CHAPTER 1:

Introduction

When the first cholera cases due to *Vibrio Cholerae* El Tor were reported in KZN in August 2000, few would have imagined that it would develop into one of the largest outbreaks yet recorded in South Africa. Coincidentally, the cholera epidemic struck at a time when the privatisation drive for water supply services was in progress. Several reports linked cholera to the water privatisation, and that the communities affected were mostly those who could not afford to pay for water services thus resorting to the use of natural water sources (Nhlapo-Hlope, 2001; Ka-Min, 2000). This popular thinking pointed to natural water sources as being a possible environmental reservoir for cholera organisms, implying that a direct link exists between the use of natural water sources, and the spread of cholera.

Although *Vibrio cholerae* is known to occur in diverse aquatic systems, there is limited knowledge about its ecological interaction with abiotic environmental factors. For that reason, an environmental approach is essential for evaluating the role of *Vibrio cholerae* in human disease. Cholera incidence is influenced by a changing micro-ecology of *V. cholerae*, vulnerability of people through exposure to health risks, resistance to infection through immunity and/or nutritional status, and environmental, socio-economic and behavioural changes (Collins, 2003). Thus in a given environment *Vibrio cholerae* may be establishment as an endemic or a recurrent pathogen. These two modes suggest the possible establishment of at least a transient environmental reservoir for cholera in the region affected (Shapiro *et al.,* 1999).

Cholera has long been recognised as a disease that reflects a complicated transmission pattern, in that multiple factors may play a role in the spread of the disease. Factors implicated in one area as being important in the spread of cholera may not be significant in another. Figure 3.1 outlines the relationships between the cholera pathogen, and the various factors that can act as possibly routes for transmission. A detailed discussion of these factors is given in more detail in Chapter 2: 2.3.4.

Historical records describe the disease cholera since the pre-Christian era affecting civilizations in Indo-Asia, China, the Middle East and Europe; where an array of myths surrounded the disease. The earlier interventions, proposed in an era of limited knowledge about infectious diseases, though well meaning, caused more harm than good. Modern medicine has taken great strides in the treatment and prevention of infectious diseases, yet even in this age of advanced technical medical interventions, cholera still instils a sense of fear in the communities it affects. Despite the abundance of scientific information on the disease and how to control it with the simple intervention of Oral Re-hydration Therapy (ORT), cholera still evades prevention.

Since 1970, when the seventh cholera pandemic first crossed over to the African continent, South Africa had experienced few imported cholera cases from neighbouring countries of Mozambique, Malawi, Angola and Zambia to name a few (Barua, 1992; WHO, 2000). Most of these cases are thought to be a consequence of migrant labourers coming to seek employment in South African mines or plantations (Isaäcson, 1974). As such, the Department of Health (DOH) of South Africa, documented cholera cases reported from all the provinces from 1980 – 2000 (DOH-Statistical Notes, 2000). According to the aforementioned record, the annual cholera cases in Kwa-Zulu, Natal (KZN) during 1980 – 2000 were the lowest in 1980, with only one cholera case, and highest in 1982 with 12 263 cholera cases.

Cholera made an unforeseen appearance on the eastern coast of South Africa in the province of KwaZulu, Natal (KZN) in 2000. Having started in August 2000, from the more urban centres of the coastal region of the province, cholera proceeded unabated to the interior of the province where no community was spared from the scourge. Despite prompt medical intervention, health education and media awareness campaigns, cholera continued to spread throughout the province of KZN. By March 2004, the official statistics of cholera cases in KZN as per Cholera Database records, stood at 158 895 cases (Dept-KZN Health, 2000). The death toll as reported in the Cholera Database was 575 persons that translated to a percentage case fatality rate of 0.36%; the lowest compared to the previous epidemics recorded in South Africa (Kustner *et al*., 1981; Küstner and du Plessis, G. 1991). An interesting feature of the epidemic is that 99% of the cases recorded by the central and provincial Departments

of Health during the peak of the epidemic were all from KZN. The remaining eight provinces reported only sporadic outbreaks or were completely spared from the disease (DOH-a, 2002).

The question then was, what were the factors that contributed to cholera reaching to epidemic proportions in KZN? This study therefore sought to understand the outbreak and the factors that possibly contributed to the spread of the cholera epidemic in KZN over the period 2000-2004. The study also called for the issues associated with the communities affected by cholera to be determined by analysing the complex and dynamic interaction of biological, socio-economic, and environmental factors over time and space. The nature of the study was such that it called for a multi faceted design to involve, not just understanding the societal aspect and trend of the disease, but also its spatial characteristics. In addition to the knowledge of the microbiology and ecology of the disease, GIS (Geographical Information System) facilitated the comparison of the disease trends and the implicated factors on a spatial level in order to determine the possible role(s) played by the different environmental and socio-economic parameters.

More specifically, the aim of the study was to investigate the possible role of the natural environment i.e. temperature, rainfall and humidity as the primary factors that influenced the spread of cholera outbreaks in KZN; on the basis of its (KZN) unique climatic conditions as compared to other areas of the Republic of South Africa (RSA). The other socio-economic and demographic factors were considered as factors that enhanced the spread of the disease. Thus a hypothesis was put forward that both the climatic conditions and socio economic variables like sanitation, clean water supply, population density, health service delivery etc., contribute to the vulnerability of communities and assist in the spread of cholera in KwaZulu-Natal. As such, the objective of the study was to contribute in the identification of factors that can be used as principles in pre-empting possible cholera outbreaks within the region. Overall, the \study demonstrated the usefulness of health data within the fraternity of water resource management in addressing issues linked to the possibilities of waterborne diseases like cholera.

CHAPTER 2:
Literature Review

"On the bed lay an expiring woman…presenting an attitude of death which…I never saw paralleled in terror…On the floor, extended on a palliasse… lay a girl of slender make and juvenile height, but with a face of a superannuated hag. She uttered no moan, gave expression of no pain, but she languidly flung herself from side to side …The colour of her countenance was that of lead- a silver blue, ghastly tint; her eyes were sunk deep into the sockets, as though they had been driven an inch behind their natural position; her mouth was squared; her features flattened; her eyelids black, her fingers shrunk, bent and inky in their hue. All pulse was gone at the wrist, and a tenacious sweat moistened her bosom. In short, Sir, that face and form I can never forget, were I to live beyond the period of man's natural age."
Dr. W.B. O'Shaughnessy's description of a cholera patient in 1831 (Cosnett, 1989).

2.1 Introduction: Cholera pandemics

Cholera is an ancient disease described by Hindus, Chinese, Arabs, Greeks and, Romans since the pre-Christian era (Russell, 1925). Documented cholera dating back to 1817, acknowledge all cholera pandemics to have originated from India, where the infection has probably been entrenched since times immemorial (Swaroop and Pollitzer, 1955; Blake, 1994). The geographical distribution harbouring the endemic foci has its centre in Bengal, in the Indian subcontinent, with a consistent and well-marked seasonal variation in individual parts of India (Swaroop and Pollitzer, 1955). The early pandemics revealed no apparent pattern of periodicity, though records show that the intervals between pandemics were no less than 5 years (Russell, 1925). Cholera, since first documented, has been around the world in seven pandemics, the latest (seventh), which is still in progress, is purported to have originated in Sulawesi, Indonesia in 1961 (Fig. 2.1). When the seventh cholera pandemic began, it was initially limited to areas in Asia and the Indian subcontinent, and later spread into the former USSR and Middle East (WHO, 2000).

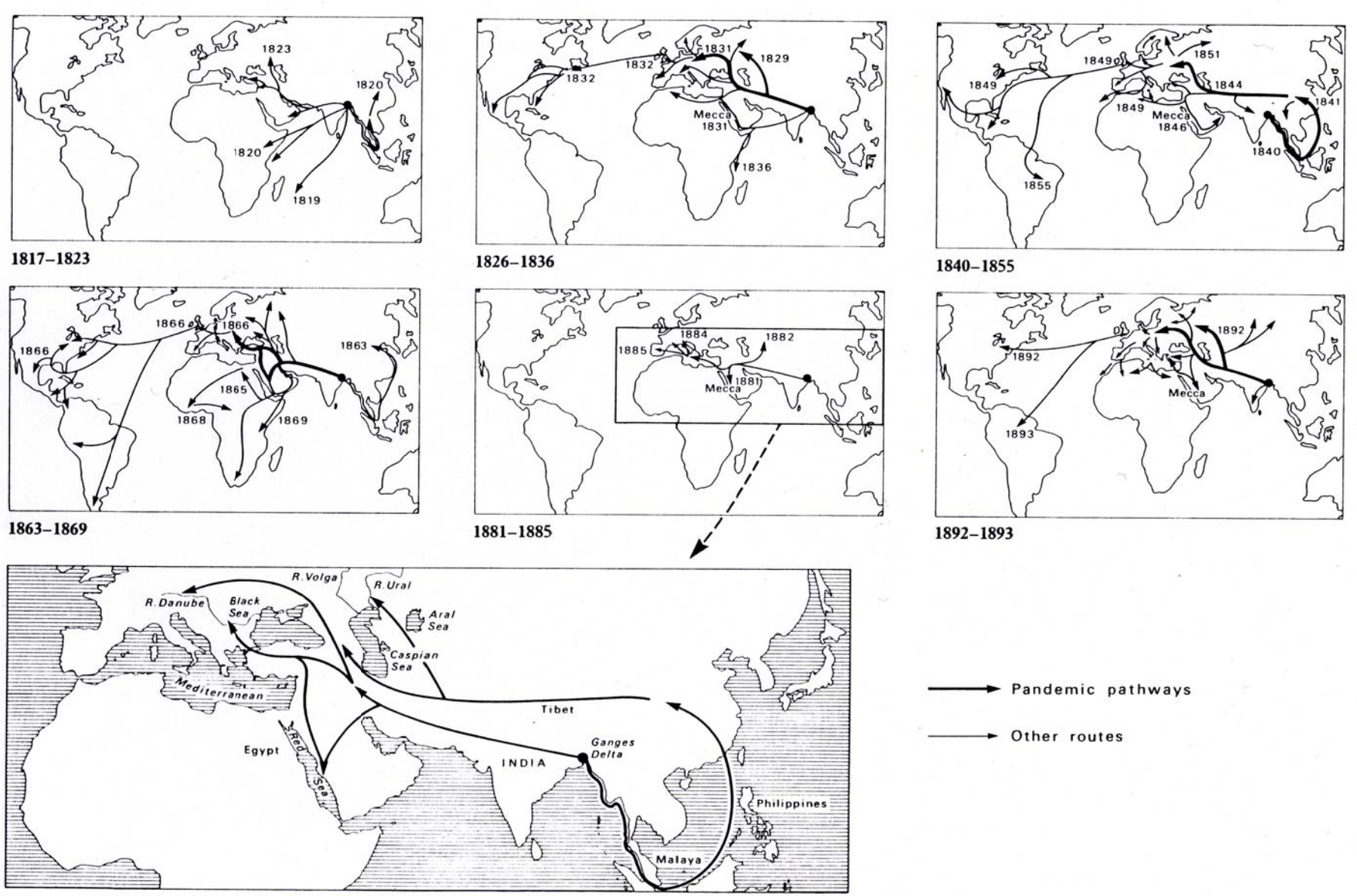

Fig 2.1. World maps of six cholera pandemics in the nineteenth century showing the main pathways followed (Adapted from: A.D. Cliff and P. Haggett. 1988. Cholera in London. In: Atlas of Disease Distributions. Analytical approaches to epidemiological data. p5-11. Blackwell Publishers. U.K.)

2.1.1 Cholera in Africa

During the 19th century five of the pandemics affected North Africa. Pilgrims returning from Mecca introduced cholera into Egypt, and the infection subsequently spread along the river Nile, into Upper Egypt and Sudan. Egypt had an outbreak of 33 000 cholera cases and 20 500 deaths in 1947 (Barua, 1992). The outbreaks of cholera in West Africa that occurred between 1868 and 1894 were thought to have followed the introduction of the disease by caravans (Swerdlow and Isaäcson, 1994). In 1970 cholera struck West Africa again, which had not experienced the disease for more than 100 years. The disease quickly spread to a number of countries and eventually became endemic in most parts of the African continent (WHO, 2000a). As the pandemic navigated its way into Africa, there were two main epidemic foci, in southern and eastern Africa (Zambia, Mozambique, Malawi and Angola) and in West Africa (Barua, 1992).

The West African epidemic, began in Guinea in August 1970 and by September of the same year, over 20 000 cases and 60 deaths were reported (Goodgame and Greenough, 1975; WHO, 1991). Initially, cases were concentrated along coastal regions and subsequently spread to the other regions by the travels of fishermen and boatmen. Between September 1970 and February 1971, epidemics occurred in Sierra Leone, Liberia, Cote d'Ivore, Ghana, Togo, Benin, Nigeria, southern Cameroon and Mali. Chad and northern Cameroon, with their desert like regions were also affected by cholera, proving that cholera could spread in drier areas (WHO, 1991). At the same time epidemics of cholera thought to have originated from the Middle East spread into Libya, Tunisia, Algeria, Djibouti, Ethiopia and Somalia. By 1971, 25 countries had reported cases of cholera to the WHO, with an overall case fatality rate of 16%. The number of deaths from cholera in Africa represented 73% of the global total for that period (Crowcroft 1994).

Since the 1970s, cholera has occurred among refugees and displaced persons in Somalia, Ethiopia, Sudan, Malawi and Mozambique. Such groups of people are particularly at risk because of overcrowding, inadequate sanitary facilities and water supplies as well as malnutrition (Moren et al., 1991; Toole and Waldman, 1990). Cholera continued to be reported by many African countries well into the 1980s with

Malawi doing so in October 1989. During the same period sub-Saharan Africa reported nearly three quarters of the global cholera cases. Countries close to South Africa, which were also affected at the time, were Angola, Mozambique and Zambia (Anonymous, 1990).

In 1991, there was a resurgence of cholera in many parts of Africa with 21 countries reporting outbreaks of cholera, the highest number since the start of the seventh pandemic on the continent in 1970. The massive outbreak of the El Tor strain of cholera among Rwandan refugees in Goma, Zaire, resulted in 70 000 cases and 12 000 deaths in July 1994 (Sánchez and Taylor, 1997). By 1996, cases of cholera notified to WHO from Africa were accounting for 93% of all reported cholera cases worldwide, with a case fatality rate of 5.7% (WHO, 1997).

Zambia experienced widespread intermittent cholera epidemics in 1991 (13 154 cases), 1992 (11 659 cases), 1999 (11 327 cases) and in 2003/2004 (2 529 cases), (CDC, 2004). In response to the 1999 cholera outbreak, there was a widespread campaign to promote in-house chlorination of drinking water supplies as well as promoting microbial safe-water storage strategies (CDC, 2004). The year 2000 saw 56 countries officially notifying the WHO of cholera, with 27 of these countries belonging to the African continent. Africa's cholera cases still accounted for the highest global total of 87%. The year 2000 witnessed major cholera outbreaks in the Comoros, Djibouti, the DRC, Mozambique, Somalia, South Africa (Kwa-Zulu-Natal) and Madagascar, which was cholera free until 1999 (Duval *et al.*, 1999). The statistics of cholera in South Africa for the year 2000 ranked third (19 667 cases) after Madagascar (29 083 cases) and the DRC (14 995 cases), though South Africa had a comparatively low case fatality rate (CFR) of 0.35% (WHO, 2001a). Overall, epidemic cholera continues to be reported every year since it was introduced in the 1970s.

2.2 The history of cholera in South Africa

Cholera outbreaks made their mark in South Africa in the 1970s, about the same time the disease was considered endemic in neighbouring Angola, Malawi, Mozambique and Zimbabwe, and was fast spreading southwards through the African continent

(Küstner *et al.,* 1981; Isaäcson, 1986). It was inevitable for cholera outbreaks to cross into South Africa considering that migrant labourers seeking employment especially in the South African mining industry came from the cholera endemic neighbouring countries (Isaäcson *et al.,* 1974). This migrant labour force was well positioned to introduce cholera into rural areas of South Africa, due to the high labour turnover rate (Isaäcson, 1986).

Endemicity in these southern neighbouring countries warranted the establishment of a surveillance system to follow up on all reported cholera cases in South Africa (Isaäcson *et al.,* 1974). The asymptomatic cholera cases identified in a Transvaal gold mine after the introduction a large-scale surveillance programme in 1974; were the earliest official records of cholera in South Africa since the onset of the seventh pandemic (Isaäcson *et al.,* 1974). These reported cases could however, hardly be considered an epidemic, at best it was an outbreak that was quickly contained. Consequently, within two months the source of the cholera outbreaks was recognized and swiftly contained by instituting a sewage surveillance system using Moore pads (Isaäcson *et al.,* 1974). The surveillance system put in place managed to isolate *V.cholerae* from sewage prior and during an outbreak of cholera. In addition to the sewage system being recognised as a source of cholera organisms, another transmission route was thought to be due to contamination of drinking water kept in open containers on the floor of acclimatization centres. This was observed during the Transvaal (Gauteng) gold mine outbreak, whereby it was hypothesized that *Vibrio cholerae* O1 might have been carried by perspiration from the perianal region of asymptomatically infected persons to the floor of the acclimatization room and subsequently infect other miners directly or possibly indirectly via the humidifying system (Isaäcson *et al.*, 1974).

Subsequent to the cholera reports from the gold mines in the 1970s, there were cholera seasonal peaks in South Africa documented between 1980 and 1985. This cholera seasonality showed a pattern, which had become familiar in other cholera endemic areas of the world, whereby cholera was expected to wane, only to be followed by a recrudescence (Isaäcson, 1986). The initial cases were all from the eastern Transvaal (Mpumalanga) close to the Mozambique border. Later on, the epidemic spread into the provinces of Natal as well as Gauteng. The overall epidemic

had an upward trend starting October 1980 to reach its peak in July 1983 and thereafter started waning until July 1987. Thus, within this particular epidemic, there were seven distinct cholera epidemic periods between October 1980 and July 1987 (Küstner and Du Plessis, 1991). Starting in October 1980, there was a cholera outbreak in Kangwane in the former eastern Transvaal (now Mpumalanga). By March 1981, there were 2,748 reported cholera cases with 36 deaths. The overall case fatality rate at the time being 1.3% (Kustner *et al.*, 1981). An epidemiological investigation into the outbreak revealed that all the patients had consumed water from an irrigation canal that served the farms they resided on. By November 1981, there was another cholera outbreak in Lebowa (Mpumalanga). Just like the epidemic in Kangwane, an investigation revealed that cholera patients had consumed water from a nearby Gumpies river (Sinclair *et al.*, 1982). The study also positively associated drinking water from water vendors with an increased risk of contracting cholera. As the cholera cases started declining, between August1982 - Jul 1987, the disease was mostly confined to the Natal province (Küstner *et al.*, 1981). In support of this observation, was a study in 1983 that screened in-patients at Eshowe hospital in Natal for cholera over a two-week period and finding a high incidence of cholera positive stools among the paediatric in-patients. This was also suggestive of endemicity within the community (Chapman and Collocott 1985). It became apparent then, that socio-economically deprived black communities, living in rural areas with relatively high rainfall, as in the former tribal homelands of Natal, KwaZulu and KaNgwane were the ones most affected by cholera outbreaks (Küstner and du Plessis, 1991).

Around the same period, there was a cholera outbreak in the Transkei (Eastern Cape) between October 1982 and September 1983 (Transkeian Dept of Health, 1982; Tshibangu and Stawski, 1984). A survey of water supply and sanitation services in rural Transkei found 87.2% of the respondents made use of natural water sources i.e. rivers, wells, springs, streams, dams and stagnant pools, as the main sources of drinking water supplies (Tshibangu, 1987). These natural water sources were susceptible to pollution and were potential carriers of pathogenic bacteria. In Transkei, cholera was one of the most common notifiable water-borne infections, often linked with the use of unprotected water supplies coupled with poor personal hygiene and unsanitary practices among the rural communities (Tshibangu, 1987).

After a decline in cholera cases since 1985, the Department of Health (DOH) released a communiqué in November 1997 warning about the spread of cholera southwards in Africa and the possibility of outbreaks in South Africa if precautionary measures were not taken. As such, provincial health facilities throughout the country were placed on alert and the necessary guidelines for managing a potential cholera outbreak were widely distributed. Bacteriological surveillance was carried out in the sewers of the major cities to detect cholera bacteria and laboratory facilities were prepared for confirming clinical diagnosis of the disease. Extensive public awareness campaigns to communities most at risk were also intensified (DOH, 1997).

Mpumalanga had another outbreak recorded early in 1998 and the use of surface water for drinking was quoted as the probable route for cholera transmission (Athan *et al.,* 1998). Mpumalanga's lowveld region is predominantly rural, an environment where clean water and adequate sanitation were often unavailable making the black communities particularly vulnerable to waterborne diseases like cholera (Athan *et al.,* 1998; Keddy and Koornhof, 1998). Considering this region borders Mozambique and Swaziland, many of the migrants casual labourers who are attracted to the banana and sugar plantations often contract cholera due to lack of sanitary facilities and safe water (Athan *et al.,* 1998; Durrheim *et al*., 2001).

2.3 Cholera – the affliction

Cholera is an acute diarrhoeal disease of humans caused by the bacterium *Vibrio cholerae*. Cholera is often confirmed through cultures and diagnostic tests of stool samples and serotyping the isolate; though the diagnosis remains primarily based on clinical findings (Weir and Haider, 2004). Onset of illness is usually rapid, with incubation periods varying from 6 hours to 5 days. Disease progression can also be rapid. The symptoms in the early stages of the disease may begin with intestinal cramping and the sudden onset of profuse, watery diarrhoea often accompanied by vomiting (WHO, 2000). In the classic clinical cases of the disease, *Vibrio cholerae* produces an enterotoxin that causes a copious, painless, watery diarrhoea that can quickly lead to severe dehydration, shock and death if treatment is not promptly given (Bennish, 1994). More than 90% of patients present with episodes that are of mild or moderate severity and these cases are difficult to distinguish clinically from other

types of acute diarrhoea; while less than 10% of ill persons develop typical cholera with signs of moderate or severe dehydration (WHO, 2000a). Severe cases are associated with a clinical picture of a patient becoming lethargic with sunken eyes and cheeks (Cosnett, 1989).

Epidemics of cholera arise after *Vibrio cholerae* is introduced in non-endemic areas where most of the population have no immunity (Glass and Black, 1992). Epidemics are often unpredictable but usually occur seasonally. Cholera exhibits periodicity in the heavily endemic region of the Indian subcontinent. This varies from year to year and seasonally as well, depending on the amount of rain and the degree of flooding (Finkelstein, 1999). Cholera appears to wax and wane in endemic regions on time scales of 3 to 6 years, a pattern that has long been recognized (Pascual *et al.,* 2002). Once an epidemic wanes, the transition to an endemic phase occurs, as a large proportion of the population is immune or semi-immune at the time. Previous immunity decreases illness in adults and higher attack rates are therefore seen in children and women of child bearing age, who act as caretakers of the young and are inevitably exposed to large inocula of *Vibrio cholerae,* capable of initiating an infection (Kolvin and Roberts, 1982; Bradley *et al.,* 1996).

2.3.1 The pathogen

Vibrio cholerae, the causative agent of cholera is a chemo-organotrophic, asporogenous, Gram negative curved bacillus, motile by means of a polar flagellum. It is a facultative anaerobic organism; oxidase positive and can tolerate alkaline conditions up to a pH of 10, but is inhibited at pH6 or below. All isolates grow at 20C^{o} and most can grow at 30^{o}C (Baumann *et al.,* 1984). Being a halophilic organism, it requires NaCl for optimum growth, thus typically found in estuarine and marine environments, whereby it can be free living or in association, with shellfish, oysters and plankton, mostly copepods (Colwell *et al.,* 1977; Hood *et al.,* 1981; Tamplin *et al.,* 1990).

Although, more than 200 recognized *Vibrio cholera* O serogroups exist, until recently only two groups of *Vibrio cholerae* strains were documented; the O1 and non-O1 group. The O1 group was considered to be the pathogenic strain capable of causing epidemic or pandemic cholera. This is because of the O1 strain's ability to produce

the cholera toxin (CT) responsible for the typical symptoms presented as cholera. The strains of the O1 group can be further subdivided into the "classic" and the El Tor biotypes, both of which are associated with epidemic cholera. During the 7th pandemic, El Tor has become endemic to Africa. It is a hardier strain than the classic biotype and survives longer in the environment (Shapiro *et al.*, 1999). *V.cholerae* O1 survives refrigeration and freezing, thus contaminated food products including those being shipped internationally, can distribute the organism far and wide from the point of original contamination (MMWR, 1991). In an epidemic situation, the source of contamination is usually the faeces of an infected person.

The non-O1 groups were generally identified as agents of sporadic cases of mild cholera-like diarrhoea in many parts of the world, and considered incapable of initiating cholera on an epidemic or pandemic scale (Blake *et al.*, 1980). This notion held true until 1992 when the causative agent for an epidemic in Bangladesh was found to be a non-O1 strain, a previously unrecognised serogroup of *V. cholerae*, now designated O139, synonym Bengal (Cholera Working Group, 1993; Shimada *et al.*, 1993; Islam *et al*., 1994). The epidemic potential of the new strain and the lack of immunity to it lead some authorities to question whether epidemics caused by the new strain may mark the beginning of the eighth cholera pandemic (Swerdlow and Ries, 1993). The potential of such a scenario is heightened when one considers that rapid transportation, frequent international travels and large population movements may support epidemics to spread faster than what has previously been the case. Within months of its appearance, *V. cholerae* O139 overwhelmed the entire Indian subcontinent and several Asian countries in a series of cholera outbreaks (Albert, 1996). By the year 2000, WHO had documented reports citing *V.cholerae* O139 as being responsible for outbreaks in 11 countries in South-East Asia (WHO, 2000).

The *V.cholerae* O1 and O139 appear to be genetically adapted to survive the entire transmission and infection cycle, i.e. from surviving the low gastric pH levels to colonization and proliferation in the ileum and finally expulsion through diarrhoea and survival in aquatic environments (Weir and Haider, 2004). As with the O1 strains, water and food seemed to be the vehicles of infection. Many family contacts of the index cases of O139 cholera were found to be infected with *V. cholerae* O139, and in many of them, the infection was asymptomatic, which is reminiscent of O1 EI-Tor

infections. Also, as with O1 EI-Tor infection, individuals of blood group O were more susceptible to O139 infection than those with other blood groups (Albert, 1996).

2.3.2 Infection and symptoms

Infection normally starts with the oral ingestion of food or water contaminated with *V. cholerae*. Subsequently, the bacteria must pass through and survive the gastric acid barrier of the stomach, then penetrate the mucus lining that coats the intestinal epithelia. The primary site of *V. cholerae* colonization is the small intestine. Inoculum size as low as 10^2 organisms may cause disease although a higher dose is probably required because of the acid sensitivity of *V. cholerae* cells, which are exposed to low pH in the gastric compartment (Cash *et al.*, 1974). The surviving bacteria adhere to and colonize the intestinal epithelial cells, eventually producing the CT and causing cholera symptoms (Reidl and Klose, 2002).

The majority of infected patients develop only mild or no illness, although the bacterium may be present in their faeces for 7-14 days. Such sub-clinical illness in most cases, resolve in 4-6 days (Sánchez and Taylor, 1997). Depending on the dose of ingested organisms, onset is usually rather sudden, with clinical manifestations ranging from asymptomatic carrier state, mild, watery diarrhoea to acute diarrhoea with characteristic rice water stools. This is a result of the toxin produced by the bacterium acting on the mucosal cells of the small intestine and stimulating production of water and electrolytes leading to profuse, watery diarrhoea, a typical feature of the disease cholera. Severe cholera cases can lead to watery stool outputs of between 500-1000ml per hour, rapidly leading to rapid dehydration and electrolyte imbalance followed by acidosis, muscular cramps, hypotension, tachycardia and vascular collapse (Keen and Bujalski, 1992).

2.3.3 Global surveillance

The International Health Regulations require governments to report all cases of the three diseases; cholera, plague and yellow fever. The aim is to provide a rapid international alert system for diseases of international public health importance (WHO, 1999). Among the acute enteric infections, cholera received the greatest attention from bodies like the World Health Organisation (WHO) because of its propensity for rapid epidemic spread. The WHO monitors countries reporting cholera

in order to follow trends in the disease over time. As a result the WHO has set up "Expert Committees" on cholera since 1951 (Barua, 1978). Just after the seventh epidemic appeared in 1961, the WHO quickly intervened by establishing Inter-Regional Cholera Teams to assist in programmes dealing with training, control, and research on the treatment and prevention of cholera. Since then, the WHO has been in the forefront in assisting epidemiological investigations and information dissemination campaigns about cholera. Nonetheless, this surveillance is by no means complete since many countries with major cholera problems do not report their cases for political, economic, or other reasons including the lack of facilities for surveillance (WHO, 2001a). Even in countries with nationwide surveillance, reporting is incomplete both because of problems of reporting and difficulty in field diagnosis of a disease with a clinical spectrum that ranges from mild to severe symptoms (Glass and Black, 1992).

Undoubtedly, cholera remains an important cause of morbidity and mortality worldwide. High incidences of the disease continue to be reported from Asia, Middle East, Africa, South and Central America. Its spread may be rapid and unpredictable because of the relative ease of transportation including the public modes of travel be it by road, rail, sea or air (Blake, 1994; WHO, 1999). Migration of people due to war or political unrest of the magnitude seen in Goma, Rwanda has contributed to entrenching cholera on the African continent (Crowcroft, 1994). As such, cholera is now endemic in many parts of the African continent (Barua, 1992; Swerdlow and Isaäcson, 1994). Endemicity of cholera carries the potential of outbreaks, which can quickly attain epidemic status, especially in developing countries where a large part of the populace live in crowded conditions with inadequate clean water supply and poor sanitation options (Barua, 1992).

2.3.4 Transmission and spread of the disease

The main vehicles of cholera transmission are water and food. Contaminated water with free-living *V. cholerae* cells are probably the main origin of epidemics, followed to a lesser extent by contaminated food, especially seafood products like oysters, crabs, and shellfish (Reidl and Klose, 2002). Cholera is a highly contagious disease, and is transmitted primarily by ingestion of faecally contaminated water by susceptible persons. Waterborne transmission has been documented as being the most

important route for the spread of cholera in Africa. Several studies in Africa have linked diarrhoeal diseases, including cholera, with drinking water from contaminated sources such as shallow wells, river water, and water contaminated while being stored (Sitas, 1986; Patel and Isaäcson, 1989; Bradley *et al.*, 1996; Shapiro *et al.*, 1999). Cholera has also been associated with bathing in contaminated river water (Acosta *et al.*, 2001). Consequently, rivers contaminated with the cholera bacterium tend to transmit the disease from one community to the other, contributing to the rapid spread of the disease. Sudden large outbreaks are usually caused by contaminated public water supplies. Thus, water plays an important role in the transmission and epidemiology of cholera, be it surface water, wastewater or seawater. *Vibrio cholerae* will survive up to 24 hours in sewage, and as long as 6 weeks in certain types of relatively impure water containing organic matter. This makes it difficult to eradicate cholera organisms from such waters, which are thus likely to remain a serious threat to public health for some time (Crowcroft, 1994).

Besides water, food has been recognized as an important vehicle for the transmission of cholera. If due care is not taken, foods are likely to be faecally contaminated during preparation, particularly by infected food handlers in an unhygienic environment (Rabbani and Greenough, 1999). Thus, in an epidemic, the source of contamination is usually the faeces of an infected person. The physicochemical characteristics of foods that support survival and growth of *V. cholerae* O1 and O139 include high-moisture content, neutral or an alkaline pH, low temperature, high-organic content, and absence of other competing bacteria. *Vibrio cholerae* can survive on a variety of foods that become contaminated through direct contact with the stools of a carrier; or by polluted water. The WHO fact sheet No. 107 (2000a) notifies that low temperatures limit proliferation of the organism and thus may prevent the level of contamination from reaching an infective dose necessary to initiate infection. Furthermore, the organism is sensitive to acidity and drying, thus commercially prepared acidic (pH 4.5 or less) dried foods are therefore without risk.

Contamination of food be it at home, during shared social functions, at markets, and during preparation by street vendors, is common, especially in developing countries where public health measures are poorly enforced by the relevant authorities. *Vibrio cholerae* can survive for 2-14 days in food and for many weeks in shellfish and

molluscs (Kolvin and Roberts, 1982). Sharing meals with persons with watery diarrhoea, eating food at a funerals, improperly cooked food, leftover food contaminated after cooking, and lack of hygienic practices e.g. washing hands before handling food are also thought to be some of the routes through which cholera spreads among communities (St. Louis *et al.,* 1990; Shapiro *et al.,* 1999).

Certain types of foods, especially seafood, i.e. fish, shellfish, crabs, oysters and clams as well as dried fish and prawns, have all been incriminated in cholera outbreaks in several countries (Acosta *et al.,* 2001; Gangarosa and Tauxe, 1992; St. Louis *et al.,* 1990). Contaminated rice, millet gruel, and vegetables have also been implicated in several outbreaks. Other foods, including fruits (except sour fruits), poultry, meat, and dairy products, have the potential of transmitting cholera (Rabbani and Greenough 1999). An investigation led by the Centre for Disease Control (CDC, 2004) during a cholera epidemic between November 2003 and January 2004 in Zambia, implicated food borne transmission via raw vegetables.

To reduce the risk of food-borne transmission of cholera, it is recommended that foods should be prepared, served, and eaten in an hygienic environment, free from faecal contamination. Proper cooking, storing, and re-heating of foods before eating, and hand-washing with safe water before eating and after defecation are important safety measures for preventing food-borne transmission of cholera (Rabbani and Greenough, 1999; WHO, 2000a; CDC, 2004). Generally, results from studies of transmission of cholera emphasize the importance of hygiene, clean water, and sanitary food handling for cholera prevention.

Altered gastric acidity induced by buffering substances predisposes a person to *Vibrio cholerae* infection. Studies showing people who had consumed acidic foods and survived *Vibrio cholerae* infection amidst an epidemic demonstrated the importance of an alkaline environment for the survival of *Vibrio cholerae* (St. Louis *et al.,* 1990). Certain life styles, like chewing of coca leaves have also been implicated in predisposing a person to *Vibrio cholerae* infection in. The slaked lime added to the coca leaves release cocaine and free bases that buffer the gastric juices rendering the stomach alkaline for hours. Thus coca chewers will predictably be more at risk of infection from a few *Vibrio cholerae* organisms than non-coca chewers. This practice

of coca chewing is common in Peru and other parts of South America where it is suggested to play a role in the transmission of *Vibrio cholerae* (Feldmeier and Krantz, 1991).

Rarely is cholera transmitted by direct person-to-person contact. Researchers from Tanzania, Malawi and Mozambique have reported nosocomial cholera infections, which they proposed spread via the person-to-person route (Cliff *et al.*, 1986; Mhalu *et al.*, 1984). Nosocomial infections were also reported from a South African hospital though as in the other African countries the exact mechanism of infection was not determined (Chapman and Collocott, 1985). However, a common feature to all these reports was that the conditions in the hospital wards were extremely overcrowded with inadequate sanitary facilities and supplies, like insufficient number of washbasins per ward and lack of hand washing soap.

2.3.5 Treatment

When cholera occurs in a susceptible community, case-fatality rates may be as high as 50% either due to lack of treatment facilities or the treatment being given too late. In contrast, a country with a well-organized diarrhoeal disease control programme could limit the case-fatality rate to less than 1% (WHO, 2000a). Clinicians should suspect cholera whilst attending to any case that involves massive, shock-producing diarrhoea, especially if the patient has travelled to a cholera-affected country or region.

By 1970, when the disease spread into Africa, there was a shift of attention to the provision of appropriate treatment such as oral re-hydration therapy, rather than ineffective vaccines (Martinez *et al.*, 1988). *Per se*, the World Health Assembly abolished the requirement of cholera vaccination for international travel as an International Health Regulation in 1973 (Martinez *et al.*, 1998). Effective treatment requires immediate replacement of the massive fluid loss by oral re-hydration salts (ORS), before conducting confirmatory diagnostic tests in the laboratory. The benefit of oral rehydration therapy (ORT) for cholera was demonstrated in 1968 (Nalin, 1968). Subsequently, this had lead to the application of the therapy to stabilise all forms of infectious diarrhoeal diseases (Pierce *et al.*, 1969). The global application of

ORT has decreased the death rates from diarrhoeal diseases by more than half in the last 30 years (Greenough III, 2004).

Therapy of acute watery diarrhoea requires replenishing water and electrolyte losses (re-hydration phase) and maintaining the water and electrolyte balance after re-hydration until the diarrhoea ceases (maintenance phase) (Nalin *et al*., 2004). The original oral re-hydration solution (ORS) formulation developed by the World Health Organization (WHO) struck a compromise between the ideal solutions for diverse disorders in cholera and non-cholera diarrhoeas, in both adults and children (Nalin *et al*., 2004). Indeed, ORS has been hailed as one of the most important medical advances of the past century, particularly because of its simplicity, low cost, and remarkable ease of use (Nalin and Cash, 1970). As such, most cases of diarrhoea caused by *V.cholerae* can be treated adequately by giving a solution of oral rehydration salts as prescribed in the WHO/UNICEF standard formulation (Duggan *et al.,* 2004). During an epidemic, 80-90% of diarrhoea patients can be treated by oral rehydration alone, but patients who become severely dehydrated must be given intravenous fluids (Bennish, 1994; WHO, 2000a). In severe cases, an effective antibiotic can reduce the volume and duration of diarrhoea and the period of vibrio excretion. Tetracycline is the usual antibiotic of choice, but resistance to it is increasing, thus its administration is not recommended. Other antibiotics that are effective against *V. cholerae* include cotrimoxazole, erythromycin, doxycycline, chloramphenicol and furazolidone (Sanchez and Taylor, 1997; O'Grady *et al* 1976; WHO, 2000a).

2.4 *Vibrio cholerae* and the environment

Recent investigations strongly suggest the existence of an environmental aquatic reservoir for *Vibrio cholerae* (Speelmon *et al.,* 2000). *Vibrio cholerae* strains are inhabitants of estuarine and marine environments where they can be free living or in association with plankton, mostly copepods (Tamplin *et al.,* 1990). Cholera has been observed to have a specific relationship with particular geographical niches, seasons and ecology (Merson *et al.,* 1978). The aquatic environment is also thought to be the habitat of the quiescent pathogenic *Vibrio cholerae* strains (Shandera *et al.,* 1983; West, 1992), although other habitats have also been suggested to support the survival

of *Vibrio cholerae* between epidemics. The association with the aquatic environment is further supported by the fact that, throughout history, and up to the present, cholera pandemics have spread by following world coastlines (Colwell and Huq, 2001). The extensive use of the Great Lakes in Africa for socio-economic activities (transport, bathing, drinking etc) have also been implicated to encourage widespread dissemination of *V.cholerae* when conditions for transmission are suitable, subsequently leading to cholera epidemic among the riverine communities (Birmingham *et al.*, 1997). This association with the aquatic environment (marine and riverine) also underscores the various biological, physical and chemical factors, which are important for the survival of *V.cholerae* in the aquatic environment (Colwell and Spira, 1992; Sánchez and Taylor, 1997). As *V.cholerae* prefers moderate salinity averaging between 0.5-3.0%, with transmission being most probable when water salinities fall in the range of 0.01-0.1% (Miller *et al.*, 1982; Singleton *et al*., 1982); implies that in estuarine environments, fluctuations in salinity will only be conducive for the transmission for *Vibrio cholerae* at certain times of the year. This may be one of the factors that support the seasonal pattern of cholera.

The seasonal behaviour of cholera is erratic and its driving factors poorly understood. Cholera seasonality in endemic areas suggests possible long-term survival of *V.cholerae* in the environment (Speelmon *et al.*, 2000). Several proposals have been put forward to explain this. Feachem (1976) suggested that *V.cholerae* survived unfavourable environmental conditions by colonising copepods or related species in the Ganges delta area. While Huq *et al*, (1983) observed that live copepods contribute significantly to the survival and distribution of the cholera organism in the aquatic environment. Thus, the seasonal cycle of persistence in the sediments, where bacterial numbers increase during plankton blooms, results in the appearance of *V. cholerae* in larger numbers capable of causing outbreaks and possibly accounting for the seasonality of epidemic cholera (Colwell, 1996; Patz *et al.*, 1996; Lipp *et al*., 2002).

On the other hand, the occurrence of sporadic outbreaks of cholera and cholera-like illnesses in areas free of sewage contamination or carriers of *V.cholerae* or both can be accounted for if the organism remains viable, though not necessarily recoverable, in brackish waters until salinity and nutrient conditions become favourable for growth (Colwell and Huq, 1994). The “viable but non culturable” state, in aquatic systems

provides a remarkably clear explanation for the phase of dormancy, survival and persistence in the environment and may explain the disappearance of *V.cholerae* between epidemics in cholera-endemic areas of the world (Byrd *et* al., 1984; Roszak *et al.*, 1984 and Colwell *et al*., 1985).

In addition to *V.cholerae* having symbiotic relationships various aquatic organisms, other modes of survival and dispersal have also been surveyed. Venkateswaran *et al.* (1989) noted that *V. cholerae* was prevalent in the aquatic environment of the United States, and its distribution is influenced by the degree of nutrients rather than the association with zooplankton. *V.cholerae* has also been found in samples of ballast water of ships docked at Chesapeake Bay (Ruiz *et al.*, 2000), suggesting that global shipping lines can disperse human pathogens through ballast water and thus merit attention as couriers of long distance dispersal of waterborne diseases. This observation partly supports Grimes *et al.* (1986) who had earlier suggested that the wastewater discharge into the aquatic environment could well be the source of nutrients, which may stimulate growth of the autochthonous pathogens rather than it being the source of the pathogens. The sampling undertaken by Ruiz *et al.* (2000) went a step further to show that ballast water, in addition to discharging nutrients into the aquatic environment, also introduces novel microbial species. *V. cholerae* may therefore be surviving in the aquatic environment using any one, a combination, or all of the means suggested.

Terrestrial environments have also been suggested as retreats for *V. cholerae* during inter-epidemic periods, like the savannahs and deserts of Africa which would be expected to be least conducive to the survival of vibrios (Feachem, 1981). Plantation land has also been suggested as a possible reservoir of *V.cholerae.* Agarwal and Shukla (1999) noted that the distribution of cholera matches the geographical distribution of sugar cane, and sugar-cane harvesting synchronises with inter-epidemic periods of cholera epidemiology in the Indian sugar-cane belt. They suggested the hypothesis that most of the sugar-cane waste that is released into drains, streams, and rivers, or used in farming to increase farm produce is sufficient to sustain the organism to its next epidemic flare up. The distribution of cholera in the mainly sugar-cane growing areas of South America, USA, Australia, Africa, south east Asia, and Japan adds credence to their hypothesis. The connection of this aspect in KZN

has yet to be established as sugar-cane plantations along the Indian Ocean coastal belt of KZN form the mainstay of the economy and agriculture.

2.4.1 Cholera epidemics and climate

The climate change at both the global and regional level fuels the debate over the effects of changes in climate on disease exacerbation in endemic areas and in their proliferation to non-endemic regions (Brown, 1996; Patz *et al.*, 1996; Rose *et al.*, 2001). Tropical regions of the world also tend to be more severely affected by infectious diseases than the temperate ones (Sattenspiel, 2000). Rainfall, runoff waters and floods have always been associated with outbreaks of waterborne diseases, considering that pathogens of faecal origins can find their way into such waters. Although the discovery of *V.cholerae* in surface waters not known to be faecally contaminated or in areas with no record of human infection have contradicted the conventional rationale of cholera being exclusively a waterborne disease (Colwell *et al.*, 1977, 1981).

Local weather conditions may have a direct or indirect effect on environmental sanitation with ensuing susceptibilities to diseases like cholera. An epidemiological feature noted in the 1980-1987 cholera epidemic in South Africa was linked to the local rainfall pattern, whereby, 99% of all cholera patients fell ill in areas with an annual rainfall of more than 600 mm (Kustner and Du Plessis, 1991). On the other extreme, water scarcity as a result of droughts or shortage of clean water will inevitably lead to unsanitary conditions that encourage transmission of pathogens like *V. cholerae* (Feachem, 1981).

Thus unravelling the mechanisms of disease dynamics will be useful in the prediction of their propagation in the different scenarios presented by climatic changes. Evidence is emerging that many ecosystems on the African continent carry risks of climate-driven threats to human health. Predisposing factors include geographic location, socio-economic status, and knowledge and attitude toward preventive measures (Anonymous, 2001). Factors, which are known to have an influence on the survival of *V.cholerae*, have been extensively studied, thus contributing to the understanding of the bacterium and the epidemiology of cholera. Notwithstanding; an aspect of cholera receiving relatively little attention until lately, is the climate, which

needs to be considered in the context of other non climatic potential drivers of the disease, such as those related to population demography and socio-economic variables.

Evidence supporting the autochtonous nature of *V. cholerae* in brackish waters and estuaries has more recently highlighted the potential significance of environmental factors to the dynamics of the disease, including its' sensitivity to climatic patterns (Tamplin *et al.*, 1990; Pascual *et al.*, 2000, Singh *et al.*, 2001). Throughout the different seasons, climatic factors such as water temperature will have a direct influence on the abundance of *V. cholerae* in the aquatic environment, or alternatively, an indirect influence on other aquatic organisms such as zooplankton, phytoplankton and macrophytes, onto which the pathogen is found to be attached to (Colwell, 1996). High ambient temperatures have been implicated in the dynamics of diarrhoeal diseases and of *V.cholerae* in Peru (Salazar-Lindo *et al.*, 1997), while sea surface temperatures (SSTs) in the Bay of Bengal have also been shown to display a bimodal seasonal cycle similar to that of cholera cases in Bangladesh (Lobitz *et al.*, 2000). Recent time series studies have shown an increase in cases associated with warmer temperatures (Singh *et al.*, 1998; Speelmon *et al.*, 2000). Existing evidence also favours the role of increased water temperature through its effect on the pathogen's growth and survival (Pascual *et al.*, 2002).

The climate-cholera link, which is likely to involve multiple pathways, is yet to be deciphered. The marked seasonality of cholera and the simultaneous appearance of cases at different locations thousands of kilometres apart in a short span of time have prompted researchers to investigate climatic and environmental drivers. Such almost simultaneous outbreaks of cholera in parts of India and South America have lead to the view that primary transmission from an environmental reservoir initiates the seasonal outbreaks of cholera in endemic regions. A case in point is Peru when in 1991, cholera revisited the country after it was last reported in 1895, almost a century of absence (CDC, 1991; Gangarosa and Tauxe, 1992). When the epidemic struck, there was an almost simultaneous appearance of the disease along the Peruvian coastline. This happened at the same time when Peru was experiencing the El Niño weather phenomenon in 1991-92, which brought rain and consequently an influx of

nutrients from land as well as warm sea surface temperatures. These climatic conditions initiated phytoplankton blooms, (a food source for zooplankton) which in turn amplified the resident zooplankton numbers, with which vibrios including the autochtonous *V. cholerae* species have a commensal or symbiotic relationship with (Colwell, 1996; Epstein *et al.*, 1993). Cholera outbreaks have been shown to almost always follow zooplankton blooms (Huq *et al.*, 1995). As phytoplankton blooms can be measured by satellite imagery, it is suggested that conditions associated with a cholera outbreak or epidemic can be monitored by satellite as well.

It is now widely accepted that the epidemiology of cholera is indisputably reliant on a complex of environmental and social factors (Miller, 1982). The information on the local climatic factors will permit a better understanding of the existing *V. cholerae* strain and its associated disease virulence, transmission, ecology and epidemiology. The growing availability of climatic data offers opportunities for retrospective and prospective analyses through remote sensing and computer processing to integrate ecological, epidemiological, and remotely sensed spatial data for developing early warning systems for epidemic cholera (Pascual *et al.*, 2002).

2.5 Socio-economic factors associated with cholera

The disease incidence of cholera is associated with several socio-economic variables, such as population density, water quality, sewer connections and poor personal hygiene. The disease can spread rapidly in areas without adequate and proper treatment of sewage and drinking water. Epidemics of cholera claimed thousands of lives in London before the physician John Snow, in 1854, demonstrated that cholera was a waterborne disease. He traced water delivered to various private pumps in the Soho neighbourhood to a public pump known as the Broad Street Pump in Golden Square. By simply removing the handle of this polluted well, he was able to stop individuals from accessing the water. He prevented contaminated water from being pumped, and thereby effectively helped to stop the 1854 cholera outbreak (Cliff and Haggett, 1988). Since then, the study of cholera outbreaks has contributed to the development of epidemiology as a branch of medical science, and also forced attention on the problem of water treatment and purification.

2.5.1 Access to basic services

The basic services required by communities are safe drinking water; sanitation; refuse collection and electricity. World wide, one billion people lack access to safe drinking water and 2.4 billion to adequate sanitation. A looming crisis that overshadows nearly two thirds of the Earth's population is drawing closer because of continued human mismanagement of water, population growth and changing weather patterns as reported by UN organizations (WHO World Water Day Report, 2001c). The United Nations set eight goals for development in its 2000 Millennium Declaration for improving the human condition by 2015 (UNMD, 2000). Goal 7 aims to ensure environmental sustainability and target 10 of this goal is to halve, by 2015, the proportion of people without sustainable access to safe drinking water and sanitation (Millennium Indicator Database, 2005; MDG, 2005). To achieve this target, an additional 1.5 billion people will require access to some form of improved water supply by 2015, that is an additional 100 million people each year (or 274 000/day) until 2015 (UNESCO).

Poor sanitation practices in highly populated areas harbouring endemic toxigenic strains are the source of occasional outbreaks due to contamination of drinking water and/or improper food preparation. Factors associated with precarious living and environmental conditions have also been implicated in cholera epidemics. A study in Brazil showed that households without tap water or sewage disposal and with an income less than or equal to the minimum wage revealed a positive association with cholera incidence (Gerolomo and Penna, 2000). In Mexico, cholera incidence was higher in coastal states than in the interior, and four times higher in the least urbanised areas compared to the most urbanised areas. Thus suggesting that areas associated with high poverty and low urbanisation be given priority in the supply of safe water and sanitation (Borroto and Martines-Piedra, 2000). Even in relatively stable countries of the developing world, where ordinary people have inadequate sanitation, future prospects are undermined by the impact of international debt on their struggling economies (Crowcroft, 1994).

2.6 Epidemic control and prevention

When cholera appears in a community it is essential to ensure three things: hygienic disposal of human faeces, an adequate supply of safe drinking water, and good food hygiene (WHO, 2000). Effective food hygiene measures include cooking food thoroughly and eating it while still hot; preventing cooked foods from being contaminated by contact with raw foods, including water and ice, contaminated surfaces or flies; and avoiding raw fruits or vegetables unless they are first peeled. Washing hands after defecation, and particularly before contact with food or drinking water, is equally important and a well-known fact (St Louis *et al.*, 1990; Kaysner and Hill, 1994; CDC, 2004).

Routine treatment of a community with antibiotics, or "mass chemoprophylaxis", has no effect on the spread of cholera (WHO, 2000). Restricting travel and trade between countries or between different regions within a country is not recommended as it may promote the suppression of information on cholera outbreaks (WHO, 1998). Setting up a *cordon sanitaire* at frontiers uses personnel and resources that should be otherwise devoted to effective control measures; and hampers collaboration between institutions and countries that should unite their efforts to combat cholera (WHO, 2000).

Limited stocks of two oral cholera vaccines that provide high-level protection for several months against cholera caused by *V. cholerae* O1 have recently become available in a few countries (WHO, 2001b). Both are suitable for use by travellers but they have not yet been used on a large scale for public health purposes. Use of this vaccine to prevent or control cholera outbreaks is not recommended because it may give a false sense of security to vaccinated subjects and to health authorities, who may then neglect more effective measures (WHO, 2001b). In 1973 the WHO World Health Assembly deleted from the International Health Regulations the requirement for presentation of a cholera vaccination certificate (WHO, 2000). As such, today, no country requires proof of cholera vaccination as a condition for entry.

Broadly speaking the literature review gives a synopsis of the disease cholera and the different factors that play a role in its transmission. It is evident that to understand

cholera whether in an endemic or epidemic form requires a multi-disciplinary approach. The following Chapter 3 outlines the rationale of the study and the overall project scope. The research approach and the methodology used are explained in detail. In effect the following chapter constitutes the foundation of the study through which outputs in the form of results were generated.