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DIARRHEA IN INFANCY

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DIARRHEA IN INFANCY

Probably the oldest definition is that of Hippocrates who wrote that it is abnormal frequency and liquidity of fecal discharges. The definition of diarrhea since that time has not changed. However, many authors start their definition with the statement that diarrhea is a symptom and not a disease (84), (35) and (32). The number of stools and the degree of looseness run more or less parallel to one another. While both have much the same diagnostic significance, this is not wholly dependable. For this reason a personal inspection of the stools, or a series of stools in chronological order, is often of determining value in evaluating a given condition, or its progress, one way or the other. There may be only two or three loose stools where there was before only one formed or pasty stool. There may be a great many, and in the severest conditions, now rarely encountered, there may be an almost continuous effort to empty the bowels with painful, uncontrollable tenesmus and eversion of the rectum. In general, the number and looseness of the stools are directly proportional to the severity of the disorder (15).

ETIOLOGY

Climate is an important factor, for the incidence is greater in warmer months for all types, and the tropical regions have more dysentery, both amebic and bacillary. Carriers are only of importance in the infectious diarrheas and in those cases usually which originate in institutions. Sex plays no part in the incidence of diarrhea in

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infancy. Age is a powerful factor, for the great majority of serious cases are seen in the first two years of life. In Cooper's (19) series of cases, 65.2% were under six months of age and only 12% were over one year of age. The greatest incidence was in those infants between three and six months of age. He explained this by the fact that many mothers stopped nursing after three months, and the formulae are better tolerated after six months. Epidemics occur with the infectious diarrheas, but the disease is usually considered to be of an endemic or sporadic nature. Immunity is important in only the infectious diarrheas. Poor hygiene and dibilitated health are factors. The condition is more prevalent in the slums, for overcrowding is usually more common in this environment. In a series of 300 cases 36% of the cases came from homes where there were families of five or more (19). Under favorable conditions of both home and medical control serious diarrheas hardly exist. The reasons are evident: Proper food, neither grossily too much nor too little; proper hygiene as to feeding regime and fresh air; reasonable clothing, neither too much nor too little; the avoidance of coddling; adequate representation of vitamins, all of which are essential to a normal state of nutrition; the absence of psychic overstimulation and fatigue; close and full cooperation between the mother and the physician; and, finally, the slightest deviation from the normal is at once reported while it is still easily rectified. Artificial feeding plays the major role, for from four to ten times as many of the cases are in artificially fed infants. Diarrhea, not always easy to explain but in some instances an accompaniment of parenteral

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infection, frequently develops in infants soon after their admission to hospitals. Meyer (62) found this practically to stop, if the patients had individual nurses. One nurse could care for two patients and it still would not occur, but if they attempted to care for more, diarrhea would occur. He found that these individually nursed infants slept as much as they did when they were home. Allergy to foods appears to produce diarrhea in some cases. Because of lowered ability to digest, diarrhea often accompanies certain endocrine disturbances, especially rickets, hypothyroidism, and also hyperthyroidism (85). In many cases it is due to contamination of the milk supply with bacteria. With the advent of certification of milk and pasteurization, the death rate and incidence from the diarrheal diseases have decreased markedly. Attempts which have been made to discover the relationship between milk with a high bacterial content and the incidence of diarrhea, seem to demonstrate that it is not the multiplicity of bacteria but their pathogenicity which is of importance in the etiology of the disease (84). Bacteriology is taken up on the etiology of the infectious diarrheas.

CLASSIFICATION

Many authors present a so called classification as to clinical types, but this is usually large and unwieldy. Talbot (84) gives one that is typical which is as follows:

Parenteral Infection
Diarrhea from Mechanical Irritation
Diarrhea due to Improper Food
Acute Intestinal Indigestion
Chronic Intestinal Indigestion
Infectious Diarrhea
Cholera Infantum

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PARENTERAL INFECTION - This clinical type is given by all authors and writers and is one of the important entities, and is one that can usually be recognized clinically. In a series of 318 cases of infantile diarrhea, Marriott (58) found 52% with parenteral infections, but in a series of 300 cases, Cooper (19) only found 40.7% with parenteral infections. In one series of autopsies, 60% showed pus in the middle ear, or the mastoid (54). However, the incidence of parenteral infections varies from year to year. Dehydration sometimes prevents the finding of some infections, notably those of the ear. The following table taken from Cooper (19) shows the incidence of parenteral infections in his series of cases:

INCIDENCE OF PARENTERAL INFEC.	NO. CASES	% TOTAL	% MORTALITY
Otitia Media	78	26.0	42.3
Bronchopneumonia	9	3.0	88.0
Pyuria	11	3.7	73.6
Furunculosis	5	1.7	60.0
Umbilical Sepsis	3	1.0	66.6
Bronchitis	4	1.3	50.0
Throat infections	1	0.0	0.0
More than one infection	11	3.7	72.7
Total	122	40.7	52.0

DIARRHEA FROM MECHANICAL IRRITATION - Diarrhea is less often caused by mechanical irritation in infants than in older children. Scybalous stools may be associated with alternating constipation and diarrhea. Ingestion of foreign bodies, such as sea sand and dirt, may result in diarrhea. On examination of the stools, the offending agent can usually be found. However, as stated above it is rarely encountered in infants, and most authors do not mention it in their series of cases.

DIARRHEA DUE TO IMPROPER FOOD (ACUTE INTESTINAL INDIGESTION) (DYSPEPSIA) - The relationship that the food itself bears to diarrheal

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disorders has been the subject of much discussion. The chief interest
lies in three directions: The effect of overfeeding, of underfeeding,
and of the medium or form in which the food is given. Overfeeding
in the sense that a given food exceeds the infant's present toler-
ance for that particular food, and that it may need to be lowered for
a time as a whole, or in one or the other of the food elements, or
be replaced by a more easily digested type of food, is a major factor
under these conditions, and would seem to be born out. Biedert (11)
emphasized the importance of ninimalnahrung, minnimal feeding, that
would just maintain a desirable state of nutrition as the important
factor in the prevention of digestive disturbances. The caloric
check on overfeeding and underfeeding advanced by Rubner and
Heubner (78), based on the known caloric requirements of breast-fed
infants, and stated in fairly definite figures for various periods
of infancy, was long in common use and still plays a minor part.
Overfeeding with different food elements was the basic consideration
in Czerny's (21) conception of Nahrschaden, and was the basis of the
so-called "percentage system" of feeding. We are today perhaps more
interested in the amounts of the different food substances, or food
elements, than in the energy quotient, the number of calories per
pound or kilogram daily, but the basic fact remains that overfeeding
as a whole, or with one or the other food elements, is an important
factor in the causation of diarrheal disorders. That we are less
interested in overfeeding than we once were is true and for reasons
evident. Our knowledge of both the science and art of infant feeding
has advanced and routine mixtures are more easily digested and are

tolerated in larger amounts than were those of several decades ago.
With such mixtures, the baby can be given a free rein as to the
amount of food he chooses to take, which could not be done safely
in the earlier period. It remains a daily observation that if an
infant gets an amount of food, qualitatively or quantitatively in
excess of his tolerance, he will be apt to vomit or have loose stools,
and that reducing the food as a whole or in part will bring about a
normal condition. Here, as elsewhere, it must be stated that the
individual tolerance for food as a whole or in part varies much in
different babies (15).

The medium, or the form in which the food mixture is given has
a very important bearing on what has just been said and will be
taken up at this point. The tolerance for a concentrated raw, sweet
milk mixture is easily overstepped. The danger of overfeeding with
boiled or evaporated milk in like concentration or probably even more
with either of these acidified, is greatly reduced and sinks to a
minimum in the use of protein milk or buttermilk (15). Not only is
this true of the milk itself, but a greater amount of sugar can be
added to the milk when given in such form as compared with raw, or
fresh sweet milk. The same is true of the fat and of the protein.

The role of the individual food elements in this connection is
by no means as sharply defined as was once thought when all of our
therapeutic procedures consisted in varying the amount, or percentage,
of the different food elements. There is too great an interplay of
a number of factors to make the matter so simple. In a well-balanced
food, little can be accomplished therapeutically by this route, as
compared with reducing the total intake or changing to a more digestible

type of food. There are, however, especially when given grossly in excess, certain symptoms or effects that can be attributed to individual food elements.

The protein has apparently little if any part in the etiology of diarrhea even if given in great excess of the infant's nutritional needs, unless it is given in raw milk without some modification of the curd. That the casein of raw milk was a factor of prime importance in the raw milk period became evident when it was changed to boiled milk and many of the troubles vanished in the transition. It cannot, however, be stated in the present state of our knowledge that the protein may not be a factor in the causation of diarrhea even if appropriately modified. One occasionally, very rarely, encounters a baby that has a number of loose, grayish alkaline, foul-smelling stools that seem to be due to an excess of casein. While fat indigestion more often yields a stool of similar appearance, notably in celiac disease, the stools under consideration occur as well with fat free milk. If it is true that the lactalbumin both delays the emptying time of the stomach and the cleavage and absorption time of the sugar, as has been advanced, then it too may play a part. In practice both possibilities may safely be ignored. The casein has even found a place in the armamentarium used in combating diarrhea (35).

The fat, when boiled sweet milk is used in excess, normally leads to a severe degree of constipation. Especially is this true if the carbohydrate is low in amount. It doubtless also plays a part in the diarrheal disorders. Again the medium is of determining significance. It is not well tolerated in raw sweet milk as a rule.

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Much larger amounts can be given safely in boiled or evaporated
milk; and in acidified milk, or protein milk, it is commonly tolerated
in amounts equal to that of whole milk. Protein milk low in whey,
hence in lactalbumin, whey salts and milk sugar, high in casein, and
with a fat content nearly that of whole milk, was devised for the
treatment of diarrheas and has been somewhat successful as a thera-
peutic food to meet this condition. In the Butter-Mehl Suppe of
Czerney-Kleinschmidt (21) the fat is derived chiefly from butter from
which the volatile fatty acids have been driven by heat, and is then
tolerated under normal conditions in amounts considerably exceeding
that of whole milk (5%). For these reasons skimmed or fat-free milk
and buttermilk are no longer used as much as they once were in com-
bating diarrheal disorders in which fat intolerance seemed to play
an important part. A peculiar type of fat indigestion with diarrhea
and gray, greasy, foul-smelling, copious stools is found in celiac
disease. Even here, there is not so much a primary fat intolerance,
as one secondary to carbohydrate intolerance, notably of starch.
Fat curds, too, are of no significance in themselves as they are
more often than not a mere by-product of diarrhea due to some other
cause.

The carbohydrates have been ascribed the leading role in the
initiation as well as in the upkeep of diarrheal disorders in arti-
ficially fed infants. The question of fermentation will be taken up
under Chronic Intestinal Indigestion or Fermentation Diarrhea.
However, at this point a few observations will be mentioned. It is

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a common observation that merely reducing the amount of carbohydrate
in the presence of a so called fermentative diarrhea does not
regularly lead to a return to normal, and that often a larger amount
will do so if given in a different form or in a different medium.
In the medium of breast milk, as we know, lactose is tolerated in-
variably up to 7%. Many babies with normal digestion will take such
amounts and even more with safety in any mixture, but there are many
exceptions. The baby that will stand a normal amount of added carbo-
hydrates, no matter what the kind of carbohydrate, when given in
boiled, or evaporated, or acidified, or protein milk, will very commonly
not stand a like amount in a raw sweet milk mixture. Furthermore,
whenever there is a "fermentative" diarrhea in an artificially fed
infant, the tolerance for carbohydrate is impaired in the highest
degree for lactose, probably somewhat less for cane sugar, and least
for dextrin-maltose preparations and starch (15). It is for this
reason that dextrin-maltose preparations have largely replaced the
other carbohydrates. If they are indicated in the presence of a
diarrhea, it naturally follows that they are less apt to initiate such
disturbance if given under normal conditions. Starch is normally
well tolerated, even surprisingly so, at a very early age as has
been dramatically demonstrated when used as a thick cereal in pylora-
spasm. In the presence of a diarrhea, it too, if given in larger
amounts will take part in the fermentative process with the other
carbohydrates (84). Different carbohydrates ferment at different
rates and at different levels in the intestinal tract and for that
reason there is a prophylactic as well as a curative action in the

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simultaneous use of a number of carbohydrates, as for example, when dextrin-maltose preparations and starch are added to the lactose already present in the milk (15).

The salts apparently take no part, or a negligible one, in the etiology of diarrhea. A former incrimination was based on premises later found to be untenable. If the salts are inadequately represented due to too little or too greatly diluted milk, they too play a part in the general undernourishment, lessened gastric and other secretions and impaired metabolism which may or may not result in diarrhea.

Underfeeding has, in recent years, been assigned an important role in the etiology of the diarrheal disorders in infancy. That it is in itself a frequent cause of diarrhea seems more than doubtful. That unwise and excessive dilution of food mixtures with a resulting inadequate supply of essential food elements, notably the protein and the salts, can keep up a diarrhea that is already present, seems well established (81). The type of infant that enters a hospital ward for a diarrheal disorder has commonly undergone this process without relief. The diarrhea may then seem due to the most obvious condition present, i. e., underfeeding, whereas the initial cause may be back of this, the factor that led to underfeeding as a therapeutic measure. Underfeeding, except under grossly ignorant conditions, is not an important cause of diarrhea (15).

CHRONIC INTESTINAL INDIGESTION - (FERMENTATIVE DIARRHEA) This type is differentiated from the preceding in only that the preceding, under proper treatment, is over in a few days (35). Some pediatricians

have admitted, however, that this type may be mainly made of cases of parenteral infections (84).

In this type of diarrhea, Colon-bacilli are supposed to migrate from the colon into the jejunum where they break down the ingested carbohydrates and thus bring about the formation of volatile fatty acids, and these acids, above all acetic acid, are said to irritate the jejunum and this give rise to catarrah.

One might furthermore control fermentation by counteracting the fermenting agent, i. e., the colon-bacillus. One way to accomplish this would be to let the child fast. For by keeping the jejunum free from food the bacilli are deprived of their nutritional substratum. The bacilli die or pass down to the lower sections of the intestinal tract where they find more favorable conditions for growth and where their metabolic products are not harmful to the organism. Hunger diets have been practically abandoned now. Replaced, for example, by buttermilk, lactic acid milk and, of course, protein milk. From the views just mentioned, their mode of action might be accounted for as follows: All these mixtures have a pH of about 4.5, a reaction antagonistic to the viability of the colon-bacilli. If a glucose culture medium with a pH of 4.5 be inoculated with colon-bacilli, fermentation will fail to appear. Substantiates the clinical observation that carbohydrates are better tolerated in an acid medium.

Another widely employed method of treating diarrhea is based upon the assumption that fermentation can be suppressed by promoting

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putrefaction, that is to say, bacterial decomposition of protein in the intestines. Hence, for example, the introduction of protein milk into the therapy of diarrhea.

As far as the significance of fermentative process in the etiology of diarrhea is concerned, one becomes sceptical when greater knowledge of the presence of colon-bacilli in the duodenum of the infant was at hand, and particularly when clinical and experimental observations obtained a clearer insight into the conditions of acidity in the duodenum. It has been found that in healthy infants, the acidity of the duodenal contents in the fasting condition varied between a pH of 6.8 and 7.6. In a case of severe atrophy with diarrhea, where colon-bacilli were present in the duodenum, Schiff (81) found an acidity corresponding to a pH of 3.2, while in a case of parenteral diarrhea he found a reaction corresponding to a pH of 7.9. In infants suffering from diarrhea, the duodenal acidity may attain such a high degree as to render bacterial fermentation impossible. Schiff (81) found that the reaction in the duodenum is not influenced by the character of the mixture given to the infant, that is, whether a sweet milk mixture or an acid mixture is given makes practically no difference, since under all conditions the juice of the duodenum is rendered acid for about two hours after a meal as a result of the passage of hydrochloric acid from the stomach, giving pH values varying between 4.5 and 5.

The theory that diarrheas result from fermentation was, however, decisively refuted when Schiff (81) was able to show that colon-bacilli

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not only attack carbohydrates but also protein and protein-split products, and above all, when he discovered the remarkable fact that colon-bacilli produce volatile fatty acid not only from sugar but also from the peptic split-products of mild proteins. He also succeeded in demonstrating that under certain conditions fermentation and putrefaction, due to colon-bacilli, can and do occur simultaneously. Thus it is obvious that the clinical conception that fermention and putrifaction are not antagonistic processes. Moreover, according to his observation, there is, theoretically at least, the possibility that when a food, rich in protein, is given, colon-bacilli may produce the same harmful acid from the protein as from the carbohydrate.

INFECTIOUS DIARRHEA (ACUTE ILEOCOLITIS; ENTEROCOLITIS; DYSENTERY; FOLLICULAR ENTERITIS; INFLAMMATORY DIARRHEA): These terms designate a group of cases in all of which the element of inflammation is predominately present. Again resorting to Hippocrates for a clinical definition: Dysentery, which means bowel trouble, is a diarrhea characterized by the presence of blood and pus, and accompanied by straining and tenesmus; and this cannot be bettered to the present day. The laboratory, however, has shown that there are two forms of dysentery which constitute twoentirely different diseases. These are bacillary dysentery and amebic dysentery. So different and distinct are these conditions that the only justification for grouping them under the heading of "dysentary" is historical usage.

Bacillary dysentery is a disease of great antiquity and of wide distribution. Throughout recorded history it has always been the

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great destroyer of armies in the field. This has been so from the
days of the Peloponnesian War to those of the World War. Very
common in tropical countries, it is also prevalent in temperate
climes. The world-wide dessemination during the World War, is the
explanation of the great increase in the last few years of acute
ileo-colitis in children (12). This increase has been noted in England
by Nabarro and Signy (66), in Germany by Kuntze (50) and in the U. S.
by Felsen (27). The mortality from 1926 to 1935 being 18.4% (12).
It is common in institutions where it spreads by cross infections or
by infected fomites. There have been reported instances of familial
outbreaks (12). The larger outbreaks are caused by contamination of
food by patients, or convalescent carriers, and especially of the
milk supply (38). As in typhoid fever, it is the chronic carrier who
is the menace to the community, but chronic carriers are important
only in asylum dysentery. (13).

The predisposing factors are: bad sanitation; factors liable to
impair the resistance of the individual, such as chilling, enervating
tropical heat, want and privation, severe physical exertion, irritation
of the intestines by coarse or indigestable food, and as a sequel to
acute febrile diseases, as measles, typhoid fever, pneumonia, diph-
theria; and hot weather; most cases occurring in the summer and early
autumn. Perhaps oftenest it occurs as an acute primary disorder not
preceded by any digestive or other disturbance (35). It is most common
in children under two years of age. In a series of 215 cases 27% were
under one year (12). The disease can occur in newborn (47). The

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distribution between sexes is equal (12). The role of flies as carriers has been demonstrated (56). Dysentery bacilli live for several days in the fly's intestine.

Ileocolitis is an infectious disease, and the exciting cause is an organism of some sort. In tropical dysentery this may be the ameba coli, and this parasite may occasionally be encountered in children in the temperate zone (69). It is the entameba coli, and entameba nana which is less prone to produce symptoms (48). Amebiasis is relatively uncommon except in the tropical climates (84).

"The bacilli credited with the causation of dysentery all belong to a natural genus which presents the following characters: They are short rods, destitute of flagella and nonmotile, forming no spores, not liquefying gelatine, negative to Gram's stain, and fermenting glucose and sometimes other sugars and alcohols without the formation of gas" (3). This was the report of Andrews' (3) Committee in 1919.

There are several varieties of Bacillus dysenteriae which can be differentiated by fermentation and agglutination methods. The organism belongs to the coliform group, being Gram-negative, but it is non-motile as stated above. From the clinical standpoint, one may include all well-recognized strains which have been found to produce typical symptoms. Of these there are four groups regarded generally as varieties of Bacillus dysenteriae, but by some as distinct species. There are the Shiga bacillus, the Flexner group, Schmitz's bacillus and Sonne's bacillus. There are, in addition, atypical, or borderline bacilli causing diarrhea of a more or less dysenteric nature.

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The cases in Gallipoli, Macedonia and Albania during the World War were mainly due to the Shiga bacillus. The Shiga bacillus is a non-mannite fermenter and produces both an exotoxin and an endotoxin upon the intestinal mucosa. The Flexner form, with which may be included the Y type of Hiss and Russell and the type of Strong, ferments mannite, it produces no exotoxin, and its endotoxin is much less active than that of the Shiga form. However, these fermentation reactions were subsequently found to be inconstant and to undergo mutation, while the Serological grouping did not conform to the cultural. Andrews (3) classified the group serologically into five races, called V, W, X, Y, Z; Y corresponding to the Hiss-Y. Schmitz bacillus does not ferment mannite, this resembling Shiga's, but it forms indol and is serologically distinct. It produces an endotoxin, but no exotoxin. Sonne's bacillus is distinguished by late acidification of lactose, strong acidification of milk, and by specific serological reactions. It also produces only an endotoxin. The Sonne bacillus has been the cause of several epidemics of dysentery of moderate severity. The Schmitz bacillus appears to cause definite dysentery, but its inclusion among the dysentery bacilli has been disputed (83). Members of the Flexner group may produce dysentery of extreme severity but on the average the infections are milder than in Shiga dysentery (83). One of the most interesting of the bacteriological phenomena is the presence of a bacteriophage in the stools of the patient. When a filtrate of the stool is added to a young culture of dysentery bacilli, the latter is first killed and

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then completely dissolved. Whether the lytic agent is an ultra-
microscopic virus as held by some (23), or is an enzyme, as is
more commonly believed, it is not possible at present to say for
certain. Besredka (8) has succeeded in producing an immunity by
feeding animals with dead bacilli, and is strongly of the opinion
that the change is not due to the production of antibodies in the
blood, but to a local immunity produced in the intestinal mucosa, a
conception which, if proved to be correct, is one of great importance.
Feemster (26) believes that the difficulty is isolating dysentery
after the first week is due to lysis as a result of the increase in
bacteriophage. This then may well be the explanation for not finding
organisms in clinical ileo-colitis, for if they are searched for in
the first three days, the chances of finding them are much better.

It should be emphasized that other organisms than the dysentery
bacillus also may be responsible for ileocolitis and, in fact, that
there seems to be a variation from year to year in those causative of
diarrheal conditions in the same locality. In some cases streptococci
are found in predominant numbers in the stools, and agglutinins may
develop in the blood. The bacillus aerogenes aapsulatus has been ob-
served at times and presumed to stand in a causative relationship,
as have the bacillus mucosus capsulatus and the bacillus pyocyaneus;
and it has been held by some that the colon bacillus may assume
pathogenicity and act primarily or as a secondary invader (35. Dif-
derent fungi have from time to time also been regarded as the in-
fectious agent (65).

The morbid intestinal changes associated with the different strains of dysentery are practically indistinguishable and especially so between the Flexner and Sonne strains, although evidences of toxemia in solid viscera are generally more pronounced in the infections due to the Flexner Bacillus (12). In dysentery as in gastro-enteritis, there is frequently a lack of correlation between severity of clinical symptoms and of morbid changes found at autopsy. In all cases the extent and the severity of the intestinal lesions varies considerably and they are most marked and are most constant in the large bowel and in the terminal ileum. The lesions tend to be of three predominant types: a - simple or acute catarrhal form; in this form the mucous membrane is congested and swollen, often covered with mucus, and the epithelium loosened in places. Small hemorrhages, usually scattered or in streaks, are seen on the surface especially upon the projecting portion of the folds, and the superficial erosions may be found; and in severe cases these shallow ulcerations may be extensive, and the whole intestinal wall may appear much thickened. Both the solitary and the agminated follicles are generally swollen and the villi are elongated and prominent. Microscopically there is found an infiltration of small cells and of numerous bacteria of different kinds in the mucous layer, penetrating even to the muscular layer in severe and long-continued cases. The lymph follicles are infiltrated. In cases which recover, the lesions disappear entirely. b - follicular or ulcerative form; in this form the disease process has usually advanced further.

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There is, here, a more or less deep ulceration in the solitary
follicles, and moderate infiltration and ulceration of the sub-
mucous and muscular layers. Cases which recover do so with cicatriza-
tion of the ulcers. c - membranous form; this form is considered the
most severe form. Here there are regions in which the entire thick-
ness of the intestinal wall becomes much swollen and stiff, with an
obliteration of the usual folds resulting from the presence of
fibrinous exudate and infiltration by round cells; and where the
membranous deposit has become detached, deep ulceration may be seen.
There is no certain relationship in ileocolitis between the severity
of symptoms and that of the lesions. All types are occasionally seen
in the same case. In the last two, edema of the bowel wall is often
a striking feature. In younger children, the morbid changes in the
bowel tend to be more diffuse, i. e. the whole of the small intestine
and the large intestine may be affected. The severer lesions (membranous
and ulcerative) are found commoner in older children than in infants.
The mesenteric lymph glands are nearly always hyperplastic and
pinkish in color. The enlargement generally being greatest in sub-
jects with intestinal ulceration, next in those cases with the mem-
branous ileocolitis and least in those cases with the congestive
catarrhal lesion. Mita and Felsen (64) observed lymphoid hyper-
plasia in dysentery and Harvey (37) is of the opinion that it is
particularly marked in the more fulminating cases.

Other morbid changes than those of the bowel are seen. Fatty
degeneration is occasionally seen in the myocardium and is constant

in the convoluted tubules of the kidneys and in the liver where
the lesion is periportal in distribution. In no instance is there
found necrosis or cellular infiltration of the liver as is found in
the other forms of diarrhea. In some instances petechial hemorrhages
are seen in the lungs and of course in some cases bronchopneumonia
may be a terminal event. The brain substance is often congested
(markedly) and edematous with increased fluid in the subararachnoid
space. There are often other morbid changes, but they are the changes
of any grave toxemia. There is no certain relationship in dysentery
between the severity of the symptoms and that of the lesions. Cases
with extensive ulceration, for instance, may sometimes exhibit but
moderate fever and little or no blood in the evacuations, while
catarrhal inflammation, although usually milder than other forms,
may continue for some weeks and end fatally without any follicular
ulceration having developed. The onset cannot be distinguished with
certainty from that of other acute intestinal disturbances. Usually,
however, the onset is sudden and severe. The temperature is from
103° to 104° F. There is often vomiting, abdominal pain, and
diarrheal movements containing undigested food. Promptly the stools
become very frequent, small, are passed with straining efforts, and
exhibit mucus either transparent or green in color, pus, fecal matter,
and more or less blood. The abdomen becomes moderately distended and
somewhat tender; the urine is scanty and may contain albumin. There
are loss of appetite, coated tongue, thirst, decided prostration and

rapid loss of weight. The tenesmus is not constant and the abdominal pain is colicky in nature; both symptoms developing or increasing at the time of evacuation of the bowels. Prolapse of the rectum is not uncommon.

The clinical findings are similar in type, but differ in degree in Flexner and Sonne infections. The Flexner infection is more toxic and produces severer intestinal symptoms, e. g. more frequent diarrhea, associated more often with blood and pus, while such cerebral manifestations as irritability, cramps, convulsions, coma and vascular disturbances as shown by pallor or cyanosis, are also as a rule commoner and more marked in the Flexner infection. Those due to the Sonne bacillus may be fulminating and fatal within 36 hours of the onset, or less. The Shiga infection is the most severe. Bojlen (13) suggests that the explanation of the variable toxicity of Sonne infections is that foreign strains introduced into a locality may prove more toxic than are those which are indigenous to it, for immunity to others may have been acquired. The general condition of the child does not appear to influence the resistance to the dysentery infection (42), or the outcome (33). In the opinion of the former, robust children are as susceptible to the dysenteric infection as are the weakly, and the latter had no death in infected marasmic infants. In children, the dysenteric toxin appears to affect the central rather than the peripheral nervous system as it does in adults, in whom toxic neuritis is a fairly frequent late complication. Loesche (51) never observed the latter in children. Other cerebral

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symptoms, e. g. encephalitic, have been observed in children with dysentery. Pulmonary complications, e. g., empyema, bronchitis, or pneumonia, are described frequently by British workers. Ocular and joint lesions are rare in children. Dysenteric infection as in other diarrheas frequently runs a very atypical course in infants, in whom the characteristic acute onset and severe clinical symptoms may be lacking and there may be little to distinguish the case from one of another form of diarrhea in the absence of blood and mucus.

CHOLERA INFANTUM: This entity has been considered to be a complication of any other form of diarrhea which has become chronic and where the infant has not responded to treatment, or who has not had any treatment, and thus has become dehydrated and toxic. Therefore, it will be discussed under complications. Bulky classifications, such as those given and more or less nocked about, have been very popular, but in the light of present knowledge, they do not seem to be very workable. So, in their place, I would like to submit what I think is one which is more practical:

    I   Diarrhea due to parenteral infection
   II   Diarrhea due to improper food. Including all ingested
        substances.
  III   Diarrhea due to infection. The dysenteries

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The first step in diagnosis is to determine whether the diarrhea is due primarily to disease in the intestinal canal or to disease

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elsewhere. This may be done by a careful physical examination which rules out disease in other parts of the body. The respiratory diseases, and otitis media, pyelitis, and the exanthemata, are, however, frequently overlooked. Occasionally tuberculosis of the mesenteric lymph nodes or intestines may cause confusion, but the sudden onset of diarrheal diseases usually eliminates the possibility of this. The diarrheas due to improper food are found by an examination of the diet and the general care of the infant. It must be remembered that not only the diet must be examined, but other substances which the infant may be ingesting, for the cause may be chemical as well as mechanical. This entity is more completely taken up in the text concerning Diarrhea due to improper food.

In the milder disturbances the stools may be merely somewhat looser, more moist or scrambled in appearance than formerly, have a nearly normal color, and are only slightly acid, or off odor. If more severe they become more watery, sink into the diaper, become greenish-yellow or green in color, and are so strongly acid that they cause local hyperemia or even excoriation of the buttocks. In the gravest type, the cholera infantum of former years, the stools may be almost continuous, with frequent spurts of a brownish, or grayish-brown, merely turbid or almost colorless, liquid, the so-called rice water stools. In this condition they are commonly alkaline in reaction and may exceed the amount of fluids ingested with a resulting ominous disturbance of water balance. Diarrhea stools usually

contain small, often quite large, soft, friable, white, or gray, sometimes greenish, fat curds and mucus. The larger, hard, amber-colored, or white, or gray, or even greenish curds are casein curds, the color varying directly in this order with the degree of diarrhea. They are insoluble in an ether and an alcohol mixture and occur almost exclusively with the use of raw milk (32). Blood and pus are not in evidence in the milder forms although there doubtless is an increase in the number of leukocytes (53). In the severer forms there may be slight evidence of macroscopic blood and there is a great deal of mucus. If there are both blood and pus in very appreciable amounts, macroscopically, there is an infection of the intestinal mucosa, quite probably a true dysentery, or ileocolitis, usually of determinable specific origin. However, as stated previously, the search must be made in the first week and better yet in the first three days, for after that it is difficult to demonstrate the dysentery bacilli (12). Also, in the diagnosis of dysentery agglutination can be used, but the use of the agglutination reaction with the patient's serum is limited, because the symptoms are sufficiently diagnostic in well-marked cases, and further, the reaction does not appear during the early acute stage. Later it may be used (71). Group or normal agglutinins are commonly present and interfere greatly with the value of the reaction in the paratyphoid types. The differences in agglutination of B. dysenteriae and the paratyphoid group are usually sharp, but infection by the types of the paratyphoid groups

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frequently can not be differentiated. An agglutination reaction is commonly present in chronic carriers. For even moderate diognostic value the serum should agglutinate one to fifty in infections with B. dysenteriae and one to one hundred with other types (71).

Isolation of the bacillus is the only method of diagnosis for certain identification of the type causing the infection. The mucous flakes in stools should be selected for plating. The methods of isolation and identification are the same as for typhoid or paratyphoid, except that the crystal violet should be omitted from the Conradi medium as the growth of many strains is inhibited more or less by anilin dyes. In acute cases, the bacilli are so abundant in the mucus of most cases that they can be readily isolated from nutrient agar plates. The isolation from carriers is not always easy. If endo medium is used, the plates should be fresh and the reaction not too alkaline. A large content of fuchsin or the presence of unreduced fuschin will inhibit the growth of the specific inhibiting agent with the Shiga Type. Veal infusion on a peptic digest basis seems to be more desirable for this group. The cultural differences can be found in any text-book of bacteriology. The actual nature of the bacillus should be verified by agglutination. The cultural characters have only tentative value (71).

In the milder diarrheal disorders, there is little if any fever. In more severe cases, there is usually some fever, and in the severest

types there is apt to be a very high rise of temperature. If the fever persists in spite of the withdrawal of food it may be assumed that there is either a parenteral infection or a true dysentery. Parenteral infections are usually readily recognized by other signs and symptoms unless the observer still clings to the erroneous idea that fever and diarrhea in infancy are always enteral in origin.

It is often extremely difficult, many times impossible, to tell in a given case whether one has to deal with a simple indigestion, or a true bacterial invasion of the intestinal mucosa. In the dysenteries, it usually becomes evident that there is an infection of the intestinal mucosa as shown by the presence of the signs elicited above. The greatest difficulty lies in a differentiation between the other condition mentioned. Fortunately the decision is not of vital importance since we know that the infections, notably prolonged infections such as dysentery, should be fed liberally throughout and that the indigestions should not be starved unduly but should be placed as quickly as tolerated on a full diet of a more readily digestible therapeutic food.

When large amounts of blood appear in the stools intussusception must always be considered. Both this and diarrhea may have a sudden onset. Intussusception, however, is accompanied by the presence of a sausage-shaped tumor in the abdomen, and the passage of stools which are composed mainly of blood, while in the diarrheal diseases the admixture of pus, mucus, and fecal matter gives a characteristic picture. If there is doubt, a rectal examination may be made, but this is rarely necessary because in the diarrheal diseases the abdomen

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becomes sunken and easily palpated. An ex-ray examination after a barium enema may determine the diagnosis.

Nervous symptoms at the onset are sometimes suggestive of meningitis. During infancy the level of the fontanel usually provides decisive evidence; in meningitis it is practically always bulging and tense; and in diarrhea, sunken, especially if the stools are frequent and profuse. If there is any doubt, a lumbar puncture will decide the diagnosis.

There is a special form of chronic diarrhea in early life which follows a prolonged course, and to which the term celiac disease or celiac affection is applied. It usually starts in the second or third year of life, and characterized by the passage of stools which are not as frequent but are bulky, pale, and offensive. Chemical examination shows an excess of split fat. The abdomen is tumid and tympanitic, and the child wasted and stunted in growth and development. This form of diarrhea is apt to simulate abdominal tuberculosis, and is often diagnosed as such; but in abdominal tuberculosis enlarged glands or a rolled-up thickened omentum may be felt, or there is ascites or evidence of tuberculosis elsewhere. Sometimes, however, a diagnosis is only possible after watching the progress of the case.

If the stools in a case of chronic diarrhea contain visible mucus and blood, and are passed with much straining, special involvement of the large bowel may be diagnosed (chronic colitis). The history will usually point to a preceding attack of acute colitis.

COURSE AND PROGNOSIS

In severe cases of dysentery, death may take place in from a few days to one week or two weeks, or longer, from exhaustion, a complicating pneumonia, or perhaps convulsions. The mortality in Marriott's (58) cases was 10% in the uncomplicated cases and 28% in the complicated cases. In the catarrhal ileocolitis of average severity the stools and intestinal symptoms may begin to improve after a week or two, the temperature gradually decline, and in four to six weeks recovery be complete. Relapses are, however, prone to occur. In mild catarrhal cases recovery may take place in two or three weeks. In follicular ileocolitis death usually results in three or four weeks, but in cases without extensive follicular ulceration recovery may take place after a tedious course of weeks and months, interspersed with frequent relapses. This form of the disease tends to run a more subacute course, the temperature after the onset not being high, the stools not frequent, and tenesmus slight. The progressive emaciation is the worst feature.

In general the prognosis in ileocolitis is much graver if ulceration has developed. The clinical symptoms are of some value in determining this, and if there is no improvement in three or four weeks and blood still persists in the stools, ulceration is probably present. The Shiga type of dysentery bacillus causes especially severe ileocolitis.

In Marriott's (58) cases a small group 17% had neither enteral nor parenteral infections, demonstrable. The average duration of the

disease was four days and the mortality was 5% as compared with the average of fifteen days and the mortality of 35% in parenteral infections. His mortality rate for parenteral infections is lower than many others have found which is usually around 50% (19).

Prognosis is also worse the younger the patient; with impaired health prior to the onset of the condition; under poor hygienic surroundings; in hot weather; and with secondary cases, or cases with complications. Cooper's (19) mortality for the first year for all types of diarrhea was 48.8%, 36% for the second year, and 73.6% under one month. The state of nutrition was also an important factor. Those infants who were within 30% of their normal weight had a death rate of 36%, and those who weighed less than 70% of their expected weight, showed a death rate of 65%. Dysentery was found in children in all states of nutrition. Results with apple therapy, banana therapy, and dyes have lowered these mortality rates for all types of diarrhea (43), (87) and (6).

COMPLICATIONS

Other than infections which have been discussed, the most important complications of severe diarrhea, no matter what the cause, are dehydration and acidosis. They are closely related and the success of treatment depends upon their recognition and correction. These symptoms occur to a greater or less degree in all types of severe diarrhea and, consequently, deserve special consideration.

DEHYDRATION is the most important symptom in diarrhea. It results from the great loss of body fluid in the diarrheal stools.

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In the acute diarrheas of infancy, dehydration and loss of weight may occur with great rapidity. The effects of dehydration are: A - Loss of weight due to the reduction in tissue water as well as to the actual breakdown of body substances which occurs in the effort to provide water for the maintenance of the normal fluid content. Fat and carbohydrate stores are first drawn upon for this purpose and later, proteins. B - Disturbances in acid-base balance usually toward the acid side. The diminished quantity of circulating fluid (anhydremia) and the consequent depression of oxidative processes in the tissues is held responsible for the excessive production of acid metabolities, e.g. lactic acid. The slowing of the renal circulation also leads to a reduced excretion of urine and retention of acids (e.g. phosphoric acid) which under normal circumstances are eliminated. C - Rise in the non-protein nitrogen of the blood. D - Rise in the body temperature as a result of the reduction in circulating fluid. E - Thirst. Under normal circumstances this serves as a signal that the water stores of the body require to be replenished. Any fall in the water content of the tissues is reflected in the glandular activities, especially of the salivary glands. Secretion is suppressed; the mouth and throat become dry and the sensation of thirst is aroused. In dehydration thirst is extreme and the mouth parched. F - Dryness, wrinkling and looseness of skin and a pinched expression to the features result from the loss of subcutaneous fat and of water from

the deeper layers of the skin. Other manifestations are, reduced intraocular tension and recession of the eyeball and depression of the fontanelle (10).

The term anhydremia is given to the condition of the loss of blood water which is simply a part of general dehydration and so results from the same causes as the latter. In anhydremia, both the protein concentration of the plasma and the red cell count are raised. The concentration of plasma protein may increase by 50% or more. The viscosity of the blood is therefore raised; the blood appears "syrupy" and flows sluggishly from an open vein. If the anhydremia persists the red cell count and the protein concentration tend to fall again as a result of red cell and protein destruction. Then an estimation of the blood concentration may fail to give a true index of the blood volume reduction. Anhydremia by abrupt reduction of water can only be obtained if the food ingested contains protein, while, with the same reduction in the intake of water, anhydremia fails to appear if the food given is free from protein (82). In the normal course of the intermediary protein-metabolism, the organism requires a definite quantity of water, and the clinical picture of intoxication; while on the other hand, allthe symptoms of intoxication fail to appear when food, free from protein, is ingested (49). In the genisis of intoxieation, the conditions prevailing in the parenteral metabolism constitute the decisive factor and not, as hitherto held, the processes in the intestinal canal, which moreover

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are but a phase in the process of intoxication and have, in fact, very little to do with the intoxication itself. Dehydration fever which is due primarily to anhydremia and has never been found to occur in the absence of anhydremia. The condition clears up as soon as enough water has been taken (29). The intoxication urinary findings may be the same as in acute nephritis or in pyuria, therefore, are spoken of an dehydration-albuminuria, cylinduria, and pyuria.

Negative anatomic and histologic findings do not necessarily exclude the presence of an infection in the disease process. In dehydration, then an infection may lead to death without leaving the slightest trace of a cellular reaction. Dehydration, therefore, interferes gravely with the cellular defense processes in the organism. Fatty degeneration of the liver is often found in intoxication, due to dehydration. If the diet is protein free, the condition was not found (82). In dehydration as in intoxication, the sugar-content of the blood is normal or increased, and the splitting up of glycogen is increased, and the resynthesis of glycogen as well as the transportation of sugar from the blood into the tissues are retarded. Abeline (1) and his co-workers observed reduction of glycogen in the liver upon feeding amines in animal experiments, so certain protein split-products may possibly play the principal role here.

An outstanding feature of intoxication is the deep respiration, a symptom of acidosis. Dehydration is also followed by acidosis. The alkali reserve sinks while the hydrogen-ion-concentration of the

blood is normal or increased, and the elimination of acids in the urine is increased. As a characteristic phenomenon of this form of acidosis, there is a practically normal total base in the blood, and a reduction of the base bicarbonate, and an increase of Cl and lactate, while the HPO showed only a slight increase. Ketonuria is absent and the elimination of ammonia in the urine is not increased in dehydration-acidosis, while the elimination of organic acids is increased(80). Best and Taylor(10) and Van Slyke(88), however, insist that there is an increased acid and ammonia excretion in the urine which is a compensatory mechanism. When the alkali reserve becomes diminished, there is a compensatory increase in the pulmonary ventilation in order to eliminate the carbonic acid more rapidly. This may be imperceptible at first, but as it becomes more pronounced the "air hunger" type of respiration develops. The lips instead of being cyonotic, as might be expected, have a cherry-red color. When acidosis is marked, the outlood is serious. If the carbon dioxide combining power of the blood falls below 20 volumes per cent the patient rarely recovers.

CHOLERA INFANTUM has many similarities to that of the acute intoxication which was discussed above. The attack is usually preceded by one of the ordinary forms of diarrhea. The choleriform symptoms develop with great suddenness. The vomiting and the diarrhea are marked. The vomitus becomes merely a greenish liquid. The stools are watery, of a greenish color, and finally almost colorless and odorless; frequent and generally large; sometimes smaller and passed every few minutes. Extreme prostration, loss

of weight, sinking and filminess of the eyes with ptosis of the
lids, shriveling of the face, depression of the fontanelle, and
pallor and wrinkling of the skin develop with an astonishing rapid-
ity; all indicating the effects of dehydration. This is shown
especially well in the skin, which, being the largest storage
place for water with the exception of the muscles, readily loses
it upon the general demand for fluid. The whole aspect of the
face is completely changed in a few hours. The temperature is
usually elevated and hyperpyrexia is common in fatal cases(35).
The pulse is weak and rapid; the respiration often irregular or
the deep and sighing breathing of hyperpnea; the urine is nearly
or quite suppressed, and may be albuminous and contain sugar; thirst
is great; the abdomen is shrunken; the tongue coated, or red and
dry; and the lips of a bright red hue. Nervous symptoms are mark-
ed. At first there is usually irritability and restlessness; lat-
er there may be a state of apathy or stupor; or coma and convul-
sions may develop. Leukocytosis is present(35) (84).

The prognosis in cholera infantum is serious and many of the
patients die. The disease may last not over two to three days.
In some instances the diarrhea and vomiting continue until death
occurs in collapse. In others there may be an abatement or even
a cessation of the G.I. symptoms, but nervous manifestations with
prostration may persist, and death may take place from convulsions
or in coma. In the case of older children the prognosis is ser-
ious but not nearly to so great a degree.

TREATMENT

In the treatment of diarrhea of the artificially fed infant, prophylaxis is of the greatest moment and that in two respects. Diarrhea must be prevented and the earliest deviation in that direction should be recognized and corrected while it is still easy to do so. The younger the infant, the truer this dictum. every effort should be made to have the infant, as nearly as possible, under as favorable hygienic and environmental conditions and medical care as have been discussed under etiology. The nature and composition of the food itself are of prime importance. Especially important is this in the new-born period and even more especially so in the absence of breast milk. As already stated, the danger of initiating a digestive, diarrheal, disorder at this period is so great with the use of a fresh, sweet milk mixture that it is safer and wiser to begin with a more readily digestible food such as evaporated or acidified milk, or protein milk. It is always safer to begin with a smaller amount of food than is necessary to cover the nutritional needs and to advance only as rapidly as conditions seem to warrant, even with these more therapeutic foods. Only after a normal adaptation to a normal amount of food had been established can one safely allow the baby to take as much as he wishes, provided he is not fed oftener than every four hours.

If a simple looseness of the stools occurs, even if there are only a few more than there have been, active treatment should be instituted. In these milder cases all that may be necessary is

to reduce the amount of food for a few days, either by diluting it, or by offering a smaller amount. It is usually futile to speculate as to whether the one or the other food element is at fault unless it is very evidently in excess of tolerance. If things do not get better promptly, or if they get worse, more radical measures are indicated(15).

In the active treatment of diarrheal disorders of all types, the following principals of treatment are stressed;

1-To combat dehydration and toxemia.

2-To obtain as complete rest for the inflamed bowel as possible; a precept which is universal in treatment of any inflamatory lesion in the body.

3-To examine carefully for evidence of parenteral infection, usually the ear, the mastoid, the nasopharynx, the paranasal sinuses, etc.

4-To institute rational dietary dietary measures during the convalescent period.

To combat dehydration and toxemia, the routine treatment of Hartmann(92) is probably the best and the easiest. This is as follows:

I; Administrationsoof Hartmann's solution which is dispensed in ampoules. One-tenth of the body weight of 100 cc. per kilogram of body weight of a mixture of isotonic sodiumr-lactate which is 1/6 molar, and isotonic or slightly hypotonic Ringer's solution in the proportions of 60 cc. to 40 cc. is administered intravenously, intraperitoneally, or subcutaneously. In addition in se-

vere cases of diarrhea with acidosis, $\frac{1}{2}$ gram of sodium bicarbonate per kilogram should be given. In very severe cases, this may have to be repeated, if the CO_2 combining power of the blood does not rise as high as expected.

II: 20cc. of citrated blood per kilogram are given intravenously for protein deficiency. This is apparently very important and should not be omitted(92).

To give the bowel a rest, only water should be given for the first 24 hours, or possibly 48 hours. Some advise a cathartic to cleanse the bowel, but with a diarrhea, the bowel should be quite clean if a cleansing enema be given. If one feels that a cathartic should be given, one teaspoonful of castor oil can be given, but it must not be given if the infant is vomiting and must not be repeated(15). In the first 12-24 hours a demulcent can be given, such as barley or rice water with some form of bismuth(90). Glucose solution can also be geven for the first 12-24 hours. Following this, the raw apple diet, pectin diet, banana diet, or protein milk in barley or rice water is given. The pectin-agar diet and regime will be described, for it is better than the raw scraped apple(92), seemingly better than the protein milk diet, and more popular than the banana diet. The following pectin-agar formula(92) will be described:

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Dextro-Maltose  # 1      175 grams
Pectin                     6 grams
Agar-agar                  8 grams
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Added to one pint of water or milk. With water, it makes 700 calories, and with whole milk, it makes 1,020 calories. For convenience, it is put in eight custard cups.

At first one custard cup of the jellis given every 3 hours,
with only water between feedings. On the second or third day,
skimmed milk issubstituted for the water as a solvent, and a
transition diet is started. This is a low fat diet which may
be composed of tea, cocoa without milk, zwieback, toast from
stale bread, bananas, cottage cheese, soups poor in fat, and lean
meat. On the fourth day or the fifth day, whole milk is substi-
tuted for the skimmed milk and the transition diet is increased.
On the sixth or the seventh day, the customary soft diet without
pectin-agar jell can be given. In a series of 24 cases(92),
the patients responded on an average in 4.79 days. The stools
remained liquid on an average of 1.3 days, and the transition to
a regular diet was possible on an average of 3.9 days. The aver-
age gain in weight for all kinds of diarrhea when treated with
pectin-agar was 50 grams per day.

The importance of examining for evidence of parenteral in-
fections has been stressed in other parts of the paper.

SUMMARY

1. Diarrhea is a symptom and not a disease.

2. Prophylaxis is of the greastest import in diarrhea.

3. The acute diarrheas can be divided into those caused by
    parenteral infection and those caused by enteral infection.
    Those caused by improper food being due to improper food.

4. That certain protein split products play a principal role in
    the genesis of intestinal intoxication.

5. The diagnosis of dysentery by clinical signs rather than
    laboratory findings.

6. The routine treatment of Hartmann in acidosis is not only good, but saves many tedious blood examinations.

7. The employment of apple or pectin-agar therapy is beneficial in all diarrheal disorders.

8. Prognosis is dependent upon: a-A rising weight curve; b-A cessation of vomiting and diarrhea; c-A return of appetite.

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