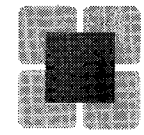
BuSpar® (buspirone HCl)

References: 1. Data on file, Bristol-Myers Squibb Company. 2. Cohn JB, Bowden CL, Fisher JG, Rodos JJ. Double-blind comparison of buspirone and clorazepate in anxious outpatients with or without depressive symptoms. *Psychopathology.* 1992;25:10-21. 3. Feighner JP, Cohn JB. Analysis of individual symptoms in generalized anxiety—a pooled, multistudy, double-blind evaluation of buspirone. *Neuropsychobiology.* 1989;21:124-130. 4. Lader M. Assessing the potential for buspirone dependence or abuse and effects of its withdrawal. *Am J Med.* 1987;82(suppl 5A):20-26. 5. Newton RE, Marunycz JD, Alderdice MT, Napolitello MJ. Review of the side-effect profile of buspirone. *Am J Med.* 1986;80(suppl 3B):17-21.

Contraindications: Hypersensitivity to buspirone hydrochloride.
Warnings: The administration of BuSpar to a patient taking a monoamine oxidase inhibitor (MAOI) may pose a hazard. Since blood pressure has become elevated when BuSpar was administered concomitantly with an MAOI, such concomitant use is not recommended. BuSpar should not be employed in lieu of appropriate antipsychotic treatment.
Precautions: ***General*** – *Interference with cognitive and motor performance:* Although buspirone is less sedating than other anxiolytics and does not produce significant functional impairment, its CNS effects in a given patient may not be predictable; therefore, patients should be cautioned about operating an automobile or using complex machinery until they are reasonably certain that buspirone does not affect them adversely. Although buspirone has not been shown to increase alcohol-induced impairment in motor and mental performance, it is prudent to avoid concomitant use with alcohol.
Potential for withdrawal reactions in sedative/hypnotic/anxiolytic drug dependent patients: Because buspirone will not block the withdrawal syndrome often seen with cessation of therapy with benzodiazepines and other common sedative/hypnotic drugs, before starting buspirone withdraw patients gradually from their prior treatment, especially those who used a CNS depressant chronically. Rebound or withdrawal symptoms may occur over varying time periods, depending in part on the type of drug and its elimination half-life. The withdrawal syndrome can appear as any combination of irritability, anxiety, agitation, insomnia, tremor, abdominal cramps, muscle cramps, vomiting, sweating, flu-like symptoms without fever, and occasionally, even as seizures.
Possible concerns related to buspirone's binding to dopamine receptors: Because buspirone can bind to central dopamine receptors, a question has been raised about its potential to cause acute and chronic changes in dopamine mediated neurological function (eg, dystonia, pseudoparkinsonism, akathisia, and tardive dyskinesia). Clinical experience in controlled trials has failed to identify any significant neuroleptic-like activity; however, a syndrome of restlessness, appearing shortly after initiation of treatment, has been reported; the syndrome may be due to increased central noradrenergic activity or may be attributable to dopaminergic effects (ie, represent akathisia).
Information for Patients – Patients should be instructed to inform their physician about any medications, prescription or nonprescription, alcohol or drugs they are now taking or plan to take during treatment with buspirone; to inform their physician if they are pregnant, are planning to become pregnant, or become pregnant while taking buspirone; to inform their physician if they are breast feeding; and not to drive a car or operate potentially dangerous machinery until they experience how this medication affects them.
Drug Interactions – Concomitant use with other CNS active drugs should be approached with caution (see **Warnings**). Concomitant use with trazodone may have caused 3- to 6-fold elevations of SGPT (ALT) in a few patients. Concomitant administration of BuSpar and haloperidol resulted in increased serum haloperidol concentrations in normal volunteers. The clinical significance is not clear. Buspirone does not displace tightly bound drugs like phenytoin, propranolol, and warfarin from serum proteins, but may displace less firmly bound drugs like digoxin. However, there was one report of prolonged prothrombin time when buspirone was given to a patient also treated with warfarin, phenytoin, phenobarbital, digoxin, and Synthroid.
Carcinogenesis, Mutagenesis, Impairment of Fertility – No evidence of carcinogenic potential was observed in rats or mice; buspirone did not induce point mutations, nor was DNA damage observed; chromosomal aberrations or abnormalities did not occur.
Pregnancy: Teratogenic Effects – Pregnancy Category B: Should be used during pregnancy only if clearly needed.
Nursing Mothers – Administration to nursing women should be avoided if clinically possible.
Pediatric Use – The safety and effectiveness have not been determined in individuals below 18 years of age.
Use in the Elderly – No unusual, adverse, age-related phenomena have been identified in elderly patients receiving a total, modal daily dose of 15 mg.
Use in Patients with Impaired Hepatic or Renal Function – Since buspirone is metabolized by the liver and excreted by the kidneys, it is not recommended in severe hepatic or renal impairment.
Adverse Reactions (See also Precautions): ***Commonly Observed*** – The more commonly observed untoward events, not seen at an equivalent incidence in placebo-treated patients, include dizziness, nausea, headache, nervousness, lightheadedness, and excitement.
Associated with Discontinuation of Treatment – The more common events causing discontinuation included: central nervous system disturbances (3.4%), primarily dizziness, insomnia, nervousness, drowsiness, lightheaded feeling; gastrointestinal disturbances (1.2%), primarily nausea; miscellaneous disturbances (1.1%), primarily headache and fatigue. In addition, 3.4% of patients had multiple complaints, none of which could be characterized as primary.
Incidence in Controlled Clinical Trials – Adverse events reported by 1% or more of 477 patients who received buspirone in four-week, controlled trials: *Cardiovascular:* Tachycardia/palpitations 1%. *CNS:* Dizziness 12%, drowsiness 10%, nervousness 5%, insomnia 3%, lightheadedness 3%, decreased concentration 2%, excitement 2%, anger/hostility 2%, confusion 2%, depression 2%. *EENT:* Blurred vision 2%. *Gastrointestinal:* Nausea 8%, dry mouth 3%, abdominal/gastric distress 2%, diarrhea 2%, constipation 1%, vomiting 1%. *Musculoskeletal:* Musculoskeletal aches/pains 1%. *Neurological:* Numbness 2%, paresthesia 1%, incoordination 1%, tremor 1%. *Skin:* Skin rash 1%. *Miscellaneous:* Headache 6%, fatigue 4%, weakness 2%, sweating/clamminess 1%.
Other Events Observed During the Entire Premarketing Evaluation – The relative frequency of all other undesirable events reasonably associated with the use of buspirone in approximately 3000 subjects who took multiple doses of the drug under well-controlled, open, and uncontrolled conditions is defined as follows: Frequent are those occurring in at least 1/100 patients; infrequent are those occurring in 1/100 to 1/1000 patients; and rare are those occurring in less than 1/1000 patients. *Cardiovascular* – frequent: non-specific chest pain; infrequent: syncope, hypotension, hypertension; rare: cerebrovascular accident, congestive heart failure, myocardial infarction, cardiomyopathy, bradycardia. *Central Nervous System* – frequent: dream disturbances; infrequent: depersonalization, dysphoria, noise intolerance, euphoria, akathisia, fearfulness, loss of interest, dissociative reaction, hallucinations, suicidal ideation, seizures; rare: feelings of claustrophobia, cold intolerance, stupor, slurred speech, psychosis. *EENT* – frequent: tinnitus, sore throat, nasal congestion; infrequent: redness and itching of the eyes, altered taste, altered smell, conjunctivitis; rare: inner ear abnormality, eye pain, photophobia, pressure on eyes. *Endocrine* – rare: galactorrhea, thyroid abnormality. *Gastrointestinal* – infrequent: flatulence, anorexia, increased appetite, salivation, irritable colon, rectal bleeding; rare: burning of the tongue. *Genitourinary* – infrequent: urinary frequency, urinary hesitancy, menstrual irregularity and spotting, dysuria; rare: amenorrhea, pelvic inflammatory disease, enuresis, nocturia. *Musculoskeletal* – infrequent: muscle cramps, muscle spasms, rigid/stiff muscles, arthralgias. *Neurological* – infrequent: involuntary movements, slowed reaction time; rare: muscle weakness. *Respiratory* – infrequent: hyperventilation, shortness of breath, chest congestion; rare: epistaxis. *Sexual Function* – infrequent: decreased or increased libido; rare: delayed ejaculation, impotence. *Skin* – infrequent: edema, pruritus, flushing, easy bruising, hair loss, dry skin, facial edema, blisters; rare: acne, thinning of nails. *Clinical Laboratory* – infrequent: increases in hepatic aminotransferases (SGOT, SGPT); rare: eosinophilia, leukopenia, thrombocytopenia. *Miscellaneous* – infrequent: weight gain, fever, roaring sensation in the head, weight loss, malaise; rare: alcohol abuse, bleeding disturbance, loss of voice, hiccoughs.
Postintroduction Clinical Experience – Rare occurrences of allergic reactions, cogwheel rigidity, dystonic reactions, ecchymosis, emotional lability, tunnel vision, and urinary retention have been reported. Because of the uncontrolled nature of these spontaneous reports, a causal relationship to BuSpar has not been determined.
Drug Abuse and Dependence: ***Controlled Substance Class*** – Not a controlled substance.
Physical and Psychological Dependence – Buspirone has shown no potential for abuse or diversion and there is no evidence that it causes tolerance, or either physical or psychological dependence. However, since it is difficult to predict from experiments the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed, physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of buspirone misuse or abuse (eg, development of tolerance, incrementation of dose, drug-seeking behavior).
Overdosage: ***Signs and Symptoms*** – At doses approaching 375 mg/day the following symptoms were observed: nausea, vomiting, dizziness, drowsiness, miosis, and gastric distress. No deaths have been reported in humans either with deliberate or accidental overdosage.
Recommended Overdosage Treatment – General symptomatic and supportive measures should be used along with immediate gastric lavage. No specific antidote is known and dialyzability of buspirone has not been determined.
For complete details, see Prescribing Information or consult your Mead Johnson Pharmaceuticals Representative.
U.S. Patent Nos. 3,717,634 and 4,182,763
MJL8-4270R2

Mead Johnson
PHARMACEUTICALS
A Bristol-Myers Squibb Company
Princeton, New Jersey 08543 U.S.A.

BOOK REVIEWS



ATUL C. MEHTA, MD, EDITOR

MAGNETIC RESONANCE IMAGING OF THE BRAIN AND SPINE
Edited by Scott W. Atlas
Raven Press

MR AND CT IMAGING OF THE HEAD, NECK, AND SPINE, 2ND EDITION
Edited by Richard E. Latchaw
Mosby-Year Book

HEAD AND NECK IMAGING
Edited by Peter M. Som and R. Thomas Bergeron.
Mosby-Year Book

THE RAVEN MRI TEACHING FILE. MRI OF THE BRAIN, VOLUME 1: NON-NEOPLASTIC DISEASE
Edited by William G. Bradley, Jr. and Michael Brant-Zawadzki
Raven Press

Magnetic Resonance Imaging of the Brain and Spine, edited by Scott W. Atlas, and *MR and CT Imaging of the Head, Neck, and Spine, 2nd Edition*, edited by Richard E. Latchaw, are the best works to date on their topics. The books complement each other, and their intended audiences differ only slightly.

Dr. Latchaw's is an all-encompassing neuroradiology text that discusses the diseases affecting the central nervous system and their various manifestations on both magnetic resonance imaging (MRI) and computed tomography (CT). This book is useful for neuroradiologists, but will be equally beneficial to general radiologists who want a comprehensive neuroradiology textbook, and to neurologists and neurosurgeons.

Dr. Atlas' contribution is a comprehensive treatise on MRI as applied to the central nervous system. This text is an essential acquisition for neuroradiologists who desire to sharpen their understanding of MRI as it relates to diseases of the brain and spine. For those without significant exposure to MRI physics, the treatment of the physics is not as easily understandable as that in Edelman and Hesselink's *Clinical Magnetic Resonance Imaging*; nevertheless, it is an excellent summary. Unlike Dr. Latchaw's book, Atlas' work does not include a discussion of ear, nose, and throat diseases below the skull base.

Both books are well written, illustrated, and referenced. I highly recommend them to the audiences detailed above. They will not be disappointed.

For the second edition of *Head and Neck Imaging*, Drs. Som and Bergeron have assembled authors who transmit their expertise in a lucid manner, enabling the reader to grasp an understanding of difficult topics, such as congenital facial and temporal bone lesions.

The book's 13 chapters cover the gamut of head and neck lesions. The first chapter discusses congenital lesions of the midface, beginning with a clear explanation of their embryology that makes subsequent radiographic analysis of the anomalies much easier to understand. The authors of this section of the book include two neuroradiologists, two plastic surgeons, a neurosurgeon, and an ophthalmologist. Their synthesis of this complex topic into a coherent whole is an ideal approach.

Dr. Som has contributed a definitive overview of imaging of the sinonasal cavity and a comprehensive treatment of the salivary glands. Temporomandibular joint (TMJ) imaging is covered in chapter 4. Co-authored by a radiologist and an orthodontist, this chapter gives the reader useful guidelines for the use of various imaging modalities for this increasingly important area. The relatively short chapter on the mandible em-

Continued on page 244

Continued from page 228

phasizes plain films and CT, but is written and illustrated well.

The chapters on the pharynx and oral cavity, parapharyngeal space, neck, larynx, orbit, visual pathways, and central skull base are superbly detailed and comprehensive. All of these chapters make extensive use of MRI. The temporal bone chapter, which concludes the book, is one of the strongest, including all pathologic conditions affecting this region. One of the most useful sections discusses vascular tinnitus, a common problem that appropriate imaging can affect significantly.

This book combines the best of both worlds: it is a comprehensive reference that is readable. Its flaws are minor: some of the MR images in the TMJ chapter are inverted, and the chapter on the mandible suffers a relative lack of MR images. The text is superbly illustrated overall and is copiously referenced. It should be in the library of every clinician or radiologist who deals with diseases of the head and neck.

Raven Press has become the "MRI house" of the industry, and the 10-volume series *The Raven MRI Teaching File* is a departure from their usual textbook approach. The series editors, Drs. Lufkin, Bradley, and Brant-Zawadzki, have assembled well-known experts in their fields to present an overview of MRI in a teaching file format. The preface states that their intention is to enable practicing radiologists to become proficient in a technique to which they might not have had sufficient (or any) exposure during training. In *MRI of the Brain, Volume 1: Non-neoplastic Disease*, they have succeeded admirably. That should not surprise anyone who is familiar with the teaching techniques of Drs. Bradley and Brant-Zawadzki.

This volume, the first of two on non-neoplastic disease of the brain, focuses on traumatic, hemorrhagic, and vascular diseases of the intracranial contents, as well as on normal and abnormal flow patterns. Each of the 100 cases is organized so that the images and clinical history are on the left-hand page, and a description of the findings, the diagnosis, a discussion, and references are on the facing page. Most of the images are of reasonably high quality, the discussions are accurate and succinct, and the references are few and pertinent. Each case takes only a few minutes to digest, and this makes the book especially useful when one does not have the time to read a more involved text. The only negative point is that the images do not always illustrate all of the abnormalities described in the text.

This is not intended to be a comprehensive reference. It will be more useful for the busy radiologist who reads MRI scans in daily work than for subspecialists in radiology. In addition, radiology residents and staff/residents specializing in neurology or neurosurgery may enjoy sitting down with this work for a quick review or introduction to MRI.

Other volumes in this series will discuss neoplastic diseases of the brain, the spine, the head and neck, the musculoskeletal system, the body, the cardiovascular system, the pediatric patient, and principles/artifacts of MRI. An enticing option is available for this series: it has been reproduced on a single videodisc which allows an interactive approach. The images can be viewed with or without the clinical history or organ system orientation. Additional images, color images, and "movie" loops are available in this expanded format as well.

SCOTT A. ROSENBLOOM, MD
Staff Neuroradiologist
Division of Radiology
The Cleveland Clinic Foundation

CHRONIC MYELOGENOUS LEUKEMIA: MOLECULAR APPROACHES TO RESEARCH AND THERAPY

Edited by Albert B. Deisseroth and Ralph B. Arlinghaus
Marcel Dekker

Since 1960, when Nowell and Hungerford first described the Philadelphia chromosome, knowledge of this chromosomal translocation has expanded steadily. Recently, this growth of knowledge has been explosive. This, the 13th volume in Marcel Dekker's series of hematology compendia, is an excellent review of the molecular biologic aspects of this disorder.

Both editors are highly regarded experts in the field of chronic myelogenous leukemia, and they have assembled a sterling group of experts to describe individual areas of this field. The M.D. Anderson Cancer Center is well represented, since the editors are from that institution.

This textbook is quite readable. The first of its five parts presents detailed analyses of the animal and viral models for chronic myelogenous leukemia. The next seven chapters deal with the bcr-abl gene and its structure. The next three chapters analyze cellular models for the disease. The next six chapters describe therapy of chronic myelogenous leukemia, with emphasis on bone marrow transplantation and its curative potential. The text ends with a chapter on future directions in research and therapy.

As with all textbooks in rapidly growing fields, some areas are not discussed. One area is autografting with cultured marrow: some feel that long-term tissue culture of chronic myelogenous leukemia marrow can eradicate the Philadelphia-chromosome-positive cells while encouraging Philadelphia-chromosome-negative hematopoietic cells to rise in number. Also not described is the significance of minimal residual disease detected by polymerase chain reaction in patients after allogeneic bone marrow transplantation.

This textbook provides the molecular biologist with a current overall analysis of the bcr-abl locus and the protein that it transcribes. On the other hand, clinicians may find the emphasis on molecular biology overwhelming, and the book is not as helpful in the daily management of patients with this disorder. Still, the book would be an excellent addition to the library of molecular biologists dealing with chronic myelogenous leukemia.

ALAN E. LICHTIN, MD
Department of Hematology and Medical Oncology
The Cleveland Clinic Foundation

ASTHMA, ITS PATHOLOGY AND TREATMENT

Edited by Michael A. Kaliner, Peter J. Barnes, and Carl G.A. Persson
Marcel Dekker

During the past decade, an explosion of information implicating chronic airway inflammation and hyperreactivity in the pathophysiology of asthma has led to a consensus that these are central features of the disease. This book, volume 49 of *Lung Biology In Health and Disease*, is a state-of-the-art summary of the pathophysiology and treatment of asthma. The editors and contributors are leading investigators from both sides of the Atlantic.

The text is well organized and readable. The first chapter summarizes recent alarming epidemiological trends in asthma mortality. The next 17 chapters examine the pathogenesis of airway hyperreactivity, including discussions of the role of neural mechanisms, various cellular components, and inflammatory mediators such as platelet activating factor and leukotrienes. The last 6 chapters detail the mechanisms of currently used agents, and consider their role in the treatment of asthma.

The work would be enhanced by an overview of the various inflammatory components discussed. Also, a chapter detailing how this new knowledge might be used clinically would be helpful. Specifically, a discussion of investigational drugs should have been included.

These shortcomings aside, the work is scholarly and up-to-date: most chapters are referenced with citations from the past 5 years. The text is augmented with schematic diagrams that interrelate components suspected of affecting the pathogenesis of asthma. The book's features make it appropriate for anyone with an investigative interest in bronchial asthma and airway hyperreactivity, and it is well suited for a medical reference library.

MANI S. KAVURU, MD
Department of Pulmonary and
Critical Care Medicine
The Cleveland Clinic Foundation