results are reproducible depends upon the use of the same medium in comparative tests. One of our strains was tested in beef heart infusion broth with and without serum. Six mg of sulfapyridine per 100 ml were required to inhibit the growth of 24,000 pneumococci in broth containing 2% serum while the same inoculum failed to grow in a concentration of 1 mg per 100 ml without serum. Similar results were obtained with brain heart infusion broth (Difco) with and without serum. Unless serum was used, however, growth from small inocula in control tubes could not be depended upon. The increased amount of sulfapyridine required in broth containing serum was probably not due to the presence of sulfonamide inhibitor in the serum[5] but rather to the stimulation of growth by the serum.

Summary. Inhibition tests using varying numbers of pneumococci in varying concentrations of sulfapyridine and sulfathiazole indicated that except for highly resistant strains, there is a straight line relationship between the amount of drug required to inhibit growth and the number of pneumococci inoculated up to about 100,000. Larger inocula were not inhibited regardless of the amount of drug present. A method is described whereby this quantitative relationship may be applied to testing the sulfonamide susceptibility of pneumococci and expressing the results in terms of the concentration of sulfonamide required to inhibit the growth of a given number of bacteria.

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Sulfonamide Chemotherapy of Mouse Pneumonitis, Meningopneumonitis and Lymphogranuloma Venereum.

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Within the last few years two new virus-like agents which form elementary bodies have been described. The first of these, the agent of meningo-pneumonitis, was isolated by Francis and Magill[1] from ferrets which had received nasal washings from humans with symptoms of grippe. The authors believed the agent to have been carried in their stock of ferrets. The second, the agent of mouse pneumonitis, was isolated by Nigg[2] from an apparently normal stock

[1] Francis T., Jr., and Magill, T. P., *J. Exp. Med.*, 1938, **68**, 147.

[2] Nigg, C., *Science*, 1942, **95**, 49.

of Swiss mice. More recent papers have shown that both these agents are related to those of the lymphogranuloma venereum-psittacosis group.[3, 4]

It has been demonstrated that the agent of lymphogranuloma venereum is one of the very few viruses or virus-like agents which is susceptible to chemotherapy with the sulfonamide drugs.[5, 6] Since two other members of this group, *viz.*, the agents of psittacosis and the very closely related one of pneumonitis,[7] are said not to be affected by the sulfonamides, it was felt that this difference in susceptibility to the action of sulfonamide drugs might be of great importance, since it might offer a clue to the mode of action of these drugs. With this in mind studies were undertaken to determine the reaction of the two new agents to sulfathiazole and sulfadiazine, the drugs found to be most effective against lymphogranuloma venereum.[6]

The results are shown in Table I. It will be seen from the experimental data with mice that both sulfathiazole and sulfadiazine were very effective against the agent of mouse pneumonitis. Both drugs, when mixed with the food (1% sulfathiazole or 0.1% sulfadiazine) were effective against at least 100 L_d 50 intranasal doses or 1 million intranasal infective doses. Moreover, the mice showed no symptoms at any time after infection and in this respect the drugs were more active than in the case of lymphogranuloma venereum where a few of the mice did show symptoms.

On the other hand, neither drug affected the action of the agent of meningo-pneumonitis whether the latter was inoculated by the intracerebral or the intranasal route. Even with larger amounts of drug (0.25% sulfadiazine, sufficient to produce an average blood level of 10 mg %, and 1.5% sulfathiazole) the intranasal infection was quite uninfluenced.

Since the results with the agent of mouse pneumonitis were obtained after intranasal infection, which is the only route by which this agent readily infects mice, and since all previous studies on chemotherapy of lymphogranuloma venereum in mice have dealt with intracerebral infection, a few experiments were made to determine the effect of both the drugs on the latter agent given

[3] Rake, G., Eaton, M. D., and Shaffer, M. F., PROC. SOC. EXP. BIOL. AND MED., 1941, **48**, 528.

[4] Eaton, M. D., Rake, G., Nigg, C., and Francis, T., to be published.

[5] Findlay, G. M., *Lancet*, 1940, **239**, 528.

[6] Jones, H., Rake, G., and McKee, C. M., PROC. SOC. EXP. BIOL. AND MED., 1941, **48**, 318.

[7] Eaton, M. D., Beck, M. D., and Pearson, H. E., *J. Exp. Med.*, 1941, **73**, 641.

TABLE I.
Representative Experiments Showing Action of Sulfathiazole and Sulfadiazine.

	Route of infection	Inoculum, 0.04 cc	Controls no drug	Concentration of drugs in food: Sulfadiazine 0.1%	Sulfadiazine 0.25%	Sulfathiazole 1.0%	Sulfathiazole 1.5%
Lymphogranuloma venereum	IN	10^{-1}	2,2,2,3,++	+,±,0,0,0		+,±,±,±,±	
		10^{-2}	4,5,++,+,±	0,0,0,0,0		±,0,0,0,0	
		10^{-3}	±,±,0,0,0				
		10^{-4}	+,±,0,0,0				
		10^{-5}	0,0,0,0,0				
Mouse pneumonitis	IN	10^{-1}		0,0,0,0,0		+,±,0,0,0	
		10^{-2}	7,7,7,8,+++	0,0,0,0,0		0,0,0,0,0	
		10^{-3}	7,7,++++,+				
		10^{-4}	8,++++,+++,+++				
		10^{-5}	++,++,++,+,±				
		10^{-6}	++,+,+,+,+				
		10^{-7}	+,+,+,+,±				
		10^{-8}	+,0,0,0,0				
Meningo-pneumonitis	IC	10^{-2}		4,5,5,5,5		5,5,5,6,6	
		10^{-3}	5,6,7	5,6,6,6		6,6,6,6	
		10^{-4}	7,7,7				
		10^{-5}	6,7,7,S,S				
Meningo-pneumonitis	IN	10^{-1}	2,2,3,3,3		2,2,3,3,3		2,3,3,3,3
		10^{-2}	5,6,6,9,9		3,3,3,4,4		3,3,4,4,5
		10^{-3}	7,8,8,10,++++				
		10^{-4}	10,++++,++++,++++,+++				
		10^{-5}	+++,+++,++,++,++				

IN = intranasal.
IC = intracerebral
2,3,4, etc. = days between inoculation and death.
±,+ to ++++ = degree of pulmonary involvement at autopsy 10 days after inoculation.
0 = showed no pulmonary involvement at autopsy 10 days after inoculation.
S = survived for 10 days.

by the intranasal route.[8] From the results included in the table it is apparent that the drugs are active against 100 L_d 50 or 1000 infective doses inoculated by this route.

The demonstration that at least two agents in this group, *viz.*, those of lymphogranuloma venereum and mouse pneumonitis, are susceptible to the action of sulfonamides is of further interest in that it draws attention to the possible relationship of this group to the agents of trachoma and inclusion blennorrhoea which are likewise susceptible to drugs of the same series. Further evidence bearing on this relationship will be published elsewhere.[9] The only other virus-like agent known to be susceptible to chemotherapy is that of heart-water fever,[10] which at present is classed with the rickettsiae.

It should be added that the authors do not believe that these investigations will necessarily have any bearing on chemotherapy of true virus diseases since evidence is accumulating which indicates that the members of the lymphogranuloma venereum-psittacosis group should be separated from the true viruses.

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Biochemical Studies of Atheromatous Animals.

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A thesis has been offered[1] suggesting that the fundamental and general causal mechanism of degenerative arterial disease is an impaired nutrition and oxygenation of the vascular wall. This thesis has been based on the production of arteriosclerotic changes by 3 general procedures: first, the use of film and emulsion-forming agents (cholesterol,[2] polyvinyl alcohol,[3] methyl cellulose,[4] etc.):

[8] Shaffer, M. F., Rake, G., and McKee, C. M., PROC. SOC. EXP. BIOL. AND MED., 1940, **44**, 408.

[9] Rake, G., Shaffer, M. F., and Thygeson, P., to be published.

[10] Neitz, W. O., *J. S. African Vet. Med. Assn.*, 1940, **11**, 15.

[1] Hueper, Wilhelm C., *Arch. Path.*, 1939, **28**, 510; *Medicine*, 1941, **20**, 397.

[2] Anitschkow, N., Experimental Arteriosclerosis in Animals, p. 271, in Cowdry, E. V., *Arteriosclerosis*, New York, The Macmillan Co., 1933.

[3] Hueper, Wilhelm C., *Arch. Path.*, 1941, **31**, 11.

[4] Hueper, Wilhelm C., *Arch. Path.*, 1942, **33**, 1.