ficial, even though the book does contain an impressive bibliography of more than 800 citations. Actually, such an accusation has little justification. A truly exhaustive search of the literature has been made, and relatively few important omissions will be uncovered even by the specialist in the field. Suggestions for improvement can, of course, be made. For instance, the text bears signs of important omissions of data and condensations of treatment that rob it of much of the richness possible to include in a larger volume. Little space is devoted to methods of collecting, cleaning and storing the seeds of hardwoods that recently have come into wide use for shelterbelt, erosion and game food planting. It is true that little has been published on hardwood seeds even though much is known. Readers particularly interested in hardwoods will find a more complete treatment in the recent nursery handbook prepared by Engstrom and Stoeckeler.[1] The discussion of periodicity of seed production could have been strengthened materially by drawing upon horticultural literature on irregular bearing of apples and other fruits. Important studies of wind dissemination by Hesselman and others merit mention. The present status and future needs in the field of tree seed research are inadequately set forth. However, throughout the several chapters suggestions for valuable research will occur to the imaginative reader. Other subjects that might have been more completely developed for the American reader include the life history of seed, provenance and the behavior of seed in their natural environment. The Swedish and German explanations on maps and diagrams shown in the text should have been translated for American readers. The book does not bring together the status of knowledge on individual species. A manual covering this subject is now under preparation by the U. S. Forest Service.

On the whole, however, the book is scholarly, readable and informative. It fills a long-felt need. Not the least of its valuable contents is the 16-page glossary of tree seed terminology that immeasurably increases its utility. It is hoped that this book will help to open the field for intensive study during the coming years.

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SPECIAL ARTICLES

CROSS-CIRCULATION AS A METHOD IN THE STUDY OF DRUG FIXATION AND POISONING

IN the endeavor to study the mode of the vago-paralytic action of amytal, two cross-circulation experiments were performed in which one animal received amytal and the other paraldehyde; the latter does not paralyze the vagus. Both drugs were given one hour previous to the beginning of cross-circulation. It was believed that if amytal did not prevent the formation of acetylcholine the partner under paraldehyde anesthesia might show cardiac inhibition and fall of blood pressure following the stimulation of the vagus of the amytalized animal. The results were disappointing, however, because before the beginning of cross-circulation the vagus of the amytalized animal was paralyzed and the vagus of the other animal was not, whereas during the progress of the cross-circulation the vagus of the amytalized partner became more responsive and the vagus of the other partner less and less responsive to faradic stimulation. This substantiated the original assumption of the authors[1] that fixed anesthetics do not actually remain permanently fixed in the tissues.

It was decided to study this problem further by administering 250 mg of barbital sodium per kgm of body weight to five dogs intravenously and wait for about 2 hours until the barbital action was at its maximum. Then each of these dogs was united with an etherized partner weighing almost three times as much and cross-circulation was begun.

The pairs of dogs used in these experiments were given 2,000 Roche Inhibitor Units of heparin (Roche) per kgm. Then the left carotid artery of the first dog was connected with the right external jugular vein of the second dog, and the right carotid artery of the second dog was connected with the left external jugular vein of the first dog. This operation was carried out by tying off the cephalic end of each vessel in the neck and inserting the ends of the U-connecting cannulae into each vessel caudally. Each of the small U-cannulae was filled with normal saline and all air expelled before the ends of the cannulae were tied in place. The bull-dog clamps were removed from both carotid arteries simultaneously when cross-circulation was begun.

The cross-circulation lasted for an hour, using ether whenever necessary for tranquilization, and after this period the partners were separated from each other and their wounds closed. The dogs receiving 250 mg of barbital sodium recovered[2] in an average time of

[1] H. E. Engstrom and J. H. Stoeckeler. 1941. Nursery Practice for Trees and Shrubs. USDA Misc. Publ. 434.

[1] Dille, Linegar and Koppanyi, *Jour. Pharmacol.*, 55: 46, 1935.

[2] Recovery-animals can stand without support. These animals were in about the same state as those receiving 50 to 70 mg of barbital sodium per kgm.

27 minutes, whereas six control dogs receiving the same dose of barbital sodium, but not cross-circulated, recovered in an average time of 29 hours.

Two dogs received 500 mg of sodium barbital per kgm of body weight and following the period of one to two hours were similarly cross-circulated to etherized partners, the pairs being of approximately equal weights. After an hour the partners were separated and both survived and were asleep for over 24 hours. Six dogs were given 500 mg of sodium barbital and they all died; the survival periods for five dogs were 127 to 235 minutes and one died in 45 minutes.

These experiments substantiate the original thesis of Koppanyi concerning the establishment of dynamic equilibrium of barbiturates in the body and show that they are not fixed in the tissues and that they may be mobilized at any time. This method of cross-circulation is proposed to study the fixation or alleged fixation of drugs, the criterions varying, of course, from drug to drug. Opiates and digitalis principles would seem to offer a particularly fruitful field for this line of study. The authors believe that few drugs if any will not be removed by cross-circulation.

The cross-circulation obviously is a method which has given excellent results in the treatment of experimental barbiturate poisoning and probably an apparatus could be constructed to provide for slow, continuous bleeding of the poisoned individuals and to replace the drawn blood at the same rate with normal plasma or compatible whole blood.

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THE ACTION OF SULFANILAMIDE COMPOUNDS ON THE LETHAL FACTOR OF BACTERIAL TOXINS

IN most gram negative bacteria the toxic factor appears to form a part of the complex O antigen,[1] and although earlier work suggested that the antigenic, and presumably the toxic portion of the endotoxin was associated with its "polypeptide" component, more recent studies[2] indicate that this component is a protein. Our studies[3] of the property which such bacterial products have of inducing hemorrhage[4] in implanted mouse tumors led to an investigation of the mode of detoxication of these antigens when introduced parenterally.

While it is generally assumed that the action of sulfanilamide compounds is one of bacteriostasis ensuing from interference with the utilization of *p*-aminobenzoic acid, our results confirm previous findings,[5,6] that sulfanilamide also markedly increases the resistance of mice to certain preformed bacterial toxins.

The toxin used in this study was prepared by growing *Salmonella typhimurium* in a medium containing citrate and dextrose as sole organic constituents. The profuse growth was killed with 2 per cent. phenol, and the suspension transferred to regenerated cellulose tubing. The contents of the tubes were simultaneously dialyzed against water and reduced to a small volume by pervaporation in a current of warm air. The phenol-free toxin was precipitated in 80 per cent. acetone, the precipitate dried with alcohol and ether, and then taken up again in water. Injected intraperitoneally into male mice weighing 20 g, 1.3 mgm of this preparation killed 50 per cent. of the animals within twenty-four hours. This amount of toxin was therefore designated as one minimum lethal dose. It was found that 2.0 MLD killed 92 per cent. of the mice, and 10.0 and 20.0 MLD killed 100 per cent.

Compounds assayed for protective effects were administered in neutral aqueous suspension by stomach tube to mice receiving simultaneously an intraperitoneal dose of toxin. In Table 1 it is seen that sulfanilamide affords almost complete protection from 2.0 MLD of the toxin, and 33 per cent. of the mice survived 10.0 MLD. Sulfathiazole and sulfapyridine were somewhat less effective. Also, if sulfanilamide is administered one hour before the toxin is injected and is followed by supplementary doses of sulfanilamide, the degree of protection against the toxin is somewhat increased.

Animals receiving toxin together with adequately protective amounts of sulfanilamide were subcutaneously given small amounts of *p*-aminobenzoic acid. As seen in the table, the effect of *p*-aminobenzoic acid in reducing the action of the sulfanilamide and thus allowing the toxin to exert its lethal effect was quite striking, and suggests that sulfanilamide and *p*-aminobenzoic acid compete for the enzymes concerned in the detoxication effect in a manner comparable to that described for bacteriostasis.

[1] A. Boivin, *Rev. d'Immun.*, 6: 86–115, 1940.
[2] W. T. J. Morgan and S. M. Partridge, *Biochem. Jour.*, 35: 1140–63, 1941.
[3] P. A. Zahl, S. H. Hutner, S. Spitz, K. Sigiura and F. S. Cooper, *Am. Jour. Hyg.*, 36: 224–42, 1942.
[4] Experiments in progress indicate a protective action by sulfa drugs against the hemorrhage inducing effects of this antigen.
[5] C. M. Carpenter, P. L. Hawley and G. M. Barbour, SCIENCE, 88: 530–1, 1938; C. M. Carpenter and G. M. Barbour, *Proc. Soc. Exp. Biol. and Med.*, 41: 255–9, 1939; C. M. Carpenter, *Proc. Soc. Exp. Biol. and Med.*, 41: 354–7, 1939.
[6] C. Levaditi and A. Vaisman, *C. R. Soc. Biol.*, 128: 463–5; C. Levaditi, A. Vaisman and L. Reinié, *Ann. Inst. Pasteur*, 61: 635–61, 1938.