Acute necrotising encephalopathy of childhood presenting with multifocal, symmetric brain lesions occurring outside Japan

I was interested in the article by Mizuguchi et al. on acute necrotising encephalopathy of childhood as a new syndrome presenting with multifocal, symmetric brain lesions. The article admirably describes the pathogenesis of this special childhood encephalopathy. I must point out however, that the authors said that they failed to find any reports of similar cases occurring outside Japan. My instructor and I previously reported a case of infants with acute encephalopathy with a striking ultrasonographic finding—"bright thalami"—suggesting panthalamic infarction. Afterwards, five more cases with similar symptoms were treated. Their clinical and neuroimaging manifestations have been reported at the 7th Congress of the International Child Neurology Association in 1994. In the same report 17 children, including 14 Japanese, were reviewed from the English literature. 1

Of the three not from Japan; two were from the United Kingdom 2 and one was from the United States. 3 At least eight other cases were presented at a local conference without publication in Taiwan.

HUEI-SHYONG WANG
Department of Pediatrics, Chang Gung Medical College, Chang Gung Memorial Hospital, 199 Yen-Hua North Road, Taipei 10591, Taiwan

Mizuguchi replies:
I am grateful to Wang for his comments on our paper. 1 Until the submission of our paper, we had been unaware of the occurrence of acute necrotising encephalopathy of childhood (ANE) outside Japan. Now Wang has made it clear that ANE is as prevalent in Taiwan as it is in Japan. Many Taiwanese patients described by Wang et al. have typical features of ANE. 2 The high prevalence of ANE in the far east implies the involvement of genetic or environmental factors pertinent to that region. Wang also reviewed patients with probable ANE reported from the United States and from England. These patients seem to have a mild form of ANE, judging from their clinical course and laboratory findings.

It is our view that the patients having CSF pleocytosis and other evidence of encephalitides, such as the one reported by Okuno et al., 3 should be excluded from ANE. Many of these patients showed a prolonged course, prominent focal signs, and asymmetric or atypical distribution of brain lesions, features that are incompatible with ANE.

JAPAN


Wu et al reply:
Cavanagh expresses his concern about the case of acute triphenyltin intoxication reported by us. 1 He claims a lack of evidence for the adverse effect of triphenyltin compounds on the nervous system in animal studies and clinical reports. Finally, he concludes that it certainly was not a case of triphenyltin intoxication.

Firstly, the formulation of the pesticide taken by our patient in a suicide attempt was carefully analysed by gas liquid chromatography coupled with a mass detector. According to animal and microwave experiments, this agent was either triphenyltin acetate or triphenyltin hydroxide. The mass spectra of these two compounds are identical in our analysis. Triphenyltin compounds are widely used as fungicidal and molluscicidal agents in Taiwan agriculture. The patient's girlfriend had hidden the crucial history from both doctor and the patient's family for some reason for the first two months after the incident. When the patient did not recover from his coma, his girlfriend finally told us the truth and provided the pesticide to doctors.

According to the comprehensive review of Bock, 2 when a high dose of triphenyltin acetate was fed to rats (250 mg/kg), rabbits (5–20 ppm), and bats (140 mg/kg), they developed muscle weakness, unsteady gait, paraesthesia in the hind limbs, tremor, and convulsion, and eventually died in a few minutes. Although increased water content of the brain and spinal cord was the only abnormal finding on pathological examination, inhibition of adenine triphosphate, protease, and amylase in brain microsomes, was reported in other studies. 3 Uncoupling of oxidative phosphorylation in the mitochondria has also been suggested as a contributor to the cellular mechanism of triphenyltin toxicity.

Although triphenyltin compounds have been regarded as less neurotoxic than alkyltin compounds, neurological manifestations in human cases with triphenyltin intoxication have been reported in some cases. 4, 5 Headache, vomiting, nausea, and impaired vision were noted in cases poisoned by triphenyltin acetate. 6 Moreover, two cases with triphenyltin intoxication had severe headache, dizziness, vertigo, transient loss of consciousness and, paraesthesia in the legs. 7 Thus it is likely that more severe neurological deficits may develop in our case who had taken a possible lethal dose of triphenyltin compound with the intention of committing suicide. He developed abdominal pain, diarrhoea, and vomiting on the first day of poisoning. Headache, blurred vision, unsteady gait, consciousness disturbance, and polymnepathy occurred subsequently. Also, systemic problems with abnormal liver function and leucopenia coincided with the neurological manifestations. These clinical features are consistent with the previous studies on animals and clinical reports.

We are grateful to Cavanagh for giving us the opportunity to reiterate the unusual case with acute triphenyltin intoxication in a suicide attempt.