dustry who wish to become better acquainted with plastics other than those with which they are thoroughly familiar.

L. M. DEBING

MANOMETRIC MEASURES

Manometric Methods. By MALCOLM DIXON. xiv + 155 pp., 20 figures. New York: The Macmillan Company. Cambridge: The University Press. Second edition. 1943. Price, $1.75.

THE manometric method, as embodied in the familiar Warburg apparatus, has become increasingly valuable to the physiologist, biochemist and more recently to other classes of investigators, particularly food technologists who have been impressed with the versatility of the technique.

Manometric manipulations, though exacting, are regarded by many with undue awe. On the other hand, there are some who have used them without sufficient regard for the pitfalls which necessarily exist in a method so delicate. This excellent little book, now in its second edition, should be most helpful to both types of investigators. The author's object—to provide a handbook for the laboratory, supplying in convenient form just that information which is likely to be required by research workers using the methods—has been fully realized.

Part I of the book comprises a discussion of principles and includes a satisfactory account of the theory involved in each of the methods described.

Part II contains a detailed description of the main methods now available: the direct and indirect method of Warburg, the first and second methods of Dickens and Simer and the method of Dixon and Keilin. A brief outline of the micro-technique is also given.

The book might have been improved by a presentation of the recent work on new applications and a description of the excellent new equipment now commercially available.

CHARLES N. FREY

SPECIAL ARTICLES

ESSENTIAL FATTY ACIDS AND LIPOTROPIC ACTION OF INOSITOL

OVER a year ago the author became interested in the possible effect of essential fatty acids on the lipotropic action of choline. If choline lowers fat in the liver by virtue of its incorporation into the lecithin molecule, then essential fatty acids, which also constitute integral parts of this phospholipid, might similarly be required before choline can exert this effect. A preliminary experiment of three weeks' duration, using rats 100 to 125 grams in weight, suggested that the essential fatty acids were not required for the action of choline, although the results obtained did suggest that choline decreases liver fat to a greater extent when these metabolites are present. However, the difference found was of questionable statistical significance. It was realized that the three-week period would not have permitted a marked depletion of the animals' stores of essential fatty acids, and an experiment of longer duration was contemplated.

In the meantime Engel's paper[1] on the relation of the essential fatty acids to the lipotropic action of choline was published. In an experiment of eight weeks' duration performed on weanling rats, Engel found that pyridoxine was required for the full lipotropic action of choline. Because of the relationship of pyridoxine and essential fatty acids in the cure of rat acrodynia, Engel determined under similar conditions the effect of essential fatty acids on the lipotropic action of choline. He found that they also augmented the lipotropic action of this substance.

[1] R. W. Engel, *Jour. Nutrition*, 24: 175, 1942.

An experiment of eight weeks' duration was devised to test the effect of essential fatty acids upon the lipotropic action of choline and also of inositol since it, too, is a constituent of certain phospholipids and its influence might be similarly affected by essential fatty acids in the diet. The basal diet chosen for this experiment consisted of 8 per cent. casein, 12 per cent. casein, 12 per cent. gelatin (both extracted with 1:1 alcohol-ether), 73 per cent. sucrose, 5 per cent. salt mixture, 2 per cent. agar, 0.015 per cent. vitamins A and D concentrate (Ayerst, McKenna and Harrison, containing 500,000 I.U. of A per gram and 50,000 I.U. of D per gram). A mixture of the B vitamins in the following amounts was injected daily in 0.5 ml physiological saline: thiamine chloride, 50 α, riboflavin, 25 α, pyridoxine, 20 α, calcium pantothenate, 100 α, nicotinic acid, 100 α. Twenty weanling rats of the Wistar strain (23 to 35 days old) were used for each group and litters were divided as evenly as possible amongst the different groups.[2] The groups were also balanced with respect to weight and sex. After eight weeks on the diet, the rats were killed by a blow on the head. Individual liver fats were determined in the usual way by saponification, acidification and extraction of the fatty acids with petroleum ether. Table 1 shows the results obtained.

This result supports Engel's statement that the lipotropic action of choline is increased in the presence of Mazola oil presumably through the action of essential fatty acids[1]. The lipotropic action of inositol on

[2] The mortality of the rats on the choline-free diets was quite high because of the development of hemorrhagic kidneys.

TABLE 1

EFFECT OF ESSENTIAL FATTY ACIDS ON LIPOTROPIC ACTION OF CHOLINE AND INOSITOL

Diet No.	Supplement per cent. of diet	Fatty acids per cent. liver weight
1. (Basal)	.....	23.4
2.	Choline chloride (0.5)	6.43
3.	Inositol (0.3)	13.3
4.	Mazola Oil (1.0)	25.3
5.	Mazola Oil (1.0) + Inositol (0.3)	27.2
6.	Mazola Oil (1.0) + Choline (0.5)	4.71

the other hand was obliterated by the inclusion of Mazola oil.[3] A possible explanation of this phenomenon might be that certain fatty acids in this oil make the diet more nearly adequate, increasing the demand for lipotropic factors and thus promoting a greater deposition of fat in the liver. But in view of the results with choline the writer believes that one must look elsewhere for the true explanation.

It is more probable that the nature of the fatty liver is changed in the presence or absence of the various supplements used. It will be recalled that choline has a relatively greater lipotropic effect on the "fat" fatty liver than on the "cholesterol" type of fatty liver, whereas with inositol, the reverse is true.[4] Only a complete analysis of the liver fats would reveal whether or not such a hypothesis is tenable. Fractionation of the fats from the livers of rats fed diets identical with those described above is now in progress and the results will be published shortly.

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STUDIES ON THE TOXICITY AND ACTIVITY OF STREPTOTHRICIN

IN 1941 Waksman and Woodruff[1] reported on the isolation and properties of streptothricin, a bactericidal substance obtained from a soil organism named *A. lavendulae*. Recently, Foster and Woodruff[2] published on the *in vitro* action of streptothricin against bacteria, fungi and yeast. However, with the exception of a short note published by Metzger[3] on the action of this agent in experimental brucellosis, nothing has appeared in the literature regarding the *in vivo* activity or toxicity of this substance. The present communication is mainly concerned with these factors.

[3] Preliminary results of current investigations indicate that the substitution of a fat devoid of essential fatty acids does not interfere with the lipotropic action of inositol.

[4] G. Gavin, J. M. Patterson and E. W. McHenry, *Jour. Biol. Chem.*, 148: 275, 1943.

[1] S. A. Waksman and H. B. Woodruff, *Proc. Soc. Exp. Biol. and Med.*, 49: 207, 1942.

[2] J. W. Foster and H. B. Woodruff, *Arch. of Biochem.*, 3: 241, 1943.

[3] H. J. Metzger, S. A. Waksman and L. H. Pugh, *Proc. Soc. Exp. Biol. and Med.*, 51: 251, 1942.

EXPERIMENTAL

Materials: The streptothricin[4] used varied in potency from 5,000 to 300,000 units[5] per gram of solid. The drug is readily soluble in water, and was administered as an aqueous solution. The mice used were of the CFI strain and weighed between 18 to 21 grams each.

Toxicity Studies: These experiments were performed in mice by administering single doses of streptothricin intravenously, subcutaneously and by mouth. The dose levels employed and the data obtained are presented in summary form in Table 1. Mice injected intravenously or subcutaneously with dose levels of 30,000 units per kgm produced no evidence of toxicity throughout the five-day observation period. Dose levels of 60,000 units/kgm (approximately 10 to 12 times the effective dose) produce some deaths when given by vein, but no untoward effect by the subcutaneous or oral route. Large doses by the subcutaneous route produced toxic signs in mice. Streptothricin was well tolerated when given by mouth in that single doses of 250,000 units per kgm appeared

TABLE 1

ACUTE TOXICITY OF STREPTOTHRICIN FOR MICE

Dose in units/kgm	No. of mice/dose	Per cent. mortality (5 days observation) i.v.	s.c.	oral
30,000	10	0	0	0
60,000	10	20	0	0
125,000	10	20	30	0
250,000	10	80	100	0
500,000	10	100	100	10
750,000	10	...	...	30

TABLE 2

BACTERIOSTATIC ACTION OF STREPTOTHRICIN IN AGAR

Organism	Units per cc of agar required to produce complete inhibition
Strep. hemolyticus 1685	32
Strep. hemolyticus MIT	256
Strep. hemolyticus M	256
Strep. viridans	> 1024
Strep. lactis	> 1024
Staph. aureus SM	16
Staph. aureus FDA	128
Staph. aureus SD	128
Staph. aureus 155	128
Diplo. pneumoniae Type I	32
B. mycoides	1024
B. subtilis	32
E. typhi	4
S. aertrycke	16
S. enteritidis	64
S. schottmülleri	16
B. flexneri	32
B. sonne	128
P. lepiseptica	32
B. proteus	512
B. pyocyaneus	256
N. meningitidis	256
E. coli	16
S. leutea	256
A. aerogenes	256

[4] The streptothricin employed in these studies was obtained from the chemists of the Research Laboratories of Merck and Co., Inc., from cultures grown by Dr. J. W. Foster.

[5] A unit of streptothricin is the minimum quantity of drug which when added to 1.0 cc of nutrient broth will inhibit a given strain of *E. coli*.