

tion of insulin the lactic acid of the blood rose to 4 to 10 times the control concentration. The rise in the lactic acid paralleled the drop in sugar.

In the diabetic subjects the ingestion of glucose produced an increase in the blood lactic acid of from 50 to 100 per cent of the control concentration. The administration of the insulin resulted in a rise in the lactic acid, paralleling the decrease in the blood sugar. In the cases of diabetes the dosage of insulin was based upon the level of blood sugar. The response of the blood lactic acid to the insulin in diabetes was much less pronounced than in the normal subjects. In both the normals and diabetics, the insulin administration produced a decrease of the inorganic phosphorus of the blood and urine, with a subsequent return to normal. Glycolysis *in vitro* was accompanied by a rise in the blood lactic acid; however this increase is not as great as the rise associated with insulin hypoglycemia. The increase in the lactic acid does not account for the entire loss in blood sugar in either case.

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The development of cutaneous hypersensitiveness following the intestinal absorption of antigenic protein.

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It has been shown by Schloss and Anderson,¹ and Anderson and Schloss² that marasmic infants frequently absorb antigenic protein from the intestinal tract in amounts sufficient to cause the appearance of specific precipitin in the blood. In many instances also, the blood has the power passively to sensitize guinea pigs to

¹ Schloss, O. M., and Anderson, A. F., Allergy to Cow's Milk in Infants with Severe Malnutrition, *PROC. SOC. EXP. BIOL. AND MED.*, 1922, xx, 5.

² Anderson, A. F., and Schloss, O. M., Allergy to Cow's Milk in Infants with Nutritional Disorders, *Am. J. Dis. Child.*, 1923, xxvi, 341.

the specific protein. It seemed of interest therefore to determine whether the enteral absorption of antigenic protein leads also to cutaneous hypersensitiveness.

Tests were made using both the cutaneous and intracutaneous methods. In no case was the reaction by the cutaneous method positive. Accordingly, the data presented in this paper is based solely on the results of the intracutaneous tests.

Solutions of the proteins in physiological saline were made up at frequent intervals. Dilutions of 1:100 to 1:1000 were employed, the strength varying with the different proteins used. Chinosol was added as a preservative. One twentieth of a cubic centimeter of the test solution was injected intradermally over the back, chest, abdomen or forearms. Readings were made at frequent intervals for one hour. Control tests were done with the solvent alone.

A reaction was considered positive only if there was a very marked urticaria-like wheal with definite irregularity of the edges—the so-called pseudopodia. In many cases there was a marked erythema or a larger wheal than shown by the control, but it was deemed wiser to disregard such reactions, and to consider positive only unquestionable reactions.

All of the intracutaneous tests described in this paper were done upon the infants who were tested by Anderson, Schloss and Myers for the presence of precipitin in the blood. As far as possible, both tests were done on the same day so that a comparison of results could be made.

It was deemed of great importance to rule out the possibility of a reaction being due to inherited hypersensitiveness. This was done in two ways. In nearly all of the cases there were repeated negative tests prior to the appearance of the positive reaction. In a few cases where the first tests were positive, subsequent negative ones were always obtained. Babies with eczema were not included.

Twenty-three marasmic infants were tested for cutaneous hypersensitiveness to cow's milk protein. Twelve showed positive reactions. There was a marked variation in the duration of cutaneous hypersensitiveness. It ranged from four days to two months or more. Five cases still showed a positive reaction, when last tested, after having been followed for periods between 2 weeks and 48 days.

In relation to the appearance of precipitins in the blood, it was found that in only one case was the precipitin test negative and the intracutaneous test positive. In eleven cases precipitin was present and the intracutaneous tests were negative. In eleven cases both tests were positive. In these eleven cases, precipitin appeared prior to the skin reactions in seven, subsequent to them in two, and at the same time in two.

These results show that a considerable number of marasmic infants develop cutaneous hypersensitiveness to cow's milk. The skin hypersensitiveness appears in most instances at about the same time that precipitin is demonstrated in the blood.

Further observations were made to determine whether ingestion of protein foods other than milk would give similar results. The first group consisted of 19 marasmic infants who ingested 6 to 12 grams of egg white a day in addition to their regular diet. On these infants, tests for precipitin were made by Anderson, Schloss and Myers. Of these nineteen marasmic infants, fifteen showed positive intracutaneous reactions to egg. There was a great variation in the duration of skin hypersensitiveness in these cases. It lasted from three days to eight months. Five infants still gave positive reactions when last tested, after having been followed from 2 weeks to 43 days. The interval between the first ingestion of egg and the appearance of positive reactions likewise showed a marked variation. The shortest period was six days and the longest seventy-four days, while the average was thirty-three days.

In relation to the appearance of precipitin, it was found that in one case there were positive skin tests and negative precipitin reactions; in three cases negative skin tests and positive precipitin tests; in one, both tests were negative; and in fourteen, both tests were positive. Of these fourteen, precipitin appeared prior to the skin reactions in eight, after them in one, and at the same time in five.

In a third group of cases sheep serum was added to the diet. The total daily amount was 30 to 60 cc. Six marasmic infants were tested and of this number one showed a positive cutaneous reaction. No conclusion as to the duration of this reaction could be drawn as the test was still positive at the end of one month. The reaction appeared thirteen days after the first feeding of sheep serum. Precipitin appeared in the blood in all of the six

cases. In the one case where both tests were positive, precipitin appeared four days after the cutaneous test became positive.

It is thus seen that, following the ingestion of foreign protein, a great number of marasmic infants develop cutaneous hypersensitiveness to the protein ingested. This skin reaction usually occurs either immediately after, or at the same time as, the appearance of antibody in the blood stream.

Further tests were then done on normal infants whose blood was examined for precipitin to determine if they likewise developed cutaneous hypersensitiveness. The first group comprised breast fed infants who, while under observation, were given complementary or supplementary feedings of cow's milk, and also very young infants who had ingested cow's milk for not more than two weeks prior to admission. Ten infants were included in this group. Of this number six showed positive intracutaneous reactions to cow's milk. Precipitin for cow's milk was present in the blood of all six cases, appearing prior to the skin reaction in one case, at the same time in four cases, and afterwards in one case.

A second group of normal infants who were fed egg white, were tested for cutaneous hypersensitiveness to egg. Eight of the 21 infants in this group gave positive reactions. The interval between the first ingestion of egg and the appearance of a positive skin reaction ranged between ten and twenty-eight days with an average interval of seventeen days. The duration of the skin hypersensitiveness varied between ten days and one month. Precipitin for egg was not demonstrated in the blood of two of the infants who developed a positive cutaneous reaction. In six cases both tests were positive. A positive precipitin reaction was obtained first in two cases, afterwards in two cases, and at the same time in two cases.

A very small group of four normal infants received sheep serum in their food. One infant showed a positive skin reaction which appeared forty days after the first feeding. The reaction was still positive two weeks after its appearance, when the last test was done. It appeared at the same time that precipitin for sheep serum was demonstrated in the blood. The small number of positive reactions which occurred after feeding sheep serum to both marasmic and normal infants might possibly be explained by the fact that the actual amount of protein ingested was much less than in the case of milk and egg.

A fourth group of normal infants was fed almond flour. Fifteen to fifty grams were added to the daily feedings. Fifteen infants were tested and of this number two showed positive skin tests. These appeared seventeen and twenty-three days after the first feeding. In both cases precipitin was present prior to the skin reactions.

These results indicate that the enteral absorption of antigenic protein by normal or marasmic infants leads not only to the appearance of a specific precipitin in the blood, but also in many cases to cutaneous hypersensitiveness. The results also indicate that there is a definite coincidence between the appearance of the skin reaction and the presence of precipitin in the blood.

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The intestinal absorption of antigenic protein by normal infants.

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In previous communications,¹ it has been shown that the blood of most marasmic infants contains precipitin for cow's milk at some period of the disease, indicating preceding enteral absorption of antigenic protein from cow's milk.

Supported by a large number of observations, it is generally assumed that in the process of normal digestion no antigenic protein product enters the blood. In a few isolated experiments, which involved feeding large amounts of protein at a single dose, absorption of antigenic protein by normal individuals has been demonstrated by Ascoli, Schloss and Worthen, and others. Most investigations of this type, however, have been negative. In a large number of normal infants, tests for precipitin for cow's milk made by us, have been uniformly negative.

¹ Schloss, O. M., and Anderson, A. F., *Allergy to Cow's Milk in Infants with Severe Malnutrition*, *PROC. SOC. EXP. BIOL. AND MED.*, 1922, xx, 5; Anderson, A. F., and Schloss, O. M., *Allergy to Cow's Milk in Infants with Nutritional Disorders*, *Am. J. Dis. Child.*, 1923, xxvi, 451.