PHARMACOLOGY OF A NEW, SYNTHETIC ANALOGUE OF RESERPINE. W. E. Barrett, R. Rutledge* and A. J. Plummer. Research Dept., CIBA Pharmaceutical Products Inc., Summit, N. J.

A synthetic derivative of methyl reserpate was found to possess sedative but not hypotensive activity. This compound, Su-7064, is methyl O-(2-tetrahydropyranyl) reserpate. In the unanesthetized dogs, intravenous doses of 250 γ, 500 γ and 1.0 mg/kg produced sedation within 30 minutes. The sedation persisted from 8 to 24 hours. Single oral doses of 2.0 to 3.0 mg/kg produced in dogs sedation or tranquilization which also lasted from 8 to 24 hours. A more detailed analysis of the pharmacological activity of this rapidly acting tranquilizing reserpine derivative will be presented.

COMPARISON OF THE EFFECTS OF CONGENERS OF LYSERGIC ACID DIETHYLAMIDE AND TRYPTOPHANE IN NORMAL HUMAN VOLUNTEERS. Henry B. Murphree, Jr.,* Elizabeth H. Jenney and Carl C. Pfeiffer. Dept. of Pharmacology, Emory University, Atlanta, Georgia.

Comparison was made in normal human volunteers of the effects of l-lysergic acid diethylamide, dl-α-methyl tryptamine, 5-hydroxytryptamine, dl-DOPA, d-DOPA and l-DOPA with d-lysergic acid diethylamide. The subjects were highly trained to recognize the effects of d-LSD and other hallucinogens. All compounds were given orally. Blood pressure, pulse rate, pupil diameter, body temperature, hand steadiness were measured at hourly intervals, and the subjects kept running diaries of subjective effects. l-LSD was previously reported by this department to have no effect in doses up to 2 mg. In this study, dosage was increased progressively to 10 mg with no effect. It was concluded that: 1) the preparation was highly pure, 2) no racemization occurred in the body, and 3) the levo- iosmer is less active than the dextro- by a factor greater than 400:1. dl-α-methyl tryptamine in a dose of 20 mg produced a subjective action similar to 50 μg of d-LSD. The effects appeared later, however, with a lag up to three hours. 5-hydroxytryptamine in a dose of 100 mg produced a fall in systolic and a rise in diastolic blood pressures together with a feeling of sedation, abdominal cramping, and muscle aching similar to those of d-LSD. Effects were delayed 6 to 8 hours after dosage. Oral DOPA produced no tangible CNS effects.

A COMPARISON OF THE EFFECTS OF IPRONIAZID AND d-AMPHETAMINE ON PSYCHOLOGICAL PERFORMANCE OF SCHIZOPHRENIC PATIENTS. Conan Kornetsky and Ogretta Humphries.* Dept. of Pharmacology and Experimental Therapeutics, Boston Univ. School of Med., Boston, Mass.

Ten chronic schizophrenic patients (6 males and 4 females) were tested on a variety of psychological tasks after the oral administration of iproniazid and d-amphetamine. Subjects were tested hourly for four consecutive hours after drug administration with the following performance tests: digit-symbol substitution, symbol copying, tapping speed, and pursuit rotor. Each subject received, on separate occasions, 100 and 150 mg of iproniazid, 10 and 20 mg of d-amphetamine, and a placebo. In addition to the various performance tests, blood pressure was recorded hourly after the drugs were given. The "double-blind" procedure was followed throughout. In contrast to an expected improvement in performance, the only statistically significant effect was a deficit in performance after 100 mg of iproniazid. Both 10 and 20 mg of d-amphetamine significantly raised systolic and diastolic blood pressure. Iproniazid caused a fall in blood pressure; however, this drop was not statistically significant.

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DOUBLE-BLIND EVALUATION OF METHAMINODIAZEPOXIDE (LIBRIUM ®). John H. Close,* John H. Gogerty and R. W. Payne. Dept. of Pharmacology and Medicine, Univ. of Okla. Sch. of Med., Okla. City, Okla.

Fourteen adult hospitalized patients of both sexes with diverse clinical diagnoses but who presented the common manifestation of severe chronic disabling agitation were entered in the present study. Alternate patients were started on Librium 10 mg. or lactose in identical capsules, identified only by code number, given t.i.d. with cross over after 4-5 weeks. The response of each patient was graded on a 5 point scale (from double minus to double plus) in terms of euphoria, depression, orientation, spontaneity, anxiety and sleeping pattern and was recorded at approximately biweekly intervals. Seven patients completed the study with a total of 90 observations per category while on Librium compared to 50 while on placebo. The total score on Librium was plus 150 while that for placebo was minus 35, with even distribution of response among the categories. Specific sustained clinical improvement occurred in 4 patients while on Librium, 1 while on placebo and 2 patients showed no substantial improvement on either medication. No toxic effects were observed with either medication.

NOISE TOLERANCE AS AN INDEX OF PSYCHOPHARMACOLOGIC RESPONSE. John H. Nodine, Tibor Bodi, Charlotte Blyn and Norman Burke (intr. by John H. Moyer). Hahnemann Medical College and Hospital, Philadelphia, Pa.

A series of noises were tape recorded, edited and standardized for intensity. The threshold intensity level necessary to produce a cutaneous galvanic response was then measured sequentially in patients with anxiety before and after various psychopharmacologic agents. The response threshold varied from 55 to 100 decibels and was found to correlate with the clinical response of the patients after treatment with phenobarbital, meprobamate, chlormezanone, two butyrophenone derivatives and placebo. The technique is promising in standardization of psychopharmacology research because it is entirely objective and is nonverbal in character.

HUMAN BIOASSAY IN PSYCHOPHARMACOLOGY. Tibor Bodi, Peter E. Siegler, Howard A. Levy, Joseph W. Slap and John H. Nodine (intr. by John H. Moyer). Dept. of Medicine, Hahnemann Medical College and Hospital, Philadelphia, Penna.

Animal assay of psychopharmacologic agents does not substitute for direct human evaluation of clinical responses to these drugs. A two stage human bioassay technique has been standardized to determine the following: a) Pharmacologic effect of the potential drug in man. b) Optimum therapeutic dose and dose response curve in man. c) Acute and chronic toxicity studies. d) Calculation of the therapeutic index (T.I.) as the ratio of the minimal daily dose, ED_{75}, producing satisfactory clinical response and the dose, TD_{25}, causing toxic effect in 25% of patients. (TD_{25}/ED_{75}) e) Double blind comparative evaluation including inert placebo and a standard active drug. Beneficial and toxic effects are recorded on a dose response card and a dose response curve is obtained by plotting the percentage of patients showing moderate and marked improvement (or toxic effects) against drug dose. Representative examples of bioassay techniques are shown and the limitations of the method discussed.