

## **A DECADE OF PROGRESS IN STATUS EPILEPTICUS 2007 TO 2017 –**

The Proceedings of the 6<sup>th</sup> London-Innsbruck Colloquium on Status Epilepticus and Acute Seizures

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This Colloquium was the 6<sup>th</sup> in a series of biannual conferences, alternating between venues in Britain and Austria, held over the last 10 years. The proceedings of each have been published (1-5) as a guide to what was discussed and the main conclusions drawn.

### **Advances in status epilepticus over the previous five colloquia**

Over the 10-year period, much has developed in the field of Status Epilepticus, we hazard to say that this is one of the fastest growing in the whole of epilepsy. This is reflected in the 5691 publications listed in Pubmed over the previous 10 years, more than were published in all the previous years on the Pubmed index. During this time, a number of new advances were made which were presented and discussed at the previous five Colloquia, and in figure 1 we have listed what we consider some of the most significant of these.

**Basic science:** The basic science understanding of the mechanisms and also the consequences of status epilepticus has advanced considerably with advances in receptor trafficking, cerebral inhibition at a cellular and system's level, synaptic function, molecular genetics, epigenetics, and experimental pharmacology. This progress in understanding of the mechanisms responsible for the failure for seizure suppression and seizure perpetuation led to new concepts in definition of status and the development of new drugs medicines for different stages of status epilepticus.

**Epidemiology:** In the field of epidemiology, there have been now good estimates of frequency of refractory and super-refractory status epilepticus (SRSE). The ageing population will lead to an increase in the incidence of status epilepticus.

**Clinical:** There have been a range of new measures to predict outcome and measures of severity which have been validated and used across different countries. There have been studies of the range of uncommon causes of status epilepticus, including genetic causes, and both clinical and pathological studies of auto-immune and mitochondrial cases. The entity of SRSE has been defined and the concept has attracted wide usage.

Electroencephalography: The EEG patterns of nonconvulsive status epilepticus (NCSE) have been better understood and the Salzburg Criteria for defining NCSE have been widely accepted.

Treatment: The advances in the use of benzodiazepine therapies 'out of hospital' using different routes of administration have been perhaps the most important public health advances in the whole of epilepsy. There have also been, for the first time RCTs in the field of established status. New treatment protocols, new drugs, and new types of treatment especially in SRSE, include ketamine, lacosamide, brivaracetam, and neurosteroids, such as ganaxolone or allopregnanolone. The better appreciation of the risks and the benefits of anaesthesia led to the development of appropriate treatment protocols.

### **The sixth symposium held in Salzburg, April 6<sup>th</sup> -8<sup>th</sup>, 2017**

The 6th Colloquium had 7 main themes: The nature of status epilepticus – experimental aspects; the nature of status epilepticus – clinical aspects; Status epilepticus in the intensive care unit; the weaning of anaesthetics; some regulatory aspects of status epilepticus; audit and registries; future perspectives – novel therapy and innovation. In addition, there was one Satellite Symposium sponsored by SAGE pharmaceuticals entitled: Clinical Controversies in the treatment of super-refractory status epilepticus (SRSE).

The faculty of 45 leaders (fig 2) in the field was drawn from 13 countries: Austria, China, Croatia, Finland, Germany, Great Britain, India, Ireland, Israel, Italy, South Korea, Switzerland and the USA. 78 posters were accepted for viewing at the congress. There were 336 delegates from 5 continents (fig 3). Financial sponsorship in the form of educational grants, without input into the programme, was provided by the following sponsors: SAGE, Eisai, UCB, Upsher-Smith, GW Pharmaceuticals, and an exhibition was held the additional exhibitors: Austrian Institute of Technology, AD-TECH/DID medical, Livanova, Epinet study group, Novartis, Electrical Geodesics, Epilog and Neuromed. The conference was awarded 15 European CME credits by the European Accreditation Council for Continuing Medical Education (EACCME).

There were 30 keynote lectures in the Colloquium. These started with a review of recent work in mitochondrial diseases and SE (Rahman), an account of new work on the circuit mechanism in SE (Kapur), new work on receptor trafficking (Kittler), Epigenetic changes in SE (Henshall), neurotrophic factors in SE (Simonato) and next generation sequencing (Lipkin). These were superb talks and show how far the field has advanced in these basic science areas. There then clinical talks on Boundary Syndromes (Shorvon) and a fascinating review of SE due to poisons in warfare (Marini). The presentation on neuroimaging of status (Meletti) demonstrated new imaging techniques for the diagnosis of SE and the study of its consequences, and the lecture on treatment gap in developing countries (Lee) shows how much remains to be done. There were then a series of talks on the ITU management of SE covering the diagnosis of nonconvulsive SE (Trinka), a new prognostic scale from China (Yuan), a review of anaesthetic

treatments (Hocker), studies of guidelines for the weaning of anaesthetics (Colquhoun), the effects of anaesthetics on the EEG (Cole), the long term consequences of ITU care in children and a new paediatric SE network (Loddenkemper), and a review of SE in the elderly (Leppik). We then led a debate about regulatory aspects of SE – covering two specific topics. The question of whether SE should be considered an entity, distinct from epilepsy, from the regulators point of view and what evidence was needed to license a drug for SE. This was followed by presentations on the Global Audit of refractory SE (Hocker and Ferlisi) and the SENSE registry (Kellinghaus). On the final day, there were a series of papers on new treatments in SE, and these demonstrated to all how fast the therapy field is moving forward. These included: Propofol hemisuccinate (Rogawski), Valnoctamide and SPD (Bialer), Brivaracetam (Trinka), Perampanel (Rohracher), neurosteroids (Rossetti) and Ketamine (Hofler). The session followed with a lecture on new modes of administration (Cloyd) and reactive oxygen species (Walker) and an update on the ESSET trial (Kapur).

There were three poster prizes awarded: Gaetano TERRONE, Italy received the award for the best poster in Basic and clinical investigations, Alexey KHOLIN, Russian Federation for Paediatric and clinical science, and Alexandra SINCLAIR, UK for the best poster in Treatment and outcome. The winners are entitled to free admission for the 7th Colloquium 2019.

## FIGURES

FIGURE 1: Some of the areas of advance on the field of status epilepticus in the last 10 years discussed in the first five of the Status Epilepticus Colloquia.

- Basic science: trafficking, cerebral inhibition, synaptic function and molecular genetics, and experimental pharmacology
- Epidemiology: frequencies
- Clinical: New definition and classification of SE, Outcome and clinical measures, uncommon aetiologies, concept of SRSE. Advanced design of clinical trials in SE (ESETT)
- Electroencephalography: EEG patterns have been clarified, criteria for the definition of NCSE
- Treatment: advances in the use of parenteral benzodiazepine therapies in 'Out of hospital' settings, RCTs and new treatment protocols, new medicines, anaesthetic treatment protocols.

FIGURE 2. Members of the Faculty of the Congress.

Abend Nicolas – United States  
 Bialer Meir – Israel  
 Basic Silvio - Croatia  
 Bauer Gerhard – Austria  
 Bleck Tom – United States  
 Cole Andrew - United States  
 Cock Hannah – United Kingdom

Ferlisi Monica – Italy  
Henshall David – Ireland  
Hocker Sara - United States  
Höfler Julia – Austria  
Jiang Wen – China  
Kälviäinen Reetta - Finland  
Kaplan Peter – United States  
Kapur Jaideep - United States  
Kellinghaus Christoph - Germany  
Kittler Josef – United Kingdom  
Kullmann Dimitri – United Kingdom  
Lee Byungin, Korea  
Leppik Ilo - United States  
Loddenkemper Tobias – United States  
Marini Ann - United States  
Meletti Stefano – Italy  
Navarro Vincent - France  
Neligan Aiden – United Kingdom  
Rahman Shamima, United Kingdom  
Rogawski Michael – United States  
Rossetti Andrea - Switzerland  
Shorvon Simon - United Kingdom  
Strzelczyk Adam - Germany  
Tan CT - Malaysia  
Trinka Eugen - Austria  
Unterberger Iris - Austria  
Walker Matthew, United Kingdom

FIGURE 3. Some of the delegates of the Congress, in the gardens of Schloß Mirabell in Salzburg, Austria.



## REFERENCES

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