

TABLE I.

Amino-acid	Drug remaining (mg per 100 cc)	% inhibition
Tryptophane	5.9	50
Tyrosine	3.6	44
Phenyl-alanine	3.2	44—
Alanine	1.8	None
Glycine	1.8	None
Histidine	2.0	None
Cystine	1.6	None
Proline	2.1	None
Control	1.9	—

From the above data, it is evident that the amino-acids containing aromatic groups are able to inhibit the adsorption of the drug by activated carbon. These experiments suggest the possibility that peptone, or certain of its constituents, may interfere with the adsorption of the drug on bacterial surfaces.

10620

Protective Action of Sulfapyridine Against Type II Pneumococcal Infections in Mice.*

RAYMOND N. BIETER, W. P. LARSON, MILTON LEVINE AND
ELIZABETH M. CRANSTON.

*From the Departments of Pharmacology and Bacteriology, University of
Minnesota, Minneapolis.*

The remarkable results obtained by Whitby¹ in the treatment of pneumococcal mouse-infections with sulfapyridine† (M. & B. 693) have led to widespread use of this sulfanilamide derivative in experimental work. Several series of experiments, herein reported, have been conducted by a method of drug-administration quite generally neglected. This method briefly consists of mixing the drug to be studied with ground food, in any concentration selected; and allowing the mice to ingest it with their food. Hunt,² working in Ehrlich's Institute, also incorporated drugs in ground animal-food. The de-

* Aided by grants from the Medical Research Fund of the Graduate School of the University of Minnesota.

¹ Whitby, L. E. H., *Lancet*, 1938, 1, 1210.

† Merck & Co., Inc., generously supplied the sulfapyridine used in these experiments.

² Hunt, R., personal communication to E. K. Marshall, Jr., 1939.

tails of this method will be reported later. The experience obtained indicates that mice eat a measurable amount of food during every 6-hour interval day and night. The food cups used are practically waste-proof. During the first 48 hours, the mice tend to eat increasing amounts; consequently, in the present experiments, the animals were placed on the diet plus drug 2 days before the inoculation. They were maintained on the diet plus drug for 10 days after the inoculation. Each mouse was kept in a separate cage. From daily weighings of food consumed, the drug-intake has been determined.

The organism used was a Type II pneumococcus isolated from a case of human lobar pneumonia. Its virulence has been maintained for more than a year by following the technic of Neufeld and Handel.³ The mice were inoculated with 0.2 cc of a 1:1296 dilution of an 8-hour broth culture, subcutaneously. This represents from 4000 to 8000 average lethal doses (50% lethal dose) of the organisms. By plate count it was determined that the mice were inoculated with from 4000 to 17,000 organisms. One hundred and ninety-nine mice were used in this study. Fifty mice were placed on 0.5%, and 49 mice on 1% sulfapyridine in food, respectively. With each of these experimental groups was included a group of 50 controls. All mice used were of 20 g body-weight.

Table I shows the average drug-intake for the 2 groups of mice, in grams per kilo of body-weight per 24 hours. It can be seen that mice on diet plus 1% sulfapyridine ingest very nearly twice as much of the drug as those on diet plus 0.5% sulfapyridine.

TABLE I.
Oral Ingestion of Sulfapyridine from Food in Grams per Kg of Mouse Body-Weight per 24 hrs.

Day	0.5% in food		1.0% in food	
	No. of mice	Intake	No. of mice	Intake
1	50	0.51	49	0.95
2	50	0.98	49	1.62
3	Subcutaneous inoculations with pneumococcus Type II.			
3	50	1.07	49	1.99
4	50	1.21	49	1.67
5	50	1.09	48	1.72
6	50	1.10	48	1.79
7	49	0.93	47	1.78
8	48	0.99	47	1.74
9	44	0.93	47	1.76
10	43	0.97	46	1.82
11	43	0.94	46	1.47
12	41	0.91	45	1.55

³ Neufeld, L., and Handel, L., *Berl. klin. Woch.*, 1912, **49**, 680.

204 SULFAPYRIDINE IN MOUSE PNEUMOCOCCAL INFECTIONS

TABLE II.
Time of Survival of Mice Treated with Sulfapyridine in Food and Inoculated Subcutaneously with 4000-8000 Lethal Doses of Pneumococcus Type II.

Control	0.5% Sulfapyridine	Control	1% Sulfapyridine
	(Time of survival in hours.)		
37	88	35.5	54.2
37	109.5	35.5	84
37	135.5	35.5	153
38.2	135.5	35.5	217
43.2	135.5	35.5	230
45.5	149	35.5	237.5
46	155	35.5	251
46	199.5	36.5	251
46	204	36.5	252
48	217.5	36.5	252
48	226	36.5	252
48.5	226	36.5	252
49	248.5	36.5	252
51.5	248.5	38.7	276
51.5	248.5	38.7	276
51.5	260.5	39.5	276
53.5	260.5	39.5	276
55	261	39.5	309
55.5	264	41	
57.5	276	42.7	
58.5	285	48	31 survivors at 60 days = 63.4%
58.5	303	49.5	
60	320	52.5	
60	320	52.5	Average greater than 230.5 hr
61	327	53	
61	336.5	55.5	
64	348	57	
65.5	360	57	
65.5		59	
65.5	22 survivors at 60 days = 44%	59	
65.5		59	
65.5		59	
65.5		59	
65.5		60.5	
65.5	Average, greater than 237 hr	60.7	
66.5		60.7	
67.5		60.7	
68.5		61.25	
68.5		62	
69.5		62	
69.5		62	
70.5		63	
72		63.5	
72		64.7	
72		69.5	
79		73.5	
79.5		79.5	
83.5		79.5	
83.5		82.5	
92.5		83.5	
Avg		Avg	
60.1 hr		52.3 hr	

Table II shows the times of survival of all the mice which in this laboratory are observed hourly. From data thus obtained, statistical analyses can be made which show definitely the significance of the experimental observations. It is believed that observations of this type are of more value to workers in this field than previous investigators have recognized.

Summary. With subcutaneous inoculations of 4000 to 8000 average lethal doses of a Type II pneumococcus in mice, the survival rates at both 30 and 60 days were (1) with 0.5% sulfapyridine in the food, 44%, and (2) with 1.0% sulfapyridine in the food, 63.4%. It is believed that the slight variations in drug-intake from day to day are more than counterbalanced by a more or less continuous drug-absorption from ingested food plus drug.

10621 P

Character of Phospholipid (Acetone Insoluble) Fatty Acids of Serum in Infantile Eczema.*

ARILD E. HANSEN.

From the Department of Pediatrics, University of Minnesota, Minneapolis.

In 1933¹ the author observed that the total fatty acids of the serum tended to be less unsaturated in infants suffering from eczema than in control infants with clear normal skin. In the follow-up studies which were made to determine which fraction or fractions of the serum lipids were involved in this phenomenon, great difficulty was encountered in finding a satisfactory method. The success in the development of a microgravimetric technic² for the determination of the phospholipid fatty acids offered the opportunity to resume the study of the serum lipids presented in this communication, in which we attempted to determine whether or not the fats of this fraction were responsible for the decreased unsaturation of the serum fats in eczema.

Seven infants ranging in age from 6 to 12 months, suffering from severe, generalized eczematous eruptions of several months' duration sufficiently refractory to necessitate hospitalization, were used in this study. Care was taken to avoid the possible interference of any

* Aided by grants from Mead Johnson and Company and the Medical Graduate Research Fund of the University of Minnesota.

¹ Hansen, Arild E., *PROC. SOC. EXP. BIOL. AND MED.*, 1933, **30**, 1198; *Am. J. Dis. Child.*, 1937, **53**, 933.

² Hansen, Arild E., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **40**, 376.