Research Foundation. Hundreds of samples from shoe factories engaged in military contracts have been examined. Specifications on shoe leathers have been suggested.

Corrosion studies have been extended to corrosion testing of underwater paints, metals and wire screening for radio equipment, corrosion resistance of certain metals used for construction of boat hulls, effect on metals of lubricating oils, and the corrosion of metals by domestic tap waters and by softened laundry waters.

In the Division of Physics and Electrical Engineering equipment has been developed for measuring the vibration characteristics of various aircraft. Useful results have been obtained. Experiments on defrosting aircraft propellors have shown that the method is likely to be applicable to service conditions. Equipment had been developed and constructed for war purposes in the following connections: (a) penetrometers for use in gas warfare (b) a chronograph for measuring muzzle velocities of guns (c) an electrical plotting device for sound ranging. Numerous tests have also been made on the armoring properties of various materials and work is in progress on the improvement of anti-aircraft projectiles. Fifteen new designs of electric meters or metering apparatus were examined and approval recommended. Investigations have proceeded on the use of Adcock aerials for long wave direction finding especially on imperfect sites and also for short wave direction finding. Extensive experiments have been carried out to determine a method of testing vapor barriers in walls. Considerable work has been done on a by-pass method of control on the heat supply in railway refrigerator cars.

In cooperation with the Department of Agriculture and the Division of Biology and Agriculture about two thousand determinations of minor elements in plant and animal material have been made by spectroscopic methods. In the sound laboratory work includes studies on the cause of flutter in gas mask valves, investigations of special telephone receivers for naval use and other new devices.

Extensive investigations of x-ray methods of inspection of castings, forgings, welds and other war materials have been continued and inspection methods and technique suitable for Canadian requirements have been developed. A small optical shop was established to experiment with various methods of producing precise optical devices and to produce certain precise optical parts for the repair of standard instruments and for the development of new equipment. A vast amount of intricate and detailed planning of heavy electrical machinery down to the smallest modern device is being carried on by the electrical engineering staff.

At the outbreak of the war representatives of the National Research Council, the Ontario Research Foundation and the Dominion Arsenal conferred with representatives of the British Purchasing Mission on the subject of munitions gauges. A gauge laboratory was gradually staffed and equipped at Ottawa and equipment was supplied to a similar laboratory set up by the Ontario Research Foundation at Toronto. Canadian manufacturers have shown an aptitude for the production of fine precision parts that bids fair to render Canada independent of outside supplies.

The National Research Council is making a substantial contribution to Canada's war effort.

SPECIAL ARTICLES

DIABETES AND INFLAMMATION[1,2]

THE condition of diabetes mellitus is known to become markedly intensified when complicated by inflammation or infection. No satisfactory explanation has ever been offered to account for the basic mechanism involved. The inflammatory reaction tends to be concomitantly increased in severity and there seems to exist a lowered resistance to infections. There are some observations indicating a diminished capacity for antibody production and a reduction in the bactericidal power of the blood.[3] The present observations attempt to explain both the enhanced degree of diabetes and the associated increased severity of the inflammatory reaction in diabetic dogs having a superimposed acute pleural inflammation.

All observations were made on dogs rendered diabetic by pancreatectomy. It is to be recalled in this connection that although this type of diabetes has many obvious points of similarities with the human form, nevertheless there are several points of differences.[4] Three groups of animals were studied as follows: (1) dogs having a pleural inflammation induced by the introduction of 1.5 cc of turpentine; (2) depancreatized dogs with a pleural inflammation induced by the same irritant, but receiving no insulin immediately preceding and during the period of inflammation; (3)

[1] Aided by grants from the Dazian Foundation for Medical Research, The International Cancer Research Foundation and the Milton Fund of Harvard University.

[2] The author had the assistance of Mr. M. A. Kadish. In the course of this study aid was also received from Miss Irene Lapouse and from Miss Joan Malkenson.

[3] R. Richardson, *Jour. Clin. Invest.*, 12: 1143, 1933; 19: 239, 1940.

[4] C. N. H. Long, Harvey Lectures, 1936–1937, p. 194, Williams and Wilkins Company, Baltimore.

depancreatized dogs with pleural inflammation but receiving repeated injections of low doses of insulin (8 to 10 units twice daily) throughout the period of study.

The presence of an acute inflammation in the right pleural cavity of dogs fails to alter the blood sugar level. On the other hand, a similar injurious reaction in a diabetic dog induces a sharp and rapid ascendency in the blood sugar from an average in the 8 dogs studied of 253 milligrams to a level of 469.1 milligrams per 100 cc. The experimental findings wholly substantiate the well-known clinical picture of a diabetic disorder complicated with infection.

What is the basic mechanism involved to explain the enhanced diabetes? There are two considerations which must first of all be borne in mind. In the first place, an inflamed area is a focus of proteolysis. This has been pointed out previously by a number of investigators including the writer.[5] The conspicuous protein catabolic process may be regarded as a cardinal feature of the inflammatory reaction. In the second place, the earlier studies, particularly of Lusk and of his school, have demonstrated that amino products of protein degradation are in the diabetic organism readily converted into sugar.[6,7] Gluconeogenesis from proteins is thus a well-recognized process. It is therefore quite possible that an inflamed area in the diabetic behaves as a focus of enhanced proteolysis, favoring thus the formation of glucose from protein breakdown; the glucose, in turn would gradually diffuse into the circulation. The accentuated degree of proteolysis would offer at the same time a reasonable explanation for the increased severity of an inflammatory reaction in diabetes. Studies were therefore carried out on both exudate and blood samples of diabetic and non-diabetic dogs to determine the degree of proteolysis at the site of an acute inflammation. Besides measuring the sugar and lactic acid, determinations were also performed on the total proteins, non-protein nitrogen, urea and amino acid nitrogen concentrations of both exudate and blood.

The results of the determinations on exudates substantiate the view that the inflamed area is an active focus of gluconeogenesis originating from increased protein breakdown. The lactic acid and sugar levels of diabetic exudates are considerably higher than encountered in non-diabetic exudates. The average increase in lactic acid is 52 per cent., while the increase in exudate sugar averages 473.6 per cent. There is a slight drop in total proteins averaging 12.56 per cent. The rise in the products of proteolysis in diabetic exudates is striking. The non-protein nitrogen is increased 89.45 per cent.; the urea, 126.3 per cent.; and the amino acid nitrogen, 74.29 per cent. These facts therefore indicate an enhanced degree of proteolysis at the site of inflammation in a diabetic animal. That these products of protein breakdown are converted to glucose by deamination is further substantiated by insulin administration. Repeated injections of this substance to depancreatized dogs with inflammation are followed not only by a drop in lactic acid and sugar concentration but also by complete inhibition of the enhanced local proteolytic processes. The total proteins, NPN, urea and amino acid nitrogen are now restored to the levels found in exudates of non-diabetic animals.

The enhanced glucose formation from proteins in the acutely inflamed area allows for the gradual penetration of this diffusible substance into the circulation. Not only is the level of blood sugar, as pointed out above, markedly raised; but there is also a pronounced rise in the concentration of non-protein nitrogen, urea and to some extent of amino acid nitrogen in the systemic circulation. This state of affairs is not referable to pancreatomy *per se*. The reflection in the blood stream of the rise in a diabetic exudate of intermediary products of carbohydrate and protein metabolism does not contradict the earlier observations of the writer on the fixation or localization of material at the site of inflammation; for, as he has pointed out, particles of smaller dimensions, and of greater diffusibility are less effectively retained in such foci. Such materials therefore gradually find their way into the circulating blood.[5,8] Inflammation *per se* in non-diabetic dogs fails to induce in the blood any increase in either protein or carbohydrate products of metabolism. Insulin administration by inhibiting gluconeogenesis from proteins at the site of inflammation likewise induces no detectable changes in the levels of the blood.

Finally, the enhanced local proteolysis in the inflamed area of a diabetic animal manifests morphological signs of cellular injury in the form of vacuolized, degenerated, and in many instances unidentifiable polymorphonuclear leukocytes. The cells studied were from areas of inflammation of several hours' to one day's duration. Comparable studies of non-diabetic exudates revealed normal appearing leukocytes. In agreement with earlier studies by the writer the character and type of the cells in exudates were found to be correlated with the pH and the lactic acid concentration.[9,10] Both the hydrogen ion and the lactic acid concentrations were found to be elevated in exudates of diabetic animals.

[5] Valy Menkin, "Dynamics of Inflammation," Macmillan Company, 1940. New York.
[6] P. G. Stiles and G. Lusk, *Am. Jour. Physiol.*, 9: 380, 1903.
[7] G. Lusk, "The Science of Nutrition," W. B. Saunders Company, 1923, Philadelphia.
[8] Valy Menkin, *Physiol. Rev.*, 18: 366, 1938.
[9] Valy Menkin, *Am. Jour. Path.*, 10: 193, 1934.
[10] Valy Menkin and C. R. Warner, *Am. Jour. Path.*, 13: 25, 1937.

In conclusion, the mechanism of enhanced diabetes with inflammation seems to be referable to an increased proteolysis in the inflamed area. The rise in protein breakdown processes is correlated both with gluconeogenesis, and with increased severity of the inflammatory reaction. The surplus glucose formed locally gradually diffuses into the circulation thus elevating markedly the blood sugar level. These studies will form the subject of a detailed forthcoming report.

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THE ACTION OF CRYSTALLINE PEPSIN ON HORSE ANTI-PNEUMOCOCCUS ANTIBODY

WE have recently shown that when diphtheria antitoxic pseudoglobulin is treated with crystalline pepsin, a cleavage of the antitoxin molecule occurs in a plane normal to the long axis and that all the reactivity remains with one fragment only.[1] We have now extended this study to horse anti-pneumococcus antibody digested with pepsin in acetate buffer at pH 4.5 according to the method of Grabar.[2]

Euglobulin fractions from several different horses containing Type I and Type II antibody[3] have been examined in the standard Svedberg oil-turbine ultracentrifuge. The different serums showed wide variations in the sedimentation constants observed in agreement with the experience of other workers.[4] Thus, for example, most of the antibody euglobulin from Type I serum No. 721–34 was concentrated in a component with $s_{20} = 7 \times 10^{-13}$ cm/sec/dyne, and relatively little heavier material was present. On the other hand, a euglobulin fraction from Type II antiserum No. 513–50 showed major components with $s_{20} = 7$, 11, 18 and 30×10^{-13} cm/sec/dyne; and specific absorption of the latter with SII indicated that the antibody was concentrated mainly in the three heaviest components. Both these preparations were among those digested with pepsin. The digested antibody was precipitated with specific polysaccharide and the specific precipitate dissociated with sodium chloride.[5] The purified, digested and dissociated antibody combines with twice as much polysaccharide per milligram antibody nitrogen as the normal antibody, in confirmation of Grabar[2] and Treffers and Heidelberger.[6] Its sedimentation constant is 5.2×10^{-13} cm/sec/dyne, suggesting a molecular weight of less than 100,000, and it is homogeneous as regards sedimentation behavior. The same sedimentation constant is obtained after pepsin treatment, regardless of the molecular weight of the antibody in the original starting material. The digested horse pneumococcus antibody combines with as much carbohydrate per milligram antibody nitrogen as normal rabbit pneumococcus antibody, and it is smaller in size.

Finally, it may be noted that digested horse pneumococcus antibody is more soluble in distilled water than is the untreated antibody, and it has been possible to utilize this property to facilitate removal of undigested antibody from the neutralized reaction mixture by simple dialysis.

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A BIOTIN-LIKE SUBSTANCE PRODUCED BY DIPLODIA ZEAE

IN the course of studies of the physiology of the two species of the genus Diplodia which most commonly cause ear rots of corn it has become apparent that at least one important difference between them is the ability of *D. zeae* (Schw.) Lév. to produce in culture some substance, apparently found in many crop plants, which is necessary for the growth of both *D. zeae* and *D. macrospora* Earle. Margolin[1] has recently reported that *D. macrospora* requires "biotin or a biotin-like substance" for growth.

That this substance may be biotin is indicated by a number of similarities between it and the biotin obtained from egg yolks by Kögl and Tönnis.[2] A concentrate was obtained by the method of Buston and Pramanik[3] from a medium which contained KH_2PO_4 .3 g., $MgSO_4$ .25 g., KNO_3 2.0 g., dextrose 30.0 g., and distilled water to make 1 liter and which had been staled for 4 or 5 weeks by *D. zeae*. This concentrate is soluble in water and alcohol but is only very slightly or not at all soluble in ether, petroleum ether or chloro-

[1] M. L. Petermann and A. M. Pappenheimer, Jr., *Jour. Phys. Chem.*, 45: 1, 1941.

[2] P. Grabar, *Compt. rend. Acad. Sci.*, 207: 807, 1938.

[3] We are indebted to Dr. Elliott S. Robinson, of the Antitoxin and Vaccine Laboratory, Jamaica Plain, Mass., and to Dr. Harold Lyall, of the New York State Laboratories, Albany, N. Y., for generous samples of pneumococcus horse serum used in this work.

[4] M. Heidelberger and K. O. Pedersen, *Jour. Exp. Med.*, 65: 393, 1937. E. A. Kabat, *Jour. Exp. Med.*, 69: 103, 1939.

[5] M. Heidelberger and F. Kendall, *Jour. Exp. Med.*, 64: 161, 1936.

[6] H. P. Treffers and M. Heidelberger, *Jour. Exp. Med.*, 73: 125, 1941.

[1] A. S. Margolin, *Proc., W. Va. Acad. Sci.*, 14 (Keyser), in *W. Va. Univ. Bul.*, Ser. 41, No. 4–II, 1940.

[2] F. Kögl and B. Tönnis, *Zeits. für Physiol. Chemie*, 242: 43–73, 1936.

[3] H. W. Buston and B. N. Pramanik, *Jour. Biochem.*, 25: 1656–70, 1931.