Influence of solar water disinfection on immunity against cholera – a review

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ABSTRACT

Cholera remains a problem in developing countries. This is attributed to the unavailability of proper water treatment, sanitary infrastructure and poor hygiene. As a consequence, countries facing cholera outbreaks rely on interventions such as the use of oral rehydration therapy and antibiotics to save lives. In addition to vaccination, the provision of chlorine tablets and hygiene sensitization drives have been used to prevent new cholera infections. The implementation of these interventions remains a challenge due to constraints associated with the cost, ease of use and technical knowhow. These challenges have been reduced through the use of solar water disinfection (SODIS). The success of SODIS in mitigating the risk associated with the consumption of waterborne pathogens has been associated with solar irradiation. This has prompted a lot of focus on the solar component for enhanced disinfection. However, the role played by the host immune system following the consumption of solar-irradiated water pathogens has not received any significant attention. The mode of inactivation resulting from the exposure of microbiologically contaminated water results in immunologically important microbial states as well as components. In this review, the possible influence that solar water disinfection may have on the immunity against cholera is discussed.

Key words | cholera, SODIS, solar ultraviolet radiation, vaccine, *V. cholerae*, waterborne disease

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INTRODUCTION

Cholera is a life-threatening waterborne disease characterised by secretory diarrhoea often accompanied by vomiting (Osei & Duker 2008). It is estimated that there are five million cases of cholera resulting in approximately 130,000 fatalities per year globally (WHO 2010). Cholera is spread through faecal contamination of water and food and is generally prevalent in resource-poor communities due to the lack of basic sanitary infrastructure and limited or no access to potable water. Various measures such as the provision of basic sanitary infrastructure and treated piped water, construction of village hospitals and immunisation, as well as proper hygiene sensitisation campaigns, have been proposed to prevent cholera outbreaks and epidemics. However, their implementation remains a global challenge (Echeverria *et al.* 1983; WHO 2011; WHO/UNICEF 2012). During an actual cholera outbreak or epidemic it is almost impossible to simultaneously implement the previously mentioned prevention measures. However, prioritisation of interventions that result in the prevention of new infections and saving of lives may be required (UNICEF 2013). Such interventions should enable the active participation of all tiers of the affected society.

Currently, the use of Oral Rehydration Solution (ORS), antibiotics and, to an extent, vaccination has been recommended as interventions to save lives and prevent new infections (WHO 2010; Date *et al.* 2011). Although these interventions are acceptable, their implementation remains a challenge due to constraints such as the cost of execution, ease of use and technical knowhow. ORS requires trained personnel on site to prepare the solution. Alternatively,

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ORS sachets could be purchased and distributed to the population facing a cholera outbreak or epidemic (UNICEF 2013). Antibiotics could be used to treat patients with cholera. However, this intervention is threatened by the emergence of more virulent strains of *Vibrio cholerae* that may be resistant to the readily available antibiotics (WHO 2010; UNICEF 2013). Vaccines may have the potential to prevent new infections if they are readily available. The unavailability and poor uptake of vaccines could be attributed to the costs and logistics involved in their preparation, shipping and storage (Date *et al.* 2011) as well as their multi-dose regimen (Date *et al.* 2011; William 2011). Furthermore, the vaccines may not be as efficacious in the affected community as previously documented in clinical trials done elsewhere (Shahjahan 2005; Ryan *et al.* 2006; WHO 2010). Vaccination of infected persons is also complicated by issues concerning the vaccination schedule and whether the affected population should stop using water from their current sources while they wait for subsequent doses of the vaccine.

Clearly an intervention that could significantly reduce the implementation costs by the affected people is required. Such an intervention should also be easy to use, sustainable (McGuigan *et al.* 2012) and compatible to the lifestyle of the people living in the affected community. Solar water disinfection (SODIS) is one of the interventions that satisfies these criteria and could be used in conjunction with the currently available prevention and crisis control interventions.

SOLAR WATER DISINFECTION

SODIS is a process in which the quality of drinking water is improved through exposure to natural sunlight in transparent vessels for a period of 6–8 hours on clear days and for 2 days during cloudy weather (Heaselgrave *et al.* 2006; Boyle *et al.* 2008; Navntoft *et al.* 2008; Ubomba-Jaswa *et al.* 2008). The process by which the disinfection occurs seems quite easy and straightforward although the underlying mechanisms are complex (Berney *et al.* 2006a, 2006b; Bosshard *et al.* 2010a). Effective bacterial inactivation is judged by the inability of the chosen microbial indicator organism to form colonies after SODIS treatment (Smith *et al.* 2000). Downes & Blunt (1877) were the first to present empirical evidence of the bactericidal effect of sunlight; however, its use to sanitise water can be traced as far back as 2000 BC (Conroy *et al.* 1996). Presently, Downes & Blunt's (1877) observations regarding the bactericidal effect of solar radiation have been refined and tested in the field by various research teams with subsequent implementation in various countries (Eawag/Sandec 2008). Studies by Acra *et al.* (1989) and Conroy *et al.* (1996) showed that the bactericidal effect resulting from solar radiation was due primarily to the ultraviolet component of sunlight.

Ultraviolet A (UVA), the most abundant component of solar ultraviolet radiation (SUVR) reaching the earth's surface, enables the formation of reactive oxygen species such as superoxide radicals, hydroxyl radicals, hydrogen peroxide and singlet oxygen. These reactive molecules, also known as photosensitisers, are formed through a process known as photo-oxidation (Elasri & Miller 1999; Sinton *et al.* 1999; Qiu *et al.* 2004; Navntoft *et al.* 2008). During SODIS, the interaction between the photosensitisers and the actively growing microorganism results in irreversible damage to the microbial catalase systems rendering them susceptible to damage from peroxide formation (Bailey *et al.* 1983; Alonso-Sáez *et al.* 2006). Furthermore, UVA through photo-oxidation blocks the electron transport chain incapacitating ATP synthesis; induces damage to the cell membrane thus inactivating transport systems; interferes with metabolic energy production and causes single strand breaks in DNA (Berney *et al.* 2006c; Bosshard *et al.* 2010a, 2010b). On the whole, UVA causes indirect multi-target damage to the microbial cellular components such as DNA, protein and lipids through the formation of photosensitisers (Joux *et al.* 1999).

Despite the fact that biological systems exposed to SUVR cause reduced functionality and destruction, there are protective mechanisms in cells that are capable of reversing some of this damage, especially at the DNA level. A number of different DNA repair mechanisms relevant to SUVR damage have been established including photo-reactivation repair, nucleotide excision repair and post replication repair and SOS repair (Diffey 1991; Arrage *et al.* 1993; Joux *et al.* 1999). However, these repair mechanisms are all dependent on the dose of SUVR (Bosshard *et al.* 2010a), the environment of exposure (Faruque *et al.* 2006; Quinones *et al.* 2006; WHO 2010) as well as cellular targets.

Impact of SODIS on the spread of waterborne diseases

The consumption of SODIS water in sub-Saharan African and various East Asian countries has reduced the percentage of individuals acquiring water borne diseases such as dysentery typhoid and cholera (Conroy *et al.* 1996, 2001; Du Preez *et al.* 2010). This has been attributed mainly to the ability of SUVR to inhibit the growth of the contaminating microorganisms, viruses such as poliovirus and giardia cysts (Heaselgrave *et al.* 2006; Quinones *et al.* 2006). The effect of SUVR on the pathogens is not dependent on their antibiotic status. Furthermore, sunlight, the primary source of SUVR, is readily available in waterborne disease endemic regions.

The epidemiological benefits of consuming SODIS water arise from beyond the technique and biology of microbial inactivation (Berney *et al.* 2006a). It is therefore important to consider the immunological effects that may originate from the consumption of SODIS water as an integral aspect of the overall benefits. The nature of the microbial constituents in water following SODIS is ambiguous (Bosshard *et al.* 2009, 2010b; WHO 2010) but may present an assortment of microbial antigenic determinants or epitopes. The consumption of SODIS water may result in an immune reaction and/or an immune response depending on how the microbial epitopes are received and processed by the cells of the immune system.

The effect of SODIS water on human mucosal immunity

The consumption of SODIS water is of great relevance to the intestinal mucosa. In this environment, a thin layer of epithelial cells separates the inner corpus from the surrounding environment. The antigen–antibody effect of SODIS occurs in the intestinal mucosal environment. The prospective antigens in SODIS water are acquired by antigen presenting cells (APCs) and transported to the mesenteric lymph nodes as well as the numerous small isolated lymphoid follicles along the wall of the intestine for presentation to T cells. Following the presentation of the antigens by the APC, the T cells are then activated with subsequent migration to all the non-lymphoid tissues (Lefrancois & Puddington 2006). An even more important component of the immune system of intestinal mucosal environment is the lamina propria (LP) tissue. The LP is a connective tissue beneath the basement membrane supporting the overlying epithelial cells of the small and large intestine. This tissue is rich in various cells of both the innate and adaptive immune system such as APCs as well as T cells (Rescigno *et al.* 1998; Guermonprez *et al.* 2002; Trombetta & Mellman 2005; Lefrancois & Puddington 2006). In the presence of any foreign material arising from the consumption of SODIS water; it is highly probable that this material may be engaged by the cells of the immune system. However, the extent of this engagement still remains unknown since presently there is virtually no published information on this matter.

The nature of antigens derived from SODIS water

Given the complex nature of the constituents of SODIS water and the possible influence it may have on the immune system, it is important to consider three crucial factors discussed by Pradeu & Edgardo (2006). The first factor requires consideration of the quantity of the antigens. In this regard it is widely known that a low antigen dose would not trigger a sufficient immune response simply because the generation of antigen specific regulatory cells is favoured (Faria & Weiner 2005). This could be the case with SODIS users during periods of an absence of outbreaks and epidemics. During such periods the concentration of *V. cholerae* in the water that a community utilises is often low (Ryan & Calderwood 2000). On the other hand, during outbreaks or epidemics the bacterial load in untreated water is high enough to cause a waterborne disease. For instance, it would take between 9 and 11 logs of *V. cholerae* cells to infect a healthy individual whereas in individuals with hypochlorhydria between 4 and 6 logs are required to cause cholera. The infected individuals excrete almost 13 logs of *V. cholerae* cells in their stool per day (Ryan & Calderwood 2000). This results in a rapid dissemination of the infection in the population because of the unavailability of adequate sanitary facilities. Solar irradiation has been shown to effectively inactivate a significant amount of *V. cholerae* cells from a bacterial dose comparable to that required to cause a cholera infection (Ssemakalu *et al.* 2012). Therefore it is possible that individuals that rely on SODIS to decontaminate their water during a cholera outbreak or epidemic

access a high antigen dose of *V. cholerae*. This may result in the generation of a proper immune response. Alternatively, such a high antigen dose may result in the unresponsiveness in T-cell function through anergy/deletion (Faria & Weiner 2005).

The second factor considers the degree of molecular difference between the new antigen and the antigens with which the immune receptors constantly interact (Avci & Kasper 2010). In developing countries, the consumption of waterborne disease causing microorganisms is apparent. Communities that regularly consume waterborne pathogens such as *V. cholerae* often develop tolerance towards these pathogens (Svennerholm *et al.* 1980). Tolerance is classically defined as the specific suppression of cellular and or humoral immune response to an antigen that has been previously encountered (Faria & Weiner 2005). Tolerance could occur when there is repeated contact with new antigens under non-immunogenic conditions and/or if there is no tissue destruction caused by the antigens. The development of tolerance towards waterborne pathogens could make vaccines generated from common pathogenic entities less effective amongst the SODIS users, as well as individuals in waterborne endemic areas (Svennerholm *et al.* 1980). Alternatively, SODIS treatment of water containing pathogens may possibly result in beneficial alteration, accessibility and preservation of the integrity of the possible epitopes. These epitopes may include proteins such as the chitin binding protein A, outer membrane protein U and unsheathed flagella (William 2011). Furthermore, the consumption of SODIS water during a waterborne disease outbreak such as cholera, if at all immunogenic, derives its epitopes from the current status of the microbial strain and hence may provide a relevant immune response.

The third factor to consider is the speed of appearance of the infrequent antigenic determinants. SODIS may induce slow or extreme rapid modifications of the antigenic epitopes thereby preventing the ability to prompt an immune response. It is also possible that SODIS may provide the right conditions for the generation of critical modifications on epitopes that could result in the induction of an immune response rather than an immune reaction.

Considering the above factors, the consumption of SODIS water may result in three major consequences discussed by Faria & Weiner (2005): (1) a non-inflammatory response marked by anti-inflammatory cytokine secretion, (2) the priming of a systematic immune response involving the production of serum antibodies as well as proinflammatory cytokines, and (3) a state of systemic and or local immunological tolerance.

SUMMARY

In this review, the relevance of SODIS in underprivileged communities is acknowledged due to the role it plays in reducing infection rates among its users (Graf *et al.* 2010; Firth *et al.* 2010). Nonetheless it is imperative to substantiate the role that SODIS water consumption may have on the immune system. Could it be possible that the consumption of SODIS water may confer significant desirable immunological effects onto the consumers? This may be true considering the benefits of SODIS in the current literature. However, empirical evidence is required to substantiate all the hypotheses put forward since the extent of protection that may be conferred onto the SODIS water consumers remains unknown. There is almost no knowledge on how the bacterial states following solar irradiation in water may influence antigen processing or development of the APCs. In our laboratory we are currently investigating some of these hypotheses so as to better understand the influence that antigens and bacterial states generated through solar irradiation of *V. cholerae* may have on the immune system.

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