detected. Effects on adrenergic, inhibitory responses have not been sufficiently investigated. A search is being made for qualitative differences in properties of various homologues in the chemical series. [*Compounds and financial support from Parke, Davis and Company.*]

Structure-activity relationship (SAR) and pharmacological peculiarities of new synthetic congeners of tetrahydrocannabinol. S. LOEWE and ROGER ADAMS (by invitation). *Dept. of Pharmacology, Univ. of Utah School of Medicine, Salt Lake City, Utah, and Noyes Chemical Laby., Univ. of Illinois, Urbana, Illinois.* Continued studies of the class of 1-hydroxy-3-alkyl-6,6,9-trimethyl-7,8,9,10-tetrahydro-dibenzopyrans (3-alkyl-R) demonstrate that variations in the 3-alkyl side-chain can produce high marihuana activity. SAR in this class is characterized by the following: 3-*n*-amyl-R has a potency (P) of 1.0, only $\frac{1}{16}$ that of the isomeric natural charas tetrahydrocannabinol; *n*-hexyl-R (pyrahexyl; P = 2.0) represents the peak potency in the 3-*n*-alkyl-R series. The P of some branched 3-side chain isomers of pyrahexyl (1-methyl-amyl; 1,1-dimethyl-butyl; 1-ethyl-2-methyl-propyl) is between 3.0 and 4.0. However, the most potent homolog in the branched 3-(1-methyl-alkyl)-R series was that with an alkyl of eight and not six C-atoms. 3-(1-methyl-octyl)-R has P = 38, *i.e.*, more than twice the potency of the most active natural congener. In some double-branched side-chain series, peak potency is also embodied in homologs with side-chains having more C-atoms than in the *n*-alkyl series. The most active of these substances is, for the time being, 3-(1,2-dimethyl-heptyl)-R (P over 100); less than one microgram per kg. elicits marked ataxia in the dog. Another potentiality is indicated in 1-methyl-nonyl-R. Its potency is only $\frac{1}{9}$th that of its next lower homolog, but its action persists for many days, whereas that of equi-effective doses of its congeners lasts several hours. Another peculiarity of SAR concerns the closely related 3-(1,1- and 1,2-dimethyl-heptyl)-Rs. Whereas, in microgram doses, the latter displays a selective marihuana activity, it is a potent convulsant when given in the threshold dose range for ataxia of the former compound. [*Assisted by grants-in-aid of research from the U. S. Public Health Service and from the Abbott Laboratories.*]

Anticonvulsant action of marihuana-active substances. S. LOEWE and LOUIS S. GOODMAN. *Dept. of Pharmacology, Univ. of Utah School of Medicine, Salt Lake City, Utah.* To elucidate further the unique neurological actions of cannabis principles and synthetic congeners, they were examined for anticonvulsant activity in rats. Natural charas tetrahydrocannabinol and its synthetic 3-*n*-hexyl ("pyrahexyl"), 3-(1-methyl-octyl) and 3-(1,2-dimethyl-heptyl) homologs were effective in the ratio of about 7:1:80: > 200 in abolishing the hindleg tonic extensor component of maximal electroshock seizures (60-cycle A.C., 150 mA., 0.2 sec., corneal electrodes). This potency ratio is rather similar to that of their ataxia potencies in the dog, thus suggesting that anticonvulsant and marihuana activity are closely related. Threshold doses were below those causing ataxia and other neurological signs. When tested for suppression of Metrazol convulsions, the same substances were found ineffective and exhibited a marked lethal synergism with Metrazol. The pattern of high anticonvulsant potency in the maximal electroshock test and absence of protection against Metrazol aligns the marihuana congeners with the diphenylhydantoin-type of anticonvulsant. Indeed, marihuana-like ataxia and catalepsy could be produced in dogs with appropriate doses of diphenylhydantoin. Anticonvulsant synergism between diphenylhydantoin and marihuana-active compounds could also be demonstrated. [*Assisted by grants-in-aid of research from the U. S. Public Health Service and the Abbott Laboratories. The cannabis congeners were synthesized by Professor Roger Adams.*]

Studies on the parenteral administration of hydrogen peroxide. ALLAN L. LORINCZ and J. J. JACOBY (introduced by J. M. Coon). *Dept. of Pharmacology, The Univ. of Chicago.* Intravenous oxygen has been used on several occasions clinically for the treatment of hypoxia and shock with reported benefit. Since in human blood, catalase rapidly decomposes hydrogen peroxide into water and molecular oxygen, studies on the parenteral administration of hydrogen peroxide solution to animals were undertaken to obtain an easily controlled and convenient method for intravascular oxygen administration.

Three per cent hydrogen peroxide exerted no deleterious effects on the blood of several animal species other than methemoglobin formation in those with very low catalase levels as shown by quantitative blood catalase activity determinations. Intravenous hydrogen peroxide tolerance in the dog and chicken was limited by methemoglobin formation, while in the rabbit and cat by gas embolism. In the cat, oxygen in the form of hydrogen peroxide could be administered intravenously at least twice as fast as in the form of oxygen gas without producing severe embolic signs.

Thirty mice given maximal subcutaneous doses of hydrogen peroxide twice daily for two weeks showed no gross or histologic deleterious effects other than temporary embolic phenomena and a 25 per cent incidence of local skin ulcers.

In the cat, intravenous hydrogen peroxide even in small amounts aggravated rather than reduced an existing hypoxia as shown by blood gas analyses. Also, little noteworthy benefit followed the use of