teremia, each animal had a local lesion (80 to 90 mm. in diameter) about the point of inoculation which presented an intense erythema and marked induration. Two of the rabbits were given 100 cc. of a 1% solution of sulfanilamide by mouth twice each day. After 3 days, the blood cultures showed no growth and at the end of 5 days the temperature had returned to normal and the local lesions had healed. Each rabbit received a total of 10 gm. of the drug during the period of treatment. It should be noted that the dose used was far in excess of that recommended in human therapy.

Both of the untreated rabbits died in 2 days. There was no reduction in the bacteremia or extent of the local lesions; neither was there a drop in the temperature of either animal. (See chart.)

Conclusion. Sulfanilamide, when given orally to rabbits in adequate doses, early in the course of experimental dermal pneumococcal infection, eliminates this microörganism from the blood stream, reduces the fever, cures the local lesion and favors recovery in most of the treated animals.

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Presence in Milk of the Extrinsic Factor of Castle.

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The extrinsic factor of Castle has been found in several protein-containing foods, such as beef muscle,[1] autolyzed yeast,[2] wheat germ,[2] and egg white.[3] From Castle's[4] more recent work, one may infer that some of the negative results obtained with protein foods other than these, were due to prolonged incubation periods, or the trial use of the materials at hydrogen ion concentrations too great for the interaction of the extrinsic and intrinsic factors. Casein[5] has been reported as giving a negative response at a pH of 2.5 to 3.5, however, more recently Taylor, *et al.*,[6] have indicated that the in-

1 Castle, W. B., Townsend, W. C., Heath, C. W., *Am. J. M. Sc.*, 1929, **180**, 305.

2 Strauss, M. B., and Castle, W. B., *New Eng. J. Med.*, 1932, **207**, 55.

3 Miller, D. K., and Rhoades, C. P., *New Eng. J. Med.*, 1934, **211**, 921.

4 Castle, W. B., and Ham, T. H., *J. Am. Med. Assn.*, 1936, **107**, 1456.

5 Castle, W. B., and Townsend, W. C., *Am. J. M. Sc.*, 1929, **178**, 764.

6 Taylor, F. H. L., Castle, W. B., Heinle, R. W., and Adams, M. A., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 566.

trinsic factor is an enzyme which has optimum action at pH 7.4 to 7.7. Because infants may be fed on whole milk alone for long periods of time without developing pernicious anemia, it would seem possible that milk which contains Caseinogen as the greatest part of its protein might contain the extrinsic factor. Because of this we have investigated the value of milk as a source of extrinsic factor with 2 pernicious anemia patients, and to 3 patients with pernicious anemia we have given partitions of milk with gastric juice to see if the extrinsic factor were contained in the whey.

All of these patients presented classical signs of pernicious anemia, 2 had had previous relapses and although 2 were negroes, all, subsequent to the experiments, have gone into remissions on liver therapy. The diets used were high in carbohydrates and lacking in meat, eggs, and whole cereals, while the patients were receiving experimental material. In Case 1, however, the patient prior to the experiment received a diet rich in meat to rule out dietary deficiency. The diets of those on whey and gastric juice were also restricted in the amount of milk foods.

Case 1. A colored female 41 years of age. For 7 consecutive days, each day, this patient was given 150 cc. of gastric juice and 960 cc. of whole milk. The protein in this mixture was not over 40 gm. The typical hematopoietic response occurred and may be seen in Table I.

The second patient to receive whole milk and gastric juice was Case No. 4. This was a male 53 years of age. The first day of the experiment he received 350 cc. of gastric juice with 960 cc. of whole milk; following this he received 7 daily doses of 150 cc. of gastric juice and 960 cc. of whole milk. In this case the milk and gastric juice were not incubated and at all times were kept cold. The day after the last dose of the milk and gastric juice mixture, the diet was changed to house ration but no antianemic substance was given. A typical hematopoietic response was obtained prior to treatment with liver extract.

These two patients not only showed the typical response of blood formation but also showed improvement in appetite and in general well-being.

After obtaining a reticulocyte response and an increase in RBC and Hb in Case 1, this patient was placed on a mixture of fresh whey and gastric juice. The fresh whey was made by the addition of 50 cc. of 5% HCl to 960 cc. of whole milk at 37°C. The clotted casein was removed. About 600 cc. of whey was collected and to this 150 cc. of gastric juice was added. This, then, was brought to

TABLE I.

Case No. 1.

Diet: High carbohydrate with no meat, eggs, or whole cereals.

	RBC mil.	Hb. %	Retic. %
2-8	1.32	35	.6
2-9	1.23	35	.7
2-10	1.5	38	.7

Start of 150 cc. gastric juice and 960 cc. of whole milk mixed and incubated 2 hours.

	RBC mil.	Hb. %	Retic. %
2-11	1.45	37	0.6
2-12	1.65	38	0.4
2-13	1.26	35	1.0
2-14			0.4
2-15	1.5	36	2.5
2-16	1.62	41	7.1
2-17	1.61	40	12.0

2-17 Last day of gastric juice and milk.

	RBC mil.	Hb. %	Retic. %
2-18	1.49	40	7.9
2-19	2.04	46	11.4
2-20	1.91	48	11.2
2-22	2.17	53	6.9
2-25	1.9	53	2.7

2-26 600 cc. fresh whey and gastric juice 150 cc. started.

	RBC mil.	Hb. %	Retic. %
2-26	1.89	53	2.5
3-9	2.03	61	1.2

This is the last day of whey and gastric juice. Patient then treated with liver extract.

Case No. 3.

Diet: High carbohydrate with no meat, eggs, or whole cereals.

	RBC mil.	Hb. %	Retic. %
4-27	1.35	48	.3

800 cc. whey made by adding 150 cc. gastric juice to 960 cc. whole milk; removing clot of casein.

4-28 600 cc. fresh whey and 150 cc. gastric juice

	RBC mil.	Hb. %	Retic. %
4-28	1.62	48	.5
4-29	1.60	49	.7

Same as 4-27.

	RBC mil.	Hb. %	Retic. %
4-30	1.34	43	1.1
5-1	1.41	46	0.7
5-3	1.77	52	0.5
5-4	1.57	48	2.6
5-5	1.70	52	3.3
5-6	1.69	49	4.2

Last material given this day.

5-7 House diet without anti-anemic substance.

	RBC mil.	Hb. %	Retic. %
5-7	1.66	53	2.9
5-8	1.66	53	2.3
5-10	1.70	53	1.4

Case No. 2.

Diet: High carbohydrate with no meat, eggs, or whole cereals.

	RBC mil.	Hb. %	Retic. %
4-9	1.89	47	
4-10	1.34	49	.3
4-12	1.61	47	.4

600 cc. of fresh whey from 960 cc. of whole milk and 150 cc. gastric juice daily. 4-11.

	RBC mil.	Hb. %	Retic. %
4-13	1.89	50	.3
4-14	2.01	51	.3
4-15	1.99	51	.2
4-16	2.11	53	.8
4-17	1.96	57	.8
4-18	2.02	56	.8

60 gm. of dried whey substituted for fresh whey daily.

	RBC mil.	Hb. %	Retic. %
4-19	2.05	57	0.7
4-20	2.12	58	1.8
4-21	2.17	60	1.3

Dried whey increased to 100 gm. daily.

	RBC mil.	Hb. %	Retic. %
4-22	1.89	52	1.5
4-23	2.09	59	1.0
4-24	1.87	51	0.9

Dried whey and gastric juice observed to be negative and discontinued. 4-25.

Case No. 4

Diet: High carbohydrate with no meat, eggs, or whole cereal.

	RBC mil.	Hb. %	Retic. %
7-16	1.27	41	1.3
7-17	1.4	38	0.8

7-18 350 cc. gastric juice and 960 cc. whole milk not incubated but kept cold.

After this day, 150 cc. gastric juice and 960 cc. whole milk were used.

	RBC mil.	Hb. %	Retic. %
7-19	1.47	39	1.0
7-20	1.40	39	1.1
7-21	1.39	39	1.1
7-22	1.40	40	3.0
7-23	1.42	40	2.2
7-24	1.45	40	3.0
7-25			4.0

Last day of gastric juice and whole milk.

	RBC mil.	Hb. %	Retic. %
7-26	1.43	41	2.2

Started on house diet without anti-anemic substance.

	RBC mil.	Hb. %	Retic. %
7-27	1.68	41	5.0
7-28	1.77	50	7.9
7-29	1.72	51	10.3
7-30	1.69	47	9.4

7-30 Started on liver therapy.

a pH of 6.8-7.0 by the addition of 10% NaOH, usually about 10-15 cc. This mixture was kept cold and 750 cc. of it was fed the patient daily for 12 days. On this mixture there was no further increase in red count nor subsequent rise in reticulocytes.

This latter experiment was repeated with Case No. 2, a colored male aged 27 years. At first he was given the fresh whey and gastric juice mixture outlined above, but after 6 days 60 gm. of dried whey was substituted for the 600 cc. of fresh whey and this was increased after 3 days to 100 gm. daily. The mixture of dried whey and gastric juice was made up to about 800 cc. in volume and the pH was adjusted to 6.8 to 7.0 by the addition of NaOH. This mixture was given for 6 days in all, which was 12 days from the start of fresh whey and gastric juice. In this time, no hematopoietic response was obtained, and the patient felt weaker, although there was no drop in blood levels. On liver extract therapy he accomplished a rapid recovery.

In these 2 cases the amount of protein given in the whey and gastric juice mixture was very small. In the fresh whey there were not over 4 gm. a day, and in the dried whey not over 12.

Case 3. The patient was a male aged 68 years. To this patient was given the filtrate from 960 cc. of whole milk precipitated with 150 cc. of gastric juice at 37° C. He received this material for 8 days, although, owing to an error after the first dose, he received fresh whey and gastric juice for 2 days, and then the above filtrate was resumed for 7 days. At the end of the ninth day a reticulocyte rise of 4.2% was elicited but no rise in Hb or RBC and the patient felt no better and showed no signs of improvement, and the experiment was discontinued. We believe it to be negative.

In this work we have treated 2 patients showing typical signs of pernicious anemia with whole milk and gastric juice while maintaining them on a diet otherwise greatly devoid of Castle's extrinsic factor. Both of these patients exhibited fair hematological responses as evidence that the extrinsic factor was present in the milk. By contrast 3 patients did not give response on gastric juice and whey, which leads us to the conclusion that the extrinsic factor was in the casein part of the milk. However, it leaves us with a query as to what might have happened if we had given 400 gm. of dried whey, which would have equalled the protein content of the 960 cc. of whole milk.