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EDITORIAL

Enteric diseases remain a major contributor to poor health outcomes in Papua New Guinea

Introduction

In 1995 this journal released a focus issue on enteric infections. In the editorial of that issue, Passey (1) discussed the impact on service delivery that was caused by the ongoing humanitarian emergencies that were occurring in Papua New Guinea (PNG) at the time, such as the conflict in Bougainville, the volcanic eruption in Rabaul, the influx of refugees from Papua Province of Indonesia (known then as Irian Jaya) and the crisis in government funding. Almost 20 years have passed since the release of the previous enteric focus issue and while the humanitarian emergencies of that time have been resolved, service delivery remains poor. This is despite a 2.2-fold increase in per capita gross domestic product (2). The recent investments in the resource sector have not yet translated into improved access to satisfactory health service delivery or the provision of basic services such as safe water supplies and sanitation, although it is recognized that provision of such infrastructure and services, in itself, will not result in improved health outcomes. In this Focus Issue of the Journal we highlight recent research into enteric diseases in PNG and discuss the progress needed for improved prevention and treatment of enteric infections.

Overview of enteric illnesses

Diarrhoeal illness is a major health issue in developing countries, particularly in children under the age of 5 years. Morbidity and mortality remain high in this age group with more than 2 million deaths per year occurring throughout the world, the majority in developing countries (3). This equates to approximately 17% of child deaths per year worldwide (4). Although mortality rates are much higher in children, diarrhoea also causes a substantial burden of disease in adults and adolescents, accounting for approximately 2.8 billion episodes of diarrhoea per year throughout the world (5).

Enteric diseases that are not primarily diarrhoeal in their presentation, such as typhoid fever, also have a high burden in developing countries. Estimates suggest that worldwide there are more than 21 million cases of typhoid per year, resulting in approximately 200,000 deaths (6).

The situation in PNG seems to reflect that of other low-income, resource-poor settings. Diarrhoeal illnesses contribute to 15% of all deaths in children aged <5 years (7). Typhoid is estimated to account for ~3% of all deaths in PNG (8). However, these estimates are based on dated and incomplete data that may not accurately represent the current situation across the entire country. This is highlighted by the thorough review of the literature pertaining to enteric illnesses in PNG by Toliman et al. (9) published in this issue. Their review provides a timely reminder of the need to obtain strong aetiological and epidemiological data on which to base decisions about future interventions.

Enteric parasites remain a neglected aspect of health in low-income countries

Until recently, parasitic infections were a largely neglected aspect of enteric illness, perhaps because these infections rarely cause mortality. However, it is now recognized that in addition to gastrointestinal symptoms, parasitic infections can have important sequelae. Soil-transmitted helminths (STHs) such as hookworms (*Ancylostoma duodenale*, *Ancylostoma ceylanicum* and *Necator americanus*), roundworm (*Ascaris lumbricoides*), whipworm (*Trichuris trichiura*) and *Strongyloides* spp. are among the most common causes of disease in humans. It is estimated that 50% of all people living in developing countries are infected with at least one STH. A study conducted in children admitted to Angau Memorial Hospital (Lae, Morobe Province) in 1981 found a high prevalence of *N. americanus* (48%), *T. trichiura* (18%), *S. stercoralis* (11%), *S. fuelleborni* (9%) and *A. lumbricoides* (6%) (10). Similarly, a study conducted in Gulf Province between 1996 and 1997 found a high prevalence (68%) of enteric helminths in children aged <5 years (11). The symptoms associated with heavy STH infections

include abdominal pain, general malaise and weakness (12). However, the real importance of STH infections is that they are regarded as one of the most important causes of physical and intellectual growth retardation (13).

Enteric protozoan infections, such as giardiasis and cryptosporidiosis, have long been considered common in PNG, but recent data are not comprehensive. *Cryptosporidium parvum* was isolated from 10% of children admitted to Goroka General Hospital (GGH) with diarrhoea between 1985 and 1990, and was more commonly isolated from cases than controls (14). Amongst children in PNG who were healthy or had pneumonia, seroprevalence for *C. parvum* was 24%, with no significant difference between sick or control children (15). The paper by Phuanukoonnon et al. (16) in this issue demonstrates that the problem of enteric parasite infection in PNG is ongoing, and is not restricted to children. In pregnant women who had no symptoms of enteric illness, protozoan and/or helminthic enteric parasites were commonly detected, often with multiple infections. On the basis of these historical and recent data, a more concerted effort to control enteric parasite infection in PNG is required.

Endemic, emerging and re-emerging enteric pathogens in PNG

In the absence of a multi-site study using currently available diagnostic methods, it is difficult to ascertain the current burden of specific pathogens in enteric diseases in PNG. However, we do know that certain pathogens are likely to play a major role in enteric diseases in PNG. Rotavirus is the most important cause of severe childhood diarrhoea in the world. Numerous studies in PNG have shown that this organism is an important cause of morbidity and mortality in children aged <5 years (14,17,18) and recent data illustrate that it remains important in children hospitalized due to acute watery diarrhoea (19).

Rotavirus surveillance is conducted by only two laboratories in PNG, using ELISA. In this issue Kas and colleagues (20) describe the evaluation of a rapid diagnostic test (RDT) for the detection of rotavirus, norovirus and adenovirus, all important causes of diarrhoea in both low- and high-income settings. The RDT performed poorly for norovirus and adenovirus, but well for rotavirus, demonstrating the potential for RDTs in rotavirus diagnosis in PNG. RDTs are unlikely to replace ELISA in current surveillance in Goroka and Port Moresby, but could enable more widespread surveillance should a rotavirus vaccine be introduced to PNG in the coming years. In settings such as PNG, where diagnostic capacity remains poor for most of the country, RDTs have considerable potential for improving the diagnosis of important treatable diseases. This has been demonstrated by the successful rollout of malaria RDTs and antimalarials in PNG. However, the use of RDTs does not negate the need for training and quality assurance to ensure the accuracy of results.

Historically, typhoid fever has been an important enteric pathogen, with research conducted in the early 1990s suggesting that the highlands region of the country had amongst the highest incidence of typhoid in the world (21). Unfortunately little research or surveillance has been done in the intervening years to monitor the burden of typhoid in PNG, in part due to the ongoing challenge of typhoid diagnosis in endemic settings such as PNG (22).

A paper published in 1999 estimated over 164 million cases of shigellosis globally, of which 99% occurred in developing countries (23). A recent shigellosis outbreak in PNG, along with concurrent infection with influenza virus (24), served as a reminder of the potentially fatal nature of *Shigella* spp., particularly in the absence of adequate health care. Unfortunately limited published data exist about the importance of *Shigella* in PNG at this time, not only in epidemics as reported by Rosewell and colleagues (24) but also as an endemic cause of enteric illness. If the PNG situation is reflective of other low-income, resource-poor settings, it is likely that *Shigella* remains a grossly neglected pathogen that warrants greater research and intervention efforts.

PNG has recently experienced the first outbreak of cholera ever recorded in this country (25). The outbreak highlighted some of the strengths and shortcomings of public health and emergency response capacity in PNG. In some locations, where there was adequate support from government and/or non-government organizations, the outbreak was contained with little mortality. However, at the national level, confirming a cholera

outbreak in remote regions, and gaining a greater understanding of the potential for other pathogens to play a role in the outbreak, was, at times, challenging (26). In this Focus Issue Horwood and Greenhill (27) provide an overview of the cholera outbreak to date, and Itaki (28) provides an insight into the response to an outbreak of acute watery diarrhoea (suspected to be cholera) in the Ambunti region, while Kas and colleagues (29) report on their investigation into the potential for other pathogens to play a secondary role in the aetiology of the cholera outbreak, and highlight some of the diagnostic challenges faced. Although cholera cases have not been reported in PNG since late 2011, there is still a threat that the outbreak strains of *Vibrio cholerae* are lurking in the country's large saline river systems (30), and ongoing surveillance of such environmental reservoirs is required.

Pigbel (or enteritis necroticans) is characterized by acute abdominal pain, vomiting of blood, bloody diarrhoea, shock and death. Pigbel occurs following the ingestion of pig meat contaminated with β-toxin-producing *Clostridium perfringens* type C. Normally the β-toxin is inactivated by the production of the pancreatic enzymes trypsin and chymotrypsin. However, in PNG a unique set of circumstances, including malnutrition, the consumption of sweet potato (which contains trypsin inhibitors) and possibly infection with *Ascaris lumbricoides*, results in the β-toxin causing necrosis of the gut (31). The introduction of a toxoid vaccine greatly reduced the incidence of pigbel in the 1980s and 1990s; previously it had been one of the leading causes of childhood death in the highlands. Unfortunately, with the discontinuation of the toxoid vaccine, cases of pigbel seem to be increasing in some areas of the highlands (32). Further surveillance and in-depth epidemiological studies are required to determine the extent of the problem and reveal suitable strategies for the prevention of this disease.

Sanitation and hygiene

The commonality between enteric diseases such as diarrhoeal/dysenteric illnesses, typhoid and parasitic infections is that research into their epidemiology has long been neglected in PNG. Most enteric diseases are largely preventable through access to safe water, improved sanitation and hygiene education, commonly referred to as WASH. Improved water and sanitation is widely regarded as one of the most important health interventions for the reduction of communicable diseases (particularly for children) in developing settings. An estimated 94% of all diarrhoeal cases, and almost 100% of STH infections, can be attributed to risk factors such as unsafe water sources, lack of sanitation and poor hygiene practices (33).

Very little research and evaluation has been published in relation to WASH in PNG since the monograph edited by Smith and Alpers in 1985 (34). The lack of recent activity in this important aspect of public health research is of concern and in this Focus Issue we provide an overview of the current status of WASH in PNG and the challenges faced (35). Moreover, Phuanukoonnon and colleagues (36) provide new insights in their paper that evaluates the behaviours associated with WASH in Hiri District of Central Province. The outcomes are indicative of a community willing to participate in, and adopt, WASH interventions when they are available.

While water, sanitation and personal hygiene are the central tenants of WASH interventions, food safety is also an important factor in the epidemiology of enteric illnesses. In many situations improved WASH would improve food safety (37,38). However, the rich history of infection through oral ingestion in PNG, most notably kuru and pigbel, demonstrates the complexity of factors that combine to cause some such illnesses (kuru should not be considered a food-borne illness as such, since consumption was during the mortuary practice of transumption, a religious practice rather than for nutritional purposes: refer to Whitfield et al. (39) for further detail). Attempts to understand the aetiology of sago haemolytic disease (SHD) is the focus of the review paper by Shipton et al. (40). It is acknowledged that SHD is considerably less prevalent than either kuru or pigbel were at their peak, and the epidemiological data of SHD to date are weak. Nonetheless, with the mechanism of the disease yet to be fully elucidated, a complex aetiology may be at play. Moreover, a review of the topic provides an important reminder of the inextricable link between food safety, nutrition and health.

Treatment and medical prevention

Severe illness and death from enteric

diseases can be prevented through relatively simple measures such as oral rehydration therapy (ORT) in the case of diarrhoeal illnesses, and mass drug administration in the case of STHs. Indeed, the development of ORT has been hailed as one of the greatest medical advancements of the 20th century (41). As Poka and Duke (42) state in this issue, ORT is the first-line treatment for acute watery diarrhoea, and in most cases should be the only treatment that is required. Even in situations where laboratory support does not exist, clinical signs and symptoms can be used with great effect to guide rehydration therapy.

Another important issue raised by Poka and Duke (42) is the overuse of antibiotics in the treatment of diarrhoea. The use of antimicrobials is poorly regulated in PNG, and we are currently witnessing a disconcerting rise in antimicrobial resistance across a variety of enteric and non-enteric pathogens (43-45). It is evident that a review of the treatment protocols needs to be implemented in PNG to counter the rise in antibiotic resistance and to ensure the effective treatment of patients; however, the paucity of culture and susceptibility data throughout the country impedes such a review.

Vaccination has proven to be an effective way of controlling some enteric illnesses, with polio being the most notable global example, and pigbel being successfully controlled during the 1980-1990s. Rotavirus could be the next enteric disease pathogen to be targeted for vaccination in PNG, given the availability of vaccines and the demonstrated role rotavirus plays in acute watery diarrhoea in PNG. Unfortunately the currently available vaccines for bacterial enteric pathogens such as *Vibrio cholerae* and *Salmonella enterica* Typhi are unlikely to offer long-term protection against cholera or typhoid fever, and vaccines for pathogens such as *Shigella* and pathogenic strains of *Escherichia coli* are not available.

Conclusions

Enteric illnesses all have one thing in common – they are spread through the faeces of an infected person. Universally accepted interventions are available for the prevention of the large majority of enteric diseases – the safe disposal of faeces through improved sanitation, improved handwashing practices to prevent introduction of pathogens into the mouth, and the supply of safe water sources to prevent the introduction of pathogens through drinking water. Adding weight to the argument for improved WASH is the impact it can also have on non-enteric diseases including acute respiratory infections and eye disease (46).

Vaccinations are now available for the most important cause of diarrhoea in children (rotavirus) and effective drugs are available for the mass treatment of communities to halt the transmission of STHs. However, in developing countries such as PNG enteric diseases are still one of the most important causes of illness and death. The millennium development goals (MDGs) were drafted as a roadmap for improvements in the quality of life for the world's poorest people, with a focus on improved sanitation and hygiene and other health interventions that would greatly reduce the burden of enteric diseases. Unfortunately many countries, PNG included, seem unlikely to meet the targets of their MDG agreements. It is evident that considerably more funds and resources need to be allocated for the prevention, treatment and surveillance of enteric diseases in PNG.

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