

The blood and spleens of 12 mice infected by the intracerebral route with the Lansing strain of poliomyelitis virus were tested for the presence of the virus after the mice became paralyzed, but no virus was demonstrated in either of these materials at that time.

Although the Lansing strain of poliomyelitis virus reaches the blood shortly after intraperitoneal and intracerebral inoculation of large doses of virus, it persists in the blood for only a short time. The time for which the virus persists in the spleen and in the blood is approximately the same. Therefore it is probable that the presence of the virus in the spleen depended upon the blood con-

tained in that organ.

Summary. The Lansing strain of poliomyelitis virus has been demonstrated in the blood and in the spleen of mice $\frac{1}{2}$ hr following the intraperitoneal inoculation of the virus. It has been demonstrated in the blood for 7 hr and in the spleen for 12 hr following intraperitoneal inoculation but not later. After intracerebral inoculation it has been demonstrated in the blood at intervals as long as $2\frac{1}{2}$ hr but in the spleen only at $1\frac{1}{2}$ hr following inoculation. The virus was not demonstrated in the spleens or blood of 12 mice when paralysis had developed following the intracerebral inoculation of the virus.

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In vitro Effects of Quinine, Atabrine and Substituted Acridine Compounds upon Gram Negative Bacteria.

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Since atabrine has been found to be a suitable chemotherapeutic agent for the treatment and prophylaxis of malaria^{1,2} and is furthermore indicated in the treatment of giardiasis,^{3,4} it appeared worthwhile to compare the *in vitro* effects of these compounds and additional substituted acridines upon other groups of microorganisms. This communication presents the effects of several such preparations upon organisms of the colon-typhoid-dysentery and related groups of gram-negative bacteria in broth.

The products tested included 3-chloro-7-methoxy-9-(1-methyl-4-diethylamino) butylamino-acridine-dihydrochloride (Atabrine); 3-chloro-7-methoxy-9-(2-hydroxy-3-diethylamino) propylamino-acridine-dihydrochloride (P-1); 3-chloro-7-methoxy-9-(2-hydroxy-eth-

ylamino) ethylamino-acridine-dihydrochloride (P-2); 3-chloro-7-methoxy-9-(4-sulfamidobenzyl) acridine (P-3); 2-ethoxy-6,9-diamino-acridine (Rivanol); 2-ethoxy-6,9-diamino-acridine lactate (Rivanol lactate); and 2-ethoxy-6,9-diamino-acridine-azo-sulfanilamide (Rivanol-azo-sulfanilamide).^{*} Quinine hydrochloride was included in these tests for comparative purposes.

Method. Dilute suspensions of 22-24 hr test cultures grown in beef extract broth were inoculated in 0.2 cc amounts in 5 cc of the broth medium containing 50 mg % concentration of one of the compounds. The inoculated drug-broth mixtures, together with control tubes lacking a drug, were incubated at 37°C. Presence or absence of visible growth was recorded at intervals of 24, 48 and 72 hr. Lack of visible growth at the end of 24 hr was taken as an indication of inhibition. In order to differentiate between bacteriostatic and possible bactericidal actions of the agents tested 1 cc of the test

¹ Hill, R. A., and Goodwin, M. K., *Am. J. Trop. Med.*, 1938, **18**, 339.

² Bispham, W. N., *Am. J. Trop. Med.*, 1938, **18**, 545.

³ Galli-Valerio, Schweiz, *Med. Wchnschr.*, 1937, **67**, 1181.

⁴ Culbertson, J. T., *J. Lab. and Clin. Med.*, 1941, **26**, 1465.

^{*} The Rivanol-azo-sulfanilamide compound was kindly supplied by Dr. Frederick Proescher, San Jose, California.

TABLE I.
Effects *in Vitro* of the Several Compounds upon *E. coli*, *E. typhosa* and *S. dysenteriae* Organisms.

Compound	48 hr observation—Organism—Strain								
	<i>E. coli</i>		<i>E. typhosa</i>					<i>S. dysenteriae</i>	
	No. 206	"M"	"B"	"M"	"H"	"R"	"Flexner"	"Sonne"	"Hiss"
Atabrine	+	0*	0	0	+	0	0*	0	0*
P-1	0	0	0	0	+	0	0	0	0
P-2	0*	0*	0	0	0*	0	0*	0	0*
P-3†	+	+	+	+	+	+	+	+	+
Rivanol	0	0	0	0	0	0	0	0	0
Rivanol lactate	0	0	0	0	0	0	0	0	0
Rivanol-azo-sulfanilamid†	0	0	0	0	0	0	0	0	0
Quinine hydrochloride	+	+	+	+	0*	+	+	+	+
Broth control	+	+	+	+	+	+	+	+	+

+ = growth.

0 = bactericidal effect.

0* = bacteriostatic effect.

† = slightly supersaturated solutions.

TABLE II.
Effects *in Vitro* of the Several Compounds upon *Salmonella*, *Aerogenes* and *Vibrio cholera* Organisms.

Compound	48 hr observation—Organism—Strain				
	<i>Salmonella</i>		<i>Aerobacter aerogenes</i>	<i>Vibrio cholera</i>	
	<i>paratyphi</i>	<i>enteritidis</i>		"Alexandria"	"Asiatic"
Atabrine	+	+	+	0	0
P-1	0	0*	+	0	0
P-2	+	+	+	0	0
P-3†	+	+	+	+	+
Rivanol	0	0	0	0	0
Rivanol lactate	0	0	0	0	0
Rivanol-azo-sulfanilamid†	0	+	0*	0	0
Quinine hydrochloride	+	+	+	0	0*
Broth control	+	+	+	+	+

See legend under Table I.

mixtures showing no growth at the end of 72 hr was transferred to 10 cc of sterile beef extract broth. Failure to obtain growth in the subculture tube was considered to be evidence of bactericidal activity on the part of the drug in the original mixture. The results of the effects of the compounds upon several strains of gram-negative bacteria, after 48 hr medication, are given in the tables.

Summary and Conclusions. In summarizing the data presented in the tables we note the following: Rivanol, Rivanol lactate, Rivanol-azo-sulfanilamid† and preparation P-1 appear to be equally effective in their antibacterial actions, *in vitro*, upon organisms representative of the colon-typhoid-dysentery group. Next in order of activity are compounds P-2 and atabrine. The remaining

drugs show little if any effect in inhibiting the growth of the bacteria studied.

Although not indicated in the tables none of the agents tested proved to be bacteriostatic for 2 strains of *Proteus vulgaris* and a strain of *Proteus morganii*. Furthermore, with but 2 exceptions the drugs failed to inhibit growth of several strains of *Pseudomonas aeruginosa*. Compound P-1 and Rivanol proved to be definitely bacteriostatic for the latter organism.

† Preliminary studies on another Rivanol-azo-sulfonamide, 2-ethoxy-6,9-diamino-acridine-azo-sulfanilamide-thiazole supplied by Dr. Proescher, during the course of these studies, indicated this preparation to be distinctly less active than Rivanol-azo-sulfanilamide against several strains of C-T-D organisms.