fluids were passed through Berkefeld N and medium Mandler filters and inoculated intracerebrally. Pharyngeal washings in bouillon from the same patients were inoculated intranasally; and after filtration, intracerebrally. About 100 mice were used in the tests but only a few became sick and died. At necropsy several of them had pneumonitis, but no other significant lesions were observed even after microscopic study of sections of the viscera. Suspensions of the lungs and spleen from several mice were reinoculated by various routes into 100 fresh mice, in a few trials to the fourth passage, without any consequence of note. Three samples of original filtered fluid from stools were inoculated into the chorio-allantoic membrane of developing chick embryos but again without results.

In December, Light and Hodes[4] reported the isolation of a filtrable agent from the stools of infants suffering from a well-known epidemic form of diarrhea of the newborn, with which they regularly produced enteritis and diarrhea in calves by intranasal inoculation. The agent was indeed an unusual one which was not regularly inactivated by boiling for 5 minutes or by heating at 70°C for 1 hour, yet it appeared to be the causative agent since it was neutralized by the serums of 6 convalescent babies.

After this publication appeared we applied the technic described using 4 stool specimens which had been preserved frozen with solidified carbon dioxide since November (2 months) and specimens from 4 patients with sporadic attacks in January. The stools were thawed, the supernatant fluids were immediately passed through medium Mandler filters and inoculated in 10 cc amounts intranasally into 8 4-week-old calves. The calves were observed for 2 months but all except one remained well. One became sick for 3 days without diarrhea a month after inoculation and died, but at necropsy no gross lesions were seen.

Summary. Attempts to isolate a filtrable infectious agent from adult patients with epidemic diarrhea, nausea, and vomiting were unsuccessful. We were unable to duplicate the results of Light and Hodes. Perhaps the virus had disappeared during preservation of the frozen stools, or was never present in the stools, or insufficient amounts of inoculum were used, or the disease in adults with which we dealt is different from that in the newborn.

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A Potentiated Chemotherapeutic Action of Sulfathiazole and Quinine.*

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In the course of an investigation on the effects of the simultaneous administration of antimalarials and sulfonamides we observed that quinine and sulfathiazole appeared to exert in mice a potentiated chemotherapeutic action against an infection with a beta hemolytic streptococcus, strain 1048M. Stuart, Powell and Bibbins[1] reported that against a streptococcal infection in mice the chemotherapeutic action of quinine sulfanilamide 3HCl was equal to but not greater than that of sulfanilamide. All other cinchona-sulfanilamide compounds tried by these investigators were less effective than sulfanilamide. Other workers, Miura,[2] Jacobi and Coenen,[3] Sattler and

* The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Woman's Medical College of Pennsylvania.

1 Stuart, E. H., Powell, H. M., Rose, C. L., and Bibbins, F. E., *J. Am. Pharm. Assn.*, 1939, **28**, 90.

2 Miura, K., *Jap. J. M. Sc., IV, Pharm.*, 1940, **12**, 209.

3 Jacobi, J., and Coenen, F., *Munchen. Med. Wchnschr.*, 1940, **87**, 723.

TABLE I.
The Protective Action of Sulfathiazole With and Without Quinine Against Hemolytic Streptococcal Infections* in Mice.

Group	No. mice	No. survived	% survived	Standard error$_p$	D/S.E.$_{D_p}$	Chances in 100 of a true difference between groups I and II
I. Sulfathiazole and quinine	71	54	76	5.07	2.38	99.1
II. Sulfathiazole	72	41	57	6.09		
III. Quinine	73	2	3			
IV. No drug	73	7	10			

* *Streptococcus hemolyticus*, strain 1048 mucoid, Lancefield group A, was the organism used for infection.

The drugs were administered for 48 hours prior to and for 168 hours subsequent to the infection. All of the survivors were placed on drug-free Purina checkers for an additional 168 hours. The survivors recorded in the table represent the number of mice living at the end of the second 168-hour period.

Tüchler,[4] and Schumacher,[5] have reported experimental and clinical data which suggest that combinations, or the concomitant administration of quinine and sulfanilamide or sulfapyridine are more effective that the sulfonamide alone.

In our experiments 289 mice were divided into 4 matched groups. Group I received sulfathiazole plus quinine ethyl-carbonate; group II, sulfathiazole; group III, quinine ethyl-carbonate; and group IV, no drug. The drugs were evenly dispersed by thorough trituration with ground Purina dog chow checkers and were fed *ad libitum*. The feeding started 48 hours before infection with the streptococci.

The number of mice shown in Column 2 of Table I represent 9 different experiments. In each of these experiments the 4 different groups were always run concurrently and the number of animals in each group in a given series was always the same. The concentration of sulfathiazole in groups I and II was the same in a given series but in the different series the concentration ranged from 0.025 to 0.3%. The concentration of the quinine ethyl-carbonate was always 0.3%. This form of quinine is almost tasteless to the human and apparently was not objectionable to the mouse.

Each mouse was injected intraperitoneally with 0.5 cc of a 1-500,000 dilution of an 18-hour blood broth culture of *Streptococcus hemolyticus*, strain 1048 M. Plate counts of the dilution before the injections showed that each animal received approximately 2500 organisms. The mice were kept on the drug for 7 days subsequent to the infection and the survivors were placed on drug-free Purina checkers for an additional 7 days.

The survivors recorded in Table I represent the animals which survived the 14-day period. The animals in Groups III and IV usually died within the first 24 hours. In Groups I and II 5 and 6 animals, respectively, survived the first 7 days but died before the 14th day. When the data from the 2 periods are analyzed in terms of the ratio of the difference to the Standard Error of the difference the chances that the difference between Groups I and II is true are 99 per 100 for each period. When the chi-square test is applied the chances that there is no difference between Groups I and II are 1.6 and 1.7 per 100 for the 2 periods. These analyses indicate that the probability of a true potentiated chemotherapeutic action of quinine and sulfathiazole is high.

Summary. Tests on 289 mice infected with *Streptococcus hemolyticus*, strain 1048M, gave evidence, with a reasonably high probability of certainty, that quinine and sulfathiazole exerted a potentiated chemotherapeutic action.

4 Sattler, A., and Tüchler, K., *Wien. Med. Wchnschr.*, 1940, **90**, 595.

5 Schumacher, G., *Munchen. Med. Wchnschr.*, 1940, **87**, 1302.