

arm and leg. An EEG demonstrated continuous widespread theta activity with sharp waves but no focal features. CSF examination and CT scan of his brain were normal, thereby failing to disclose a focal lesion to explain the clinical picture. Chlorambucil was discontinued and function returned to the right arm and leg over the next 7 days. However, these investigators correctly identified the possibility of cerebrovascular disease contributing to their patient's neurologic changes, given his strong history of angina and peripheral vascular disease, suggesting diffuse atherosclerotic disease.

The mechanism of chlorambucil-induced neurotoxicity has not been established. Subcortical structures have been suggested as the primary site of neurologic insult.² Lion et al¹⁰ found ¹⁴C-labeled chlorambucil distributed in subcortical structures in cats. They also suggested that myoclonic seizures were the reaction pattern of an immature CNS.

Albuminum hydroxide¹¹ and chlorambucil administered to children are the only pharmacologic agents that have been previously described to cause myoclonic seizures in humans. There have been no reported cases of chlorambucil-induced myoclonic seizures in adults. In this present case, the onset of myoclonic seizures while being administered chlorambucil, the gradual abatement of the myoclonus after the discontinuation of chlorambucil, the lack of previous seizure or movement disorders, the patient's EEG similarities to chlorambucil-induced EEG changes in children and animals with myoclonus, the absence of any other complicating or alternative diseases causing myoclonus, and the lack of recurrence after the discontinuation of chlorambucil — all provide support that chlorambucil did indeed precipitate this patient's myoclonic seizures. We cannot speculate about the diverse implications this case presents to the suggested mechanisms of chlorambucil neurotoxicity.

We would conclude that myoclonic seizures are rare in patients receiving chlorambucil and that elderly patients should have careful neurological follow-up if chlorambucil is prescribed in doses exceeding the recommended daily maximum of 0.2 mg/kg. Further clinical, EEG, and pharmacologic studies in adults, especially elderly patients, who are prescribed chloram-

bucil are necessary to delineate the mechanism and site of chlorambucil neurotoxicity.

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REFERENCES

1. Cadman E, Drislane F, Waldron JA Jr, et al: High-dose pulse chlorambucil-effective therapy for rapid remission induction in nodular lymphocytic poorly differentiated lymphoma. *Cancer* 50:1037-1041, 1982
2. Pradhan SN, Marsan CA: Chlorambucil toxicity and EEG "centrencephalic" patterns. *Epilepsia* 4:1-14, 1963
3. Wolfson S, Olney MB: Accidental ingestion of a toxic dose of chlorambucil — Report of a case in a child. *JAMA* 165:239-240, 1957
4. Green AA, Naiman JL: Chlorambucil poisoning. *Amer J Dis Child* 116:190-191, 1968
5. Williams SA, Makker SP, Grupe WE: Seizures: A significant side effect of chlorambucil therapy in children. *J Pediatr* 93:516-518, 1978
6. Byrne TN Jr, Moseley TAE III, Finer MA: Myoclonic seizures following chlorambucil overdose. *Ann Neurol* 9:191-194, 1981
7. Ammenti A, Reitter B, Muller-Wiefel DE: Chlorambucil neurotoxicity: Report of two cases. *Helv Paediat Acta* 35: 281-287, 1980
8. Blank DW, Nanji AA, Schreiber DH, et al: Acute renal failure and seizures associated with chlorambucil over-dose. *J Toxicol-Clin Toxicol* 20:361-365, 1983
9. Naysmith A, Robson RH: Focal fits during chlorambucil therapy. *Postgrad Med J* 55:806-807, 1979
10. Lion P, Testa GF, Semerano A: Periodic myoclonic epilepsy in the kitten: an experimental study on the reactivity of the immature brain. *Electroenceph Clin Neurophysiol* 28:213-214, 1970
11. Griswold WR, Reznik V, Mendoza SA, et al: Accumulation of aluminum in a nondialyzed uremic child receiving aluminum hydroxide. *Pediatrics* 71:56-58, 1983

ERRATA

In the article by McDermed et al "Clinical Pharmacokinetics of High-Dose Metoclopramide in Cancer Patients Receiving Cisplatin Therapy" (*Journal of Clinical Oncology* 3:1400-1408, 1985), an error was made in the second column on page 1401 that altered the meaning of an equation. The correct equation appears below.

$$Vd = \frac{\text{dose} \times (1 - e^{-k_{el}t})}{t'k_e [C_p^3 - (C_t^2) (e^{-k_{el}t})]}$$