Treatment of Diarrhea

We Have the Solution (ORS)—What is the Problem?

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Diarrhea is a top cause of global child death

About 535,000 deaths of children 1-59 months were attributed to diarrhea in 2014, globally.¹

¹ UNICEF A Promise Renewed Report 2015
*Excludes neonatal deaths, which make up a significant burden of under-five deaths, but have unique causes that must be addressed separately.
ORS – The Most Important Medical Advance of the 20th Century

THE LANCET
AUGUST 1978

Water with Sugar and Salt

The discovery that sodium transport and glucose transport are coupled in the small intestine, so that glucose accelerates absorption of solute and water, was potentially the most important medical advance this century.\(^1\) It opened the way to oral hydration treatment for severe diarrhoea—the main cause of infant death in the developing world.
Fluid Therapy for Diarrhea

1831-32
- Description of physiologic disturbances in diarrhea
- Use of intermittent saline and alkali in cholera

1930-50s
- Use of IV fluids

1950s
- Use of ORS in United States
Mass Accidental Salt Poisoning in Infancy
A Study of a Hospital Disaster
Oral Rehydration Therapy USA
Early 1980’s

Not Recommended – concern
Re. Hypernatremia
Genesis 19:26

... but his (Lot’s) wife, from behind him, looked back; and became a pillar of salt...
MECHANISM OF ORAL REHYDRATION

INTAKE:
A: NONE

B: ISOTONIC SALT SOLUTION
WATER, ELECTROLYTES
SMALL BOWEL

RESULT:
DIARRHOEA ISOTONIC DEHYDRATION
MORE DIARRHOEA ISOTONIC DEHYDRATION

C: ISOTONIC SOLUTION OF SALT AND GLUCOSE
WATER, ELECTROLYTES
SMALL BOWEL

GLUCOSE, WATER, ELECTROLYTES
WATER, ELECTROLYTES

DIARRHOEA
HYDRATION IS MAINTAINED OR CORRECTED
Water Absorption Rates from Different Salt and Glucose Solutions by 30cm of Healthy Small Bowel

<table>
<thead>
<tr>
<th>Solution Perfused</th>
<th>Saline</th>
<th>Glucose-Saline Mixtures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Glucose Concentration Millimoles</td>
<td>0</td>
<td>5.6</td>
</tr>
</tbody>
</table>

Water Absorption in mL per Hour

Sladen and Dawson 1969 Clin Sco 38, 199
<table>
<thead>
<tr>
<th>Year</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1966</td>
<td>Success of ORS in adults with cholera (Bangladesh and India)</td>
</tr>
<tr>
<td>1970</td>
<td>Success of ORS in children with cholera (India)</td>
</tr>
<tr>
<td>1978</td>
<td>Adoption of the WHO ORS formulation</td>
</tr>
</tbody>
</table>
THE SOLUTION (ORS)
DIARRHOEA
MALNUTRITION

WEIGHT CHART
... Usual dietary intake is achieved, usually in 7 to 8 days.

“...half of what we teach you here is wrong –

Unfortunately, we don’t know which half…”

-Lisa Sanders, New York Times
Randomized Trial: Early vs. Delayed Feeding Duration of Diarrhea

**Mean Duration (±SEM), Hours**

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>SEM</td>
<td>5</td>
<td>10</td>
</tr>
</tbody>
</table>

* * P<0.001

Pediatrics 76; no 2 Aug 1985
## Reduced Osmolarity ORS

<table>
<thead>
<tr>
<th></th>
<th>R-ORS</th>
<th>WHO ORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (mmol/L)</td>
<td>75</td>
<td>90</td>
</tr>
<tr>
<td>Potassium</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Chloride</td>
<td>65</td>
<td>80</td>
</tr>
<tr>
<td>Citrate</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Glucose</td>
<td>75</td>
<td>111</td>
</tr>
<tr>
<td>Osmolarity (mosm/L)</td>
<td>245</td>
<td>311</td>
</tr>
</tbody>
</table>
Reduced Osmolarity ORS Solution

- Stool output is reduced by 25-30%
- Vomiting is reduced by 30%
- The need for unscheduled IV fluids is reduced by more than 35%
- A group of experts recommended that:
  - a single ORS solution be used, with 75 mEq/l of sodium and 75 mmol/l of glucose, and a total osmolarity of 245 mOsmol/l
  - this reduced osmolarity ORS be used in place of standard ORS for treatment of adults with cholera
# Therapeutic Effects of Zinc Supplementation on Acute Diarrheal Severity

## Table

<table>
<thead>
<tr>
<th>Country</th>
<th>Diarrhea Outcome</th>
<th>Percent Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>Frequency</td>
<td>59% ▼</td>
</tr>
<tr>
<td>India</td>
<td>Frequency</td>
<td>18% ▼</td>
</tr>
<tr>
<td>India</td>
<td>Frequency</td>
<td>39% ▼</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>Output</td>
<td>28% ▼</td>
</tr>
<tr>
<td>India</td>
<td>Output</td>
<td>38% ▼</td>
</tr>
</tbody>
</table>

Statistically significant reduction\(^2\) in:

- All-cause mortality by **46%** (RR 0.54, 95% CI 0.32–0.88)
- Diarrhea-related hospital admission by **23%** (RR 0.77, 95% CI 0.69–0.85)

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\(^1\)Baqui. Effect of Zinc in the Prevention and Treatment for Childhood Diarrhea and Pneumonia. \(^2\)Bhutta et al. Interventions to address deaths from childhood pneumonia and diarrhoea equitably: what works and at what cost? Lancet. 2013 Apr 20;381(9875):1417-29 (*Statistical significance*)
2004 UNICEF/WHO Recommendation on Diarrhea Management

Treatment should include:

- Liberal use of low-osmolarity Oral Rehydration Solution to correct and prevent dehydration
- Zinc supplementation for 10-14 days to shorten duration and severity of diarrhea
- Continued feeding and additional fluids
Diarrhea Mortality Over the Years

Since 1980, over 60 million lives have been saved due to ORS.
Percent of children with diarrhea in the previous 2 weeks who received zinc
(Based on available data from the Demographic and Health Survey and Multiple Indicator Cluster Survey)

Among countries analyzed, most reported zinc coverage was <5%.

Figures courtesy of Amnesty LeFevre et al. Personal Communications. Manuscript under development.
Percent of children with diarrhea in the previous 2 weeks who received ORS
(Based on available data from the Demographic and Health Survey and Multiple Indicator Cluster Survey)

Among countries analyzed, most reported ORS coverage was 30-45%.
Opportunities

Moving forward to prevent child morbidity and mortality from diarrhea
Strategies for Preventing and Treating Pneumonia

- **Protection**
  - Breast feeding promotion
  - Hand washing promotion
  - Zinc supplementation
  - Adequate nutrition
  - Reduce indoor air pollution

- **Prevention**
  - Vaccinations
    - New: Pneumococcal, Hib
    - Routine: Measles, pertussis
  - HIV prevention

- **Treatment**
  - Improve care seeking behavior
  - Community case management
  - Health facility case management
  - Antibiotics

Strategies for Preventing and Treating Diarrhea

- **Protection**
  - Breast feeding promotion
  - Hand washing promotion
  - Vitamin A and Zinc supplementation
  - Adequate nutrition
  - Safe water and sanitation

- **Prevention**
  - Vaccinations
    - New: Rotavirus
    - Routine: Measles
  - HIV prevention

- **Treatment**
  - Improve care seeking behavior
  - Community case management
  - Health facility case management
  - Low-osmolarity ORS
  - Zinc

Many interventions and treatment strategies are identical
Conditions Necessary for Successful Program Coordination

• Clear WHO policy
• Clear strategies
• International funding and support

Communication and feedback between global, national, and local levels

Global Level

National Level

Local Level

• Clear national policies
• Political commitment
• Appropriate funding
• Improved management

• Strong supply procurement
• Health worker training
• Monitoring and evaluation
Commitments to Reduce Child Mortality

• A Promise Renewed for Child Survival:
  Reduce under-5 mortality to 20/1000 live births or less in all countries by 2035

• Target reduction
  – Reduce pneumonia mortality to <3/1000 live births by 2025
  – Reduce diarrhea mortality to <1/1000 live births by 2025
  – Virtually eliminate these deaths by 2035

Commitments to Reduce Child Mortality

• Reaching the targets will require
  – Increased immunization coverage to 90%
  – Scale up of other interventions to 80%

• Scaling up existing interventions could prevent
  – 67% of under-5 pneumonia deaths by 2025
  – 95% of under-5 diarrhea deaths by 2025

• To end preventable pneumonia and diarrhea deaths by 2025, the cost will be about US$6-7.15 billion

Conclusions

• Globally, enormous strides have been made in reducing diarrheal mortality and morbidity.

• But over half a million children continue to die each year and millions of children are hospitalized, resulting in enormous economic and social burden.

• Studies from various settings have shown that new interventions like rotavirus vaccines have the potential to significantly reduce child diarrheal deaths and hospitalizations.

• Many powerful strategies are available but coordinated and comprehensive approaches are required for optimal results.

• We need political will, mobilization of resources, accountability, and community engagement and mobilization to implement these powerful strategies.
Thank You