lations are based are correct, then we have here a type of culture whose composition may be deliberately changed in opposite directions by varying the environment, *i. e.,* solid or liquid media, without influencing the rate at which new variants arise from the culture. If the commoner forms of dissociation differ only quantitatively from the phenomena here described, then studies on bacterial dissociation must be concerned with 2 distinct phenomena: (1) The rate of origin of the new variant cells (primary rate of variation). (2) The environmental factors which make it possible for the new variant cells to grow to sufficient numbers to be detected in culture.

7769 P

Isolation of a Specific Ascorbic Acid (Vitamin C) Oxidase.

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An extract of Hubbard squash oxidizes both the synthetic and the natural ascorbic acid (vitamin C)* with great rapidity. This is due to an enzyme having an optimum pH of 5.83 to 5.96. It may be obtained and purified by extracting the squash (edible part) with twice its weight of 30% ethyl alcohol for 10 minutes. The centrifuged and filtered fluid is treated with an equal volume of acetone, which causes a yellow sticky substance to precipitate. This may be washed free of yellow pigment with acetone, dissolved in water and reprecipitated with acetone. A third precipitation yields a preparation, which after drying *in vacuo* over sulphuric acid has an activity 500 times that of the original extract.

This preparation is water soluble and gives slight protein tests. Alcohol and saturated solutions of neutral salts, however, do not precipitate it. It is digested (inactivated) by trypsin. A polysaccharide accompanies the enzyme in the above precipitation. We have found no way of removing it thus far.

This enzyme differs in various ways from the "hexoxidase" which v. Szent-Györgyi[1] discovered in cabbage leaves, *e. g.,* the

* We are indebted to Professor v. Szent-Györgyi for a sample of l-ascorbic acid and to the Hoffman La Roche Co. for some of their synthetic l-ascorbic acid (Redoxon).

[1] Szent-Györgyi, A., *Science,* 1930, **72**, 125; *J. Biol. Chem.,* 1931, **90**, 385.

hexoxidase is precipitated by saturated $(NH_4)_2SO_4$ solution; it oxidizes not more than about 25% of the substrate, whereas the enzyme of the squash oxidizes 100% very rapidly. Moreover, the kinetics of our preparation point to the presence of a single enzyme. Substances thus far tested, such as cysteine, tyrosine, glutathione, and phenols, are not affected. We suggest, therefore, that the enzyme responsible be designated "ascorbic acid oxidase".

It requires the presence of atmospheric oxygen, which plays the rôle of hydrogen acceptor. The oxidized ascorbic acid may be reduced to its original state by hydrogen sulphide. The enzyme is remarkably stable to dialysis, oxygen and carbon monoxid. Hydrogen sulphide, however, inactivates it.

For ascorbic acid estimation, Tillmans and associates'[2] 2,6-dichlorobenzenoneindophenol method was employed.

7770 P

Carcinomatous Changes in Virus-induced Papillomas of the Skin of the Rabbit.

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The Shope rabbit papilloma, a skin growth caused by a virus,[1] has been shown to possess the characters whereby tumors are recognized.[2] When given opportunity, as on implantation within the host, the growth frequently looks and behaves like a malignant neoplasm. The present report is concerned with instances in which skin papillomas caused by the virus have spontaneously become carcinomatous. The change has been noted in 5 of 10 domestic rabbits with growths existing 4 to 8 months.

During the early weeks of its development after virus inoculation the papilloma enlarges laterally, but later it is restricted by scar tissue and builds outwards only. At first it overlies the skin appendages, but these disappear after a time and it becomes bedded somewhat more deeply. The malignant change may first attract attention when a fissure exuding serosanguineous fluid opens in the midst

[2] Tillmans, J., Hirsch, P., and Hirsch, W., *Z. Untersuch. Lebensmittel*, 1932, **63**, 1.

[1] Shope, R. E., *J. Exp. Med.*, 1933, **58**, 607.

[2] Rous, Peyton, and Beard, J. W., *J. Exp. Med.*, 1934, **60**, 701.