early as 6 to 8 hours after injection, and rose to a maximum in about 48 hours. At that time, the entire liver parenchyma was involved, all hepatic cells being distended with lipid globules. A progressive loss of liver lipids was noted after that time despite continued ethionine injections.

One group of rats was fed the stock diet to which had been added 0.1 per cent DL-ethionine. Although the food intake varied widely (0-14 g per day, average of 5 g per day), the effect on the pancreas was no different from that observed when the ethionine was injected.

Comment. It has been known since 1924 that fatty livers developed slowly in depancreatized dogs kept alive with insulin, and that the addition of raw pancreas prevents this fatty change(11). The finding that a similar type of fatty liver occurs in dogs subjected to complete ligation of their pancreatic ducts has led to the view that the release of pancreatic juice into the intestinal tract is necessary for inhibiting the deposit of excessive amounts of fat in the liver. This led us to question whether the fatty liver found in the DL-ethionine-treated rats resulted from destruction of their pancreatic acinar tissue. However, the rapid onset of this fatty change would appear to cast doubt on the possibility that it results from loss of the external secretion of the pancreas.

The view that ethionine inhibits protein synthesis has been expressed by Simpson *et al.* (12). The rapid depletion of zymogen granules and the loss of cytoplasmic basophilia (presumed to reflect the nucleoprotein content of the cell) might be construed to support this view(13-18). It should be stressed, however, that a direct toxic action of the administered ethionine (or a derivative) upon the acinar tissue is not ruled out.

Summary. 1. The effects of daily administration of 50 or 100 mg of DL-ethionine on the rat pancreas is described.

2. Degenerative changes in the acinar tissue occurred as early as 12 hours after a single injection of 50 mg DL-ethionine.

3. Daily injections of 50 or 100 mg in nonfasted rats, for 2 weeks, resulted in almost complete obliteration of the acinar tissue accompanied by fibrous proliferation.

4. No histological evidence of islet damage was observed with these dosages.

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Received July 11, 1950. P.S.E.B.M., 1950, v74.

Passive Transfer of Atopic Hypersensitiveness in Man by Means of Leucocytes.* (18074)

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Lawrence(1) has recently demonstrated, in man, the local passive transfer of the delayed type of cutaneous hypersensitiveness to tuberculin by the intracutaneous injection, into normal recipients, of viable leucocytes obtained from the blood of tuberculin-sensitive

* Aided by a grant from the Celia Antonoff Research Fund.

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donors. Chase(2) had previously succeeded in passively sensitizing normal guinea pigs to the delayed type of sensitivity to tuberculin and to chemicals(3) by the injection of leucocytes obtained from peritoneal exudates of sensitized animals. In the present communication, the writers report the local passive transfer of the immediate whealing type of cutaneous reaction which is mediated by the atopic reagin, employing as the skin-sensitizing agent the viable washed leucocytes obtained from the blood of atopic skin-sensitive patients. The experimental method represents a variation from the passive transfer technic originally described by Prausnitz and Küstner(4) in that the transfer was effected by the donor's leucocytes instead of his blood serum.

Methods. Viable leucocytes were obtained from the heparinized venous bloods of allergic patients according to the technic of Minor and Burnett(5) which employs bovine fibrinogen, Fraction I (Armour), to hasten the sedimentation of the erythrocytes. The white blood cells which remained suspended in the plasma were isolated by centrifugation and washed two or four times in Tyrode solution in Machlett capillary-tip tubes, according to the method described by Lawrence(1). Microscopic examination of the cellular sediment after 2 washings revealed a mixture of leucocytes and erythrocytes in which the viable white cells predominated. The average yield from each 10 ml of donor's blood was 0.028 ml of cellular sediment. This sediment, resuspended in 12 times its volume of Tyrode solution, was used for passive local sensitization. Rigid precautions for the maintenance of sterility were enforced throughout the entire procedure.

Sedimented erythrocytes, obtained from the same blood samples which provided the leucocytes, were washed twice and resuspended in Tyrode solution by the same technic employed for the white blood cells. This erythrocytic suspension was also used for attempts at passive local sensitization.

To determine whether plasma, in the dilution which remained in the white cell suspension, could produce passive local sensitization, 0.03 ml of cell-free plasma was treated as though it were cell sediment. It was "washed" (diluted) with 2.0 ml of Tyrode solution and centrifuged in a Machlett tube. With 0.03 ml of "sediment" of this mixture, the "washing" (dilution) process was repeated. Finally, 0.03 ml of the "sediment" was diluted with 12 times its volume of Tyrode solution and used for attempts at passive sensitization.

Sensitized cutaneous sites were also prepared with 1:5 dilutions of the supernate obtained when the plasma was centrifuged to remove the leucocytes.

The passive transfer technic employed in these experiments followed the principles outlined by Walzer and Bowman(6) for indirect testing in atopic hypersensitiveness. Normal nonatopic adults who showed completely negative reactions to skin tests with the concentrated allergens to be employed in the studies were chosen as recipients.

Sites were prepared on the outer aspects of the recipient's arms by the intracutaneous injection of 0.05 ml of the sensitizing substances. At the sites injected with leucocytes, induration and erythema developed, which usually lasted for from three to seven days. Persistence of the inflammation beyond this time rendered the sites unfit for testing. The injection of the erythrocyte suspensions and the serum preparations produced little or no inflammation.

The allergenic extracts used for testing were those routinely employed for diagnosis and treatment in the Allergy Clinic. They were prepared according to the technic of Coca and Milford(7) and standardized on the basis of their total nitrogen content. The ragweed, timothy, and English plantain pollen extracts were made in January, 1950. Because the

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TABLE I.
Passive Transfer of Sensitivity to Ragweed Produced with Leucocytes of H. R.

Recipient	Date of sensitization	Allergen tested (mg N/ml)		Reactions obtained on cutaneous sites prepared with: H. R. leucocytes washed 2×	H. R. leucocytes washed 4×	Normal leucocytes washed 2×	H. R. plasma dilution 1:5
P	4/ 7/50	Ragweed	0.1	+	±		++
P†	4/25/50	,,	0.1	+	±		
I	4/27/50	,,	0.1	+	±		
D	5/ 1/50	,,	0.1	+			+±
P	5/ 6/50	Timothy	0.1	0			
K	5/17/50	Ragweed	0.1	+			
		Timothy	0.1				±
PR	6/19/50	Ragweed	0.1*	+		0	
		,,	0.2	±			
P	6/19/50	,,	0.2	+			
		,,	0.1*	±		0	
		Rabbit epithelium	0.05	0			
		Timothy	0.1*	0			
W	6/19/50	Ragweed	0.1*			0	
		,,	0.2			0	

* Freshly prepared extracts.

† Sites on this recipient prepared with twice-washed erythrocytes and with a serum dilution control reacted negatively to tests with ragweed 0.1.

Reactions to tests with above allergens on normal cutaneous sites of recipients were uniformly negative.

potency of the pollen extracts gradually diminished with age, fresh extracts of timothy and ragweed pollens were prepared in June, 1950.

The cutaneous sites on the recipients were tested for hypersensitiveness seven days after their preparation. About 0.02 ml of the allergenic extract was injected into the site and into adjacent normal skin as a control. Positive reactions at sites prepared with leucocytes tended to develop slowly and reached their peak in from 20 to 30 minutes. The larger positive reactions at the leucocytic sites consisted of a wheal and erythema similar to positive reactions on plasma-sensitized sites. Palpation of the reactions at leucocytic sites, however, often revealed a deep-seated edema, which tended to outlast reactions at the plasma-sensitized sites. It was, therefore, necessary to evaluate reactions by palpation as well as by inspection. Pruritus, if present at all, was of a mild degree.

Since the tests with allergens on normal skin produced uniformly negative reactions as a result of the preliminary screening of the recipients, the results of passive transfer tests were evaluated solely on the basis of the reactions at the sensitized sites after twenty minutes. They were graded as follows:

0 = Negative—Site unchanged; 0± = Negative plus—Barely perceptible edema; ± = Slight minus positive—Definite, but small amount of edema, with faint erythema; + = Slight positive—Wheal, at least 0.5 cm in diameter, with surrounding erythema; ++ = Moderate positive—Wheal, approximately 1.0 cm in diameter, with surrounding erythema; +++ = Marked positive—Wheal, larger than 1.0 cm in diameter, with surrounding erythema.

The viable leucocytes used for passive sensitization were obtained from patients with bronchial asthma or hay fever who were attending the Allergy Clinic. They varied widely in the degree of their clinical and cutaneous sensitivities as well as in their serum titers for atopic reagins. None were sensitive to an unusually pronounced degree. Leucocytic suspensions from normal, nonatopic subjects were also used as controls.

Because of convenience, H.R., a hospital interne, aged 27, was used repeatedly as a source of leucocytes (Table I). He had been troubled with hay fever caused by ragweed pollen for two seasons. Symptoms rarely occurred during the grass (timothy) season. He

TABLE II.
Summary of Passive Transfer Studies with Leucocytes from Allergic Patients.

Donor; Diagnosis; Skin reactions	Recipient	Date	Allergen tested (mg N/ml)	Reactions obtained on cutaneous sites prepared with: Leucocytes washed 2×	Leucocytes washed 4×	Serum control	Plasma: Dilution	Plasma: Result
T.C. male, 26 yr	P	4/ 6/50	Rabbit epith. 0.05	+			1:5	++
Asthma	G	4/17/50	" " 0.05	±	0±			
Rabbit epith. 0.001 ++±	D	4/22/50	" " 0.05	±	0			
S.F. female, 30 yr	W	3/13/50	Ragweed 0.1	+		0	None	+++
Ragweed hay fever	K	5/29/50	" 0.1	±				
" 0.001 +			" 0.2	±				
" 0.01 +++			Timothy 0.1	0±				
Timothy 0.1 ++			Saline	0				
M.S. female, 45 yr	D	4/10/50	Ragweed 0.1	±		0	1:5	++
Ragweed hay fever	PR		" 0.2	+		0		
" 0.0001 ++			Plantain 0.1	0				
" 0.001 ++±			Timothy 0.1	0				
" 0.01 +++			Cat epith. 0.01	0				
Timothy 0.1 ++±								
Plantain 0.1 ++								
Cat epith. 0.01 0								
S.E. male, 27 yr	P*	4/ 4/50	Ragweed 0.1	±	0		1:5	++
Ragweed hay fever								
" 0.001 +								
" 0.01 +++								
V.P. male, 11 yr	T	3/28/50	Ragweed 0.1	0	0			
Asthma			" 0.2	0	0			
Ragweed 0.001 +	P		" 0.01				None	++±
" 0.01 +++								

* Sites on this recipient prepared with twice-washed erythrocytes reacted negatively to tests with ragweed 0.1.
Reactions to tests with above allergens on normal cutaneous sites of recipients were uniformly negative.

reacted to intracutaneous tests with pollen extracts as follows:

Ragweed	0.0001	+
"	0.001	++±
"	0.005	+++
Timothy	0.1	+
Plantain	0.1	+±

Titration of the reaginic content of his blood serum by the serum dilution method of Coca and Grove(8) with an extract containing 0.01 mg N ml showed a titer of 1:64 to ragweed and 1:4 to timothy.

Results. Cutaneous sites on five different recipients prepared with the leucocytes of ragweed-sensitive donor, H.R., responded regularly with positive reactions to tests with ragweed in every instance (Table I). Two tests on these sites with timothy pollen and one with rabbit epithelium gave negative reactions. Sites prepared with a suspension of twice-washed erythrocytes and with the serum dilution control of H.R. did not react to tests with ragweed. Leucocytes from a nonsensitive donor failed to sensitize the recipient's skin to ragweed. Washing the leucocytes of H.R. 4 times instead of twice diminished but did not eliminate their specific skin-sensitizing property. The weak reaction to timothy pollen obtained on the plasma site could not be elicited on leucocytic sites.

In studies with leucocytes obtained from 5 other atopic patients, positive transfers were obtained in 4 (Table II). With the cells of T.C., local cutaneous sensitivity to rabbit epithelium was induced in 3 recipients. Skin-sensitizing antibodies to ragweed were transferred with leucocytes of 3 of the remaining four patients. All sites prepared with suspensions of erythrocytes, with serum dilution controls, and with viable leucocytes from nonsensitive donors gave negative reactions to tests with ragweed. The relatively weak sensitivities to timothy and plantain in patients S.F. and M.S. were not transferred with their leucocytes.

Failure to transfer sensitivity to ragweed occurred with the leucocytes of patient, V.P., an 11-year-old male, with a positive skin reaction to ragweed, but with no clinical history of pollen sensitivity. This patient's plasma readily transferred ragweed sensitivity.

Discussion. The positive reactions elicited in these experiments on sites sensitized with leucocytes were specific and definite, but no reaction greater than one-plus was obtained. The fact that the leucocytes were provided by donors with sensitivities of only average intensity may account, in part, for the relatively weak transfers. The inflammatory reaction which followed the sensitizing injection at the leucocytic sites was undoubtedly an important factor in reducing the intensity of the response of these sites to subsequent tests with allergens. Tests with weak solutions of histamine on leucocyte-prepared sites showed a diminished response as compared to that obtained on normal adjacent skin similarly tested at the same time. Moreover, experience obtained in the testing of sites sensitized with serum has revealed that the specific as well as the nonspecific responsiveness of passively sensitized sites is reduced by the inflammation which results from the sensitizing injection(9).

Conclusions. 1. The intracutaneous injection of viable leucocytes obtained from the bloods of atopic subjects who respond with immediate whealing reactions to skin tests with common allergens may specifically and locally sensitize the skin of normal recipients.

2. Red blood cells obtained from the same donors lack this skin-sensitizing property.

The authors gratefully acknowledge the technical assistance of Sonia Stroyman.

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Received July 12, 1950. P.S.E.B.M., 1950, v74.