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<i>Issue Date</i>	<i>Closing Date</i>	<i>Issue Date</i>	<i>Closing Date</i>
March-April	February 1, 1993	May-June	April 1, 1993
July-August	June 1, 1993	September-October	August 2, 1993
		November-December	October 1, 1993

MIDWEST

RESIDENCY PROGRAM DIRECTOR — Grant Medical Center seeks a Board Certified family physician for the position of Program Director of the Family Practice Educational and Residency Training Program. The Director will plan, organize, direct, monitor and evaluate the clinical educational activities associated with the family practice residency education programs. This longstanding university affiliated Program is ACGME approved to train 36 residents in a 450-bed full service tertiary care medical center. The anticipated date of hiring is March 1993. The Directorship is a tremendous opportunity for the individual with appropriate clinical, administrative, and teaching experience. Send a letter of application and Curriculum Vitae to: Benjamin Humphrey, M.D., Chairperson, Search Committee, Department of Medical Education, Grant Medical Center, 111 S. Grant Ave., Columbus, OH 43215. Phone: (614) 461-3290; Fax: (614) 341-2205.

FAMILY PRACTITIONERS — Primary care community health center with 20 providers seeks additional family practitioners, and OB/GYN. Competitive salary, academic affiliation, load repayment, paid malpractice, flexible benefit package. NHSC and IDPH eligible. Medical Director position also available for experienced primary care provider who desires part-time clinical and part-time administrative practice. CV to John F. Frana, Executive Director, Crusader Clinic, 120 Tay Street, Rockford, Illinois 61102. Phone: (815) 968-0286.

NORTHEAST

UPSTATE NEW YORK — Primary Care Opportunities — Eisenbud & Associates, Inc., a health care consulting firm specializing in physician recruitment, has been retained by several hospitals in rural, suburban and urban areas in the Northeast to help them recruit board certified/board eligible physicians. Emergency medicine and locum tenens opportunities also available. Our clients offer: generous compensation packages; relocation assistance; all fees and expenses paid; and positions in partnership, group, HMO and hospital practice settings. If

interested, please call or send CV to: Barbara G. Eisenbud, Eisenbud & Associates, Inc., 757 Panorama Road, Villanova, PA 19085. Phone: (800) 342-2890, FAX: (215) 527-7732.

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MEDICAL DIRECTOR — needed for HIV clinic in beautiful SW Florida. Full time responsibilities include: medical examinations, clinical drug trials and ARNP supervision. Experienced or recently trained internist, FP, or ID, preferred. Send resume to: Comprehensive Care Clinic, 150 East Ave. S., Sarasota, FL 34237.

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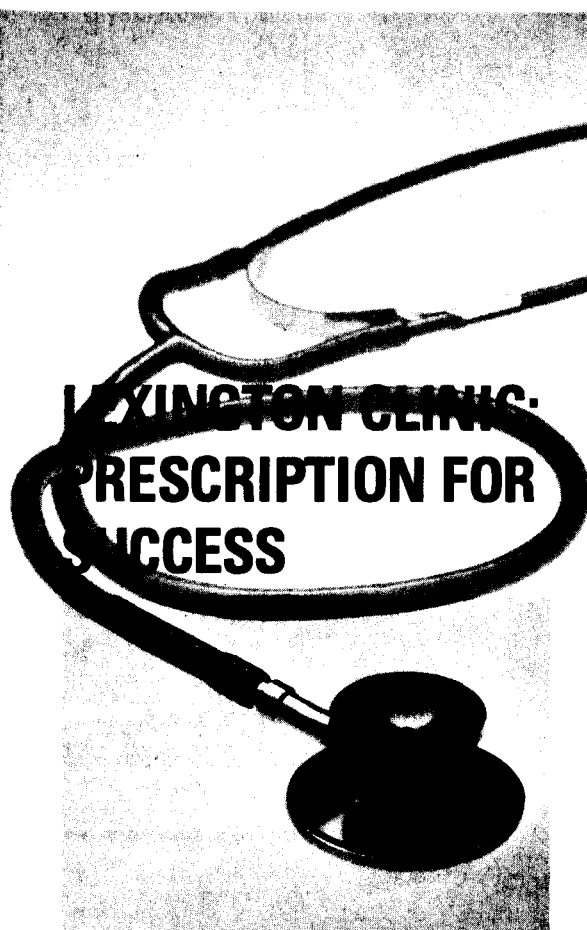
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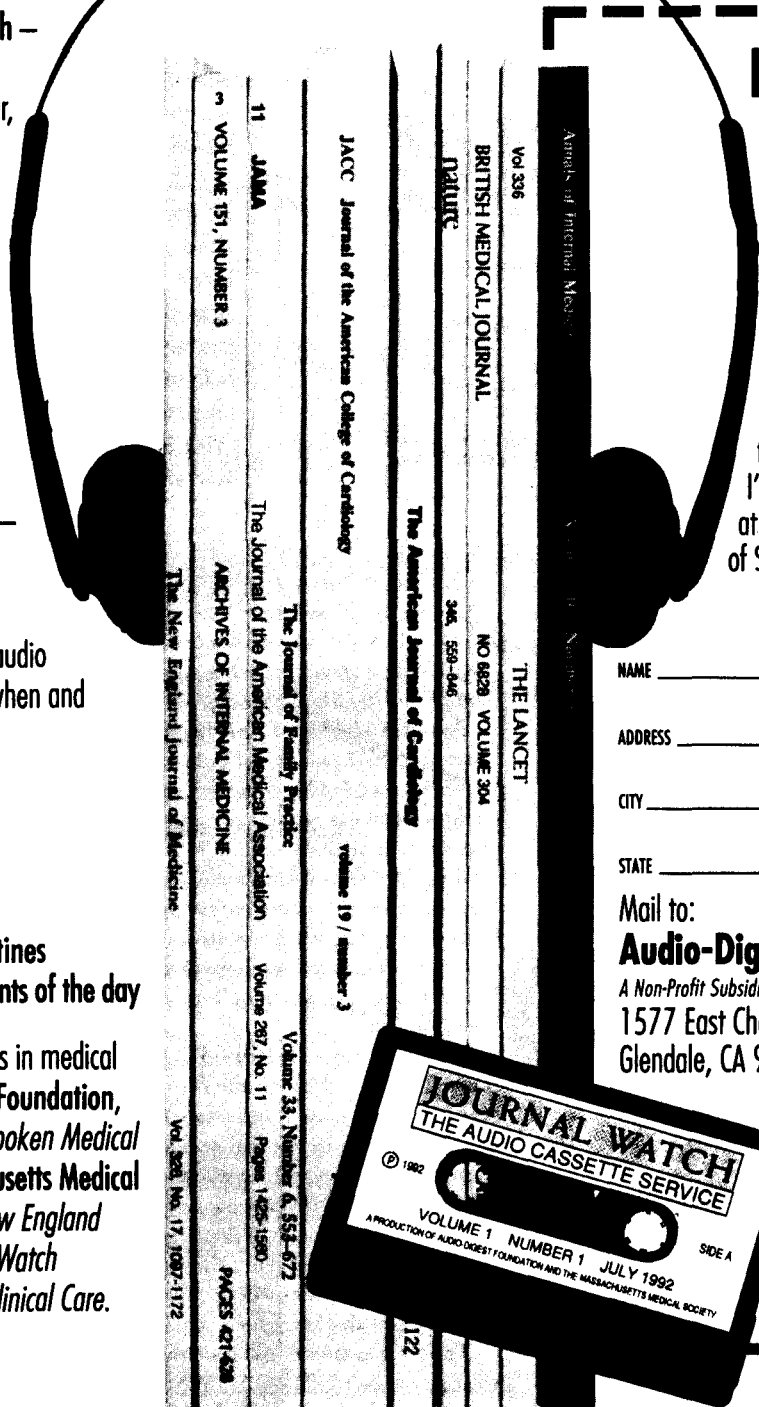
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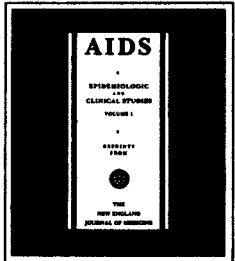
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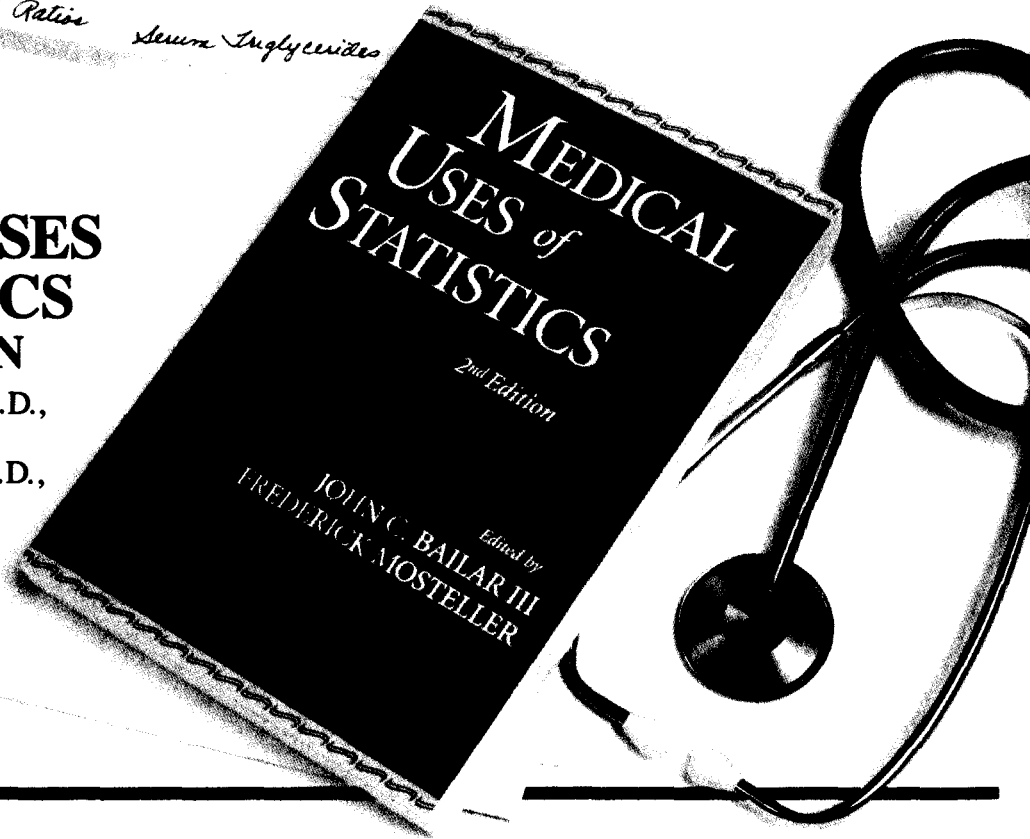
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CONTRAINDICATIONS: SECTRAL is contraindicated in: 1) persistently severe bradycardia; 2) second- and third-degree heart block; 3) overt cardiac failure; 4) cardiogenic shock. (See WARNINGS)

WARNINGS: Cardiac Failure: Sympathetic stimulation may be essential for support of circulation in patients with diminished myocardial contractility and inhibition by β -adrenergic receptor blockade may precipitate more severe failure. Although β -blockers should be avoided in overt cardiac failure, SECTRAL can be used cautiously when heart failure is controlled with digitalis and/or diuretics. Digitalis and SECTRAL impair AV conduction. Withdraw SECTRAL if cardiac failure persists. **In Patients Without a History of Cardiac Failure:** In patients with aortic or mitral valve disease or compromised left ventricular function, continued depression of the myocardium with β -blockers over time may lead to cardiac failure. Digitalize patients at first signs of failure, and/or give a diuretic and observe closely. Withdraw SECTRAL if cardiac failure persists.

Exacerbation of Ischemic Heart Disease Following Abrupt Withdrawal: Abrupt discontinuation of some β -blockers in coronary artery disease patients may exacerbate angina; in some cases, myocardial infarction and death have been reported. Caution such patients against interruption of therapy without a physician's advice. Even in the absence of overt ischemic heart disease, withdraw SECTRAL gradually over a period of about two weeks; observe carefully and advise patients to minimize physical activity during this time. (If desired, patients may be transferred directly to comparable doses of an alternative β -blocker without interruption of β -blocking therapy.) If exacerbation of angina occurs, restart full-dose anti-anginal therapy immediately and hospitalize patient until stabilized.

Peripheral Vascular Disease: β -antagonists reduce cardiac output and can precipitate/aggravate arterial insufficiency in patients with peripheral or mesenteric vascular disease. Exercise caution and observe such patients closely for progression of arterial obstruction.

Bronchospastic Diseases: Patients with Bronchospastic Disease Should, in General, Not Receive a β -Blocker. Because of its relative β_1 -selectivity, low doses of SECTRAL may be used cautiously in such patients who do not respond to, or cannot tolerate, alternative treatment. Since β_1 -selectivity is not absolute and is dose-dependent, use lowest possible dose of SECTRAL initially, preferably in divided doses. Make bronchodilator, e.g., theophylline, or a β_2 -stimulant, available in advance with instructions for use.

Anesthesia and Major Surgery: The necessity/desirability of withdrawing β -blockers prior to major surgery is controversial; the heart's impaired ability to respond to β -adrenergically mediated reflex stimuli may enhance the risk of excessive myocardial depression during general anesthesia. Difficulty in restarting and maintaining the heartbeat also has been reported with beta-blockers. If treatment is continued, take special care when using anesthetics that depress the myocardium; use lowest possible SECTRAL dose. SECTRAL, like other β -blockers, is a competitive inhibitor of β -receptor agonists, so its effects can be reversed by cautious administration of such agents (e.g., dobutamine or isoproterenol). Symptoms of excessive vagal tone (e.g., profound bradycardia, hypotension) may be corrected with atropine.

Diabetes and Hypoglycemia: β -blockers may potentiate insulin-induced hypoglycemia and mask some symptoms such as tachycardia, dizziness and sweating are usually not significantly affected. Warn diabetics of possible masked hypoglycemia.

Thyrotoxicosis: β -adrenergic blockade may mask some clinical signs (tachycardia) of hyperthyroidism. Abrupt withdrawal of SECTRAL may precipitate a thyroid storm in patients suspected of developing thyrotoxicosis.

PRECAUTIONS: Impaired Renal or Hepatic Function: While there are no U.S. studies, foreign published experience shows that acebutolol has been used successfully in chronic renal insufficiency. Acebutolol is excreted via the G.I. tract, but the active metabolite, diacetolol, is eliminated mainly by the kidney. A linear relationship exists between renal clearance of diacetolol and creatinine clearance (Cl_{Cr}); reduce daily dose of acebutolol by 50% when Cl_{Cr} is less than 50 mL/min and by 75% when it is less than 25 mL/min. Use cautiously in patients with impaired hepatic function.

SECTRAL has been used successfully and without problems in elderly patients in U.S. clinical trials without specific dosage adjustment. However, in the elderly, lower maintenance doses may be required because bioavailability of SECTRAL and its metabolite are approximately doubled.

Information for Patients: Warn patients, especially those with evidence of coronary artery disease, against interruption or discontinuation of SECTRAL without physician supervision. Although cardiac failure rarely occurs in properly selected patients, advise patients to contact a physician if signs or symptoms suggestive of impending CHF, or unexplained respiratory symptoms, develop.

Warn patients of possible severe hypertensive reactions from concomitant use of α -adrenergic stimulants, e.g., nasal decongestants used in OTC cold medicines and nasal drops.

Clinical Laboratory Findings: SECTRAL, like other β -blockers has been associated with development of antinuclear antibodies (ANA). In prospective clinical trials, patients receiving SECTRAL had a dose-dependent increase in the development of positive ANA titers. Symptoms related to this laboratory abnormality were infrequent. Symptoms and ANA titers were reversible upon discontinuation of SECTRAL.

Drug Interactions: Catecholamine-depleting drugs may have additive effects when given with β -blockers. Observe patients treated with both agents closely for evidence of marked bradycardia or hypotension which may present as vertigo, syncope/ presyncope, or orthostatic changes in blood pressure without compensatory tachycardia. Exaggerated hypertensive responses have been reported from use of β -adrenergic antagonists with α -adrenergic stimulants, including those in OTC cold remedies and vasoconstrictive nasal drops. Nonsteroidal anti-inflammatory drugs may blunt antihypertensive effects of beta-blockers.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Chronic oral toxicity studies in rats and mice, at doses 15 times the maximum recommended (60 kg) human dose, did not indicate carcinogenic potential for SECTRAL. Diacetolol, the major metabolite in man, was without carcinogenic potential in rats at doses up to 1800 mg/kg/d. SECTRAL and diacetolol also had no mutagenic potential in the Ames Test. No significant impact on reproductive performance or fertility was found in rats following SECTRAL or diacetolol doses of up to 240 or 1000 mg/kg/d, respectively.

Pregnancy: Teratogenic Effects: Pregnancy Category B: No teratogenic effects were seen in rat or rabbit reproduction studies utilizing SECTRAL doses that were, respectively, approximately 31.5 and 6.8 times the maximum recommended human dose. At this dose in the rabbit, slight fetal growth retardation was noted; this was considered to be a result of maternal toxicity (evidenced by reduced food intake, lowered rate of body weight gain, mortality). Diacetolol studies (doses up to 450 mg/kg/d in rabbits and up to 1800 mg/kg/d in rats) showed no evidence of fetal harm other than a significant elevation in postimplantation loss with 450 mg/kg/d, a level at which food consumption and body weight gain were reduced in rabbit dams; there was a nonstatistically significant increase in incidence of bilateral cataract in rat fetuses from dams treated with 1800 mg/kg/d. There are no adequate and well-controlled trials in pregnant women; SECTRAL should be used during pregnancy only if potential benefit justifies risk to the fetus.

Nonteratogenic Effects: Human studies indicate that acebutolol and diacetolol cross the placenta. Neonates of mothers who received acebutolol during pregnancy have reduced birth weight, decreased blood pressure, and decreased heart rate.

Labor and Delivery: Effect on labor and delivery in pregnant women is unknown. Animal studies have shown no effect of SECTRAL on the usual course of labor and delivery.

Nursing Mothers: Acebutolol and diacetolol appear in breast milk (milk: plasma ratio of 7:1 and 12:2, respectively). Use in nursing mothers is not recommended.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: SECTRAL is well tolerated in properly selected patients. Most adverse effects have been mild, not required therapy discontinuation, and tended to decrease as treatment duration increases.

The incidence of treatment-related side effects (volunteered and elicited) derived from U.S. controlled clinical trials in patients with hypertension, angina and arrhythmia follows. Numbers represent percentage incidence for SECTRAL (N = 1002) versus placebo (N = 314), respectively.

Cardiovascular: Chest pain 2%, 1%; Edema 2%, 1%. **CNS:** Depression 2%, 1%; Dizziness 6%, 2%; Fatigue 11%, 4%; Headache 6%, 4%; Insomnia 3%, 1%; Abnormal dreams 2%, 1%. **Dermatologic:** Rash 2%, 1%. **Gastrointestinal:** Constipation 4%, 0%; Diarrhea 4%, 1%; Dyspepsia 4%, 1%; Flatulence 3%, 1%; Nausea 4%, 0%. **Genitourinary:** Micturition (frequency) 3%, <1%. **Musculoskeletal:** Arthralgia 2%, 2%; Myalgia 2%, 0%. **Respiratory:** Cough 1%, 0%; Dyspnea 4%, 2%; Rhinitis 2%, <1%. **Special Senses:** Abnormal Vision 2%, 0%.

The following selected (potentially important) side effects were seen in up to 2% of SECTRAL patients: **Cardiovascular:** hypotension, bradycardia, heart failure. **CNS:** anxiety hyper/hypoesthesia, impotence. **Skin:** pruritus. **Gastrointestinal:** vomiting, abdominal pain. **Genitourinary:** dysuria, nocturia. **Liver and Biliary:** small number of reported cases of liver abnormalities (increased SGOT, SGPT, LDH). In some cases, increased bilirubin or alkaline phosphatase, fever, malaise, dark urine, anorexia, nausea, headache, and/or other symptoms have been reported. In some cases, symptoms and signs were confirmed by rechallenge. Abnormalities were reversible upon drug cessation. **Musculoskeletal:** back and joint pain. **Respiratory:** pharyngitis, wheezing. **Special Senses:** conjunctivitis, dry eye, eye pain. **Autoimmune:** extremely rare reports of systemic lupus erythematosus.

Incidence of drug-related adverse effects (volunteered and solicited) based on SECTRAL dose is shown below. (Data from 266 hypertensive patients treated for 3 months on a constant dose.)

Body System	400 mg/day (N = 132)	800 mg/day (N = 63)	1200 mg/day (N = 71)
Cardiovascular	5%	2%	1%
Gastrointestinal	3%	3%	7%
Musculoskeletal	2%	3%	4%
Central Nervous System	9%	13%	17%
Respiratory	1%	5%	6%
Skin	1%	2%	1%
Special Senses	2%	2%	6%
Genitourinary	2%	3%	1%

Potential Adverse Effects: Certain adverse effects not listed above have been reported with other β -blocking agents and should be considered as potential adverse effects of SECTRAL.

CNS: Reversible mental depression progressing to catatonia, an acute syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuro-psychometrics.

Cardiovascular: Intensification of AV block (see CONTRAINDICATIONS). **Allergic:** Erythematous rash, fever with aching and sore throat, laryngospasm, respiratory distress.

Hematologic: Agranulocytosis, nonthrombocytopenic and thrombocytopenic purpura. **Gastrointestinal:** Mesenteric arterial thrombosis, ischemic colitis.

Miscellaneous: Reversible alopecia, Peyronie's disease. The oculomucocutaneous syndrome associated with prolapia has not been reported with SECTRAL.

Keep at room temperature, Approximately 25°C (77°F).

3482-5 6/21/89