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POSSIBLE DISINFECTION OF ORAL REHYDRATION SOLUTIONS:

Notes from November 13, 1980 Meeting

with

Drs. Richard Cash and Lincoln Chen

AID/DSPE-C-0080
931117600

REASON FOR THIS REPORT

Recently, the question of whether or not to consider the introduction of a disinfectant into oral rehydration packages was raised. Disinfection should at least be considered it is contended, since most households in Third World countries do not have access to safe water. Several problems are however attendant upon the use of a disinfectant in this capacity, among them possible chemical interactions with other components of the package, biologic reactions with the inflamed gut, and problems of cost, taste and acceptability. Because of these problems, it was thought useful to hold a serious discussion of the issues before deciding to routinely include a disinfectant in OR packages. Drs. Richard Cash and Lincoln Chen of the Harvard School of Public Health were invited as guest consultants and a group of AID technical personnel was gathered[1].

[1]For a list of attendees, see Attachment IV.

POSSIBLE DISINFECTION OF ORAL REHYDRATION SOLUTIONS:

Notes from November 13, 1980 Meeting with Drs. Richard Cash and Lincoln Chen

Drs. Cash and Chen began their discussion with DS/HEA and WASH staff by posing two questions. The first question was:

> "As drinking water in LDC's is often contaminated, should an effort be made to insure the potability of oral rehydration solutions?

Dr. Chen presented data from the following studies which illustrate that the growth of micro-organisms is supported in OR solutions.

1) Richard Guerrant in Brazil (now Department of Geographic Medicine, University of Virginia, Charlottesville) found E. Coli, after 24 hours, in concentrations of 10^5 per 100 ml in OR solutions made up by villagers regardless of the initial purity of the water to which the salts were added

2) Gerry Keusch at Harvard found the follcwing numbers of E. Coli in various OR solutions. Note: These solutions consisted of river water, added E. Coli and oral therapy salts.

Time (hrs)	1	4	8	16
E. Coli	10^1	10^{1-2}	10^4	10^6

The discussion then dealt with many questions about ORS and ORT with potential for field research. These questions are summarized in Attachment I.

The first question raised was, "Are there negative effects (e.g. reinfection or prolongation of the diarrheal episode) of drinking contaminated ORS, given that the gut is already inflamed?" the answer to this question is unknown but the suggestion was made that Mike Levine at the University of Maryland might be able to include an approach to this question in his volunteer diarrheal studies. It should be noted, however, that the results of either animal or human adult studies of this question might not be directly applicable to children under five; thus one might argue for using a natural experiment in an on-going oral rehydration therapy field project.

Dr. Cash pointed out that it is important to know at what point the water in the OR solution is contaminated: at the water source? in vessels used for transport from the source to the home? during storage in the home? by the person who mixes up the solution (fingers, spoon)? or from the ORS salts themselves (especially since the ingredients, sugar and salt, are supportive of bacterial growth.

If it can be assumed that the contamination of the solution during the mixing or from the salts is negligible, what options could be considered for water purification: e.g. adding a bactericidal agent to the water storage vessels in the home? boiling the water to be used (this method was criticized because of its high fuel and time costs)? addition of a disinfectant to the ORS packet? Finally, a paper has been recently received by the Near East Bureau which suggests that exposure of the mixed solution to the sun's ultraviolet irradiation for one hour has a significant bactericidal effect (see Attachment II). Does this approach appear to be feasible?

Not much work has been done with regard to what substances might be used as a disinfectant in the ORS. Vic Wehman mentioned potassium permanganate as a possibility. Halogens such as

chlorine or bromine have the disadvantage that they oxidize the glucose, reducing its physiological benefit. Iodine, although not as strong an oxidant, has the disadvantage of an unpleasant taste.

Questions remaining to be answered about disinfectants themselves include:

> "What disinfectant(s) would have a high bactericidal/viricidal activity? be realtively inert with regard to the ORS components? not negatively affect the shelf-life of the ORS packet? be palatable? be of low cost? be chemically inert in relation to metal ions frequently found in untreated water such as Fe^{+++} Mn^{++}?"

A further important question is, "What would be the effect of the disinfectant on the inflamed gut?"

These questions are researchable. One might undertake laboratory studies to evaluate the relative effectiveness of various disinfectants under a variety of conditions. A later field study as part of an on-going ORT program could help to answer questions about the taste acceptibility and the effects on an already compromised gut. A summary of the research literature already available on this question appears as Attachment III.

A "danger" of the "disinfectant addition" strategy is that it may start an uncontrolled series of suggestions concering vitamin, mineral and protein supplementation. The argument might be made that a child with diarrhea needs the addition of certain nutrients as well as fluid and electrolytes.

Another caution raised was whether the benefits of a purified (safer?) OR solution would be worth the costs. Dr. Shapiro of

UNICEF was quoted as estimating the cost of adding purifiers to be about 1/2 cent per packet or about a 13¢ increase in the cost of the UNICEF packet (now 6.4 cents). The money invested in adding disinfectants to ORS, which at this time is not known to have any benefit, might be used, for example, to provide:

1) appropriate mixing containers or markers,
2) improved public education about ORT,
3) greater numbers of packets,
4) improved distribution strategies,
5) assistance to countries to produce their own ORS packets, and
6) efforts to improve habits related to water supply and personal hygiene.

With these cautions in mind, some discussion was then devoted to alternatives to any water purification strategy, i.e. reducing the size of the packet or instructing the mothers to dispose of the ORS solution after a specific period of time.

The second question posed by Drs. Cash and Chen as fundamental to the first one, was:

> "Does the provision of potable drinking water improve health (morbidity, mortality, nutrition and fertility)?"

Dr. Chen commented that the frequency of diarrhea was not a good outcome variable to use in water quality studies because of the cultural variability in definition of diarrhea and the physiological variability in susceptibility to diarrhea. Quite simply, there is no one-to-one correlation between the number of micro-organisms in a quantity of water and the incidence of diarrhea. Many other variables having an impact on the overall level of health and nutritional status influence a person's susceptibility to diarrhea.

Dr. Chen suggested that measures of nutritional status can be more precisely measured and are outcomes which might be used to determine if improvements in water supply actually improve health status. Dr. Chen sketched out the schematic which appears below, to illustrate his point.

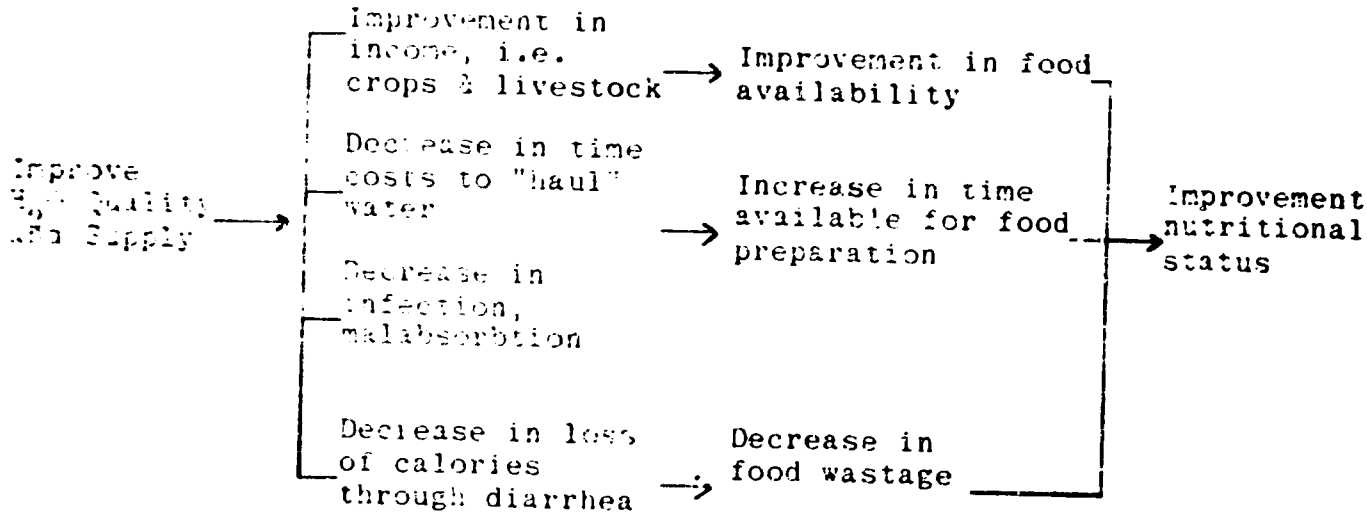

Fig. 1 Relationship of improved water supply to improved nutritional status.

The meeting ended with the point being made that many questions regarding ORT and ORS were not as yet answered, not only questions about the inclusion of disinfectants. Given what is now known, there did not seem to be much support for including a disinfectant in ORS packets, although a shift in this opinion might be warranted when further research has been done. Drs. Cash and Chen recommend further study of ways to provide safe domiciliary water supplies, and for "rethinking" the whole water supply and health model.

ATTACHMENT I: POSSIBLE ORS/ORT RESEARCH QUESTIONS

1. Biomedical:

Are there negative effects (e.g. reinfection or prolongation of the diarrheal episode) of drinking contaminated ORS, given that the gut is already inflamed?

2. Operational:

a. Would it be possible, feasible and effective (as determined by an improved quality of ORS) to combine instruction of village health workers (VHW) and mothers in preparation and use of ORS, with emphasis on use of clean carrying and storage vessels? VHW training might also include teaching water source protection and methods for promoting improved water use habits.

b. Is there an improvement in mothers' learning about ORS preparation when teaching is done at the clinic level in comparison with teaching done at home? What teaching approaches and aids are most effective in each setting?

3. Bio-chemical:

a. What chemical compounds and in what forms might be used for disinfection of water vessels in homes?

b. What chemical compounds might be added to ORS packet materials to prevent the growth of micro-organisms when the contents are mixed with contaminated water? These compounds should be inert with respect to the ORS components and metal ions found in untreated water, palatable and not negatively affect the shelf-life of the packet, nor the inflamed gut.

c. Might a less expensive and relatively safe chemical compound be added which would suddenly change color when the OR solution reached a certain level of contamination.

5. Product Development

a. Are there significant advantages which can be gained by changing the ORS package size or shape?

b. What instructions are effective in insuring that the mother correctly mixes and uses ORS?

c. Are there siginificant benefits to flavoring or coloring the ORS to make it more acceptable as a "medicine" for oral rehydration?

ATTACHMENT II: DISINFECTION OF ORAL REHYDRATION SOLUTIONS BY SUNLIGHT

By: Aftim Acra, Yester Karahagopian, Zeina Raffoul, and Rashid Dajani*

The World Health Organization (WHO) has recently intensified its efforts to promote and expand diarrhoeal disease control programmes in developing countries by means of oral rehydration therapy within the framework of primary health care. WHO strategy aims at the delivery of oral rehydration solutions (ORS) containing glucose (or sucrose) and salts of sodium and potassium for all cases of diarrhoea, especially in infancy.[1] This communication addresses one of the concerns in the use of ORS, the microbiological safety of solutions prepared with contaminated water. We wish to share our observatons that simple exposure to sunlight of ORS contained in transparent vessels renders these solutions bacteriologically safe, without deterioration of the ingredients.

In the course of a study on the small-scale disinfection of water for home use by exposure to sunlight, we have observed that sunlight destroys bacteria, including pathogens.[2] These findings prompted experiments to determine the applicability of this simple, inexpensive technology to disinfection of ORS prepared with contaminated water. For this purpose 15 liters of bulk ORS were prepared by dissolving the requisite amount of salt-sugar mixture recommended by WHO[3,4] in chlorine-free tap water contaminated with fresh sewage. One liter of this solution was transferred into each of 15 sterile polyethylene bags (Liquid - Tite fluid containers Falcon, Dickinson and Co., Oxnard, CA, USA). These bags are graduated up to 2.5

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liters, and have a wall thickness of 0.13 mm and screw cap closures. Spectral transmittance curves of specimens of the polythylene material, as well as of polypropylene sheets and pyrex glass, have shown that the high transmittance values fall appoximately in the range of 260 to 700 nm, with minimum transmittance occuring below about 230 nm. Accordingly, the near UV light and the visible light components of sunlight would be transmitted equally well by containers made of these materials.

Two experiments were run on different occasions according to the following protocol: 3 sets of 3 bags each were exposed to direct sunlight, 2 bags were kept in the dark, and 2 others were kept under room conditions (artificial and natural light). Samples of the ORS bulk solution taken at 0 hr., and of those contained in the experimental bags were examined bacteriologically at set intervals by applying techniques using solid media as described in Standard Methods.[5] However, in the case of the bags exposed to sunlight, one bag from each of the three replicate sets was used for examination at the prescribed intervals to avoid any interruption of exposure to sunlight. The results, given in Tables I and II, indicate that a zero coliform count/ml of ORS, which is considered to be a rather stringent requirement, were attained in about one hour. Similar results were obtained in some 50 experiments using highly contaminated water contained in an assortment of vessels made of transparent glass or plastic, and having different colours and shapes.[2] The rise in temparature of the test ORS not exceeding $5^{o}C$ on exposure to sunlight for 2 hours leads to the conclusion that in this case heat is not a factor involved in the destruction of micro-organisms. It appears that the germicidal action is due to solar radiation in the

near UV range (300 to 400 nm). It was also shown by analysis that the $NaHCO_3$ did not undergo any change in concentration, and that the pH value of 8.33 remained constant. This shows that $NaHCH_3$ and CO_2,[6] is not significantly affected by this technique. The inability of the microorganisms to regrow 24 hours after solar irradiation allows for storage or transport of treated ORS.

These findings, indirectly supported by evidence derived from the literature on the viricidal activity of sunlight,[7-10] clearly demonstrate the effectiveness of this simple technique for the preparation of potable ORS. the use of graduated vessels made of transparent, colourless or blue tinted, plastic or glass presents an additional advantage. Solar irradiation of polluted water intended for ORS preparation and for drinking is suggested as a useful alternative approach which provides both curative and preventive measures.

We thank Kalouste Gulbenkian Foundation Lisbon, and Dr. Eugene Gangarosa for their financial and moral support, respectively.

ATTACHMENT III: ORAL REHYDRATION FLUIDS: TO DISINFECT OR NOT TO DISINFECT A PRELIMINARY REPORT OF A LIMITED LITERATURE SEARCH

Purpose of Search

Some concern has arisen over the question of the quality of water used for mixing oral rehydration fluids. While oral rehydration has been proven effective in the prevention and treatment of dehydration from diarrhea, authors are unanimous in recommending that the safest water possible be used in these solutions (Parker, 1980; WHO, 1978) and that a fresh solution be prepared at least every 24 hours (Wells et al, 1980; Sack et al, 1978; Cash, 1979), the latter to avoid problems of bacterial growth in fluids kept over prolonged periods. That organisms can grow in ORS has been demonstrated by Wells et al (1980). V. cholerae appears to grow less well because of inhibition by acid by-products of metabolism (Feldman, 1980).

The question to be addressed by the literature search and subsequent activities is, therefore, how best to assure safe water for use in mixing ORS. Several optional approaches exist, not all of which are equally advantageous. They are discussed below.

Optional Modes of Assuring Safe Water for ORS

Doing nothing

Parker, et al, (1980) suggests that the overriding importance of getting water and electrolytes into a dehydrated child, makes relatively unimportant the question of the quality of the water used, so that a recommendation to use the "cleanest available water" and to dispose of any unused fluid after 24 hours is made.

This approach, however, begs the question of how clean is clean. Some communities with only very polluted water supplies as their option would be hard put to fulfill the criteria.

To do nothing implies that the possibility of introducing a new inoculum of potential pathogens to an already inflamed gastrointestinal tract poses no problem. Despite the paucity of knowledge on the physiologic alterations attendant upon infection of the intestinal mucosa by various organisms, it does appear that so-called "secretory" diarrhea is less vulnerable to the ill effects of a new dose of organisms than "invasive" diarrhea, where the damage to tissues is more

severe. Most infant diarrhea in developing countries is of the former type (Rowland and McCollum, 1978), but one cannot rule out the latter in the individual case. Nor can one rule out the possibility of introducing a sufficient dose of an invasive organism.

The size of the infective does must also be considered. Most investigators contacted felt that a dose of organisms sufficient to cause a renewed infection would be rare even without efforts to protect the water supply. What seems to occur is a resurgence of symptoms 2-3 days after diarrhea has once abated with the use of ORS. This phenomenon may reflect a lag in the growth rate of the newly introduced organisms (Sack, 1980).

In the long run, in terms of the ultimate outcome of a given case of diarrhea, the previous nutritional status of the infant probably exerts more influence than the quality of water used in mixing the ORS.

Boiling

A WHO working group (1975) recommends boiling and cooling any water of "doubtful quality" to be used in preparing ORS. Because of the obstacles of scarce and costly fuel, time for the process and the urgency of getting fluids into the child, however, Cash (1979) and others recommend against using this option.

What is needed then is more rapid, yet effective disinfectant.

Adding a chemical disinfectant to the water

Iodine shows the most promise as a potential disinfectant to be included in ORS. it holds several distinct advantages over chlorine or bromine.

- it is more stable than either Cl or Br.
- It is much less reactive with the glucose in the ORT package.
- It is an excellent cysticidal as well as a bactericidal agent.

Globaline (triglycine hydroperiodide) was suggested

which has proven effectiveness, low reactivity with glucose, and productive of minimal change in odor and taste. It was originally developed for use in the canteen disinfection program of the US Army.

Johnson suggests adding a sufficient quantity of Globaline to ORT packages to handle waters of variable contamination, i.e., a single amount placed in all packages no matter what the quality of water. The more polluted the water, the longer the standing time necessary before use.

Several questions arise, however, in considering the use of a disinfectant:

- What is the reaction of the compound with the inflamed gut? No satisfactory answer could be obtained, with respect to either irritation of or increased absorption through the inflamed intestine.

- In view of the standing time necessary for more contaminated water, where there is chance for a larger inoculum of organisms and a greater bacterial growth potential in the ORS, it might be better to add the disinfectant to the water stored in the home (assuming such to be the case).

Wider ramifications

What of the possibility of doing something of a more permanent nature about the quality of water available for mixing ORS? There is a trend in ORT circles toward more community level packaging and distribution of ORT packets. Despite problems of impurities, short shelf life, and less quality control, the involvement of local people, and the possibility of dispelling the aura of a magical cure, make this approach attractive.

A workshop on Integrating Oral Rehydration Therapy into Community Action Programs (Washington, D.C., 19-21 March, 1980) discussed the realtive advantages and disadvantages of various means of mixing and distributing ORT packets. No conclusions were reached although community-based systems were emphasized. Surprising was the failure to even mention focusing community action on the quality of water used, whether at the source, in transport, or in domestic storage. Unless community based pro-

grams of preventing and treating diarrhea and dehydration encompass these concerns, programs will be permanently dependent upon the use of disinfectants.

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ATTACHMENT IV: ATTENDEES AT MEETING ON DISINFECTION OF ORAL REHYDRATION SOLUTIONS 13 DECEMBER, 1980

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Ms. Veronica Elliott
Mr. Donald Ferguson
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Dr. Clifford Pease
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Mr. Victor Wehman
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