

der (*Ateles geoffroyi*), black spider (*Ateles ater*), black howler (*Alouota palliata insonans*), and white face (*Cebus capucinus capucinus*). They were nearly all juvenile, weighing between one and 2 kilos. The filtrates fed were from staphylococcus broth cultures after 2 to 3 days' growth; their gastro-intestinal toxicity for man was in each instance established by their effect in 2 cc.-10 cc. amounts on human volunteers. Thirteen monkeys were fed amounts ranging from 5 cc.-20 cc. A rubber catheter was introduced into the stomach, and measured amounts of the filtrate were slowly injected by a graduated syringe. In five (2 red spiders, 2 black howlers, 1 black spider) definite symptoms were observed of a similar character to those described in human subjects.¹ These animals suffered from marked diarrhea and showed lack of appetite; they remained huddled in a corner and apparently experienced abdominal pain. The onset of the symptoms occurred about 2 hours after the filtrate was administered, corresponding to what is observed in man. In one instance vomitus was found on the floor of the cage. The condition of malaise lasted for approximately one day, after which recovery appeared to be complete. In one animal, however, the diarrhea persisted for about 8 days. In 3 other animals symptoms of slight malaise were noticed; these were perfectly definite in character, such as weakness, sluggishness and lack of interest in food, but were not accompanied by active gastro-intestinal disturbances. The other 5 animals were not visibly affected by the feeding. One of the monkeys that had diarrhea after being fed 10 cc. of filtrate on March 2 manifested slight malaise when given 20 cc. of a less potent filtrate 10 days later.

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Changes in the Reducing Substances in the Liver and Muscle in
Experimental Streptococcus Septicaemia.

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This paper deals with the effect of experimental streptococcus septicaemia upon reducing substances in the liver and muscle of rabbits. It was recently shown¹ that during the course of such an

¹ Jordan, Edwin O., PROC. SOC. EXP. BIOL. AND MED., 1930, 27, 421.

¹ Linton, R. W., J. Exp. Med., in press.

infection the blood sugar tends to become less concentrated. The average blood sugar level for normal rabbits was 135 mg. per 100 cc. of blood, using the micromethod of Folin.² At the terminus of the experimentally induced septicaemia, which always ends fatally, the average blood sugar was about 30 mg. per 100 cc. less than the normal.

While the terminal concentrations of blood sugar are not at hypoglycaemic levels, it was nevertheless thought of interest to study the decrease further, especially in view of the fact that the other blood changes pointed to a large production of acid *in vivo* by the streptococcus. Since the work of Hopkins and Parker,³ it has been recognized that the tissues are the site of infection in experimental streptococcus septicaemia. The defenses of the body are in the tissues, and here also the organisms proliferate, those appearing in the blood having been passively carried away from tissue foci of infection. In spite of the profound changes which occur in the blood,¹ it is felt that these alterations simply reflect the more fundamental disturbances occurring in the tissues.

Septicaemia was produced in rabbits by the intravenous injection of from 0.5 cc. to 0.75 cc. of a 24-hour broth culture of *Streptococcus hemolyticus*. In the 7 experimental animals the resulting infections reached fatal terminations in from 2 to 8 days. Tissues were removed from the rabbits just at death, or the animals were killed at a period when the non-protein nitrogen had risen to an abnormal level. It was found in the earlier work that a rise in this constituent could be used as a guide to the time at which the animal had entered the terminal period of the disease, and had an expected survival of only a few hours. The 8 animals in the control series were killed by a blow on the neck. They had not been starved before their tissues were taken. Ten to 12 gm. of liver, and 6 to 8 gm. of muscle from the abdominal wall were taken from each rabbit. In the experimental animals, heart's blood cultures were positive for *Streptococcus hemolyticus* in each case.

The extraction of the tissues, precipitation of the protein, and determination of the total reducing substance, non-fermentable substance, and true sugar were carried out according to the procedure of Trimble and Carey.⁴

The amounts of total reducing substance, non-fermentable substance, and true glucose in liver and muscle are given in Tables I and

² Folin, O., *J. Biol. Chem.*, 1928, **77**, 421.

³ Hopkins, J. G., and Parker, J. T., *J. Exp. Med.*, 1918, **27**, 1.

⁴ Trimble, H. C., and Carey, B. W., Jr., *J. Biol. Chem.*, 1931, **90**, 655.

II. The former contains the figures for the normal series, and the latter the data on the infected animals. Table II also shows the length of survival after the injection of the streptococcus.

TABLE I.
Total Reducing Substance, Non-fermentable Substance, and True Sugar in the Liver and Muscle of Normal Rabbits, in mg. per 100 gm. of Fresh Tissue.

Rabbit No.	Liver			Muscle		
	Total Reducing Substance	Non-fermentable Substance	True Sugar	Total Reducing Substance	Non-fermentable Substance	True Sugar
1	64.52	7.55	56.97	8.61	5.69	2.91
2	58.3	6.4	51.9	9.27	4.67	4.59
3	47.4	6.6	40.8	10.7	6.2	4.5
4	95.2	9.95	86.25	8.75	4.45	3.65
5	76.8	7.9	68.9	7.0	—	—
6	45.0	4.2	40.8	9.0	—	—
7	56.18	6.49	49.69	6.79	3.89	2.9
8	43.19	4.78	38.41	7.28	4.16	3.12
Average	60.82±3.91	6.73±0.38	54.21±3.91	8.42±0.33	4.84±0.22	3.61±0.18

TABLE II.
Total Reducing Substance, Non-fermentable Substance, and True Sugar in the Liver and Muscle of Rabbits in the Terminal Stage of Septicaemia due to *Streptococcus hemolyticus*, in mg. per 100 gm. of Fresh Tissue.

Rabbit No.	Liver			Muscle			Survival after Infection. Days
	Total Reducing Substance	Non-fermentable Substance	True Sugar	Total Reducing Substance	Non-fermentable Substance	True Sugar	
1	35.64	3.49	32.15	5.14	3.31	1.83	8
2	23.31	5.24	18.07	4.14	3.88	0.26	5
3	14.05	3.51	10.54	2.57	1.41	1.16	2
4	36.1	5.89	30.21	4.1	3.3	0.8	3
5	33.1	5.15	27.95	—	—	—	3
6	17.75	5.08	12.67	3.56	2.29	1.27	3
7	9.48	3.16	6.32	3.57	3.18	0.39	3
Average	24.2±2.56	4.5±0.24	19.7±2.4	3.84±0.2	2.89±0.21	0.95±0.14	

The relations between the total reducing substance, non-fermentable substance, and true sugar in the livers and muscles of the 2 groups may be expressed as follows: The non-fermentable substance of normal rabbit liver is approximately one-tenth of the total; in infected rabbits it is more variable, but usually represents one-fifth or one-sixth of the whole. That is to say, while both constituents are reduced, the true sugar undergoes a greater proportionate reduction than the non-fermentable substance. The actual reduction can be estimated by a comparison of the average values. The average for the total reducing substance drops from 60.82 mg. to 24.2 mg.,

for the non-fermentable substance from 6.73 mg. to 4.5 mg., and for the true sugar from 54.21 mg. to 19.7 mg.

The data derived from the study of the muscles lead to similar deductions. In the normal animals, the non-fermentable substance makes up slightly more than 50% of the total; infected animals' muscles, on the other hand, have about three-quarters of the total reducing substance in the form of non-fermentable constituents. Here again the proportionate reduction is greater for the true sugar than for the non-fermentable substance. The actual reduction, in so far as it is shown by the averages, goes from 8.42 mg. to 3.84 mg. for the total reducing substance, from 4.84 mg. to 2.89 mg. for the non-fermentable substance, and from 3.61 mg. to 0.95 mg. for the true sugar.

In the work reported above,¹ it was suggested that the production of organic acids *in vivo* by the streptococcus played an important rôle in bringing about the death of experimentally infected animals. In view of the fact that the organisms grow in the tissues, especially in the muscles, in contrast to the blood, in which they probably do not grow, the present findings suggest strongly that tissue glucose serves as the source of the acids produced by the streptococcus. Under these conditions, the gradually lowered blood sugar would result from an increasingly large transfer of glucose from blood to tissue, with a consequent drain on the liver. In this connection it is interesting to note that the protein-free extracts of infected liver are water-clear, while similar extracts of normal liver have the decided opalescence of glycogen solutions. Hopkins and Parker³ have shown that the liver of even a susceptible animal will destroy large numbers of streptococci in the early part of the infection, while the organisms begin at once to grow in the muscles. Thus the liver, since it contains few parasites or none, and is therefore not being drained of glucose by their growth, is in a position to furnish sugar to the muscles where proliferation is rapid and destruction of the organisms slight or absent. In the last stage of the disease, however, the streptococci begin to proliferate in the liver itself, and the glucose concentration of the blood is still further lowered. The evidence is not clear for a separate "toxic effect" of the streptococci, which might be supposed to act apart from and in addition to the purely biochemical changes in bringing about the death of the animal.

Conclusion. The concentrations of total reducing substance, non-fermentable substance, and true glucose have been determined in the livers and muscles of rabbits in the terminal stages of acute strep-

tococcus septicaemia. These concentrations are found to be significantly lower than those in normal rabbits.

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A Thermoregulated Foot Cradle for the Treatment of Peripheral Vascular Disease.

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When the circulation to an extremity is impeded the ability to maintain the proper temperature of the part may be seriously impaired. Therefore it seemed that patients with gangrene of the feet due to peripheral vascular disease might be benefitted by discovering and maintaining the temperature optimum for the circulation in their feet. This preliminary communication is submitted because of the relief from pain which has followed this procedure in 3 cases, two of diabetic and one of arteriosclerotic gangrene.

Each patient had a spot of dry gangrene on one great toe. The local lesions had been treated by placing the feet in a bed cradle containing an electric bulb permanently lighted, but pain had persisted.

Procedure. The threatened feet were placed in a large water bath equipped with a stirring device and heating unit. At the initial temperature, about 31°, the patients complained that the cold caused pain, and the skin was pale and blue with patches of deeper cyanosis near the gangrenous areas. As the temperature was gradually raised (about 1°C. in 5 min.) the pain lessened and the color improved. At a temperature of 34° in 2 patients, 35° in the third, pain disappeared completely and the color of the feet approached the normal. After the temperature had risen another degree pain and cyanosis returned. Increasing pain and deepening cyanosis accompanied a further rise of temperature. Therefore 34° or 35° appeared to be the optimum temperature for the feet of these patients.

After discovering the optimum temperature, a foot cradle* equipped with a thermoregulator was placed upon the patient's bed and the gangrenous foot kept in it constantly. The thermometer

* This cradle was demonstrated at the scientific exhibit of the American Medical Association meeting at Philadelphia, June, 1931.