OneWorld Health, a drug development affiliate of PATH

Diarrheal Disease

Diarrheal disease accounts for approximately 1.3 million deaths annually in children under five years of age—it is the second most common cause of death in young children after pneumonia. Survivors who are inadequately treated suffer from long-term health problems. Although the adoption of oral rehydration therapy (ORT) has significantly reduced infant mortality by treating dehydration (the cause of death), ORT does not reliably shorten the duration or severity of diarrhea, leading to inconsistent adoption and widespread non-compliance. With about 2 billion cases of diarrheal diseases globally every year, there is an urgent need for safe and affordable anti-diarrheal drugs to be used in conjunction with ORT.

What is diarrheal disease?

A major challenge to combating diarrhea is the number of disease-causing pathogens including bacteria, viruses, and parasites: acute watery diarrhea (AWD), which is characterized by rapid fluid loss and dehydration is caused by pathogens such as cholera, *E. coli*, and rotavirus; dysentery (or bloody diarrhea) is caused by pathogens such as *Shigella* and *Entamoeba*; persistent diarrhea can be caused by numerous bacteria, viruses, parasites (such as *Giardia*), and other factors. Both AWD and dysentery can be fatal, especially if the child is malnourished or suffers repeated bouts of infection. The primary cause of death from diarrheal diseases is dehydration. As dehydration worsens, thirst, restlessness, decreased skin turgor, and sunken eyes progress to diminished consciousness, rapid and feeble pulse, and undetectable blood pressure. Studies suggest that diarrhea within the first two years of life has long-term, lasting effects on growth, fitness, cognition, and school performance.

Geographic distribution and prevalence

Diarrheal diseases are a global problem, but are especially prevalent in developing countries in conditions of poor environmental sanitation, inadequate water supplies, poverty, and limited education. The epidemiology of diarrheal diseases in many developing countries is still poorly understood. Prospective studies, surveillance systems, and outbreak investigations have attempted to describe the epidemiology of diarrheal diseases. Incidences vary by region, season, and with the timing of epidemics, such as outbreaks of cholera. Generally, the highest incidence occurs in children in their first two years of life, followed by a decline with increasing age.

OneWorld Health responds

OneWorld Health (OWH) is working to address various aspects of cholera and other diarrheal diseases. In 2011, OWH received US Food and Drug Administration approval to proceed to phase 1 trials for its investigational new drug iOWH032 to treat secretory diarrhea as a result of diseases like cholera. This new synthetic drug reduces fluid loss and is designed to be used in conjunction with ORT, providing faster relief of diarrhea symptoms and encouraging wider adoption and compliance of ORT. iOWH032 is scheduled to enter phase 2 trials in 2012. OWH is also collaborating with Anacor Pharmaceuticals to discover antibacterial compounds for treating bloody diarrhea (shigellosis) and with the Center for World Health and Medicine to identify potential anti-secretory drug candidates.

Additional Resources

Black RE, Cousens S, Johnson HL, et al. Global, regional, and national causes of child mortality in 2008: a systematic analysis. *The Lancet*. 2010;375(9730):1969–1987. Available at: www.thelancet.com/journals/lancet/article/PIIS0140-6736%2810%2960549-1/fulltext. Accessed April 9, 2012.

World Health Organization diarrhoeal disease fact sheet page. Available at: http://www.who.int/mediacentre/factsheets/fs330/en/index.html. Accessed April 9, 2012.

Centers for Disease Control and Prevention website. Available at: www.cdc.gov. Accessed April 9, 2012.

Defeat DD website. Available at: www.defeatdd.org. Accessed April 9, 2012.

Very few treatments for specific diarrheal pathogens exist. In many parts of the world, diarrhea is routinely treated with antibiotics, regardless of the underlying cause. However, antibiotics are ineffective against many pathogens, and indiscriminate use of such drugs contributes to resistance in many different bacterial pathogens.

Oral rehydration therapy (ORT), which counters dehydration associated with diarrhea, has been the cornerstone of international programs for the control of diarrheal diseases and has greatly reduced mortality due to dehydration. However, while ORT is extremely useful, it does not treat the cause or the symptoms of diarrhea directly.

There is an urgent need for the development of safe, effective, and affordable drugs for people suffering from diarrheal diseases.

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April 2012

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