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Salmonella enterica Serovar Typhi and Paratyphi Responsible of Typhoid and Paratyphoid Fevers Transmitted by Environment and Food

Somda Namwin Siourimè[1,2]✎, Bonkoungou Ouindgueta Juste Isidore[2,3], Traoré Yves[1], Savadogo Aly[1]

[1]Laboratoire de Biochimie et d'Immunologie Appliquée (LABIA). UFR en Sciences de la vie et de la terre. Ecole Doctorale Sciences et Technologies. Université Ouaga I Pr Joseph Ki-Zerbo, 03 BP 7021 Ouagadougou 03, Burkina Faso.
[2]Laboratoire National de Santé Publique (LNSP), 09 BP 24 Ouagadougou 09, Burkina Faso.
[3]Laboratoire de Biologie Moléculaire d'Epidémiologie et de Surveillance des agents Transmissibles par les Aliments (LaBESTA). UFR en Sciences de la vie et de la terre. Ecole Doctorale Sciences et Technologies. Université Ouaga I Pr Joseph Ki-Zerbo, 03 BP 7021 Ouagadougou 03, Burkina Faso.

Abstract: This study deals with *Salmonella enterica* serovar Typhi and Paratyphi responsible of typhoid and paratyphoid fevers transmitted by environment and foods. Typhoid and paratyphoid fevers are systemic diseases caused by the bacteria *Salmonella* Typhi and *Salmonella* Paratyphi, respectively. Humans are the only reservoir for *Salmonella* Typhi (which is the most serious), whereas *Salmonella* Paratyphi also has animal reservoirs. Humans can carry the bacteria in the gut for very long times (chronic carriers), and transmit the bacteria to other persons (either directly or via food or water contamination). Although *S.* Typhi *and S.* Paratyphi are strictly adapted to humans, both serovars can remain viable in the environment, surviving in water and underlying sediment for days to weeks. Foods are susceptible to be contaminated and transport *Salmonella* include vegetable products such as lettuce. In developping countries, typhoid and paratyphoide fever were generally treat with using antimicrobial such as quinolones, and cephalosporin. Patients were not responding to the most available antibiotics of choice. Some patients, because of ignorance and lack of financial means, prefer street drugs, so they practice self-medication. Those practices can enhance the antibiotics resistances genes. As the ultimate solution for the prevention and eradication of paratyphoid fever, it is essential to improve sanitation such as the provision of safe water and food as well as enhanced public health awareness.

Keywords: *Salmonella* Typhi and Paratyphi, typhoid and paratyphoid fever, epidemiology, antibiotic resistance, environment, food.

Introduction

Salmonella enterica subsp. enterica, belonging to *Enterobacteriaceae*, is a gram-negative, zerotolerant, rod shaped, facultatively anaerobic bacterium. *Salmonella enterica* serovar Typhi (*S.* Typhi) and Paratyphi (*S.* Paratyphi A, *S.* Paratyphi B, *S.* Paratyphi C), the causative agent of typhoid and paratyphoid fever, is transmitted primarily by ingestion of contaminated food and water ; also their are an exclusive human pathogen and the cause of typhoid fever, a major global public health concern (Parry *et al*., 2002; Raffatellu *et al*., 2008; Crump and Mintz, 2010; Dougan and Baker, 2014; Wain *et al*., 2015). According to the World Health Organization (WHO) (2014), the annual toll of typhoid and paratyphoid fever reaches 20.6 million cases and about 223,000 deaths. Typhoidal *Salmonella* serotypes, such as Typhi and Paratyphi A, B and C, on the other hand, may initiate enteric fever. Especially, *S.* serovar Paratyphi A has recently begun to take over *S.* serovar Typhi as the main agent of enteric fever in many Asian countries (Teh *et al.*, 2014). Thus, global progressive increase of paratyphoid fever worldwide (Sharland *et al*., 2016) has turned into a main health problem, especially in developing countries such as African's countries, China and Pakistan (Richa and Kashi, 2016). Both *S.* Typhi and *S.* Paratyphi encode typhoid toxin, an unusual AB family exotoxin, which is largely absent from non-typhoidal *Salmonella enterica* serovars

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Somda Namwin Siourimè (Correspondence)
landsom60@yahoo.fr
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(Haghjoo and Galan, 2004; Spano *et al*., 2008). Previous studies have shown that administration of purified typhoid toxin to experimental animals can reproduce most of the pathognomonic symptoms of typhoid fever, thus placing this toxin at the center of the pathogenesis of this disease (Song *et al*., 2013). Unlike all known AB toxin family members (Beddoe *et al*., 2010; Merritt and Hol, 1995), typhoid toxin exhibits a unique *A2B5* organization with two enzymatically active ‘‘A’’ subunits, *PltA* and *CdtB*, linked to a homopentameric ‘‘B’’ subunit made up of *PltB* (Song *et al*., 2013). Typhoid toxin is targeted to cells by its *PltB* B subunit, which interacts with specific glycans on the surface, glycoproteins podocalyxin 1 (on epithelial cells) or *CD45* (on myelocytic cells) (Song *et al*., 2013). Recent studies have shown that typhoid toxin has unique binding specificity for human glycans (Deng *et al*., 2014; Galan, 2015; Yang and Song, 2016), which is consistent with the observation that typhoid fever occurs only in humans.

Salmonella carried by fresh produce irrigated with dirty water has been indicated as a vehicle for a growing number of enteric disease outbreaks (Jacobsen and Bech, 2012; Kusumaningrum *et al*., 2012). Use of feces-contaminated water to irrigate the produce has been reported to lead contaminating of soil and vegetables with *Salmonella* for an extended period of time (Ongeng *et al*., 2011). Consumption of vegetable contaminated are responsible of salmonellosis.

Interestingly, *Salmonella* can adhere to and invade a wide variety of cell types, from kidney epithelial cells to macrophages (Finlay and Falkow, 1990; Yang and Song, 2016). This pathogenic bacteria is one of the invasive bacteria that can induce the expression and up-regulation of several proinflammatory cytokines in human intestinal epithelial cell lines (Saarinen *et al*., 2002).

In developing countries, typhoid and paratyphoid fever were generally treat to using antimicrobial such as quinolones, and cephalosporin. Patients were not responding to the most available antibiotics of choice. Some patients, because of ignorance and lack of financial means, prefer street drugs, so they practice self-medication. Those practices can enhance the antibiotics resistances genes (Somda *et al*., 2017). It is now generally accepted that the main risk factor for the increase of resistance to pathogenic bacteria is the anarchic use of antibiotics. The aim of this study was to investigate epidemiology and antimicrobial resistance level of *Salmonella enterica* serovars Typhi and Paratyphi in environment and food.

I- Generalities on typhoid and paratyphoid fever

1. Definitions and characteristics

Typhoid and paratyphoid fever are afections caused by *Salmonella enterica* serovar Typhi and Paratyphi (A, B and C). It is a potentially severe and occasionally life-threatening febrile illness (Anna *et al*., 2016). Typhoid and paratyphoid fevers are distributed worldwide. They are endemic in low-hygiene developing countries (Asia, Africa, South America) and are rare and predominantly sporadic in developed countries (metropolitan France) where most cases are imported after a stay in an endemic area. Humans are the only source of these bacteria; no animal or environmental reservoirs have been identified. Typhoid and paratyphoid fever are most often acquired through consumption of water or food that has been contaminated by feces of an acutely infected or convalescent person or a chronic, asymptomatic carrier. Transmission through sexual contact, especially among men who have sex with men, has been documented rarely (Anna *et al*., 2016). The incubation period is usually 8 to 14 days but can vary from 3 days to 1 month (Crump and Heyderman, 2015). Typhoid fever typically manifests as symptoms associated with prolonged fever associated with headache, abdominal pain and other gastrointestinal symptoms (Imanishi *et al*., 2014). Clinical expression may also be atypical or moderate or even unapparent especially in endemic countries. Paratyphoid fevers are generally less severe than typhoid fever.

2. Mode of transmission

Transmission is via the fecal-oral route. Overwhelmingly, transmission is indirect by the ingestion of water and food contaminated with feces and/or urine. Transmission by direct person-to-person contact can occur but is rare (Bakers *et al*., 2011). Chronic carriers transmit typhoid by contaminating food as a consequence of unsatisfactory hygiene practices (WHO, 2014). Little is know about chronic paratyphoid carriage.

Food was identified as the source of paratyphoid A infection following an outbreak among travellers returning from Nepal (Woods *et al*., 2006; Bakers *et al*., 2011; Meltzer *et al*., 2014). To explain the higher incidence of paratyphoid in returned travellers, authors of a Swedish study of enteric fever (typhoid fever or paratyphoid fever) surmised that travellers are more likely to be exposed to food from street vendors infected by *S.* Paratyphi than to persons carrying *S.* Typhi (Ekdahl *et al*., 2005). Imported foods (sauerkraut, ham, sausage, broiler chicken, eggs) have also been associated with outbreaks of typhoid (Katz *et al*., 2002).

Although *S. Typhi and S.* Paratyphi are strictly adapted to humans, both serovars can remain viable in the environment, surviving in water and underlying sediment for days to weeks (Chandran *et al.*, 2015). Foods susceptible to transport *Salmonella* include vegetable products such as lettuce. The fresh produce consumption is encouraged because of its health benefits; however, fresh produce can be contaminated with human pathogens in any stage of the food supply chain, which increases the risk of foodborne outbreaks (Lynch *et al*., 2009; Ge *et al.*, 2013). Hygienic conditions are needed for these fresh produce for consumption to avoid contamination.

3. Pathogenesis and virulence of *Salmonella*

Salmonella is an invasive enteropathogenic bacteria. If contaminated water or food is swallowed, they reach the small intestine where they multiply (Crump *et al*., 2015). They destroy the brush border of the intestinal cells and then penetrate the epithelial cells by invagination of the membrane. The bacteria continue their intracellular multiplication inside vacuoles. Intestinal invasion by *Salmonella* induces an inflammatory response causing ulcers responsible for the secretion of water and electrolytes (Garai *et al*., 2012). *Salmonella* has an arsenal of virulence factors that play a role at different stages of the infectious process. To interact with the host cell, *Salmonella* will involve attachment factors (*mis*L genes), penetration and intracellular survival (*orf*L genes), virulence factors combine those not specific to pathogenic serovars represented by: lipopolysaccharide (LPS), fimbriae or pili and the flagella, and those said to be specific to pathogenic serotypes whose essential genetic support is constituted by islands of pathogenicity, however virulence plasmids (*spv*RABCD) and phages have shown a role in this virulence (Hacker & Kaper, 2000; Guiney and Fierer, 2011; Smith *et al.*, 2012). Non-specific virulence factors play a role in attachment, persistence and intestinal and systemic colonization (*inv*A), mucus crossing (*pip*D), and good internalisation by macrophages in the peritoneal cavity (*orf*L). These roles in virulence studied in vivo on cell cultures, and in vitro on animal experimental models is controversial little known. The major contribution in the virulence of *Salmonella* is linked to the various tools and mechanisms of virulence codified by islands of pathogenicities constituted mainly by: type III secretion systems (TTSS), effectors secreted by TTSS, fimbriae, of iron capture (Garai *et al.*, 2012).

In typhoid salmonellosis, bacteria reach the mesenteric lymph nodes and then multiply before part of the bacterial population passes into the lymphatic stream and then bloodstream causing systemic infection. (**Figure 1**).

Acording to Guiney and Fierer (2011), the *spv* locus is strongly associated with strains that cause non-typhoid bacteremia, but are not present in typhoid strains. The *spv* region contains three genes required for the virulence phenotype in mice: the positive transcriptional regulator *spvR* and two structural genes *spvB* and *spvC*. *SpvB* and *spvC* are translocated into the host cell by the *Salmonella* pathogenicity island-2 type three secretion system. However recent studies notified that *Salmonella* Typhi and Paratyphi arbored spvR genes, this may justify the possibility of transferring genes from non-typhoid Salmonella strains to typhoid strains via the environment (Somda *et al*., 2017).

4. Epidemiology of *Salmonella* Typhi and Paratyphi

Salmonella is one of the leading causes of food-borne diseases worldwide. Typhoid and paratyphoid fevers are reported in both developing and developed countries.

An estimated 22 million cases of typhoid fever and 200,000 related deaths occur worldwide each year; an additional 6 million cases of paratyphoid fever are estimated to occur annually. Each year in the United States, approximately 300 culture-confirmed cases of typhoid fever and 100 cases of paratyphoid fever are reported (Anna *et al*., 2016). More than 80% of reports of typhoid fever and superior 90% of reports of paratyphoid fever caused by *Salmonella* Paratyphi A are of travelers to southern Asia (Crump and Mintz, 2010; Johnson *et al.*, 2011). Other areas of risk include East and Southeast Asia, Africa, the Caribbean, and Central and South America (Anna *et al*., 2016).

In 2010, typhoid fever incidence rates ranged from inferior 0.1 cases per 100,000 population in Central and Eastern Europe and Central Asia, to 724.6 cases per 100,000 population in Sub-Saharan Africa. In the same year, paratyphoid incidence rates ranged from 0.8 cases per 100,000 population in North Africa/Middle East to 77.4 cases per 100,000 population in Sub-Saharan Africa and South Asia (Buckle *et al*., 2012). In 2010, enteric fever was responsible for an estimated 190,000 deaths and more than 12.2 million disability-adjusted life years.

In the industrialized countries, most typhoid fevers are contracted during a trip abroad. In France, between 2004 and 2009, 615 cases of typhoid fever were reported, 176 cases of paratyphoid fevers to *S.* Paratyphi A, 82 to *S.* Paratyphi B and 6 to *S.* Paratyphi C. In 91% of the cases, fever Typhoid was acquired during a stay in endemic areas, mainly in Africa and the Indian subcontinent. This proportion is 88% for paratyphoid fevers (Aubry and Gaüzère, 2015).

In Democratic Republic of Congo, epidemic's typhoid fever occurred in Kikwit in 2011-2012, causing 2065 cases in 13 weeks with 154 complications and 31 deaths (Aubry and Gaüzère, 2015). In Gabon, it has been reported that *Salmonella* Typhi and Paratyphi reaches 46% of strains isolated from diarrheal diseases (Okome-Nkoumou *et al*., 2001). In Mali and Burkina Faso, a study showed a high rate of typhoid *Salmonella* isolated from people suffering from diarrheal diseases (Timbiné, 2014). In Lagos, Nigeria, the study of 235 stools isolated 42 strains of *Salmonella* including 19 *Salmonella* Typhi (45.2%), 7 *Salmonella* Paratyphi (Akinemi *et al*., 2007).

In Burkina Faso, infections due to *Salmonella* remain a concern for children. In 2011, one study reported a lower prevalence of *Salmonella* in children younger than 5 years, in 2.3% (Nitiema *et al*., 2011). Two years later, another study reported an overall prevalence of 9% (Bonkoungou *et al.*, 2013). In 2014, a study conducted in rural areas in children under five showed an overall prevalence of 6% (Dembélé *et al*., 2014). This may suggest that infections caused by these enterotropathogens are increasing in children in Burkina Faso. In 2016, a study carried out in the three countries of the sub region showed that the serotype Paratyphi B was predominantly 42% (20/48), 35% (22/63) and 30% (6/20); followed by Typhi 13% (6/23), 22% (14/23) and 15% (3/23), followed by Paratyphi C 19% (9/48), 11% (7/63) and 20% (4/20) followed by Paratyphi A 6% (3/48), 11% (7/63) and 10% (2/20) serotypes respectively for the Burkina Faso, Mali and Niger (Bawa *et al*., 2016).

5. *Salmonella* Typhi and Paratyphi in environment and food

Since the early recognition of the role of water in the transmission of typhoid fever Steele *et al*. (2016), it has been demonstrated that improvements in access to clean water and improved sanitation result in dramatic reductions in typhoid fever–related death rates in many settings. It is clear that as access to safe water and improved sanitation are being developed, this should dramatically reduce the exposure to *S.* Typhi and *S.* Paratyphi bacteria in the environment and, thus, enteric fever disease.

In this numerous of foodborne infections, salmonellosis is the most frequent infection with a great number of serotypes and intoxications caused with lethality in 1% cases (Ao *et al.*, 2015). The increase in food-borne outbreaks may be attributed to two factors: the improved surveillance of *Salmonella* contaminations of fresh produce over the years and the growing consumption of fresh produce due to a shift in people's eating habits toward healthier lifestyles where more vegetables and fruits instead of meat are consumed. It is predicted that consumption and production of fresh produce will continue to rise (Dubowitz *et al*., 2014; Li *et al*., 2014). Given that irrigation water can be a source of *Salmonella* contamination of vegetables, the prevention of outbreaks could be accomplished by consistent monitoring of the presence of *Salmonella enterica* in water supplies.

Among the most foodborne infections with *Salmonella*, the lettuce takes up a significant place. *Salmonella* Paratyphi has long been reported as a common cause of foodborne gastroenteritis (Hur *et al*., 2012). In Burkina Faso, rains shortage leads to the practice of the farming irrigated by barrage or waste water (**figure 2**) (Somda *et al*., 2017). Due to the vicinity, waste water from university hospital Yalgado Ouédraogo, the biggest hospital in the country is released into a canal which flows nearby the dam. It is the case of the truck farmer production. The dirty water in particular those of the stoppings and the gutter ones are used for the vegetables irrigation (Somda *et al*., 2017). Theses vegetables mainly lettuce are generally contaminated by the enteric bacteria in particular *Salmonella* Typhi and Paratyphi from this contaminated water (Traoré *et al*., 2015). According to Petterson *et al*. (2010), the consumption of the fruit and vegetables constitutes a factor of potential risk of infection by bacteria enteropathogens such as *Salmonella* and *Escherichia coli* O157. Cases of food poisoning related to the contaminated vegetable ingestion were identified a little everywhere in the world (Wendel *et al*., 2009). Among the factors generally implicated in the contamination of vegetables appears the irrigation water (Koffi-Nevry *et al*., 2011). A recent study showed high prevalence of *Salmonella* from lettuce in Burkina; the distribution of serotypes of *Salmonella* from lettuce samples comprised *Salmonella* Typhi 1%, *Salmonella* Paratyphi 50% (Somda *et al*., 2017). These finding supports the well-documented role of the presence of *Salmonella* in waste water and animals feces in environmental contamination in Burkina Faso as in some others developing countries (Kagambèga *et al.*, 2013; Traoré *et al*., 2015).

Food histories are generally only collected if the case is suspected to have acquired their illness locally and if there is no history of international travel for them and all of their household type and other contacts;

generally foods are non typhoidal *Salmonella* reservoirs.

Figure 2: A= Canal located upstream of the Tanghin reservoir, B= Canal behind the Yalgado Ouedraogo Hospital (Pics Somda, 2015).

II- Antibiotics used to treat typhoid and paratyphoid fevers

In the treatment of diarrhea, the most important is the equilibre maintenance of the hydroelectric. The other treatments are complementary, including antibiotic therapy in of diarrhea of bacterial origin. Naturally, all antibiotics used agains Gram- bacteria were efficient agains *Salmonella* (**figure 3**). Generally all wild strains of *Salmonella* are susceptible to antibiotics. Nowadays many *Salmonella* serovars have developed resistance to antibiotics.

1. Factors favoring the development of resistance

Several factors favor the development of resistance:
- The treatment of a viral disease (Rotavirus diarrhea) by antibiotics, whereas these are effective only on bacteria. In the case of inappropriate treatment, antibiotics attack the bacteria of the natural flora of the organism, causing them to develop resistance mechanisms and, during a bacterial infection, these bacteria of the flora by conjugation can transfer their resistance genes to pathogens bacteria;
- An inappropriate choice of antibiotic is therefore ineffective against the bacteria involved
- A poor take of the treatment by the patient (stop too fast, forget certain catches, substitution by another inadequate antibiotic)
- Resistant bacteria will be able to spread by direct contact with a person carrying the treated infection. This leads to major problems in hospitals, particularly in "at-risk" units, in long-stay facilities or retirement homes where fragile patients are present in a small space (Mainardi *et al*., 1996; WHO, 2014).

According to World Health Organization (WHO), the phenomenon of resistance to antibiotics has become an increasingly important public health problem in the world. When bacteria become resistant, the disease is likely to persist and may become potentially fatal. This also entails:
*an increase in the prescription of antibiotics;
*a reduction in the range of therapeutic choices (limited choice of antibiotics);
*longer lengths and hence costs of hospitalization;
*increased morbidity and mortality of infected patients.
- The environment plays a role in the spread of resistance; antibiotics used in farming in fish farming or in arboriculture are found in native form or metabolites in soils and waters or they maintain a selection pressure (Kummerer *et al*., 2009). Manure application techniques, or even sludge from sewage treatment plants, maintain this phenomenon (**figure 4**). Effluents and sewage treatment plants (STEP) are considered to be genuine "hot spots" that promote horizontal exchanges of genetic materials due to high bacterial concentrations, the presence of bacteria of different origin (human, animal, environmental), in an environment rich in organic matter, and in the presence of hundreds of antibiotic molecules or their metabolites (Baquerau *et al*., 2008).

2. *Salmonella* Typhi and Paratyphi resistant to antibiotics

Antibiotics using to treat infectious diseases, has conducted bacteria to develop the defenses against their. Bacteria are living beings, they evolve and their genes change to cope with changing situations. As a result, they are able to adapt to antibiotics, sometimes very quickly after their introduction. They become "resistant" and the treatment therefore ineffective. Some bacteria are resistant to several antibiotics, they are called "multiresistant". The resistance of bacteria can be natural or acquired. Bacteria have developed mechanisms to resist antibiotics. Four main mechanisms explain the resistance:
- A change in the site of antibiotic fixation;
- The synthesis of antibiotic-inactivating proteins;

- A decrease in the permeability of the bacterial wall which leads to an insufficient concentration of antibiotic inside the bacterium;
- Active efflux of antibiotics.

Frequent use of classical first-line antimicrobials such as ampicillin, chloramphenicol and co-trimoxazole has led to the emergence and global spread of multidrug resistant (MDR) *S.* Typhi strains in the 1970s and 1980s (Rowe *et al*., 1997; Wain *et al*., 2003). As a result, third-generation cephalosporins and fluoroquinolones (FQs) were advocated by the WHO (WHO, 2003). Recently, resistance to third-generation cephalosporin in *S.* Typhi strains has also been reported from other countries (Al Naiemi *et al*., 2008; Kumarasamy and Krishnan, 2012). Azithromycin has been used as an empirical drug for treatment of uncomplicated typhoid fever, but sporadic reports of resistance to azithromycin pose a problem for selecting suitable antimicrobials for typhoid treatment (Rai *et al.*, 2012; Hassing *et al*., 2014). Multidrug resistance in *S.* Typhi is conferred by the presence of resistance genes carried especially on the IncHI1 plasmids, but chromosomally translocated MDR locus has been reported in recent studies (Holt *et al*., 2011; Wong *et al*., 2015). FQ resistance in *S.* Typhi can be attributed to mutations in the quinolone resistance-determining regions (QRDRs) of topoisomerase genes or acquisition of plasmid mediated quinolone resistance (PMQR) genes (Chau *et al*., 2007; Geetha *et al*., 2014; Das *et al*., 2016). Global emergence of drug resistant *S.* Typhi isolates has been shown to be mediated by the dissemination of a specific lineage H58 across Asian and African countries (Wong *et al*., 2015).

Resistant bacteria are transferred from foods and animals to man via the food chain. After the ingestion of contaminated foods, commensal and pathogenic bacteria in the gut can exchange mobile genetic elements mediating resistance. Recent epidemiological studies have revealed that human infections with resistant *Salmonella* spp. are associated with prolonged illness, an increased risk of invasive disease and hospitalization, and excess mortality (Mąka and Popowska, 2016).

A recent study in Burkina Faso, from 94 *Salmonella* Typhi and Paratyphi in lettuce showed that all isolates were susceptible to imipenem, gentamicin, ceftriaxone, cefotaxime and ciprofloxacin. In contrast, a low antimicrobial resistance to tetracycline 22 %, amoxicillin+clavulanic, amoxicillin, ampicillin, chloramphenicol, nalidixic-acid and trimethoprime-sulfamexazol respectively 7 %, 6 %, 5 %, 4 %, 3 %, and 2 % was observed (Somda *et al*., 2017).

III- Prevention :

1. Foods and water

Safe food and water precautions and frequent handwashing are important in preventing typhoid and paratyphoid fever. Although vaccines are recommended to prevent typhoid fever, they are not 100% effective; therefore, even vaccinated travelers should follow recommended food and water precautions. For paratyphoid fever, these precautions are the only prevention method, as no vaccines are available (Anna *et al*., 2016). For example using ultraviolet C irradiation and chemical sanitizers were very efficient to disinfected lettuce and fresh vegetable. Recent studies showed that ionizing radiation, such as gamma ray and electric beam, has been frequently examined for its potential of inactivating the internalized pathogens in fresh produce (Chimbombi *et al*. 2011; Ge *et al*., 2013) and it was shown as an effective physical disinfectant to inactivate the human pathogens with low fluency in food without generating toxic hazards or making food radioactive, which has been confirmed by World Health Organization. Compared with the ionizing radiation methods, the application of ultraviolet light has grown steadily in various fields such as water, wastewater, aerosol, surface and food as its germicidal effect was firstly described by Ge *et al.* (2013).

In case of suspicion all identifiable contacts should:
- receive information about the disease, mode of transmission and the importance of hygiene, in particular hand washing before eating and preparing food, and after going to the toilet;
- be advised to exclude themselves (see Isolation and restriction below) and present to their medical practitioner should symptoms develop within the month following contact with an infectious case or their own return from a typhoid/paratyphoid endemic area.

2. Vaccine

There has been interest in typhoid fever vaccination for several decades, and although there has also been progress in developing control solutions for typhoid, this progress has been somewhat stilted in many regions.

It is essentially based on two new anti-typhoid vaccines:
- Oral vaccine Ty21a in the form of capsules and oral suspension,
- Injectable polyosidic Vi vaccine (Typhim Vi®, Typherix® Vaccine) these vaccines can be used in children over 2 years of age and adults.

Indications for vaccination:

- School-aged and / or pre-school children in areas where typhoid fever is a problem
Public health in these age groups,
- Travelers traveling to destinations where the risk of typhoid fever is high.

Vi polysaccharide vaccine is well tolerated. It is prescribed by subcutaneous or intramuscular injection. He ensures rapid and durable protection for 3 years, revaccination of children every 3 years. He protects only against *S.* Typhi.
Vaccination against typhoid fever is also recommended for the control of outbreaks epidemics. Immunization programs against typhoid fever must be implemented in other efforts to combat the disease, including health education, quality of water and sanitation and training of health professionals in the diagnosis and treatment of treatment (Aubry and Gaüzère, 2015).

Conclusion

Safe food and water precautions and frequent handwashing are important in preventing typhoid and paratyphoid fever. Although vaccines are recommended to prevent typhoid fever, they are not 100% effective; therefore, even vaccinated travelers should follow recommended food and water precautions. Furthermore, the guidelines and training for treatment of enteric fever cases in Africa are sorely needed to help mitigate the inappropriate use of antimicrobial treatment. Classic water safety and access to sanitation development remain powerful tools for the control of typhoid fever, yet the huge economic costs and long timelines are unlikely to provide a short- to middle-term solution. As the ultimate solution for the prevention and eradication of paratyphoid fever, it is essential to improve sanitation such as the provision of safe water and food as well as enhanced public health awareness.

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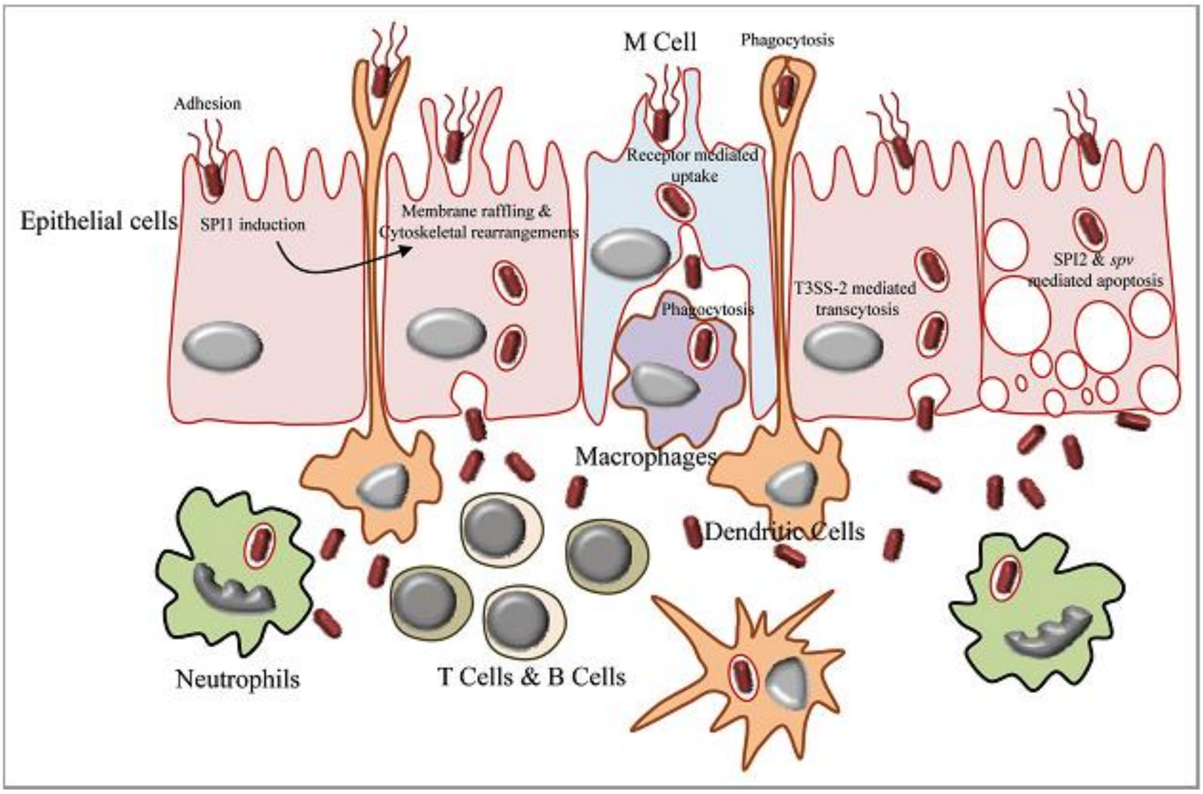

Figure 1 : Breaching of gut epithelia by *Salmonella*. The mode of entry of *Salmonella* in gut lumen varies according to type of cell encountered on the gut epithelium. The M cells take up the bacteria by means of receptor mediated endocytosis, whereas dendritic cells engulf them by phagocytosis. The membrane of epithelial cells is modified by

the action of SPI1 to facilitate the entry of bacteria. Once inside the gut lumen, Salmonella is being taken up by macrophages, T cells, B cells, neutrophils, etc. (Garai *et al*., 2012).

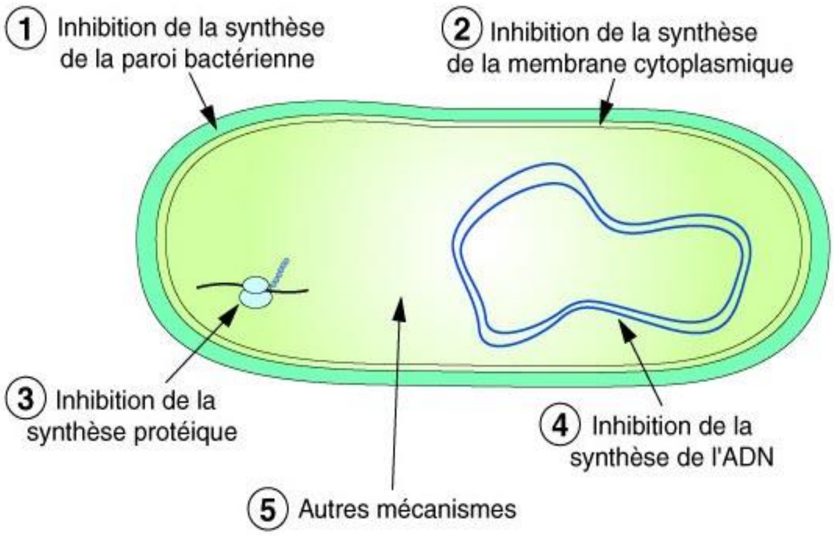

Figure 3: Sites and modes of action of different classes of antibiotics (www.123bio.net/cours/antibio/modedaction.html) consulter le 10/02/2016.
1: β-Lactamines, (paroi)
2: Polypeptides, aminosides et macrolides (cytoplasmique membrane)
3: Tetracyclines, (ribosomes)
4: sulfamides, (DNA)
5: quinolones, fluoroquinolones (RNA polymerase).

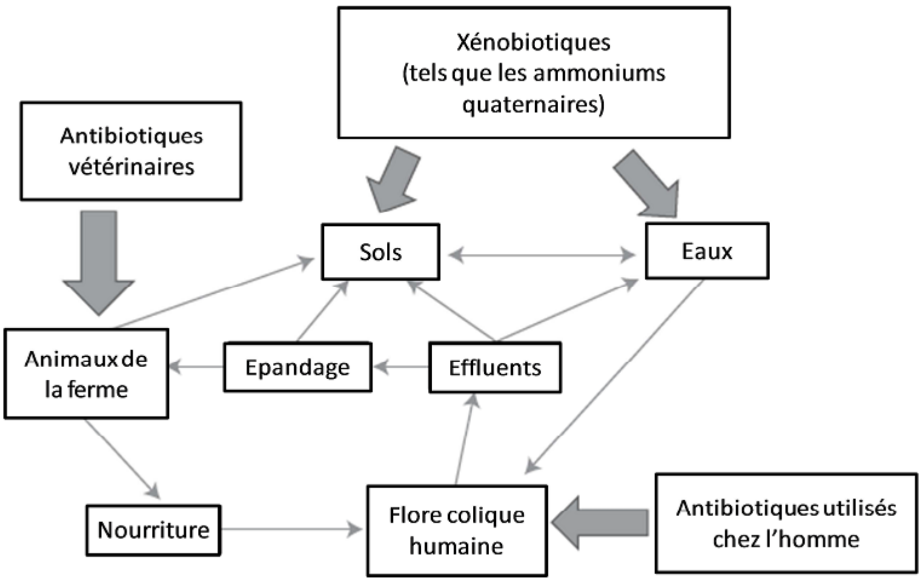

Figure 4: Flow of resistance genes in different ecosystems.