isolation contained no complement-fixing antibodies to the agent, though it was not known whether they came from the same source as the original animals.

Discussion. In these experiments a rickettsia-like organism was isolated from guinea pigs injected with blood from a patient with pretibial fever, a recently described disease of unknown etiology. It was not possible to demonstrate the presence of significant titers of complement fixing or agglutinating antibodies to this agent in the human sera. The technics employed were satisfactory for detecting these antibodies in the sera of recovered guinea pigs. Neutralization tests in guinea pigs were unsatisfactory, as is the case with most rickettsial diseases. In view of these negative findings, the origin of the agent is in doubt. Unfortunately, all of the human blood was used up at the time of the original inoculations, and no additional cases of pretibial fever appeared during the 1943 season. It is hoped that more information as to the source of the agent can be obtained in the future.

A search of the literature has failed to show a guinea pig disease similar to the one described. Mochkovski[4] reported the occurrence of a chronic rickettsiosis in the mononuclear cells of guinea pig blood. His paper describes the morphology of the organism and does not refer to the biological characteristics of the agent.

[4] Mochkovski, C., *C. R. Soc. de biol.*, 1937, **126**, 379.

Summary and Conclusions. An agent pathogenic for guinea pigs has been isolated. The organisms appeared as small pleomorphic bacillary forms, staining red by the Machiavello method and gram negative. They were larger than the known rickettsia, as well as *P. tularensis* and *Brucella,* and were immunologically distinct from them. They grew fairly well in the yolk sac of the fertile hen's egg but were not cultivated on artificial media. The host range was limited to the guinea pig except when enormous doses were given.

After a short incubation period, peritonitis was produced in the guinea pig, for which the agent was highly virulent, and a specific immunity resulted in recovered animals. The inflammatory reaction in the tissues was characterized chiefly by the presence of mononuclear cells. The organism appeared predominantly intracytoplasmic in impression smears of the spleen.

The origin of the organism is in doubt. It has not been possible to identify it with any known group of pathogenic agents, but at present it may be termed "rickettsia-like" for descriptive purposes.

Most of the immunological procedures and much of the animal work was done at the National Institute of Health, United States Public Health Service, Bethesda, Maryland, through the courtesy of the Director.

The author wishes to express his appreciation for the assistance and advice so fully extended by the various members of the Commission on Acute Respiratory Diseases and the technical staff.

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Alleviation by Raw Liver of Anorexia Produced by Sulfapyridine.

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The administration of sulfapyridine to dogs in blacktongue did not interfere with the alleviation of symptoms by nicotinic acid but did prevent weight restoration.[1,2] Raw liver,

[1] West, R., PROC. SOC. EXP. BIOL. AND MED., 1941, **46**, 369.

[2] Schaeffer, A. E., McKibbin, J. M., and Elvehjem, C. A., *J. Biol. Chem.*, 1942, **144**, 679.

TABLE I.
Effect of Liver on Sulfapyridine Induced Anorexia in Rats.

Sulfapyridine, %	Liver	Initial rat wt, g	Total wt gain, g	Basal diet consumption, g per day
—	—	204	51	15.2
1	—	201	17	10.5
1.5	—	196	2	9.3
2	—	197	4	8.9
—	5% powder	189	49	13.4
1.5	" "	206	0.6	6.4
—	5% concentrate	202	56	14.7
1.5	" "	193	5.4	7.9
—	2 g raw per day	221	36.5	16.7
1.5	" " " " "	215	13.2	12.9
—	5 " " " "	237	35	15.4
1.5	" " " " "	230	18	11.2
—	10 " " " "	178	48	11.5
1.5	" " " " "	180	38	9.1
—	Raw liver *ad lib.*, no basal diet	97	29	—
1.5	" " " " " " "	101	30	—

however, counteracted the sulfapyridine effect. The weight loss in blacktongue is due to anorexia[3] and it seemed possible that the effects observed with sulfapyridine were not due to a specific interference with nicotinic acid metabolism by the drug but rather to a sulfapyridine-induced anorexia. In the present work it has been found that raw liver counteracts sulfapyridine-induced anorexia in normal rats and dogs.

Experimental. Rats. The basal ration used in these experiments was as follows: casein, 25; sucrose, 57; cottonseed oil, 10; cod liver oil, 3; salt mixture,[4] 5. Each 4 kg contained thiamine, 12 mg; riboflavin, 20 mg; calcium pantothenate, 120 mg; pyridoxine, 12 mg. When sulfapyridine or whole dry liver powder was included in the diet an equivalent amount of sucrose was omitted. Raw pork liver was liquefied in a Waring blendor and sulfapyridine incorporated in the brei to provide the same concentration (dry weight) used in the basal diet. The raw liver and basal diet were fed in separate vessels and, except when the liver was offered *ad libitum,* the liver was always completely consumed. The results are presented in Table I and are expressed as the mean values obtained with groups of 12 male rats (Vanderbilt strain) each for 14 days.

Sulfapyridine fed as 1.5% of the diet produced a satisfactory decrement in appetite and growth rate. It has been demonstrated[5] that such growth failure is due largely to the relative anorexia. Whole liver powder* and a concentrated liver extract† were without effect in this connection. The addition of raw liver to sulfapyridine-containing diets induced some increased consumption of the basal diet and definitely increased growth. Finally sulfapyridine was fed with raw liver alone and then appeared to be without effect although growth on raw liver as the sole foodstuff was inferior to that on the basal diet.

Dogs. Four adult male mongrels were offered a diet consisting of yellow corn meal, 80; casein, 8; cottonseed oil, 10; cod liver oil, 1; and $CaCO_3$, 1. To this was added 2 volumes of water and the whole was cooked for one hour. Twice weekly each dog was given a

[3] Handler, P., and Dann, W. J., *J. Biol. Chem.*, 1942, **145**, 145.

[4] Drummond, J. C., and Watson, A. F., *Analyst*, 1922, **47**, 235.

[5] Harris, J. S., and Kohn, H. I., *J. Pharm. Exp. Ther.*, 1943, **78**, 56.

* Wilson and Company, Chicago, Ill.

† Lederle Laboratories, Inc., Pearl River, N.Y.

TABLE II.
Effect of Liver on Sulfapyridine Induced Anorexia in Dogs.

Dog	Initial wt, kg	Basal ration Period 1		Sulfapyridine Period 2		SP and liver Period 3		Liver only Period 4	
		Food intake, g/day	Final wt, kg	Food intake, g/day	Final wt, kg	Food intake, g/day	Final wt, kg	Food intake, g/day	Final wt, kg
A	11.3	1100	10.7	400	9.9	950	10.4	1150	11.6
B	8.8	1150	9.4	750	8.6	1000	9.8	1050	9.9
C	10.5	950	10.6	550	10.0	1100	11.2	1100	11.8
D	9.7	1200	10.2	900	9.3	1050	9.9	1400	11.4
Mean	10.1	1100	10.2	650	9.5	1025	10.3	1150	11.2

capsule containing thiamine, 3 mg; riboflavin, 3 mg; nicotinic acid, 10 mg; pyridoxine, 3 mg; calcium pantothenate, 20 mg; and choline chloride, 1.0 g. After 10 days on the basal diet sulfapyridine administration was started. The drug was given in tablets 3 times daily in sufficient quantity to produce a fasting morning blood level of 3-5 mg %. Ten days later each dog was offered 100 g of raw liver daily and sulfapyridine administration continued. During the fourth 10-day period the drug was withheld but the raw liver feeding continued. The results are given in Table II.

Sulfapyridine administration produced an average decrease of 58% in the food consumption of these dogs. The raw liver was consumed well and, in addition, considerably alleviated the anorexia. In a series of similar experiments, with the same animals, sulfapyridine failed to affect appetite when a stock ration containing cooked horse meat was employed.

From these data it is apparent that oral administration of sulfapyridine produces anorexia in rats and dogs. When raw liver was then added to the diet of rats a definite improvement in their growth rate was found although their appetites were not so markedly restored. However, raw liver added to the diets of dogs almost completely prevented the anorexia. The failure of blacktongue dogs to gain weight when treated with sulfapyridine and nicotinic acid[1,2] can probably be explained by the secondary anorexia produced by the sulfapyridine, since the same phenomena have now been observed with normal dogs. The possibility still remains that the *modus operandi* of sulfapyridine in this regard does involve nicotinic acid metabolism as this mechanism is still obscure. Nor is there as yet a satisfactory explanation of the effects of raw liver. It is possible that liver increases the appetite and general well being of these animals by a mechanism quite independent of that which is disturbed by sulfapyridine.

Summary. Sulfapyridine produced anorexia and consequent growth failure and weight loss in normal rats and dogs. This was counteracted by the inclusion of raw liver in the diet, but not by dry liver powder or concentrated liver extract. The failure of nicotinic acid to induce weight restoration in sulfapyridine-treated blacktongue dogs while raw liver does stimulate weight gains may perhaps be explained on the same basis.

The author's thanks are due to the Duke University Research Council for a grant-in-aid of this work.