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## Chemotherapy of Experimental Rabies of Rats.

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Of the various viral diseases that have been investigated chemotherapeutically *lymphogranuloma inguinale* alone has responded uniformly favorably to treatment with certain aromatic sulfur compounds; a high percentage of cures has been obtained in both the experimental<sup>1-4</sup> and the clinical disease.<sup>5-7</sup>

The response of certain of other viral diseases to chemotherapy has been negligible or slight. Regarding canine distemper, just as many unfavorable<sup>8-10</sup> as favorable<sup>11-13</sup> papers have been published. The reported therapeutic action of 2,4-diaminoazobenzene-4'-sulfonamide in choriomeningitis of mice,<sup>14</sup> was not confirmed.<sup>15-17</sup> Presumably massive infections with influenzal virus were unaffected,<sup>14, 15</sup> whereas favorable results were claimed when the infecting dose was known to be small.<sup>18, 19</sup>

Chemotherapeutic experiments with the viruses of poliomye-

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- <sup>1</sup> Levaditi, C., *Compt. rend. soc. biol.*, 1938, **128**, 138.  
<sup>2</sup> Levaditi, C., *Ibid.*, 1938, **128**, 875.  
<sup>3</sup> Levaditi, C., *Ibid.*, 1938, **129**, 490.  
<sup>4</sup> MacCallum, F. O., and Findlay, G. M., *Lancet*, 1938, **2**, 136.  
<sup>5</sup> Hamilton, G. R., *Military Surgeon*, 1938, **83**, 431.  
<sup>6</sup> Shaffer, L. W., and Arnold, E., *Arch. Dermatol. and Syphilol.*, 1938, **38**, 705.  
<sup>7</sup> Shropshire, G., *Illinois M. J.*, 1938, **74**, 153.  
<sup>8</sup> Dickerson, V. C., and Whitney, L. F., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **38**, 263.  
<sup>9</sup> MacIntyre, A. B., and Montgomerie, R. F., *Brit. M. J.*, 1938, **1**, 875.  
<sup>10</sup> Plummer, P. J. G., Mitchell, C. A., and Walker, R. V. L., *Can. J. Comparative Med.*, 1938, **2**, 139.  
<sup>11</sup> Dochez, A. R., and Slanetz, C. A., *Science*, 1938, **87**, 142.  
<sup>12</sup> Larsen, C. E., *J. Am. Vet. Med. Assn.*, 1938, **46**, 197.  
<sup>13</sup> Marcus, P. M., and Necheles, H., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **38**, 385.  
<sup>14</sup> Rosenthal, S. M., Wooley, J. G., and Bauer, H., *Pub. Health Rep.*, 1937, **52**, 1211.  
<sup>15</sup> Levaditi, C., *Compt. rend. soc. biol.*, 1938, **127**, 958.  
<sup>16</sup> Ronse, M., *Ibid.*, 1938, **127**, 845.  
<sup>17</sup> Findlay, G. M., and MacCallum, F. O., *Brit. M. J.*, 1938, **1**, 875.  
<sup>18</sup> Climenko, D. R., Crossley, M. L., and Northey, E. M., *J. A. M. A.*, 1938, **110**, 2099.  
<sup>19</sup> Oakley, C. L., *Brit. Med. J.*, 1938, **1**, 895.

litis,<sup>20-22</sup> fibroma and myxoma,<sup>21, 22</sup> encephalitis,<sup>10, 14, 15</sup> yellow fever and Rift-valley fever,<sup>17</sup> as well as foot-and-mouth disease<sup>15</sup> have yielded negative results.

The purpose of this report is to record briefly the results obtained with sulfanilamide\* and sodium sulfanilylsulfanilate† in rats infected with fixed rabic virus.

The brain of a rat that died 7 days after intracranial infection with fixed rabic virus was macerated with 10 cc of saline under aseptic conditions. The resulting suspension was injected intracranially in 0.1 cc amounts into 29 etherized rats by the technic reported previously.<sup>23</sup> Treatments consisting of 150 mg of drug suspended in 0.5 cc of 15% gum acacia were given orally immediately following infection and repeated once daily for a total of 8 days.

TABLE I.  
Mortality-rate of Treated and Untreated Rats Infected with Fixed Rabic Virus.

	Daily Dosage, mg	No. of rats	No. of rats dying on days following infection					
			5	6	7	8	9	10
Control	None	9	—	—	8	—	—	1
Sulfanilamide	150	10	—	1	3	—	4	2
Sodium sulfanilylsulfanilate	150	10	1	—	1	—	—	8

Table I shows that the drugs in the doses used were incapable of saving the lives of the infected animals, although a slight prolongation of life was obtained. These results are not necessarily conclusive of the impotency of the 2 drugs because no attempt was made to titrate the infectious material and because the infecting dose employed was unnecessarily heavy and the route of injection was "unnatural." The error of drawing conclusions from chemotherapeutic experiments in which the infecting dose has been improperly adjusted is well illustrated in certain papers reporting negative results with sulfanilamide-therapy of pneumococcal infections.

*Conclusions.* Against a heavy infecting dose of fixed rabies virus administered intracranially to rats, the oral administration of sulfanilamide or of sodium sulfanilylsulfanilate resulted in a slight prolongation of life but failed to save the life of any animal.

<sup>20</sup> Toomey, J. A., and Takaes, W. S., *Arch. Pediat.*, 1938, **55**, 307.

<sup>21</sup> McKinley, E. B., Aeree, E. G., and Meek, J. S., *Science*, 1938, **87**, 43.

<sup>22</sup> Rhodes, A. J., and van Rooyen, C. E., *Brit. Med. J.*, 1938, **1**, 924.

\* Synthesized and donated to us by the Monsanto Chemical Co., St. Louis, Mo.

† Synthesized and donated to us by the Calco Chemical Co., Bound Brook, N. J.

<sup>23</sup> Cooper, F. B., Gross, Paul, and Lewis, M., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **38**, 835.