

## Focal Point

### Serendipitous antiepileptics

The uses of valproate as an antiepileptic drug and as a mood stabiliser agent are among the most quoted examples of serendipitous drug discoveries. In 1881, the American chemist Beverly Burton synthesised valproic acid as an organic solvent.<sup>1</sup> It was only after over 80 years of its use as a solvent that its clinical use as an antiepileptic drug was recognised.

In 1963, Georg Carraz tried to examine the antiepileptic activity of herbal khelline compounds, which were dissolved in valproate as a solvent, and found that all the substances he tested had antiepileptic properties. Recognising the need to run an appropriate control, he then tested the solvent used for these khelline solutions and found that it too was effective in controlling seizures, leading him to deduce that the antiepileptic properties were in the solvent itself.<sup>2</sup> Soon after, Carraz developed valpromide, which was thought to be more lipophilic and therefore have greater penetration in the CNS than valproate. He collaborated with a psychiatrist, Sergio Boreselli, who used it in trials in patients with epilepsy and found that the agent was also associated with mood stabilisation.<sup>3</sup>

Another serendipitous moment in antiepileptic drug discovery occurred when Alfred Hauptmann, a psychiatry resident in the Psychiatry Clinic of the University Medical Center Freiburg in Germany, accidentally discovered the efficacy of phenobarbital as an antiepileptic medication in 1911. The young Hauptmann was responsible for the care of inpatients with epilepsy. He found that it was nearly impossible for him to rest, because of the constant occurrence of seizures in patients in his unit. Hence, he decided to administer low doses of hypnotics to his patients to help them, and in turn, himself, sleep through the night. He was surprised that patients who received phenobarbital had a reduction in the frequency and severity of seizures.<sup>4</sup> Phenobarbital was soon widely accepted as a potent antiepileptic medication.

*Taha Nisar, Harry Sutherland-Foggio, Walter Husar*

- 1 Burton B. On the propyl derivatives and decomposition products of ethylacetoacetate. *Am Chem J* 1882; **3**: 385–95.
- 2 Carraz G, Darbon M, Lebreton S, Beriel H. Propriétés pharmacodynamiques de l'acide n-dipropylacétique et de ses dérivés. *Thérapie* 1964; **19**: 469–75.
- 3 Carraz G. A propos de deux nouveaux antiépileptiques de la série n-dipropylacétique. *Encephale* 1965; **54**: 458.
- 4 Hauptmann A. Luminal bei epilepsie. *Munch Med Wochenschr* 1912; **59**: 1907–09.

## Lifeline

**Simiao Wu** is a neurologist and researcher working in the Department of Neurology at West China Hospital, Sichuan University in Chengdu, China. Her research focuses on the management of stroke. She is currently investigating approaches for outcome prediction and management of patients with severe ischaemic stroke. She is also interested in investigating interventions for the recovery of post-stroke fatigue.

### What has been the greatest achievement of your career?

Publishing in *The Lancet Neurology* and receiving a grant from the Young Scientists Fund of the National Natural Science Foundation of China to support my first independent research on ischaemic stroke.

### What inspires you?

The unanswered questions that I encounter in clinical practice, for example, high mortality of malignant brain oedema after stroke, inspire me to investigate underlying disease mechanisms and possible solutions.

### What do you think is the most neglected field of medicine at the moment?

Current research for patients with stroke is more focused on pathological issues, whereas mental wellbeing and the social needs of patients and their families are sometimes neglected.

### If you had not entered your current profession, what would you have liked to do?

I would have liked to be a lawyer. I enjoy communicating with people, which is something that both doctors and lawyers do.

### Who were your most influential teachers, and why?

Ming Liu (West China Hospital, Sichuan University, Chengdu, China), my MD supervisor, inspired me to begin a career in stroke medicine and guided me to be an academic neurologist. My PhD supervisors Gillian Mead and Malcolm MacLeod (University of Edinburgh, Edinburgh, UK) encouraged and trained me to be an independent researcher. Peter Sandercock (University of Edinburgh, Edinburgh, UK) has constantly supported my career in stroke research.

### What is your idea of a perfect day?

My day starts with meeting the patients in the clinic, doing laboratory research in the afternoon, having dinner with my family, and then reading a book before bed.

### If you wrote an autobiography, what would be the title?

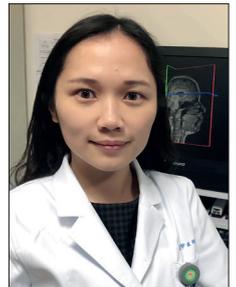
A Traveller and Explorer.

### What was your first experiment as a child?

I poured orange juice into milk, which curdled the milk.

### What is the best piece of advice you have received?

When you face difficult times, do not be angry but keep calm and focus on solving the problem.



See [Series Lancet Neurol](#) 2019; **18**: 394–405