amino acids (Difco) were added, each in a concentration of 50 ppm, to a culture solution containing 5 ppm of selenium as sodium selenite. Table I shows that at least four of these substances—bactotryptone, neopeptone, sodium caseinate and proteose peptone—approximately doubled the accumulation of selenium, and smaller increases were obtained with the other substances tested. It may be noted also that water extracts of alfalfa hay and of string beans had a marked effect in increasing selenium absorption.

TABLE I

INFLUENCE OF VARIOUS PROTEINS AND AMINO ACIDS IN THE CULTURE SOLUTION ON THE ACCUMULATION BY CORN SEEDLINGS OF SELENIUM SUPPLIED AS SODIUM SELENITE

Protein or amino acid in culture solution, 50 ppm.	Selenium series (5 ppm. Se as Na_2SeO_3)		Control series* (No selenium)
	Se content of plants, ppm.	Ave. dry wt. of tops, g.	Ave. dry wt. of tops, g.
Bactotryptone	471	0.90	2.23
Neopeptone	420	0.87	2.10
Sodium caseinate	413	0.92	2.26
Proteose peptone	396	0.95	3.37
Alanine	324	0.78	2.27
Tyrosine	264	1.02	2.63
Cystine	253	1.00	2.87
Tryptophane	205	1.12	2.20
Control	192	1.14	2.47
Alfalfa hay extract ..	319	0.80	1.17
Control	143	1.27	2.20
String-bean extract ..	285	0.84	0.83
Control	132	0.66	1.04

* Analysis showed that these plants contained no selenium.

Fig. 2 shows that increasing the concentration of

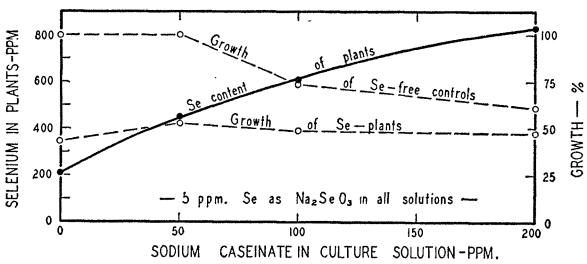

FIG. 2

sodium caseinate in a solution containing 5 ppm of selenium as sodium selenite brought about a progressive increase in the accumulation of selenium by the corn plants. With 200 ppm of sodium caseinate, the corn plants stored 830 ppm of selenium, or four times the concentration accumulated in the absence of the protein. It is of interest in this connection to note that the toxicity of selenium to rats has been found to be markedly reduced by a high proportion of protein, particularly casein, in the diet.[4]

In conclusion, it may be suggested that soils naturally high in nitrogenous organic substances may allow greater selenium accumulation by crop plants and native grasses than soils low in such substances. It would be expected that preparation of a grain field in a seleniferous area by plowing under a leguminous crop might markedly increase the absorption of selenium by the grain. Corn, other cultivated grains and native grasses, though unable to rival the true indicator plants, might nevertheless be capable of significant activity as selenium accumulators and converters in a soil rich in organic material.

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[4] R. A. Gortner, Jr., *Jour. Nutrit.*, 19: 105–112, 1940.

FACTORS INFLUENCING CAPILLARY PERMEABILITY IN THE VITAMIN E DEFICIENT CHICK[1]

INCREASED permeability of capillaries resulting in diffuse hemorrhage and exudation of plasma, as well as in increased migration of intravenously injected colloidal dyes into the tissues, was found by us to be an outstanding feature of vitamin E deficiency in chicks.[2, 3, 4, 5]

A further study of this condition has shown that it is possible to influence the intensity of this symptom very much by certain modifications of the diet which do not affect the vitamin E content.

Thus the appearance of exudates can be delayed and the incidence and severity of the symptom reduced by lowering of the concentration of soluble salts in the diet, whereas a high concentration of such salts—phosphates or sodium chloride—has the opposite effect. By suddenly raising the content of soluble salts considerably, exudates in the pericardium and the peritoneum and edema of muscle tissue can be produced as a regular symptom, whereas such exudates are rare on the same diet with low salt content. This observation affords some explanation as to why Bird and Culton[6] found the symptoms to be more severe on their diet (which contained 54 per cent. of dried skim milk and 1 per cent. of sodium chloride) than on our previously used diet, which has a lower salt content.

Acceleration of the onset of exudates can also be obtained by incorporating a trace of histamine in the

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[2] H. Dam and J. Glavind, *Nature*, 142: 1077, 1938.

[3] *Idem, Nature*, 143: 810, 1939.

[4] *Idem, Skandinavisches Archiv f. Physiologie*, 82: 299, 1939.

[5] *Idem, Die Naturwissenschaften*, 28: 207, 1940.

[6] H. R. Bird and Th. G. Culton, *Proc. Soc. Exp. Biol. and Med.*, 44: 543, 1940.

diet or by raising the cholesterol content to about 1 per cent. That a high fat content in the diet favors the symptoms has previously been reported.[7]

These observations are interpreted by the assumption that certain regions of the capillary systems of the E-deficient chick are unable to withstand even the normal osmotic pressure of the blood and that the capillaries are easily damaged by histamine or an abnormally high supply of cholesterol as well as by other possible changes in the milieu with which the capillary wall is in contact.

The fact that fat and cholesterol favor the symptom suggested to us that it might be desirable to test the effect of some lipotropic substances.

Incorporation in the vitamin E deficient diet of 2 per cent. Lipocaic, a water-soluble preparation from pancreas (L. R. Dragstedt, *et al.*)[8] gave a high degree of protection against exudates even if the diet contained a relatively high amount of salts such as 7.2 per cent. of McCollum's salt mixture number 185. A chemical test showed that the effect of the lipocaic preparation could not be due to contamination with vitamin E. Inositol was then tested because Gavin and McHenry[9] have reported that this substance has a similar lipotropic effect as lipocaic. 1.5 per cent. of inositol in the diet was found to give a high degree of protection, whereas 1.1 per cent. of choline chloride was without any effect. Ineffective also was 5 per cent. gum arabic and 2 per cent. of acetone treated soy bean phosphatide was nearly ineffective.

This is believed to be the first instance where non-lipoid substances of animal origin have been found to counteract a symptom of vitamin E deficiency. An investigation as to whether these substances will also counteract other symptoms of lack of vitamin E, as well as a study of the protective factor in the lipocaic preparation and the way in which it acts, should be of importance in the elucidation of the mode of action of vitamin E.

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MECHANISM OF SULFONAMIDE ACTION. II. INHIBITION OF BACTERIAL RESPIRATION BY SULFANILAMIDE AND BY ITS INACTIVE ISOMERS

UNTIL very recently the only valid method for the study of sulfonamide action was based upon chemotherapeutic experiments, using animals infected with pathogenic bacteria. Recent investigations of the competitive inhibition of sulfonamides by *p*-aminobenzoic acid have shown that this antagonism can be made the basis of a suitable *in vitro* method.[1] The mechanism of the sulfonamide action is not clearly revealed by the *in vivo* experiments, and even the *in vitro* experiments based upon *p*-aminobenzoic acid antagonism involve the over-all process of bacterial growth in measuring sulfonamide activity. A recent report by Sevag *et al.*[2] attracted our attention because it was an attempt to study chemotherapeutic action of sulfonamides on a less intricate system. Our experiments using this method have convinced us that the inhibition of bacterial respiration by high concentrations of sulfonamides should not be regarded as typical sulfonamide action. We have found, for example, that the respiration of resting cells of *Escherichia coli*, *Staphylococcus aureus* or of *Streptococcus pyogenes* prepared after the manner of Sevag, is inhibited by the meta and ortho derivatives of amino benzenesulfonamide just as by sulfanilamide itself. The data in Table I show that of the two chemotherapeutically inactive isomers, the meta form behaves exactly as sulfanilamide, while the ortho form gives considerably more inhibition.

TABLE I

EFFECT OF .04 M SULFANILAMIDE AND ITS ISOMERS ON BACTERIAL RESPIRATION ON GLUCOSE IN M/60 PHOSPHATE BUFFER IN AIR

	Control		Sulfanilamide		Metanilamide		Orthanilamide	
pH	6.2	7.2	6.2	7.2	6.2	7.2	6.2	7.2
E. coli Q_{O_2}	37	38	25	24	26	25	12	11
Inhibition			32 per cent.	37 per cent.	30 per cent.	34 per cent.	67 per cent.	71 per cent.
Staph. aureus Q_{O_2}	63	51	41	38	39	35	23	30
Inhibition			35 per cent.	25 per cent.	38 per cent.	31 per cent.	63 per cent.	41 per cent.
Strep. pyogenes Q_{O_2}	55	50	44	36	44	36	35	29
Inhibition			20 per cent.	28 per cent.	20 per cent.	28 per cent.	36 per cent.	42 per cent.

E. coli is a typical fecal strain.
Staph. aureus is F.D.A. strain.
Strep. pyogenes is strain 1896 M obtained from Dr. J. S. Lockwood, University of Pennsylvania.

[7] H. Dam, J. Glavind, I. Prange and J. Ottesen, Royal Danish Academy of Science, *Biological Communications*, 16: 7, 1941.

[8] L. R. Dragstedt, C. Vermeulen, W. C. Goodpasture, P. B. Donovan and W. A. Geer, *Archives of Internal Medicine*, 64: 1017, 1939.

[9] G. Gavin and E. W. McHenry, *Jour. Biol. Chem.*, 139: 485, 1941.

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[2] M. G. Sevag and M. Shelburne, *Jour. Bact.*, 43: 411–462, 1942.