Federal Government contributed more than $1,400,000 for protection and reforestation in cooperating states. Cooperative fire protection was extended to several million acres which had not previously been covered. The work of growing and distributing trees for forest planting also was enlarged.

DISCUSSION

CRYSTALLINE AMYLASE

NORTHRUP and Kunitz's recent announcement, in these columns, of the crystallization of trypsin, the pancreatic protease, prompts us to record here the crystallization of pancreatic amylase also.

From buffered alcohol-water solutions of pancreatic amylase, freshly purified by methods previously described from this laboratory, crystals have been obtained which show enzymic activity almost as high as the maximum observed in the highly purified preparations of this enzyme as previously prepared and studied.

The crystalline amylase is obtained as very minute isotropic elongated crystals which exhibit slight double refraction. Professor P. F. Kerr, of our department of mineralogy, to whom we are indebted for the crystallographic examination, reports further that the index of refraction as determined by immersion is approximately 1.54.

In view of the protein or protein-like nature of the crystals and their very slow deposition from the alcoholic systems, it is exceedingly important to work with a very small temperature gradient and in the region of hydrogen-ion activity corresponding to the isoelectric point.

The hydrogen-ion activity of the solution is adjusted by means of phosphate buffers in such concentration that they are not separated out at the temperatures employed. Both formation and yield of crystals are very dependent upon the hydrogen-ion activity of the system.

Careful study and rigorous observance of the best experimental conditions thus far found make it possible to obtain crystals with regularity; but as yet only in very small amounts. Furthermore, the crystals are so minute, so light and so unstable that even after they have been formed they must be handled by means of highly specialized and very time-consuming technique.

Hence it appears inevitable that further progress must be exceedingly slow and it therefore seems best to record, at this preliminary stage of the work, the fact that this much-studied and presumably typical amylolytic enzyme has been obtained in crystalline form, even if as yet only upon a small scale.[1]

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[1] Contribution No. 661 from the Department of Chemistry, Columbia University, New York.

PSYCHIC ANALOGUES OF ALLERGY

WHEN a foreign protein comes in contact with the tissue cells of a normal organism these become irritated and enter upon a cycle of unwonted metabolic change, the results of which appear in a week or two.

The first of these results is a specific hypersensitiveness toward the foreign protein in question so that thereafter infinitesimal quantities of the latter may be able to irritate the cells.

Experiment has made it obvious that the acquirement of specific sensitization goes hand in hand with the development of extraordinary powers within the tissue cells for rapid destruction, digestion or neutralization of the offensive foreign protein. The effective cellular agents in these reactions we know as *antibodies*. Their varieties and qualifications transcend our knowledge.

While the details of these cellular evolutions are exceedingly complex it is manifest that they are all coordinated to effect a purpose; to protect the body against a foreign poison; to endow it with what we call immunity toward the harmful substance which first irritated the cells.

Study of the pathogenesis of various infections leads irresistibly to the conclusion that, by and large, the essence of all infectious diseases inheres in the foreign proteins liberated in the body through the presence of invading microbes. Obviously no range of human endeavor is more fraught with problems affecting human welfare than that which is concerned with the understanding and control of the poisons leading to immunity.

There are doubtless several ways by which the biological status of immunity may be attained, but only one concerns us here—that, namely, in which the foreign protein or "antigen," as it is called, on entering the normal body has been able in the course of a few days to excite the latter to develop essentially new vital powers objectively witnessed by specific hypersensitiveness and defensive antibody reactions. The normal body which has undergone such a course of cellular training is now said to be "immune" toward that particular antigen, or microbe, which started the disturbance. It is characteristic of the immune state that the body which has acquired it responds at once with defensive reactions calculated to inhibit or destroy the irritating antigen whenever thereafter the latter makes a new invasion.

It might safely be predicted that all future contests

between the assaulted organism and the intruding pathogens must be determined on a merely quantitative basis according to the number and virulence of the latter.

When these factors are small enough the prepared defenders of the body destroy the invaders without perturbation, and gain strength by the exercise; the conscious mind is oblivious of the danger which had threatened its citadel.

But in actual experience or at the will of the experimentalist the number and virulence of the intruding microbes may surpass the abilities of the prepared mechanisms of defense. For the invaded host the contest then concerns, as it were, not the occasional criminal helpless before the bar of justice, but a national enemy threatening subjugation of a whole people. The result can only be determined by a war. In vital statistics this war is classified as "disease"; for the experimentalist its activities are broadly expressed by the word "allergy." Allergy implies a defensive reaction against a particular antigen in a prepared subject. The energy of the conflict is a function of the parity and the powers of the contenders. A decisive ending may signify the victory of either contestant. It may be assumed that in the scheme of Nature there is a definite purpose behind all these cellular changes in an animal which follow its infection with pathogenic microbes and culminate after some days in an allergic state capable of explosive physiological reactions under the stimulus of reinfection. Indeed, as will be indicated in a contribution as yet unpublished, the manifestation of allergy is not saved up like gifts for Christmas, ready for a grand celebration when a set time is reached; on the contrary, there is reason to believe that allergy, which includes specific hypersensitiveness and altered reaction, is initiated in the tissue cells at their earliest intercourse with invading germs. Nevertheless we can not admit that the ultimate purpose of nature is merely to develop in protoplasm a capacity for explosive disintegration. Rather her aim is peace—to be achieved by war only when necessary. And peace is complete immunity.

Nevertheless, the establishment of acquired immunity, either through the accident of disease or the intention of experiment, is commonly bound up with the inflammatory reactions of allergy which, like a club in the hands of a blind ally, may strike friend or foe alike.

The protection of the host through the tissue and functional reactions of allergy is so constant a concomitant of reinfection, or as the French prefer to say, super-infection, that a majority of the leaders in immunology assume that the sword of accomplishment in the establishment of immunity is allergy itself, or that allergy is the indispensable directive force of reactions through which immunity is established.

Calmette,[1] himself a proponent of this view, squarely states the paradox that the same allergic reaction in the host which under favorable conditions holds in check or forthwith destroys the microbic enemies of reinfection may, when the cellular responsiveness is enfeebled, turn upon its master and hasten his dissolution.

The distinguished American spokesman for the same point of view, Allen K. Krause,[2] closes a series of brilliant experimental researches aimed at the identification of allergy as the essential and effective agent of immunity, with the frank confession that, in spite of all demonstrated probabilities in favor of his theme, there still lacks convincing proof that his thesis is sound.

Now come Rich and McCordock[3] who, in a bold and most instructive essay, flatly deny that allergy is the essential basis of immunity. According to them the evidence of facts is decidedly against rather than in favor of such a view. While admitting that allergic reaction may at times favor protection of the host, such a relation is casual and not essential. The nub of their argument consists in the known lack of parallelism between the intensities of allergy and immunity. Either may be conspicuously weak while the other is correspondingly strong.

The whole argument seems to have reached a stalemate. The fast accumulating wealth of immunological facts finds no general law for their classification. There lacks a shibboleth—touchstone of fealty as between cell and microbe.

It has occurred to the writer that our philosophy of biological reaction may need a new point of view, less narrowly mechanistic than we can expect from our laboratories of to-day.

No physical proofs can be offered, only suggestive analogies from the psychic phase of that life of which, it is commonly agreed, allergy and immunity represent quasi-functions of the soma.

Consider pain. How negligible in health and well-being! Yet were there no such sensation it is safe to predict that animal life would not long persist. Consider fear, the warning forerunner of impending evil; the advocate of protective preparation. How universal and all-controlling this emotion and that

[1] A. Calmette, "L'Infection bacillaire de la Tuberculose chez l'homme et chez les animaux," 1920.

[2] A. K. Krause, and Krause with Willis or Peters, Numerous contributions to the *Amer. Rev. of Tuberculosis.*

[3] A. R. Rich and H. C. McCordock, *Bull.* Johns Hopkins Hospital, xliv, 273, 1929.

sensation. These two incidentals of the psychic life would be monstrously out of place in a trouble-free Eden, in our fool-a-day world they unite to make the cornerstone of human activities.

Using words of broad signification, we may assume that through fear the mind keys the body to instant defensive response for mutual protection. But there was not always a mind. It is a late sublimation of protoplasmic function.

But it is inconceivable that communities of living cells should have failed in the essentials of defensive reaction while waiting the development of a psychological organ. The elaboration of a technique of immunity must have kept pace step by step with the lethal powers of poisonous foes, else sooner or later must the defenseless race have succumbed. It seems probable that this technique accomplishes its purpose of immunity through two different methods.

The immigration of limited numbers of aliens into a growing country adds power to the population when they become assimilated without confusion. What we call "natural immunity" may find its analogue in some such process. But a common historical event has been a mass invasion of one people by another where the issue is not fusion, but conquest of one by the other. In such a case the national spirit of the invaded people is aroused to mobilize their mechanisms of defense, and these may or may not be adequate for victory.

But there is no likeness whatever between the national spirit and the military operations which it called into being. They have different rôles in the warfare. They may combine in a powerful union or, isolated, each may hurry to self-destruction.

The national spirit senses constantly the state of the country in its relations with alien peoples, always with a view of future possible conflict. Defense mechanisms of many kinds, each adjusted to deal with incipient trouble, are trained to go automatically into action. It may be plausibly maintained that this awareness of the country's interests, which is an attitude of the national spirit, finds an analogue in what is termed "allergy" in the phenomena of animal reinfections.

Allergy is the excitement-energy which precipitates the activities of prepared mechanisms of various kinds, here with violent inflammation and high fever, there with the gentle solution and disintegration of foreign germs and poisons without trace. Its whole import and reason for existence is protection of the organism—immunity. The more perfect and powerful that immunity, the less noise of conflict, the less evidence of allergy. But when the strongholds of the defenders are carried by assault—then allergic agony is futile to protect.

These analogues do not in themselves form admissible evidence, but they may broaden that field of suggestion from which the clews to most lines of productive research are picked.

No propaganda for the generation of public opinion can compare in speed and effectiveness with that universal hypersensitiveness to its own products which the growth of tubercle bacilli in a remote corner of the body has for the whole animal organism.

Physicists now soberly tell us that in the last analysis matter and energy are but different phases of the same something. Perhaps disputing biologists may come to see in vitalism and mechanism complementary views of the same subject.

As pain, fear and national spirit may be regarded teleologically as stimuli to conservative defensive reactions on the part of living units or communities, so perhaps we may properly consider allergy to represent a kindred agency which both generates hypersensitiveness to noxious inclusions and stimulates the body cells to form and operate defensive mechanisms against them. According to this view, in the language of social life, allergy is *in* immunity, but not *of* it.

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LEAF DIAGNOSIS AND THE INTERPRETATION OF FERTILIZER REQUIREMENTS OF PLANTS

WITH an enthusiasm and tenacity that is reminiscent of Pasteur, H. Lagatu and L. Maume, of l'Ecole Nationale d'Agriculture de Montpellier, have made numerous investigations during the past ten years and published *in extenso* on this subject.[1] Recently some of this literature has been widely distributed among the agricultural experiment stations in the United States and elsewhere and has found partial recognition in this country.[2, 3]

The main principles enunciated by the authors are that when one of the major elements—nitrogen, phosphorus or potassium—is omitted from a fertilizer the other two will be absorbed proportionally more, thus leading to unbalanced nutrition, disturbed metabolism and reduced yield. These conclusions are contrary to the widely accepted and amply verified "Law of the Minimum" (Liebig) as applied to nutrition of plants. Experimental data from which

[1] *Compt. Rend. Acad. Sci.*, 179: 782, 932, 1924; 180: 1179, 1925; 182: 653, 1926; 184: 229, 1927; 188: 1062, 1929; 190: 389, 1137, 1516, 1930; 191: 579, 1930. *Compt. Rend. Acad. Agr.*, 13: 437, 548, 1927, and 14: 762, 1928. "Le diagnostic foliaire de la pomme de terre," *Ann. Sci. Agron.*, 47: 5: 596, 1930.

[2] SCIENCE, 70: 382, 1929.

[3] SCIENCE, 72: 425, 1930.