

Proceedings
of the
Society
for
Experimental Biology and Medicine

VOL. 55

APRIL, 1944

No. 4

SECTION MEETINGS

ILLINOIS

University of Chicago

March 14, 1944

MINNESOTA

University of Minnesota

March 15, 1944

ROCKY MOUNTAIN

Denver, Colo.

February 25, 1944

DISTRICT OF COLUMBIA

George Washington University

March 30, 1944

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**Negative Results in Studies of Epidemic Diarrhea, Nausea and Vomiting
of Unknown Cause.**

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Because of the absence of any demonstrable bacterial cause, several investigators suspected the syndrome called epidemic diarrhea, nausea and vomiting to be caused by a filtrable virus acting either on the central nervous system¹ or on the gastrointestinal tract.² The nature of the infection, its probable air-borne transmission and its appearance in explosive outbreaks concurrently in widely scattered places supports this view. There is reason to believe that certain viruses may cause primary gastro-enteritis in man, but until recently^{3,4} none was thought to be par-

ticularly enterotropic, except perhaps the virus of poliomyelitis.

A widespread epidemic in Philadelphia in November, which involved 20% of our student body, provided material for study.⁵ Food poisoning was excluded. Bacteriologic examination of stools and pharyngeal secretions from 10 carefully studied patients revealed none of the usual bacteria or other parasites commonly associated with enteritis and no unusual ones. Diarrheal stool samples from 5 patients were spun at slow speed in the centrifuge, and the supernatant fluid was inoculated orally, intranasally, and rectally into young white mice. Samples of the same

¹ Rischel, A., *Ugeskr. Laeg.*, 1935, **97**, 1285; Henningsen, E. J., *Ugeskr. Laeg.*, 1936, **98**, 45; Bradley, W. H., *Brit. Med. J.*, 1943, **1**, 309; Miller, R., and Raven, M., *Brit. Med. J.*, 1936, **1**, 1242.

² Boardman, W. W., *Am. J. Med. Sci.*, 1939, **196**, 833.

³ Silva, M., *Hospital*, Rio de Janeiro, 1940, **18**, 1015; Baker, J. A., *J. Exp. Med.*, 1943, **78**, 435.

⁴ Light, J. S., and Hodes, H. L., *Am. J. Pub. Health*, 1943, **33**, 1451.

⁵ Reimann, H. A., Price, A. H., and Hodges, J. H., *Epidemic Diarrhea, Nausea and Vomiting of Unknown Cause*, to be published.

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 Hodes⁴ 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 Bibbins¹ 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. Wechschr.*, 1940, **87**, 723.