

Correspondence

MONITORING CHILDREN TREATED WITH CARBAMAZEPINE

The question of monitoring patients taking anticonvulsants has been reviewed previously.^{1,2} During carbamazepine monotherapy, complete blood counts (CBC) and alanine transaminase (ALT) were measured at intervals in 23 children attending a Pediatric Neurology clinic during 1990 and 1991. The results were reviewed retrospectively. The mean age was 10.3 years (SD 3.7 yrs). Prior to starting carbamazepine CBC and ALT were measured in 19 and 14 respectively. In two, high white cell counts (WCC) on the day of a seizure, were excluded from the figures. Maintenance doses were mean 13.09 mg/kg/day (SD 4.68). The patients were followed for a mean 15.6 months (SD 6.7). The results were divided into those obtained during the first 8 weeks of treatment (22 samples) and those after 8 weeks (62 samples). Drug levels showed compliance in all except for two late in their course of treatment.

Two patients had drug reactions. A 14.5-year-old girl developed petechiae with thrombocytopenia (platelet count $28 \times 10^9/l$) at 13 days. A 12-year-old girl developed a hypersensitivity reaction at four weeks. Three developed leukopenia. A 15-year-old boy had leukopenia ($WCC < 4 \times 10^9/l$) from 4 weeks to 8 months. He had a transient neutropenia ($1.3 \times 10^9/l$) at 8 weeks. He was asymptomatic, his dose was not changed and the leukopenia resolved. Another 15-year-old boy had a transient neutropenia ($1.4 \times 10^9/l$) at 2 weeks. He also had transient leukopenia on two occasions at 2 weeks and 10 months. A 15-year-old girl had a transient leukopenia at 9 weeks. Two patients had transient elevations of ALT, 109 and 94 μ/l (normal 4-30 μ/l) which on repeat were normal. No symptoms of infection were reported. Another had elevation in ALT (59-65 μ/l) over a period of a month associated with a chest infection. Paired t-tests were performed on all CBCs comparing before and during the first 8 weeks treatment (12 patients), and before and after 8 weeks treatment (16 patients). There was no significant decrease ($P < 0.05$) in WCC, lymphocytes, granulocytes nor hemoglobin (Hb). Platelet counts did show a significant decrease ($P < 0.05$) both during first 8 weeks and after 8 weeks. No platelet count fell below the normal range.

The incidence of hematological abnormalities with carbamazepine has been reviewed.^{3,4} The reported incidence of aplastic anaemia is 5.1/million, agranulocytosis 1.4/million and leukopenia 10%.⁴ It is not clear whether sequential monitoring can identify patients at risk for the rare serious reactions. Guidelines from the ad hoc committee for the Canadian Association for Child Neurology, regarding blood monitoring during anticonvulsant therapy, suggest performing base line CBC and liver function tests, warning patients of reactions and testing only if symptomatic.¹ A reply to these guidelines suggested testing young patients treated with valproic acid. Another author also recommended base line blood work and no further monitoring except in high risk groups.² In the present 23 children two clinical reactions occurred prior to routine monitoring and abnormal results did bring 5 back for further testing. Laboratory results did not alter treatment in any. Therefore in this small group of patients

treated with carbamazepine and guidelines above (1) would have been appropriate.

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2. Pellock JM, Willmore LJ. A rational guide to routine blood monitoring in patients receiving antiepileptic drugs. *Neurology* 1991; 41: 961-964.
3. Hart RG, Easton JD. Carbamazepine and Hematological Monitoring. *Ann Neurol* 1982; 11: 309-312.
4. Pellock JM. Carbamazepine Side Effects in Children and Adults. *Epilepsia* 1987; 28 (Suppl 3): S64-S70.

RE: CURRENT STATUS OF RADIOSURGERY FOR ARTERIOVENOUS MALFORMATIONS

To the Editor:

We were interested in the scientific and economic ramifications of the "review article" by Schwartz and colleagues entitled, "Current status of radiosurgery for arteriovenous malformations", published in the Canadian Journal of Neurological Sciences 1991; 18: 499-502. This "review article", by a group that had treated only 18 AVM's at the time of publication of that report, seems somewhat premature especially since many strong conclusions are reached. There are many statements and conclusions stated in this paper that we would like to address.

First, the authors state that two competing technologies exist for the delivery of focused photon irradiation. We would like to emphasize that although a competition might exist between the manufacturers of various devices, there should exist no scientific competition. The International Stereotactic Radiosurgery Society was formed to amalgamate the experiences of neurosurgeons, radiation oncologists, and medical physicists using various techniques of focused irradiation and to share and combine results. As a result one should not feel threatened by other technologies.

Second, Schwartz et al. described at length the concept of radiosurgical accuracy using their modified linear accelerator system. They state that the treatment error vector for angiographically selected targets has a value of 0.3 mm and that CT scanning is even less accurate than angiography. The gamma unit with a fixed radiation delivery system has a radiation delivery accuracy less than 0.3 mm, and accuracy is significantly dependent upon the neurosurgeons skill at interpreting the stereotactic images as well as target selection. A recent paper by Woo et al. from their linear accelerator center¹ now reports a clinically observable discrepancy of 4 mm between the mechanical and radiation isocenters using their system. They have identified the cause of this discrepancy to be the gantry head sag of their linear accelerator and have made recommendations for their device to help correct this. It seems that the physical problems associated with some linear accelerator systems are still being worked out, and that institutional quality assurance must be paramount.

Third, they state that the cost of the gamma unit is at least \$5 million to purchase and install. This figure is incorrect. They state that the cost of modifying a linear accelerator to deliver a focused radiation dose is between \$50,000 and \$100,000. That may be the cost that their group paid, but certainly most of the linear accelerator systems elsewhere in the world have cost much more than that, especially since many have developed their own treatment planning systems. They also state that operating costs are embedded in the cost of running the radiotherapy unit – in a provincial health care system, the government still pays the costs regardless of which departmental budget it may fall under. In fact in a ten year cost-estimate analysis developed by Epstein et al., Brown University, the cost of the Gamma Knife is *less* than that of a linear accelerator provided that the same number of patients are treated, when mechanical and personnel costs are considered (personal communication).

Fourth, they state some of the linear accelerator results for the treatment of AVM's and compare these to published results using the gamma unit. Their system is based on the linear accelerator system initially developed in Montreal, and the results for treatment of AVM's at that center have now been reported in the Canadian Journal of Neurological Sciences.² In the treatment of 36 patients, 27 had two year angiographic follow-up and only 11 (41%) were completely obliterated. This seems lower than the results reported at our institution^{3,4,5} as well as by some other linear accelerator centers.

Finally, their statement that "it is certain that there will be very few gamma units because of their high cost and limited application" cannot be further from the truth. There are more than 10 gamma units now in the United States, and more than 30 across the world. The comment "there will not likely be sufficient cases to sustain even a few gamma units in North America" does not appear to be true because all centers seem to be quite busy. The average site treats 160 patients per year; more than 5,000 to date worldwide and more than 2,000 in 1991 alone (approximately 900 patients at the University of Pittsburgh since August 1987.) Their final comment that "any hospital or health system that is contemplating the acquisition of a gamma knife can expect to have a facility that is over-priced and underutilized" would be challenged by many of the socialized health care systems of European countries that have purchased gamma units (including Norway, Italy, Spain, France, Austria, Czechoslovakia and England). Many of the productive linear accelerator radiosurgery groups that we know and converse with, do not appear to be threatened by gamma unit radiosurgery, but rather seem to benefit from the scientific information we all share. We believe that in a peer review journal of such stature as The Canadian Journal of Neurological Sciences, in which we ourselves have published, that a "review" article should review, not editorialize with unsubstantiated comments.

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REPLY

To the Editor:

We are responding to the Letter to the Editor written by Drs. Douglas Kondziolka and Dade Lunsford of the University of Pittsburgh, in response to our article entitled, "Current status of radiosurgery for arteriovenous malformations", published in the Canadian Journal of Neurological Sciences, 18: 499-502, 1991.

First, we wish to reassure Drs. Kondziolka and Lunsford that we do not feel threatened by Gamma Knife technology.

We are concerned, however, that Drs. Kondziolka and Lunsford may have left readers with the mistaken impression that we deliver radiosurgical treatments using a linac based system on which a 4 mm discrepancy between the mechanical and radiation isocentres has been demonstrated. No patients have been treated on that unit. Woo¹ has provided a salutary warning against the indiscriminate use of linear accelerators which have not been adequately commissioned for the purpose of radiosurgery. The specifications of the linear accelerator system presently delivering radiosurgery at the Toronto-Bayview Regional Cancer Centre have been published elsewhere² and in our view, they match the capabilities of the Gamma Knife.

As far as costing is concerned, we would be pleased to learn Drs. Kondziolka and Lunsford's estimates for the purchase and installation of a Gamma Knife. We believe the cost advantage for a linear accelerator system will only be realized through the modification of existing equipment as discussed in our article rather than with the acquisition of a unit dedicated to radiosurgery.

Our group has always been pleased to share information through the medical and scientific literature. The benefit derived will in part depend on the care with which it is read.

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- Woo MK, O'Brien P, Gillies B, et al. Mechanical and radiation isocenter coincidence: An experience in linear accelerator alignment. *Med Phys* 1992; 19: 357-359.
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