TABLE I.
Influence of Pathogenizing Substances on Agglutination of the 0901 Strain by Anti-O Serum (Titer 1:10,000).

Substance tested	Concentration, %	End of the agglutination titer
Dextran (*L. mesenteroides*)	0.1-0.25	1:10,000
	0.5-1.0	1: 1,000
	2.0	negative at 1:100
Levan (*A. levanicum*)	0.1-0.5	1:10,000
	1.0	1: 5,000
	2.0	negative at 1:100
Mucin	1.0	1:10,000
	2.0	1: 2,000
	5.0	negative at 1:100
Pectin	0.1-0.2	1:10,000
	0.5	1: 1,000
	1.0	1: 100
	2.0	negative at 1:100
Glycogen	0.5	1:10,000
	1.0	1: 2,000
	2.0	1: 1,000
Starch	1.0-2.0	1:10,000
	5.0	1: 200
Inulin, gum acacia, cellulose (cotton)	0.1-5.0	1:10,000

ence of any of the inhibiting substances (dextran, levan, mucin, pectin), however, no measurable quantities of antibody N were taken up by the cells. These observations accord with the findings of Keefer and Spink[4] concerning the effect of mucin on the bacteriolysis of gonococci by whole blood and immune serum.

[4] Keefer, C. S., and Spink, W. W., *J. Clin. Invest.*, 1938, **17**, 23.

Summary. The union of O-antibody by *E. typhosa* is completely inhibited by dextran, levan, and pectin at 2% concentration and by mucin at 5% concentration. Reduction of agglutination titer occurs in the presence of starch (5%) and glycogen (1-2%). Inulin, gum acacia, and acid-degraded cotton cellulose in 5% concentration are without this effect.

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Influence of Nitrogen Mustards on the Antibody Response.*

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The absence of infection in the leucopenic phase following nitrogen mustard therapy of lymphomas suggests that some specific protective mechanism persisted despite the demonstrable widespread damage to the hemopoietic system. The role of lymphocyte in the antibody response[1,2] suggests the lym-

* This study was supported in part by a grant from the Committee on Growth, American Cancer Society.

[1] Ehrich, W. E., and Harris, T. N., *J. Exp. Med.*, 1942, **76**, 335.

phocytotoxic nitrogen mustard compounds may influence the antibody reaction.

Method. To elucidate this relationship, the response to typhoid vaccine 1 cc intramuscularly, in a single dose and in 3 weekly doses was followed at 3-7-day intervals by agglutination titration with dilutions of 1 to 10 to 1 to 5120. A control group of 3 rabbits was given typhoid vaccine 1 cc intramuscularly and the agglutination titre followed through its peak response of 1 to 1280 on the 21st day until the titre had fallen. On the 80th to 95th day, nitrogen mustard (methyl bis β chlorethyl amine) 1 mg per kg (total dose 2 mg) was injected intravenously every 5 days for 4 doses. No increase in the antibody titre similar to the anamnestic reaction was observed. A second control group of 3 rabbits received injections of 1 cc typhoid vaccine intramuscularly for 3 weeks with a resulting increase in antibody titre to 1-5120 in the third week. Nitrogen mustard 1 mg every 4 days was given for 3 doses. There was no summation of titre but a decline to 1-1280 over the following week occurred.

A group of 3 rabbits was given nitrogen mustard at a dose of 0.5 mg per kg weight (1 mg total dose) every 4 days for 9 weeks. On the 25th day, when the lymphocyte count had fallen to 30% of the pretreatment level, typhoid vaccine 1 cc was given intramuscularly. The antibody titre increased only 1-80 3 weeks later, while the controls reached a titre of 1-1280. Another group of 3 rabbits received a similar dose of nitrogen mustard for 7 weeks. On the 18th day, 3 weekly doses of 1 cc typhoid vaccine were initiated. The treated group showed an antibody titre of 1-320 in the third week as compared to a control level of 1-5120.

The antibody response following simultaneous injection of typhoid vaccine and nitrogen mustard was investigated to determine to what extent this cytotoxic material might interfere with the antibody response. Typhoid vaccine 1 cc intramuscularly was given on the first day and nitrogen mustard 0.5 mg

TABLE I.
Typhoid Agglutination Titers Following Intravenous Injection of Nitrogen Mustard.

Group		No. rabbits	Weeks 0	1	2	3	4	5	6	7	11	12	13
1	Control anamnestic	3	0	1/320	1/640	1/1280	1/640	1/320	1/80	1/10	1/10	0	0
			*	*	*	‡	‡				8	1/10	0
2	Control summation	3	0	1/80	1/640	1/5120	1/1280	Died				9	10
3	Preantigen and concurrent	3	0	0	0	0*	0	1/40	1/80	1/40	1/10	1/10	
4	Preantigen and concurrent	4	1/20	1/20	1/20	1/160*	1/320*	1/80*	1/40				
5	Simultaneous antigen and nitrogen mustard	3	0*	1/160	1/160	1/80	1/160	1/80	1/80				

* Typhoid vaccine 1 cc, 500 million bacteria intramuscularly.
† Methyl-bis-β chlorethyl-amine hydrochloride 2 mg intravenously every 5 days, 4 doses.
‡ Nitrogen mustard 1 mg every 4 days.

[2] Dougherty, T. F., and White, A., *Endocr.*, 1944, **35**, 1.

per kg weight (total dose 1 mg) was given every 4 days for 4 weeks. The antibody titre rose to 1-160 as compared to a control titre of 1-1280.

Comment. The studies of Ehrich[1] have shown that the lymphocytes from lymph of a regional node draining an extremity into which antigen has been injected contain an increased titre of antibody on the fourth to sixth day. Dougherty and White[2,3] have shown that corticosterone will produce a lymphopenia and that the decrease in these cells, with their dissolution is associated with a rise in the antibody titre. Since the nitrogen mustards produce a toxic lymphopenia which is apparent in the peripheral blood[4] and lymph node[5] within 4 days, it might be expected that this toxic dissolution would result in the increase of antibody. With this in view, the nitrogen mustard was given after the normal antibody curve had fallen but no rise in titre similar to the anamnestic reaction was seen. No summation of titre occurred when nitrogen mustard was given at the peak of the antibody response.

These findings do not contest the role of the lymphocyte in antibody formation but suggest that the toxicity of nitrogen mustard interferes with the antibody forming mechanism of the lymphocyte. This hypothesis is supported by the suppression of the antibody formation in animals receiving antigen following pretreatment and concurrent treatment with nitrogen mustard. The dosage used in these experiments are 10-fold or more than that given in human therapy and an investigation of the antibody response in the human is now in progress. It is of interest to mention that in the human given a course of 25 mg nitrogen mustard, the leucopenic phase coincides with a period of active regeneration of the hemopoietic system.[6]

Summary. 1. The lymphocytotoxic effect of the nitrogen mustards will not produce an anamnestic reaction or summation of the antibody titre in the rabbit.

2. Pretreatment and concurrent administration of nitrogen mustard suppress the antibody response to typhoid antigen.

[3] Dougherty, T. F., White, A., and Chase, S. H., PROC. SOC. EXP. BIOL. AND MED., 1944, **56**, 28.

[4] Jacobson, L. O., Spurr, C. L., Barron, E. S. G., Smith, T. R., Lushbaugh, C., and Dick, G. F., *J. A. M. A.*, 1946, **132**, 263.

[5] To be published.

[6] Spurr, C. L., Jacobson, L. O., Smith, T. R., and Barron, E. S. G., A.A.A.S. Gibson Island Conf. on Cancer, *Chemotherapy of Tumors*, in press; *Cancer Research*, 1947, **7**, 51.

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Chemotherapeutic Action of Streptomycin and of Streptomycin with a Sulfone or Sulfadiazine on Tuberculosis.

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Previously published experiments[1] have shown that streptomycin and promin used together in the treatment of experimental tuberculosis in guinea pigs produced a chemotherapeutic effect greater than the sum of effects from the individual components. Equally good results were later reported from the combined use of streptomycin and another sulfone, sodium salt of 4-amino,4'-galacturonylaminodiphenylsulfone.[2] The supply of streptomycin, however, was then so limited that no experiments could be made

[1] Smith, M. I., and McClosky, Wm. T., *Pub. Health Rep.*, 1945, **60**, 1129.

[2] Smith, M. I., McClosky, W. T., and Jackson, E. L., *Am. Rev. Tub.*, in press.