Nicoli presented that microbubble administration during prolonged 2-MHz transcranial Doppler (TCD) improves recanalization with long-term functional outcome in acute stroke patients treated with IV tPA for isolated M1 occlusion. His cohort was 31 cases with TCD only, and 23 TCD+ microbubbles. The best results were obtained for those whose initial NIHSS score was <15. Hemorrhagic transformation was documented in 1.2% of the cases.

Sad to report, your correspondent was prevented from hearing the *sessions on heart and brain, management and economics* and the *symposium on thrombolytic therapy in acute stroke* at the Hotel Rey Juan Carlos I, chaired by the host, A. Chamorro. It featured A. Davalos, J.B. Fiebach and T. Jovin. The day ended with symposia No. 1 Servier, No. 2 SIECV (Sociedad Iberoamericana de Enfermedad Cerebrovascular), No. 3 Lundbeck, No. 4 ev3 and No. 5 Bayer.

Thursday, 27 May 2010, was even more crowded, with a total of 33 individual sessions. In room J, like many other rooms filled beyond capacity, the *minisymposium III – invasive treatment strategies for acute ischemic stroke*, was chaired by W.D. Heiss and M. Fisher, featuring 4 speakers. M. Mazighi discussed personal experience with IA and IA-IV thrombolysis.

H. Mattle reviewed personal experience and the literature in *intracranial mechanical recanalization – a neurologist's view*. He noted the best prognostic factors for outcome were recanalization and a low initial NIHSS score, lower age and available collaterals, time not seeming to be as important. A series of slides showed the advantages of and disappointments from mechanical clot extraction. Bridging IV with IA treatment offered some advantages. For added mechanical clot extraction efforts, he proposed patients with some of the following characteristics: NIHSS score ≥ 10 ; stroke >6 h earlier; central occlusion of the anterior circulation; rescue therapy after failed IV therapy; basilar artery occlusion (unclear if IV was equal to IA thrombolytic therapy), and stroke patients with anticoagulation or in pregnancy. Responding to a question from the floor, he commented that it is not clear yet whether to use endovascular or tPA treatment alone for short basilar occlusion. He also left the question unanswered whether there is an open window beyond 8–12 h, but then treatment does not seem to improve the outcomes of patients.

T. Liebig offered a *neuroradiologist's view*. He noted that a high NIHSS score usually means major occlusion, low likelihood of recanalization and little improvement

even if successful. He showed the 7 devices commonly used for clot extraction, claiming that multimodality approaches can lead to a 10% increase in effect of reperfusion. NIHSS score improvement by >4 points occurred in 65% of the MCA occlusions he presented. He noted that the angiogram-to-reperfusion time was slowly falling from 75 to 40 min on average. He also discussed the use of stents, noting the techniques copied from cardiology, but also including intracranial self-expanding stents. The SARIS (Statin on Atherosclerosis and Vascular Remodeling Assessed with Intravascular Sonography) trial of 20 patients achieved good perfusion. He held out hope the stents may suppress the local thrombogenic focus, and reviewed concerns whether perforators could be occluded. Examples were presented of the use of temporary stents to keep the arteries open until a local occlusion is cleared away, the stent then being removed. Some were subject to repeated deployment. He noted some occlusions that had been delodged could migrate to previously unaffected territories. His experience included 104 patients. Some of the cases had been treated after full-dose tPA failure. The Solitaire stent was used as an anchor to advance the catheter to the occlusion site and extract the occlusion. Citing successes, he also acknowledged complications, including subarachnoid hemorrhage, parenchymal hemorrhage, clot migration, vessel perforations, inability to retrieve the implant, and dissections, concluding with the comment that some of the best recanalizations have yielded the worst outcomes.

J. Jolkkonen closed with a discussion of *animal models of intravascular cell therapy*. His work was drawn from work with rodents at the University of Eastern Finland. Although migration of implants to the infarcted areas has been seen from intraventricular injection and some from direct brain injection, to date human trials have also been of no proven value. Intravascular delivery of human umbilical cord blood to a rodent femoral vein has yielded no clinical improvement. Only a few cells were found in the rat brain, most of the cells went to the liver and spleen.

In other meeting rooms, parallel sessions were held: *stroke progress A; etiology of stroke and risk factors; acute stroke, emergency management, stroke units and complications; experimental studies A; acute stroke – current treatment*, and a *minisymposium* at the Hotel Rey Juan Carlos I on *neuropsychiatric complications of stroke*. After the coffee break, the auditorium was the site of the *European Stroke Network symposium*, chaired by U. Dirnagl and S. Meairs, featuring talks by C. Iadecola, A. Planas, N. Rothwell, L. Sorokin and A. Meisel. Parallel sessions were held on: *stroke prevention; etiology of stroke and risk*

factors; acute stroke emergency management, stroke units and complications B; experimental studies B; vascular biology, and intracerebral/subarachnoid hemorrhage and venous diseases. Poster session blue occurred during the lunch hour.

In the afternoon, the auditorium was used for the ESC/ESO (European Stroke Organization) Symposium, chaired by P. Michel and V. Caso. Three subjects were reviewed in gentle debates: (a) TIA cases should be treated in TIA clinics, not admitted to stroke units; (b) patent foramen ovale – close high-risk patients versus never close, and (c) should patients with an unknown time window be treated with recombinant tPA?

Parallel oral afternoon sessions were held on: *epidemiology of stroke; small vessel disease and white matter disease A; acute cerebrovascular events – TIA and minor stroke; acute stroke clinical patterns and practice A; rehabilitation and reorganization after stroke A; intracerebral/subarachnoid hemorrhage and venous diseases B*, and *behavioral disorders and poststroke dementia*.

After the coffee break, a well-attended session held at the Hotel Rey Juan Carlos I was the *minisymposium V – update on the treatment of carotid stenosis*, which was chaired by M.M. Brown and J.L. Mas. M. Brown, reviewing his recent publications on the subject, concluded stenting was not as safe as surgery.

A. Mackey, from the Hôpital l'Enfant Jesus, a major contributor to the just-published CREST, showed data indicating women did not have a higher stroke or death rate, and that those aged >75 years suffered a higher rate of strokes from stent. The data came from 108 US and 9 Canadian sites. Those eligible had symptoms for <180 days and carotid stenoses of $\geq 50\%$ by angiogram or $\geq 70\%$ by ultrasound, and were ineligible if they had severe coronary artery disease or cardiac ejection fraction of <35%. Follow-ups were at 3 months, then semiannually. During the years of the trial, 2000–2008, 47% of the participants (1,181) had been asymptomatic. The 5-year stroke event rate for stenting was 8.6%, for surgery 8.4% (hazards ratio: 1.08; $p = 0.69$). The procedure-related stroke and death rates were the lowest yet reported. Although cranial neuropathy and myocardial infarction were more frequent with surgery, interventional stroke rate and disability were higher with stenting, rising with age of >70 years. The current follow-up is 5 years, and NIH proposals have been submitted in favor of 10 years.

The session was continued by P. Rothwell, who addressed the question: *who is at highest risk of stroke associated with carotid stenosis?* His extensive literature review demonstrated that the risk of stroke by decades as a

function of degree of carotid stenosis is definitely falling, which raises the issue of whether there is a benefit from the procedure(s) for asymptomatic patients.

J.L. Mas posed the question: *is stenting as safe as endarterectomy?* Reviewing the results from the EVA 3, Space, ICSS and CREST, he noted the results for each group were the same, also by protocol, and by intention to treat. The Kaplan-Meier curves all looked fairly flat after the procure-related events. EVA 3 also showed an age-related complication rate for stenting comparable to that found in the CREST.

H. Sillesen closed with a clear indication for improving outcomes of medical therapy over the past few decades, and a declining evidence of stroke risk from carotid stenosis. He noted the presence of carotid stenosis now predicts a risk of death more than of stroke. He cited evidence that dual antiplatelet therapy was better than single; statins, treatment for hypertension, and changes in lifestyle have improved outcomes to an extent that the next issue is whether stent or surgery will be subject to reevaluation. The attendees were facing a sober reappraisal of current therapies.

As if these presentations were not enough, the day closed with 3 satellite *symposia*: No. 6 *Uriach*; No. 7 *stroke devices*, and No. 8 *Allergan*. On the closing day, 3 *symposia* dealt with (a) *challenging stroke cases*, (b) *body temperature and stroke*, and (c) *antihypertensive treatment in acute stroke and prevention*, as first in 2009 coorganized by the ESC and the European Society of Hypertension. In parallel oral sessions were discussions on: *metaanalysis and reviews; vascular imaging*, and *small vessel stroke and white matter lesions*. They were all very well attended and, in contrast to previous years, all research data were heavily discussed in vivid interaction among speakers, chairpersons and the audience.

C. Iadecola, New York, was invited as guest speaker to give the *ESC lecture 2010* about *amyloid, hypertension and cognitive dysfunction*; his review of this extremely important research areas, filled by many examples of his own and his group's outstanding contributions, was vividly applauded by a large audience of nearly 2,000 people still present after the 3 days of this meeting.

The ESC 2010 was one of the best attended and, scientifically, certainly the most busy and successful of the ESCs ever organized. Twenty years after its foundation, M.G. Hennerici invited all physicians, scientists and members of the international stroke community all over the world to join the 20th ESC in Hamburg, Germany, May 24–27, 2011.