SPECIAL ARTICLES

THE SENSITIZING PROPERTIES OF THE NUCLEIC ACIDS AND THEIR DERIVATIVES

THE chemical relationships between the nucleic acids and their physiological degradation products have been intensively studied; the part that these compounds may play in immunological phenomena, however, has never been investigated. Preliminary studies indicate that they may bear a fundamental relationship to pollen sensitization. The authors have found that individuals who gave positive skin reactions, when injected intradermally with ragweed pollen extract, likewise gave positive reactions when similarly tested with dilute solutions of nucleic acids and many of their derivatives. These reactions, so far demonstrated in a series of fifty ragweed pollen-sensitive human beings, appears to parallel the sensitivity of these individuals to ragweed pollen, regardless of the occurrence of symptoms of hay-fever. Only an occasional reaction has been observed in a group of forty non-allergic control cases, most of whom were normal individuals but some of whom were patients suffering from a variety of unrelated diseases. Likewise, five cases who gave positive reactions to animal danders, dust and foods, but not to ragweed pollen extract, also failed to react to the nucleic acid group of compounds.

The skin reactions elicited by the nucleic acids and their derivatives were the typical, immediate, wheal-erythema type. Such reactions were obtained uniformly upon the intradermal injection of $8\,\gamma$ (.008 mg) of either thymus or yeast nucleic acid (neutralized before injection). Three crystalline nucleotides prepared from yeast nucleic acid, namely, adenine, guanine and cytosine nucleotides, gave positive reactions in doses of $2\,\gamma$ (.002 mg). Likewise, crystalline adenine nucleotides prepared from beef heart muscle, beef pancreas and tea leaves reacted in the same manner. The simple purine salts, adenine sulfate, guanine chloride, hypoxanthine nitrate, xanthine nitrate and sodium urate all gave positive reactions in doses of $1\,\gamma$ (.001 mg), as did also the simple pyrimidine uracil. Allantoin, the chief end product of purine metabolism in most mammals except man, likewise gave positive reactions. The simple compound urea has also given typical reactions.

The compounds mentioned above, with the exception of urea, are all concerned in the metabolism of the nucleic acids and all contain a purine or pyrimidine ring structure. The alkaloid caffein (which contains the purine ring) and the amino acid d.l. histidine mono-hydrochloride (which contains the imidazole ring) gave consistent reactions, but the amino acid l. proline (which contains the pyrrolidine ring) reacted less frequently.

A skin-sensitizing antibody to yeast nucleic acid, muscle and yeast adenine nucleotides, caffein, allantoin, histidine and urea has been demonstrated so far in the serum of ten individuals reacting to these compounds.

Severe constitutional reactions were produced in two patients, when only 0.02 mg of two adenine nucleotides, prepared from yeast nucleic acid and from beef muscle, respectively, were used. For this reason only the small doses described above were employed in skin testing sensitive individuals.

WALTER L. WINKENWERDER
MARY V. BUELL
JOHN EAGER HOWARD
THE JOHNS HOPKINS UNIVERSITY

A POSSIBLE RELATION BETWEEN MANGANESE, SUNLIGHT AND WINTER HATCHABILITY OF HEN'S EGGS

IT has been observed at this station (unpublished data) that slipped tendon occurs more frequently in the heavy breeds of chickens that are raised in batteries in contrast to those that are raised out-of-doors on wire screens. Since the discovery of the relation of manganese to slipped tendon, little attention has been given to the effect of sunlight on this condition. Evidence that the manganese requirements of laying hens may be increased in the absence of sunlight is indicated by hatchability records obtained during the past two years.

It was found that a mash consisting of 45 parts of yellow corn, 15 of wheat bran, 15 of middlings, 5 of alfalfa leaf meal, 1.5 of granite grits, 1.5 of limestone grits, 1 of cod liver oil and 16 parts of soy-bean oil meal was improved for egg hatchability by the addition of 85 parts per million of manganese. This ration contained adequate amounts of vitamin D; however, during the fall and winter months (September to April) the average per cent. of hatchability of the fertile eggs laid by the hens fed this ration without added manganese was 48.1. The corresponding groups which received added manganese produced eggs having an average hatchability of 62 per cent. When there was adequate sunlight during the late spring and early summer, there was little significant difference in the egg hatchability between these two groups. The increase in hatchability of the eggs from the group on the basal ration appears to be correlated with increased sunlight. Hatchability of these eggs increased to an average of 70 per cent. as compared to 75 per cent. hatchability of the eggs from the manganese-fed group. The effect of sunlight on the hatchability of the eggs from the basal group is shown very clearly in Fig. 1.

The bi-monthly hatchability of eggs laid by the first group (low manganese) was compared with the corresponding variations in temperature and hours of

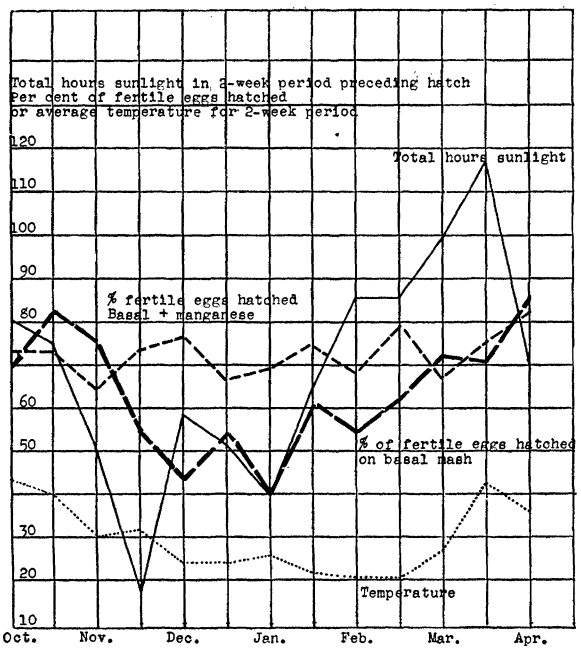

FIG. 1. The effect of manganese, sunlight, and temperature on hatchability of hen's eggs.

sunlight. The correlation was found between the total hours of sunlight during the 2-weeks period preceding the time the eggs were laid and the hatchability of the eggs. The period of diminishing per cent. of hatchability followed shortly after the period during which the total hours of sunlight diminished. Likewise the improvement in hatchability followed the increase in sunlight. There was no correlation between the fall or rise in the mean temperature and the per cent. of hatchability. Byerly, Titus, Ellis and Nestler[1] also have reported that hatchability of eggs from hens on a high soy-bean oil meal ration was markedly improved when the hens had direct access to sunlight. Since there was no fall in the hatchability of eggs from groups receiving added manganese, there must have been a borderline deficiency in the manganese content of the ration. During the spring, when there was adequate sunlight, this deficiency was eliminated, as was shown by the nearly equal hatchability of the two groups. That the vitamin D of cod liver oil was not a factor in the effect of sunlight has been shown by a number of experiments.

What explanation can be given for this apparent sparing action of sunlight on a hen's requirement for manganese can not be stated at present.

J. B. CHRISTIANSEN
J. G. HALPIN
E. B. HART

UNIVERSITY OF WISCONSIN

[1] T. C. Byerly, H. W. Titus, N. R. Ellis and R. B. Nestler, *Jour. Poultry Sci.*, 16: 323, 1937.

THE ELECTROPHORETIC ANALYSIS OF ANTIPNEUMOCOCCUS HORSE SERA

RECENT work has indicated that the antibody activity of antipneumococcus horse serum is associated with proteins which differ from the principal globulins of normal horse serum in both molecular weight[1] and electrical mobility.[2] These antibodies are heavier than the principal globulins and electrophoretic observations have indicated that they move with a velocity intermediate between those of the β and γ components of normal sera.[2]

We have made electrophoretic[3] measurements upon a number of antipneumococcus horse sera and of antibody concentrates from them. Our results differ from the foregoing in showing that the antibody activity in all our preparations has the same electrical mobility as the ordinary γ-globulin. This is illustrated in Fig. 1, which reproduces the Longsworth[4] mobility-concentration patterns of an antipneumococcus horse serum before and after absorption of the serum with specific polysaccharides. This photograph was made with a bivalent Types I and II antiserum; similar results have been obtained with a bivalent serum against Types IV and VIII pneumococci. The measured mo-

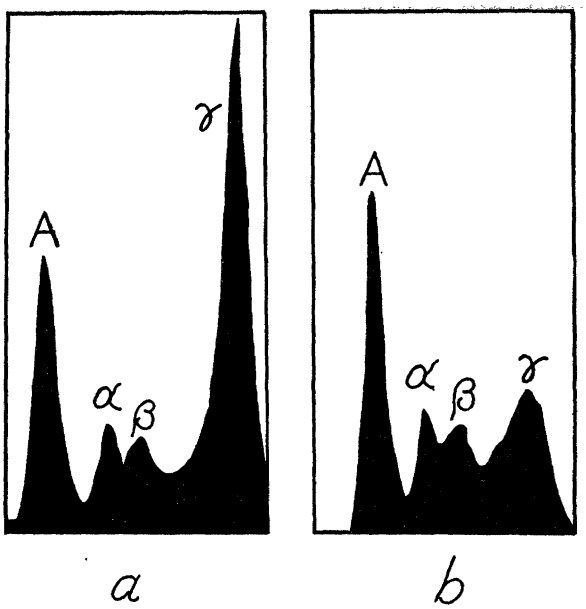

FIG. 1. Longsworth patterns of (a) unabsorbed and (b) absorbed antipneumococcus horse serum No. 6639. The albumin peak is designated by A, the globulin peaks by α, β, γ. The decrease in area of the γ-peak on absorption is evident.

[1] J. Biscoe, F. Hercik and R. W. G. Wyckoff, SCIENCE, 83: 602, 1936; M. Heidelberger and K. O. Pedersen, *Jour. Exp. Med.*, 65: 393, 1937.

[2] A. Tiselius and E. A. Kabat, SCIENCE, 87: 416, 1938; *Jour. Exp. Med.*, 69: 119, 1939.

[3] A. Tiselius, *Trans. Faraday Soc.*, 33: 524, 1937.

[4] L. G. Longsworth, *Jour. Am. Chem. Soc.*, 61: 529, 1939.