of both Salmonella and meningococcus produced similar effects not only in their inhibition of succinic-dehydrogenase but also on the carbohydrate metabolite concentration of tissues. Since the enzyme inhibition occurred in a few minutes after the injection of the endotoxin, it is reasonable to assume that the inhibition of this enzyme activity plays an important role in the mechanism responsible for the changes in carbohydrate metabolite concentration in the poisoned rabbit tissues. The mechanism of this enzyme inhibition and its effect on carbohydrate metabolism is being investigated in detail.

Summary. The intravenous injection of meningococcal or Salmonella endotoxin into rabbits produced increase in blood glucose, lactic acid and inorganic phosphorus. This was followed by hypoglycemia which could be observed before the death of the animal. Liver and muscle glycogen decreased while lactic acid content of the tissues increased. The pyruvic acid content of blood and tissues showed a significant decrease. Succinic dehydrogenase in both muscle and liver was markedly inhibited. Cytochrome oxidase activity was not affected.

The Na-ascorbate used in the enzyme assays was generously supplied by Van Patten Pharmaceutical Company, Chicago.

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Passive Cellular Transfer of the Tuberculin Type of Hypersensitivity.*

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Chase[1] recently reported that the tuberculin type of hypersensitivity was transferred passively to normal guinea pigs by injection of the cells of peritoneal exudate, lymph nodes or spleen of guinea pigs sensitized to tuberculin by the injection of heat-killed tubercle bacilli. The passively conferred sensitivity was transient, lasting about 5 days. This is a significant achievement as the failure passively to transfer tuberculin sensitivity has been adduced as a basic distinction between the tuberculin and the anaphylactic or Arthus types of hypersensitivity.[2] It was hoped that, if confirmed, the passive cellular transfer of tuberculin hypersensitivity might provide a method suitable for the elucidation of the underlying chemical factors in the induction and development of this peculiar allergic phenomenon. The repetition of Chase's studies was therefore undertaken.§

Materials and Methods. The materials and methods were essentially those used by Chase[1] in his experiments. White albino guinea pigs of both sexes were sensitized to tuberculin by subcutaneous injection into the groin of heat-killed human tubercle bacilli suspended in mineral oil[3,4,5] and aquafor. Usually 2.5 mg of dried bacillary growth was suspended in a total inoculum of 1 ml for each animal. Five to 9 weeks later, when cutaneous sensitivity to

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‡ Contribution No. 1153.

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§ Since these confirmatory studies have been completed another group of workers reported successful repetition of Chase's experiments. Cummings, M. M., Hoyt, M., and Gottshall, R. Y., *Pub. Health Rep.*, 1947, **62**, 994.

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TABLE I.
Reactions to Tuberculin in Guinea Pigs Injected with Cells from Normal and Tuberculin-sensitized Guinea Pigs.

No. and type donor animals	Volume and type material transferred to each recipient*	No. of recipients*	Avg reaction (mm) of recipients 24 hr after injection of tuberculin†	and 48 hr	No. tuberculin pos.‡ No. tested
15 sensitized	0.5 ml peritoneal cells	3	8 × 9, i, e	12 × 13, i, e	3/3
16 "	0.65 " " "	4	8 × 8, i, e	10 × 12, i, e	3/4
4 "	— " "	1	8 × 8, e	12 × 15, i, e	1/1
2 "	— " "	1	7 × 7, i	10 × 10, i, e	1/1
9 "	2.0 ml splenic cells	3	10 × 9, i, e	12 × 12, i, e	3/3
9 "	2.0 " lymph node cells	3	10 × 10, i, e	12 × 12, i, e	2/3
9 "	19.0 " defibrinated blood	3	9 × 9, i, e	10 × 11, i, e	1/3
9 "	20.0 " citrated blood	3	8 × 8, i, e	11 × 11, i, e	1/3
12 "	8.0 " serum	4	0	0	0/4
16 normal	0 70 " peritoneal cells	4	0	0	0/4
16 "	2.25 " splenic cells	4	0	0	0/4

* For example, in the first group peritoneal cells from 15 sensitized animals were divided into 3 parts and injected into each of 3 animals; in second group, cells from 16 animals were divided into 4 parts, and so on.

† Reactions to second injection of tuberculin 48 hours after passive transfer. i = induration; e = erythema; 0 = negative.

‡ In first group, for example, 3 out of 3 animals tested reacted positively to tuberculin; in second group 3 out of 4, and so on.

tuberculin was found to be definite and intense, exudates were evoked in the sensitized guinea pigs by the intraperitoneal inoculation of 30 ml of mineral oil. Forty-eight hours later the peritoneal cavities were flushed out with citrated-Locke's solution containing 0.25% gelatin. The washings were placed in a separatory funnel and allowed to stand. After the oil had risen the aqueous layer was collected and centrifuged lightly for several minutes. The sedimented cells, about 0.15 ml from each animal, were resuspended in citrated gelatin-Locke's solution and again centrifuged. The washed cells were suspended in about 4 ml of gelatin-Locke's solution and immediately inoculated intraperitoneally into male albino guinea pigs. The differential cell count of the suspension before inoculation revealed about 25% polymorphonuclear leukocytes, 35% lymphocytes, and 40% mononuclears.

Twenty-four and 48 hours after the cell-transfer the recipient animals were tested for tuberculin sensitivity by intradermal injection of 1:2 or 1:4 Old Tuberculin from which the glycerin had been removed by precipitation with cold alcohol.[6]

As a control each animal was also skin-tested with 0.1 ml of 1:2 or 1:4 glycerin broth which was deglycerinated in the same manner as was the Old Tuberculin. It had been previously determined that these concentrations of "deglycerinated" tuberculin and broth were the highest not producing visible reactions upon injection into the skin of normal, unsensitized guinea pigs. The cutaneous response to all test inoculations was measured 24 and 48 hours after inoculation of the test material.

Cells from the spleen and lymph nodes and, in a few instances, whole defibrinated or citrated blood and serum from sensitized animals also were employed in the attempt to transfer sensitivity. It is important to note that smears of the lymph node cell suspensions revealed that approximately 95% of the cells were small or medium-sized lymphocytes and 5% monocytes. As controls corresponding types of cells from normal, unsensitized guinea pigs were inoculated into normal guinea pigs.

Results. Pertinent data and results of these experiments are summarized in Table I. In order to conserve space the uniformly negative results of control injections of "deglycerinated" broth and of all tests 24 hours after the cell transfer are omitted from the table.

[6] Chase, M. W., personal communication.

In general the data confirm Chase's results on the passive transfer of tuberculin hypersensitivity with the further observation that whole blood may occasionally transfer sensitivity. In a few instances by means of daily skin tests it was found that the passively conferred sensitivity lasted only 4 or 5 days. The occasional failures in transfer of sensitivity with peritoneal exudate or lymph node cells have not been satisfactorily explained.

Discussion. It should be emphasized that the positive tuberculin reactions elicited in the recipient animals were of the delayed type typical of reactions in animals actively sensitized by injection of tubercle bacilli.[2] The reactions rarely appeared much before 24 hours and were at their height of intensity 48 to 72 hours after injection.

It is interesting to note that sensitivity was transferred in 2 instances by injection of whole blood from sensitized animals. This is not surprising as Chase has found recently[6] that the buffy coat separated from the red cells of the blood may passively transfer sensitivity. These observations and the demonstration of typhoid agglutinins in the buffy coat from the blood of immunized rabbits[7] suggest a wider than hitherto supposed participation of the white cells of the blood in immunological phenomena.

The positive results employing suspensions containing about 95% lymphocytes are indicative of the possible preeminence of this cell in the transfer of sensitivity. The specific lysis of a portion of small mature lymphocytes from blood or spleen of tuberculous mice and guinea pigs upon contact with tuberculin[8] may be related to the ability of lymphocytes to transfer sensitivity. The recent implication of lymphocytes as cells which synthesize antibodies[9] may or may not be a related finding, as it has not been shown so far that antibodies are involved in the development of tuberculin hypersensitivity.[2] The demonstration[10] that cells from tuberculin-sensitive animals may retain their sensitivity to the toxic action of tuberculin after several transplants in tissue culture would seem to rule out the role of circulating antibodies in this phenomenon.

Work is proceeding in the attempt to isolate the factor responsible for the transfer of sensitivity. Thus far efforts to transfer sensitivity by means of various crude extracts of the cells have been completely negative. In the endeavor to determine whether the cell transfer is a general phenomenon, cell transfer of the delayed type of pneumococcus sensitivity in rabbits[11] has been tried. Thus far these experiments also have proven unsuccessful.

Summary. 1. In confirmation of Chase's studies, the tuberculin type of hypersensitivity has been transferred passively to normal, unsensitized guinea pigs by injection of the cells of peritoneal exudate, lymph nodes, spleen, and whole blood of tuberculin-sensitive guinea pigs. The passively conferred sensitivity lasted 4 or 5 days.

2. The transfer of sensitivity by injection of whole blood taken with other observations suggests that the white cells of the circulating blood may participate more widely than previously believed in immunological phenomena.

3. The positive results employing suspensions containing 95% of lymphocytes suggest that this cell type may be of great importance in the transfer of sensitivity.

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