It is natural that different individuals, according to their training and circumstances, should feel differently about these matters, so also the same individual at different times. But one feels that some of the things done, such as the evacuation of the three great museums at San Diego, which would have contributed greatly to the education of the men in service, has resulted from a feeling of indifference to cultural values on the part of those in authority. Let us hope that in the days to come the better life which we now see through dark glasses may not only restore our civilization but make it far more interesting and serviceable to the average man.

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## DEVELOPMENTS IN SCIENCE

*Forward with Science.* By ROGERS D. RUSK. Alfred A. Knopf Company. 307 pp. $3.50.

THIS book by Rogers D. Rusk, is intended as a guide to non-scientists, to keep them in touch with the present developments in science and to review for them some of the philosophical implications, as well as to describe the practical consequences of the thought of the past two decades. It is not intended to be a text and therefore fits into the category of the other books explaining science to the layman, such as the familiar ones by Jeans and Eddington.

Dr. Rusk sets forth for the average layman the points of view which have been developed by science in recent times and outlines some of the interesting results. He starts out by explaining the triumphs of modern physical science and discusses the structure of matter and the newly discovered fundamental particles. He then shows us immediately how these particles are used. He devotes one chapter to the electron microscope, another to x-rays, and still others to artificial radio-acitvity and atomic energy. Then Rusk describes cosmic rays and reviews the evidence for the age of the earth. The remainder of the book is devoted to a more philosophical view of the problems posed by modern science. The author explains the difficulties of the mechanistic view and the importance of the development of the wave and probability concepts which form the basic operational philosophy of modern physics. His later chapter headings are suggestive, as "Reaching for the Stars," "Does Nature Make Sense?", "Man Outgrows Mechanism" and "Human Freedom and Destiny."

Finally, toward the end of the book Rusk also considers science and destruction. He attempts to set at ease the minds of those who worry about the destructive forces unleashed by science by reminding them that science provides power and tools for the use of mankind and that it is not the fault of science that some of these tools have been used by misguided persons for destructive purposes.

Dr. Rusk, being himself a physicist, is, of course, thoroughly conversant with his subject and cites extensively the original fundamental and significant experiments. He has clearly explained the rather complex ideas which have been formulated and developed by the leaders of present-day physical thought, such as Heisenberg, de Broglie, Schrodinger and Bohr. Since physics has grown during the past ten years to vast dimensions it is impossible to do justice to all phases of it in a book of this length. One is therefore left with the feeling at the end of many chapters that more should have been added about the subject and that the arguments and treatments are incomplete. Also, in reading the book a physicist would feel that in Dr. Rusk's development of the subject he departs from the classical order of presenting the material. This departure from the traditional presentation tends to give the impression that the author jumps around too much for so broad a field and does not always finish the ideas which he has started to explain. On the other hand, many of the facts in the book are excellent and certainly reflect the current thought in physics. Many of us have felt, as does Dr. Rusk, that the philosophical point of view developed by Jeans and Eddington had gone beyond the true province of science, particularly in Jeans' discussion of determinism and in his famous conclusion that since physics is mathematical, therefore God must be a mathematician. It is most encouraging therefore to hear a fellow physicist point out the difficulties with this point of view and to hear him explain the feelings which have been commonly shared by many of us in this field.

On the whole, Rusk has done a good job, and has presented the subject to the layman in a most interesting and readable book.

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# SPECIAL ARTICLES

## RETARDATION OF RANCIDITY BY SULFHYDRYL COMPOUNDS

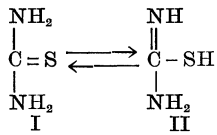
BIOLOGICAL antioxidants, as food constituents, are attracting increasing attention. Apart from the tocopherols, which Mattill and his associates first demonstrated as having antioxygenic potency,[1, 2] crude

[1] H. S. Olcott and H. A. Mattill, *Chemical Reviews*, 29: 257, 1941.

sources of the vitamin B complex have also, recently, been recognized as potent antioxidants.[3, 4, 5]

In the course of investigations dealing with the retardation of rancidity in dried milks,[5] thiourea was examined as a possible antioxidant for fat. It has been claimed that thiourea is a good stabilizer for ascorbic acid[6] but its possible antioxygenic effect on fats required special study. From such experiments[5] it became evident that thiourea is capable of acting as a fat antioxidant, but only in the presence of water.

It is plausible to assume that the antioxygenic properties of thiourea (I) can be attributed to the sulfhydryl residue in its tautomeric form, isothiourea (II).



This idea carries with it several practical implications which are open to experimental verification.

1. Iso-thioureas having a substituent attached to the sulfur atom should not exhibit antioxygenic properties. On the other hand, *N*-substituted thioureas having a hydrogen atom available for enolization should act as antioxidants.

2. Other sulfhydryl compounds, for instance, cysteine (but not cystine), should also be good antioxidants, at least *in vitro*.

3. $Cu^{++}$ and $Fe^{+++}$ ions should inhibit the antioxygenic potency of sulfhydryl compounds.

Experiments were set up to test the above postulates. For the assay method a modified dried system[7] was used, composed of cornstarch (18 gram), redistilled linoleic acid (3.5 gram) and antioxidant (43 mg), with or without the addition of water (1 gram of water replacing 1 gram of starch) and of $CuSO_4$ (10 mg in the total mixture). The ingredients were thoroughly mixed and incubated at 30°. On the eighth day the fat was extracted with $CHCl_3$ and the iodine number determined.

The experimental results contained in Table I indicate the correctness of the assumption, according to which, sulfhydryl-compounds by virtue of their free sulfhydryl radical retard the development of rancidity in fat, but only in the presence of water and in the absence of copper salts (also of ferric salts, and possibly of other inhibitors of the sulfhydryl radical).

TABLE I

EFFECT OF WATER AND OF $CuSO_4$ ON THE ANTIOXYGENIC POTENCY OF SULFHYDRYL COMPOUNDS AND OF HYDROQUINONE-MONOBENZYLETHER

| Antioxidant (0.2 per cent.) | $H_2O$ per cent. | $CuSO_4$ mg. | Iodine No. Exper. 1 | Iodine No. Exper. 2 |
|---|---|---|---|---|
| Cysteine | 0 | 0 | 43.5 | |
| Cysteine | 4.65 | 0 | 113.8 | 114.1 |
| Cysteine | 4.65 | 10 | 46.6 | 42.4 |
| Cystine | 0 | 0 | 54.5 | |
| Cystine | 4.65 | 0 | 55.9 | |
| N-Acetylthiourea | 0 | 0 | 55.4 | |
| N-Acetylthiourea | 4.65 | 0 | 122.0 | 128.5 |
| N-Acetylthiourea | 4.65 | 10 | 81.7 | 48.7 |
| S-Methylisothiourea | 0 | 0 | 51.2 | |
| S-Methylisothiourea | 4.65 | 0 | 49.6 | 56.3 |
| S-Methylisothiourea | 4.65 | 10 | .... | 44.5 |
| Thiourea | 0 | 0 | 54.8 | 64.5 |
| Thiourea | 4.65 | 0 | 120.2 | 125.2 |
| Thiourea | 4.65 | 10 | 47.8 | 48.7 |
| Thiouracil | 0 | 0 | | 64.8 |
| Thiouracil | 4.65 | 0 | | 140.9 |
| Thiouracil | 4.65 | 10 | | 57.0 |
| Hydroquinone-Monobenzylether | 0 | 0 | | 138.4 |
| Hydroquinone-Monobenzylether | 4.65 | 0 | | 141.2 |
| Hydroquinone-Monobenzylether | 4.65 | 10 | | 137.1 |
| Control (no antioxidant) | 0 | 0 | 60.5 | 55.3 |
| Control (no antioxidant) | 4.65 | 0 | 63.5 | 57.3 |
| Control (no antioxidant) | 4.65 | 10 | 50.3 | 50.9 |

It is improbable that the effect of the copper salt is due to its inherently pro-oxygenic character rather than its effect in blocking the sulfhydryl group. If the former were the case the strong antioxidant, hydroquinone-monobenzylether, should also be inactivated by the copper ion. Such inactivation, however, could not be demonstrated (Table I).

The special interest in the retardation of autoxidation of fats by sulfhydryl compounds lies primarily in the unexpected finding that *fats* are protected by such antioxidants only in the presence of *water*. In the second place, this same phenomenon may shed light on the mechanism under-lying the hypometabolic state in rats fed certain sulfonamides as well as thiourea and its derivatives.[8, 9, 10] Thiourea and thiouracil have been found to be effective also in thyrotoxicosis in man.[11, 12]

Similar to the effect of sulfhydryl compounds on the enlargement of the thyroid of the rat, there has been found a definite synergism in this respect between p-aminobenzoic acid and sulfonamides[10] as op-

[2] See also K. Hickman, *Ann. Rev. Biochem.*, 12: 353, 1943.

[3] P. György and R. Tomarelli, *Jour. Biol. Chem.*, 147: 515, 1943.

[4] D. F. Clausen, R. H. Barnes and G. O. Burr, *Proc. Soc. Exp. Biol. and Med.*, 53: 176, 1943.

[5] M. B. Williamson—To be published.

[6] See W. R. Fearon, *Brit. Med. Jour.*, 2: 95, 1942.

[7] P.György, R. Tomarelli, R. P. Ostergard and J. B. Brown, *Jour. Exp. Med.*, 76: 413, 1942.

[8] J. B. Mackenzie, C. G. Mackenzie and E. V. McCollum, SCIENCE, 94: 518, 1941.

[9] C. G. Mackenzie and J. B. Mackenzie, *Endocrinology*, 32: 185, 1943.

[10] E. B. Astwood, J. Sullivan, A. Bissell and R. Tyslowitz, *Endocrinology*, 32: 210, 1943.

[11] E. B. Astwood, *Jour. Am. Med. Asn.*, 122: 78, 1943.

[12] R. H. Williams and G. B. Bissell, SCIENCE, 98: 156, 1943.

posed to their normal antagonism in bacteriostasis. A direct antioxygenic reaction might be the cause for this synergism which hitherto has defied any plausible explanation. The enhancing effect of p-aminobenzoic acid on sulfonamides in the retardation of rancidity in fat has recently been experimentally demonstrated.[13]

More experimental evidence is needed before the link between antioxygenic activity of thiourea and related substances and their effect on metabolism and the thyroid gland can be regarded as established.[13]

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## VITAMIN $B_6$ DEFICIENCY ANEMIA IN THE DOG[1]

HYPOCHROMIC microcytic anemia typical of vitamin $B_6$ deficiency in puppies and adult dogs has been produced in this laboratory consistently, thus confirming the work of others.[2,3,4,5,6] The synthetic basic diet used was high in protein and consisted of the following ingredients: casein 40 per cent., sucrose 36, cotton seed oil 18, cod liver oil 2, mineral salts[7] 4 per cent. This diet is essentially free from all members of the vitamin-B complex.

### EXPERIMENTAL GROUPS

*Group I*—consisting of nine animals—received in addition to the basic diet seven synthetic members of the vitamin B complex as follows: thiamin 1.4 mg, riboflavin 0.7 mg, nicotinic acid 6 mg, inositol 6 mg, pantothenic acid 6 mg, para aminobenzoic acid 6 mg, and choline 30 mg per dog per day, but no vitamin $B_6$. All these dogs developed the hypochromic microcytic anemia observed in dogs lacking vitamin $B_6$. The initial hemoglobin of these dogs averaged 15.5 grams. This rose to a peak of 18.8 grams in approximately 7 weeks, then declined to values averaging 7.7 grams after 22 weeks on the diet. For other blood values see Table I.

*Group II.* As a control group five puppies were placed on the same régime except that vitamin $B_6$ was given as a supplement (6 mg per dog per day) from the beginning of the experiment along with the other seven synthetic vitamins. Much to our surprise under these conditions the blood values (determined every two weeks) followed a pattern quite similar to that of the vitamin $B_6$ deficient animals (Fig. 1). Their initial hemoglobin values averaged 14.5 grams. These rose to a high value of 18.6 grams in 4 weeks, then declined gradually to 9.4 grams over a period of 20 weeks.

*Group III.* As an additional control group, 4 animals (1 adult and 3 puppies) received the basic diet altered to contain brewers' yeast, as a source of all the B-complex vitamins, at a level of 10 per cent., replacing an equivalent amount of carbohydrate. The initial hemoglobin values in this group averaged 14.5 grams, rose to a peak of 19.8 grams after 17 weeks on the diet and then returned to a value around 18 grams, a level which was maintained throughout the rest of the experiment.

*Group IV*—composed of 4 puppies—received the same yeast control diet as group III, but in addition these animals received the eight synthetic vitamins given to group II and in the same daily amounts. Here the average initial hemoglobin was 13.5 grams with a peak averaging 20.5 grams after 21 weeks and a subsequent return to a value around 18 grams. Fig. I illustrates the contrast in behavior between the animals receiving only synthetic vitamins and their yeast controls.

One puppy of group I after being depleted of vitamin $B_6$ was subsequently treated with vitamin $B_6$ and later with brewers' yeast. The results substantiated the findings in groups II and III. At the end of the depletion period of 36 weeks this dog had a Hgb. of 6 grams, a red blood count of 4,570,000 and a hematocrit of 18.5 volumes per cent. Treatment with vitamin $B_6$ resulted in the usual prompt rise in hemoglobin, which increased 4 grams in 6 days with a corresponding rise in the other blood values. The hemoglobin then gradually rose to 15.5 grams in 10 weeks with a corresponding RBC of 6,720,000 and a hematocrit of 41.9. The hemoglobin could not be

[13] In preliminary experiments (in collaboration with Dr. R. M. Tomarelli) hydroquinone monobenzyl ether (0.5 per cent. in the diet) has no effect on the size of the thyroid in rats when administered for fourteen days. In this connection it should be noted that the effect of various antioxidants depends, to a large extent, on the substrate on which they are tested.

[1] Evidence that vitamin factors found in brewers' yeast in addition to vitamin $B_6$ are essential for maintaining hemoglobin in the dog.

[2] Only two adult dogs were used, one in Group I, the other in Group III.

[3] P. J. Fouts, O. M. Helmer, S. Lepkovsky, and T. H. Jukes, *Jour. Nutrition*, 16: 197, August, 1938.

[4] P. J. Fouts, O. M. Helmer, and S. Lepkovsky, *Am. Jour. Med. Sci.*, 199: 163, 1940.

[5] H. J. Borson and R. S. Mettier, *Proc. Soc. Expt. Biol. and Med.*, 43: 429, 1940.

[6] J. M. McKibbin, A. E. Schaefer, D. V. Frost and C. A. Elvehjem, *Jour. Biol. Chem.*, 142: 77, 1942.

[7] Mineral salt mixture: Bone meal (steamed), 57.8 per cent.; sodium chloride, 24.4 per cent.; lime stone (oyster shell flour), 12.2 per cent.; iron sulfate (U.S.P.), 3.7 per cent.; magnesium oxide (U.S.P.), 1.2 per cent.; copper sulfate (reagent), 0.3 per cent.; manganese sulfate (reagent), 0.1 per cent.; zinc oxide (reagent), 0.1 per cent.; cobalt carborate, 0.1 per cent.; potassium iodide, 0.1 per cent.