Availability of antiepileptic drugs: Politicians’ roles

To the Editors:

Recently, Baftiu et al. published a very nice and important paper entitled: “Availability of antiepileptic drugs across Europe.” In their study, they observed that the main reasons for poor access to antiepileptic drugs (AEDs) in European countries were lack of regulatory approval, high prices, and reimbursement restrictions. There were large gaps in AED availability across European countries, especially between high-income countries and the others. The newest AEDs were not available in lower-income countries. These authors concluded that their findings raise major concerns about the quality of epilepsy care in many European countries.

Findings in the study of Baftiu et al. are important and valid. In fact, the dramatic situation in the world is the presence of even a more strikingly huge gap in epilepsy care between high-income countries and poor nations. In a recent study from the Democratic Republic of Congo, only 33% of the people with epilepsy had received any AEDs, indicating a treatment gap of 67%. In a systematic review investigating global disparities in the epilepsy treatment gap, the authors concluded that the gap was >75% in low-income countries, whereas many high-income countries had gaps of <10%. During the past decade or so, many health care professionals and physicians around the world have developed or proposed creative ways to overcome the challenges and to provide better care for patients with epilepsy in resource-limited settings. These kinds of actions have often resulted in significant changes regionally. However, poor income, lack of resources, regulatory approval, and high prices are apparently not the only factors that play significant roles in lack of access to AEDs and appropriate epilepsy care. In a recent study, we observed that the hardship by the international economic sanctions imposed on the Iranian people in the past few years caused poor access to AEDs in some patients with epilepsy. Compared to the period before the intensification of sanctions, the price of some AEDs (e.g., levetiracetam) increased up to 300% after intensification of the sanctions. None of the newest AEDs (i.e., lacosamide, perampanel, and rufinamide) have become available in Iran.

In brief, physicians, researchers, and other health care professionals around the world will continue their endeavor to provide the best care possible for all patients including those with epilepsy, but from a patient care perspective, it is necessary that politicians facilitate decisions that make the life, health, and well-being of ordinary people more affordable and without hardship.

ACKNOWLEDGMENT

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DISCLOSURE

The author has no conflict of interest to disclose. I confirm that I have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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REFERENCES


Postencephalitic epilepsy in children and adults: Etiology matters

To the Editors,

I read with great interest two studies on postencephalitic epilepsy (PE) published this year in Epilepsia,
the first in the adult population by Singh et al.,\(^1\) and the second in children by Pillai et al.\(^2\) Both studies retrospectively analyzed frequency and risk factors for the development of epilepsy in large cohorts of patients admitted to the hospital with encephalitis of viral, autoimmune, or unknown origin. The strength of these works was Indeed the long-term follow-up, which was a median time of 43 months in the first study and 7.3 years in the second. PE was defined as the need for continued use of antiepileptic drugs for at least 12\(^1\) or 24\(^2\) months after the resolution of acute encephalitis, respectively. Using this definition, the frequency of PE was 29.9\% in the adult population and 21\% in children. Importantly, but unsurprisingly, both studies conclude that features predictive of PE were the presence of seizures and status epilepticus during the acute encephalitis stage. Brain magnetic resonance imaging (MRI) abnormalities were also associated with the development of PE. I want to congratulate Dr Singh, Dr Pillai, and their colleagues for these results, but I would like to bring one issue to the authors’ attention. When examining the relationship between different etiologies of encephalitis and risk of subsequent PE, the two studies come to opposite conclusions. In fact, Singh et al. found that PE was more common in autoimmune encephalitis (46.5\%) as compared to infectious encephalitis (34.9\%). However, the etiology of encephalitis was not recognized to be predictive of the development of PE. To the contrary, Pillai et al. stratified the patients in a “high risk group” for PE—the herpes simplex virus (HSV) group—and a “low risk” class, including patients with anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis. Remarkably, none of the nine patients with anti-NMDAR described had developed epilepsy, despite the fact that seven of them had acute seizures. I believe that this difference deserves mention and propose four possible explanations. First, the propensity to cause seizures in response to the same neural surface antibody could vary depending on the age of the patient, as observed previously.\(^3\) Second, a subgroup of the HSV patients may have developed epilepsy due to an unrecognized, infection-induced, anti-NMDAR encephalitis. Pillai et al. stated that 103 (80\%) of 129 non-ADEM (Acute Disseminated Encephalomyelitis) patients were tested for serum autoantibodies, but it is possible that patients with an initial diagnosis of HSV encephalitis later relapsed due to an immune-mediated process, as described recently in numerous reports.\(^4,6\) Third, the fact that patients with voltage-gated potassium channel (VGKC)–complex antibodies were unrepresented in the children group could have played a role. Fourth, differences in immunotherapies used among the two groups, with varying results in controlling seizures due to an immune-mediated pathogenesis. The emerging role of autoimmune encephalitis in causing seizures and new-onset refractory status epilepticus in adults was recently confirmed in a multicenter retrospective study.\(^7\) Prospective studies with extensive antibody testing are needed to quantify the real burden of PE depending on the diverse etiologies.

**Disclosure**

I have no conflicts of interest to disclose. I confirm that I have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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**References**


**In response: Postencephalitic epilepsy in children and adults: Etiology matters**

To the Editors:

We would first like to congratulate Pillai et al. for performing a valuable study that looked into the predictors of postencephalitis epilepsy (PE) in the pediatric population and also Dr. Alberto Vogrig for analyzing the study of Pillai et al. and our study together and highlighting the important similarities and differences between the studies.\(^1,2\) Dr. Vogrig came up with four possible explanations for the discrepancies in the conclusions between the two studies, particularly in one variable, that is, etiology. We agree with the possible explanations; however, there is one major difference in patient categorization between the two studies that also deserves to be highlighted. All the patients in our study were categorized as having viral infection.
encephalitis, only if they had a positive antibody titer in the cerebrospinal fluid (CSF), a positive polymerase chain reaction (PCR), or CSF culture or histopathologic findings, whereas autoimmune encephalitis was defined by the presence of specific antibodies in the CSF or histopathologic evidence on brain biopsy. Thus, all the patients in these two categories had a confirmed diagnosis, and for the patients who didn’t meet the above criteria, they were categorized as unknown/others. Instead, Pillai et al. included the confirmed, probable, and possible diagnoses as viral and autoimmune encephalitis. This might be important because in their cohort, the majority of PE in infectious encephalitis was caused by Herpes simplex virus (HSV) (6 of 11 PE cases) and only 4 of 9 cases had a confirmed HSV diagnosis. Meanwhile, the majority of confirmed cases had enterovirus (17/20), and only 4/14 of them had PE. In addition, acute disseminated encephalomyelitis (ADEM) is a disease more common in children, and Pillai et al. had only five cases of antibody-confirmed autoimmune encephalitis (all with anti-N-methyl-D-aspartate receptor [NMDAR] antibodies). It is therefore possible that the studies might have shown more similar results if PE had been compared in only the confirmed cases or in cases with similar etiologies. We were not able to confirm the role of encephalitis etiology in the risk of PE using multivariate analyses because we considered that our cohort size was insufficient to perform a reliable multivariable analysis.\(^1\) We agree that larger prospective studies with extensive antibody and serology testing in cases of encephalitis are necessary to better quantify PE across diverse etiologies.

**DISCLOSURE**

Both authors have no conflicts of interest to disclose. We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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**REFERENCES**

DISCLOSURE

Neither of the authors have any conflict of interest to disclose. We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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REFERENCES


In response: Comment on outcome following multiple subpial transection in Landau-Kleffner syndrome and related regression

To the Editors:

We thank Dr. Kheder and colleagues for their letter and we are grateful for their comments.

The authors of Outcome following multiple subpial transection in Landau-Kleffner syndrome and related regression discussed focusing on those with a classic Landau-Kleffner syndrome (LKS) presentation prior to publication. It was decided that because this is such a variable population and the proportion of classic LKS cases in the surgery and nonsurgery groups was equivalent, the analysis would focus on the group as a whole, as this is more representative of what presents clinically. However, in response to the letter from Dr. Kheder and colleagues, we have repeated the main analysis with the classic LKS only subgroup below. Given the small sample size in this subgroup analysis, the findings should be interpreted with some caution.

At baseline, significant differences between the surgery and nonsurgery groups remained for age at presurgical assessment (t (−2.3), p = 0.03) and laterality of discharges (χ² = 7.3, p = 0.03). In this classic LKS subgroup, there was no significant difference between the surgery group (n = 11) and the nonsurgery group (n = 15) in language or nonverbal reasoning category levels at baseline or at follow-up (see appendix Table S2 for language category at both time points’). There remained no significant difference between groups for change in language category over time, with improvement in three from the surgery group and seven from the control group, no change in five from the sur-
gery group and five from the control group, and deterioration in two from the surgery group and two from the control group.

At follow-up, there were no significant differences between the surgery and nonsurgery groups in electrical status epilepticus during sleep (ESES) outcome, seizure outcome, adaptive functioning, or quality of life. Seizures at follow-up ($β = −0.64$) remained the most significant predictor of quality of life ($F = 10.42$, $R^2 = 0.41$, $p = 0.01$), with age at regression becoming nonsignificant (note that “diagnosis” was removed from the regression model).

Overall, the main findings of this subgroup analysis are similar to the whole sample analysis, with similar outcomes for both the surgery and nonsurgery groups. This supports our original conclusion that there is insufficient evidence that multiple subpial transection in LKS produces substantial benefits over and above the recovery seen in patients who do not undergo surgery.

**Disclosure**

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Michelle Downes, Rebecca Greenaway, Maria Clark, J. Helen Cross, Nicola Jolleff, William Harkness, Marios Kaliakatsos, Stewart Boyd, Brian G. R. Neville

1. UCL Institute of Child Health, London, United Kingdom; and
2. Great Ormond Street Hospital for Children NHS Trust, London, United Kingdom

**Reference**


**Regional Congresses**

**11th Asian & Oceanian Epilepsy Congress**

13–16 May, 2016
Hong Kong
Website: www.epilepsyhongkong2016.org

**9th Latin American Congress on Epilepsy**

20–23 August 2016
Cancún, Mexico
Website: www.epilepsycancun2016.org/

**12th European Congress on Epileptology**

11–15 September, 2016
The Prague Congress Centre, Czech Republic
Website: www.epilepsyprague2016.org

**Upcoming Chapter Congresses**

**Annual Meeting of the Swiss League Against Epilepsy and the Swiss Society for Sleep Research, Sleep Medicine and Chronobiology (SSSSC)**

28–29 April 2016
Basel, Switzerland

**Ukrainian League Against Epilepsy**

Age and gender aspects of epilepsy through the prism of time

12–14 May 2016
Lviv, Ukraine
Congress website: http://www.rimon.in.ua
Information: lepilep@i.ua

**10th Turkish National Epilepsy Congress**

12–15 May 2016
Euphoria Aegean Resort Hotel, Seferihisar-Izmir, Turkey
Registration contact: epilepsi2016@flaptour.com.tr | Information: irseltezer@yahoo.com.tr

38th Italian League (LICE) National Epilepsy Congress
8–10 June, 2016
Rome, Italy
Congress website

Brazilian Epilepsy Congress
9–11 June, 2016
Recife, Brazil

21st Korean Epilepsy Congress
17–18 June 2016
Seoul, South Korea

Joint British and Irish Chapters Annual Scientific Meeting
5–7 October 2016
Clontarf Hotel, Dublin, Ireland
Congress Website

Canadian League Against Epilepsy Biennial Scientific Meeting
14–16 October 2016
Quebec City, Quebec
Congress Website
Abstract submission now open: How to submit an abstract
Abstract submission deadline: June 1, 2016

Other Congresses

1st International Training Course on Neuropsychology in Epilepsy
10–15 April, 2016
Château de Rosay, France
Information flyer
Contact: Neuropsychology Course Secretariat: sarah-ra@unimelb.edu.au

14th International Child Neurology Congress (ICNC)
1–5 May 2016
Bridging Worlds; Child Neurology from a Global Perspective
Amsterdam, the Netherlands
Website: http://icnc2016.org/

3rd International Course on Drug Resistant Epilepsies
8–14 May 2016
Tagliacozzo, Italy
For more information contact Federico Vigevano: federico.vigevano@opbg.net or Nicola Specchio: nicola.specchio@opbg.net
Announcement | Program

4th International Conference on Molecular Neurodegeneration (ICMN 2016)
9–11 May 2016
Coex, Seoul, Korea
Website: www.icmn2016.org | Brochure

7th Caucasian Summer School
24–26 May 2016
Epilepsy: Pharmacological and Alternative Treatment
Tbilisi, Georgia
Announcement | Program | Application
Contact: Nana Tatishvili: n_tatishvili@hotmail.com or Sofia Kasradze: sofiakas@gmail.com

Baltic Sea Summer School on Epilepsy (BSSSE 10)
5–10 June 2016
Trakai, Lithuania
Announcement

2nd East-European Course on Epilepsy
8–10 June 2016
Romania
For more information contact Dana Craiu: dcraiu@yahoo.com or Stanislav Groppa: stgroppa@googlemail.com
Practical Neurology for Junior Doctors 2016

9 June 2016
Newcastle upon Tyne, UK
Information: Edwin Jabbari edwin.jabbari@nhs.net

2nd East-European Course on Epilepsy and SRIE Summer School

15–17 June 2016
Cheile Gradistei, Romania
Information flyer | Program | Registration form

9th International Epilepsy Colloquium: Surgical and targeted treatments for acquired lesions

22–24 June 2016
Westminster, London, UK
Congress website: www.activateevents.com/9thiec 2016

International Summer School on Imaging in Epilepsy (SuSIE)

26–29 June, 2016
Rauischholzhausen Castle, Marburg, Germany
Program, registration and more information on website: www.imaging-in-epilepsy.org

13th Eilat Conference on New Antiepileptic Drugs (EILAT XIII)

26–29 June, 2016
Madrid, Spain
www.eilatxiii.com | Email eilatxiii@target-conferences.com

18th annual meeting of Infantile Seizure Society

1–3 July, 2016
International Symposium on Acute Encephalopathy in Infancy and Its Related Disorders (ISAE)
Chiyodaku, Tokyo, Japan
Website: http://square.umin.ac.jp/isac2016/

2016 Hemispherectomy Conference

8–10 July 2016
Broomfield, Colorado
Website: http://www.brainrecoveryproject.org/events/2016-hemispherectomy-conference-and-family-reunion/

2016 San Servolo international advanced course: Brain Exploration and Epilepsy Surgery

10–22 July 2016
San Servolo (Venice), Italy
Designed for neuroscientists and neurologists with a documented background in epilepsy research and a special interest in epilepsy surgery.
Course directors: Ingmar Blümcke (Germany) and Laura Tassi (Italy)
Sponsored by ILAE, Fondazione Istituto Neurologico Carlo Besta
Information | Contact: epilepsysummercourse@univiu.org

Dianalund Summer School on EEG and Epilepsy (DSSEE3)

17–23 July 2016
Dianalund, Denmark
Advanced, interactive, practically-oriented course on EEG and its application in the field of epilepsy with many hands-on sessions
Announcement

4th Neuropathology Summer School

31 July–4 August 2016
Erlangen, Germany
For more information contact Ingmar Blumcke: bluemcke@uk-erlangen.de

15th Asian Oceanian Congress of Neurology (AOCN 2016)

18–21 August 2016
Advanced Education in Neurology in Asian Oceanian Region
Insights into the latest research, developments and treatments. Including high-level plenaries, interactive symposia, poster and platform opportunities for free papers, state-of-the-art review course, workshops and debates on hot topics and ample networking opportunities
Fundamental Mechanism of Epilepsy International Conference: Excitatory-Inhibitory Signaling Balance as Therapeutic Target in Epilepsy
26–27 August 2016
Montreal Neurological Institute of McGill University, Canada
Focused on roles played by ligand-gated signaling in epileptiform synchronization and epileptogenesis.
More information and registration

4th International Summer School for Neuropathology and Epilepsy Surgery (INES 2016)
29 August–2 September
West China Hospital, Sichuan University, Chengdu, P.R. China
Flyer

14th European Congress on Epilepsy and Society
15–16 September 2016
Prague, Czech Republic
Website: www.epilepsyandsociety.org

5th Global Symposium on Ketogenic Therapies
20–24 September 2016
Treating epilepsy, brain cancer, autism and cognitive disorders
Banff, Alberta, Canada
Website: http://www.ketoconnect.org/

5th International Summer School for Neuropathology and Epilepsy Surgery (INES)
6–9 October 2016

2nd meeting on Immunity and inflammation in epilepsy (IIE2016)
13–15 October 2016
Milan, Italy
For more information contact: Stephan.Rueegg@usb.ch

Annual Meeting of the German-Swiss-Austrian Epilepsy Working Group DACH-AK
Excellence discourse epileptology: I. Clinical epileptology, II: Electrophysiology (EEG, MEG)
20–22 October 2016
Meeting Venue: Prien, Germany
Course directors: Hermann Stefan, Margitta Seeck, Eugen Trinka
Registration ends 15 September 2016

The 27th International Symposium on the Autonomic Nervous System
2–5 November 2016
San Diego, California
Information: Anita Zeller: zeller.anita@mayo.edu
Website: www.americanautonomicsociety.org
Deadline for abstract submission is June 1, 2016.

2017 Congresses

6th London-Innsbruck Colloquium on Status Epilepticus and Acute Seizures
6–8 April, 2017
Salzburg, Austria
www.statusepilepticus.eu