and from them virus was isolated.

Since the number of available *C. tarsalis* was very limited no attempt was made in these preliminary experiments to infect them by feeding on an experimental animal, for in the laboratory they feed much more satisfactorily on blood-soaked cotton. However, we have infected other mosquitoes by permitting them to feed on a chicken 48 hr after a subcutaneous inoculation of the St. Louis virus. Finding *C. tarsalis* infected in nature is evidence that it becomes infected by some natural means, probably by feeding on an infected animal host.

In addition to *C. tarsalis, Culex coronator* Beyer was shown to be capable of transmitting the St. Louis virus to chickens. This latter species is potentially important in the lower Rio Grande Valley, where the work was done. In this area during an epidemic of encephalitis in 1941 antibodies to the St. Louis virus were found in the sera of man and domestic animals.[6]

Summary and Conclusions. *Culex tarsalis* has been demonstrated to be infected in nature with St. Louis encephalitis virus and to be capable of transmitting it. Furthermore, it fits well into the epidemiological picture encountered in the Yakima Valley, Washington. We can therefore safely conclude that this species is a natural vector. This is the first instance in which a mosquito has fulfilled these 3 criteria for incrimination as a vector in respect to St. Louis encephalitis virus. *C. pipiens* previously has been shown to be capable of transmitting this virus in the laboratory and the same has just been demonstrated for *C. coronator*. In addition, these experiments demonstrate that the chicken may serve as a satisfactory reservoir of virus. This is undoubtedly shared by other birds for we have previously shown that virus may be isolated from the blood of a dove following the bite of infected *C. pipiens*[5] and unpublished work indicates that ducks may serve as reservoirs.

Collection of the larvæ for the second experiment was made by Mr. R. B. Eads, entomologist, Texas State Health Department. Valuable laboratory assistance was rendered by Mrs. Margaret Gray and Miss Margaret Smith, Hooper Foundation.

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Influence of Diet on Action of the Sulfonamide Drugs.*

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The importance of diet in the normal physiology of the liver and in the protection of the liver from the action of such damaging substances as chloroform and carbon tetrachloride has been brought to the attention by many investigators.[1-7]

Since we found that sodium sulfapyridine exerts a definite and characteristic effect on the levels of blood sugar and liver glycogen,[8] we wished to study the effects of various diets on the action of sodium sulfapyridine and sodium sulfathiazole in rats. The diets used to date are Purina Dog Chow Checkers

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TABLE I.
Effects of Various Diets on Action of Sodium Sulfapyridine and Sodium Sulfathiazole.

Diet	1	2	3	4	5	6	7	8	9	10	11	12	13	Condition
Purina	5	138.6	6.08	4.39	12.4	14.4	+18	90	3.67	161.3	1.00	1.00	0	Controls
Dog Chow	13	139.0	5.55	3.99	12.8	13.2	+26	116	1.22	51.8	33.95	41.91	5.97	Sodium Sulfapyridine
Checkers	10	135.8	5.92	4.36	11.0	13.2	+23	97	3.19	141.4	11.08	13.04	1.96	Sodium Sulfathiazole
High	4	116.0	5.26	4.53	5.7	4.0	— 6.2	96	1.64	76.0	1.36	1.36	0	Controls
Protein	10	118.4	5.46	4.61	6.6	6.4	— 0.2	191	1.11	53.2	46.24	52.55	6.31	Sodium Sulfapyridine
High Carbohydrate	3	113.7	5.69	5.00	8.6	6.7	— 1.7	88	6.70	341.5	1.22	1.22	0	Controls
	9	114.8	4.81	4.19	8.8	7.3	+ 2.1	137	1.58	68.9	54.75	60.32	5.56	Sodium Sulfapyridine
High Fat	4	131.0	6.22	4.75	5.7	4.5	+ 6.5	76	1.23	57.6	1.50	1.50	0	Controls
	4	139.5	5.97	4.28	5.4	4.7	+ 1.2	107	1.22	52.1	32.09	36.82	4.73	Sodium Sulfathiazole

1. No. of rats.
2. Body wt.
3. Liver wt.
4. Liver as % of body wt.
5. Avg daily intake (g).
6. Intake during last 24 hr.
7. Gain or loss in body wt during last week.
8. Blood sugar, mg%.
9. Glycogen, % of liver wt.
10. Glycogen, mg per 100 g body wt.
11. Concentration of free drug in blood, mg%.
12. Concentration of total drug in blood, mg%.
13. Concentration of drug in combined form, mg%.

as the balanced diet, and experimental diets in which protein, carbohydrate and fat form about 87% of the caloric value of the diet.[9]

In these studies the rats were kept on the special diets for one week, and were not fasted before the experiment. The daily food intake and gain or loss in body weight during the last week were recorded. This information, together with the blood sugar, liver glycogen (expressed both as per cent of liver weight and as mg per 100 g of body weight), free, total and acetylated levels of the drug in the blood is shown in Table 1.

One dose of the drug to be studied was given by intraperitoneal injection. 7.5% solutions were used; 1 cc per 100 g of body weight was given. The animals were killed 3 hr later.

It will be noticed that the administration of sodium sulfapyridine to rats that have been on the balanced diet leads to a decided decrease in liver weight, an increase in blood sugar and a decrease of 68% in liver glycogen (calculated from mg of liver glycogen per 100 g of body weight). The changes which follow the administration of sodium sulfathiazole are in the same direction but less marked; the level of the drug in the blood was lower in this group.

On the high protein diet the livers of the control rats were heavier than on the balanced diet. The liver weight increased after the administration of sodium sulfapyridine so these livers were much heavier than the corresponding livers on the balanced diet. The increase in blood sugar was much greater although the values in the control rats on the two diets are almost the same. The most significant finding is the less marked decrease in liver glycogen. The decrease after administration of sodium sulfapyridine is 30% on the high protein diet compared with 68% on the balanced diet, although the level of the drug in the blood is higher in the former rats. This suggests that with sodium sulfapyridine there is less interference with the factors which control liver glycogen if rats have been fed a high protein diet during the preceding week. Studies are in progress with other concentrations of sodium sulfapyridine.

The heaviest livers were found in rats on the high carbohydrate diet. After the administration of sodium sulfapyridine there was a decrease in liver weight and an increase in blood sugar. Although the level of liver glycogen in the control rats is much higher than in the control rats on the balanced diet, the decrease of 79% is greater than that of 68% found on the balanced diet.

The effects of a high fat diet on the action of sodium sulfapyridine have not yet been studied. A few observations on sodium sulfathiazole have been made. The administration of this drug leads to a decrease in liver

[9] Greisheimer, E. M., and Johnson, O. H., *J. Nutrition*, 1930, **3**, 297.

weight and an increase in blood sugar; these changes are more marked than they were on the balanced diet; the level of the drug in the blood is higher. The decrease in liver glycogen is of the same order as on the balanced diet.

In conclusion, it appears that a high protein diet decreases the effect of sodium sulfapyridine on liver glycogen, while a high fat diet does not appear to increase the susceptibility of the liver to the action of sodium sulfathiazole.

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Sulfonamides and the Blood pH.*

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In a previous paper (Wertenberger[1]) on the effect of single doses of some of the sulfonamide preparations upon blood pH, it was shown that intraperitoneal injections of the sodium salts of sulfapyridine (sodium 2-para-amino-benzene-sulfonamido pyridine) and sulfathiazole (sodium 2-para-amino-benzene-sulfonamido-thiazole) produced a marked rise in blood pH, while sulfadiazine (2-sulfanil-amido-pyrimidine) showed only a slight rise.

Since the sulfonamides are most frequently given by mouth, this study was extended to include a comparison of the effects produced by oral and intraperitoneal administration.

Method. Albino male rats from a standard strain of approximately the same age and weighing between 100 and 150 g were used. The animals were kept on a standard diet (Purina Dog Chow Checkers) for one week before treatment. All rats were fasted for 18 hours before the experiment.

The blood pH was determined electrometrically with the glass electrode using the Behrmann-Fay[2] blood chamber as previously described (Wertenberger[1]).

Drug concentrations in the blood were determined by the method of Bratton and Marshall[3] using the photoelectric colorimeter.

A sufficient amount of blood was withdrawn at one time for both the pH and drug concentration determinations in all of the experiments except two.

Results and Discussion. A total of 147 rats was used for this study and the data are summarized in Table I. Sodium sulfapyridine and sodium sulfathiazole produce a marked rise in blood pH when given intraperitoneally and the blood level is high.

This shift does not occur, however, when the drugs are given orally and the blood level is much lower. In the series run 6 hours after treatment, there was a slight rise in the blood pH with sulfapyridine but none with sulfathiazole even though the concentration in the blood had risen to about one-third of the concentration observed after intraperitoneal injection.

The effect of sulfathiazole is not quite as marked, however, and the blood levels are lower and show the least conjugation. This latter fact was observed by Van Dyke and co-workers[4] who found that sulfathiazole is more rapidly metabolized and undergoes less conjugation than sulfapyridine.

Sodium sulfadiazine by intraperitoneal injection was studied in a series comparable to those previously run on sulfapyridine and

* Supported by Grant No. 460 to Doctor Esther M. Greisheimer from the Committee on Therapeutic Research, Council on Pharmacy and Chemistry, American Medical Association.

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