

PRESCRIBING INFORMATION – UK AND ROI REBIF 8.8 MICROGRAMS AND 22 MICROGRAMS SOLUTION FOR INJECTION REBIF® 22 MICROGRAMS SOLUTION FOR INJECTION REBIF® 44 MICROGRAMS SOLUTION FOR INJECTION. Interferon beta-1a

**Presentation** Rebif 8.8 and 22: Pre-filled glass syringe containing 8.8µg or 22µg of Interferon beta-1a in respectively 0.2 or 0.5ml. Rebif 22 or 44: Pre-filled glass syringe containing 22µg or 44µg Interferon beta-1a in 0.5ml. **Indication** Treatment of relapsing multiple sclerosis. Efficacy has not been demonstrated in patients with secondary progressive multiple sclerosis without ongoing relapse activity. **Dosage and administration** Initiate under supervision of a physician experienced in the treatment of multiple sclerosis. Administer by subcutaneous injection. Recommended dose: Weeks 1 and 2: 8.8µg three times per week (TIW); Weeks 3 and 4: 22µg TIW; Week 5 onwards: 44µg TIW (22µg TIW if patients cannot tolerate higher dose). Limited published data suggest that the safety profile in adolescents aged 12–16 years receiving Rebif 22 TIW is similar to that in adults. Do not use in patients under 12 years of age. Prior to injection and for 24hrs afterwards, an antipyretic analgesic is advised to decrease flu-like symptoms. Evaluate patients at least every second year of the treatment period. **Contraindications** History of hypersensitivity to natural or recombinant interferon beta, or to any of the excipients; treatment initiation in pregnancy; current severe depression and/or suicidal ideation. **Precautions** Inform patients of most common adverse reactions. Use with caution in patients with previous or current depressive disorders and those with antecedents of suicidal ideation. Advise patients to report immediately any symptoms of depression and/or suicidal ideation. Closely monitor patients exhibiting depression and treat appropriately. Consider cessation of therapy. Administer with caution in patients with a history of seizures and those receiving anti-epileptics, particularly if epilepsy is not adequately controlled. Closely monitor patients with cardiac disease for worsening of their condition during initiation of therapy. Patients should use an aseptic injection technique and rotate injection sites to minimise risk of injection site necrosis. If breaks in skin occur, patients should consult their doctor before continuing injections. If multiple lesions occur, discontinue Rebif until healed. Use with caution in patients with history of significant liver disease, active liver disease, alcohol abuse or increased serum ALT. Monitor serum ALT prior to the start of therapy, at Months 1, 3 and 6 and periodically thereafter. Stop treatment if icterus or symptoms of liver dysfunction appear. Treatment has potential to cause severe liver injury including acute hepatic failure. Full haematological monitoring is recommended at Months 1, 3 and 6 and periodically thereafter. All monitoring should be more frequent when initiating Rebif 44. New or worsening thyroid abnormalities may occur. Thyroid function testing is recommended at baseline and if abnormal every 6–12 months. Use with caution in, and closely monitor patients with, severe renal and hepatic failure or severe myelosuppression. Serum neutralising antibodies may develop and are associated with reduced efficacy. If a patient responds poorly and has neutralising antibodies, reassess treatment. Use with caution in patients receiving medicines with a narrow therapeutic index cleared by cytochrome P450. Women of childbearing potential should use effective contraception. Limited data suggest a possible increased risk of spontaneous abortion. During lactation, either discontinue Rebif or nursing. If overdose occurs, hospitalise patient and give supportive treatment. **Side effects** In the case of severe or persistent undesirable effects, consider temporarily lowering or interrupting dose. *Very common:* flu-like symptoms, injection site inflammation/reaction, headache, asymptomatic transaminase increase, neutropenia, lymphopenia, leucopenia, thrombocytopenia, anaemia. *Common:* injection site pain, myalgia, arthralgia, fatigue, rigors, fever, pruritus, rash, erythematous/maculo-papular rash, diarrhoea, vomiting, nausea, depression, insomnia. Serious side effects include: injection site necrosis, hepatitis with or without icterus, severe liver injury, anaphylactic reactions, angioedema, erythema multiforme, erythema multiforme-like skin reactions, seizures, thromboembolic events, suicide attempt, Stevens–Johnson syndrome, dyspnoea. Consult the Summary of Product Characteristics for more information relating to side effects. **Legal category** POM **Price** Rebif 8.8 and 22: 6 (0.2ml) + 6 (0.5ml) syringes – £563.33. Rebif 22: 12 syringes (0.5ml) – £624.77. Rebif 44: 12 syringes (0.5ml) – £829.61. For prices in Ireland, consult distributors Allphar Services Ltd. **Marketing Authorisation Holder and Numbers:** Sero Europe Ltd, 56 Marsh Wall, London, E14 9TP; EU/1/98/063/007; 003 & 006 **For further information contact:** UK: Merck Sero Europe, Bedfont Cross, Stanwell Road, Feltham, Middlesex, TW14 8NX. Tel: 020 8818 7373. **Republic of Ireland:** Merck Sero Europe, 3013 Lake Drive, Citywest Business Campus, Dublin 24. Tel: 01 4661910 **Date of Preparation:** February 2009.

Adverse events should be reported. Reporting forms and information can be found at [www.yellowcard.gov.uk](http://www.yellowcard.gov.uk). In the Republic of Ireland information can be found at [www.imb.ie](http://www.imb.ie). Adverse events should also be reported to Merck Sero Europe Limited – Tel: +44(0)20 8818 7373 or email: [medinfo.uk@mercksero.com](mailto:medinfo.uk@mercksero.com)

#### References:

1. Giovannoni G *et al.* *Mult Scler* 2009; **15**(2):219–228.
2. PRISMS Study Group. *Neurology* 2001; **56**:1628–1636.
3. Kappos L *et al.* *Neurology* 2006; **67**:944–953.
4. Gold R *et al.* *Eur J Neurol* 2005; **12**:649–656.

Date of preparation: February 2009.

REB09-0035

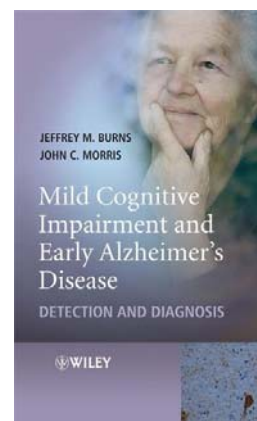


## Mild Cognitive Impairment and Early Alzheimer's Disease. Detection and Diagnosis

Identification of early, preferably presymptomatic, Alzheimer's disease (AD) is now deemed the most likely way to achieve meaningful therapeutic intervention, through use of disease-modifying agents when these become available. Although there are some existing texts on mild cognitive impairment (MCI; e.g. see review in *ACNR* 2003;3(5);23), a new volume may be thought welcome, especially when one of the authors (John Morris) has been an important player in the field.

This slim volume covers neuropathology, detection, aetiology, and treatment of MCI, as well as presenting three case histories. As to be expected, the emphasis is that of the Washington University group, with diagnosis of early AD based largely on subjective information gathered from a reliable informant, rather than depending on patient performance in cognitive test batteries (e.g. pp 65–68, and case histories), with immediate commencement of symptomatic therapy when diagnosis is made (p71; of course, not possible in UK if following NICE guidance). The distinction of “worried well” (= self-report of lapses in memory retrieval) from incipient AD (= loss of self-appreciation) is helpful (p53).

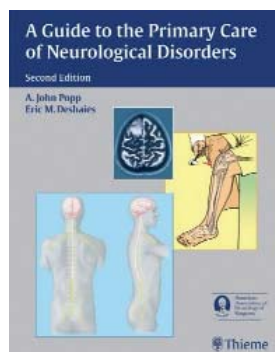
This book will serve as a useful introduction for those approaching this area for the first time, although experienced cognitive neurologists will already be familiar with much of the content. However, the book is seriously marred by inadequate proof-reading and/or copy-editing. There are many typographical errors (e.g. “Neurotic and inflammatory responses”, p85), a non-existent figure is referred to (p64), factual errors occur (surely 18, not 15, patients developed meningoencephalitis in the AN1792 amyloid vaccine trial? p88), a note to “add a reference” has not been deleted from the text (p54), and the references are inconsistent, being neither sequential nor in alphabetical order, beginning at reference 12. With the exception of the first 11 references, none are more recent than 2004 (indeed one 2004 reference is “in press”). If I may indulge in some amateur sleuthing in textual criticism, I would speculate that the book was originally written in 2004, then languished until 2006 when additions were tacked on, rather than fully integrated into the text; perhaps the two authors wrote their sections separately. The other consequence of this is that parts of the book are seriously out of date, e.g. trials of cholinesterase inhibitors in MCI (p69) have now been published; “more than 50” presenilin 1 mutations described (p103; now in fact more than 160). Likewise, the 2007 revised diagnostic criteria for AD, which suggest elimination of the MCI category, are not discussed. ♦



**Author:** Burns JM, Morris JC  
**Published by:** John Wiley, 2008  
**Price:** £21.00  
**ISBN:** 9780470319369

**Reviewed by:**  
 AJ Larner,  
 Cognitive Function Clinic,  
 WCNN, Liverpool, UK.

# A Guide to the Primary Care of Neurological Disorders, Second Edition



Editors: Popp JA, Deshaies EM  
 Published by: Thieme, 2007  
 Price: \$79.95  
 ISBN: 978-1-58890-525-3

Reviewed by:  
 CAH Fisher,  
 Marches Surgery,  
 Leominster, UK.

A primary care neurology textbook edited by two American neurosurgeons may raise eyebrows. As will a glance at the list of contributors – ten neurologists, fourteen neurosurgeons, four psychiatrists, two radiologists... The list goes on, and yes, does include two primary care physicians (one in private practice). The result is a text with scope way beyond that required by a British GP, but hidden within it are some nuggets worth finding.

This is a thoroughly American book, as witnessed by references to websites, and the recommended reading at the end of each chapter. As a paperback, it is somewhat unwieldy in its sub-A4 size. The text is dense, with few diagrams, and those that there are can be daunting (e.g. the neuroanatomy of the vestibular apparatus) or of no practical use (that showing the Hallpike manoeuvre would be of no help to anyone not experienced in its use). Tables abound, and some of these are of much greater value – that outlining medication options for essential tremor has led me to try mirtazapine for a patient. The index is excellent and without doubt it is through this that the book should be accessed.

The text is divided into four sections, covering an overview of “primary care and the neurosciences”, diagnosis (in general terms), diagnosis and management of common neurological symptoms, and finally, management of specific conditions. Chapter 1 provides a remarkably informed description of the nature and role of primary care, written by a paediatric neurosurgeon! But only the most dedicated would plough on through subsequent chapters, describing the history and scope of the neurosciences, with a strong American emphasis, and legal and ethical issues of the same (though reference to the issue of physician-assisted suicide in Oregon is interesting). A chapter on ambulatory nurses is of no relevance to UK practice, and another purporting to describe the effective use of diagnostic tests was a dry list of statistics. In section 2 (diagnosis) there is only the briefest review of symptoms, though it is good to be reminded that “TIAs very seldom cause loss of consciousness or memory”. A rather poor description of examination techniques includes some unfamiliar suggestions, such as examination of the ethmoid arteries and the Shirley Wray sign. By contrast, much detail is given in sections on neuroimaging and neurophysiological tests, surely of limited use to even an American family physician.

In section 3, there is more of interest to be found. A whole chapter dedicated to low back pain would be more expected in an orthopaedic text, and UK readers will note a complete absence of reference to “red flags”. But it is interesting to note that “home cervical traction” is recommended for cervical disc herniation – perhaps worthy of consideration this side of the Atlantic. We are also reminded that vertebroplasty may have a role in compression fractures of the

spine. In a chapter on headache there is reference to the use of barbiturate compounds (butalbital) for acute relief of tension headache and, interestingly, advice to increase doses of amitriptyline up to 125mg in prevention, or to try fluoxetine. The author of the headache chapter repeats his salutary warning that use of analgesics should be restricted to no more than 2-3 days per week, and opiates to just one day per week. Dripping 4% lignocaine into the nostrils is less familiar advice!

*This is a thoroughly American book, as witnessed by references to websites, and the recommended reading at the end of each chapter*

Section 4 probably contains most of interest, though once again there are whole chapters that might be better placed in other texts, including a whole one on hearing loss, and another on psychiatry. There are good overviews of neuropathies and myelopathies, movement disorders, neuro-ophthalmology, and dementia/delirium, including the hardly required dictum “early diagnosis of dementia can be difficult”. In managing the latter, “daily supplementation with vitamin E is now accepted as standard practice”, and thioridazine is still advocated as an option for management of agitation. A detailed chapter on coma and brain death could simply have been excluded, as could much of others on head injury, spinal injury, and “The Role of the Emergency Department...” An otherwise useful account of cerebrovascular disease has no reference to the ABCD stratification of TIAs, but those on neuro-oncology, infections and MS provide good overviews, and another covering neurology applied to paediatrics is an unexpected bonus.

In these days of ready and quick access to clinical information via one’s PC, the role of textbooks is perhaps in decline, and it is difficult to imagine this one making it onto the shelves of many British GPs. But for those lucky enough to have access to a copy, it can certainly provide some useful insights as a reference text. A third edition would benefit from UK input if it is to aspire to a readership in this country. ♦

If you would like to review books for ACNR, please contact Andrew Larner, Book Review Editor, c/o rachael@acnr.co.uk