#### Volume 31 Number 3 August 2004



#### THE CANADIAN JOURNAL OF **Neurological Sciences** LE JOURNAL CANADIEN DES Sciences Neurologiques



Joseph Babinski (1857 - 1932)



Neurenteric cyst

#### **EDITORIALS** 291 Headaches in Childhood

- Joseph Dooley
- 293 Therapeutic Brain Stimulation Both Excitation and Inhibition Required Zelma HT Kiss

#### **REVIEW ARTICLES**

295 Progress in Clinical Neurosciences: Pharmacotherapies for the Secondary Prevention of Stroke

CMP Daniel G. Hackam and Moira K. Kapral

304 Revised 2004 International Classification of Headache Disorders: New Headache Types Jonathan P. Gladstone, David W. Dodick

#### **ORIGINAL ARTICLE**

- 315 Mixed Migraine and Tension-type: A Common Cause of Recurrent Headache in Children Shashi S. Seshia
- 319 Chronic Daily Headache in Children and Adolescents
- CALL Shashi S. Seshia
- 324 Prevalence of Reported Migraine Headaches in Canadian Adolescents K.E. Gordon, J.M. Dooley, E.P. Wood
- 328 Pallidal Deep Brain Stimulation in Cervical Dystonia: Clinical Outcome in Four Cases H.A. Eltahawy, J. Saint-Cyr, Y.Y. Poon, E. Moro, A.E. Lang, A.M. Lozano
- 333 Thalamic Deep Brain Stimulation for Essential Tremor: Recommendations for Long-Term Outcome Analysis
- I.D. Putzke, R.E. Wharen, Jr., A.A. Obwegeser, Z.K. Wszolek, J.A. Lucas, M.F. Turk, R.J. Uitti
- 343 Electrocardiogram Artifacts Caused by Deep Brain Stimulation Constantine Constantoyannis, Brett Heilbron, Christopher R. Honey
- 347 Comparison of Monitoring Techniques for Intraoperative Cerebral Ischemia David W. Rowed, David A. Houlden, Lee M. Burkholder, Amanda B. Taylor

#### 357-397 See Contents Pages

#### **30TH ANNIVERSARY HISTORICAL ARTICLE**

398 The Anatomical Substratum of Pain: Evidence Derived from Morphometric Studies on Peripheral Nerve P.K. Thomas

#### NEUROIMAGING HIGHLIGHT

404 Submitted by: Nabil Hussain, Ashok Srinivasan, Scott Paquette, Charles Agbi, Cheemun Lum

**CASE REPORTS** See Contents Pages

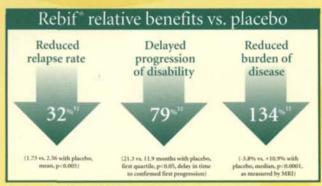
#### HISTORICAL NEUROSCIENCE

422 Charcot et Babinski: au-delà de la simple relation professeur-élève Rami Massie

#### SUPPLEMENT 2

11th Biennial Canadian Neuro-Oncology Meeting. May 28-30, 2004 Abstracts S1

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\* Randomized, double-blind, placebo-controlled trial. Rebif 44 mcg TIW group (n=184), Rebif 22 mcg TIW group (n=189), placebo group (n=187).<sup>3</sup>

 $\Delta$  Fictitious case may not be representative of results for the general population.





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Results of the 44 mcg TIW dose at 2 years.



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- 343 Electrocardiogram Artifacts Caused by Deep Brain Stimulation

Constantine Constantoyannis, Brett Heilbron, Christopher R. Honey 347 Comparison of Monitoring Techniques for Intraoperative Cerebral Ischemia

David W. Rowed, David A. Houlden, Lee M. Burkholder, Amanda B. Taylor

- 357 Electrophysiological Evaluation of Peripheral and Autonomic Involvement in Leprosy Aysun Soysal, Turan Atay, Tacettin Ozu, Baki Arpaci
- 363 TAU Mutations are not a Predominant Cause of Frontotemporal Dementia in Canadian Patients Anastasia Levchenko, Yves Robitaille, Michael J. Strong, Guy A. Rouleau
- 368 Structural Abnormalities are Similar in Familial and Nonfamilial Mesial Temporal Lobe Epilepsy Fabio Thadeu Ferreira, Eliane Kobayashi, Íscia Lopes-Cendes, Fernando Cendes
- 373 Collision Frequency in Elite Hockey on North American versus International Size Rinks Richard Wennberg
- 378 Neurologic Course, Endocrine Dysfunction and Triplet Repeat Size in Spinal Bulbar Muscular Atrophy Michael Sinnreich, Eric J. Sorenson, Christopher J. Klein
- 383 Malaysian Siblings with Friedreich Ataxia and Chorea: A Novel Deletion in the Frataxin Gene

Siân D. Spacey, Blazej I. Szczygielski, Sean P. Young, Juliette Hukin, Kathy Selby, Terrance P. Snutch

- 387 Trends in Hospital Admission for Stroke in Calgary T.S. Field, T.L. Green, K. Roy, J. Pedersen, M.D. Hill
- **394** Exacerbation of Pre-existing Epilepsy by Mild Head Injury: a Five Patient Series *P.C. Tai, D.W. Gross*





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Sciences Neurologiques

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#### NEUROIMAGING HIGHLIGHT

404 Submitted by: Nabil Hussain, Ashok Srinivasan, Scott Paquette, Charles Agbi, Cheemun Lum

#### CASE REPORTS

- 406 Lymphocytic Hypophysitis with a Long Latent Period Before Development of a Pituitary Mass Rene W.G. Wong, Teik Chye Ooi, Brien Benoit, David Zackon, Gerard Jansen, Adam Telner
- 409 Modafinil in Endozepine Stupor. A Case Report Sharon Scott, Iftekhar Ahmed
- 412 Intraparenchymal Supratentorial Neurenteric Cyst Edward Kachur, Lee-Cyn Ang, Joseph F. Megyesi
- 417 Magnetic Resonance Diffusion Weighted Imaging in CME Cerebral Fat Embolism

G.B. Marshall, V.R. Heale, L. Herx, A. Abdeen, L. Mrkonjic, J. Powell, R.J. Sevick, W. Morrish

#### HISTORICAL NEUROSCIENCE

- 422 Charcot et Babinski: au-delà de la simple relation professeur-élève *Rami Massie*
- 427 Letters to the Editor
- 430 Books Received
- 430 Book Reviews
- 433 Calendar of Events
- 434 Notes and Announcements
- 434 Erratum
- A-10 Information for Authors
- A-15 Preliminary Program 40th Canadian Congress of Neurological Sciences – Ottawa, ON
- A-56 Advertisers Index

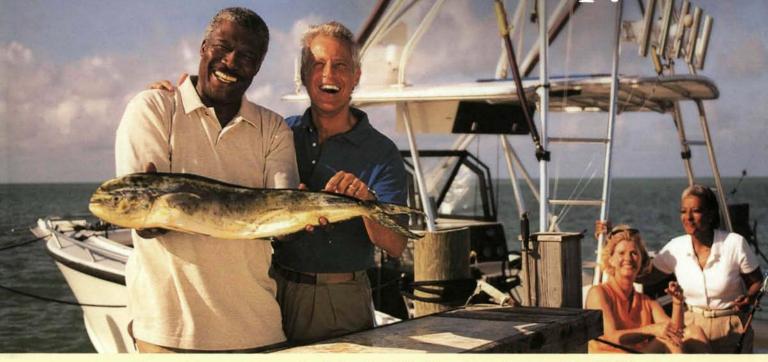
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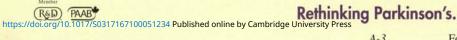
References: 1. Korczyn AD et al. Dosing with ropinirole in a clinical setting. Acta Neurologica Scandinavica 2002;106:200-204. 2. Rascol O et al. A five-year study of the incidence of dyskinesia in patients with early Parkinson's disease who were treated with ropinirole or levodopa. N Eng J Med 2000;342(20):1484-1491. 3. Product Monograph of REQUIP® (ropinirole hydrochloride), GlaxoSmithKline, March 2004

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A-3





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References:

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   Maelicke A, Albuquerque EX. Eur J Pharmacol 2000;393:165-170.
- tt Exception drug status

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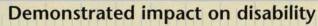


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A-7



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‡ Open label trial for children (n = 72) treated for ≥ 3 months. Average dose of 10 mg/kg/day.
§ CMS adverse events: Somolence (30,1%), distriness (28,3%), ataxis (21,2%), speech disorders (16.8%), nystagmus (15.0%), paresthesia (15.0%), nervousness (15.9%), difficulty with concentration/attention (8.0%), confusion (9.7%), depression (3.0%), anarota (5.3%), language problems (5.5%) and most oproblems (3.5%) and most oproblems (3.5%) and most oproblems (3.5%). In an audit of 1446 adults and 303 children, there appeared to be a similar pattern of adverse events.
\*\* The long-term effects of weight loss in pediatric patients are not known.

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REFERENCES: 1. TOPAMAX\* topiramate Tablets and Sprinkle Capsules Product Monograph, May 11, 1999. 2. Kamin M, Kraut L, Olson W. Dose optimization of topiramate as add-on therapy in adults with treatment-resistant partial-onset seizures Neurology 1999;52 (Suppl 2):A525-526. 3. Glauser TA, Elterman R, Wyllie E et al. Open label topiramate in paediatric partial epilepsy Epilepsia 1997:38 (Suppl 3):94. 4. Rosenfeld WE et al. Topiramate and concomitant weight loss. Epilepsia 1997:38 (Suppl 3):94.

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among the references. Reference citations should not include unpublished presentations or other non-accessible material. Books or chapter references should also include the place of publication and the name of the publisher. Examples of correct forms of reference follow:

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.

• *Illustrations* Submit five original sets of illustrations. We will not return illustrations; therefore, authors should keep negatives for all photographs. Submit high quality glossy black and white photographs preferably 127 x 173 mm (5" x 7"). This includes graphs and diagrams. Do NOT send photocopies of illustrations. Original artwork and radiographs should not be submitted. The additional cost of coloured illustrations must be borne by the author; quotations are available upon request from the Journal office. Identify each figure with a label at the back indicating top, figure number and first author. Letters and arrows applied to the figures to identify particular findings should be professional appliques suitable for publication. Photomicrographs should include a calibration bar with a scale indicated on the figure or in the legend. Legends for illustrations should be typed on a separate page from the illustrations.

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• *Review articles* on selected topics are also published. They are usually invited, but unsolicited reviews will be considered. It is recommended that authors intending to submit review articles contact the Editor in advance.

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is required, patients may be started 10 ma ++ When a >45% LDL-C reduction start at 10 mg. 20 mg. 4 at 40 mg o.d.

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25-56% 2

> 39-60% LDL-C

TC/HDL-C 29-44

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beyond

# LIPITOR has a leading edge clinical research program exploring new areas that may extend beyond lipid control<sup>4</sup>

LIPITOR is an HMG-CoA reductase inhibitor (statin). LIPITOR is indicated as an adjunct to lifestyle changes, including diet, for the reduction of elevated total cholesterol, LDL-C, TG and apolipoprotein B in hyperlipidemic and dyslipidemic conditions (including primary hypercholesterolemia, combined [mixed] hyperlipidemia, dysbetalipoproteinemia, hyper-triglyceridemia and familial hypercholesterolemia) when response to diet and other non-pharmacological measures alone has been inadequate.

LPTOR also raises HDL-cholesterol and therefore lowers the LDL-C/HDL-C and Total-C/HDL-C ratios (Fredrickson Type lla and llb)

Less than 2% of patients discontinued therapy due to adverse experiences. Most common adverse effects were constipation, diarrhea, dyspepsia, flatulence, nausea, headache, pain, myalgia and asthenia.

LIPITOR is contraindicated: During pregnancy and lactation; active liver disease or unexplained persistent elevations of serum transaminases exceeding 3 times the upper limit of normal; hypersensitivity to any component of this medication. pid levels should be monitored periodically and, if necessary, the dose of LIPITOR adjusted based on target lipid levels recommended by guidelines.

Caution should be exercised in severely hypercholesterolemic patients who are also renally impaired, elderly, or are con-comitantly being administered digoxin or CYP 3A4 inhibitors.

Liver function tests should be performed before the initiation of treatment, and periodically thereafter. Special attention should be paid to patients who develop elevated serum transaminase levels, and in these patients, measurements should be repeated promptly and then performed more frequently.

Demonstrated delayed time to first ischemic event in stable More than 57 million patient-years of experience<sup>3</sup> CAD patients<sup>34</sup> (n=341, *p*=0.03) A A EXPERIENCE EVIDENCE

⁺ A powerful demonstrated effect across key lipid parameters¹

A

EFFICACY

in patients with stable coronary artery disease and LDLC at least 3.0 mmol/L in patients referred for percutaneous transluminal coronary angioplasty (PTCA). Patients were randomized for 18 months to LIPITOR 80 mg daily or to PTCA with usual medical care which could include lipid metabolism regulators. The results of the AVERT study should be r The Atorvastatin Versus Revascularization Treatments (AVERT) study examined the effect of intensive lipid-lowering considered as exploratory since several limitations may affect its design and conduct. In the medical-treated group The results also suggest that intensive treatment to target. LDL-C levels with LIPITOR is additive and complementary to angoplasty and would benefit patients referred for this with LIPITOR there was a trend for a reduced incidence of ischemic events and a delayed time to first ischemic event.

**Pfizer** procedure.

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For brief prescribing information see pages A-38, A-39

A-11

NEW PRE-FILLED DILUENT SYRINGE (PFDS) NONACIDIC-pH INJECTION\*

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#### + DEMONSTRATED EFFICACY

 Reduces relapse frequency and severity in RRMS<sup>2-4</sup>

pH 7.1 to 7.8 when reconstituted.

 Clinical significance has not been established.
 Prospective, multicentre study. Patients with RRMS were randomly assigned to self-administer either Betaseron 250 µg s.c. every other day or interferon beta-1a 30 µg i.m. once weekly. Scans were analyzed centrally by independent investigators who were unaware of treatment allocation and clinical PAAS (RAD) characteristics of patients.

https://doi.org/10.1017/S0317167100051234 Published online by Cambridge University Press

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60% relative risk reduction (29% absolute risk reduction; p<0.001) in the appearance of new T<sub>2</sub> lesions with Betaseron<sup>®</sup> (n=76) vs. interferon beta-1a i.m. (n=73) after two years (comparative clinical significance has not been established)<sup>‡5</sup>



BETASERON® (interferon beta-1b) is indicated for the reduction of the frequency of clinical exacerbations in ambulatory patients with relapsing-remitting multiple sclerosis and for the slowing of progression in disability and the reduction of the frequency of clinical exacerbations in patients with secondary-progressive multiple sclerosis.

The safety and efficacy of BETASERON<sup>®</sup> in primary-progressive MS have not been evaluated. Efficacy of treatment for longer than two years has not been substantially demonstrated in relapsing-remitting multiple sclerosis (RRMS).

The most common side effects related to BETASERON<sup>®</sup> in patients with RRMS are: flu-like symptom complex (76%); fever (59%); chills (46%); injection site reactions (85%); myalgia (44%); asthenia (49%) and malaise (15%).

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#### 25 Years Ago in the Canadian Journal of Neurological Sciences

SPONTANEOUS DISSECTION OF CERVICO-CEREBRAL ARTERIES

C. Miller Fisher, Robert G. Ojemann And Glenn H. Roberson

SUMMARY: Sixteen cases of spontaneous dissection of the cervical internal carotid artery (6 verified) are described. The mean age was 45 years. The clinical picture varied from simply headache and a bruit to hemiplegia and aphasia. Eleven patients had transient ischemic attacks. Headache, facial pain, a subjective bruit, oculosympathetic palsy and transient monocular blindness were present in various combinations in two-thirds of cases and their presence suggested the correct diagnosis. Examples of suspected dissection of the intracranial internal carotid, middle cerebral, posterior cerebral and extracranial vertebral arteries are also presented. Spontaneous dissection is more common than the literature indicates.

Can. J. Neurol. Sci. 1978;5: 9

#### MICROVASCULAR ANASTOMOSIS FOR CEREBRAL ISCHEMIA IN 19 PATIENTS: A PRELIMINARY REPORT

P.J. Murray

SUMMARY: The general principles of bypass surgery as they affect the cerebral circulation are reviewed. The preliminary results of an extracranial intracranial bypass operation performed on a group of 19 patients suffering from cerebral ischemia are presented. The results of the surgery compare favorably with those published in the literature. Can. J. Neurol. Sci. 1978;5: 21

#### BRAIN METABOLISM AND ARTERIAL ACID-BASE BALANCE FOLLOWING BILATERAL CAROTID OCCLUSION IN NORMOTENSIVE AND EXPERIMENTAL HYPERTENSIVE RATS

M. Fujishima, Y. Morotomi, K. Tamaki, Y. Nakatomi, J. Ogata, S. Takishita, K. Kumamoto, K. Fukiyama and T. Omae

SUMMARY: The effects of bilateral common carotid artery occlusion on brain metabolism and arterial acid-base balance were studied in normotensive and experimental renovascular hypertensive rats.

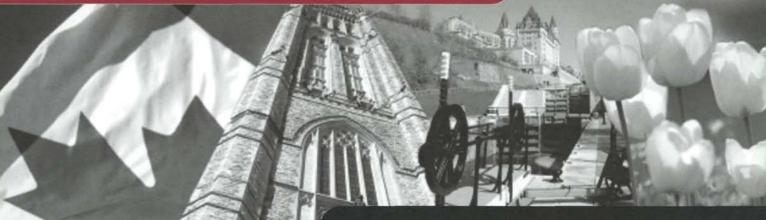
One hour after carotid occlusion in hypertensive rats, supratentorial lactate increased to 383% and lactate-pyruvate ratio to 280% of the controls, while adenosine triphosphate (ATP) decreased to 69%. These metabolic changes were thought to be due to cerebral ischemia. Arterial  $pCO_2$  was lowered and the pH was raised in the hypertensive animals due to cerebral ischemia induced hyperventilation. In the normotensive rats, carotid occlusion had minimal effects on cerebral metabolism and arterial acid-base balance.

These results suggest that hypertensive rats are more susceptible to cerebral ischemia caused by carotid occlusion than normotensive rats. Increased cerebrovascular resistance in hypertension is discussed as a casual factor in cerebral ischemia.

Can. J. Neurol. Sci. 1978;5: 27



#### 40E ASSEMBLÉE ANNUELLE DU CONGRÈS CANADIEN DES SCIENCES NEUROLOGIQUES



#### P R O G R A M M E P R O V I S O I R E

#### Tuesday, June 14th, 2005

Neurobiology Review Course ALS Strategies for Quality Life/Quality Care Movement Disorders Video Session Epilepsy Video Session

#### Wednesday, June 15th, 2005

Spinal Course Epilepsy – Consensus and Controversies in Epilepsy EMG Neuroanatomy EEG Brain Tumours - Current Standard and Advances in Neuro-Imaging for Treatment of Brain Tumours MRI in MS and Stroke and Functional MRI Sleep – Review and Update in Neurology-Related Pediatric and Adult Sleep Disorders Welcome Reception

#### Thursday, June 16th, 2005

Plenary Session I - Peripheral Nerve Platform and Poster Sessions Grand Rounds Dementia

#### Friday, June 17, 2005

Plenary Session II - Education and Manpower Platform and Poster Sessions Plenary Session III - Rehabilitation – Joint Session with Canadian Association of Physical Medicine and Rehabilitation Friday Night Social

#### Saturday, June 18th, 2005

Mini-symposia: A Pain in the Head Maximizing CME/Maintenance of Certification Opportunities Neurocritical Care Child Neurology Day – Advances in the Diagnosis and Treatment of Pediatric Neuromuscular Diseases Stroke

Multiple Sclerosis



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#### **Once-a-week AVONEX® – Efficacy that Lasts:**

- 37% reduction in the probability of disability progression at 2 years (21.9% vs. 34.9%; p=0.02).<sup>1.5</sup>
- 32% reduction in annual exacerbation rate over 2 years (0.61 vs. 0.90; p=0.002).<sup>5</sup>
- Significant reduction in the number (0.8 vs. 1.6; p≤0.05) and volume (p=0.03) of Gd-enhanced lesions at 2 years<sup>Ω,#,5</sup>, and in the number of new and enlarging T2 lesions over 2 years (2.0 vs. 3.0; p=0.002).<sup>#...5</sup>
- Delayed worsening in brain atrophy during the second year (p=0.03).\*.45
- Delayed worsening in cognitive function demonstrated on 2 neuropsychological parameters (Information Processing/Memory<sup>†</sup>, p=0.011 and PASAT<sup>\*</sup> p=0.023).<sup>405</sup>

AVONEX<sup>®</sup> (Interferon beta-1a) is indicated for the treatment of relapsing forms of MS and for the treatment of people who have experienced a single demyelinating event, accompanied by abnormal Magnetic Resonance Imaging (MRI) scans with lesions typical of MS, to delay the onset of clinically definite multiple sclerosis (as determined by a second demyelinating event), and to decrease the number and volume of active brain lesions and overall disease burden (as identified by MRI scans). Before initiating treatment with AVONEX<sup>®</sup>, alternate diagnoses should first be excluded.

AVONEX<sup>®</sup> is generally well tolerated. The most common side effects associated with treatment are flu-like symptoms, muscle ache, fever, chills, and asthenia. AVONEX<sup>®</sup> should be used with caution in patients with depression and in patients with seizure disorders. Patients with cardiac disease should be closely monitored. Routine periodic blood chemistry and hematologic tests are recommended during treatment with AVONEX<sup>®</sup>.<sup>5</sup>

£ Comparative clinical significance has not been established. ¶ Kaplan-Meier methodology, AVONEX\* n=158, placebo n=143. \* AVONEX\* n=85, placebo n=87.  $\Omega$  Using the Mann-Whitney rank-sum test. AVONEX\* n=83, placebo n=82. # The exact relationship between MRI lindings and clinical status is unknown. \*\* Analyzed by Wilcoxon rank-sum test. AVONEX\* n=78, placebo n=80. + As measured by brain parenchymal fraction in a retrospective analysis, n=140, AVONEX\*; 68, placebo: 72.  $\Delta$  The clinical correlation and significance of these findings require further assessment. † AVONEX\* 67, placebo 70, n=137. \* AVONEX\* 77, placebo 71, n=148.  $\diamond$  As demonstrated in the second year of the Phase III pivotal trial.

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Bayer HealthCare Biological Products Division



Gamunex<sup>™</sup> is contraindicated in individuals with known anaphylactic or severe systemic response to immune globulin (human). Individuals with severe, selective IgA deficiencies (serum IgA <0.05 g/L) who have known antibody against IgA (anti-IgA antibody) should only receive Gamunex<sup>™</sup> with utmost cautionary measures.

Immune globulin intravenous (human) products have been associated with renal dysfunction, acute renal failure, osmotic nephrosis and death. Patients predisposed to acute renal failure should be administered the minimum concentration of human immune globulin products at the minimum rate of infusion.

Please see complete Prescribing Information on adjacent pages.

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#### Innovative manufacturing process.

- Novel process designed to protect fragile IgG molecules."
- Utilizes new caprylate/chromatography process as an effective alternative to solvent-detergent for inactivating and removing enveloped viruses.<sup>1</sup>

#### Excellent tolerability profile.

 In a study of 97 ITP patients, 90% of adverse events were mild-to-moderate and transient.<sup>1\*</sup>

#### Designed with convenience in mind.

- Liquid 10% formulation reduces volume load vs 5% formulations.<sup>11#</sup>
- High maximum infusion rate reduces infusion time,"
- 5 months room temperature storage.<sup>14</sup>
- · Osmolality similar to physiologic osmolality.
- No added sugar stabilizers (such as sucrose or glucose),!
- \* Most common adverse events reported in a study of 97 ITP patients: headache (50%), vomiting (13%), fever (10%), nausea (10%), rash (6%), back pain (6%).
- † Initial infusion rate is 0.01 to 0.02 mL/kg body weight/min for 30 minutes; if well tolerated, the rate may be gradually increased to a maximum of 0.14 mL/kg body weight/min.
- ‡May be stored at room temperature (≤ 25°C) for 5 months during first 18 months of manufacture after which product must be used or discarded.
- § Based on sizes of studies listed in Product Monographs of IGIV products currently marketed in Canada.
- ¶Double-blind trial of 172 PID patients randomized to Gamunex<sup>™</sup> or Gamimune<sup>®</sup> N, 10%.
  \*\*Double-blind trial of 97 ITP patients randomized to Gamunex<sup>™</sup> or Gamimune<sup>®</sup> N, 10% response rate by day 7.
- t†1TP study above; maintenance rate (≥50 x 10° for 7 days); p=0.066. ‡‡ Comparative clinical significance unknown.
- Most common adverse events reported in PID were: cough increased (1, 7%) hand above (0, 9%) for (0, 1%) and a bar matting (0, 9%)

(1.7%), headache (0.8%), fever (0.1%) and pharyngitis (0.8%). https://doi.org/10.1017/S0317167100051234 Published online by Cambridge University Press New Gamunex<sup>™</sup> trials design.

- Largest pivotal trials in IGIV in patients with primary humoral
   immunodeficiency (PID) and idiopathic thrombocytopenic purpura (ITP).<sup>4</sup>
- Head-to-head comparison in more than 350 patients vs Gamimune<sup>®</sup> N, 10%.<sup>1</sup>

#### Proven efficacy in immune replacement therapy.

Reduced the annual rate of validated sinopulmonary infection in PID (Gamunex<sup>™</sup>: 0.18 vs Gamimune<sup>®</sup> N, 10%: 0.43, p = 0.023).<sup>¶</sup>

#### Proven efficacy in immunomodulatory therapy.

- Gamunex<sup>™</sup> demonstrated excellent response rates in chronic ITP (100%) and acute ITP (90%).<sup>20™</sup>
- Excellent duration of platelet response (Gamunex<sup>™</sup>: 74% vs Gamimune<sup>®</sup> N, 10%: 60%).<sup>2</sup><sup>™</sup>



For brief prescribing information see pages A-42, A-43

A-19

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- Réduction de 35 % après neuf mois (0,50 {n = 113} c. 0,77 {n = 115} placebo, moyenne, p = 0,0077)'.
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Au cours des essais comparatifs, les effets indésirables le plus fréquemment associés à l'utilisation de COPAXONE® et dont l'incidence était supérieure à celle qui a été observée chez les sujets qui recevaient le placebo étaient les suivants : réactions au point d'injection (2,4-66,4 % c. 0-36,5 %), vasodilatation (27,2 % c. 11,1 %), douleur thoracique (26,4 % c. 10,3 %), asthénie (64,8 % c. 61,9 %), infection, douleur, nausées (23,2 % c. 17,5 %), arthralgie (24,8 % c. 17,5 %), anxiété et hypertonie (35,2 % c. 29,4 %).

Traitement au long cours de la SP rémittente G.P. - S.E.N.C. Montréal (Quibec) HIA IL versity Press A-21

2000 2001 2002 2003 200

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Pour documentation voir pages A-49, A-50, A-51

#### 25 Years Ago in the Canadian Journal of Neurological Sciences

CYTOCHEMICAL LOCALIZATION OF ADENYLATE CYCLASE IN BROKEN CELL PREPARATIONS OF THE CEREBRAL CORTEX

S. W. French, D. S. Palmer and M. Caldwell

SUMMARY: Broken cell preparations derived from rat cerebral cortical grey matter were studied cytochemically to localize adenylate cyclase (AC) activity in subcellular organelle membranes. AC activity was localized by visualizing reaction product in brain particulate fractions by electron microscopy. Activity was found in the endoplasmic reticulum, on the inside of the inner mitochondrial membrane and on both leaflets of the nuclear membrane. Reaction product was found in the postsynaptic density area of most synapses. The reaction product tended to be more prominent in the presence of flouride. A synaptosome-rich fraction was shown to have NE stimulated AC activity which was blocked in vitro by both an  $\alpha$ - and a  $\beta$ -blocker and *in vivo* by propranolol.

Can. J. Neurol. Sci. 1978;5: 33

#### ANESTHESIA IN MULTIPLE SCLEROSIS

C. Bamford, W. Sibley and J. Laguna

SUMMARY: The effect of general anesthesia on 42 multiple sclerosis (MS) patients who underwent 88 episodes of general anesthesia was analyzed. One patient experienced a relapse after a procedure under general anesthesia, which is compatible with the natural history of the disease. A literature review revealed little information on this subject or on the use of particular anesthetic agents in MS. Our experience with spinal and local anesthesia is reported. In the evaluation of the former our limited data suggested that spinal anesthesia is less preferable than other alternatives in MS. Local anesthetics had a benign effect on the course of MS.

Can. J. Neurol. Sci. 1978;5: 41

#### MICROANGIOGRAPHY AND VASCULAR PERMEABILITY OF THE SUBEPENDYMAL MATRIX IN THE PREMATURE INFANT

Sachio Takashima and Kenzo Tanaka

SUMMARY: The microvascular architecture of the subependymal matrix in premature infants was studied with microangiography and benzidine stains. This revealed that the subependymal matrix is the end zone or the border zone between cerebral arteries and the collection zone of the deep cerebral veins. Focal hypoxic changes of this subependymal matrix may occur in hypoxemia and ischemia because of the characteristic architecture.

The vascular permeability of these vessels was studied in rabbits using three different molecular weights of FITCdextran. Vascular permeability was increased in the subependymal matrix by hypoxia and especially by hypoxia associated with an increased venous pressure. These findings may be related to the pathogenesis of subependymal hemorrhage in prematurity.

Can. J. Neurol. Sci. 1978;5: 45



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pH de 7,1 à 7,8 après la reconstitution.

LES

<sup>†</sup> L'importance clinique n'a pas été établie.

Étude prospective et multicentrique. On a assigné les patients aléatoirement soit au groupe qui devait inistrer 250 µg de Betaseron par voie s.-c. tous les deux jours, soit à celui qui devait s'administrer 30 µg d'interféron bêta-1a par voie i.m. une fois par semaine. Les clichés ont été analysés par un service central de chercheurs indépendants qui ne connaissaient pas le traitement que recevaient CCPP (R&D) les patients ni leurs caractéristiques cliniques.

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#### + SOINS PERSONNALISÉS

- Un appel suffit pour parler à votre infirmière de SEP LeParcours<sup>™</sup>
- Soutien spécialisé de SEP LeParcours<sup>™</sup> pour répondre à vos besoins et à ceux de vos patients atteints de SEP

#### + RÉSULTATS SIGNIFICATIFS OBSERVÉS À L'IRM<sup>†</sup>

 Diminution de 60 % du risque relatif (diminution de 29 % du risque absolu; p < 0,001) d'apparition de nouvelles lésions T<sub>2</sub> avec Betaseron<sup>®</sup> (n = 76) comparativement à l'interféron bêta-1a i.m. (n = 73) après deux ans (la signification clinique comparative n'a pas été établie)<sup>‡5</sup>



BETASERON est une marque déposée de Berlex Canada inc.
 M<sup>C</sup> SEP LeParcours est une marque de commerce utilisée sous licence par Berlex Canada inc.

BETASERON<sup>®</sup> (interféron bêta-1b) est indiqué pour réduire la fréquence des poussées cliniques chez les patients ambulatoires atteints de sclérose en plaques rémittente. Il est également indiqué pour ralentir la progression de l'incapacité et réduire la fréquence des poussées cliniques chez les patients atteints de sclérose en plaques progressive-secondaire.

L'efficacité et l'innocuité de BETASERON® dans la SEP progressiveprimaire n'ont pas été évaluées. On ne dispose pas de données probantes sur l'efficacité du traitement de la SEP rémittente au-delà de deux ans.

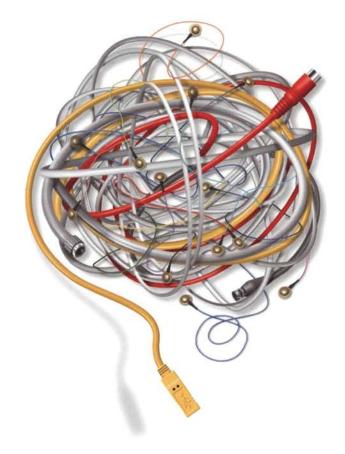
Chez les patients atteints de SEP rémittente, les effets indésirables les plus courants liés à l'utilisation de BETASERON<sup>®</sup> sont : syndrome grippal (76 %) ; fièvre (59 %) ; frissons (46 %) ; réactions au point d'injection (85 %) ; myalgie (44 %) ; asthénie (49 %) et malaise (15 %).

POUR PLUS DE DÉTAILS SUR LES MISES EN GARDE ET LES PRÉCAUTIONS, VEUILLEZ CONSULTER LA MONOGRAPHIE DE PRODUIT FOURNIE SUR DEMANDE AUX PROFESSIONNELS DE LA SANTÉ.





#### From uncontrolled



New Keppra connecting excellent profiles in efficacy and tolerability

#### Effective control of seizures

- Shown to provide up to 4 out of 10 refractory patients with  $\ge$  50% reduction in partial onset seizures (p < 0.001)
- Rapid clinical improvement demonstrated by week 2 during a 14-week evaluation period (p < 0.001)"</p>



For more information, please refer to the complete Keppra Product Monograph.

Keppra is indicated as adjunctive therapy in the management of patients with epilepsy who are not satisfactorily controlled by conventional therapy.

The most significant CNS adverse events were somnolence (Keppra 15% vs placebo 10%) and asthenia (Keppra 14% vs placebo 10%), behavioural/psychiatric symptoms (nonpsychotic: Keppra 14% vs placebo 6%; psychotic: Keppra 1% vs placebo 0%) and coordination difficulties (Keppra 3% vs placebo 2%). These adverse events were observed in controlled clinical trials with concomitant AEDs.

NOW FULL BENEFIT COVERAGE ON QUEBEC AND SASKATCHEWAN FORMULARIES

#### to control

#### Generally well tolerated

- Favourable adverse event profile
- Adverse events not dose dependent<sup>2</sup>
- Low discontinuation or dosage reduction (Keppra 14.3% vs placebo 11.7%) due to adverse events'

#### Efficacy and manageability right from the start

- Starting dose of 1000 mg/day (500 mg bid) shown to be effective and may be adjusted to a maximum of 3000 mg/day if required
- No blood level monitoring required
- No drug/drug interactions' with other AEDs, warfarin, digoxin or between Keppra 500 mg bid and a combination oral contraceptive (0.03 mg ethinyl estradiol and 0.15 mg levonorgestrel)<sup>§</sup>
- § Note: Pharmacokinetic interaction studies with contraceptives have not been conducted covering the full recommended dosage range of Keppra. Physicians should advise their female patients to be alert to any irregular vaginal bleeding or spotting and report any occurrences. Data from a 38-week multicentre, randomised, add-on, double-blind, placebo-controlled, parallel-group trial. Study consisted of a 4-week titration period followed by a 14-week evaluation period. Patients received either levetiracetam 1000 mg/day (n = 98), 3000 mg/day (n = 101) or placebo (n = 05). (a = 95). Facilitati weekly seizure frequency was reduced over placebo, at week 2 of the evaluation period, by 24.9% (1.120/1.406) for Keppra 1000 mg/day and 38.6% (0.918/1.406) for Keppra 3000 mg/day. The percentage of patients achieving ≥ 50% seizure reduction from baseline after the 18-week titration and evaluation period was 7.4% for placebo, 37.1% for Keppra 1000 mg/day and 39.6% for Keppra 3000 mg/day. † Based on observations in clinical studies
- C<sub>max</sub> of levetiracetam's metabolite (ucb L057) was approximately doubled in presence of probe-necid. Renal clearance of ucb L057 decreased by 60% in presence of probenecid.





#### PORTRAIT OF A FAMILY HISTORY

#### HISTORY DOESN'T HAVE TO REPEAT ITSELF

Roger, History of angina.

> Died age 57 of MI.

#### Help Reduce the Risk of CV Death by 7 6%<sup>1</sup>

(p<0.001; 6.1% vs. 8.1%)

Alice, History of diabetes and high total cholesterol.

Died age 62 of stroke.



GUARDING AGAINST CV DEATH

ALTACE is indicated in the treatment of essential hypertension, normally when beta-blockers and diaretics are inappropriate. It may be used alone or in association with thiazide diaretics. ALTACE is indicated following acute myocardial infarction in clinically stable patients with signs of left ventricular dysfunction to improve survival and reduce hospitalizations for heart failure.

Results from the HOPE study showed that ALTACE improved survival in patients by reducing the risk of CV death by 26% (*p*<0.001; 6.1% vs. 8.1%). ALTACE may be used to reduce the risk of MI, stroke, or CV death in patients over age 55 who are at high risk of CV events because of a history of CAD, stroke, peripheral artery disease, or diabetes accompanied by at least 1 other CV risk factor such as hypertension, elevated total cholesterol levels, low HDL levels, cigarette smoking, or documented microalbuminuria.

Like other ACE inhibitors, ALTACE is not recommended for pregnant or lactating women and should be used with caution in patients with renal insufficiency. The most frequent adverse events occurring in clinical trials with ALTACE monotherapy in hypertensive patients who were treated for at least 1 year (*n*=651) were: headache (15.1%); dizziness (3.7%); asthenia (3.7%); chest pain (2.0%). Discontinuation of therapy due to clinical adverse events was required in 5 patients (0.8%).

The reasons for stopping treatment were cough (ramipril 7.3% vs. placebo 1.8%); hypotension/dizziness (1.9% vs. 1.5%) and edema (0.4% vs. 0.2%).

#### ALTACE is the most prescribed ACEI among cardiologists.

\*IMS Health Canada: Canadian CompuScript Audit, Year 2002 Total Prescriptions

(R&D) PAAB Product Monograph available to physicians and pharmacists upon request.

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