DISCUSSION

THE DISCOVERY OF INSECT TRANSMISSION OF PATHOGENIC MICRO-ORGANISMS

THE recent quotation which appeared in this journal[1] on "The Seventieth Birthday Anniversary of Theobald Smith" brings to mind another pioneer on studies of insect transmission of pathogenic micro-organisms, one who is frequently ignored by writers of medical text-books and of books and articles for popular consumption. Reference is being made to Merton B. Waite, the able plant pathologist who discovered, and first published in 1891,[2] that bees often carry the bacillus that is responsible for that disastrous scourge on pear, apple and other fruit-trees popularly known as fire-blight.

It is not at all surprising that investigators and "popularizers" of human and animal diseases should have overlooked the work of a plant pathologist, and it can not truthfully be said that the latter group are freer from sin in ignoring the work of other pathologists than their medical brethren. It is just another illustration of the great difficulty involved in coordinating knowledge, even though the branches run so closely parallel to each other as human, animal and plant pathology. The chief difference between Waite's work and Smith's is that while the former was studying a "passive" insect carrier the latter was working with an "active" one. Coming at a time when learned doctors were still arguing as to whether or not there could be such a thing as a bacterial disease in the plant kingdom, Waite's discoveries were truly remarkable. He not only helped settle that dispute[3] but made such further advances in the knowledge of bacterial diseases of plants, particularly the one mentioned above, that it has kept plant pathologists busy checking Waite's work up to this very day. While some of his views expressed more than thirty-five years ago may have to be discarded, there can be no question that as far as insect transmission of pathogenic micro-organisms is concerned his proof was ample. The great Erwin F. Smith has the following to say of this work:[4]

Waite isolated the pear-blight organism, grew it in pure cultures and proved its infectious nature by inoculations. With such proved cultures he sprayed clusters of pear flowers in places where the disease did not occur and obtained blossom-blight, and later saw this give rise to the blight of the supporting branch, found the organism multiplying in the nectar and re-isolated it from the blighting blossoms. On some trees he restricted the disease to the sprayed flowers by covering them with mosquito netting to keep away bees and other nectar-sipping insects. On other trees where the flowers were not covered he saw bees visit them, sip from the inoculated blossoms and afterwards visit blossoms on unsprayed parts of the tree, which then blighted. Finally he captured bees that had visited such infected blossoms, excised their mouth parts, and from these, on agar-poured plates, obtained *Bacillus amylovorus*, with colonies of which he again produced the disease. These experiments were done in several widely separated localities with identical results. I saw them and they made a great impression on me.

In conclusion it may be of interest to point out that Theobald Smith and Merton Waite were both members of the same institution when their epoch-making discoveries on insect transmission of disease-producing agents were made, one working in the animal division and the other in the plant division. Although Waite's first announcement of this phenomenon preceded Smith's[5] by two years the two men had evidently worked on insect transmission more or less at the same time and independent of each other. Waite, it should be noted, is still connected with and actively engaged in that remarkable public institution, the U. S. Department of Agriculture.

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THE RATE OF ABSORPTION OF EPINEPHRINE FROM THE SUBCUTANEOUS TISSUE

IT is experimentally established that the subcutaneous injection of 1 mg of epinephrine per kilo does not lead to a rise in blood pressure of rabbits, cats and dogs. This is generally ascribed to the fact that epinephrine is absorbed very slowly from the subcutaneous tissue. A five times smaller dose which we used in work on carbohydrate metabolism Cannon[1] designates as "huge" and as "far beyond physiological limits," because he believes that subcutaneously injected epinephrine leads to disturbances in circula-

[1] SCIENCE, 70: 193–194, 1929.

[2] *Bot. Gaz.*, 16: 259, 1891; *Proc.* Amer. Assoc. Adv. Sci., 1891: 315, 1892; *Trans.* Peninsula Hort. Soc. Fifth Ann. Session, pp. 32–34, 1892.

[3] The very heavy verbal artillery fired at the time by Erwin F. Smith at Alfred Fischer has tended to drown out the extremely modest verbal offerings of Waite and others. Up to the present moment he has not published a full account of his early experiments although enough, fortunately, has appeared in various horticultural and agricultural journals to enable one to get a fair view of his work.

[4] "Bacterial Diseases of Plants," Philadelphia, 688 pp., 1920.

[5] Bur. Anim. Ind., U. S. Dept. Agr. Bul. 1, 1893.

[1] W. B. Cannon, *Physiol. Reviews*, 9: 399, 1929.

tion. This belief can only be based on the tacit assumption that subcutaneously injected epinephrine is absorbed very rapidly into the blood stream, which is contrary to accepted experimental evidence. Since the discovery of the glycosuric action of epinephrine twenty-seven years ago, our dose of 0.2 mg per kilo and larger doses have been used in virtually hundreds of animal experiments by a great number of authors. In view of this the criticism of Cannon, if it were well founded, would be of far-reaching importance and it may therefore be worth while to examine the evidence he sets forth. First he calculates the equivalent of our dose of 0.2 mg per kilo of rat for a man of 70 kilos and arrives at the figure of 14 mg. This *argumentum ad hominem* can not impress those who know that the sensitivity of various species to drugs and hormones shows the greatest variation. There can be no doubt that the rat, rabbit, cat and dog are less sensitive to subcutaneously injected epinephrine than man. Secondly, Cannon states that pronounced physiological effects were obtained in rats with one twentieth of our dose. He does not mention the mode of application of epinephrine or describe the nature of the physiological effects observed. It is true that the *intravenous* injection of 0.001 mg of epinephrine per kilo per minute raises the blood pressure of rats, but this argues in our favor because experiments made in this laboratory have shown that the *subcutaneous* injection of our dose which is two hundred times larger has no effect on blood pressure. Hence, the absorption from the subcutaneous tissue must proceed at a rate less than 0.001 mg per kilo per minute which is, according to Cannon, within the physiological range. The dose we injected was *non-glycosuric* in animals rich in glycogen.[2] Absence of glycosuria under these conditions is generally accepted as evidence that the dose is moderate. Glycosuria appeared only when epinephrine was injected in conjunction with glucose feeding.[3] Cannon argues that the highest blood sugar in these experiments came early and was associated with the lowest glycosuria, and he concludes from this that the "huge doses disturbed the circulation." The figures on which Cannon bases this argument are as follows. Average sugar excretion from 0 to one hour 12 mg, from one to two hours 13 mg, from two to three hours 15 mg and from three to four hours 15 mg. It needs hardly to be emphasized that the increase in the average sugar excretion from 12 mg in the first hour to 15 mg in the last hour is not significant and Cannon's criticism is therefore ill-based. The rather constant sugar excretion from hour to hour was used for the following argument. It is definitely known that epinephrine acts only as long as it enters the blood stream. Since the glycosuria persisted for four hours, the absorption of epinephrine from its subcutaneous depot must have persisted for at least that length of time and from this it was calculated that the rate of absorption was well within physiological limits. This could recently be confirmed experimentally by determining the amount of epinephrine remaining unabsorbed in the subcutaneous tissue of the rat at various time intervals after the injection. In experiments to be reported in extenso elsewhere the following average values were obtained. Recovered after one hour 65 per cent., after two hours 52 per cent., epinephrine still present after four hours. This is direct evidence that the absorption proceeds at a very slow rate and shows that Cannon's assumption that our results were due to overdosage is unfounded. It would also seem that the mere fact that smaller doses of epinephrine than those used by us still influence metabolism can hardly invalidate our results.

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[2] C. F. Cori and G. T. Cori, *J. Biol. Chem.*, 79: 321, 1928.

[3] C. F. Cori and G. T. Cori, *J. Biol. Chem.*, 79: 343, 1928.

THE CHEMICAL NATURE OF ENZYMES

IN his "Outlines of Biochemistry" Dr. Ross Aiken Gortner reviews Willstätter's conception of the structure of enzymes as follows:

> Both Willstätter and Oppenheimer take the view-point that enzymes are amphoteric electrolytes which exist in a particular colloidal state. Willstätter discusses this question at considerable length, the conclusion being that enzymes contain a special reactive group which either combines with, or possesses some particular affinity for, definite groupings in the substrate, thus accounting for the specificity of enzyme behavior. This special reactive group is attached to a colloidal carrier, and enzyme action is determined in part by the affinity of the active group for the substrate and in part by the colloidality of the entire aggregate. He notes that when the colloidal properties of the aggregate are destroyed, then the activity of the enzyme likewise disappears.

Recently, in connection with a study of the insoluble tyrosinase of the velvet bean seed coat the writer prepared an aqueous solution from a mushroom (species not yet determined) which, when filtered through ordinary filter-paper appeared to be very clear and was found to possess marked activity toward the chromogen, 3.4-dihydroxyphenyl alanine, a constituent of velvet bean cotyledons. This filtrate was dialyzed over night in a cellophane dialyzing tube and the dialysate was found to be quite active,