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Wm. R. Bartle,
Department of Pharmacy,
Sunnybrook Medical Centre,
University of Toronto,
Toronto, Ontario M4N 3M5

Reply From Authors

We thank Dr. Bartle for the comments on our recent article (Albright and Bruni, 1984). We agree that cimetidine can elevate
phenytoin levels through inhibition of hepatic drug metabolizing
enzymes. Cimetidine may also elevate plasma levels of other
antiepileptic drugs such as the benzodiazepines.

The purpose of our article was to review the most frequently
reported and most significant drug interactions of the antiepileptic
drugs, rather than to present all the drug interactions reported.
Additional drugs that may elevate phenytoin levels include
nortriptyline, phenylbutazone, clofibrate, furosemide, imipra-
mine, sulfonamides, propranolol and phenothiazines. Drugs
that may lower phenytoin levels include folate, pyridoxine, and
diazoxide.

Carbamazepine plasma levels may be elevated with the
concomitant use of propoxyphene, erythromycin and triacetylo-
deandomycin (Dravet et al., 1977) and clinical intoxication may
occur.

We agree with Dr. Bartle that when an additional drug is
added to the treatment regimen of a patient on antiepileptic
drugs closer monitoring of plasma levels is required to detect
possible pharmacokinetic drug interactions.

P.S. Albright
J. Bruni

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CHOLECYSTOKININ HYPOTHESIS OF TOURETTE
SYNDROME

To The Editor:
The neuropeptides constitute a large proportion of the
putative neurotransmitters within the brain. Not surprisingly,
peptides are affected in a number of neurological disorders.
The etiology of Tourette Syndrome (TS), a juvenile-onset
neurological disorder characterized by chronic, fluctuating
motor tics and involuntary vocalizations, is unknown, but
may involve neostriatal mechanisms. Most evidence exists
for a defect in dopamine (DA) neurotransmission, possibly a
supersensitivity of DA receptors (Friedhoff, 1982). Treatment
with DA receptor blockers, such as haloperidol, leads to
clinical improvement in many, but not all, TS patients.
These agents have numerous adverse side effects.

The primary defect in TS might be in cholecystokinin-
octapeptide (CCK) mechanisms. This neuropeptide coexists
with DA in mesencephalic neurons projecting to cortical and
limbic forebrain regions. By contrast, striatal CCK appears
to arise in neurons in the caudalstratum and/or piriform cortex
and amygdala (Meyer et al., 1982). Despite this lack of
localization to the same neurons, CCK has a direct effect on
DA receptor function in the striatum. The binding of CCK
to its receptor leads to a direct decrease in DA receptor number
in this brain region (Fuxe et al., 1981). A decreased striatal
CCK transmission could lead to an apparent overactivity of
DA systems through the loss of such DA receptor modulation.
Treatment with a DA receptor blocker would not address
such a deficit directly, possibly explaining the lack of
efficacy of this agent in some patients. CCK and related peptides
appear to have neuroleptic-like activity, both in animal tests
(Van Ree et al., 1983) and in humans with neuroleptic-
resistant schizophrenia (Nair et al., 1983). Therefore, we
believe that pharmacotherapies designed to increase striatal
CCK transmission would lead to more effective treatments
for patients with Tourette Syndrome.

Henrik K. Kulmala,
Department of Medical & Surgical Neurology,
Texas Tech University Health Sciences Center,
Lubbock, Texas 79430

Sakkubai Naidu,
John F. Kennedy Institute
Baltimore

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ERRATUM

In the paper “Spinal Epidural Lipomatosis” published in the
August 1984 issue (1984; 11:383-386), the name of one author
was inadvertently omitted and wrong initials were used for
another. The list of authors for this article should read N.A.
Russell, G. Belanger, B.G. Benoit, D.N. Preston, J.E. Latter,
D.L. Finestone and G.W. Armstrong.