Studies on the metabolism of C\textsuperscript{14} carboxyl salicylate. Edward L. Alfen*, H. George Mandel* and Paul K. Smith. Dept. of Pharmacology, The George Washington Univ. School of Medicine. In the dog 1 gm. of C\textsuperscript{14} carboxyl-salicylate (10 μc. per gm.) was injected intravenously. Pooled urine was analyzed, using a 24-plate countercurrent distribution between pH 4.6 citrate buffer and amyl alcohol. Chemical, spectroscopic and radioactive assay indicated approximately one-half free salicylate, one-fourth hydroxyl-glycuronate, one-fifth salicylurate and none one-tenth gentisate.

In patients a similar dose yielded one-half salicylate, one-third glycuronates, one-tenth free salicylate and a few per cent gentisate. Hydrolysis of the glycuronate fraction did not yield gentisate or salicylate. After exhaustive extraction with ethyl acetate-alcohol mixture, chromatography of the glycuronate fraction indicated two glycuronates, only one of which gave a free-hydroxyl group test. These experiments are further evidence that, in man, glycuronates of salicylate are formed on either the hydroxyl or carboxyl groups. No evidence for the “acidoduraminsalicilico” of Baldoni was found.

In the rat no radioactivity appeared in the expired carbon dioxide after salicylate.

Pharmacologic effects of betaine hydrazide hydrochloride. John D. Archer, Joyce K. Howard and Joe B. Nash (introduced by G. A. Emerson). Univ. of Texas Medical Branch, Galveston. Betaine hydrazide HCl inhibits histidine decarboxylase and histaminase in vitro, but fails to protect sensitized guinea pigs from anaphylaxis (Nash et al., q.v.). The intraperitoneal LD\textsubscript{50} of betaine hydrazide HCl for white mice is about 450 mg./kg. Death occurs within 20 minutes from respiratory failure accompanying clonic convulsions. Phenobarbital, glucose, atropine and epinephrine are not effective antidotes. There is little cumulative toxicity. The compound is weakly cholinergic, as evidenced by salivation, urination and defecation, but not miosis, on parenteral administration. It is 1/6500 as effective as acetylcholine on the guinea pig ileum in vitro, but, in the intact dog, it affects neither the epinephrine response nor the tone or motility of the duodenum or ileum. Depressor doses in dogs are not potentiated by phystostigmine, but are fully inhibited by atropine. Acute toxicity in dogs involves bronchial constriction not effectively antagonized by atropine. Betaine HCl is not cholinergic in equimolecular amounts.

Phase-boundary potentials of atropine. T. C. Barnes and R. Beutner. Dept. of Pharmacology, Hahnemann Medical College of Philadelphia and Medical College of Alabama, Birmingham. The electrical action of drugs runs parallel with biological effects. In these experiments in each case the dose of atropine was given to 20 gm. mice and 200 ml. of saline in the oil-cell (from the same solution). One mg. produced 40 mv. negativity in the oil-cell and 0 mortality in mice; 2.4 mg. gave 52 mv. negativity and 33% mortality; 6 mg. produced 64 mv. and 100% mortality. These experiments suggest that many drugs such as atropine act on living tissue by generating phase-boundary potentials. The transient cerebral stimulation can be explained by this hypothesis. The effect of acetylcholine can be antagonized by atropine in vitro as in vivo. Thus 0.01% acetylcholine produces 50 mv. negativity in the oil-cell but only 10 mv. negativity after 0.01% atropine. Chemicals with positively charged phase-boundary potentials provide an antidote for atropine in vitro. Thus after atropine followed by sodium lauryl sulfonate the acetylcholine potential attains nearly its original value of 43 mv. negativity. It is possible that a similar antidote for atropine might be demonstrated in vivo. Experiments on the isolated rabbit gut are in progress.

Acute toxicity and antagonism of N-octyl bicycloheptene dicarbazimide (NOBD). Robert O. Bauer (introduced by George L. Maison). Dept. of Pharmacology, Boston Univ. School of Medicine. Previously observed fine tremors in animals exposed to NOBD via their respiratory tree (Fed. Proc., 8: 723, 1949) suggested an action on the central nervous system. This report supports this contention.

Lethal doses of NOBD intraperitoneally in rats or mice initiate within 30 minutes clonic unilateral