MASSIVE CARBAMAZEPINE POISONING

The clinical features in 28 consecutive adult cases of laboratory confirmed massive overdosage with CBZ alone treated in an intensive care unit during the period 1981-1991 are reported from Southern Hospital, Karolinska Institute, Stockholm, Sweden. Serum levels at or above 40 mg/L were significantly associated with an increased risk of serious complications including coma, seizures, respiratory failure and cardiac conduction defects. Two patients died. In 61% CBZ had been used therapeutically for the treatment of epilepsy. Five patients with repeated generalized seizures despite CBZ concentrations above 40 mg/L were controlled with diazepam or clonazepam intravenously. Ataxia, vertigo, nystagmus, diplopia, dysarthria, and/or dyskinesia were recorded in 11 cases (39%). Multiple dose activated charcoal was administered routinely. (Hojer J et al. Clinical features in 28 consecutive cases of laboratory confirmed massive poisoning with carbamazepine alone. <u>Clin Toxicol</u> Sept 1993;<u>31</u>:449-458). (Reprints: Dr Jonas Hojer, Medical Intensive Care Unit, Sodersjukhuset (Southern Hospital), S-118 83, Stockholm, Sweden).

COMMENT. An increased risk of seizures was a sign of CBZ overdose in this study, but in at least six previous reports, one involving 26 well documented cases in children, carbamazepine induced exacerbation of seizures at therapeutic dose levels. (see <u>Ped Neur Briefs</u> June 1987; <u>Progress in Pediatric Neurology</u>, 1991, pp 108-9). The epileptic syndromes worsened by CBZ included childhood absence, Lennox-Gastaut, myoclonic epilepsy, focal frontal lobe, and generalized tonicclonic epilepsy. A slow withdrawal of the CBZ results in improved seizure control.

PHENOBARBITAL IN NEONATAL SEIZURES

Phenobarbital plasma levels 24 hrs after a loading dose, and drug level variations after intravenous maintenance doses, were studied in 25 newborns with seizures admitted to a neonatal intensive care unit at the Maternity-School Hospital of Vila Nova Cachoeirinha, Sao Paulo, Brazil. With a mean loading dose of 19 mg/kg for both term and pre-term infants and a mean maintenance dose of 4 mg/kg/day, a mean plasma level of 23 mcg/ml was obtained at 24 hrs, and therapeutic levels between 15 - 40 mcg/ml were sustained at 4, 7, 14 and 21 days. A tendency towards drug accumulation in the first week and lower levels after 7 days requires frequent monitoring and dose adjustments. Seizure control without EEG confirmation was obtained in 64%. Phenytoin iv was required in addition in 7 infants and clonazepam in 5. Side effects were limited to infants with severe neurological impairment. (Gherpelli JLD et al. Phenobarbital in newborns with neonatal seizures. A budy of plasma levels after intravenous administration. Brain & Development July/Aug 1993;15:258-262). (Respond: Dr JLD Gherpelli, Sevico de Neurologia Infantil,

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COMMENT. For newborns and infants < 3 months who require *phenytoin*, the recommended loading dose is 12-20 mg/kg and the maintenance dose is 2-4 mg/kg/d, with 8-12 hr dosing intervals (Leppik IE. <u>Epilepsia</u> 1992;<u>33</u>, <u>Suppl 4</u>:S32). Phenytoin levels may be modified by phenobarbital because of an increased metabolism during chronic therapy. Phenytoin elimination half-life varies with age: preterm neonate 75 hr; neonate 21 hr; infant and child 7 h; and adult 24 h.

VASCULAR DISORDERS

CEREBROVASCULAR ABNORMALITIES AND CELIAC DISEASE

Cortical vascular abnormalities including pial angiomatosis and fibrosis of small veins are described in a 12 year old girl with celiac disease, occipital calcifications, and folate deficiency who underwent surgery for intractable complex partial seizures at the Montreal Neurological Institute, Canada. She was first diagnosed with Sturge-Weber syndrome without nevus flammeus. A right occipital resection was performed and was followed by seizure remission. Subsequently, low folic acid levels and iron deficiency anemia led to a diagnosis of celiac disease. Antigliadin antibodies were 182 arbitrary units (normal: < 25), and small bowel biopsy showed villous atrophy. A gluten-free diet with folate, vitamin E, and iron supplementation resulted in improved appetite and weight increase. (Bye AME et al. Cortical vascular abnormalities in the syndrome of celiac disease, epilepsy, bilateral occipital calcifications, and folate deficiency. <u>Ann Neurol</u> Sept 1993;<u>34</u>:399-403). (Respond: Dr Anderman, Montreal Neurological Hospital, 3801 University St, Montreal, Quebec, Canada H3A 284).

COMMENT. The pathological abnormalities in this case were considered similar but not identical to those in Sturge-Weber syndrome. A syndrome of celiac disease, epilepsy, and cerebral calcifications, resembling Sturge-Weber syndrome, has been reported frequently, especially in Italy (Gobbi G et al. <u>Lancet 1992;340:439;</u> Tiacci C et al. <u>Epilepsia 1993;34:528;</u> Piattella L et al. <u>Child's Nerv Syst 1993;9</u>:172.).

Patients with occipital cerebral calcification of unknown cause and patients with celiac disease should receive an EEG, followed by an MRI if the EEG is abnormal. A new, rapid, noninvasive screening test for celiac disease, a strip-AGA (antigliadin antibody) test, performed on a drop of whole blood, is described from the Instituto per l'Infancia, Trieste, Italy (Not T et al. <u>PPediat</u> Sept 1993;<u>123</u>:425-7).