The keynote in the treatment is promptness. If the food can be stopped and the alimentary tract emptied within a few hours after the onset of symptoms, most infections can be aborted.

The results of antidysenteric serum treatment were disappointing. It, too, was apparently helpful in proportion to the shortness of the time which elapsed between the beginning of the illness and the injection of the serum. Its use is perfectly harmless under anti-septic precautions.

The prophylactic injection of the serum into susceptible babies may prove to be an advisable procedure.

The alterations in the body produced by the action of the dysentery bacillus may be those of an acute toxemia only, or in addition there may be set up more or less destructive lesions of the lower bowel. In this latter process streptococci and other organisms may play a part. The constant change noticed in all cases was the enlargement (serous infiltration) of the mesenteric lymph glands.

THE BACILLUS DYSENTERIÆ (SHIGA) IN ITS RELATION TO THE DIARRHEAL DISEASES OF INFANTS.

A CLINICAL STUDY OF TWO HUNDRED AND THIRTY-SEVEN CASES.*

L. EMMETT HOLT, M.D.

Professor of Pediatrics in the College of Physicians and Surgeons.
NEW YORK CITY.

The early history of the work done on the dysentery bacillus has been so often published that it need not be repeated here. It is to Duval and Bassett that the credit is due of first pointing out the fact that this organism played an important part in the diarrheal diseases of infancy. Working under the direction of Dr. Flexner at the Thomas Wilson Sanitarium, Baltimore, in the summer of 1902, Duval and Bassett studied 53 cases of diarrheal disease in infants and young children, in 42 of which they demonstrated the presence of the dysentery bacillus. After a considerable number of positive cases had been found, 25 cases were taken successively and from 19 of these the dysentery organism was isolated. They established the connection between the organism and the disease by obtaining positive agglutination reactions in a very considerable number of their patients.

In the autumn of 1902, at my suggestion, Dr. Martha Wollstein, at the Babies' Hospital, began a systematic study of the cases of acute disturbance of the intestine, and continued the investigations until the following May, in order to discover whether this organism would be found in winter cases as well. She studied, in all, the discharges from 114 patients, representing almost every phase of acute intestinal disorder; in 39 of the 114 cases the dysentery bacillus was found. It was never absent where the clinical picture was a definite one of acute disturbance characterized by the presence of blood and mucus in the stools.

In 1903, under the general direction of Dr. Flexner, the Rockefeller Institute undertook to continue this investigation by making simultaneous observations at different centers, with a view of throwing further light on the relationship existing between the dysentery bacillus

and diarrheal diseases in summer. Work was carried on in New York at the Babies' Hospital, Nursery and Child's Hospital, Vanderbilt Clinic, Foundling Hospital, Infirmary for Women and Children, Bellevue Hospital; in Baltimore, in the out-patient department of Johns Hopkins Hospital and the Thomas Wilson Sanitarium; in Boston, at the Floating Hospital, and at the Children's Hospital in Philadelphia.

The bacteriologic reports of this investigation have been edited by Dr. Flexner and have recently been issued. The present paper is a summary of the clinical reports of 237 cases in which the dysentery organism was present. These cases were observed by the following persons:

Drs. John Howland and L. E. La Pétra, Vanderbilt Clinic	62 cases.
Dr. Louise Cordes, Infirmary for Women and Children	26 cases.
Dr. Samuel Amberg, Baltimore	19 cases.
Dr. Louis M. Warfield, Bellevue Hospital	7 cases.
Dr. J. H. M. Knox, Jr., Thomas Wilson Sanitarium	43 cases.
Dr. Robert Hastings, Boston Floating Hospital ..	28 cases.
Dr. R. G. Freeman, New York Foundling Hospital ..	7 cases.
Dr. Dorothy Reed, Babies' Hospital	45 cases.

Several of these persons have already published their individual reports. It is the purpose of the present paper to combine the results of the investigations of the summer of 1903 to see what light they have thrown on our conception of summer diarrheas of infants, and especially what results have been obtained, and in the future what may be expected from the serum treatment.

Considerable new light has been thrown on the subject of diarrheal diseases in infants and young children by this investigation, although much still remains to be done. The summer was not a particularly fortunate one for such an investigation, as it proved to be an unusually cool season, and the diarrheal diseases were neither so frequent nor so severe as in average years.

Several points were prominently brought out by the different clinical observations:

1. The infection with the *B. dysenteriae* occurs under quite a wide variety of conditions. It is seen in breast-fed infants as well as in those artificially fed.

2. It occurs (a) as an acute primary infection in children previously well; (b) as a subacute infection without previous acute symptoms; (c) coincident with or following other acute diseases, such as measles, pneumonia, etc.; (d) it is often seen as a terminal infection in children suffering from extreme malnutrition or marasmus.

3. It occurs as a mild intestinal disorder with few symptoms, and these hardly more marked than those belonging to intestinal indigestion; also with local symptoms of considerable severity, yet with very little fever or constitutional depression; and finally, in its most severe form, with both local and constitutional symptoms of great severity.

4. It is not a disease of any one locality, having been seen with great and about equal frequency in all the large cities—New York, Boston, Philadelphia and Baltimore—where investigations were carried on; the only variation in type being that in the warmer cities the proportion of severe acute cases was rather larger. Nor is the disease one of tenements and hospitals, a number of the cases observed being in children living under the best surroundings, even in the country. In its prevalence, it appears to be as widespread as are summer diarrheal diseases.

PREVIOUS DIET.

The clinical reports include observations on 237 cases. The previous diet was studied in most of these in the

* Read at the Fifty-fifth Annual Session of the American Medical Association, in the Section on Diseases of Children, and approved for publication by the Executive Committee: Drs. S. W. Kelley, H. M. McClanahan and John C. Cook.

hope of gaining some information as to the mode of entrance of the organism into the body. Of the cases observed, 26 were previously breast-fed. While in most of these the infection was a mild type, some were severe and even fatal. That these attacks were, as a rule, milder than most of those seen, may be in part at least explained by the better physical condition, and consequently the greater resistance of the breast-fed infants. That so many attacks were seen in nursing infants shows that we must seek for some other mode of entrance of the specific organisms than with the milk. Possibly it may be the water, although in this the dysentery bacillus has not yet been found. The practice of boiling water for the use of infants is seldom followed in the tenements, and water in some form was given to almost all the children. No special relation of the infection to any other food or any special kind of feeding could be discovered.

RELATIVE FREQUENCY OF INFECTION.

The relative frequency of infection with the dysentery bacillus as compared with other diarrheal diseases of infancy can not be definitely stated from these reports. In only two groups of cases were systematic examinations made of consecutive cases. In the others, the cases for examination were more or less selected, and hence it is impossible to draw conclusions from them as to relative frequency. The two groups of consecutive cases were those from the Vanderbilt Clinic, a summer series reported by Howland and La Fétra, and those from the Babies' Hospital, a year-round series, reported by Reed. In the first group of cases the dysentery bacillus was found in 62 of 64 cases examined. They included every sort of intestinal disturbance attended by diarrhea. These figures, however, do not prove that in every instance this organism was the cause of the disturbance. In some of the cases the number of dysentery bacilli was apparently very small; sometimes only one or two colonies were discovered after a prolonged and careful search. But their presence even in such small numbers is interesting as showing possibly how mild attacks might develop into severe ones.

In this connection I should like to refer to some studies just completed at the Babies' Hospital by Dr. Wollstein on the stools of normal children. During the past winter and spring, observations have been made on 56 children with a view of determining (1) whether dysentery bacilli were present in the stools of normal infants; (2) whether they could be obtained postmortem from scrapings of the mucosa of children dying from other diseases.

Stools of 32 children, all under 18 months of age, were studied with great care by the following method: Patients who had been in the hospital several days and had been observed to have normal discharges were selected. The colon was washed out with one or two quarts of a saline solution, after which a cathartic, castor oil or citrate of magnesia, was administered. All stools passed in the next ten hours were studied. In no instance were dysentery bacilli discovered.

In a series of 24 cases studies were made of scrapings from the intestinal mucosa in children dying from diseases other than intestinal. In 21 no dysentery bacilli were found. They were present in 3 cases, but 2 of these presented rather marked evidences of inflammation of the intestinal mucous membrane, not suspected during life; while in the third a history was obtained of a previous attack of diarrhea, and this case showed swelling of Peyer's patches and some congestion of the mucous membrane of the colon.

In one entire year's service at the Babies' Hospital about one-half of all the cases exhibiting clinical evidence of acute disorders of the intestinal tract showed dysentery bacilli.

These observations indicate that dysentery bacilli are an important etiologic factor in the intestinal diseases of young children, both in winter and in summer; but that they are present in a much larger proportion of cases in summer than in winter.

CLINICAL TYPES.

Of the cases studied, 91 were classed as examples of severe infection. These were characterized by much mucus and generally blood in the stools, usually fever, but not always high, and by marked general prostration. There were 81 examples of moderately severe infection, in which there was much mucus and often blood in the stools, some fever but not much constitutional depression. There were 63 examples of mild infection, in which the constitutional symptoms were very few; blood was seldom present; there was little or no fever; but the stools almost always contained mucus. These figures indicate only that mild infections are very common; their relative frequency, however, is probably much greater than is stated here, since by several observers only severe cases were taken for examination.

The types of disease were essentially the same at all places where the observations were made. Infection with the dysentery bacillus was associated with almost every sort of intestinal disturbance accompanied by diarrhea, with, however, one notable exception, viz., the severe acute intestinal intoxication called "cholera infantum," with its sudden violent onset, protracted vomiting, high temperature, frequent serous discharges, great prostration, early collapse and often early death. There was only one case which at all approached this type, and this lacked some of the essential features. The infection with the *B. dysenteriae* is associated rather with the inflammatory forms of diarrhea, and of all degrees of severity, the mildest and the most severe, the acute, the protracted and subacute; occurring both as a primary disease and a secondary disease, often occurring in institutions during the summer as a terminal infection in infants suffering from marasmus, exactly as does bronchopneumonia under similar circumstances in winter.

Up to the present time the organism has not been found in cases of chronic intestinal indigestion in infants and older children, even though mucus was present in the stools in considerable amount. In this series of cases there were observed no chronic cases such as have been described in adults where bacilli were found after many months. The cases of long duration which were studied in infants were usually free from bacilli at the end, death being due to progressive marasmus.

The most characteristic clinical type and the one with which the organism was almost invariably found associated, was the acute febrile form with stools containing much mucus and usually streaked with blood. For these cases the term "infantile dysentery" would seem the only proper appellation. This type seems so distinctive that we may safely regard it as a separate and distinct disease.

TYPES OF ORGANISM.

Of the 237 cases studied clinically, the "Flexner-Harris" or "acid" type of organism was present in 207, the true Shiga in 23, and both organisms were present in 7. No difference could be observed in the clinical manifestations in the different forms of infection. Further-

more, the relative frequency of the different types was nearly the same in all places where the observations were made.

Whatever may be said of the dysentery of adults, it would appear from these data that in infants and young children, in our large eastern cities, it is the acid type of organism rather than the true Shiga with which we are chiefly concerned.

MORTALITY.

Of the 237 cases reported, 73 were fatal. This gives little idea of the gravity of the dysentery infection, since it is well known that the result in all forms of intestinal disease in infants depends on nothing so much as on the age and previous condition of the patients. Considerably more than half the total number, 139, were observed in hospitals. It was among these patients also that nearly all the deaths occurred, as might have been expected. The poor general condition of these patients and the late date of beginning treatment had most to do with determining the results. Again, in several it was noted that the patients recovered from the acute diarrhea but died subsequently from marasmus. Cases of this kind were seen in almost all the groups.

In all acute disorders of the intestinal tract complex conditions are present. No infection or intoxication can occur without producing marked functional derangement of digestion. In some cases the infection is slight, while the digestive disturbance is severe. The two bear a general but by no means a constant relation to each other. The child's symptoms may be due almost entirely to the indigestion and very little to the infection. These conditions stand in the way of success by serum treatment. While we may be able to combat the infection by the serum, it may be without any power to improve the digestive disturbance. It also has a bearing on the question of diet during the attacks.

DIET DURING THE ATTACK.

The necessity of stopping milk during severe acute infections is universally agreed on. There is, however, some difference of opinion in regard to the desirability of withholding milk from cases of moderate severity, without temperature, where the disease seems to be limited to the large intestine. In these cases the symptoms from which the child suffer are chiefly those of wasting from chronic indigestion. There seems to be little doubt from the experience at the Babies' Hospital and Vanderbilt Clinic, that many of these cases do much better on a properly modified milk than on other substitutes employed, such as broth, barley water, albumin water, etc., with which the loss of weight is very rapid. In such cases the infection seems to play a minor part and the indigestion a major part, and, therefore, one should not have his attention too much on the presence of a specific infection, but should manage the child's diet according to general principles, as in other forms of acute or subacute intestinal indigestion. The mere presence of dysentery bacilli in the stools is, therefore, in itself no reason for withholding milk, and its intelligent use seems to give much better results than the substitutes usually employed.

PREVENTION.

The fact that the dysentery infection is contagious seems to be established, but how and to what degree is not yet proven. In four instances, small ward epidemics were noted. From present experience a high degree of contagion does not seem probable. The spreading takes place most likely through the discharges. This calls at-

tention to the necessity for disinfection and the closest attention to prevent contamination of food or water by persons handling the child's napkins. The rule followed in the Babies' Hospital is a good one for all institutions, viz., that the nurse in charge of the children's napkins shall not at the same time have anything to do with the food or the feeding.

SERUM TREATMENT.

In all there were 83 cases in which the anti-dysenteric serum was employed; 38 of these were fatal. On the whole, the results were disappointing. No unfavorable symptoms followed its use in any case. In a few instances eruptions, usually urticaria, followed, as occasionally after diphtheria antitoxin. In only 12 cases did a noteworthy improvement appear to follow its administration. A careful study of the cases in which the serum was used does not make the results quite so bad as at first appears. Too much evidently was expected. The physicians had in mind the striking effects seen after diphtheria antitoxin. These were observed in no instance, and it is doubtful if they ever will be. The conditions in the intestines are very complex and in no way comparable to those which are present in diphtheria. Great disturbances of digestion are in most cases present, and the consequences of this remain long after a specific infection may have disappeared. Difficulties were found in the use of the serum. The quantity in the strength in which it was used was large. The mothers of dispensary patients would not allow its use except in severe cases, and often would not return for a second dose. A brief summary of the cases seems desirable.

Freeman's Report.—Seven cases treated; all hospital patients; in 2 the attack followed measles; one child had diphtheria and pneumonia. In 4 cases no improvement. In 3 improvement apparently occurred, but 2 died later from marasmus long after the intestinal symptoms had disappeared. The only case which recovered was that of a nursing child. Full doses were given, all but one receiving from 5 to 10 doses of 10 c.c. each.

Howland's and La Ftra's Report.—Ten cases treated; all dispensary patients. Serum used only in the severe cases. Two children received but a single dose; result unknown, as they did not return; 2 died, one moribund when treatment was begun, the other recovered from diarrhea, but died long after from marasmus; 2 showed decided improvement after the serum. In the other 4, no apparent effects. Rarely more than 2 doses of 10 c.c. given.

Amberg's Report.—Ten cases treated; 2 hospital patients, 5 private practice, 3 not stated. Of the 5 severe cases, 3 ended fatally, 1 improved and 1 recovered; of the 6 moderately severe cases, 5 recovered, 1 improved. Only one case received an injection on the first day and one on the second day; 3 had been sick four to six days and 6 more than one week. Six cases received two doses and 4 five doses of 10 c.c. each.

Warfield's Report.—Seven cases treated; 2 observed in tenements, 5 hospital cases; 4 died. Two were moribund when the serum was given and one other had pneumonia; 3 apparently benefited by the serum. Two patients received but two doses; all the others received much larger quantities, one patient being given 150 c.c.

Hastings' Report.—Fourteen cases treated; all hospital patients. Serum was used only in the severe cases. Seven of these were fatal. Details of the fatal cases only are given; one of these was moribund at the time of the administration, one died in the seventh week of the disease; 5 were in poor condition at the time of the attack. No striking improvement seen in any case.

Know's Report.—Twenty cases treated; of these 9 were fatal. Three cases apparently improved from the serum; in 17 apparently no improvement.

Cordes' Report.—One severe case seen late, no apparent effect.

Reed's Report.—Fourteen cases; all hospital patients; nearly all severe infections. Temporary improvement seen in several, permanent improvement in none. In 9 cases only one 10 c.c. dose was given.

Such, in brief are the facts regarding the use of the serum in the 83 cases in which it was employed. That decided improvement appeared to follow its use in only 12 of the patients is not very encouraging. Several factors worked against success. In a large proportion of the cases it was used late in the disease. Again, it was as a rule used only in the most severe cases; and, finally, at the beginning of the season no rules had been formulated as to the size and frequency of doses, hence it is evident that many of the doses were too small. Four patients were moribund at the time the serum was given. Of the 83 cases, 67 were hospital patients, and all familiar with hospitals for infants know the class of patients referred to.

The conditions of success, however, are, first, that it must be used early, before serious lesions have developed or before the patient's general nutrition has been too profoundly impaired. The latter refers particularly to cases in young infants. The second point is that experience shows that the serum must be used in repeated doses, one or two doses given each day and continued for several days if the attack is severe. I can not myself feel from a study of these reports and from personal observation of some of these patients, that an adequate trial of the antidyenteric serum has yet been made. The favorable cases for its use are surely not the subacute infections, where the symptoms relate much more to the functional disturbance of digestion and the resulting impairment of the child's nutrition, than to the specific toxemia of the dysentery bacillus; nor again can anything be expected from it in attacks which develop late in a condition of marasmus in hospital patients. The promising cases are rather the sharp acute attacks with symptoms of severe infection occurring in infants or older children with some powers of resistance. In other words, in patients where the real problem is to combat the infection, and not to maintain the nutrition of patients, which even before the infection was a matter of the greatest difficulty.

Inasmuch as at present nearly two days are required for a bacteriologic diagnosis, and as the agglutination reaction is seldom present until the end of the first week of the disease, if used at all, the serum must be injected on a clinical diagnosis. Its use would then be indicated in children taken with acute intestinal symptoms with blood and mucus in the stools, or with very much mucus in the stools with fever and symptoms of general infection. The serum surely must be used early, and it must be given repeatedly, since what is desired is to stop a process and not to neutralize a toxin.

All rules as to dosage and frequency must at present be tentative. From the experience of the past summer it would appear that a dose of at least 10 c.c. should be used daily in a moderate case, this being repeated two or three times daily in a severe case.

Since we have no means at present of differentiating clinically the cases in which the infection is with the acid or Flexner-Harris and with the true Shiga type, it would seem best to use a serum from animals immunized against both types of the organism, or that from animals immunized against the acid type, since by far the largest number of cases in young children are of this variety. Although the serum obtained from ani-

mals immunized with true Shiga is not without some effect in infections with the acid type, and vice versa, this is much less than when the animals are injected with the special type of organism concerned.

A beginning only has been made with the use of the antidyenteric serum. A much more extended trial and on more carefully selected cases is necessary before definite statements can be made as to its value.

14 West Fifty-fifth Street.

SOME FINDINGS IN SUMMER DIARRHEAS OF CHILDREN.*

JOHN C. COOK, M.D.

CHICAGO.

These cases came under observation during July and August, 1903, and are reported to show the relative frequency of some bacteria not ordinarily given prominence in this relation. The study was begun with the hope of making some clinical deductions from the microscopic findings and to trace, if possible, any bacterial relations between the buccal cavity and intestinal disorders.

Twenty-nine cases in all were observed and cultures were simultaneously made from mouth and fecal discharges, and observed as nearly together as possible, but much of the work was not completed owing to the sanitarium closing before all the cultures were worked out.

No note will be made of the ordinary inhabitants of the canal, such as colon groups, staphylococcus, etc., but only such as may have some pathologic bearing on the clinical findings.

CASES 1, 2 and 3.—Nothing of value was found, notwithstanding that there were some clinical features present, such as vomiting and loose bowels, which were found in other cases bacteriologically more interesting.

No. 4.—Breast-fed; aged four months; diagnosis of enteritis. Gave history of from five to six loose, offensive movements daily for four or five days; temperature from 96 to 100; vomited frequently. Cultures were taken from oral cavity and bowel movements, but nothing was found but pink yeast bacilli and staphylococci from the mouth.

No. 5.—Aged six months. Came to sanitarium July 27, with normal temperature and history of from three to five loose brownish bowel movements a day. On the fourth day after admission a curdy exudate appeared in the roof of the mouth and on the inside of the cheeks, and some on the outside of the gums, resembling thrush a little. With this came a slight rise of temperature and loose greenish movements, six to eight a day. This condition was not influenced by treatment for more than a day at a time, when it would lapse back to the same state, and the child died on August 18. Cultures from mouth and movements both showed *Bacillus pyocyaneus*. A postmortem was not permitted.

No. 6.—Entered the sanitarium July 6, with temperature 103; three or four loose green bowel movements in twenty-four hours; vomited once or twice. Child was 18 months old and fairly well nourished; had been nursed for first two months of life, when the supply failed; since had been fed on diluted cow's milk. Cultures from oral cavity showed nothing out of the ordinary. *Bacillus pyocyaneus* was found in the culture from bowel movements. Child left the sanitarium on August 4, not in good condition.

No. 7.—Aged nine weeks; normal temperature; partially breast-fed and partially on store milk diluted; frequent green bowel movements; vomited occasionally. *Bacillus pyocyaneus* in bowel movements only. Did not return.

* Read at the Fifty-fifth Annual Session of the American Medical Association, in the Section on Diseases of Children, and approved for publication by the Executive Committee: Drs. S. W. Kelley, H. M. McClanahan and John C. Cook.