1981 YEAR BOOK OF CLINICAL PHARMACY

WOOLLEY

The YEAR BOOK of

Clinical Pharmacy

1981

Edited by

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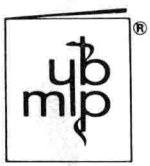

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Preface

Peter Drucker has stated that the measure of the executive is the ability to "get the right things done." This observation seems to be particularly true of the practicing health professional, for whom getting the right things done means being prepared and able to intervene for the benefit of the patient. In modern therapeutics, maximum effectiveness requires continuous adjustment to an enormous volume of new information, reappraisal of technique and application of sound pharmacologic principles to therapy of the individual patient.

But how does the busy practitioner keep up to date? The periodical literature is clearly a fundamental source of new information, but today the reporting of therapeutic advances is awesome in its dimensions. The number of journals is large, the information is often incremental and the special interest character of research aims can often obscure, to name just a few factors. The intent of this YEAR BOOK OF CLINICAL PHARMACY is to tackle some of these problems in a pleasant, meaningful and time-tested way.

The YEAR BOOK concept, namely, the annual presentation of selected published articles in condensed form (more detail than the conventional abstract) with illustrations and editorials, has been an important factor in continuing professional education for 80 years. Each year, hundreds of thousands of health professionals study and learn from the YEAR BOOKS. While the YEAR BOOK is intended to be studied at leisure, it can also be useful for periodic reference and review. Subject and Author Indexes are provided for this purpose.

The articles in this first YEAR BOOK OF CLINICAL PHARMACY were selected with three objectives in mind: (1) that they contain information which would correlate theory with practical therapeutics, (2) that they would acquaint the reader with evolving concepts and (3) that they would provide a basis for judgment in the selection of therapeutic agents. In preparing the editorials, an effort was made to briefly review the pharmacology of the major drugs involved.

The introduction of this new YEAR BOOK OF CLINICAL PHARMACY hopefully will add a new dimension to continuous learning and contribute meaningfully to the professional excellence of its readers.

Bruce H. Woolley, Pharm. D.
November, 1980

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Anesthetic and Analgesic Agents

Anesthetic Agents

Hypertension and Anesthesia: Cause for Concern. David A. Cross and Jack R. Collins[1] (Jewish Hosp. of St. Louis) review the anesthetic management of hypertensive patients. It is estimated that elevated arterial pressure is found in 20% of the United States' population, only half the hypertensive patients are known, only half the known hypertensives are treated and only half the treated hypertensives are adequately treated and controlled. Hypertension is the most significant risk factor in cardiovascular mortality.

Distinct hypertension is a blood pressure of 160/95 mm Hg, and borderline hypertension is a pressure of 140/90 mm Hg. With the use of available drugs singly or in combination, it is possible to control blood pressure adequately in most patients. Whereas normalization of pressures should be the goal, even partial lowering gives significant benefit.

Because of the theoretical hazards of unresponsive hypotension during anesthesia, discontinuation of some types of antihypertensive therapy before administration of anesthesia has been recommended. However, because untreated hypertension constitutes a serious risk to patients having anesthesia and surgery, before anesthesia the antihypertensive therapy should not be withdrawn without a compelling reason.

Administration of elective anesthesia to patients of any age with unevaluated, untreated or uncontrolled systolic hypertension is difficult to justify. A single elevated blood pressure reading in a patient before operation deserves further investigation, even if surgical delay is necessary. Hypertension should be evaluated, treated and controlled preoperatively in patients having nonemergency surgery regardless of their degree of lability. Patients whose blood pressure is adequately controlled with antihypertensive medication should be evaluated for cardiovascular or renal disease; their status should be optimal from both standpoints before administration of elective anesthesia. The pharmacologic actions of antihypertensive agents should be taken into account when anesthetic agents and techniques are chosen for a treated hypertensive patient.

Acute hypertension that is seen immediately after laryngoscopy and intubation is usually best treated with an increase in anesthetic depth. If an idiopathic hypertensive crisis appears on emergence from anesthesia in the recovery room, the use of vasodilator drugs such as diazoxide, chlorpromazine, trimethaphan or sodium nitroprusside is

(1) South. Med. J. 71:161–165, February, 1978.

indicated. The use of sodium nitroprusside is preferred because of its rapid onset and short duration of action.

The untreated or uncontrolled hypertensive patient who needs emergency surgery presents a difficult situation. If a rapid sequence or awake tracheal intubation is planned, and if time permits, blood pressure should be controlled with nitroprusside prior to induction. Although the use of topical anesthesia in the candidate for awake intubation is controversial, its use is justified in the patient with uncontrolled hypertension. If spinal or epidural analgesia is planned, its effects on blood pressure should first be determined, with the means of rapidly lowering blood pressure readily available.

▶ [Anesthetic management of hypertensive patients has been a problem for quite some time. Adequate control of blood pressure is of prime importance and is best achieved prior to induction of anesthesia. This article, in which the authors review the problem and present their opinions as to proper patient management, should be of interest to anyone who is involved in the use of these agents.] ◀

Toxic Effects of Local Anesthetics are discussed by Rudolph H. de Jong[2] (Univ. of Illinois Med. Center, Chicago). Toxic actions of local anesthetics affect structures contacted directly by the drug and those more distant organs reached by drug absorbed or injected into the circulation. Although most local anesthetics are free from tissue-irritating properties, traumatic injection, high drug concentration, delayed absorption and other mechanical factors may cause microscopic and occasionally macroscopic tissue damage.

In vivo effects of local anesthetics on blood elements are negligible. Vasodilation, though demonstrable in the laboratory, contributes little to hypotension from local anesthetic overdose. Allergic manifestations to local anesthetics are extremely rare and are virtually limited to ester-linked agents.

The central nervous system mirrors the concentration of the anesthetic in the blood. The higher the blood level, the more profound the effect of the anesthetic on the brain. A dose-related spectrum of cerebral effects is seen. Two ways of minimizing central nervous system toxicity of local anesthetics exist: control at the source and control at the central target. Source control over toxicity is exerted by total dose administered and by rapidity of drug entry into the bloodstream. A vasoconstrictor such as epinephrine incorporated into the anesthetic solution shows absorption and reduces the peak blood level. The blood level, however, can creep up insidiously when a steady-rate infusion is administered. Brain toxicity can be reduced by pharmacologic and physiologic means that render it less susceptible to local anesthetic-induced convulsions. Diazepam raises the brain's seizure threshold to lidocaine and can successfully abort ongoing convulsions.

The first concern in treating an intense drug reaction is to prevent patient injury, as may result from uncontrolled movements of a convulsion. The patient should be breathing adequately and have an unobstructed airway. Cardiac rhythm and rate, peripheral perfusion and blood pressure should be monitored closely.

▶ [The authors review many of the direct and indirect toxic effects reported with the use of

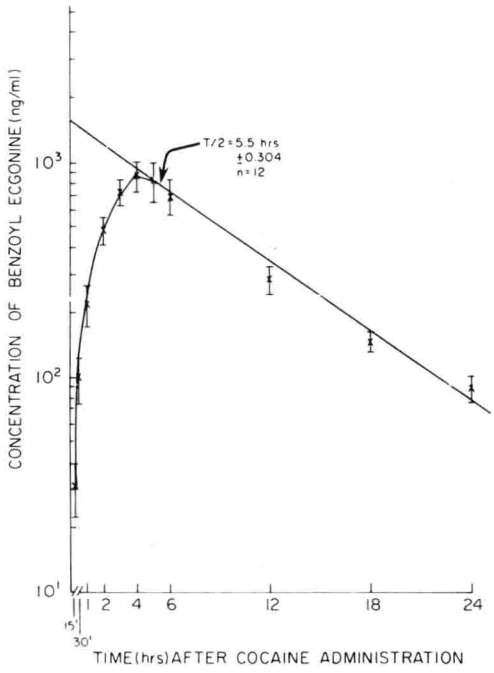
(2) J.A.M.A. 239:1166–1168, Mar. 20, 1978.

local anesthetics. Their conclusions are well taken, and those who administer these agents should be familiar with proper safeguards. It would seem apparent that this knowledge is the basis for any type of drug therapy.] ◀

Metabolism of Intranasally Applied Cocaine was studied by Michael E. Johns, Ann R. Berman, John C. Price, Richard C. Pillsbury and Robert L. Henderson[3] (Walter Reed Army Med. Center). Little is known about the metabolism and toxicity of cocaine in man, a drug clinically in use for almost 100 years. The introduction of a radioimmunoassay (RIA) procedure for detecting cocaine metabolites in the urine and serum serves as a valuable adjunct to other methods used to detect cocaine. The procedure is specific for benzoylecgonine, the major metabolite of cocaine.

The appearance of significant amounts of benzoylecgonine in the serum 15 minutes after topical application to the nasal mucosa (Fig 1) substantiated the fact that cocaine is readily absorbed and metabolized. A peak level in the plasma was found from 4 to 6 hours after topical administration. Absorption of the drug from the nasal mucosa lasted as long as 3 hours. The half-time clearance of the metabolite from serum was 5.5 hours. After hydrolysis of cocaine, the metabolites were excreted in the urine. Twenty-four hour urine samples col-

Fig 1.—Concentration curve of benzoylecgonine in serum as related to time after application of 200 mg cocaine intranasally, showing peak level, half-life and clearance from serum as average for the 12 patients. (Courtesy of Johns, M. E., et al.: Ann. Otol. Rhinol. Laryngol. 86:342-347, May-June, 1977.)



(3) Ann. Otol. Rhinol. Laryngol. 86:342–347, May–June, 1977.

lected from 8 patients showed a mean of 20.1 ng benzoylecgonine per ml.

Establishing a maximum safe dose for cocaine is not a simple matter. Many variables must be evaluated, including route of administration, anatomical site of application, method of application and rate of metabolism. Further studies of the metabolism and toxicity of cocaine used in the clinical setting are needed. The least amount of cocaine necessary to perform a procedure should be used. A test dose should be applied in small amounts prior to application of the total dose to observe for rare idiopathic reactions. A knowledge of the clinical signs and symptoms of cocaine toxicity and the availability of the necessary drugs and equipment to treat such a reaction should be prerequisite to the use of cocaine.

▶ [These data show that cocaine is readily absorbed and metabolized when applied intranasally. However, the authors express concern that establishing a maximum safe dose is a difficult matter and many variables must be considered. Any physician who prescribes cocaine should be familiar with the signs and symptoms of cocaine toxicity and have the expertise for adequate monitoring for rare idiopathic reactions.] ◀

Anti-inflammatory Agents

Multicenter Comparison of Naproxen and Indomethacin in Rheumatoid Arthritis. Naproxen is a nonsteroidal anti-inflammatory, analgesic drug of low toxicity that was recently introduced in the United States for the treatment of rheumatoid arthritis. J. J. Castles *et al.*[4] report a double-blind crossover comparison of naproxen and indomethacin in 132 patients with rheumatoid arthritis at six centers. Naproxen was used in a dose of 250 mg twice daily or 500 mg at bedtime and indomethacin in a dose of 25 mg 4 times daily. Only ambulatory outpatients with classic or definite rheumatoid arthritis were included in the study. The age range was 21–70 years. The 16-week double-blind phase was preceded by a single-blind placebo period carried out for 2 weeks.

Treatment was evaluable in 107 patients with the disease for an average of 8.7 years; 80% were in the American Rheumatism Association (ARA) functional class II. Efficacy evaluations, based on objective indices of arthritis activity, such as number of clinically active joints, walking time and duration of morning stiffness, were nearly identical for the three regimens. A single daily dose of naproxen was as effective as the twice-daily treatment. Adverse central nervous system effects were fewer with naproxen than with indomethacin. The two drugs had comparable adverse gastrointestinal effects. The only serious adverse effect was a gastric ulcer in a patient with a history of ulcer disease who received naproxen.

Naproxen and indomethacin produced similar relief of rheumatoid symptoms in this study. Few adverse effects occurred with either drug, but each treatment period lasted only 1 week. Single daily naproxen dosage gave results comparable with those of twice-daily treatment. The general equivalence of these regimens could prove ad-

(4) Arch. Intern. Med. 138:362–366, March, 1978.