

The Canadian Journal of Neurological Sciences

Le Journal Canadien des Sciences Neurologiques

SPECIAL FEATURES

- Editorial Review: Therapeutic Trials in Multiple Sclerosis** J.H. Noseworthy, T.P. Seland and G.C. Ebers **355**
- Editorial Review: Migraine: New Views on an Old Theory** John Edmeads **363**

ORIGINAL ARTICLES

- Posterior Column Dysfunction in Cervical Spondylotic Myelopathy** D.J. MacFadyen **365**
- Management of Acute Subdural Hematomas from Aneurysmal Rupture** Bryce Weir, Terence Myles, Moe Kahn, Falah Maroun, David Malloy, Brien Benoit, Michael McDermott, Douglas Cochrane, Gerard Mohr, Gary Ferguson, Felix Durity **371**
- Intermittent Treatment of Febrile Convulsions with Nitrazepam** Michel Vanasse, Pierre Masson, Guy Geoffroy, Albert Larbrisseau and Pierre C. David **377**
- A Method for Measurement of Arterial Concentration of Cerebral Blood Flow Tracer for Autoradiographic Experiments** Devidas Menon, Mirko Diksic, Ernst Meyer, Kazuhiro Sako and Y. Lucas Yamamoto **380**
- Spinal Epidural Lipomatosis: A Complication of Glucocorticoid Therapy** N.A. Russell, G. Belanger, B.G. Benoit, D.N. Latter, D.L. Finestone and G.W. Armstrong **383**
- Recurrent Aseptic Meningitis Secondary to Intracranial Epidermoids** Werner J. Becker, Gordon V. Watters, Jean-Pierre de Chadarevian and Michel Vanasse **387**
- Oculoskeletal Myopathy with Abnormal Mitochondria** V. Bril, N.B. Rewcastle, J. Humphrey **390**
- Brain Abscess Due to *Petriellidium boydii*** François Dubeau, Louis E. Roy, Johanne Allard, Michel Laverdiere, Suzanne Rousseau, Fernand Duplantis, Jean Boileau and Jacques Lachapelle **395**
- Inflammatory Myelopathy Presenting as a Cystic Intramedullary Spinal Cord Lesion** B.I. Tranmer, T.A. Gray, W.J. Horsey, C.G. Gonsalves **399**
- Relapsing Polychondritis with Multifocal Neurological Abnormalities** J. Willis, E.A. Atack, G. Kraag **402**
- Les Abrégés du Congrès Québécois de la Recherche Clinique en Sciences Neurologiques** **405**
- BOOK REVIEWS** **412**
- CALENDAR OF EVENTS** **415**



The Official Journal of

The Canadian Neurological Society
 The Canadian Neurosurgical Society
 The Canadian Society of Clinical Neurophysiologists
 The Canadian Association for Child Neurology



FOR THE HEAD PAIN PUZZLE...

FIORINAL[®]

Two stat
for **TENSION**
headache

SANDOZ[®]
▼▼▼

Complete headache therapy
Sandoz Canada Inc., Dorval, Quebec H9R 4P5

Fiorinal contains: ASA/caffeine/butalbital
Full prescribing information available on
request.

[®]TM
PAAI
CCFP
PMA
ACIM

THE CANADIAN JOURNAL OF NEUROLOGICAL SCIENCES LE JOURNAL CANADIEN DES SCIENCES NEUROLOGIQUES

Editor

Robert G. Lee
Calgary

Editorial Board

Albert J. Aguayo
Montreal

Henry J.M. Barnett
London

Paul Bédard
Quebec

Henry B. Dinsdale
Kingston

Guy Geoffroy
Montreal

Alan Hudson
Toronto

Yves Lamarre
Montreal

Associate Editor

André Barbeau
Montreal

Bernard Lemieux
Sherbrooke

William J. Logan
Toronto

Morton Low
Vancouver

Thomas P. Morley
Toronto

Thomas J. Murray
Halifax

Donald Paty
Vancouver

Sidney J. Peerless
London

Founding Editor

Robert T. Ross
Winnipeg

Terry Picton
Ottawa

Jean Reiher
Sherbrooke

Leo P. Renaud
Montreal

Barry Rewcastle
Calgary

Harvey B. Sarnat
Calgary

Matthew W. Spence
Halifax

William G. Tatton
Toronto

Bryce Weir
Edmonton

Book Review Editor

T. Peter Seland
Calgary

Editorial Assistant

Sally Gregg
Calgary

THE EDITORIAL BOARD wishes to publish original work in the basic and clinical neurosciences on the understanding that it has not been and will not be published elsewhere. Review articles on timely subjects will be accepted. Manuscripts must be in triplicate including illustrations. One of the copies must be the original, ribbon copy. Manuscripts should be typed double spaced, on white paper.

Papers will be accepted in French or English. All papers should be accompanied by a short résumé in both languages. The résumé translation will be done by the editorial board if requested.

Papers should be identified only by the full name of the author, or authors, and the name of the place in which the work was done.

ILLUSTRATIONS: Photographs should be unmounted on glossy paper and show magnification scale. They should be marked on the back with figure number, title of paper and name of author.

Diagrams should be in India ink and large enough to be informative after reduction.

All illustrations should be referred to as figures, numbered consecutively, not included in the body of the text and all captions should be typed on a separate piece of paper.

Colored illustrations cannot usually be accepted unless the author is prepared to assist with the cost of reproduction.

REFERENCES to authors outside the context of the sentence should read (Name, Year). i.e. "However, a recent study (Bird and Iverson, 1975) showed a decreased, etc." Authors mentioned within the context of the sentence should read Name (Year), "i.e. . . . twenty years since Ecker and Reimenshender (1951) demonstrated, etc." References should be typed in alphabetical order on a separate sheet and include author's name, initials, year, title, publication, volume first and last page, i.e. Isacson, P. (1967). Myx-oviruses and autoimmunity. *Progress in Allergy*, 10, 256-292. Abbreviations should be the same as those used in *Cumulated Index Medicus*.

Textbook references should include name of text, author's name, page number, publisher and city.

REPRINTS: Fifty reprints will be supplied free if ordered when the galley proofs are returned. More may be ordered at a nominal charge. Corrections and changes in the galley proofs, apart from printer's errors may be charged to the author.

This journal is indexed by **Index Medicus**, **Excerpta Medica** and **Current Contents — Clinical Practice and Life Science**.

SUBSCRIPTIONS: This journal is issued four times a year. The annual rate is \$40.00 for Canada and the U.S.A. \$44.00 elsewhere. Internes, Residents, Pre- and Post-Doctoral Students, \$20.00 per annum. Single copies \$12.00 each.

ADVERTISING: Enquiries regarding advertising space and rates should be directed to LEX LTD, 431 Alden Road, Markham, Ontario L3R 3L4. Telephone — (416) 477-2030.

Suite 390, 3333 Cavendish Blvd., Montreal, Quebec H4B 2M5 — (514) 487-4412-4.

All communications, manuscripts, subscriptions, etc., should be sent to the Editor, Canadian Journal of Neurological Sciences, Rm. 1443, Faculty of Medicine, University of Calgary, 3330 Hospital Drive N.W., Calgary, Alberta, Canada T2N 4N1. Telephone (403) 283-4072.

COPYRIGHT © 1984 by THE CANADIAN JOURNAL OF NEUROLOGICAL SCIENCES INC. No part of this journal may be reproduced in any form without the prior permission of The Canadian Journal of Neurological Sciences. ISSN 0317-1671.

Published in conjunction with the University of Calgary Press.

Printed by McAra Printing Limited, 105, 2507 - 12th Street N.E., Calgary, Alberta T2E 7L5

Mailed under second class registration number 3307. Postage paid at Calgary, Alberta.

PUBLICATIONS COMMITTEE

John Wherrett
Toronto

Andrew Eisen
Vancouver

Terry Myles
Calgary

John Tibbles
Halifax

CANADIAN NEUROLOGICAL SOCIETY

President
Past-President
Vice-President
Secretary-Treasurer

Robert F. Nelson
Thomas J. Murray
Thomas P. Seland
Garth M. Bray
1650 Cedar Avenue,
Montreal, P.Q.
H3G 1A4

Council:
Monique Lefebvre-d'Amour
Jean Pierre Bouchard
William McCormick
Donald Calne
Ali Rajput
Thomas Feasby

CANADIAN NEUROSURGICAL SOCIETY

President
Past-President
President-Elect
Secretary-Treasurer

Stanley Schatz
Leslie Ivan
Charles Tator
Alain Godon
12361 Notre-Dame-des Anges Street
Montreal, Quebec
H4J 2C3

Council:
Jacques Boucher
Mohamed Khan
Hart Schutz
Barry Purves
Brien Benoit
Renn Holness

CANADIAN SOCIETY OF CLINICAL NEUROPHYSIOLOGISTS

President
Past-President
Secretary-Treasurer

Warren Blume
Andrew Eisen
Terry Picton
Ottawa General Hospital
501 Chemin Smythe Road
Ottawa K1H 8L6

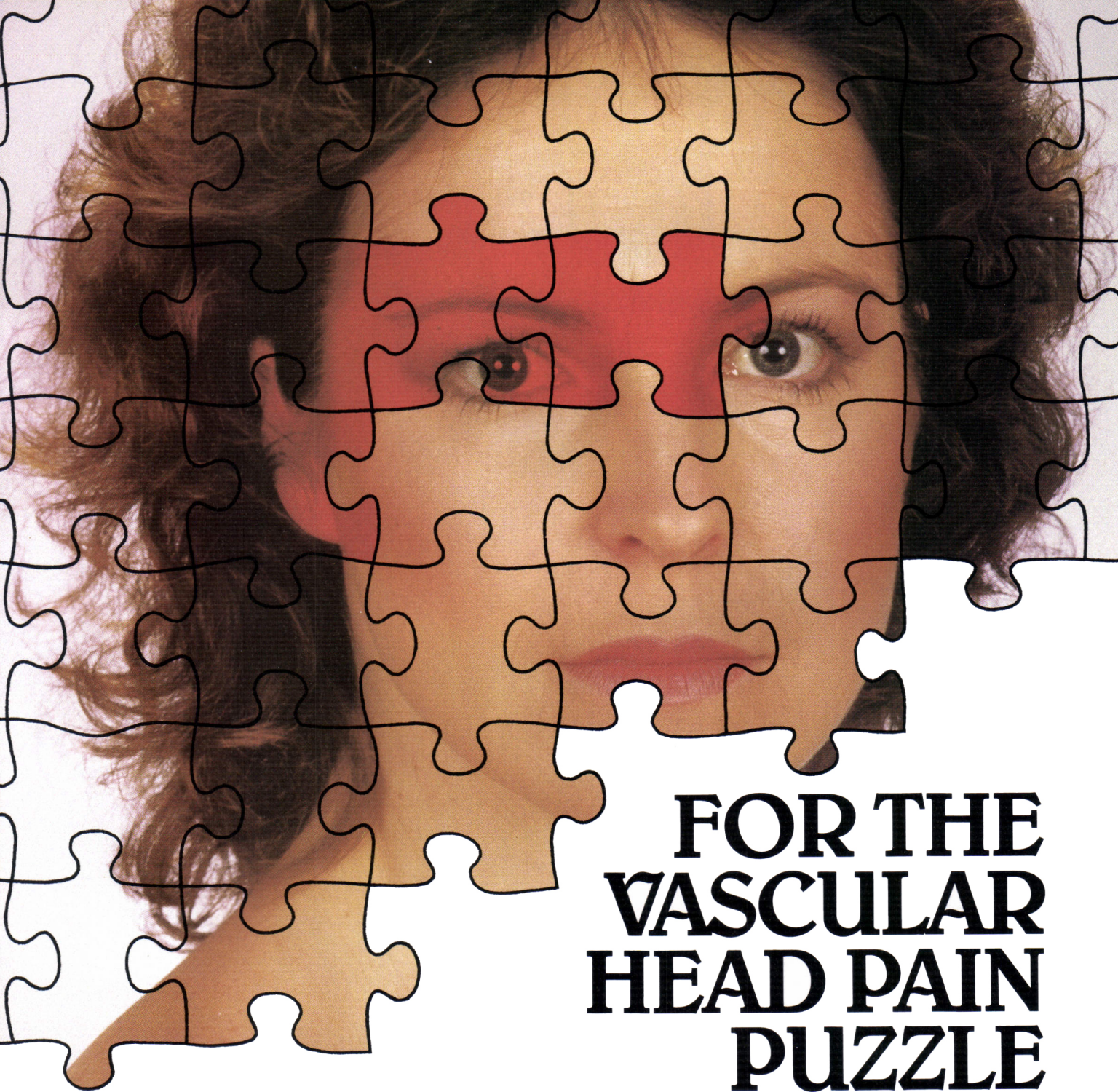
Council:
Peter Ashby
Gordon Blair
Monique D'Amour
Michael Jones
Sherrill Purves

CANADIAN ASSOCIATION FOR CHILD NEUROLOGY

President
Past-President
Vice-President
Secretary-Treasurer

Frederick Andermann
Rosalind Curtis
R. Haslam
Daune L. McGregor
Hospital for Sick Children
555 University Ave.
Toronto M5G 1X8

Council:
Peter Humphreys
J.U. Crichton
A. Larbrisseau



FOR THE VASCULAR HEAD PAIN PUZZLE



CAFERGOT[®]
To ABORT acute
vascular headache

SANDOMIGRAN[®] DS
PROPHYLAXIS for chronic
recurring vascular headache

SANDOZ[®]

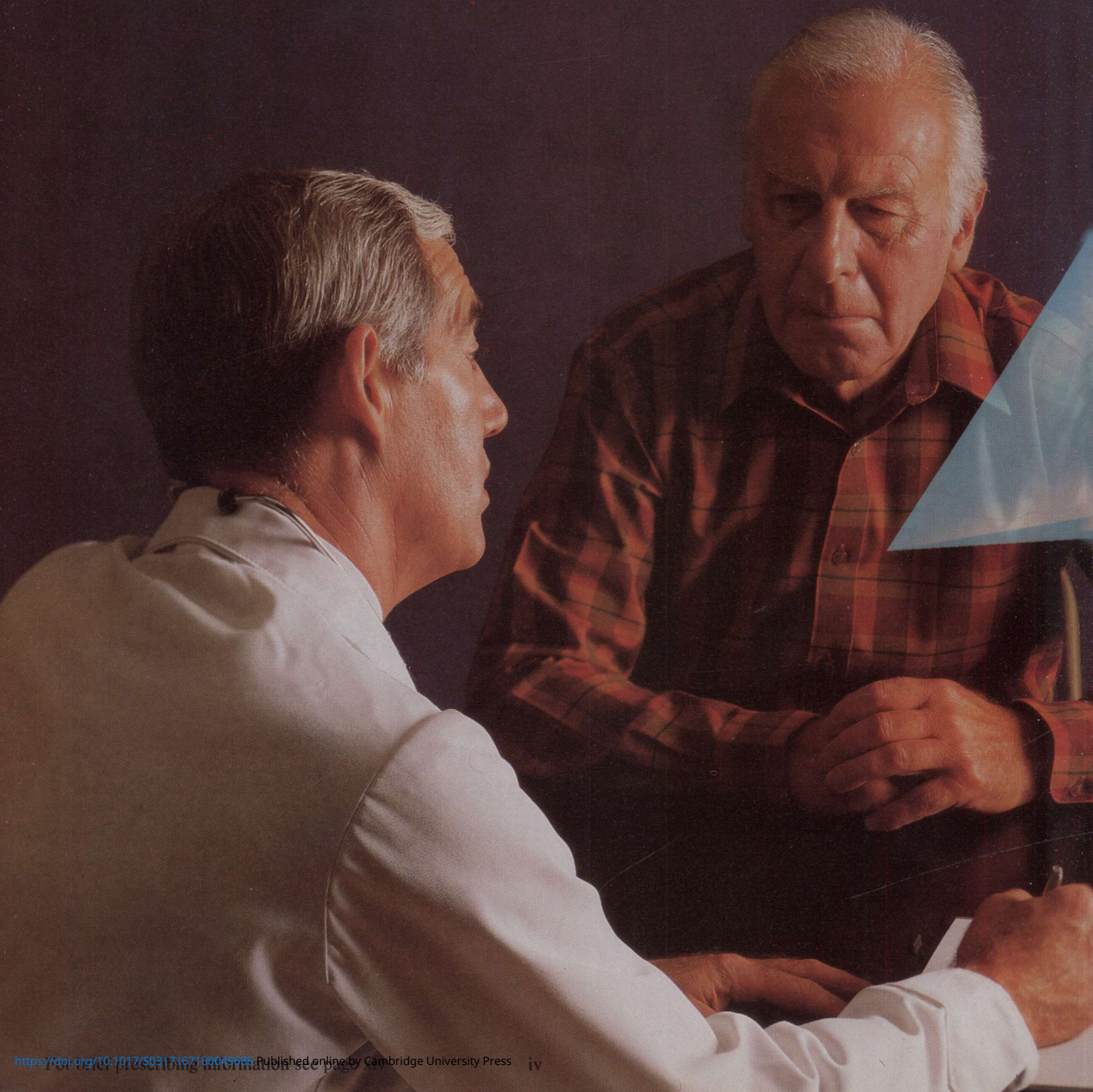


Complete headache therapy
Sandoz Canada Inc., Dorval, Quebec H9R 4P5

Cafergot contains: ergotamine tartrate/cafeine [®]TM
Sandomigran DS contains: pizotyline
Full prescribing information available on request.  

Combat the Threat of Thrombosis ...

Choose Asasantine[®] for Your Patients
with Coronary Artery Disease



"Increased platelet activity may have an important role in inducing intimal damage and vasospasm"¹

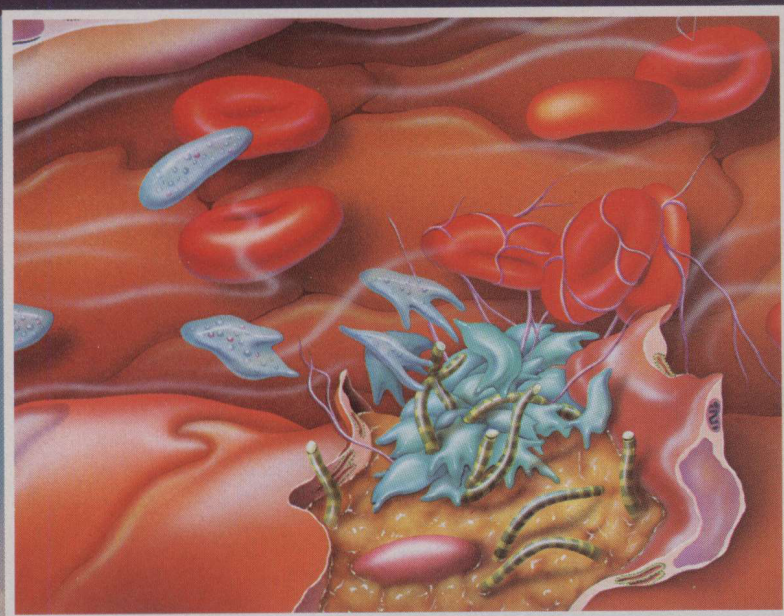
"Whatever the precise sequence of events, formation of platelet aggregates in the coronary vessels could limit blood flow and either cause the ischemic event or result in deterioration of already compromised blood flow to the myocardium."²

Asasantine[®] Normalizes Platelet Reactivity

Asasantine[®] capsules contain 75 mg Persantine[®] (dipyridamole) plus 330 mg ASA. Clinical trials demonstrate the effectiveness of this combination in reducing platelet adhesion and aggregation, and subsequent thrombus formation. Consequently, Asasantine[®], is an important choice of therapy in preventing recurrent myocardial infarction.

Asasantine[®] Reduces Coronary Incidence

- 1 capsule T.I.D.
- Minimal side effects
- No cardiovascular-related contraindications



Asasantine[®]



**Boehringer
Ingelheim**

PAAB
CCPP

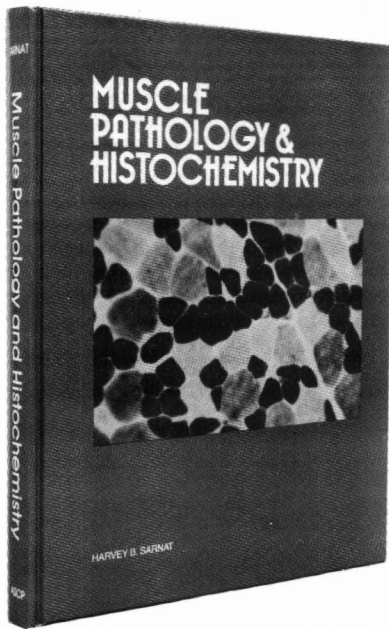
Boehringer Ingelheim (Canada) Ltd. / Ltée
977 Century Drive, Burlington, Ontario L7L 5J8

Evomatic® 8000

**- completely integrated system
for evoked potential testing**

- ★ Galvanically isolated patient unit
- ★ One preamplifier for each electrode
- ★ Fully computerized operation
- ★ Powerful signal averaging and data processing
- ★ 60 user-defined programs stored on one disc
- ★ Color display combined with finger-touch operation
- ★ 1000 points per channel with 12-bit resolution
- ★ Multi-functioning stimulators for auditory, visual and somatosensory evoked
- ★ Storage of full patient journal including curves, patient data and text
- ★ Eight color plotter printouts
- ★ Built-in IEEE-488 interface
- ★ Expandable from 1 to 8 channels
- ★ Designed for ease of operation





MUSCLE PATHOLOGY & HISTOCHEMISTRY

HARVEY B. SARNAT, MD

Associate Professor of Pediatrics,
Pathology & Clinical Neurosciences
University of Calgary Faculty of Medicine
Calgary, Alberta

- A full color atlas with 207 color photomicrographs
- Methodology on tissue preparation for histochemical & histologic studies
- Detailed discussions of histochemical stains as interpretive aids in muscle biopsies
- Over 1,000 references

This text atlas provides you with interpretive clinical correlations to increase diagnostic skills in light microscopy of muscle biopsy. This in-depth reference stresses the difficult diagnostic problems of the muscular dystrophies, inflammatory, congenital and metabolic myopathies, and the recognition of neurogenic disease of muscle. It discusses the morphologic changes in striated muscle that are associated with neurogenic and myopathic processes, developmental muscle disorders, and the value of histochemical stains in the interpretation of muscle biopsies. This textbook atlas also permits the identification of distinguishing features of various myopathies at the light microscopic level. It is an important procedural and interpretive reference for every laboratory.

YES, I want to order the text atlas *Muscle Pathology and Histochemistry* by Harvey B. Sarnat.

TEXT
Cat #AD/16-1-034-00
\$75.00

TEXT & 216 SLIDES
Cat. #AD/15-1-034-00
\$175.00

Total _____

Name _____

Shipping & Handling Add 5% _____

Address _____

IL Residents add 6% tax or
note sales tax exemption _____

TOTAL _____

City _____ State _____ Zip _____

Day Phone () _____

ASCP Member No. _____

Bill me P.O. No. _____

Check enclosed. Make payable to ASCP
Charge to: VISA MasterCard

Card No. _____

Inter. No. _____ Exp. Date _____

Signature _____

**PHONE ORDERS; call
TOLL FREE:
800-621-4142**
(In Illinois, call: 312-738-4890)

**MAIL TO: ASCP
P.O. Box 12075
Chicago, IL 60612**

Contact ASCP for quantity discounts.
Please allow 4 to 6 weeks for delivery.
Prices subject to change without notice.
Prices slightly higher outside U.S.



**A.S.C.P.
PRESS**

Epival[®] divalproex sodium

Prescribing Information

ACTION: Epival (divalproex sodium) has anticonvulsant properties, and is chemically related to valproic acid. Although its mechanism of action has not yet been established, it has been suggested that its activity is related to increased brain levels of gamma-aminobutyric acid (GABA). The effect on the neuronal membrane is unknown. Epival dissociates into valproic acid in the gastrointestinal tract.

Peak serum levels of valproic acid occur in 3 to 4 hours. The serum half-life (t_{1/2}) of valproic acid is typically in the range of 6 to 16 hours. Half-lives in the lower part of the above range are usually found in patients taking other anti-epileptic drugs. A slight delay in absorption occurs when the drug is administered with meals but this does not affect the total absorption. Valproic acid is rapidly distributed throughout the body and the drug is strongly bound (90%) to human plasma proteins. Increases in dose may result in decreases in the extent of protein binding and variable changes in valproic acid clearance and elimination. The therapeutic plasma concentration range is believed to be from 50 to 100 µg/mL. Occasional patients may be controlled with serum levels lower or higher than this range. A good correlation has not been established between daily dose, serum level and therapeutic effect.

Elimination of valproic acid and its metabolites occurs principally in the urine, with minor amounts in the feces and expired air. Very little unmetabolized parent drug is excreted in the urine. The principal metabolite formed in the liver is the glucuronide conjugate. See "Metabolism" subsection regarding statement on other metabolites in the urine.

See WARNINGS section regarding statement on fatal hepatic dysfunction.

INDICATIONS AND CLINICAL USE: Epival (divalproex sodium) is indicated for use as sole or adjunctive therapy in the treatment of simple or complex absence seizures, including petit mal. Divalproex sodium may also be used adjunctively in patients with multiple seizure types which include absence.

In accordance with the International Classification of Seizures, simple absence is defined as a very brief clouding of the sensorium or loss of consciousness (lasting usually 2-15 seconds) accompanied by certain generalized epileptic discharges without other detectable clinical signs. Complex absence is the term used when other signs are also present.

CONTRAINDICATIONS: Epival (divalproex sodium) should not be administered to patients with hepatic disease or significant dysfunction, it is contraindicated in patients with known hypersensitivity to the drug.

WARNINGS: Hepatic failure resulting in fatalities has occurred in patients receiving valproic acid. These incidences usually have occurred during the first 6 months of treatment with valproic acid. Serious or fatal hepatotoxicity may be preceded by non-specific symptoms such as loss of seizure control, malaise, weakness, lethargy, anorexia, and vomiting. Patients and parents should be instructed to report such symptoms. Because of the non-specific nature of some of the early signs, hepatotoxicity should be suspected in patients who become unwell, other than through obvious cause, while taking Epival (divalproex sodium).

Liver function tests should be performed prior to therapy and at frequent intervals thereafter especially during the first 6 months. However, physicians should not rely totally on serum biochemistry since these tests may not be abnormal in all instances, but should also consider the results of careful interim medical history and physical examination. Caution should be observed when administering Epival to patients with a prior history of hepatic disease. Patients with various unusual congenital disorders, those with severe seizure disorders accompanied by mental retardation, and those with organic brain disease may be at particular risk.

In high-risk patients, it might also be useful to monitor serum fibronogen and albumin for decrease in concentrations and serum ammonia for increases in concentration. If changes occur, divalproex sodium should be discontinued. Dosage should be titrated and maintained at the lowest dose consistent with optimal seizure control.

The drug should be discontinued immediately in the presence of significant hepatic dysfunction, suspected or apparent. In some cases, hepatic dysfunction has progressed in spite of discontinuation of drug. The frequency of adverse effects particularly elevated liver enzymes may increase with increasing dose. Therefore, the benefit gained by improved seizure control by increasing the dosage must be weighed against the increased incidence of adverse effects sometimes seen at higher dosages.

Use in Pregnancy: According to recent reports in the medical literature, valproic acid may produce teratogenicity in the offspring of human females receiving the drug during pregnancy. The incidence of neural tube defects in the fetus may be increased in mothers receiving valproic acid during the first trimester of pregnancy. Based upon a single report, it was estimated that the risk of valproic acid exposed women having children with spina bifida is approximately 1.2%. This risk is similar to that which applies to non-epileptic women who have had children with neural tube defects (anencephaly and spina bifida). Animal studies have demonstrated valproic acid induced teratogenicity, and studies in human females have demonstrated placental transfer of the drug. Multiple reports in the clinical literature indicate an association between the use of anti-epileptic drugs and an elevated incidence of birth defects in children born to epileptic women taking such medication during pregnancy. The incidence of congenital malformations in the general population is regarded to be approximately 2% in children of treated epileptic women, this incidence may be increased 2 to 3-fold. The increase is largely due to specific defects, e.g. congenital malformations of the heart, cleft lip and/or palate, and neural tube defects. Nevertheless, the great majority of mothers receiving anti-epileptic medications deliver normal infants.

Data are more extensive with respect to diphenylhydantoin and phenobarbital, but these drugs are also the most commonly prescribed anti-epileptics. Some reports indicate a possible similar association with the use of other anti-epileptic drugs, including trimethadione, paramethadione, and valproic acid. However, the possibility also exists that other factors, e.g. genetic predisposition or the epileptic condition itself may contribute to or may be mainly responsible for the higher incidence of birth defects.

Anti-epileptic drugs should not be discontinued in patients to whom the drug is administered to prevent major seizures, because of the strong possibility of precipitating status epilepticus with attendant hypoxia and risks to both the mother and the unborn child. With regard to drugs given for minor seizures, the risks of discontinuing medication prior to or during pregnancy should be weighed against the risk of congenital defects in the particular case and with the particular family history.

Epileptic women of child-bearing age should be encouraged to seek the counsel of their physician and should report the onset of pregnancy promptly to him. Where the necessity for continued use of anti-epileptic medication is in doubt, appropriate consultation is indicated.

Nursing Mothers: Valproic acid is excreted in breast milk. Concentrations in breast milk have been reported to be 1 to 10% of serum concentrations. As a general rule, nursing should not be undertaken while a patient is receiving Epival (divalproex sodium).

Fertility: Chronic toxicity studies in juvenile and adult rats and dogs demonstrated reduced spermatogenesis and testicular atrophy at doses of valproic acid greater than 200 mg/kg/day in rats and 90 mg/kg/day in dogs. Segment I fertility studies in rats have shown that doses up to 350 mg/kg/day for 60 days have no effect on fertility. The effect of Epival (divalproex sodium) and valproic acid on the development of the testes and on sperm production and fertility in humans is unknown.

LONG-TERM TOXICITY STUDIES IN RATS AND MICE INDICATED A POTENTIAL CARCINOGENIC RISK.

PRECAUTIONS: Hepatic dysfunction: See CONTRAINDICATIONS and WARNINGS.

General: Because of reports of thrombocytopenia and inhibition of platelet aggregation, platelet counts and bleeding-time determination are recommended before instituting therapy and at periodic intervals. It is recommended that patients receiving Epival (divalproex sodium) be monitored for platelet count prior to planned surgery. Clinical evidence of hemorrhage, bruising or a disorder of hemostasis/coagulation is an indication for reduction of Epival (divalproex sodium) dosage or withdrawal of therapy pending investigation.

Hyperammonemia with or without lethargy or coma has been reported and may be present in the absence of abnormal liver function tests; if elevation occurs the divalproex sodium should be discontinued.

Because Epival (divalproex sodium) may interact with other anti-epileptic drugs, periodic serum level determinations of concurrently administered anti-epileptics are recommended during the early part of therapy. (See Drug Interactions). There have been reports of breakthrough seizures occurring with the combination of valproic acid and phenytoin.

Epival (divalproex sodium) is partially eliminated in the urine as a ketone-containing metabolite which may lead to a false interpretation of the urine ketone test.

There have been reports of altered thyroid function tests associated with valproic acid; the clinical significance of these is unknown.

Driving and Hazardous Occupations: Epival (divalproex sodium) may produce CNS depression, especially when combined with another CNS depressant, such as alcohol. Therefore, patients should be advised not to engage in hazardous occupations, such as driving a car or operating dangerous machinery, until it is known that they do not become drowsy from the drug.

Drug Interactions: Epival (divalproex sodium) may potentiate the CNS depressant action of alcohol.

There is evidence that valproic acid may cause an increase in serum phenobarbital levels, by impairment of non-renal clearance. This phenomenon can result in severe CNS depression. The combination of valproic acid and phenobarbital has also been reported to produce CNS depression without significant elevations of barbiturate or valproic acid serum levels. Patients receiving concomitant barbiturate therapy should be closely monitored for neurological toxicity. Serum barbiturate drug levels should be obtained, if possible, and the barbiturate dosage decreased, if indicated.

Primidone is metabolized into a barbiturate, and therefore, may also be involved in a similar or identical interaction.

There is conflicting evidence regarding the interaction of valproic acid with phenytoin (See PRECAUTIONS - General). It is not known if there is a change in unbound (free) phenytoin serum levels. The dosage of phenytoin should be adjusted as required by the clinical situation.

The concomitant use of valproic acid and clobazepam may produce absence status.

Caution is recommended when divalproex sodium is administered with drugs affecting coagulation, e.g. acetylsalicylic acid and warfarin.

ADVERSE REACTIONS: The most commonly reported adverse reactions are nausea, vomiting and indigestion. Since valproic acid has usually been used with other anti-epileptics, it is not possible in most cases to determine whether the adverse reactions mentioned in this section are due to valproic acid alone or to the combination of drugs.

Gastrointestinal: Nausea, vomiting and indigestion are the most commonly reported side effects at the initiation of therapy. These effects are usually transient and rarely require therapy. Diarrhea, abdominal cramps and constipation have also been reported. Anorexia with some weight loss and increased appetite with some weight gain have also been seen.

CNS Effects: Sedative effects have been noted in patients receiving valproic acid alone but are found most often in patients on combination therapy. Sedation usually disappears upon reduction of other anti-epileptic medication. Ataxia, headache, nystagmus, diplopia, asterixis, "spots before the eyes", tremor, dysarthria, dizziness, and incoordination have rarely been noted. Rare cases of coma have been reported in patients receiving valproic acid alone or in conjunction with phenobarbital.

Dermatologic: Transient increases in hair loss have been observed. Skin rash and petechiae have rarely been noted.

Endocrine: There have been reports of irregular menses and secondary amenorrhea in patients receiving valproic acid.

Abnormal thyroid function tests have been reported (See PRECAUTIONS).

Psychiatric: Emotional upset, depression, psychosis, aggression, hyperactivity and behavioural deterioration have been reported.

Musculoskeletal: Weakness has been reported.

Hematopoietic: Thrombocytopenia has been reported. Valproic acid inhibits the second phase of platelet aggregation (See PRECAUTIONS). This may be reflected in altered bleeding time. Bruising, hematoma formation and frank hemorrhage have been reported. Relative lymphocytosis and hypofibrinogenemia have been noted. Leukopenia and eosinophilia have also been reported. Anemia and bone marrow suppression have been reported.

Hepatic: Minor elevations of transaminases (e.g. SGOT and SGPT) and LDH are frequent and appear to be dose related. Occasionally, laboratory tests also show increases in serum bilirubin and abnormal changes in other liver function tests. These results may reflect potentially serious hepatotoxicity (See WARNINGS).

Metabolic: Hyperammonemia (See PRECAUTIONS). Hyperglycemia has been reported and associated with a fatal outcome in a patient with pre-existing non-ketotic hyperglycemia.

Pancreatic: There have been reports of acute pancreatitis occurring in association with therapy with valproic acid.

SYMPTOMS AND TREATMENT OF OVERDOSAGE: In a reported case of overdose with valproic acid after ingesting 36 g in combination with phenobarbital and phenytoin, the patient presented in deep coma. An EEG recorded diffuse slowing, compatible with the state of consciousness. The patient made an uneventful recovery.

Naloxone has been reported to reverse the CNS depressant effects of valproic acid overdose.

Because naloxone could theoretically also reverse the anti-epileptic effects of Epival, it should be used with caution.

Since Epival tablets are enteric-coated, the benefit of gastric lavage or emesis will vary with the time since ingestion. General supportive measures should be applied with particular attention to the prevention of hypovolemia and the maintenance of adequate urinary output.

DOSAGE AND ADMINISTRATION: Epival (divalproex sodium) is administered orally. The recommended initial dosage is 15 mg/kg/day, increasing at one week intervals by 5 to 10 mg/kg/day until seizures are controlled or side effects preclude further increases.

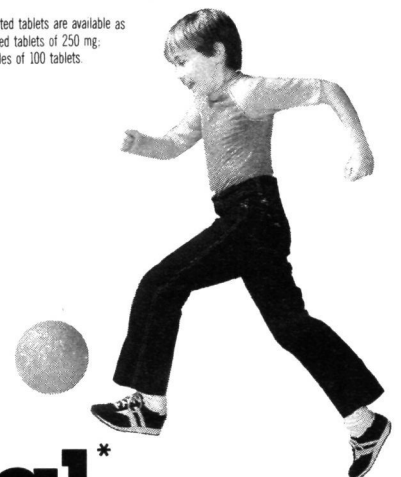
The maximal recommended dosage is 60 mg/kg/day. When the total daily dose exceeds 125 mg, it should be given in a divided regimen (See Table).

The frequency of adverse effects (particularly elevated liver enzymes) may increase with increasing dose. Therefore, the benefit gained by improving seizure control must be weighed against the increased incidence of adverse effects.

kg	Weight lb	Total daily dose (mg)	Table of Initial Doses by Weight (based on 15 mg/kg/day)		
			Dose 1	Dose 2	Dose 3
10-24.9	22 - 54.9	250	125	0	125
25-39.9	55 - 87.9	500	250	0	250
40-59.9	88 - 131.9	750	250	250	250
60-74.9	132 - 164.9	1,000	250	250	500
75-89.9	165 - 197.9	1,250	500	250	500

As the dosage of divalproex sodium is raised, blood levels of phenobarbital and/or phenytoin may be affected (See PRECAUTIONS). Patients who experience GI irritation may benefit from administration of the drug with food or by a progressive increase of the dose from an initial low level. **The tablets should be swallowed without chewing.**

AVAILABILITY: Epival (divalproex sodium) enteric-coated tablets are available as salmon-pink colored tablets of 125 mg, peach-colored tablets of 250 mg, lavender-colored tablets of 500 mg. Supplied in bottles of 100 tablets.



Epival[®] divalproex sodium

a better way to a better life

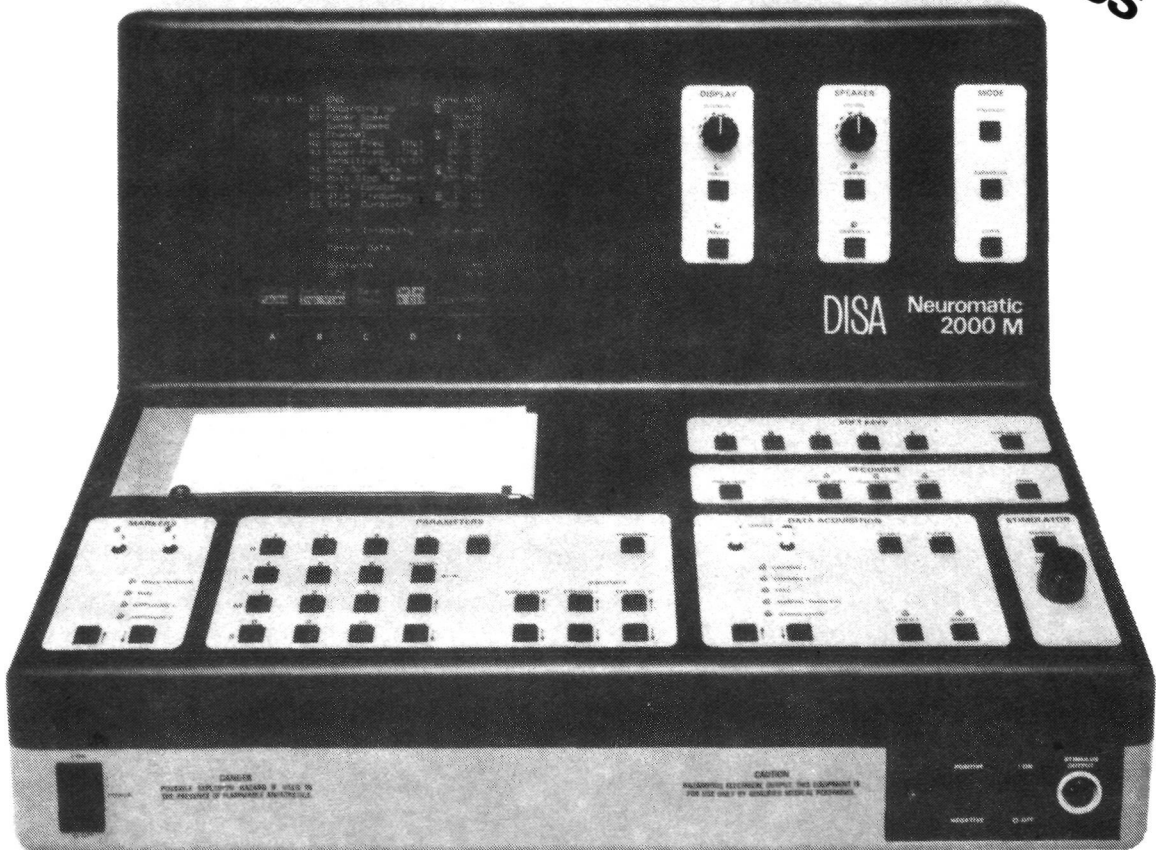
PHARMACEUTICAL PRODUCTS DIVISION
ABBOTT LABORATORIES, LIMITED
MONTREAL, CANADA H4P 1A5

MEMBER
PMAC PAAB
*TM

Neuromatic® 2000

- a proven success

now
C and M
types

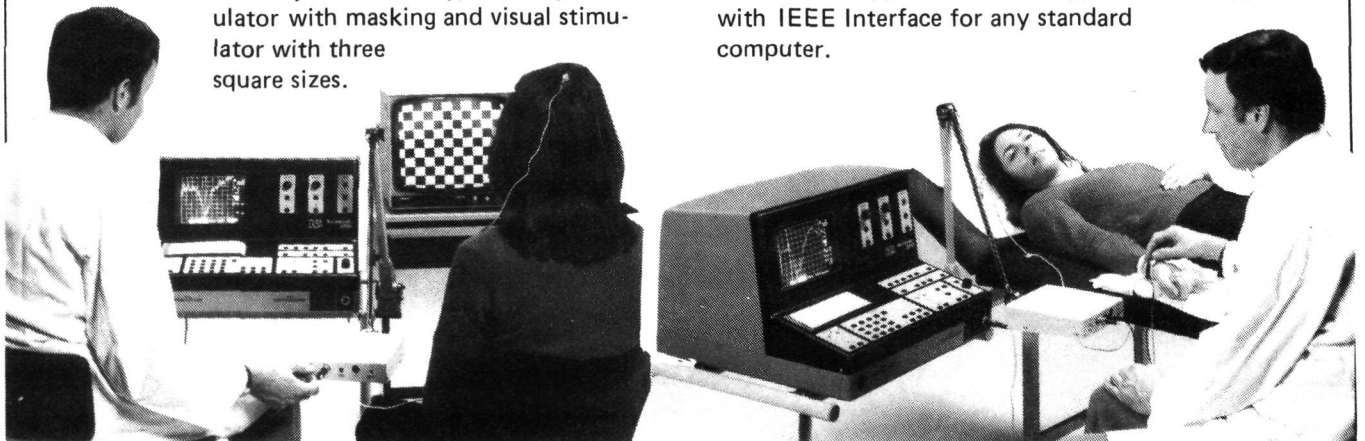


Neuromatic® 2000 C — the Combined Neuro-Myograph for Clinical Electromyography and Evoked Potentials

The Neuromatic® 2000 C has powerful averagers with rejection facility, auditory stimulator with masking and visual stimulator with three square sizes.

Neuromatic® 2000 M — the Myograph for Clinical Electromyography

The Neuromatic® 2000 M has superior amplifiers and powerful averagers with rejection facility. Both the C-type and the M-type can be supplied with IEEE Interface for any standard computer.



with Tegretol[®]

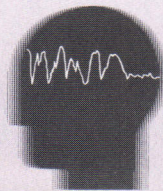


...this may well be
the only sign of
epilepsy

Tegretol[®] provides excellent seizure control without the penalty of excessive sedation; without hyperplasia of gingival mucosa, without hypertrichosis; *and with minimal impairment of cognitive function.*^{1, 2, 3}

So give your epileptic patients a better chance at a more normal lifestyle. With Tegretol right at the start.

Tegretol[®]



Because there's no substitute for experience.

Geigy

Mississauga, Ontario
L5N 2W5

PAAB
CCFP
G-3161

A new and better way to prescribe valproic acid

Epival* is divalproex sodium, a new form of valproate in enteric-coated tablets that minimize gastric upsets.¹ Epival is bioequivalent to valproic acid, with comparable anticonvulsant effectiveness.²


New 125-mg tablet improves compliance

Epival is offered in a 125-mg enteric-coated tablet which is easier to swallow than large capsules, and better accepted than syrup. 250-mg and 500-mg enteric-coated tablets are also available.

in simple and complex absence

Epival
divalproex sodium

a better way to a better life

 PHARMACEUTICAL PRODUCTS DIVISION
ABBOTT LABORATORIES, LIMITED
MONTREAL, CANADA H4P 1A5

1. Wilder BJ et al. Gastrointestinal tolerance of divalproex sodium. *Neurology* 1983; 33(6): 808-811.
2. Data on file. Abbott Laboratories.
*TM