Diarrheal disease in infancy and early childhood—especially repeat, prolonged episodes—can have long-term consequences on a child’s growth, cognitive development, and ability to do well in school. There is also a growing body of research linking diarrhea in early childhood to increased risk factors for non-communicable diseases, such as diabetes, cardiovascular disease, and obesity. In this brief, we discuss the long-term impact of childhood diarrhea in general—not specifically rotavirus gastroenteritis.

Childhood diarrhea, especially repeated and prolonged bouts, can have a long-term impact on growth and development.
ENTERIC INFECTIONS AND MALNUTRITION

Studies have shown that diarrheal infections, especially recurrent ones, can lead to malnutrition and poor growth in a young child living in impoverished conditions. This is true even among children born with normal weight and who start off growing at a normal rate. Once they are weaned and start getting enteric infections, their growth may falter.

Why do diarrheal illnesses in early childhood result in poor growth? Diarrhea increases the need for more energy and nutrients (proteins, fats, micronutrients), while also decreasing a child’s appetite and food intake. At the same time, repeat infections damage the wall of the small intestine, by blunting the millions of finger-like villi that enable the gut to rapidly absorb nutrients. This results in the child having less ability to absorb what he or she eats.

This malabsorption of important nutrients and poor appetite can lead to poor weight gain—a sign of acute malnutrition. Over the long term, it can also lead to stunting (reduced growth in height) as a result of chronic malnutrition. In one study in the Gambia in the 1980s, newborns followed for one year had a mean weight-for-age deficit of 1.2 kilograms—half of which was attributed to diarrheal diseases.

Malnutrition, in turn, weakens the body’s defenses against further episodes of diarrhea, continuing the vicious cycle of diarrhea and malnutrition. Malnourished children therefore have more frequent and longer diarrheal illnesses. In one study in Northeast Brazil, children under 5 years of age who were underweight for their age had twice as many days of diarrhea than better nourished children and their illnesses lasted, on average, 73% longer.

**FIG. 1 THE VICIOUS CYCLE OF ENTERIC INFECTIONS, MALNUTRITION, AND LONG-LASTING EFFECTS**

*Adapted from Guerrant, et al, 2013*
Two community-based clinical trials in Karachi, Pakistan (5) and Northern Ghana (6) that followed groups of children over time found that having diarrhea increased the risk of pneumonia or acute lower respiratory illness (ALRI) in the following 2–4 weeks among young children living in settings with high rates of malnutrition and diarrhea. Any case of diarrhea in the past two weeks increased the risk of ALRI or pneumonia by 61% in Ghana and by 31% in Pakistan in children under 5 years of age. More than two-thirds (68%) of all ALRI episodes in Ghana were, in fact, preceded by a diarrheal illness in the prior two weeks. (7)

Both studies found a strong correlation between the risk of pneumonia (or ALRI) and the duration of diarrhea in the previous two weeks. In Pakistan, each additional day of diarrhea increased the risk of getting pneumonia within that timeframe by 6% in children under 5 and by 9% in children under 12 months, after adjusting for weight-for-age and various socio-economic variables (e.g., household income, parents’ literacy). (5) The added risk of ALRI per additional day of diarrhea in the Ghana study was 8% in children under 5. (6)

The studies estimated that more than one-quarter (26%) of ALRI cases in Ghana and 6% of pneumonia cases in Pakistan in children under five were attributable to having had diarrhea in the previous two weeks, and thus could have been avoided if the recent diarrheal illness had been prevented. Possible factors that may increase the risk of acute respiratory illness among young children include the loss of zinc (in stool), dehydration, and the loss of electrolytes that can result from diarrhea, especially severe diarrhea. All of these may increase a child’s susceptibility to new infections, including ALRI, especially in children who already have compromised immunity due to malnutrition. (7)

In contrast, a similar study in Brazil in a population with considerably lower rates of malnutrition, diarrhea, and child mortality than in Pakistan and Ghana did not find any relationship between pneumonia and recent diarrheal illnesses. (6)

Preventing diarrhea through interventions such as improved water, sanitation, and zinc supplementation, while reducing the duration and severity of diarrhea—for instance, through oral rehydration therapy, zinc treatment, and antibiotic therapy for bacterial enteric infections—can therefore have a “multiplier effect” in areas with high rates of malnutrition and diarrheal disease by also preventing pneumonia, the number one cause of death in children under 5 worldwide.
STUNTING

Stunting is very common in impoverished settings and can be more common than children being underweight (weight-for-age). In a study in Bangladesh conducted in 2008–09, 16% of children were born with stunted height (height-for-age Z score or HAZ of <-2), but, by the age of 12 months, 42% of them were stunted. This can result in adults in low-resource countries being 10–15 cm (4–6 inches) shorter than those in wealthier countries.

Children can recover weight following a diarrheal illness, but this catch-up growth is less common with height and occurs at a slower rate. In a pooled analysis of nine prospective studies examining growth and diarrhea in five countries in Africa, South America, and Asia, only 6% of children stunted by 6 months of age reached a normal height by 24 months of age, and only 7% of those stunted by 18 months of age recovered from stunting by the age of 2.

While many of these studies cannot determine if the diarrhea caused the stunting or the stunting caused the diarrhea, a study in Peru that followed a group of children from birth found that there was a two-month delay between diarrheal episodes and evidence of stunting. This suggests that the diarrhea led directly to the children being stunted. And as in the above studies, the greater the burden of diarrhea in a child, the greater the degree of stunting. Children who experienced diarrhea 10% of the time during their first two years of life were, on average, 1.5 cm shorter by 24 months of age than children who never had diarrhea. Children stunted by 6 months of age were likely to be stunted permanently.

Even enteric infections that don’t result in diarrhea (sub-clinical infections) can cause stunting. Frequent infections can cause chronic inflammation of the intestine, which has been found to be a major contributor to poor growth in infants. In the Malnutrition and Enteric Disease (MAL-ED) study that followed impoverished children from birth in eight sites in Asia, Latin America, and Africa, children with high levels of exposure to gut bacteria, viruses, and parasites were shorter and lighter at 2 years of age than children with low exposure.

Studies have shown that among major infectious diseases in children, diseases of the intestines are especially likely to affect a child’s growth. This suggests that interventions to reduce diarrheal diseases—such as improved water and sanitation systems, health education, zinc supplementation, probiotics, as well as vaccination against enteric infections—can help to reduce malnutrition in young children as well.

Many studies show a link between stunting and diarrheal diseases and enteric infections in early childhood. In the nine-study analysis mentioned above, the odds of stunting before the age of two years—a critical period of growth—increased 13% with every five episodes of diarrhea, and 16% with every 5% increase in the total number of days with diarrhea by 24 months of age. The authors estimated that five or more diarrheal episodes before the age of 24 months accounted for 25% of stunting in these children.

Similarly, in a study in Bangladesh, the average prevalence of diarrhea in children under the age of 5 years at any one time—13%—accounted for 20% of the stunting in this population. If these children had had no diarrhea in their first five years of life, they would have been an estimated two centimeters (>¾ of an inch) taller by age five.

In Brazil, children under the age of 5 who were found to be stunted when measured were almost twice as likely (1.9 times) to have diarrhea in the next two months than non-stunted children, when controlling for age, toilet facilities, previous diarrheal episodes, and other variables.

FIG. 2 CHILDREN > 3 YEARS OF AGE WITH STUNTING IN A SHANTYTOWN IN N.E. BRAZIL EXPERIENCED LONGER AND MORE FREQUENT EPISODES OF DIARRHEA

<table>
<thead>
<tr>
<th>Degree of stunting</th>
<th>Diarrhea-weeks per child-year</th>
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<tbody>
<tr>
<td>Normal</td>
<td></td>
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<tr>
<td>Stunted</td>
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<tr>
<td>Severely stunted</td>
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<table>
<thead>
<tr>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
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THE LONG-TERM EFFECTS OF STUNTING AND REPEAT ENTERIC INFECTIONS ON COGNITIVE DEVELOPMENT

The strong connection between height-for-age at age 2 and cognitive and school performance found in several studies is likely the results of a “compounding, cumulative effect of diarrhea and malnutrition”. (14)

How does stunting or a high burden of diarrhea in early childhood result in less schooling and poorer performance in school? One possibility is that chronic malnutrition—manifested by stunting—results in deficiencies of nutrients critical to brain development. Even more so than length and weight measures, the MAL-ED study found that head circumference measures were most linked with cognitive scores at age 2. (15) Repeat diarrheal infections—by damaging the wall of the intestine and by causing chronic inflammation—can also reduce the ability of the gut to absorb critical nutrients, such as zinc, iron, and fatty acids, as well as micronutrients that are crucial to the development of the brain during the first two critical years of life. (16-18) This may explain why some studies showed that diarrhea alone—even without malnutrition—affected performance on intelligence tests.
IMPACT ON SCHOOL PERFORMANCE

There is worldwide evidence that a heavy burden of diarrheal disease in early childhood harms a child’s mental development years later—including school readiness and school performance—either directly or indirectly as a result of stunting.

Latin America, Asia, and Africa

An analysis of around 8,000 children from low- and middle-income countries in Latin America, Asia, and Africa estimated that, after controlling for such variables as socio-economic status and mother’s education, children stunted by age 2 completed, on average, around one year less of schooling and were 16% more likely to have ever failed a grade than their non-stunted peers.\(^{(19)}\)

An analysis of data from four studies in Latin American and Asian countries found that poor length-for-age at the age of 2, but not overall burden of diarrhea during the first two years of life, predicted scores on various intelligence tests given later in childhood.\(^{(20)}\) However, children in a Brazilian shantytown who had more than five episodes of diarrhea by the age of 24 months performed significantly worse on two out of three intelligence tests given at ages 5–12 years than children with a lesser burden of early childhood diarrhea.\(^{(16)}\) This was true even when controlling for stunting and underweight. Socio-economic variables, such as household income and mother’s education, were not contributing factors, since they were similar among the groups of children with and without high burdens of diarrhea. This suggests that diarrhea in early childhood had an impact on children’s cognitive development independently of malnutrition.

Jamaica

A study of around 200 stunted and non-stunted children in Jamaica found that, when socio-economic factors, age, and other confounding variables were taken into account, children stunted by age 2 performed significantly worse than non-stunted children on reading, spelling, and arithmetic tests given at age 11 or 12.\(^{(21)}\)

Brazil

Other studies also link diarrhea in early childhood to school readiness and performance, regardless of whether or not they had been stunted. A study from Brazil found that on average, each episode of diarrhea delayed the start of school by 0.7 months, when family income and other socio-economic factors were taken into account.\(^{(14)}\) This relationship remained statistically significant even when stunting and underweight were taken in to account.

Pakistan

For children in rural Pakistan, the total number of days with diarrhea by age 2 or age 5 was negatively correlated with math scores. At the same time, stunting and underweight did not make a significant difference in these test scores.\(^{(22)}\)
According to several long-term studies conducted in Latin America and India, people who had been stunted or underweight by the age of 2 years had higher rates of risk factors for cardio-vascular disease, such as high blood pressure and high levels of HDL cholesterol and triglycerides, when they became adults than people who had not been malnourished in early childhood. They also had higher rates of pre-type 2 diabetes (insulin resistance and glucose intolerance).

A link between diarrhea disease in early childhood and an increased risk for non-communicable diseases (NCDs) was also made in a study of adults 25–37 years of age in Guatemala who had participated in a nutrition intervention study when they were young children. Each 1% increase in the number of days that infants 0–6 months old had diarrhea increased their odds of developing hypertension, metabolic syndrome (a set of risk factors that precede type 2 diabetes) and obesity each by 3% when they became adults.

The cumulative effect of repeat enteric infections, stunted growth, and the increased risk of developing chronic diseases and obesity has been labeled by some experts as a “triple burden.” It is believed that chronic inflammation due to infections and insufficient intake of calories in early childhood may play a role in increasing the risk of NCDs in adulthood.

REFERENCES

Diarrheal disease in early childhood is part of a cycle of infection and malnutrition common in impoverished settings.

Diarrheal infections—especially repeat, prolonged episodes—before the age of 2 years are an important contributor to stunting.

A heavy burden of diarrheal disease in early childhood can harm a child’s cognitive development years later, either directly or as a result of stunting, resulting in poorer school achievement.

There is also evidence that stunting, as well as a heavy burden of diarrheal disease in early childhood, can increase the risk of cardiovascular disease, type 2 diabetes, and obesity in adulthood.

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