The Canadian Le Journal Journal of Canadien des Neurological Sciences Sciences Neurologiques



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XXVIIIth Canadian Congress of Neurological Sciences June 16-19, 1993 Toronto, Ontario

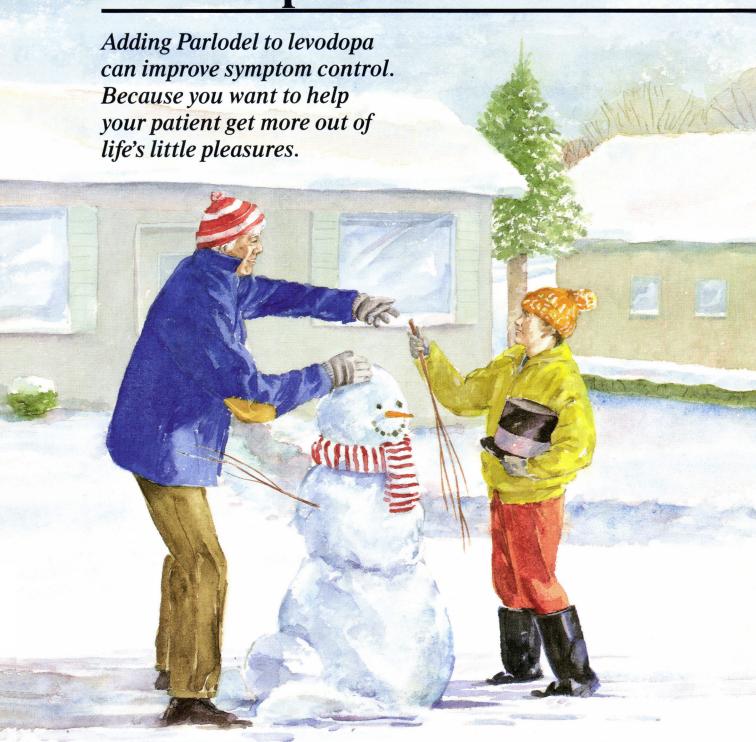
The Official Journal of

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The Canadian Association for Child Neurology

Volume 19, No. 4

November 1992

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Le Journal Canadien des Sciences Neurologiques

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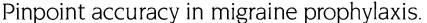
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Journals

Yang JF, Fung M, Edamura R, et al. H-Reflex modulation during walking in spastic paretic subjects. Can J Neurol Sci 1991; 18: 443-452.

Chapter in a book

McGeer PL, McGeer EG, Amino acid neurotransmitters. *In*: Siegel GJ, Albers RW, Agranoff BW, Katzman R, eds. Basic Neurochemistry. Boston: Little, Brown & Co., 1981: 233-254.

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Rx Summary

Antiparkinson Agent

Indications and clinical use:

As an adjunct to levodopa (with or without a decarboxylase inhibitor) in the management of the signs and symptoms of Parkinson's disease

In newly diagnosed patients before symptoms begin to affect the patient's social or professional life, at which time more efficacious treatment becomes necessary.

Contraindications:

In patients with known hypersensitivity to Eldepryl, Eldepryl should not be used in patients with active peptic ulcer, extrapyramidal disorders such as excessive tremor or tardive dyskinesia, or patients with severe psychosis or profound dementia. Eldepryl should not be used with meperidine (Demerol or other trade names). This contraindication is often extended to other opioids.

Warnings (Selective vs non-selective inhibition of MAO-B):

Eldepryl should not be used at daily doses exceeding those recommended (10 mg/day) because of the risks associated with non-selective inhibition of MAO. It is prudent, in general, to avoid the concommitant use of Eldepryl and fluoxetine (Prozac)

Warnings to patients:

Patients should be advised of the possible need to reduce levodopa dosage after the initiation of Eldepryl therapy. The patients should be advised not to exceed the daily dose of 10 mg. The risk of using higher doses of Eldepryl should be explained, and a brief description of the "hypertensive crisis" ("cheese reaction") provided.

Precautions:

Some patients given Eldepryl may experience an exacerbation of levodopa associated side effects, presumably due to the increased amounts of dopamine reacting with supersensitive post-synaptic receptors. These effects may often be mitigated by reducing the dose of levodopa by 10-30%

NURSING MOTHERS: It is not known whether Eldeptyl is excreted in human milk. Because many drugs are excreted in human milk, consideration should be given to discontinuing the use of all but absolutely essential drug treatments in nursing women.

PEDIATRIC USE: The effects of Eldepryl in children under 18 have

Laboratory Tests:

No specific laboratory tests are esential for management of patients on Eldepryl. Transient or continuing abnormalities with tendency for elevated values in liver function tests have been described in long term therapy. Although serious hepatic toxicity has not been observed, caution is recommended in patients with a history of hepatic dysfunction. Periodic routine evaluation of all patients is however appropriate.

Drug Interactions:

The occurence of stupor, muscular rigidity, severe agitation and elevated temperature has been reported in a man receiving selegiline and meperidine, as well as other medications. These symptoms were resolved over days when the combination was discontinued. This case is typical of the interaction of meperidine and MAOIs Other than the possible exacerbation of side effects in patients receiving levodopa therapy, no interactions attributed to the combined use of ELDEPRYL and other drugs have been reported. It is also prudent to avoid the combination of ELDEPRYL and fluoxetine

Use during Pregnancy:
The use of Eldepryl during pregnancy has not been established.
Therefore, Eldepryl should be given to a pregnant woman only if the potential benefits outweigh the potential risks.

Adverse reactions:

A) IN COMBINATION WITH LEVODOPA
THE SIDE EFFECTS OF ELDEPRYL ARE USUALLY THOSE ASSOCIATED WITH DOPAMINERGIC EXCESS. ELDEPRYL MAY POTENTIATE THE SIDE EFFECTS OF LEVODOPA, THEREFORE ADJUSTMENT OF THE DOSAGE OF LEVODOPA MAY BE REQUIRED. ONE OF THE MOST SERIOUS ADVERSE REACTIONS REPORTED WITH ELDEPRYL USED AS AN ADJUNCT TO LEVODOPA THERAPY ARE HALLUCINATIONS/CONFUSION, PARTICULARLY VISUAL HALLUCINATIONS

Other reactions include nausea, dizziness, faintness, abdominal pain, dry mouth, vivid dreams, dyskinesias and headache.

B) IN MONOTHERAPY

The incidence of adverse reactions occurring in trials using Eldepryl as monotherapy has not been fully reported to date. Serious adverse reactions include depression, chest pain, myopathy and diarrhea. Other reported adverse reactions include insomnia, headache, nausea, dizziness and vertigo.

In prospective clinical trials, the following adverse effects (listed in decreasing order of frequency), led to the discontinuation of Eldepryl: Nausea, hallucinations, confusion, depression, loss of balance, insomnia, orthostatic hypotension, increased akinetyic involuntary movements, agitation, arrhythmia, bradykinesia chorea, delusions, hypertension, new or increased angina pectoris and syncope. Events reported only rarely as a cause of discontinuation of treatment include anxiety, drowsiness/lethargy, nervousness, dystonia, increased episodes of freezing, increased tremor, weakness, excessive persperation, constipation, weight loss, burning lips/mouth, ankle edema, gastroitestinal bleeding and hair loss.

The recommended dosage of Eldepryl as monotherapy in newly diagnosed patients, or as adjunct to levodopa (usually with a decarboxylase inhibitor) is 10 mg per day administered as divided doses of 5 mg each taken at breakfast and lunch. When ELDEPRYL adjunctive therapy is added to the existing levodopa therapeutic regime, a reduction, usually of 10 to 30% in the dose of levodopa (in some instances a reduction in the dose of Eldepryl to 5 mg/day) may be required during the period of adjustment of therapy or in case of exacerbation of adverse effects. Doses higher than 10 mg per day should not be used. There is no evidence that additional benefit will be obtained from the administation of higher doses. Furthermore, higher doses will result in a loss of selectivity of Eldepryl towards MAO-B with an increase in the inhibition of type

There is an increased risk of adverse reactions with higher doses as well as an increased risk of hypertensive episode ("cheese reaction")

Supplied:

Eldepryl 5 mg tablets, available in bottles of 60 tablets.

References:

1. The Parkinson Study Group. Effect of Deprenyl on the Progression of Disability in Early Parkinson's Disease. New Eng Journ 321, 1364-1371, November 1989. 2. Eldepryl (selegiline hydrochloride) Product Monograph, December 1990. 3. Myllyla VV, Sotaniemi KA, Vuorinen JA, Heinonen EH. Selegiline as initial treatment in de novo parkinsonian patients. Neurology 1992; 42, 339-343. 4. Tetrud JW, Langston JW. The Effect of Deprenyl (Selegiline) on the Natural History of Parkinson's Disease. Science, August 1989, vol. 245, 519-522. 5. Myllyla VV, Sotaniemi KA, Vuorinen J. Heinonen EH. Selegiline (deprenyl) as primary treatment in Parkinson's disease. Selegiline therapy in early Parkinson's disease. July 1990, 19-24. 6. Langston JW in Lees A. Deprenyl in Parkinson's Disease: Guidelines for Clinicians. North American Round Table Series, No. 1, 1988, 1-26. 7. DuVoisin RC in Lees A. Deprenyl in Parkinson's Disease: Guidelines for Clinicians. North American Round Table Series, No. 1, 1988, 1-26.

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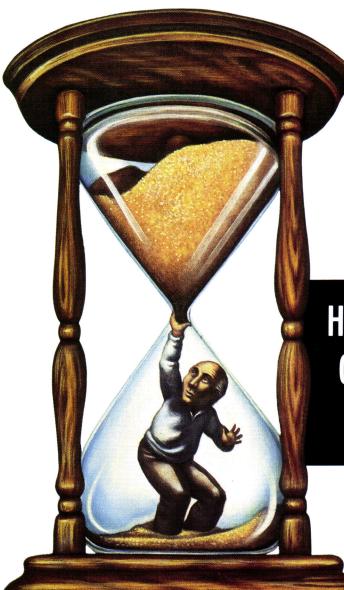
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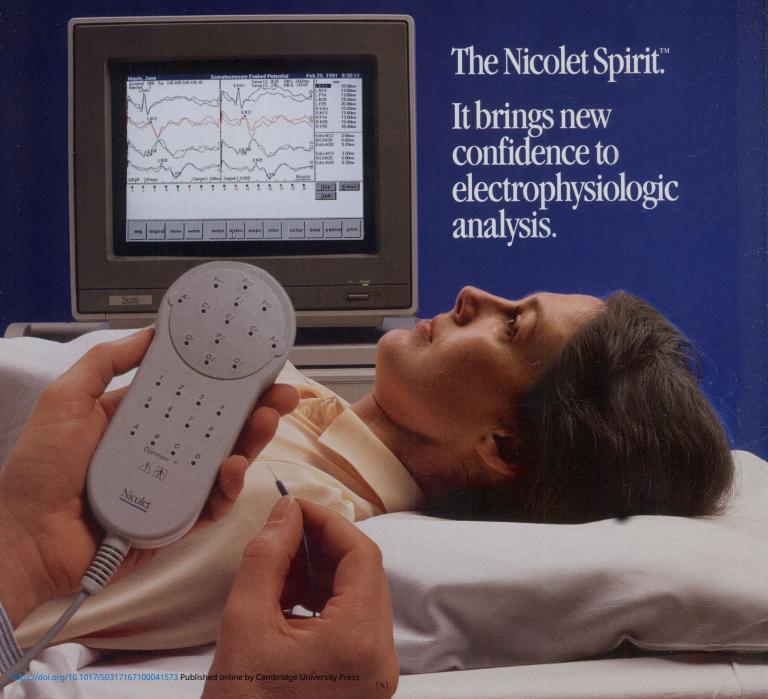
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For brief prescribing information see page xxiv

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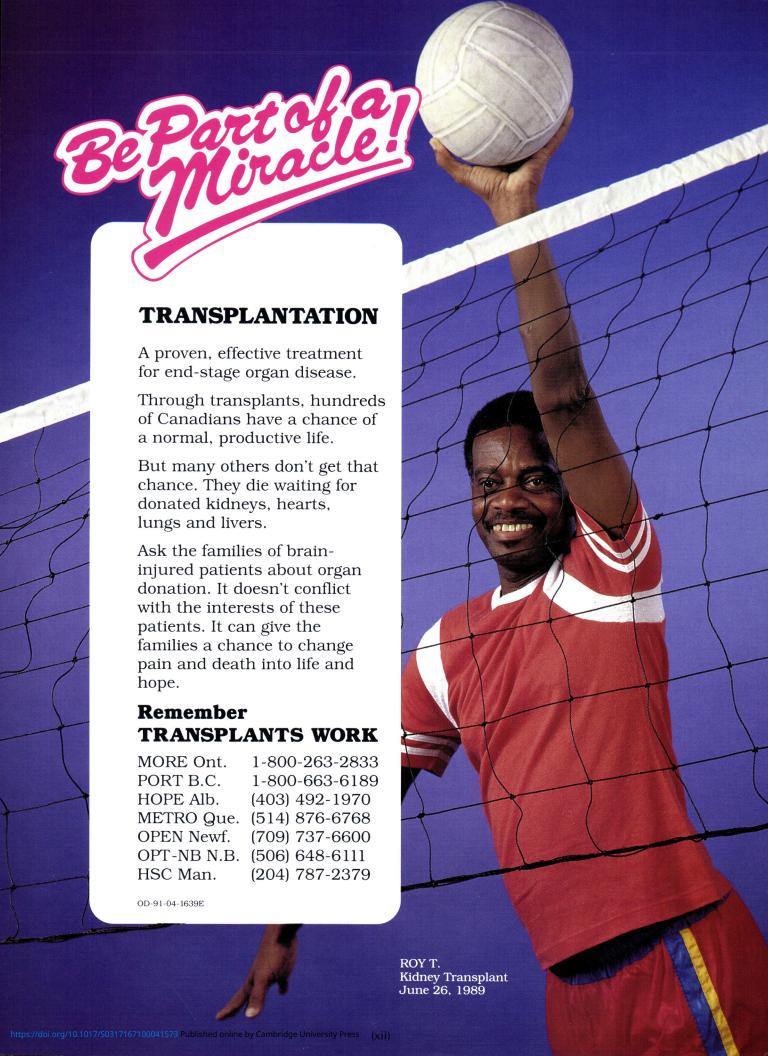
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(xiii)

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For years, valproate has been regarded as an excellent choice for the control of absence seizures. 1.2

In addition to its proven efficacy in simple and complex absence seizures, ^{2,3} valproate has been shown to be as effective as previous standards in controlling primary generalized seizures with tonic-clonic manifestations.⁴ Epival* tablets have a special enteric-coating designed to reduce GI upset⁵ and are bioequivalent to Depakene*.⁶

Compared to most antiepileptics, Epival has been shown to have minimal effects on behaviour and cognition⁷ and relatively less interactions with commonly-prescribed medications.^{8,9}

Today's consensus favours monotherapy wherever possible. And no other single agent can provide this spectrum of efficacy in the management of primary generalized seizures.





HELPING TO MEET TODAY'S THERAPEUTIC GOALS

