In two purified preparations, prepared from the second alcoholic extract, after boiling with $Ba(OH)_2$, no ether soluble substance (fatty acids) could be found, nor after treatment with 25 per cent H_2SO_4, could reducing substances be demonstrated. Pepsin and trypsin did not decrease the potency of a purified preparation. The addition of lecithin to the first alcoholic extract, when the mixture contains 99 per cent of lecithin expressed in dry material, enhances the potency four times.

The examination of the extract of streptothrix has been retarded because of the lack of a highly potent serum, and because of the rapid drop of potency of the serum available.

The smallest amount of the alcoholic extract giving complement fixation was 0.006 mgm. The activation of this extract by the addition of lecithin is very striking. The antigen and lecithin were mixed in alcoholic solution. In a mixture containing 0.2 per cent of the alcoholic extract an activation 200 times was observed.

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Local Hypersensitiveness in Tuberculous Guinea Pigs.

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The plan of the experiments described in this note was suggested to us by the papers of Lewis and Loomis[1] on allergic irritability.

Guinea pigs shortly after a tuberculous infection, during the interval when the tuberculin sensitiveness usually appears, were treated with egg white, and later the skin sensitiveness toward egg white and the appearance of precipitins and complement fixating antibodies in the blood serum were examined. Non-tuberculous guinea pigs were treated and observed in the same way.

Table I contains the observations with one series of animals. The other series, together with the detailed description of the observations, will be published later.

Six control guinea pigs were treated together with the series described in the table; three were treated like the guinea pigs 1-3

TABLE I.

No. of guinea pig	Treatment of the guinea pig	Skin reaction on the 8th day after treatment; 0.1 mgm. egg white (dry weight) intracutaneously. Reaction after			Precipitation	
		6 hours	24 hours	48 hours	9 days after the treatment	13 days after the treatment
1	Guinea pigs 1-3	20x20 lsw.	25x25 lsw.	no reaction	10000++	300000++
	The 8th, 11th and 13th day				100000±	1 million±
2	after the infection, 0.1, 0.5 and	ssw.	25x25 sw.	17x17 sw.	100++	1 million++
	1.5 mgm. egg white (dry		10x10 bn.	9x9 n.	10000±	
3	weight)	28x28 lsw.	30x30 lsw.	no reaction	10—	1000±
					1000—	
4		20x20 sw.	25x25 lsw.	15x15 lsw.	1000++	300000++
	Guinea pigs 4-6, in the same		6x6 bn.	5x5 n.	10000±	1 million±
5	days as former, 0.03, 0.15 and	18x18 ssw.	25x25 lsw.	20x20 sw.	1000++	1 million++
	0.5 mgm. egg white.		9x9 bn.	10x10 n.	10000±	
6		no sw.	20x20 sw.	14x14 sw.	100—	10000±
			8x5 bn.	6x8 n.	10000—	300000±
7		18x18 ssw.	30x25 lsw.	20x20 lsw.	1000++	300000++
	Guinea pigs 7-9, in the same			10x10 bn.	10000±	1 million±
8	days as former, 0.01, 0.03 and	20x20 sw.	20x20 ssw.	no reaction	100±	100±
	0.1 mgm. egg white.				1000±	10000±
9		25x25 sw.	30x30 lsw.	25x25 lsw.	1000++	1 million++
			11x11 bn.	12x12 n.	10000±	

With the skin reaction, the numbers signify mm. sw. = swelling; lsw. = large swelling; ssw., = slight swelling; n = necrosis; bn. = beginning necrosis. With the precipitation, the numbers signify the highest dilution of native egg white giving a strong (++) or a slight (±) reaction with the dilution 1:2 of the serum.

of the table, three with larger doses. Only one of these guinea pigs, treated with the larger amounts of egg white, has shown a small reaction, fading in 24 hours, in the eighth day after treatment. The same guinea pig gave a faint precipitation with the dilution of egg white from 1:10 to 1:5000. After more prolonged treatment, we found in correspondence with former observations, a quite extensive wheal, which disappeared in 36 hours, after intracutaneous injection of egg white. At the same time, we found precipitation with higher dilutions of the egg white (in one serum 1:10,000, in another 1:100,000), but with all dilutions the precipitation appeared only later, and remained faint compared with the precipitation given by the serum of the tuberculous guinea pigs. Even after prolonged treatment we found no complement fixation with the serum.

It is at once visible from the table that, corresponding to the observations of Lewis, there is a very great difference in the precipitin formation between the normal and infected animals. The same difference is present concerning the antibodies responsible for the complement fixation. The serum of several infected guinea pigs has shown a titer of 1:250 or 1:160 in the complement fixation test. As these antibodies appear only later in the serum, they are not included in the table. In the tuberculous animals, treated even with the smallest dose of egg white (0.14 mgm.) and very soon after treatment, severe necrotic skin reactions were observed.

Two types of severe local hypersensitiveness, leading in the tests to tissue destruction, are known: the Arthus phenomenon, mainly observed in the rabbit, and the tuberculin reaction and similar reactions found in certain chronic diseases. It is undecided whether these two types of local sensitiveness are essentially different, or, though they differ considerably in appearance, the underlying mechanism for both is the same. To which of these two types does the sensitiveness observed by us belong? Is it an Arthus phenomenon, the observation of which was made possible in the guinea pig by the great increase of the antibody production caused by the tuberculous infection? Although a thorough discussion of this question has to be postponed until more experience is gained, some observations are worth mentioning now.

The connection between the antibody content of the serum and

the local sensitiveness, although a general parallelism is present, is not so close that the serum antibodies could be held responsible for the sensitiveness. For instance, animals 1 and 6 of the table are exceptions to the rule. The sensitiveness appears earlier than the serum antibodies. The large increase of the antibodies from the 9th to the 13th day after treatment described in the table, was not followed by a corresponding increase of sensitiveness. All experiments for transferring the sensitiveness with blood serum to tuberculous and non-tuberculous animals, remained unsuccessful. We tried to transfer by three methods: the injection of larger amounts of serum (6 and 3 cc.) intracardially; the technic used for the testing of atopic reagins; and the injection of the mixture of serum and egg white in the skin.

The amount of egg white needed both for the sensitizing, and for the production of skin reaction, is very small. There is no indication in our table that the smallest amount used by us (0.14 mgm.) represents the smallest sensitizing dose. With somewhat larger amounts of egg white (13 mgm.) we obtained markedly less sensitization than with the smaller doses. Two hundredths mgm. egg white caused necrotic skin reaction in several animals, and .004 mgm. a marked reaction. Usually in a tuberculin sensitive animal and the protein substances of the tubercle bacillus, the corresponding doses are about .005 and .001 mgm.

The development and appearance of the reactions show considerable variation. In certain cases, in a few hours after the injection of egg white, a 20 to 30 mm. well circumscribed red wheal forms with considerable swelling. In some cases the redness and swelling increases until the next morning; then in 12 hours disappears. (Guinea pigs 1, 3, 8 and all the non-infected controls, after energetic treatment with egg white, reacted in this manner.) In other cases showing an early reaction, a hard swelling and necrosis develops later. But some of the strongest reactions appeared during the night and have shown the appearance and characteristics of the intracutaneous tuberculin reaction, with perhaps the one difference that the necrosis developed earlier than in the tuberculin reaction. Without having more experience, and without examining different antigens, it is impossible to evaluate the significance of the similarities and differences between our reaction and the tuberculin reaction.

With egg-globulin, we obtained similar sensitization to that of

the crude egg white. In a small series with crystallin egg-albumin and ovomucoid, no sensitization leading to necrotic reaction was obtained.

Although the observations at our disposal do not permit the identification of the described sensitiveness with the tuberculin sensitiveness, the conclusion seems at hand that the mechanism underlying both is similar. The tuberculous infection creates in an unknown manner the conditions necessary for the development of the local sensitiveness, as well as the conditions for an increased antibody production, which are not specific to a certain antigen. The protein substances of the tubercle bacilli, as any foreign protein substance which is present in the organism, determines the specificity of the sensitiveness. It is a very interesting problem whether in the resistance against the tuberculous infection, which we observe always as the result of a slight infection, the same factors are at work—a non-specific altered reaction of the organism and a specific reaction made possible by the former.

[1] Lewis, P. A., and Loomis, D., *J. Exp. Med.*, 1924, xl, 503; 1925, xli, 327; 1926, xlii, 263.

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The Effect on Blood Sugar of Injections of Bacteria.

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Intercurrent infection unfavorably influences the course of diabetes. Graham[1] finds that infection may be instrumental in precipitating the diabetic into a state of coma. Graham[1] and also Rabinowitch[2] report that infection diminishes the potency of insulin. The dosage required to lower the blood sugar to a certain level is much greater in a diabetic in whom infection is present than in one without this complication. Clinical evidence is accumulating with reference to the fact that infection, focal or generalized, may be an etiological factor in *diabetes mellitus*. Rosenow has recently demonstrated a relation between focal infection and this disease.[3]