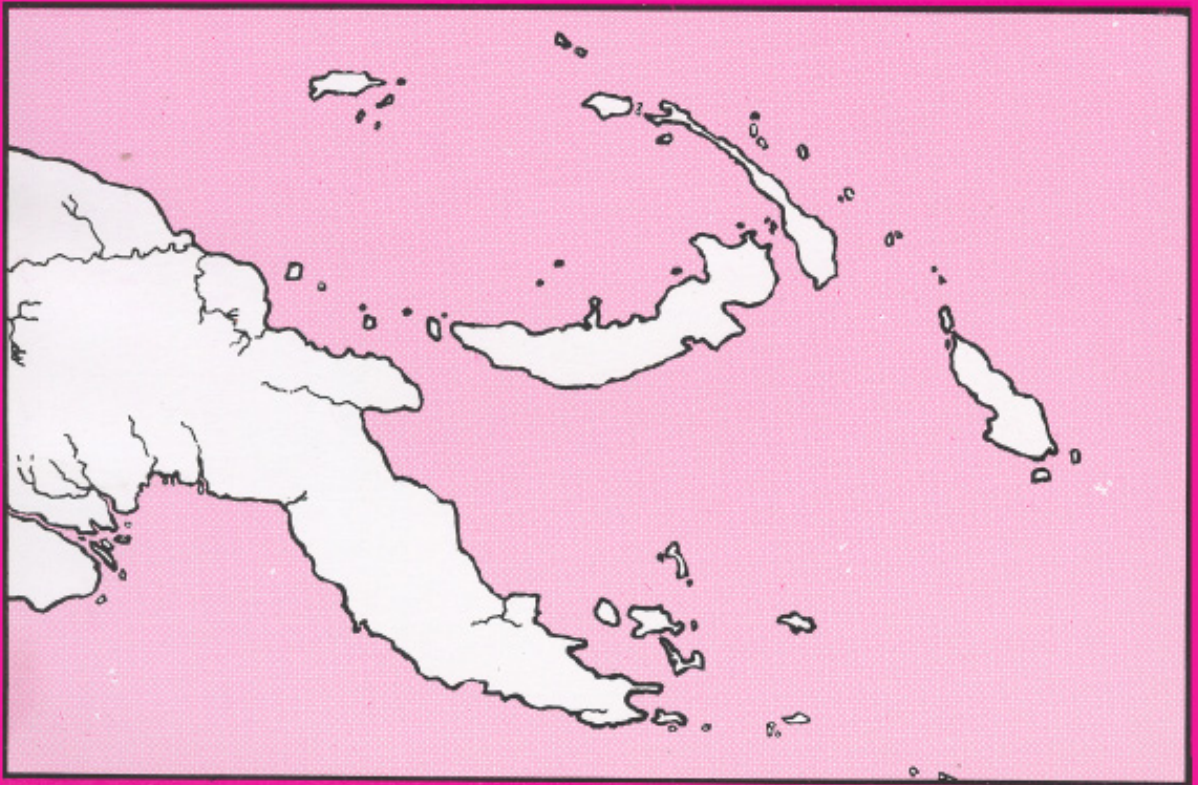


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CONTENTS

EDITORIAL

- A case for the introduction of a rotavirus vaccine in Papua New Guinea *A.R. Greenhill, M.H. Danchin, W. Pomat and P.F. Horwood* 129

Neglected Diseases

ORIGINAL ARTICLES

- Challenges of diagnosing leprosy in a rural low-endemic setting in Papua New Guinea
K. Yaku, N. Berry, C. Asuak, J. Kumai and R.A. Wangnapi 134
- Towards elimination of yaws in Papua New Guinea *W. Houinej, R.A. Wangnapi, J. Wangi, M.Y. Abdad, M. Marks, L.N. John, S.V. Bieb and O. Mitjà* 137
- Shigellosis: a truly neglected disease in Papua New Guinea *E. Malau, J. Mosse, P.F. Horwood and A.R. Greenhill* 147

ORIGINAL ARTICLES

- Bacterial profile and antimicrobial susceptibility patterns in primary surgical infections at Modilon Hospital, Papua New Guinea *J.M. Kuzma, F.W. Hombhanje, J. Pawiying and M.V. Hombhanje* 155
- "I have a heart to help the mothers": 25 years of the Village Birth Attendant Program in Milne Bay Province, Papua New Guinea *L.M. Vallety, R. Paul, B. Naidi, J. Morewaya, G. Kariwiga, A. Vallety, C. Morgan and C.S.E. Homer* 164
- Sociocultural barriers to access and utilization of birth delivery services in a rural area of Papua New Guinea *N. Ipi, J.D. Vince and G.L. Mola* 178
- Factors associated with lower extremity amputation in patients presenting with diabetic septic foot: a prospective case series *J.G. Nuli, C. Breria, K. Lapu and I. Kevau* 187
- A pilot study of the quality of life among cancer patients attending the Ambulatory Cancer Clinic at Port Moresby General Hospital, Papua New Guinea *G. Gende and S. Mwadede* 191
- Herbal products utilization among patients with HIV/AIDS in East Sepik Province, Papua New Guinea: a pilot survey to determine the prevalence *C. Manineng, M. Baigry, E. Trowalle and F.W. Hombhanje* 196

CASE REPORT

- Wandering spleen with torsion of the pedicle: a case report *J.G. Nuli and K. Lapu* 204

LETTER TO THE EDITOR

- Microscopic observation of *Rodentolepis nana* eggs in a faecal specimen *F.W. Hombhanje, M.V. Hombhanje and J. Pawiying* 207

OBITUARY – TRIBUTES TO DR REGINA WANGNAPI

- Dr Regina Wangnapi – going above and beyond the call of duty *H.W. Unger* 209
- In memory of Regina Alice Wangnapi-Taput *M. Ome-Kaius* 211
- Dr Regina Wangnapi *L. Robinson* 213

PEER REVIEWERS

215

MEDICAL RESEARCH PROJECTS IN PAPUA NEW GUINEA

216

MEDLARS BIBLIOGRAPHY

218

EDITORIAL

A case for the introduction of a rotavirus vaccine in Papua New Guinea

It is widely recognized that improving child health remains one of the great challenges facing Papua New Guinea (PNG). The poor health outcomes of the nation's children are often cited; nonetheless, the statistics are worthy of reiteration. PNG has an infant (children less than 1 year old) mortality rate of 50/1000 live births, and a childhood mortality rate (aged <5 years) of 60/1000 live births. These figures are the worst in the Pacific, and equate to the death of approximately 13,000 children each year (1). Collectively, infectious diseases such as pneumonia, malaria, tuberculosis, diarrhoeal diseases, meningitis and HIV (human immunodeficiency virus) infection are leading causes of morbidity in PNG, and account for approximately half of all deaths (2). The burden of many of these infectious diseases, particularly pneumonia and diarrhoea, is greater in children than in adults.

Clearly, there is no silver bullet for improving child health in PNG or other low-income countries but some recent interventions have improved child health outcomes. There is evidence to suggest that malaria transmission has decreased in recent years with interventions such as long-lasting insecticidal nets (3), which no doubt has had a positive impact on infant and child health. Improved treatments including oxygen for children with severe respiratory infections (4) and updates to antimicrobial treatment guidelines in the face of growing antimicrobial resistance (5) are likely to optimize recovery from severe infections such as pneumonia and meningitis. Other than implementation of oral rehydration solution, few recent strategies have improved health outcomes for children suffering from diarrhoea in PNG, despite diarrhoea being recognized as a leading cause of morbidity and a significant contributor to mortality in PNG (6).

The World Health Organization (WHO) and United Nations Children's Fund (UNICEF) list vaccination as one of the most successful and cost-effective interventions to reduce child mortality (7). Arguably, the

most important interventions introduced in PNG in the last decade have been vaccines efficacious against *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae* (pneumococcus), the two leading bacterial causes of meningitis and pneumonia. Unfortunately, a lack of systematic aetiology studies pre- and post-vaccine introduction makes it difficult to quantify the reduction of morbidity and mortality associated with these vaccine programs. It is predicted that widespread global adoption of vaccines for pneumococcus and Hib could result in a reduction in overall under-five mortality by 11% and 4%, respectively (8). Given the high burden of pneumonia in children in PNG, and the reported role of Hib and pneumococcus in invasive disease (9), similar reductions in mortality could be expected in PNG.

To further improve the health of children in PNG we need to continue to invest in existing child health interventions, including but not limited to those mentioned above, and carefully consider future interventions. Based on current PNG rotavirus surveillance data, stated health priorities for PNG, and consideration of the global impact of rotavirus vaccines in countries in which they have been introduced (10-12), PNG must prioritize the introduction of a rotavirus vaccine.

Diarrhoeal illnesses are the second most common cause of mortality in children under the age of five years, after pneumonia, causing 700,000 deaths globally each year, as estimated by Walker et al. in 2013 (13). Although diarrhoeal illnesses result from a wide variety of aetiological agents, a leading cause of severe childhood diarrhoea is rotavirus. In 2004, before the 2007 rollout of the current rotavirus vaccines, it was estimated that approximately 500,000 children died each year from rotavirus infections (14). The true number of deaths due to rotavirus may be lower given the recognized role of *Shigella* and other pathogens in acute watery diarrhoea and, after 2007, the impact that the rotavirus vaccine may have had since the estimate of 500,000 deaths per annum in

2004. Nonetheless, rotavirus is an important cause of moderate and severe diarrhoea (15).

Diarrhoeal diseases are a major health burden in PNG (6); and there is longstanding evidence that rotavirus is a major cause of diarrhoeal disease in children (16-20). There have been no recent case-control studies investigating the cause of diarrhoea in PNG, reflecting the reluctance of the international funding community to provide monetary support to enable studies to investigate the aetiology of high-burden diseases in this country. However, one previous case-control study (17) and recent rotavirus surveillance (16,20) provides insight into the likely contribution that rotavirus plays in childhood morbidity in PNG. The case-control study, conducted at the Goroka Hospital in 1985-1990, investigated the causes of diarrhoea leading to hospitalization of children. In that study, Howard et al. detected rotavirus in 23% of cases (17). The more recently completed surveillance in Eastern Highlands Province has yielded a similar proportion of positive samples from symptomatic patients (16,20). These detection rates are higher than those observed in cases in the Global Enteric Multicenter Study (GEMS), conducted on children <5 years of age in seven low-income countries, where approximately 17% of participants were rotavirus positive (15).

Two efficacious rotavirus vaccines have been introduced into the vaccination schedules of many countries worldwide: RotaTeq, licensed by Merck & Co; and Rotarix, licensed by GlaxoSmithKline Biologicals. As of May 2016 there were 81 countries that had introduced a rotavirus vaccine into their national immunization program. Within the Western Pacific Region, ie, those countries neighbouring PNG, 7 countries have introduced the vaccine: Australia, Fiji, Kiribati, Marshall Islands, Federated States of Micronesia, New Zealand and Palau (21). There are new rotavirus vaccines in development that are expected to offer benefits the two existing vaccines currently do not offer, such as lower cost and birth dose administration (22).

The first licensed rotavirus vaccine, Rotashield®, was withdrawn nine months post-licensure in the United States in 1999 due to a confirmed association with intussusception (23). There was an apparent 37-fold increased risk of intussusception in the

3-7 days after dose 1, or approximately 10-20 cases per 100,000 doses. However, large Phase 3 studies of Rotarix and RotaTeq found no evidence of an association. Subsequent post-licensure studies have found a 4- to 5-fold increased risk of intussusception in the 7 days after dose 1 of Rotarix or RotaTeq, which equates to approximately an additional 2 cases of intussusception per 100,000 first doses (24,25). As such, the vaccines have been introduced broadly with strict upper age limits of administration and ongoing global safety surveillance. The benefits of rotavirus vaccination clearly outweigh the risks, as recognized by the WHO Strategic Advisory Group of Experts (26).

A recent meta-analysis of the effectiveness of rotavirus vaccines in 19 low- and middle-income Latin American and Caribbean countries found that rotavirus vaccination was effective in reducing severe cases of rotavirus gastroenteritis by 82% and hospitalization due to rotavirus by 85% (Rotarix) and 90% (RotaTeq) (27). Clinical trials of the two oral attenuated rotavirus vaccines have demonstrated high efficacy against severe rotavirus disease (28,29) in high-income countries but both vaccines have substantially lower efficacy, and a more rapid waning of protection, in low-resource settings (30). Several hypotheses have been suggested to explain this gradient in vaccine efficacy between lower- and higher-income countries, including maternal antibodies (31), micronutrient deficiencies, microbial overload on mucosal surfaces and alteration of the microbiome (32). Studies to date have not shown that limitation of breastfeeding before and after rotavirus vaccine administration improves the immune response (33,34) and studies providing additional doses of vaccine or supplementation for specific micronutrient deficiencies are underway. Solutions to this problem are still needed and will require further research to determine if the immunogenicity of rotavirus vaccines can be boosted during immunization in children from developing countries. Despite the lower efficacy in low-income settings relative to high-income settings, the actual benefit of rotavirus vaccination is probably higher in low-income countries, where the burden of severe rotavirus disease and mortality is greatest.

In a 2013 edition of the *Papua New Guinea Medical Journal* we were fortunate to be able to dedicate an entire issue to enteric

diseases. This provided a timely opportunity to reflect on the burden of gastrointestinal diseases in PNG, particularly with the cholera outbreak of 2009-2011 (35) fresh in the minds of health professionals, researchers and policy makers. Although the cholera outbreak served as a stark reminder of how vulnerable people living in PNG are to gastrointestinal infections, there have been few (or no) policy changes or multisite interventions aiming to decrease the burden of gastrointestinal infections in PNG. Improving access to safe water, sanitation and hygiene (collectively termed WASH) is arguably the most important intervention to improve health in all age groups in PNG (36,37). However, unlike the case with most gastrointestinal diseases, improvements in safe water sources and sanitation have little effect on the burden of rotavirus infection (38). Vaccination is one of the only interventions proven to be effective in preventing childhood infection with rotavirus. This highlights the need for an integrated and multi-faceted approach to reduce the burden of gastrointestinal diseases. There are a myriad of interventions, and we should learn from the approach taken to the control of malaria, where multiple interventions have been proposed (39) and subsequently adopted (to varying degrees of success) in a coordinated and cohesive approach globally. In PNG a coordinated approach has also been proposed (40), with some success in the coordination of efforts of the private and public sector (41). The introduction of a rotavirus vaccine is likely to improve health outcomes of children in PNG, while also contributing to a decrease in the overall burden of gastrointestinal disease. Thus a rotavirus vaccine is likely to be an important component of a coordinated approach to combat gastrointestinal disease in PNG.

In the aforementioned enteric disease special issue of the Journal, Pamela Toliman and colleagues contributed an excellent review of the aetiology of diarrhoea in PNG (42). The review included a section on rotaviruses, and the authors postulated that "the introduction of a rotavirus vaccine may be possible in the near future". The introduction of a rotavirus vaccine in PNG would be consistent with the WHO recommendation that all countries include the rotavirus vaccine in their national immunization program (26). Moreover, it would appear to be consistent with PNG's health priorities. Although the introduction of the rotavirus vaccine is not

specifically stated in the current PNG National Health Plan, the Plan does recognize the need to improve child survival and reduce the burden of communicable diseases as key strategic areas (6). Moreover, the PNG National Child Health Plan acknowledges a potential role for the rotavirus vaccine in reducing deaths from diarrhoea in PNG (43). Unfortunately, consistency with stated policy does not ensure success, and adding another vaccine to PNG's Expanded Programme on Immunization is not without financial, human resource and logistical costs. With these factors in mind now is the time to plan for the introduction of a rotavirus vaccine and, like the efforts to combat malaria in PNG, the plan should draw on the many private and public sector organizations that have a vested interest in improving the health of children in PNG.

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Challenges of diagnosing leprosy in a rural low-endemic setting in Papua New Guinea

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SUMMARY

Papua New Guinea reached elimination of leprosy at the national level in 2000 with a prevalence of 0.7/10,000 population. In a District Health Centre on Karkar Island in the Madang Province of Papua New Guinea there have been 5 cases reported in the last 15 years, the last of which was 10 years ago. We report a case of leprosy that was overlooked at the Outpatient Department resulting in delayed treatment due to the lack of trained staff and the unavailability of appropriate drugs. The patient was referred to the Disease Control Unit at the Modilon Provincial Hospital and commenced on multidrug therapy 5 weeks after the initial diagnosis. This case report highlights the importance of continuous health care provider training and community awareness on diseases that have been eliminated in some provinces but not others.

Introduction

Leprosy or Hansen's disease is a chronic granulomatous infectious disease caused by the intracellular bacillus *Mycobacterium leprae* that affects skin and peripheral nerves. It is a neglected tropical disease that is diagnosed clinically based on the presence of one or more of the following cardinal signs: hypopigmented or reddish anaesthetic skin lesion(s); thickened peripheral nerves with loss of sensation in the area of distribution; and a positive skin smear for acid-fast bacilli. Delayed diagnosis and treatment is associated with nerve impairment and physical deformities. The implementation of multidrug therapy (MDT) has led to the widespread decline in the prevalence of leprosy (1).

In 1991 the Forty-fourth World Health Assembly declared its commitment through the World Health Organization (WHO) to eliminate leprosy as a public health priority disease by the year 2000, with the aim of reducing the prevalence of leprosy to less than one case per 10,000 at the national level (2). In addition, the Enhanced Global Strategy

2011-2015 for reducing the disease burden aimed to reduce the rate of new leprosy cases with grade 2 (visible) disabilities by at least 35%, compared with the baseline in 2010 (0.25/100,000), by the end of 2015 (3).

Although Papua New Guinea (PNG) reached leprosy elimination status at the national level in 2000, leprosy is still reported in all provinces and remains endemic in six (4). The Leprosy Mission has been working alongside the National Department of Health (NDoH) to roll out programs to integrate leprosy services into general health services, especially the training of the Disease Control Officers, starting in the 6 endemic provinces, namely, Western, East New Britain, Central, Gulf, West Sepik and the National Capital District, as well as in 5 other districts (Bogia, Alotau, Wewak, Central Bougainville and Lae) that are hotspots in low-endemic provinces. As part of the 2011-2015 National Leprosy Control Program, the Provincial Disease Control Officers are the chosen focal points for leprosy program implementation. It is expected that the training will move from the provincial level to the district level, to Church-

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based organizations and eventually to all health facilities. The aim of the control program was to sustain the national elimination status and to eliminate leprosy in the 6 endemic provinces by the end of 2015.

We present a case of leprosy found at one of the Church-based health facilities, whose cadres of health workers have not had training on one of the leprosy programs in the last 10 years.

Case report

The patient was a 50-year-old woman with no family history or past medical history of leprosy. She presented to the Outpatient Department of the District Health Centre complaining of discoloured skin patches on her body with no other associated symptoms for a period of four months. She was diagnosed as a case of fungal skin infection and treated with ketoconazole. Despite completion of antifungal treatment, she returned to the Outpatient Department with the same complaint and was told to wait for another month to see if there would be any improvement before returning.

A month later, she returned with the same complaint. A team of visiting clinicians working at the Outpatient Department recognized the hypopigmented lesions and further examination revealed the skin patches to be anaesthetic (Figures 1 and 2).

A slit-skin smear performed by the visiting

team was said to be negative for acid-fast bacilli and was discarded by the laboratory staff without a second opinion due to the confusion on the procedures that were involved in sending the slide to the provincial hospital. Nevertheless, MDT was commenced and treatment supplies were organized through the Provincial Disease Control office. The patient improved on medication with no reported reactions. Furthermore, all household contacts were examined and found to have no symptoms or signs of leprosy.

Discussion

The 2011-2015 Enhanced Global Strategy for reducing the burden of leprosy is expected to reduce the occurrence of new cases and lower the transmission of the disease in communities. In a weekly epidemiological record in 2012, WHO emphasized that National Leprosy Programs should focus on underserved populations and inaccessible areas to improve diagnosis and treatment (3). The country's challenge is to provide sustainable services for patients who have been on treatment and for those new cases who will visit health facilities, especially in areas where leprosy is no longer endemic. It is well recognized that when a disease is no longer considered a public health problem, complacency and reduced priority often result in the resurgence of the disease. In a resource-limited setting, where dermatology services are not available, it is vital that leprosy diagnosis and treatment is continuously taught at all medical, paramedical and nursing



Figure 1. Hypopigmented skin lesion on the back.



Figure 2. Anaesthetic skin patch on the right upper arm.

schools and that awareness continues as part of the public health campaigns of the NDoH.

Studies in other countries where leprosy has been eliminated and has become a rare skin disease have found that health care providers lack skills and have poor knowledge of the early diagnosis of leprosy (5), and this is likely to be the same for PNG.

Delaying commencement of treatment in this case was a result of the lack of clinical diagnostic skills and not knowing where to refer the patient. We recommend that a standard operating procedure including control guidelines as a tool for the early diagnosis of leprosy should be made available for each province and be distributed to every health facility. The present case report strongly reaffirms the 2011-2015 Mission of the National Leprosy Control Program (4) and highlights the need for a country-wide sustainable leprosy service that can lead to upskilling of health care providers, timely case detection, appropriate MDT treatment, prevention of disabilities, rehabilitation of people affected with leprosy and awareness of leprosy as a neglected disease.

Consent

Written consent was obtained from the patient for publication of this case report and the photographs.

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Towards elimination of yaws in Papua New Guinea

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SUMMARY

Yaws is a chronic infectious disease caused by *Treponema pallidum* subsp. *pertenue*, which causes disease of the skin, bones and joints and is spread by skin-to-skin contact. Most cases are seen in young children living in rural remote communities in coastal areas. A major campaign to eradicate yaws between 1953 and 1958, by mass treatment of affected communities with long-acting, injectable penicillin, reduced the number of cases by 95% in Papua New Guinea (PNG), but yaws has reappeared in recent years. In the period 2008-2015 PNG reported >25,000 cases per year, and the country is currently home to about 40% of all the cases of yaws in the world. In 2012, one oral dose of azithromycin was shown to be as effective as intramuscular penicillin in the treatment of the disease, and the World Health Organization launched a new initiative to eradicate yaws by 2020. The new treatment policy recommends mass azithromycin treatment of the entire population in endemic areas. Continued vigilance for the development of macrolide resistance in *T. pallidum* ssp. *pertenue* will be important as the drug is introduced into public health practice.

Introduction

Yaws is a chronic infectious disease caused by *Treponema pallidum* subsp. *pertenue*, which is spread by skin-to-skin contact in warm humid environments, mainly among children. The disease consists of primary, secondary and tertiary phases. The first sign of infection is a localized papilloma or a solitary yellow-brown crusted ulcer. Secondary lesions consist of smaller multiple skin excrescences

or scaly plaques, and osteoperiostitis of long bones. In some individuals, such inflammation leads to severe deforming bone lesions. The aim of the treatment of yaws is both to halt the progression of disease by curing the infection and to stop transmission to susceptible individuals. Tissue injury occurring during the early stages of infection resolves completely following adequate therapy, but tissue damage occurring during the late stages of infection is irreversible (1).

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Yaws was the first disease to be targeted for eradication by the World Health Organization (WHO), and mass screening and treatment programs led by WHO in the 1950s reduced the global prevalence by more than 95% (2). It has since re-emerged as an important public health problem in several regions of the world, including Papua New Guinea (PNG).

Ongoing research in PNG has led to updated recommendations for clinical decision-making, particularly in the areas of diagnostic testing and the use of antibiotics. The recent demonstration that a single oral dose of azithromycin is as effective as injectable penicillin in the treatment of yaws has prompted renewed interest in the possibility of yaws eradication (3).

Epidemiology

Yaws was highly prevalent in PNG before the 1950s with more than 20,000 annually reported cases (4,5). A nation-wide mass treatment campaign targeting the entire population of PNG took place between 1953 and 1958, covering more than 90% of the population (6). The campaign was successful: only 2352 cases were reported in 1959, and fewer than 500 cases were reported each year until 1973. A slight increase in the number of cases was recorded between 1973 and 1978, but it did not exceed 1000 cases per year (7), and most of them occurred in rural areas, in Bougainville and around Rabaul in East New Britain (8). The disease was rarely reported in the highland districts and thought to be nonexistent in the Central Province and Port Moresby (9). Consequently, yaws was removed from the national list of reportable diseases by the Ministry of Health.

In 1978 there was a rapid increase of yaws cases on Karkar Island, Madang Province, that prompted a mass treatment campaign targeting the entire population of the island (8). Although the mass treatment was reported to have covered more than 90% of the population, the island continued to report cases of yaws.

In the middle 1980s, there was a resurgence of yaws with more than 5000 cases annually. Clusters of cases were reported in the provinces of East and West Sepik, East and West New Britain, New Ireland and Milne Bay. An outbreak in Yilui village, West Sepik Province, affected 35% of the population

(193 clinical cases) (8). In the Kiriwina and Trobriand Islands of Milne Bay Province, a number of cases among children were also reported in 1984 (10). In 1988, another outbreak was reported on Karkar Island, in the village of Takia, where 6% of the population presented with early yaws lesions (11).

Between April 2000 and September 2001, the Nine Mile Clinic in Port Moresby identified 494 cases which were confirmed by serological tests (12). Most of the cases originated from people living in settlements with poor access to clean water and electricity.

Nowadays yaws is again a nationally notifiable disease through the National Health Information System (NHIS) monthly reports that are being collected via forms from hospitals, health centres and aid posts throughout the country. In the period 2008-2012 PNG reported >25,000 cases per year; 19,824 yaws cases were reported in 2013, 29,886 in 2014 and 28,584 in 2015 (Figure 1). Six provinces are currently considered very highly endemic (ie, ≥ 1000 cases in 2015), including New Ireland, West and East New Britain, Morobe, Madang and North Solomons, whilst six provinces are considered highly endemic (ie, 500- <1000 cases in 2015), including National Capital District (NCD), Milne Bay, Enga, Oro (Northern), West Sepik, and East Sepik (Figure 2). The prevalence is lower in the Highlands Region, where 15 districts reported less than 10 yaws cases in 2015.

According to the latest WHO figures, PNG is currently home to about 40% of all the cases of yaws in the world (13). Other high-endemic countries are the Solomon Islands (12,372 in 2012) and Ghana (8980 in 2012). The number of active infections is below 300 cases per year in Benin, Cameroon, Central African Republic (CAR), Republic of the Congo, Democratic Republic of Congo (DRC) and Togo but without formal programs for active case-finding it is likely that there is under-reporting from all of these countries.

Bacteriology

Treponemes are Gram-negative spirochaetes which cannot be cultured in vitro (2). They divide slowly (every 30 hours), have a characteristic corkscrew-like motility and can move through gel-like environments such as connective tissue. They are rapidly killed by

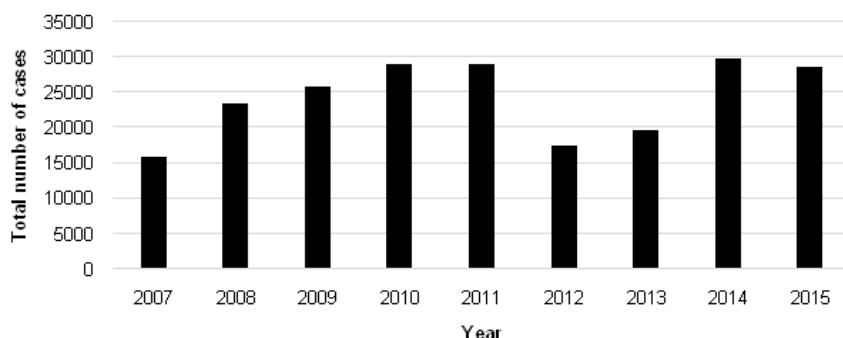


Figure 1. Total number of reported yaws cases by year in Papua New Guinea, 2007-2015.

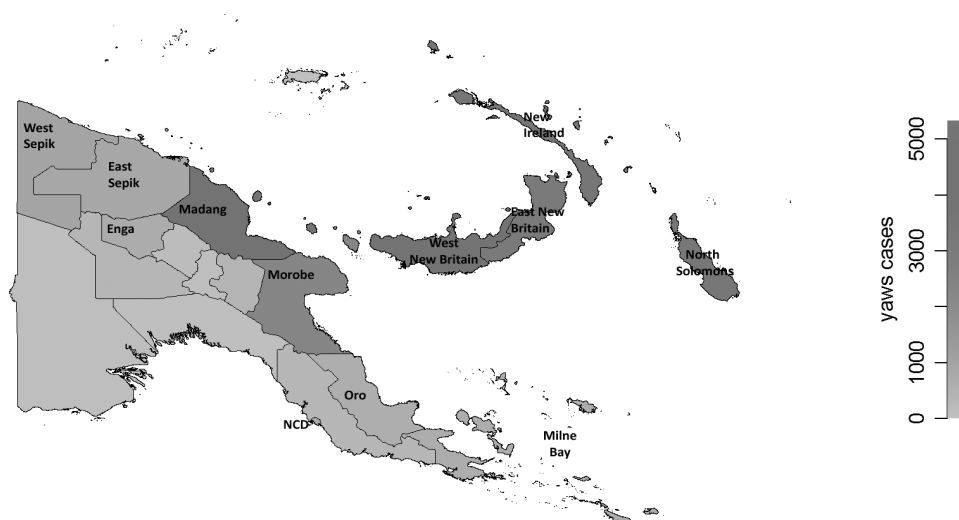


Figure 2. Geographic distribution of yaws in Papua New Guinea in 2015. NCD = National Capital District

drying, oxygen exposure or heating, and cannot survive outside the mammalian host. The four pathogenic treponemes are morphologically and serologically indistinguishable, and share at least 99% DNA sequence homology (14). Yaws is caused by *Treponema pallidum* ssp. *pertenue*. Whole genome sequencing has demonstrated that the genome of *T. pallidum* ssp. *pertenue* differs by only 0.2% from that of *T. pallidum* ssp. *pallidum*, the causative organism of venereal syphilis. The phylogenetic relationship between different subspecies of treponemes is not clear, as very few isolates of the non-venereal subspecies are available (15).

Clinical features

The clinical features of yaws consist of

primary, secondary and tertiary stages. If left untreated, the infection may become latent at any time, with only serological evidence of infection. Relapses have been reported up to 10 years following initial infection (1).

The initial or primary lesion (known as a 'mother yaw') appears at the site of inoculation on an exposed part of the body 2-12 weeks after inoculation. It usually starts as a localized papule, which may develop into a large nodule 2-5 cm in diameter that ulcerates. Ulcers are usually non-tender and have a characteristic granular surface reminiscent of a raspberry (hence the name 'framboesia') (Figure 3). Ulcers often exude a yellow discharge that may dry to form a crust. The primary lesion is most commonly found on the legs and ankles (65 to 85% of cases)

(16). Without treatment the ulcer usually heals after 3-6 months, regressing into a pitted scar with dark margins.

Secondary lesions, which are the result of lymphatic and haematogenous spread of organisms, appear from a few weeks to 2 years after the primary lesion. Arthralgias and malaise are probably the most common, albeit non-specific symptoms of secondary yaws; up to 75% of children aged under 15 years with yaws presented with arthralgia in PNG (16). Secondary skin lesions consist of multiple smaller excrescences, often resembling the initial papule, that may ulcerate. A generalized eruption may cover a region of the body or the whole body. In secondary yaws, early osteoperiostitis of the proximal phalanges of the fingers (dactylitis) or long bones (forearm, tibia or fibula) may result in nocturnal bone pain or swelling (17).

A small proportion of cases (<10%) develop tertiary stage lesions after 5 years or more of untreated infection. The late-stage skin lesions are characterized by gummatous nodules with necrotic tissue destruction, followed by debilitating scarring and contracture. At this stage, yaws can cause disfigurement and long-term disabilities.

Differential diagnosis

Yaws shares clinical features with a number of other conditions common in the tropics. The primary lesion of yaws may be mistaken

for cutaneous leishmaniasis, tropical ulcer (a typically painful and malodorous ulcer caused by anaerobic fusobacteria and *Treponema vincentii*) or pyoderma.

An important recent finding has been the emergence of *Haemophilus ducreyi* as a common cause of chronic skin ulceration in yaws-endemic communities (18). These lesions are extremely difficult to distinguish clinically from yaws lesions and may be found in patients who are both seropositive and seronegative for yaws (19). In a cohort study in PNG during a yaws elimination campaign, *H. ducreyi* DNA was found by PCR in 54 (74%) of 73 individuals with ulcers. There are also reports of *H. ducreyi* as a cause of non-genital skin lesions from the Solomon Islands (19), Vanuatu and Ghana (20). Further work to delineate the epidemiology, clinical features and treatment responsiveness of this emerging pathogen-disease association is urgently needed to better understand the role of *H. ducreyi* in chronic skin ulceration.

Diagnosis

T. pallidum is not viable ex vivo, which has limited the value of direct diagnostic methods. Whilst dark-field microscopy allows visualization of spirochaetes (2), the skills and equipment required are not available in most locations, even in relatively high-income settings. Instead, diagnosis has rested on combinations of serological assays and, more recently, nucleic acid amplification tests



Figure 3. Yaws ulcers before and after treatment.

(NAATs).

As with venereal syphilis, serology has been the mainstay of laboratory diagnosis. Serological testing traditionally involves a non-specific, non-treponemal antibody test followed by a more specific treponemal test for diagnostic confirmation. The venereal disease research laboratory (VDRL) and rapid plasma reagin (RPR) tests are referred to as non-treponemal tests and detect antibodies to a variety of antigens including cardiolipin. These tests may give rise to biological false positives, but more accurately reflect active disease activity and can be used as a test of cure (21), since titres fall following successful treatment. They are often performed on serial dilutions of serum to give a quantitative titre, defined as the reciprocal of the highest dilution that yields a positive result. *T. pallidum* particle agglutination (TPPA) and haemagglutination (TPHA) assays are used to detect *Treponema*-specific antibodies. Once positive, these tests usually remain positive for life (22).

A major challenge for clinicians and epidemiologists has been that the pathogenic treponemes are serologically indistinguishable. Given the considerable epidemiological and clinical overlap between the syndromes, this continues to represent a major barrier to accurate data on the incidence and prevalence of yaws. However, as syphilis is less likely to occur in children (except via congenital transmission), serologically confirmed cases of suspected yaws in children are still most likely to reflect true yaws.

Serological assays do require access to laboratory facilities, which are rarely available to the remote communities where yaws is endemic. Rapid diagnostic tests (RDTs)

have proved effective in the diagnosis of syphilis (23) and a number of evaluations of their performance in diagnosing yaws have recently been undertaken. In PNG, an RDT test – the Dual Path Platform (DPP) – that detects both treponemal and non-treponemal antibodies (Chembio Diagnostic System Inc., New York, USA – Figure 4) showed excellent performance in confirming the diagnosis of yaws in patients with suspected clinical lesions (24).

The DPP is read by naked eye and can assist in distinguishing between current and past infection. A current infection is characterized by the appearance of three red/magenta lines in the window of the device: a treponemal line or T1, a non-treponemal line or T2 and a control line or C. Visible T1 and C lines with no visible T2 is interpreted as an old or previously treated case. Visible T2 and C lines with no visible T1 is interpreted as a false-reactive test. A nonreactive result is demonstrated by the appearance of only the C line. When compared with TPHA, the DPP treponemal line (T1) had a sensitivity of 88.4% and specificity of 95.2%. By comparison with the RPR test, the DPP non-treponemal line (T2) had a sensitivity of 87.9% and specificity of 92.5%.

In the Solomon Islands the DPP was shown to be of use for community surveillance and mapping (25). The sensitivity of the test kit was lower than reported in PNG, but it should be noted that this predominantly reflects the lower antibody titres found in screening asymptomatic individuals. These tests may help to improve reporting practices for yaws world-wide.

The key value of the DPP test resides in the



Figure 4. Point-of-care Dual Path Platform (DPP) yaws assay.

non-treponemal T2 element, which provides rapid and accurate results for field diagnosis of active untreated yaws infection with only a finger-stick blood sample. Increased use of the DPP RDT will allow improvements in the accuracy and validity of national yaws surveillance systems and facilitate an improved understanding of the world-wide epidemiology of yaws.

Polymerase chain reaction (PCR) assays have been developed for the diagnosis of venereal syphilis, but could also be adopted for the diagnosis of yaws. To distinguish between subspecies of *T. pallidum* combined PCR and sequencing has traditionally been required and this has only been available at research laboratories. A multiplex PCR for the subspecies level identification of treponemal infections has now been developed (26). The method to differentiate among subspecies relies on molecular identification of genetic signatures that are specific for *T. pallidum* ssp. *pertenue*. PCR has also emerged as a tool for diagnosing other causes of skin lesions in yaws-endemic populations, including *H. ducreyi* and *Mycobacterium ulcerans*.

Another molecular test of pivotal importance for those involved in the diagnosis and treatment of human treponemal infections is represented by the assay to detect the point mutations in the 23S rRNA genes known to confer resistance to azithromycin (and macrolides in general), the antibiotic that WHO is planning to use in the new eradication campaign for yaws and endemic treponematoses (27). Macrolide resistance in *T. pallidum* is associated with a single A to G mutation occurring at either position 2058 or 2059 of the 23S ribosomal RNA gene (28). Multiplex PCRs capable of differentiating treponemal subspecies and detecting mutations associated with azithromycin resistance are under development and may play a role in molecular surveillance for drug resistance during the WHO yaws eradication campaign.

Treatment

According to the PNG Standard Treatment book for children (2016 edition) (29), skin ulcers larger than a 10 toea coin that are not suspected to be yaws or have a negative RPR test can be treated with amoxycillin orally 3 times daily for 3 days. If the ulcer does not get better then the treatment should be

changed to a broad-spectrum antibiotic such as cotrimoxazole orally twice daily for 5 days and tinidazole orally once daily for 3 days. If the sores are raised or the RPR test is positive then yaws is considered the most likely diagnosis and first-line treatment is either a single dose of intramuscular benzathine penicillin or azithromycin 30 mg/kg orally stat. Treatment of contacts is also recommended. In our experience non-yaws ulcers are mainly caused by two different types of infection: skin strains of *Haemophilus ducreyi*, which are susceptible to amoxycillin, and polymicrobial infections related to *Corynebacterium diphtheriae* and *Fusobacterium nucleatum*. Therefore the currently recommended first-line treatment with amoxycillin is appropriate for the majority of non-yaws skin ulcers except for those where anaerobes are involved; these will respond to second-line treatment with antianaerobic antimicrobials.

Long-acting penicillin (single intramuscular dose) has been the mainstay of treatment for yaws for the past 60 years. Therapeutic levels of penicillin can be achieved by giving repeated doses of short-acting benzylpenicillin preparations (ie, aqueous benzylpenicillin) or by a single intramuscular injection of the slowly absorbed, repository benzylpenicillin preparations (ie, benzathine penicillin). The WHO-recommended regimen consists of 1.2 million units for adults and 0.6 million units for children (30), the dosing being lower than for syphilis. However, there is no definite knowledge about the total dosage of penicillin required for the satisfactory treatment of yaws and PNG standard treatment guidelines continue to recommend the higher dose of 2.4 and 1.2 million units, respectively.

Despite extensive use of the antibiotic, *T. pallidum* remains extremely susceptible to penicillin, with no compelling evidence that resistance has emerged. There have been a few reports in PNG of treatment failure following treatment with penicillin (11). Clinical relapse among treated cases on Karkar was reported to be 8% at 22 months. Whilst these findings might be interpreted as suggesting that yaws cases in this area had decreased susceptibility to penicillin, the difficulty of distinguishing treatment failure from reinfection makes the significance of these findings uncertain. The major drawbacks of injectable penicillin have been the requirement for trained medical staff to administer treatment, concerns over sterilization of needles and the risk of

transmitting other infections, and possible risk of anaphylaxis. Also, administration by injection challenges the acceptability of and adherence to the treatment.

The macrolide antibiotic azithromycin was previously shown to be effective in treating venereal syphilis. A landmark paper published in 2012 compared a single oral dose of azithromycin (30 mg/kg) to benzathine penicillin in the treatment of primary and secondary yaws (31). Azithromycin was non-inferior to penicillin, with clinical and serological cure in 96% at 6 months of individuals randomized to treatment with azithromycin. Efficacy of azithromycin was 91% for patients with primary stage lesions and 100% for patients with secondary stage disease, including polyarthralgia or bone pain and swelling.

Similar findings were reported among 500 patients with confirmed primary yaws skin lesions in Ghana (C. Kwakye, personal communication). Clinical outcomes were similar to those seen in PNG, and the serological response at 6 months was superior in the azithromycin group to that in the penicillin group.

The main advantage of azithromycin is oral administration versus parenteral administration of benzathine penicillin. Oral azithromycin is safe and easy to administer and avoids the need for injection, no trained staff are needed to treat cases in remote areas, infection and anaphylactic shock control measures are not necessary, and treatment is more acceptable to communities who need it. Azithromycin needs only to be taken once (single dose), which improves patient compliance compared to all other oral antibiotics for yaws, such as doxycycline or erythromycin, which require multiple dosages for 7 days or more.

Azithromycin can be used in pregnancy, but the safety profiles of benzathine penicillin and erythromycin have been better established. Benzathine penicillin and erythromycin are therefore preferred treatments in pregnant women.

One area of concern is the possibility of resistance to azithromycin, which is now widespread in sexually transmitted strains of *T. pallidum* (27). Monitoring for the development of resistance in *T. pallidum* ssp. *pertenue* will

be an extremely important component of the WHO yaws eradication strategy.

Patient monitoring after treatment

Patients with yaws should be examined four weeks following administration of antibiotic treatment. In most cases, complete healing of the primary and secondary lesions is observed within this period of time. Failure of an early-stage yaws lesion to heal within four weeks is considered evidence of treatment failure. Patients with clinical treatment failure should be treated with an alternative agent. Microbiological studies may help to distinguish whether the non-healing lesion is due to infection by an alternative pathogen.

Patients should also undergo follow-up non-treponemal testing at 6 and 12 months after treatment. Assessing the serological response to treatment is frequently difficult, and definitive criteria for cure have not been established. The RPR or VDRL titres usually decline within 6 to 12 months; in most cases, they become negative within less than two years. Serological treatment failure is defined as a ≥ 4 -fold increase in the RPR titre or titre persistently ≥ 64 over 12 months. Many experts suggest that a ≤ 4 -fold decrease in titre should be included in this category. Patients who do not have an appropriate decline in serological titre should be managed with another course of treatment. Most serologically defined treatment failures are thought to be caused by reinfection following treatment rather than by relapse or true antibiotic resistance. In addition, it is important to ensure that all household and community contacts are treated to decrease the risk of reinfection.

Mass treatment for yaws eradication

Yaws is a potentially eradicable disease since the diagnosis and treatment are relatively straightforward. There is evidence of a possible animal reservoir of yaws in Africa (32), which may interfere with elimination efforts in Africa, but no such reservoir has been identified in the Pacific.

In 2007, experts and delegates from endemic countries agreed on a renewed effort to assess yaws burden and restart activities for disease control (33). In 2012, WHO officially launched a road map to accelerate work to eradicate yaws. This was ignited by the potential use of azithromycin to fight the

disease. WHO set a target of 2020 for global yaws eradication (3).

The approach to eradication, called the 'Morges Strategy', is centred on community mass treatment with a single dose of oral azithromycin (30 mg/kg, maximum 2 g) to be given to entire populations in areas known to harbour yaws. Benzathine penicillin may be used as an alternative for individuals who are allergic to macrolides. For use in pregnancy, the recommended antibiotic is also benzathine penicillin at a dose of 1.2 million units. Mass treatment is followed by surveys every six months to detect and treat remaining cases. In the interval between surveys, local health facilities must treat infected individuals and their close contacts. The eradication of yaws will be declared when no new active cases are reported over 3 successive years, supported by evidence of no transmission among children younger than 5 years.

The efficacy of this approach was demonstrated in a study of mass treatment performed in rural villages on Lihir Island, Papua New Guinea (34). Of 16,092 residents, 83% received mass treatment with single-dose azithromycin and were monitored for one year; the prevalence of active yaws decreased from 2.4 to 0.3%, and the prevalence of latent yaws with high-titre seroreactivity (rapid plasma reagin ≥ 16) decreased from 18.3 to 6.5%, with a near absence of high-titre seroreactivity in children 1 to 5 years of age. No evidence of macrolide resistance was observed.

Notwithstanding, we are yet to determine how many rounds of mass drug administration of azithromycin are required to achieve eradication. The research conducted in Lihir Island suggests that the best strategy might consist of 3 rounds of mass treatment (OM and others, unpublished data).

Addressing the issue of drug resistance during mass treatments for yaws requires efforts along several fronts, including tracking use of macrolides for other purposes (and ensuring that the correct dose for yaws is administered), monitoring patients for treatment failure (and switching to an alternative regimen) and analysing clinical specimens from patients who fail treatment for mutations that confer macrolide resistance (if feasible). Integration of molecular techniques will be necessary to facilitate monitoring for the emergence of macrolide-resistant strains

of *T. pallidum* spp. *pertenue*. Surveillance for treatment failure and resistance to azithromycin is important because there is biological evidence that antibiotic pressure can select for resistant strains of venereal syphilis (35).

Health education and improvement of social conditions can contribute to halting the spread of the treponematoses. Supportive measures for the eradication of yaws include: strengthening access to primary health care; training clinicians to detect and treat patients; general health education; improvement in the standard of living and in personal hygiene; and providing soap, water and clothing to children (36).

A final remark should be made regarding the possibility of integrating yaws diagnosis and treatment with existing programs that tackle other neglected tropical diseases (NTDs). PNG has a working program that provides mass drug administration (MDA) for lymphatic filariasis. By integrating MDA for both diseases, further efficiency would be promoted. Moreover, integration is also possible in the domain of diagnosis. There is room for promotion of mass screening campaigns tackling diseases with similar manifestations which are co-endemic in PNG, such as leprosy, Buruli ulcer (*Mycobacterium ulcerans* infection), scabies, tinea imbricata and yaws. If put in place, these would also result in further efficiency, both in terms of cost-saving and of disease identification. Integration would therefore contribute to the overall strengthening of the country's health system.

A number of operational challenges need to be overcome for PNG to achieve elimination of yaws – defined as the absence of active yaws and latent yaws (serological negativity for *T. pallidum* spp. *pertenue* infection in children younger than 5 years of age) for 3 consecutive years (Table 1). First, mass treatment and targeted treatment programs need to be effectively deployed in all yaws-endemic communities. Second, yaws elimination efforts will be conducted by local health systems that must keep high priority on other infectious disease control programs, such as deworming in children and malaria and filariasis elimination efforts. The right stakeholders need to be identified to allow execution of control programs in areas where public health infrastructure is constrained by

TABLE 1**ACTIVITY PLAN FOR YAWS ELIMINATION IN PNG**

Milestone	Activities
Mapping	Review routine surveillance data in districts currently reporting and not reporting yaws
Strengthened political commitment and resource mobilization at all levels	Develop advocacy material and training materials
Strengthened partnership and intersectoral collaboration	Conduct stakeholder analysis
Capacity building and community mobilization	Adapt technical and print guidelines/training materials for yaws eradication
Improved case detection rate	Organize house-to-house visits by village health workers/volunteers to identify suspected yaws cases
Implement high-coverage mass treatment (100%) in endemic areas	Drug procurement and logistics/operational costs
Supportive supervision and monitoring ensured	Develop checklist
Enhance surveillance	Development of a strategy integrating robust diagnostics such as point-of-care serological tests and new molecular tests
	Implement community-based surveillance
	Conduct serosurveillance in children aged under 5 years from implementation units
Validation missions conducted	Establish a national review committee for validation of yaws data

limited human and financial resources. Third, progress toward the elimination of yaws needs to be monitored by means of point-of-care serological surveys for latent yaws in children. Finally, maintaining high levels of community participation in treatment and monitoring will be essential.

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Shigellosis: a truly neglected disease in Papua New Guinea

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SUMMARY

Diarrhoeal diseases still affect many people, especially children living in impoverished and under-developed settings. In Papua New Guinea (PNG) diarrhoea remains one of the leading causes of hospitalization and a major cause of death. Here, we focus on the role of *Shigella* in diarrhoeal illness in PNG, and provide an overview of the causative organism and the illness. A review of the available data on the aetiology of diarrhoea in PNG suggests that shigellosis is a major cause of diarrhoeal illness. Since shigellosis can cause protracted and life-threatening illness an appreciation of the burden of shigellosis is important to aid in the development of optimal prevention and control strategies. Treatment strategies for all cases of moderate-severe diarrhoeal illness should centre on rehydration, but where antimicrobial treatment is required consideration should be given to the increasing antimicrobial resistance observed in *Shigella* isolates in PNG.

The global burden of diarrhoeal diseases and shigellosis

Diarrhoeal diseases remain one of the greatest contributors to morbidity and mortality globally, particularly among children less than 5 years of age. Of all infectious diseases, diarrhoea remains the second leading contributor to disability-adjusted life years (DALYs) – only ranking behind pneumonia. This high burden remains the case despite an approximate 50% decline in the burden of diarrhoeal illness between 1990 and 2010 (1,2). It is pertinent to note in the context of 'tropical' diseases that diarrhoea causes more all-age illness than malaria or tuberculosis (2), yet has attracted considerably less attention in recent years. Diarrhoeal diseases, along with pneumonia, appear to fall into a group of what might be described as truly neglected diseases. These two diseases have not received the attention and funding that malaria, tuberculosis and HIV (human immunodeficiency virus) infection have over

the past decade, and neither do they feature in the list of neglected diseases published by the World Health Organization (WHO) (3).

One of the challenges in addressing the high burden of diarrhoeal diseases is the myriad of aetiological agents that cause gastrointestinal infections. It is difficult to ascertain which pathogens are the greatest contributors to the burden of diarrhoeal disease, and thus which pathogens warrant targeted intervention. Despite the challenges of determining the cause of diarrhoeal diseases, recent studies and analyses of the data suggest that *Shigella* is one of the most important causes of diarrhoea (2,4). Indeed, *Shigella* has been recognized as a major contributor to the burden of diarrhoeal disease for almost two decades (2,5), although until recently there was a lack of strong aetiological data to support the epidemiological modelling. With the recent global enteric multicentre study (GEMS) (4) we now have irrefutable evidence that *Shigella* is a major contributor to

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diarrhoeal disease in children in low-income countries.

The GEMS study investigated the burden and aetiology of diarrhoeal disease in infants and young children in developing countries. *Shigella* is one of the four leading pathogens responsible for causing moderate-severe diarrhoea in children. Moreover, unlike other leading causes of diarrhoea such as rotavirus, *Cryptosporidium* and *Escherichia coli*, a child's chances of being infected with *Shigella* increased with age within the first 5 years of life (4). Although older children and adults are generally less susceptible to moderate-severe diarrhoeal illness, shigellosis does occur in these populations as well. Indeed, shigellosis is the second leading cause of diarrhoeal mortality amongst all ages globally (6). Thus *Shigella* is an important cause of moderate-severe gastrointestinal illness from infancy all the way through to, and including, adulthood.

While the greatest burden is in low-income settings where sanitation and hygiene are lacking, diarrhoeal diseases can also affect people in high-income settings. In countries such as the United States and Europe, *Shigella* is often found amongst children attending day-care centres, migrant workers, people living in correctional facilities, men who have sex with men, travellers visiting developing countries, and in communities struck by natural disasters or conflict (7).

Based on these global findings and the limited country-specific data currently available for Papua New Guinea (PNG), it is likely that *Shigella* is a major contributor to the burden of diarrhoeal illness in PNG. In this review we provide an overview of *Shigella* and shigellosis, provide an insight into the possible burden of shigellosis in PNG, and review other issues pertinent to shigellosis such as treatment, sanitation and hygiene.

An overview of *Shigella* and shigellosis

Shigella is a Gram-negative, non-motile, non-spore-forming, facultative anaerobic bacillus belonging to the family Enterobacteriaceae. *Shigella* is closely related to *E. coli*, an organism commonly present in the gut of many birds and mammals (7,8). Most strains of *E. coli* are non-pathogenic, though some strains cause disease of the gastrointestinal tract and other organ systems. *Shigella* spp. have a genome akin to that of *E. coli*, though

with the deletion of some segments of the genome and the acquisition of numerous insertion sequences. There are similarities in the pathogenesis of infection with *Shigella* and some of the diarrhoeagenic strains of *E. coli*, in particular the enteroinvasive *E. coli* (8).

The *Shigella* genus consists of four species: *S. dysenteriae*, *S. flexneri*, *S. boydii* and *S. sonnei* (7). Based on genetic analysis these four species of *Shigella* could be more accurately considered different varieties of a single species; however, the four species remain due to historical, epidemiological and clinical considerations. While the greatest burden is in children living in low-income settings (5), the pathogen can readily infect people of all ages living in both developing and industrialized settings. Humans are the only natural host, and therefore the main reservoir, for *Shigella*; however, the organism will survive in water and on foods. Reflecting this, transmission is primarily through the faecal-oral route from person-to-person contact (predominantly from inadequate basic hygiene practices), and also through the consumption of contaminated food and water supplies.

The distribution of each species varies according to socioeconomic circumstances: *S. sonnei* is the most common of the four species to be found in high-income settings (7,9). In low-income settings *S. flexneri* is considered the most common (5,7), with *S. dysenteriae* and *S. boydii* also present. Moreover, it appears that as countries transition to middle-income status the epidemiology of circulating strains also transitions. This supposition is based, in part, on the findings of von Seidlein et al.: *Shigella* surveillance across six Asian countries over 4 years found *S. flexneri* to predominate in Bangladesh, Pakistan, Indonesia, China and Vietnam, while *S. sonnei* accounted for most cases in Thailand. It was postulated that this difference in distribution may correspond to Thailand's rapid progression towards being a middle-income country (10). The findings of Vinh and colleagues seem to concur with this theory, with a shift in species distribution from *S. flexneri* to *S. sonnei* in southern Vietnam (11).

A similar phenomenon was observed as early as the 1960s in countries such as Israel, the United States of America and parts of Europe. Circulating *Shigella* species

transitioned from the once predominant *S. dysenteriae* to *S. flexneri* and *S. sonnei*, with the latter gradually becoming the predominant species in developed countries (12). It was postulated that this gradual rise of *S. sonnei* infections may be related to the increase of antimicrobial resistance (12), though other factors may also contribute.

Shigella is highly infectious: ingestion of as few as 10-100 bacteria can cause infection. Incubation time depends on the species serotype causing infection: typically 1-3 days, but can range from 12 hours to 7 days (13,14). Infection with *Shigella* is often characterized by blood and/or mucus in stools (dysentery). However, these symptoms are not always present in infected people, with the disease often resulting in diarrhoea without dysentery. A mild case of shigellosis may result in fever, fatigue, malaise, anorexia and watery, non-bloody diarrhoea. These symptoms are similar to those caused by other enteric pathogens, and therefore it can be difficult to distinguish these causes clinically one from the other (7). In severe cases, severe abdominal cramps, dysentery and sometimes seizures occur (7,9). Shigellosis can result in death. There are multiple virulence factors and mechanisms of pathogenesis that can lead to mortality, including dehydration, intestinal complications and decreased immune function and nutritional status leading to co-infection (7).

The burden of shigellosis in Papua New Guinea

According to PNG's current national health plan for 2011-2020, diarrhoeal diseases are one of the five most frequent illnesses reported, with approximately 40 people per 1000 presenting to hospital outpatients and/or health centres annually with diarrhoea-related illness (15). Over 200 people per 100,000 of the population are admitted for diarrhoea-related illnesses. Age-specific data on the burden of diarrhoea are not provided in the current health plan, but the burden is likely to be highest in children. Data published by the WHO (16) state that 9% of deaths occurring in children less than 5 years of age in 2012 were diarrhoea related. However, this could be an underestimation of the true burden of diarrhoeal disease in PNG because of poorly recorded and documented outpatient records. Indeed, other WHO published data state that diarrhoeal illness accounted for 14% of deaths

in children aged 1 month to 5 years of age in 2013, with no appreciable decrease in the burden over the past 14 years (17). Moreover, the impact of diarrhoeal diseases on the general health of children, and therefore their susceptibility to other causes of death, may not be fully accounted for in these estimates.

Despite recognition that diarrhoea is an important cause of morbidity and mortality in PNG, particularly among children, data on the aetiology of diarrhoeal disease in PNG are lacking. The most robust data come from a case-control study by Howard and colleagues (18), although the data are now dated, with recruitment completed a quarter of a century ago. The study found *Shigella* to be one of the most important aetiologies for children hospitalized with diarrhoea in Goroka, Eastern Highlands Province (EHP), being detected in 13% of cases. Recently, surveillance by our research team, conducted in the same setting and a similar cohort (children hospitalized with diarrhoea in Goroka, EHP), found *Shigella* spp. and rotavirus to be the most commonly detected pathogens, with *Shigella* detected in 26.6% of children (19). In another recent study, focusing on both children and adults presenting with diarrhoea to hospital outpatients or an urban health clinic, *Shigella* was isolated from 22% of all study participants (20). On the basis of the aforementioned studies, it appears that *Shigella* remains an important pathogen in the Eastern Highlands of PNG.

Other studies provide evidence of the nation-wide distribution of *Shigella*. The first case report of *Shigella* infection in PNG (which was then the Territory of Papua and New Guinea under Australian administration) was by Morahan in 1968 (21). This study occurred over a 33-month period from March 1965 to November 1967. Faecal specimens were collected from the Wewak Hospital and other hospitals in the Sepik districts. A total of 907 stool samples were obtained from 848 persons, of which 90 were *Shigella* positive. *S. flexneri* was the most common species isolated (and was responsible for two fatal cases of shigellosis), followed by *S. sonnei* and then *S. boydii* (21).

In early 1987, Schuurkamp and colleagues (22) monitored food handlers in PNG working at Ok Tedi Mine. The mining company had to re-enforce their premedical health checks on all potential food handlers following two cases

of typhoid fever imported from the highlands. An initial screen of 155 food handlers and 85 non-food handlers resulted in the isolation of *Shigella* sp. from 2.6% of food handlers and 3.5% of non-food handlers; all were asymptomatic carriers. A second survey of 160 food handlers including those from private fast-food establishments detected one *S. boydii* infection in a local fast-food shop staff member. *S. boydii* and *S. sonnei* were responsible for the majority of *Shigella* infections experienced on site (22). This study demonstrates that asymptomatic carriage of *Shigella* occurs in PNG, a finding supported by our recently obtained unpublished data.

In 2009, following an epidemic caused by multidrug-resistant *S. flexneri* in four provinces in PNG, a review of antimicrobial susceptibility of *Shigella* spp. isolated at the Port Moresby General Hospital was conducted. Of 3419 faecal samples cultured between 2000 and 2009, approximately 4% were positive for *Shigella*, with a majority of *S. flexneri* isolates showing antimicrobial resistance to amoxycillin, chloramphenicol and cotrimoxazole (23). However, there are few data from other parts of the country. In 2013 there was an outbreak of shigellosis in a settlement camp near Bulolo, Morobe Province. There were an estimated 1200 cases, with five fatalities (24), making it one of the largest outbreaks of shigellosis ever reported in the scientific literature.

Shigellosis likely to be under-recognized as a cause of illness in PNG

As with many infectious diseases, the exact burden of shigellosis in PNG is unknown. Detailed aetiological data pertaining to two of the most important infectious diseases in PNG, namely pneumonia and diarrhoea, are lacking, as highlighted in previous editions of the Medical Journal in recent years (25-27). This is largely attributable to the country's lack of resources and diagnostic capabilities (28,29).

Diagnosis is a challenge in PNG given the limited resources available in most health facilities; issues with storage and transportation of samples are also problematic, which contributes to the challenges faced with performing proper laboratory diagnosis. These issues are very important for *Shigella* diagnosis, particularly to the cultivation and isolation of the organism,

which appears to be more susceptible to loss of viability in transport than many other enteric pathogens. Once faecal samples are collected they need to be processed within a few hours to maximize chances of recovery of the organism. Additionally, *Shigella*'s close relationship with other members of the Enterobacteriaceae family makes it difficult to differentiate *Shigella* spp. from other closely related species including *E. coli*. Training for local health and laboratory staff in the proper collection, handling and storage of faecal samples, in conjunction with improved diagnostic procedures and techniques, could help improve *Shigella* spp. detection (29).

Approximately 87% of PNG's population live in rural settings (15); diarrhoeal diseases and acute respiratory infections occur at higher incidence in these rural communities (16). There is poor access to clean water and proper sanitation facilities, which increases the risk of communities acquiring gastrointestinal illnesses (20,29,30). Access to general health services is difficult and nearly a third of all aid posts in the country have closed since Independence in 1975 (28,31). Communities living in the urban poor regions of major towns and cities also experience similar problems.

On the basis of recent data, it would seem that: a) *Shigella* remains an important gastrointestinal pathogen in PNG; b) it is difficult to ascertain the exact burden of *Shigella* throughout the country due to the variable range of detection rates in recent studies (4% of stool samples in Port Moresby, compared to ~25% detection rate in Goroka) (19,20,23,32), which may reflect differences in sensitivity using culture methods; however, when specific efforts are made to detect the pathogen (by culture or polymerase chain reaction [PCR], as conducted in Goroka) *Shigella* is commonly isolated (19,20); and c) there has been no appreciable decrease in the burden of shigellosis in the Eastern Highlands Province over the past two decades. Our recent studies suggest shigellosis is the second leading contributor to diarrhoea in children hospitalized with diarrhoeal illness (19), and a leading cause of diarrhoea in children and adults (20).

Treatment

The optimal treatment and management of diarrhoeal diseases requires an understanding of the cause of the disease,

which unfortunately is not currently obtainable in most settings in PNG. However, irrespective of the cause hydration is central in the treatment of diarrhoea, and is especially important in children. With this in mind, treating diarrhoea based on severity of illness is routinely conducted in PNG (33,34) and can ensure adequate health outcomes in the absence of aetiological data. In children with mild diarrhoea with no signs of dehydration parents are advised to give extra fluids; oral rehydration solution (ORS) is recommended for children with moderate cases of diarrhoea and signs of dehydration; while intravenous fluid is recommended for patients with severe diarrhoea and severe dehydration. Continued breastfeeding of babies is strongly advised to reduce the severity of diarrhoea and complications of malnutrition, which can be experienced in infants and young children; and zinc supplementation is also recommended (33,35-37).

Antibiotics are overused in the treatment of diarrhoea (35,36); however, evidence of shigellosis warrants their use. Such evidence usually comes in the form of dysentery. Ciprofloxacin is the recommended antibiotic for both children and adults with dysentery (33-36). Previously it was cotrimoxazole (or nalidixic acid or ampicillin) (35), but with the rise of antimicrobial resistance reported globally and also observed in recent studies in PNG the recommendations for the antibiotic treatment of shigellosis were updated (33,34). Two recent studies have reiterated the need for the change in antimicrobial treatment regimens. Rosewell and colleagues reported that *Shigella* was commonly resistant to amoxycillin, chloramphenicol and cotrimoxazole (23); these findings also concurred with the more recent study conducted by our research team (20).

The current practice of recommending treatment of dysentery with ciprofloxacin is appropriate given that *Shigella* is the most common bacterial cause of dysentery and circulating strains are commonly resistant to other antibiotics (20,23). However, shigellosis does not always result in dysenteric stools. Indeed, in our recent surveillance of children hospitalized with acute watery diarrhoea, children with dysentery were excluded from the surveillance; yet *Shigella* was detected in 26.6% of children. The standard treatment manual for children recommends chloramphenicol, if antibiotics are required,

for treatment of diarrhoea. Our recent data (19,20) suggest that the most common bacterial cause of diarrhoea (in the absence of dysentery) is *Shigella*. Given the high rates of resistance to chloramphenicol in *Shigella* (~80% resistance or intermediate resistance found by Rosewell et al. and Greenhill et al.) (20,23), treatment with chloramphenicol may be of little benefit to the patient.

Future considerations

Increased and sustained effort is required to lower the burden of all causes of diarrhoea in PNG and of shigellosis in particular. The importance of access to safe water, sanitation and hygiene (ie, WASH) cannot be overstated. Challenges in the uptake of such measures exist (30,38) but the impact on diarrhoeal illness, and indeed overall health, would be significant (30). Indeed, two recent large outbreaks of gastrointestinal illness in PNG, namely cholera and shigellosis, could have been avoided or drastically reduced with access to and uptake of WASH in the country's rural majority and urban poor communities (24,28). Vaccines, currently under development for *Shigella*, may form an important component of control strategies in the future.

Routine diagnosis of diarrhoeal disease is rarely conducted in PNG. Port Moresby General Hospital laboratory is the only laboratory to regularly conduct diagnosis; even there an average of ~350 samples were tested annually between 2000 and 2009 (23). From a public health perspective there would be benefits for PNG if there was improved diagnostic capacity, as witnessed during the cholera outbreak (29). Culture and susceptibility testing should be conducted in the major provincial capitals, with a view to introducing technologies suitable for use in resource-poor settings in the future to supplement traditional diagnostic methods. Given the resistance of *Shigella* to multiple antibiotics, ongoing antimicrobial susceptibility testing is imperative in PNG.

Conclusions

A major impediment to the control of diarrhoeal disease is the multiple aetiologies responsible. However, current evidence suggests that *Shigella* is a leading cause of diarrhoea (and dysentery) in PNG. Increasing our understanding of the epidemiology of

shigellosis throughout PNG will help further our understanding of the burden of disease, and could assist patient management. Control of diarrhoeal diseases needs to be both broad and targeted in approach. Improved hygiene and sanitation would result in a decrease in the burden of all-cause diarrhoea and shigellosis alike; however, such WASH interventions will take considerable time to implement. Treatment of diarrhoea according to the relevant guidelines is recommended. The primary focus of treatment should remain rehydration; however, the judicious use of antibiotics, preferably ciprofloxacin, is appropriate in probable cases of shigellosis (which may or may not present with blood or mucus in the stools).

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Bacterial profile and antimicrobial susceptibility patterns in primary surgical infections at Modilon Hospital, Papua New Guinea

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SUMMARY

Primary surgical infections are the second most common cause of surgical admission and contribute considerably to morbidity and mortality of surgical patients in developing countries. This study aimed to determine a bacterial profile and antimicrobial susceptibility patterns in primary surgical infections. **Methods:** This was a prospective cross-sectional study including 150 patients diagnosed clinically as primary surgical infections. Antibiotic susceptibility testing was done on the isolates using the disc diffusion method. **Results:** Positive cultures were obtained from 122 patients; Gram-positive bacteria were responsible for 48% (n = 59), Gram-negative for 39% (n = 48), mixed flora for 10% (n = 12) and *Candida* for 2% (n = 3) of primary surgical infections. The alarming finding was that 78% of *Staphylococcus aureus* were resistant to oxacillin (MRSA) and 83% resistant to cephalosporins, whilst 3 isolates showed intermediate resistance to vancomycin. Gram-negative isolates also demonstrated antibiotic resistance. **Conclusions:** This study provides recent baseline data both on the bacterial profile and the antibiotic susceptibility patterns in primary surgical infections in the Papua New Guinean setting and it should guide therapeutic policies in the country. There is a growing need for surveillance of the local microbiological epidemiology and for antimicrobial stewardship to ensure that the empirical use of antibiotics is appropriate.

Introduction

Primary surgical infections (infections contracted outside the hospital) contribute considerably to morbidity and mortality of surgical patients in developing countries. In the last decade there have been a limited number of reports on the bacterial profile and antibiotic susceptibility patterns of primary surgical infections in Papua New Guinea (PNG) (1,2). One of the most common pathogens responsible for surgical infections is *Staphylococcus aureus*, which has been isolated from more than half of suppurative infections in both high- and low-middle-income countries (3,4). *S. aureus* has demonstrated the ability to develop resistance to many antimicrobial agents leading to long hospital stays and increased mortality worldwide (5,6). Methicillin-resistant *S. aureus*

(MRSA) strains are becoming increasingly multiresistant, and have recently developed resistance to vancomycin, which has been used successfully to treat MRSA for many years (7,8).

Despite various policies implemented to combat bacterial resistance over the past decade, several studies have shown that rates of MRSA have increased steadily (9). The changing scope of pathogenic bacterial flora as well as their antibiotic susceptibility patterns requires constant surveillance to provide updated information for a rational antibiotic policy. Inappropriate use of antimicrobial agents, both in surgical prophylaxis and treatment, not only increases the cost of health care but also exposes the patient to potential drug toxicity and raises the risks of the development and spread of

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antimicrobial resistance (10). Antimicrobial resistance poses an important challenge to health systems because of the increased complication rates and costs associated with procedures and treatment connected with infection eradication (11).

This study aimed to determine the common bacteria responsible for primary surgical infections and to assess the antibiotic susceptibility patterns against common antibiotics used for treating hospitalized patients in PNG.

Objectives of this study were:

1. To determine the distribution of bacterial pathogens isolated from primary surgical infections such as septic arthritis, osteomyelitis, cellulitis, pyomyositis, abscesses and peritonitis.
2. To assess the antibiotic susceptibility patterns of common pathogens causing primary surgical infections.

Methodology

Study design

A prospective cross-sectional study of 150 patients with primary surgical infections admitted to the surgical unit of Modilon General Hospital between February 2015 and November 2015 was conducted to determine the bacterial profile and the antimicrobial susceptibility patterns of the causative organisms. Diagnosed primary surgical infections included septic arthritis, acute and chronic osteomyelitis, cellulitis, pyomyositis, abscesses and peritonitis. Patients' variables were recorded on standard research forms and included: age, sex, white blood cell count (WBC), temperature, antibiotic regimen (type, dose, duration, route), surgical treatment, infection site, culture data, and other clinical variables. The nutrition status for children was measured as percentage of desired body weight for age (normal 80-100%, underweight 60-79%, severe malnutrition less than 60%). The study was approved by the Divine Word University Research Ethics Committee (No UREC 2-2012).

Inclusion and exclusion criteria

Consecutive patients with clinically diagnosed surgical infections admitted to

the surgical ward were enrolled in the study after obtaining informed consent from them or from guardians/attendants. Primary surgical infections are defined as those that require surgical intervention as a part of the treatment regimen and are distinguished from postoperative (surgical site), post-traumatic wound and nosocomial infections in surgical patients. Patients who had subclinical infection, who refused informed consent or who withdrew their consent in the course of the study were excluded from the final analysis.

Sampling procedure

Pus swab specimens were aseptically obtained from surgical sites before the wound was cleaned with an antiseptic solution. The specimens were collected on sterile cotton swabs. Care was taken to avoid skin contamination. Where appropriate, deep tissue specimens were collected intra-operatively. The samples were placed in Stuart Transport Medium for transport to the laboratory soon after being obtained and were accompanied by a request form containing personal data, time, date and site of collection. In the laboratory, the specimens were registered and macroscopically examined before the preparation of smears for Gram staining and culture on blood agar and MacConkey agar.

Microscopic examination and culture

Smears were air-dried, heat-fixed and stained by Gram's technique. Gram staining and colony characteristics were used to differentiate the organisms isolated. Biochemical tests were conducted to confirm the species. Antibiotic susceptibility testing was conducted on the isolates using antibiotic-impregnated discs (Oxoid, Australia). Specimens were classified as susceptible, intermediate or resistant according to the Clinical and Laboratory Standards Institute Guidelines (12). Antibiotic susceptibility testing involved different groups of antibiotics depending on the type of pathogen. We determined antimicrobial susceptibility for *S. aureus* isolates to chloramphenicol, gentamicin, cotrimoxazole, ceftazidime, oxacillin, erythromycin, ciprofloxacin and vancomycin; for *Streptococcus* spp. to penicillin, chloramphenicol, tetracycline, cotrimoxazole, erythromycin and ceftazidime; and for Gram-negative bacteria to ampicillin, chloramphenicol, tetracycline, gentamicin, ceftazidime and ciprofloxacin.

Patient management

Patients were managed according to clinical protocols related to particular clinical diagnoses. Initial antibiotic therapy was empirically determined. When Gram-positive flora was suspected, flucloxacillin was used combined with chloramphenicol in the more severe infections. Gentamicin was usually initially selected for suspected Gram-negative bacteria. Antibiotic management was modified later on the basis of the results of susceptibility tests.

Data analysis

The data were analysed using the computer software SPSS version 15. Simple descriptive data were summarized as arithmetic mean with standard deviation (mean \pm SD) and percentage representation for categorical data.

Results

Demographic characteristics

We investigated the microbiological profile and antibiotic susceptibility of 150 patients who presented to the surgical unit and were diagnosed with primary surgical infections. 12 patients had mixed flora thus each providing two samples for analysis, which in total gave 162 samples in the laboratory data. Table 1 presents the demographic characteristics of the participants.

All participants had been administered one or two antibiotics before the sample taking and the most commonly used antibiotics were flucloxacillin and chloramphenicol (Table 1). A relatively low white cell count for the participants could be explained by them being on antibiotic treatment for a few days before admission.

Bacterial profile

Of the 162 bacterial cultures 40 (25%) showed no growth, including those from patients with septic arthritis (17/31, 55%) and chronic osteomyelitis (3/32, 9%) (Table 2). Of the 122 positive cultures obtained, Gram-positive bacteria accounted for 48% (n = 59), Gram-negative bacteria for 39% (n = 48), mixed flora for 10% (n = 12) and *Candida* for 2% (n = 3) (Table 2).

Our findings showed that *S. aureus* was the main causative microorganism (overall 44%, n = 54 out of 122 positive cultures) for most of the primary surgical infections except for peritonitis, where *Escherichia coli* was the dominating isolate (Table 2). Of note is that in chronic osteomyelitis and septic arthritis all isolates of *S. aureus* were oxacillin resistant (MRSA). Three patients with chronic osteomyelitis who had been subjected to prolonged antibiotic therapy in primary care developed *Candida* infection (Table 2). While cellulitis is typically caused by Gram-positive bacteria, 3 out of 7 of our cases of cellulitis yielded Gram-negative bacteria (Table 2).

Antibiotic susceptibility

78% of *S. aureus* were resistant to oxacillin while 3 bacterial isolates showed intermediate resistance to vancomycin (Table 3). Resistance to oxacillin implies that *S. aureus* organisms would generally be β -lactamase-resistant to penicillins including methicillin, cloxacillin and flucloxacillin. Most of the *S. aureus* strains (83%) were also resistant to ceftazidime. Our findings showed a high susceptibility of *S. aureus* to ciprofloxacin (100%), gentamicin (98%) and erythromycin (94%). Gram-negative bacteria demonstrated a high susceptibility to ciprofloxacin (98%), gentamicin (91%) and ceftazidime (73%) and reduced susceptibility to ampicillin (11%) and chloramphenicol (42%) (Table 3). We also detected Gram-negative bacteria resistant to multiple drugs, eg, *E. coli* susceptible only to ceftazidime or *Klebsiella pneumoniae* susceptible only to ciprofloxacin.

Discussion

Bacterial profile

Our findings revealed that Gram-positive bacteria (48%) dominated over Gram-negative bacteria (39%) as the cause of primary surgical infections. In particular, *S. aureus* accounted for 44% of all primary surgical infections. Likewise, recent studies from high- and low-income countries reported that *S. aureus* was responsible for more than half of all suppurative surgical infections (3,4). In our study, *S. aureus* was found in all cases of pyomyositis and 60% of acute osteomyelitis. A similar rate of *S. aureus* was observed in studies from high-income countries, ranging from 50% to 90% (13-15).

TABLE 1

DEMOGRAPHIC FEATURES OF 150 PATIENTS WITH PRIMARY SURGICAL INFECTIONS ADMITTED TO MODILON GENERAL HOSPITAL, PAPUA NEW GUINEA, 2015

Variable	Mean (\pm SD) or number	Percentage
Age	23 (\pm 17.85)	
Sex:		
Male	99	66
Female	51	34
Haemoglobin (g/dl)	10.19 (\pm 2.15)	
White cell count ($\times 10^9$ /l)	8.35 (\pm 1.15)	
Nutrition:		
Normal	120	80
Underweight	28	19
Severe malnutrition	1	1
Smoking:		
Yes	30	20
No	120	80
Diagnosis:		
Abscess	39	26
Septic arthritis	31	21
Acute osteomyelitis	6	4
Cellulitis	10	7
Pyomyositis	9	6
Peritonitis	30	20
Chronic osteomyelitis	25	17
Pre-sample antibiotic:		
Flucloxacillin	91	61
Chloramphenicol	117	78
Gentamicin	78	52

SD = standard deviation

Although *S. aureus* remains the most common bacterial pathogen in chronic osteomyelitis (11/26, 42%), in our study half of the infecting bacteria (13/26, 50%) were Gram-negative including mixed infections. The second most common infecting organisms found in chronic osteomyelitis were *Klebsiella* and *Pseudomonas aeruginosa* (14%). Chronic post-traumatic osteomyelitis is commonly polymicrobial and *P. aeruginosa* has been found as the second most common infecting organism (20%) (16). In 3 patients with chronic osteomyelitis who were under a long duration of antibiotic treatment, *Candida*

sp. was isolated.

Antibiotic susceptibility

The alarming finding of our study was that overall 78% of *S. aureus* strains were MRSA (Table 3) while in chronic osteomyelitis and septic arthritis all strains were MRSA (Table 2). The incidence of MRSA varies in different studies from 1.6% to 90% (4,9,17,18). Recent reports from high- and low-income countries point out that community-acquired methicillin-resistant *S. aureus* (CA-MRSA) is responsible for an increasing incidence of infections

TABLE 2

BACTERIAL ISOLATES ASSOCIATED WITH PRIMARY SURGICAL INFECTIONS AT MODILON GENERAL HOSPITAL, PAPUA NEW GUINEA, 2015

Microorganism	Frequency of specific microorganisms in various types of primary surgical infections							
	Abscess (39 patients)	Pyomyositis (9 patients)	Cellulitis (10 patients)	Acute osteomyelitis (6 patients)	Chronic osteomyelitis (25 patients)	Septic arthritis (31 patients)	Peritonitis (30 patients)	Total (150 patients)
<i>Staphylococcus aureus</i>	18 (8 MRSA)	7 (5 MRSA)	3 (3 MRSA)	3 (2 MRSA)	11 (11 MRSA)	10 (10 MRSA)	2	54 (39 MRSA)
<i>Escherichia coli</i>	1	-	2	-	2	-	23	28
<i>Klebsiella</i>	1	-	-	-	4	1	3	9
<i>Pseudomonas aeruginosa</i>	-	-	1	-	4	-	1	6
<i>Streptococcus</i> group A	1	-	1	-	2	1	-	5
<i>Enterobacter</i>	-	-	-	-	1	2	1	4
<i>Haemophilus influenzae</i>	2	-	-	-	-	-	-	2
<i>Providencia</i> sp.	-	-	-	-	-	-	2	2
Diphtheroids	1	-	-	-	-	-	-	1
<i>Hafnia alvei</i>	1	-	-	-	-	-	-	1
<i>Staphylococcus</i> coagulase-negative	1	-	-	-	-	-	-	1
<i>Proteus</i> sp.	-	-	-	-	1	-	-	1
<i>Candida</i>	-	-	-	-	3	-	-	3
<i>Streptococcus</i> not group A	1	-	-	2	-	-	1	4
<i>Acinetobacter anitratus</i>	-	-	-	-	1	-	-	1
No growth	14	2	3	1	3	17	-	40
Total	41	9	10	6	32	31	33	162

MRSA = methicillin-resistant *Staphylococcus aureus*

TABLE 3

SUMMARY OF ANTIBIOTIC SUSCEPTIBILITY TESTS OF BACTERIA OBTAINED FROM PRIMARY SURGICAL INFECTIONS IN PATIENTS FROM MODILON GENERAL HOSPITAL, PAPUA NEW GUINEA, 2015

Microorganism	Antibiotic susceptibility as percentage (susceptible number/total tested)									
	Penc	Amp	CMP	Te	Gn	SXT	Caz	Cip	Ox	Ery
<i>Staphylococcus aureus</i>			81% 35/43	97% 28/29	98% 50/51	80% 16/20	17% 6/35	100% 36/36	22% 11/50	94% 49/52
<i>Streptococcus</i> group A	100% 5/5		100% 5/5	100% 5/5		40% 2/5			50% 2/4	100% 5/5
Total Gram-negative		11% 5/45	42% 23/55	44% 23/52	91% 48/53	41% 18/44	73% 41/56	98% 39/40		

Penc = penicillin
Amp = ampicillin
CMP = chloramphenicol
Te = tetracycline
Gn = gentamicin
SXT = Septrin (cotrimoxazole)
Caz = ceftazidime
Cip = ciprofloxacin
Ox = oxacillin
VA = vancomycin
Ery = erythromycin
*3 bacterial isolates had intermediate resistance to vancomycin

among children (13,19,20).

Cross-resistance of MRSA to cephalosporins, carbapenems and other beta-lactam antibiotics is common (21). In our study 83% of MRSA were resistant to ceftazidime while in another study from Brazil 29% were resistant to cefuroxime (22). It was confirmed that if an isolate becomes resistant to a third-generation cephalosporin, it will also be resistant to all first- and second-generation cephalosporins (21). Whilst our study found high susceptibility of MRSA to some of the other antibiotics, resistance to other groups of antibiotics has been widely reported (4,22,23). The proportion of MRSA strains resistant to different antibiotics varies in different studies: for erythromycin from 7.8% to 98% (4,24), and for chloramphenicol from 34% to 88% (4,23).

Interestingly, 7% of *S. aureus* in this study showed intermediate resistance to vancomycin despite the fact that this antibiotic is generally not available in the country. Although vancomycin has been regarded as reliable against MRSA strains, vancomycin-intermediate *S. aureus* strains which respond poorly to this antibiotic are now increasingly reported (25). De novo resistance to rifampicin or fluoroquinolones (eg, ciprofloxacin) is uncommon among MRSA; however, it was indicated that each of these antibiotics should not be used as monotherapy because of the rapid development of resistance during therapy (26).

Our study has also demonstrated the presence of resistant Gram-negative organisms. Overall Gram-negative bacteria were resistant to ampicillin in about 90% of cultures, to chloramphenicol, tetracycline and cotrimoxazole in about 60%, to a third-generation cephalosporin in 27%, to gentamicin in 9% and to ciprofloxacin in 2%. High rates of resistance to antibiotics among Gram-negative organisms has been reported by many authors (9,11,22,27,28). Whilst multidrug-resistant *P. aeruginosa* (MDRPA) is being detected with increasing frequency (22,27), in our study we noted only *E. coli* and *Klebsiella* strains as being resistant to multiple antibiotics.

Limitations of the study

This study has several limitations. Firstly, due to a relatively small sample size and single hospital location, generalization of the results

should be made with caution. Secondly, because the specimens were taken at different time-points of patients' hospitalization and after patients had received antibiotic treatment, the results need to be interpreted within these contexts. We were thus not able to clearly differentiate between community- and hospital-acquired MRSA. Blood cultures may have strengthened our findings, but were not feasible and prior administration of antibiotics would have provided a low return (14).

Antimicrobial stewardship

About two-thirds of our specimens were taken within 48 hours of admission, which suggests that our bacterial profile predominantly reflects community-acquired infections. However, in this study all patients had received antibiotics for varying duration before admission. A recent report from the World Health Organization (WHO) (29) stated that "inappropriate and irrational use of medicines provides favorable conditions for resistant microorganisms to emerge and spread". When the full course of a prescribed antimicrobial is not taken or when poor-quality antimicrobials are used resistant microorganisms can emerge and spread (29). Forty years ago it was shown that the increase of gentamicin usage paralleled the increase of gentamicin-resistant Gram-negative organisms (30). Conversely, other reports have shown a reduction in the incidence of infections by resistant microorganisms after reduction in the use of third-generation cephalosporins (31).

A variety of factors contribute to the increase of antimicrobial resistance. These include not only suboptimal use of antimicrobials both for prophylaxis and treatment, but also ineffective hospital infection control practices, increased length of hospital stay, in particular intensive care unit stays, increased use of invasive devices and catheters, antibiotic use in agriculture, and increasing national and international travel (32,33).

Many individuals and groups have proposed solutions to the global threat of antimicrobial resistance (21,29). Recommendations include improving the effectiveness of infection control programs in hospitals, the education of health workers on appropriate antimicrobial applications, antimicrobial resistance surveillance programs in hospitals, computer-

based monitoring of the use of antimicrobial agents, and funding for more clinical and basic research on antimicrobial resistance. To combat antibiotic resistance, the WHO recently recommended more prudent antibiotic use, for instance not using antibiotics when benefit is minimal (eg, in common colds), starting from narrow-spectrum antibiotics whenever possible and using optimal dosages and regimens. In addition, WHO pointed out that the need for antibiotic therapy can be reduced by preventing infections through vaccination, infection control measures and improved sanitation (29). The current literature review by WHO showed that improvement of hand washing procedures is a simple and cost-effective measure in reducing incidence of intra-hospital MRSA infections (34).

Because of marked local differences in conditions, antibiotic use and bacterial susceptibility, it is of paramount importance that local infection surveillance programs be conducted in hospitals to provide therapeutic guidelines for rational use of antimicrobials (9,29). Monitoring and optimization of antimicrobial use is one of the most important factors in reducing the emergence and spread of antimicrobial-resistant pathogens (9,35). More research is needed into antimicrobial resistance, new antibiotics and regimens and improving prevention of infection (21).

Conclusions

Our data indicate the need for access to newer antibiotics, such as linezolid, clindamycin or vancomycin, to treat the increasing numbers of patients with MRSA infection. There is a growing need for well-designed surveillance of the local microbiological epidemiology and for antimicrobial stewardship to ensure that the empirical use of antibiotics is appropriate. This study of the bacterial profile and antimicrobial susceptibility patterns provides baseline data to guide the development of rational and updated antibiotic-prescribing guidelines in PNG.

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“I have a heart to help the mothers”: 25 years of the Village Birth Attendant Program in Milne Bay Province, Papua New Guinea

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SUMMARY

In many low-resource settings an estimated one-third of all births take place unsupervised with traditional and non-traditional villager birth attendants the only providers of care during pregnancy and childbirth. The training of village birth attendants (VBAs) in Milne Bay Province began in 1991, and has continued during a period of significant shifts in national and international public health policy. As part of a wider provincial-wide review of the VBA program we undertook 6 focus group discussions, 13 in-depth interviews and 8 key informant interviews in three districts in Milne Bay Province in 2014. In this paper we describe the role, responsibilities and function of VBAs, and the challenges facing both VBAs and those involved in their training and in supporting their work in the community. In this setting, VBAs continue to assist women during childbirth, and are frequently having to try and manage difficult obstetric complications with little or no support from their communities or local health facilities. Some VBAs reported being called too late by the community, with insufficient time to refer women on to a health facility, resulting in maternal deaths. Many VBAs continued with their practice, motivated by a heartfelt desire to serve, despite feeling ‘neglected’ and ‘overlooked’, while others continued because of their religious convictions and dedication to help their communities. There is an urgent need to better define what VBAs can and should do in this setting, what communities can realistically expect of their VBAs, and how professional health care workers can work more constructively with this long-standing cadre of lay health workers. There is a need for all health facilities and VBA trainers to support their VBAs, and to fully recognize the often difficult situations VBAs are required to work in while continuing to advocate for supervised, health facility births.

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Introduction

In many low-resource settings, traditional birth attendants (TBAs) remain an important provider of maternity care (1,2), assisting 31-44% of all births (3). Frequently with no formal health training and little connection to the mainstream health systems a TBA is “a person who assists the mother during childbirth and who initially acquired her skills by delivering babies herself or through an apprenticeship to other TBAs” (4).

Despite decades of training TBAs, there is limited evidence to support the impact of this informal cadre of health workers on maternal and neonatal mortality (1,5,6), although there is some evidence that trained TBAs have contributed to the successful implementation of maternal and newborn health interventions (1,7-10). In recognition of the importance of access to skilled care during childbirth, a shift in global policy in 1997 focussed on the importance of having a skilled birth attendant at every birth (11,12), thus excluding TBAs from a role in childbirth management and reducing support for TBA programs world-wide (12,13). A skilled attendant is “an accredited health professional – such as a midwife, doctor or nurse – who has been educated and trained to proficiency in the skills needed to manage normal (uncomplicated) pregnancies, childbirth and the immediate postnatal period, and in the identification, management and referral of complications in women and newborns” (11). The most appropriate role for TBAs as providers of care during childbirth remains unclear, particularly in settings where maternal and neonatal mortality are highest. There is some evidence to suggest that collaboration between active TBAs and formal health services can have significant benefits (14) and a recent *Lancet* series on midwifery noted the need for maternal health programs to establish such mechanisms (15).

Papua New Guinea (PNG) has one of the highest maternal mortality ratios (MMRs) in the world with 594 to 733 maternal deaths per 100,000 live births (16,17). Overall, only 37% of births take place at a health facility, attended by professional health care workers (17). Although PNG differs from other low-resource settings in lacking any longstanding culture of TBA practice (18), the training of similar cadres of birth attendants, typically referred to in PNG as village births attendants (VBAs), has taken place throughout the

country over the past three decades. VBAs are estimated to attend approximately 7% of community-based births (19).

A program to train VBAs in the Trobriand Islands of Milne Bay Province (MBP) (Figure 1) began in 1991, and has been active and evolving since that time. At inception, the program was supported by the provincial health office and United Nations Children's Fund (UNICEF). The initial aim of the program was to identify and refer ‘high-risk’ women for health facility births, and for VBAs to assist births in the community for ‘low-risk’ women. VBAs received training in antenatal care, hygienic birth, danger signs in pregnancy, childbirth and the newborn, and the importance of early breastfeeding. VBAs also received instruction on the interpretation of a specifically designed ‘antenatal feedback chart’, a reporting tool completed for each woman by the antenatal clinic staff to provide key information from the antenatal clinic to the VBA, including whether the woman was considered high- or low-risk. Training also included general health education, personal hygiene, environmental health, family planning, sexually transmitted infections and infant nutrition. Training methods, including use of visual aids and practical instruction, also evolved over this time. On completion of their training, all VBAs were provided with a ‘VBA kit’ – a small tin containing items such as soap, gloves, plastic sheet, cord ties and scalpel blades for cord-cutting to promote clean, hygienic births.

In 1995 a major shift in scope extended the program from the Trobriand Islands to the mainland of Milne Bay Province. A number of further shifts in strategy and policy have affected the program since that time, including a broader village health volunteer (VHV) program developed by the National Department of Health (NDoH) in the early 2000s. The VHV program was designed to consolidate a variety of discrete village-based lay health workers, including VBAs, community-based distributors, ‘marasin meri’ (women who distribute medicines), village health promoters and village health assistants into one community-based program. The VHV program aimed to: “improve the health of individuals, families, clans, and villages through health assistance from ‘trained’ villagers” (VHV program manager's guide, prepared by the NDoH in 2003). By the end of 2014, over 500 VHV/VBAs had been trained

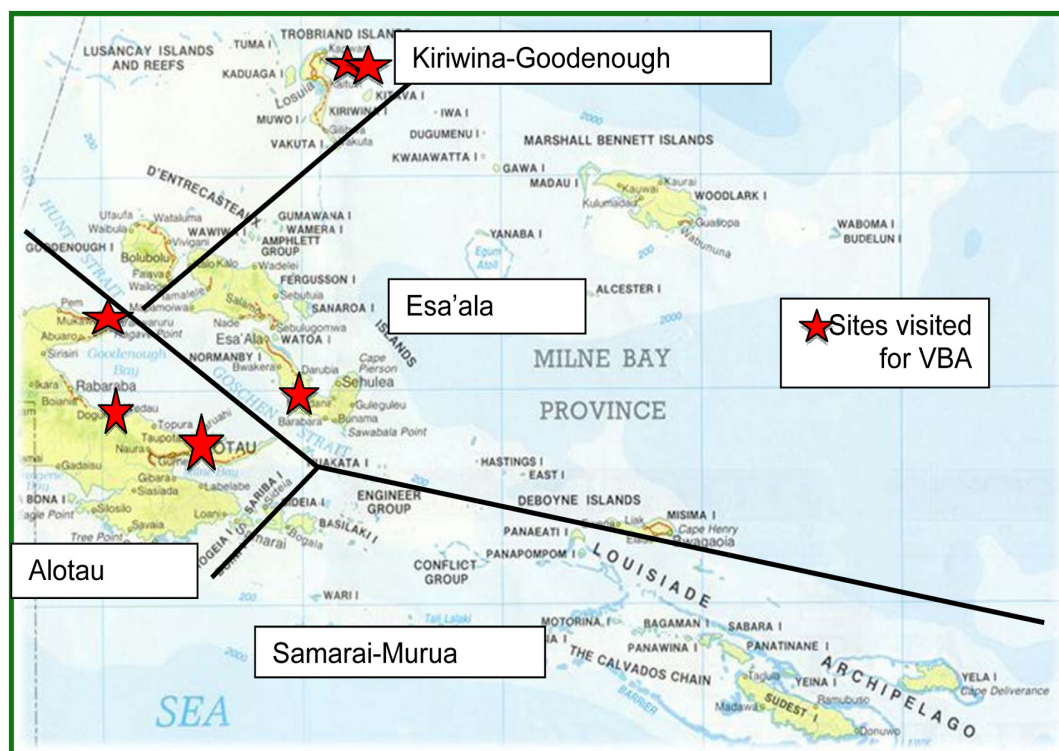


Figure 1. Map of Milne Bay Province, indicating the 4 districts and highlighting sites visited during the review.

across all four districts in Milne Bay Province, of whom around half were reported to be active and performing VBA activities, including attending births. A smaller proportion of VBAs were reporting on their activities, such as the number of births assisted, maternal and newborn deaths, and community-level education (personal communication, Family Health Services, Milne Bay Province).

Many communities in MBP remain remote with over 160 islands and a mountainous mainland making access to health services problematic. Approximately half (49%) of all women in MBP give birth unsupervised; 3-22% are assisted by a VBA (17,20). Concerned with the low uptake of supervised births, and a high maternal mortality ratio, estimated to be 587 per 100,000 live births (21), the Milne Bay Provincial Health Authority (MBPHA) requested a review of the VBA program as part of a broader maternal health program review. In this paper, we describe the current situation of VBAs in MBP, the roles and functions of VBAs, and the challenges

facing both VBAs and those who provide their training and ongoing support.

Methods

Study locations and selection of participants

As part of a broader, descriptive study we undertook focus group discussions (FGDs) and semi-structured interviews with VBAs in six purposively selected sites, from three districts in MBP: Losuia and the Outer Islands, Trobriand Islands, Kiriwina-Goodenough District; Sewa Bay, Normanby Island, Esa'ala District; and Huhuna/Garuahi, Dogura and Cape Vogel, Alotau District (Figure 1). Sites were selected to ensure the participation of VBAs from a variety of settings, and included remote island communities and those having road access to formal health services. VBAs were selected based on the geographical location of the village, their availability and their willingness to meet with the review team. All VBAs who agreed to meet with

the review team did so on the pre-arranged, allocated day. Individual interviews allowed for a more detailed narrative on a one-to-one basis and allowed for more intimate details to be discussed. Interviews were conducted between September and December 2014, and were supplemented by observation and informal discussions at health facility and community level. We also undertook key informant interviews with health professionals from preventive and curative health services, who were purposively selected for their experience with the VBA program in MBP.

All FGDs and key informant interviews were undertaken in English with the use of an interview guide. 9 of the semi-structured interviews were conducted in English; the remaining 4 were undertaken in the local language ('tok ples') with questions and responses translated at the time of the interview. A study-specific questionnaire allowing multiple responses and open-ended questions was used during the semi-structured interview. All interviews took place in the community, in a quiet area where participants did not feel concerned about being overheard. All FGDs and key informant interviews were digitally audio-recorded, with consent from each participant. Additional field notes were gathered from informal discussions and observations at the community level. Some of these discussions took place on an individual level but most were undertaken as part of a wider community group, during which time community members were able to discuss their thoughts and feelings about the positive and negative aspects of the VBA program.

All interviews were undertaken by one researcher (LMV), with the assistance of a second co-investigator (RP) when a translator was required. Review of all data, including audio-recordings and questionnaires, was undertaken by one member of the research team (LMV). Data from questionnaires were entered into an Excel spreadsheet; transcripts were managed using NVivo 9, a qualitative software data package.

Transcripts were reviewed by one member of the research team (LMV) and a qualitative content analysis approach (22), with continuous comparison, was used to develop a coding framework. Throughout the coding process the framework was developed and modified as new themes emerged. All data are presented in a descriptive nature.

Ethical considerations

Ethical approval was gained from the Papua New Guinea Institute of Medical Research (PNGIMR) Institutional Review Board (IRB), the Medical Research Advisory Committee (MRAC) of Papua New Guinea and the Medical Research Committee of the Milne Bay Provincial Health Authority.

Written informed consent was obtained for all semi-structured interviews. Oral consent was gained for those participating in the key informant interviews and FGDs. To ensure anonymity, the names of VBAs and informants, their village or position of work are not referred to in this paper.

Findings

Overview

23 VBAs participated in 6 FGDs, and 13 VBAs took part in semi-structured interviews (Table 1). 8 key informant interviews were conducted with health professionals from preventive and curative health services in MBP.

The majority of VBAs were aged over 45 years. Most were married; a minority were widowed or separated. Most VBAs had received only early primary education; none reported education above grade six. A few had received no formal education. All except one VBA had previously given birth; parity ranged from one to eight. The majority of VBAs did not use a health facility for the birth of their last born child.

VBAs and key informants described a broad range of experiences and knowledge in relation to the VBA program, from training and practice to challenges reflecting both individuals and the program.

VBA training

The majority of VBAs were originally selected by their community based on their prior experience assisting mothers to give birth in the community. All reported that their initial training took place between 1990 and 1999 (Table 2). Training typically comprised a three-week residential course, used a combination of visual aids and practical experience, and was led by an experienced maternal health nurse or midwife VBA trainer.

TABLE 1

FOCUS GROUP DISCUSSIONS AND SEMI-STRUCTURED AND KEY INFORMANT INTERVIEWS

Interview type	Number
Focus group discussions	6
Losuia, Kiriwina-Goodenough District	1
Cape Vogel, Alotau District	2
Dogura, Alotau District	3
Semi-structured interviews	13
Losuia and Outer Islands, Kiriwina-Goodenough District	7
Normanby Island, Esa'ala District	2
Huhuna and Dogura, Alotau District	4
Key informant interviews	8
Losuia and Outer Islands, Kiriwina-Goodenough District	3
Normanby Island, Esa'ala District	1
Alotau, Dogura and Cape Vogel, Alotau District	4

Only one VBA was assisting mothers without having received such training: she was instructed in the village by another VBA.

Most VBAs had received only one refresher course since their initial training and most had not received any refresher training for at least eight years (Table 2). VBAs in one site reported attending other training courses, for example, training in home-based care for HIV (human immunodeficiency virus) infection, but had not received any training relating to their role as a VBA.

VBA practices

The majority of VBAs were supporting births in their community. In some sites, there was confusion over the number of VBAs ever trained, those currently active and those who had stopped working. In some sites, health facility staff stated that there were no active VBAs. However, in these same sites VBAs described how they continue to be called upon by the community, particularly when a difficult birth was encountered. Both VBAs and key informants commonly stated that VBAs were not reporting on their activities and they did not know the number of births attended by VBAs.

Provision of antenatal care

VBAs reported undertaking antenatal care tasks, including abdominal palpation, listening to the fetal heart, checking for fetal movement, checking for swelling of lower limbs, and providing safe childbirth messages, including the importance of attending the antenatal clinic and attending the health facility for a supervised birth. There was general agreement among most VBAs that the antenatal feedback chart was no longer in place.

Attending births

All but one VBA described continuing to attend births in the village. Most reported attending births during the year of the study (2014), and around half had attended births in the month preceding the study. Some VBAs also reported bringing women to the aid post or health centre to give birth, whereupon the VBA attended the birth, although not always under the supervision of a trained health care worker. In two sites, VBAs reported that they have fewer women giving birth in the village, as more are attending the health facility, attributing this to a new incentive program (the gift of a 'baby bundle') that began in 2013 as

TABLE 2

VILLAGE BIRTH ATTENDANT TRAINING AND YEARS OF PRACTICE

	Year trained	Years working as VBA	Refresher courses attended	Last refresher attended	Currently practising as VBA
VBA 001	1990	24	3	2004/2006	Yes
VBA 002	1995	19	4	2004/2006	Yes
VBA 003	1995	19	2	2004/2006	Yes
VBA 004	No formal training	3	N/A	N/A	Yes
VBA 005	1994	20	1	1996	Yes
VBA 006	Before 2000	>14	4+*	2004/2005	Yes
VBA 007	Before 2000	>14	1	2004/2005	No
VBA 008	1999	15	2	2006	Yes
VBA 009	1999	15	1	2006	Yes
VBA 010	1996	18	1	before 2005	No
VBA 011	1999	15	1	before 2005	No
VBA 012	1995	19	1	Do not know	Yes
VBA 013	1995	19	1	Do not know	Yes
FGD 001	Between 1994 and 1996	18-20	1	Do not know	Yes
FGD 002	Between 1997 and 1999	15-17	0	-	Yes
FGD 003	Between 1996 and 1999	15-18	0	-	2 Yes/2 No
FGD 004	Between 1996 and 1998	16-18	1	2002	3 Yes/1 No
FGD 005	Between 1996 and 1997	17-18	1	Do not know	Yes
FGD 006	Between 1997 and 1999	15-17	0	-	Yes

VBA = village birth attendant

FGD = focus group discussion

*Was yearly until VBA trainer left

an initiative of the Milne Bay Provincial Health Authority and an independent charity (23).

VBAs reported advising women to attend the health centre to give birth, especially if they considered the women to be high risk – primigravid or multiparous woman, or with a known previous problem such as postpartum haemorrhage (PPH) – or if a complication was

recognized. However, the majority of VBAs reported that women in their communities often did not adhere to the advice and remained in the village to give birth. VBAs stated that they would frequently be called too late to refer the woman to the health facility, leaving the VBA no alternative but to assist the woman. VBAs also described some women giving birth while on the way to the health facility:

"...many they deliver on the way.....I have got many babies I delivered on the way [to the health centre]..." FGD 3

Managing complications

All but one VBA could recall experiencing complications when assisting women in the community. Premature birth, long labour (more than a whole day or a whole night – 12 hours) and malpresentation were some of the complications they had experienced. Most VBAs could describe how they managed particular complications, including referring women to the health facility, assisting mothers with breech presentation and management of transverse lie with hand presentation, as described by one VBA:

"...I pushed the hand right back up inside and told the mother to walk around more to get the contractions to come stronger... when she came back to me the baby was sleeping properly (vertex presentation)..." VBA 1

The most commonly mentioned complications were postpartum haemorrhage and retained placenta. Reported management of PPH included pressing and rubbing the abdomen to "rub up a contraction", raising the mother's buttocks, and providing oral fluids before transferring the mother to the nearest health facility. One VBA described how she managed a retained placenta:

"...after the cord snapped, I rubbed the tummy to remove the placenta..." VBA 6

Many VBAs credited a strong Christian faith with providing strength and guidance, particularly during a difficult birth, as one VBA describes:

"...one mother had a twin pregnancy...one baby was born with the head first and was OK, but for the other one the buttocks came first...I didn't know what to do – it was my first time to see this...I felt for the arms and pulled them down [one by one] and then I waited for the baby. Before [I assisted the mother] I said my prayer, then when I was caring for the mother the [other] VBA was on her knees in the corner [praying]..." VBA 4

In another site, VBAs mentioned the use of holy water and holy oil, which was rubbed

onto the abdomen and perineum to assist in a safe birth:

"...since 2011 we give holy water. If a mother fails to deliver and feels weak we give her holy water which she drinks to get strength. Now we are using that holy water and holy oil... they drink holy water and [we] rub them with holy oil..." FGD 1

Maternal deaths

While many of the VBAs could recall maternal deaths in the community there was widespread agreement that these deaths mostly occurred when women were not attended by the VBA. Reflecting on such experiences, some VBAs described being called too late, only when a problem was recognized, leaving no time to refer, and without the means to save the mother, as one VBA in a FGD describes:

"[One] mother died with the placenta inside, then later baby died...yes [I did deliver mother]...it [placenta] was really hard to come out...it was raining and flooding and was too hard [to bring her down]...poor lady, I really miss her...that's only my first mother [who died], my delivery was no good and I was really scared...I couldn't help her." FGD 4

Reports of deaths in the presence of a VBA described unsuccessful attempts at management or referral. One VBA described a mother who gave birth without supervision, with the family only calling the VBA when they were unable to remove the placenta. The VBA tried to refer the mother to the health centre but she died on the beach while awaiting a small boat for referral transport. Another reported:

"One mother died...she had PPH...we were trying to transfer her to the health centre and the mother died...it just happened too quickly...in 2012..." FGD 3

One community-based key informant hypothesized as to why he felt maternal deaths occurred:

"...from what I have seen is that most of the problems that led to maternal deaths are through ignorance by mothers themselves, who fail to listen to the advice they are given. They fail to do such, to obey and they

encounter that [problems]..." KI 6

Neonatal outcomes

Stillbirths and early neonatal deaths were mentioned by a number of VBAs. Some VBAs spoke of the reasons why they felt the deaths occurred, recognizing premature births, malpresentation, big babies and 'broken cords' as reasons for stillbirths. When discussing complicated births, VBAs frequently reported instances of a positive outcome for the mother but a number of neonatal deaths. One VBA described how she managed a breech presentation:

"...it came out by the bum-bum, it's very hard for me, it's very risky...I can't [do it], it's only the health centre [staff] but we have to use what we have learnt from our training and make [do] our best to help the mother...and [get] the baby to come out...I turned one leg out and I turned and took the other leg out, I tried my best. The normal one [birth] is OK but the difficult one...the baby had already died, but the mother was alright..." FGD 6

VBAs recognized many newborn outcomes could have been better if the birth had taken place at the health facility. Early neonatal deaths were often reported, including reports of babies being born 'flat' (in need of resuscitation). For those reporting babies born 'flat' the commonly reported management was to immerse the infant in cold water to stimulate it to cry, advice they reported having been given during their VBA training. When discussing stillbirths, some VBAs reported macerated stillbirths and some suggested that congenital anomaly was the cause of many stillbirths.

Challenges

Health system support

Since the inception of the VBA program a number of respondents reported that the program has gradually deteriorated, as described by one key informant:

"...[at] the launch of the VBA program [in early 1990s] there was support, but the program has gradually collapsed...the downfall of the program is not only because of lack of donor support but also lack of support by the community, health staff and

politicians..." KI 8

Some of this is attributed to lack of funding and financial support, but some to lack of support across VBA program coordinators, VBA trainers and health facility staff. One of the consistent messages expressed in all sites, by individuals and groups, was that of a breakdown in the overall coordination of the program. Even in sites with an active trainer, VBAs reported minimal follow-up and no refresher training or continuing support. Most VBAs reported that they have never been visited by their VBA trainer in their village. VBAs also reported that little support was provided by the health clinic team during routine maternal and child health clinic patrols conducted in their communities.

While many VBAs reported lack of support from or interaction with professional staff at health facilities, there were some exceptions. One nurse at an aid post mentioned that VBAs make a big difference to her work load, as they come into the facility with the woman in labour, providing not only support to the woman in labour but also to the health care worker who worked alone at that site. Having worked in areas without VBAs she saw the program as a positive contributor and worked closely with the VBAs. In other sites, health facility staff, key informants and VBAs felt that integration of VBAs with the formal health system was constrained by high staff turnover, the loss of trainers in particular areas and the absence of any handover to new health facility staff.

One of the biggest challenges reported by most VBAs was their lack of medical supplies needed to assist at births. Supply was typically dependent on stock availability at the health facility, which if limited was held back from VBAs. This was reported as often leaving VBAs without gloves, cord ties or cord clamps, or clean blades to cut the baby's umbilical cord. One VBA described:

"...we used shopping plastic [bags] to tie [cover] our hands...or rice plastic [bag]..." FGD 2

Some VBAs reported attending births in their community using their bare hands. Clean scissors or sharpened bamboo was used to cut the umbilical cord. In one district, VBAs from two different sites spoke of having their VBA kits taken away from them by health facility staff as a disincentive for village births.

These VBAs were also actively dissuaded from assisting mothers using the pretext of the risk of HIV infection. Even when stripped of equipment, VBAs felt vulnerable as they continued to be called to assist mothers giving birth in the village, as one VBA in a FGD describes:

"I send them down [the mothers]...I have no things to use to deliver them. Because when we had refresher we came here... they stop us not to deliver the mothers at home because of this HIV disease...they [said they] must deliver here. We came and that was what they told us and we left all our kits here, not [allowed] to take them home, they stopped [us] to take the kits and go and look after the mothers at home. I thought they would repack it [the VBA kit] and give back [to me]...but they didn't...I was a bit worried, sometimes I use my bare hands to do my service...no gloves.....but I really love my job." FGD 4

Community and family support

Overall, VBAs reported that they did not have enough, if any, support from the communities which they served. A few VBAs expressed a desire for help with their gardens and to maintain their houses. Some VBAs had help maintaining crops in their garden, and some had food prepared for them after assisting a mother to give birth. However, those who reported community assistance noted this as inconsistent, with most of the support coming from the VBA's own family. In two communities, the local-level government (LLG) had built a 'birthing house' for VBAs to attend women during childbirth and as a place for women to rest post-partum. While this was acknowledged as supportive, the VBAs were disappointed that the building remained unfinished in one community, without a water supply, with the result that they were unable to use it and needed to continue to attend to women in their own houses. The lack of support for VBAs was reflected on by one key informant:

"The VBA program has done a lot of good for the community but the question is how much has the community done to help the VBAs..." KI 8

Key informants reported a lack of support at the community level for many of the VBAs. However, in one very remote site, a key

informant described how one community was supporting their VBAs through training and providing a regular monthly payment, to show their support and appreciation:

"...the LLG is sustaining the VBA program and has funded two refresher courses for VBAs, and also the LLG is setting to paying each VBA K30 every month for their work." KI 2

Most of the married VBAs had supportive husbands, but two said their husbands wanted them to stop working or receive payment for their work. The issue of receiving payment was also highlighted during one FGD with VBAs recognizing that other individuals providing services at the village level (peace officers, councillors etc) receive regular payments. When asked what kind of support VBAs would like, many mentioned aspects of community assistance that would help their practice. These suggestions included: some form of payment to enable them to easily take their reports into the health centre; funds for referrals for antenatal care visits or for women in labour; and funds for kerosene for lamps and soap and gloves to ensure clean births.

"...[the community support us], give us food, help in our gardens, sometimes they collect money and give us K5 every 3 months..." FGD 1

Motivations and personal issues

Many VBAs reported continuing with their work in spite of feeling unsupported, stating they enjoyed what they do and want to help mothers in their communities. Many of the VBAs were motivated by a heartfelt desire to serve despite the lack of support, although from their descriptions it could be argued that they are being neglected and overlooked. Other VBAs continue because of their commitment to God, for example:

"I have a heart to help the mothers. I love the mothers and want to save them." VBA 8

"Only God knows [how hard we work]...but we are very happy, very happy to do our work, we are saving God's people...ours is our promise to God..." FGD 2

On an individual level, other challenges faced by VBAs relate to their personal circumstances. Although in some sites VBAs

are themselves training younger VBAs to ensure services are continued, ageing VBAs and poor health was a concern for many. One younger VBA in a FGD expressed:

"As for me, about that old mother there [refers to another VBA] – with your own eyes you can see she is very old...see how she looks like now, are you really thinking that she will do that work, seeing that it looks like she is very old..." FGD 6

For many VBAs, the reality of facing complications of childbirth, such as stillbirths and PPH, was too personally distressing. One VBA in a FGD described that she had stopped practising following an incident in the village:

"...for me I was working and the mother died [in 2006]...only the baby survived, the mother passed away... she had too much bleeding... and I got scared to do any more and so I stopped working..." FGD 3

Some VBAs reported working alongside another VBA, either from their own or another village – this was particularly the case if it was felt that there was a problem. In one setting the VBAs explained that it was important to have two VBAs so that, if something went wrong, not just one VBA could be blamed.

Despite the challenges, many VBAs who took part in this study maintained a good sense of doing whatever they could, given the circumstances, as one group of VBAs mentioned:

"Just a few weeks ago there was mother at []...they were trying to rush her to health centre. The mother was not expecting to have twin babies...one was delivered on the way and with the second one they were trying to check any more inside and the mother pushed and there's another baby... it was funny...they all got shock." FGD 3

Discussion

Almost 25 years after the training of VBAs began in Milne Bay Province, this cadre continues to support women during childbirth in remote and rural areas. A range of situations were reported whereby VBAs were called to assist a birth in the community, including: lack of transport; being called when labour had progressed too far for referral; being called only when problems were

noticed; and women giving birth on the way to a health facility. Despite some conflicting opinions about whether VBAs are assisting births or not, the findings of this review suggest that VBAs continue to support births many years after training, without supervision or formal support from the health system or their community and without the availability of essential equipment such as gloves and cord ties/clamps to support a clean birth. The findings of this review indicate that VBAs are meeting a community-perceived need (ie, care during childbirth) that the formal health system currently fails to fully address in this setting. While VBAs report assisting births, they experience situations where their training, skills, equipment or workplace are sadly insufficient to manage obstetric complications, with some women dying while awaiting or undergoing referral. Many VBAs, through their continuing practice, have gained a detailed understanding of the complications of childbirth and the realities of maternal and perinatal death, learnt through the often harsh lived experience of assisting vulnerable women as they progress through pregnancy and childbirth.

The importance of striving for supervised, health facility births, with good quality care during childbirth for all women, is undeniable (12,24) and is supported in PNG through national policy (25). However, the reality in Milne Bay Province, as in much of PNG, is that many communities are far from ready, or able, to manage this transition, as is the health system; this is seen in failings of infrastructure and a crippling shortage of a suitable health workforce, especially midwives (26,27). Many communities in MBP are remote and rural, with difficult terrain and open waters to navigate, and long distances to cover when trying to reach a health facility. Such barriers have previously been documented from PNG and elsewhere, as have barriers relating to timely decision-making and seeking care (7,28-31). Whether through choice or circumstances, women in such remote and poor settings, the very groups with the highest maternal and neonatal mortality rates, are the least likely to access and receive adequate health care (7,32). In the absence of skilled health care, community-based care, such as through VBAs, is often the only support available to women during pregnancy and childbirth (3). However, the lack of support and follow-up of VBAs by trainers or managers, coupled with the lack of coordination with professional health

workers in this setting, raises major concerns. A number of commentators have envisaged a useful role for TBAs (and by extension VBAs) in maternal health in other settings, such as supporting and accompanying women to health facilities and early initiation of breastfeeding (14,33-35), which are not being realized in MBP. Experiences from other low-resource settings suggest that improved supervised birth attendance can be gained through better integration of VBAs with formal health systems, more regular support supervision and annual refresher courses, and the use of VBAs to help understand and overcome local obstacles to health service utilization (14,33,34).

This study highlighted the grass-roots confusion that can result when national health policy shifts. The 2003 national VHV program and policy initiative intended to consolidate VBAs with other community-based health volunteers. However, this review has demonstrated that the volunteers, child-bearing women and their communities, and professional health staff, all continued to refer to VBAs as a distinct cadre, based on their training, and saw them as having a distinct role focused on pregnancy and childbirth care. There was further confusion among key informants who stated that they had received a directive from the National Department of Health in 2012 that all VHVs (VBAs) must stop assisting mothers giving birth in the community, instead referring them for a supervised, health facility birth. This directive was referred to during this review, with both VBAs and key informants reporting that VBAs were no longer to assist childbirth in the community. In one site VBAs were denied essential supplies to support their practice in the community. But the realities of childbirth in remote locations lacking in transport or health services meant that many VBAs were placed in extraordinarily difficult situations as they continued to be called upon for care that their community believed they were trained to provide. This exposed not only VBAs to risk of infection, but rendered a VBA unable to provide a clean birth experience, putting women and their newborn infant at increased risk of infection. While the policies may have been based on sound evidence, their implementation in this situation cannot be said to have advanced public health, or progressed reductions in MMR and neonatal mortality.

In Milne Bay Province, efforts to improve

supervised births are being addressed by providing women who give birth at a health facility with a 'baby bundle' incentive gift. This initiative is complemented by the training of health care workers in emergency obstetric care, and the establishment of an emergency phone line direct to the Labour Ward at Alotau Provincial Hospital (23,36). However, such efforts need to be accompanied, in the short term at least, by interventions to improve the safety of births that still, by necessity, take place outside of health facilities (37). This must include making better use of the VBA cadre that has such a long history in this province. There is a continuing need not only to define the VBA role in this particular setting but also to identify a strategy that will both support them in the community and integrate them with professional health care workers in the health facilities, including specific strategies of how VBAs can assist women (and their families) to make their way to health facilities in the last weeks of pregnancy to await birth and thereby benefit from the safety of a professionally supervised facility birth. In areas with active VBAs, training in evidence-based interventions enabling first aid care for selected maternal and newborn complications could be a viable interim strategy (35). In addition, practices described by VBAs that are potentially harmful to women and their newborn infants (pressing on the fundus and immersing the neonate in cold water) need to be promptly addressed in this setting. Given the number of VBAs in this study who spoke about PPH and retained placenta, and the prominence of PPH as a cause of maternal death in PNG, VBAs should be informed of the importance of early initiation of breastfeeding both for prevention of PPH and for the health of the neonate. Supported by evidence internationally is the potential benefit of community-based health care workers to distribute or administer misoprostol to prevent PPH following home births (38-40); such an intervention warrants consideration in remote, hard-to-reach areas.

This study is unusual because comprehensive reviews of VBA programs in PNG are not commonly publicly reported. It has a number of limitations, not least of which is that we only spoke to VBAs willing to share their experiences. In addition some interviews and community discussions took place in local languages, which were translated as the dialogue progressed. It is possible that some meaning and depth were lost during the

translation. While both VBAs and members of the community could recall maternal and neonatal deaths, given the nature of this study it was not possible to identify all maternal deaths in this area. As such we were unable to ascertain if the training of VBAs has saved the lives of women. It is acknowledged that there are many other VBAs who did not meet with the review team, either through choice or circumstances. Due to unforeseen circumstances and time constraints, we were unable to reach all sites with VBAs. More engagement with the community, particularly including men, could have revealed further insights. However, the sites visited have a long history of VBAs within their communities and, given that findings were similar across all sites, with different constraints, it is reasonable to assume that the findings accurately reflect the broader VBA program in MBP.

Conclusion

VBAs in this setting continue to support women during childbirth in their communities. Many are managing difficult obstetric complications with little or no knowledge or skill about these complications and without support from their communities or local health facilities. There is an urgent need to better define what VBAs can and should do in this setting, what their communities can expect, and how professional health care workers can work more constructively with this long-standing cadre of lay health workers.

The wider strengthening of facility-based maternal health services must remain an increasingly urgent priority, but while it is awaited, there is a need for all health facilities and VBA trainers to support their VBAs, recognizing the often difficult situation they are working in, and to emphasize that safer birth is only possible if the VBA assists the mother to get to a health facility for supervised birth.

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Sociocultural barriers to access and utilization of birth delivery services in a rural area of Papua New Guinea

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SUMMARY

A cross-sectional descriptive study using qualitative and quantitative methods was carried out in November 2012 to determine the reasons for the very low facility delivery rate in the Imbongu District of the Southern Highlands Province. 300 women of childbearing age (15-45 years) who had delivered either in Imbongu District health facilities or villages within the previous 24 months were interviewed using a structured questionnaire. Two focus groups with women and one focus group with the officers in charge of health facilities were held. The women who delivered at health facilities were more likely to have been educated to primary school level and above, to be less than 36 years of age, to have attended antenatal clinic and to have had the support of their male partner or male relative than the women who delivered in the village. Customary beliefs, run-down health facilities, poor staff attitude and concerns over the possibility of a male birth attendant were major reasons for women avoiding facility delivery. If maternal mortality rates are to fall in the district, urgent attention is needed to make the health facilities more attractive and user-friendly, and to find other ways of persuading mothers to deliver in them.

Introduction

The Southern Highlands Province is one of 22 provinces in Papua New Guinea (PNG). It is characterized by steep mountain ridges and deep valleys and its largely rural population of approximately one million people live in scattered villages and hamlets. Road access is limited and rough and many villages can only be reached on foot – making delivery of health services very difficult. At the time of this study the province had 200 aid posts, 52 health subcentres, 8 health centres, 5 district hospitals and 1 provincial hospital. Imbongu is one of eight districts in the province. Approximately one-fifth of the 100,000 population are women of childbearing age.

The 2006 National Demographic and Health Survey (DHS) reported a maternal mortality ratio (MMR) of 730 maternal deaths per 100,000 live births (1). 75% of all maternal deaths result from severe bleeding (particularly

postpartum haemorrhage), puerperal sepsis, preeclampsia and eclampsia, complications from delivery and unsafe abortion (2). These complications require skilled obstetric care and there is a very strong correlation between unsupervised delivery and maternal death (3,4). The role of a skilled birth attendant, defined by the World Health Organization (WHO) as “an accredited health professional – such as midwife, doctor or nurse – who has been educated and trained to proficiency in the skills needed to manage normal (uncomplicated) pregnancies, childbirth and the immediate postnatal period, and in the identification, management and referral of complications in women and newborns” (5), in preventing maternal death (and neonatal death) cannot be overemphasized. “A health centre intrapartum-care strategy can be justified as the best bet to bring down high rates of maternal mortality” (3).

The very low uptake of supervised birth by

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women in PNG is a major contributory factor to the alarmingly high MMR. In 2010 only 40% of PNG pregnant women were reported as having supervised births and the figure for Southern Highlands Province was only 17% (6). Figures for Imbongu District indicated that only 18% of pregnant women attended one antenatal visit and only 4.4% had supervised births (7).

For a typical home delivery in rural PNG there is no power supply, no access to clean running water, rudimentary toilet facilities, no health professionals for assistance, and no vehicle to transfer the mother if something goes wrong (and sometimes there is not even road access).

The study aim was to investigate why the rate of supervised deliveries in Imbongu District is so low, in spite of relatively good road access from most villages to a health facility.

The study objectives were:

- to identify women who gave birth within the previous 24 months in Imbongu District
- to compare the profiles of women giving birth in the village with those who had supervised births
- to understand women's reasons for having a home birth
- to identify circumstances and actions that may improve the rate of supervised facility births in the district.

Methods

The study was a cross-sectional descriptive study using qualitative and quantitative methods carried out in November 2012.

The delivery room and postnatal wards in the six health facilities in Imbongu District were thoroughly inspected, taking note of the water supply, the state of the toilet and shower block, the condition of the delivery room and delivery bed, the availability of delivery packs, drugs and equipment (eg, vacuum extractor), and the light source.

A sample size of 300 was determined using the standard formula, with 95% confidence

intervals and a desired precision of $\pm 5\%$, based on a population of 22,644 women of childbearing age and a crude birth rate of 32/1000. Convenience sampling was used to select women in the childbearing age group (15-45 years) attending the maternal and child health (MCH) clinics at each of the district health facilities who had delivered either in Imbongu District health facilities or villages within the previous 24 months and who had lived in the Imbongu District for more than one year. A pretested structured questionnaire designed to obtain information on demographic and sociocultural factors related to childbirth and their own experience was administered to the women by trained research assistants following informed consent. Data were checked for consistency by the first author. Sociodemographic quantitative data (including age, education status, distance from a health facility and antenatal attendance) were analysed using the SPSS 19 program. The Pearson Chi-squared test was used to compare categorical variables of those mothers who had delivered in a health facility with those who had delivered in the village. Odds ratios and 95% confidence intervals were generated for variables showing highly significant differences between the two groups, and multivariate logistic regression was used to determine confounding.

Three focus group (FG) discussions lasting between 30 and 35 minutes were conducted among 20 women and health professionals. One group, selected by convenience sampling, consisted of women who had given birth in a health facility. A second group, similarly selected, consisted of women who had given birth in the village. The third group comprised officers in charge (OICs) from different health facilities. At the focus group discussions the topic of factors contributing to village births was introduced. Mothers were encouraged to discuss the reasons for home birthing and how to improve the coverage for health facility birth. Structured questions were not used, but participants were guided to stay on the topic. Handwritten diary notes were made of the points articulated during the discussions and subsequently analysed and classified under specific themes as outlined by Parahoo (8).

The research proposal was approved by the School of Medicine and Health Sciences, University of Papua New Guinea (UPNG) Research Committee and permission for the

study was given by the Southern Highlands Provincial Health Adviser. A simple witnessed consent form was completed by the participants either by signing or by marking with a thumbprint.

Results – Quantitative Studies

Of the 300 women interviewed, 84 (28%) had given birth to their last child in a health facility and 216 (72%) in the village.

Sociodemographic and related characteristics

Characteristics of the women giving birth in the health facility and the village are compared in Table 1.

Women giving birth in the health facility were more likely to be less than 36 years of age, to have had primary or higher education, to have attended antenatal clinic at least once and to live less than a full day's walk from the nearest health facility than those giving birth in the village. They were also more likely to have had the support of their husband or a male relative during their pregnancy – and during transfer to the health facility.

Human factors adversely influencing the decision to access health facilities for childbirth

All participants were asked to choose one of five reasons for women not accessing a health facility for childbirth and to give their

TABLE 1

COMPARISON OF WOMEN GIVING BIRTH IN A HEALTH FACILITY WITH THOSE GIVING BIRTH IN THE VILLAGE

	Facility birth No (%) n = 84	Home birth No (%) n = 216	p value
Age (years):			
15-25	37 (44)	42 (19)	
26-35	31 (37)	95 (44)	
36-45	16 (19)	79 (37)	<0.001
Education:			
None	10 (12)	88 (41)	
Primary	26 (31)	94 (44)	
Secondary	37 (44)	33 (15)	
Tertiary	11 (13)	1 (0.5)	<0.001
Distance (time to walk) to health facility:			
Short walk	25 (30)	47 (22)	
Within 2 hours	30 (36)	70 (32)	
Half a day	19 (23)	40 (19)	0.036
Full day	10 (12)	59 (27)	0.007
Attended ANC at least once	69 (82)	118 (55)	<0.001
Number of ANC visits:			
Nil	15 (18)	97 (45)	
One	5 (6)	16 (7)	
Two	15 (18)	19 (9)	
Three	19 (23)	32 (15)	
Four	30 (36)	52 (24)	<0.001
Assistance from husband or other male relative	54 (64)	69 (32)	<0.001

ANC = antenatal clinic

preference for the type of attendant at their next birth. The responses are shown in Table 2. Whilst both groups indicated cultural factors as important in the decision to give birth at the village rather than the health facility those who had given birth at the health facility also indicated that the poor status of the facility and adverse staff attitudes were likely to have a strong influence on women's decisions. They also postulated that having an unskilled birth attendant at the health facility was likely to be a deterrent. Both groups showed strong preference for female health workers or – in the case of those who had delivered in the village – a female village birth attendant (VBA). The possibility of a male attendant was a stronger deterrent for those mothers who had given birth in the village than for those who had had facility births – but was still an issue for the latter group. Similar proportions of the groups had paid delivery fees either at the health facility or to a VBA in the village.

Physical infrastructure at health facilities

Although women (and the community) could not be expected to have detailed knowledge about the physical state of health facilities and the equipment available in them,

the views of the women concerning the poor state of the health facilities were borne out by the inspection which found that of the 6 health facilities, 1 had no water supply and another required major maintenance, 4 did not have a vacuum extractor, 2 did not have a delivery bed, 2 had no delivery packs, 2 had no appropriate drugs, 2 were dirty, 1 had no toilet or shower and in 1 the toilet also required maintenance. All had a delivery light or lamp.

Measures to increase proportion of facility births

Responses requiring the choice of one of four questions concerning how mothers could be motivated to give birth at the health facility are shown in Table 3. The choices were the provision of food, napkins and soap; having only female health workers attend delivery; building more community health posts; and training more VBAs to assist mothers from the village to facilities.

Differences between the two groups were not significant. Ensuring female staff at the health facility and building more community health posts were the two commonest answers in both groups.

TABLE 2

POSSIBLE FACTORS INFLUENCING MOTHERS AGAINST A HEALTH FACILITY CHILDBIRTH AND THEIR PREFERENCE FOR BIRTH ATTENDANT AT THEIR NEXT BIRTH

	Facility birth No (%) n = 84	Village birth No (%) n = 216	p value
Reasons for avoiding facility birth:			
Culture	22 (26)	74 (34)	<0.001
Possibility of male birth attendant	11 (13)	69 (32)	
Poor health facility	25 (30)	34 (16)	
Staff attitude	14 (17)	24 (11)	
Unskilled health professional	12 (14)	15 (7)	
Preference for birth attendant:			
Female health worker	66 (79)	120 (56)	<0.001
Village birth attendant	0	53 (25)	
Self	5 (6)	26 (12)	
Male or female health worker	12 (14)	17 (8)	
Other woman	1 (1)	0	
Fee payment for previous birth	27 (32)	55 (25)	0.39

Principal factors associated with giving birth in a health facility

Uncorrected and corrected odds ratios for those variables for which there were highly significant differences between the two groups are shown in Table 4. Education (primary or above), the support of husband or male relative, and having at least one antenatal attendance at a health facility were independently associated with health facility birth. Age of greater than 35 and distance of a day's walk to the health facility were negatively associated on bivariate analysis but these associations were influenced by confounding.

Results - Qualitative Studies

Several common themes emerged during

focus group discussions as to why women gave birth in the village and not in the health facilities.

Poor staff attitudes

Poor staff attitudes were frequently cited as a strong factor influencing women against facility delivery.

"My first delivery was a male infant delivered at Mendi Hospital. The nurses in the delivery room said, 'Do you wash, did you bring a baby blanket, napkins, soap?' and aggressively talked hard on me and I was embarrassed and ashamed. They hit me on my buttock when I did not cooperate with them throughout the delivery process, even laughed at me when I was struggling

TABLE 3

WOMEN'S OPINIONS ON MOTIVATION FOR FACILITY BIRTHS

	Facility birth No (%) n = 84	Village birth No (%) n = 216	p value
Only female staff to attend birth	39 (46)	67 (31)	0.055
Build community health posts	26 (31)	76 (35)	
Provide food and other materials	13 (15)	41 (19)	
Train more VBAs	6 (7)	32 (15)	

VBA = village birth attendant

TABLE 4

FACTORS ASSOCIATED WITH HEALTH FACILITY BIRTH

Parameter	Unadjusted odds ratio	p value	Adjusted odds ratio	p value
Education (primary and above)	5.09 (2.49-10.39)	<0.001	4.65 (2.20-9.83)	<0.001
Attendance at antenatal clinic	3.82 (2.06-7.09)	<0.001	2.99 (1.52-5.89)	0.001
Support from husband or male relative	3.84 (2.26-6.50)	<0.001	2.45 (1.36-4.41)	0.003
Age above 35	0.38 (0.20-0.70)	0.002	0.53 (0.27-1.02)	0.076
One day's walk to facility	0.36 (0.17-0.74)	0.006	0.55 (0.25-1.24)	0.15

to deliver with the strong pain. ...So I promised not to deliver again at the health facilities and deliver the second baby in the village. I came to antenatal clinic today for the nurse to tell me the position of the baby.” (FG1)

This sentiment was expressed by mothers who chose facility birth because of the risks of dying in the village.

“I have seen mothers dying with retained placenta and loss of blood. I live quite a distance away but I always make it my business to go and give birth at the facility. I felt ashamed of being naked in the eyes of the health workers but many of us think of our life and go for delivery at the facilities. Most of the female health workers say bad words which hurt our feelings but we still go for delivery. For these reasons many mothers don’t go and give birth at the facilities.” (FG1)

Poor staff attitude was recognized as a deterrent by the OICs.

“If we treat the mothers like our own relatives they will like our services and access the facilities for delivery.” (FG3)

Poor health facilities

The poor condition of the health facilities was another important reason against facility delivery, and was often linked to the need to ensure adequate numbers of female health workers.

“Though I live close to the health facility, I delivered the third child in the village due to no qualified nurses at the centre. It doesn’t have water supply to the delivery room, no delivery bed, it doesn’t have bathroom toilet and no separate room for delivery. Majority of the health workers are male and I don’t like to give birth in the eyes of males even if the delivery room is provided in the near future. Currently all the mothers here are delivering in the village; however, to motivate the mother to deliver at the health facilities, the Health Division must provide a delivery bed at the centre, allow only females to do deliveries and allocate more female nurses to work at the health centres.” (FG2)

The OICs of the health centres were well

aware of the reasons why health facilities were not better utilized and showed frustration with the health authorities.

“I talked to the District Health Officer regarding this issue many times to fix the delivery room and it has fallen on deaf ears all the times. If the Provincial Health Authorities want the supervised births to improve and motivate mothers to give birth at the centre, they must come and fix the delivery room.” (FG3)

“The Division of Health in the province was told verbally and in written form to provide female nurses for the facility but this request did not eventuate and females don’t want to come to give birth when males are working at the facility.” (FG3)

Lack of support from husbands

Lack of support from husbands was discussed, with some women agreeing that this should be a legislative issue. It was felt that polygamy contributed to this lack of support and consequent failure to attend health facilities. Women indicated that many husbands regarded women as unclean during the delivery process and did not assist because of the fear of contamination.

“Our husbands think that we are unclean so they could not assist us very much during the delivery process. I know many women are dying due to childbirth but I am still delivering in the village because I can’t help it when time occurs for delivery; there is nobody to assist me. The village birth attendants in my village assist us to deliver when we go and see her for assistance but now she can’t assist, when she doesn’t have the hand gloves and other items like gauze.” (FG2)

Distance from health facility

Distance from the health facility and the need to provide health facilities closer to the village were linked with the other reasons.

“The reason for delivering in the village was, Mendi hospital is far away and I have no money for PMV fare and have no money to purchase food items while in hospital. My husband has three wives and is good at making us pregnant but doesn’t care about the outcome of his sexual pleasure.” (FG2)

Women had faith in the VBAs but they were not always available or able to assist, and it was recognized that they would not be able to help in a serious complication.

"The village birth attendant does lot of deliveries there, when she has the hand gloves and gauze, but currently her relatives stop her from this job due to fear of HIV/AIDS infection." (FG2)

"I live close to the health centre but don't go to the health facility and give birth there. I am a mother of two children and delivered one at hospital and one in the village. Most of the mothers there delivered in the village with the assistance of the village birth attendant. We have seen mothers dying with postpartum haemorrhage in the villages and request many times to the Provincial Health Office at Mendi to allocate a female nurse for the health centre, but this request did not result in any change." (FG2)

Discussion

Women who had their last birth in a health facility were more likely to be younger, of higher education status, to have attended antenatal clinic and to have had support from a male member of the family than those who had given birth in the village. The possibility of a male attendant, unwelcoming and unprofessional staff attitudes, and run-down and inadequately staffed health facilities were strong deterrents to health facility births.

Findings from this study are consistent with those from other low- to middle-income countries. A Kenyan study (9) found that women with no or low education did not access the health facilities, and that the timing and frequency of antenatal visits were significantly associated with education of the mothers and their partner. Lack of privacy, presence of male health staff, poor quality of care and adverse attitude of health workers towards the delivering mother contributed to home deliveries among rural Laotians (10) and similar findings have been reported from studies in Ethiopia (11), Nigeria (12), Kenya (13) and Tanzania (14).

Distance is often cited as a factor in deterring women from facility delivery. A study from West Java, Indonesia (15) found that physical distance and financial limitations were two major constraints. In two recent

studies from Goroka, in the Eastern Highlands Province of Papua New Guinea, distance and transport as well as decision-making processes and customary beliefs influenced whether women did or did not reach a facility to give birth even though both women and men were aware of the risks of village delivery (16,17). Distance was a major factor in the high maternal mortality ratio in the remote parts of Milne Bay Province (18). In our study, distance was also a factor in bivariate analysis but there was significant confounding.

It is well recognized that charges made at health facilities are a strong deterrent (3). In spite of the fact that PNG National Health Policy forbids the charging of fees for giving birth, family planning services and antenatal care in the public health system, our study found that fees were charged to one-third of those delivering in the health facility and a quarter of those delivering in the village. Even when facility charges are not made, the costs of transport and of food and other essentials are significant considerations. Women in our study felt that the supply of food and other items would increase the facility birth rate. A recent study from Milne Bay described an increase in supervised birth following the introduction of 'mother and baby gifts' as incentives (19). Whether or not such an intervention is sustainable in the long term is questionable.

VBAs have been trained in some parts of PNG for many years (20,21). In this study they had assisted 18 (8%) of those women delivering in the village. The assistance of the VBAs was valued, and during focus group discussions it was suggested that more VBAs should be trained and that there should be more community health posts (CHPs) in the district. However, there are limitations to the role of the VBA and indeed of the CHP and its staff. It is accepted that assistance at normal delivery is helpful and that basic care of the newborn such as cord care may prevent neonatal death. CHP staff are trained to recognize risks and early signs of complications of labour and delivery, to provide obstetric first aid and refer women who have risk factors and early signs of complications to a health facility equipped and staffed to provide appropriate obstetric care.

The role of the VBAs is to assist all pregnant women to attend antenatal clinic for regular check-ups and a health facility for

supervised birth, and indeed this is National Department of Health (NDoH) policy. Once birth complications, such as prolonged labour, abnormal presentations, antepartum or postpartum haemorrhage or preeclampsia develop, there is very little any village-based health worker can do to alleviate the situation, and most do not have referral capacity.

In a recent study from East Sepik, increased use of services provided by village health volunteers (VHVs) in the rural communities occurred concomitantly with a decline in health facility usage for assisted delivery (22). Whilst there may be several reasons to explain this it is at least possible those women in the rural communities did not appreciate the limitation of care provided by the volunteers and that the presence of such volunteers resulted in the belief that village delivery would be safe and delivery in a health facility unnecessary.

In a recent study from Somaliland traditional birth attendants (TBAs) were paid each time they brought women to a facility for delivery. Instead of conducting home births and only referring women to facilities when a complication developed, the TBAs accompanied mothers to nearby facilities for delivery and postnatal care, resulting in increased deliveries at health facilities and prevention of many obstetrical complications (23). Whilst a similar policy in which VBAs or other community members could be utilized may be feasible in some areas of PNG it would only work if mothers were assured of being managed in the birthing process by a competent, friendly female birth attendant, in a pleasant well-equipped health facility.

Maternal mortality will not be significantly reduced by increasing the numbers of health workers in the community, but rather by providing access to high-quality health facilities where labour can be monitored and interventions carried out by appropriately trained staff (3). Whilst it is unrealistic to plan for every pregnant woman to deliver in a tertiary health facility, it is feasible to improve care provided at health centres and district hospitals to meet the NDoH minimal standards. The limited but important role of VBAs and VHVs needs to be appreciated. CHPs should be able to provide antenatal care, to determine high-risk pregnancies and to encourage – and possibly accompany – the expectant mother to go to a properly equipped and staffed health facility for a supervised

delivery.

There are a number of limitations to this small study, conducted among women attending MCH clinics at health facilities. A larger study including women in the remote villages would have generated further information and a focus group discussion with young married men would have provided added insights. The information obtained from the questionnaire survey was limited by the single answer format. Women were likely, for example, to have had more than one reason – and perhaps all the reasons offered – for not accessing health facilities. Notwithstanding these limitations, the study has provided valuable information.

Conclusions

Traditional beliefs about childbirth and traditional male attitudes to women will take many years to change, but it is hoped that following the introduction of 'free' primary education, increased access to secondary education and improved socioeconomic status of rural communities the proportion of women opting for facility birth in health facilities close to their homes will improve over the foreseeable future. In the short to medium term, the option of community health facility-based childbirth can and must be made more available and attractive. Health facilities must be upgraded to include the basic requirements for skilled obstetric care and must be staffed by qualified female birth attendants. All health workers need to appreciate the positive effects resulting from a welcoming and friendly professional behaviour.

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Factors associated with lower extremity amputation in patients presenting with diabetic septic foot: a prospective case series

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SUMMARY

The rapid demographic changes occurring in the Pacific island countries, including Papua New Guinea, have led to a rapid increase in the prevalence of non-communicable diseases. Surgical services in Papua New Guinea are seeing a marked increase in admissions for diabetic septic foot (DSF). Lower extremity amputation is common, although specific criteria for this procedure are lacking. We report a prospective case series of 20 patients admitted to the Surgical Ward of Nonga General Hospital with DSF from October 2013 to July 2014. Patients who had lower extremity amputation were younger, had a higher level of HbA1c and a higher Wagner ulcer score than those managed conservatively.

Introduction

The earliest survey of diabetes mellitus (DM) in Papua New Guinea (PNG) was done by Hingston and Price in 1962, using glycosuria for screening and the glucose tolerance test for confirmation (1). The prevalence of DM according to their findings was 0.2%. Campbell in 1963 reported that only 10 patients with diabetes were admitted to Port Moresby General Hospital (PMGH) over a 3-year period (2). Since then, various authors have shown that the prevalence is increasing. Certain ethnic groups in PNG such as the Tolais and the Wanigela community at Koki in Port Moresby have some of the highest prevalences of DM in PNG (3). Martin and colleagues found that diabetic patients in Port Moresby and Rabaul have a high frequency of complications including proteinuria, neuropathy and lower limb amputations (4). Kuzma and colleagues reported increasing numbers of diabetic foot ulcers admitted to PMGH from 2003 to 2008 (5). The development of diabetic foot is a

complex process involving the neurological, vascular and musculoskeletal systems. The primary underlying cause of these changes is the increasing level of glucose resulting in non-enzymatic glycosylation at the molecular level (5). In PNG the prevalence of diabetic foot disease is affected by sociocultural factors such as walking barefoot, low education, lack of knowledge about the complications of diabetic foot and the low socioeconomic status of patients (5). Diabetic foot complications are responsible for 18% of all admissions related to DM (6). Approximately 15% of all diabetic patients will present at some point in their lives with a foot ulcer, with a 5-year recurrence rate of 66-70% (6). Diabetic septic foot (DSF) is a major health problem and major lower extremity amputation (LEA) is the most feared complication of diabetes. It increases morbidity and mortality and reduces the patient's quality of life (7).

The population of East New Britain Province is estimated to be around 220,000. At Nonga General Hospital (NGH) an average

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of 3 diabetic amputations are performed each month with an average of 36 diabetic amputations per year. This represents about 5% of the surgery work load. In 2013, 50% of the mortality in the Surgery Department at NGH was from complications of diabetes and diabetic septic foot. These figures represent a significant disease burden for the hospital – one which is likely to increase in the coming years.

In PNG, health care resources to deal with the diabetic septic foot are limited. Sophisticated investigative tools such as ankle brachial index measurements, Doppler sonography and angiography are not available. The management is based on the experience of the general surgeon. In contrast, in developed countries, the management of DSF involves a multidisciplinary approach including orthopaedic, vascular and plastic surgeons and other disciplines such as physiotherapy and nutritional services (8).

Methods and Materials

We performed a prospective case series study on 20 consecutive patients presenting to the Surgery Department of Nonga General Hospital with diabetic septic foot between October 2013 and July 2014.

Patients with diabetic coma, hypertension and prior history of heart disease, kidney disease or any other serious co-morbidities were excluded from the study.

Informed written consent was obtained from all patients. The study was approved by the Chief Executive Officer and Director of Medical Services of the Nonga General Hospital.

We used a standard sliding scale treatment regimen with short-acting subcutaneous insulin (Actrapid) given on a 6-hourly basis to control blood sugar and standard intravenous antibiotics, namely chloramphenicol 1 g and flucloxacillin 1 g 6-hourly, to cover infections. Patients who were anaemic were transfused. Debridement was the first option of management.

Details of the patient's age, gender, HbA1c level, white cell count, haemoglobin level and Wagner ulcer grade were documented. Data were entered and analysed using SPSS version 20.

The Wagner classification is shown in Table 1.

Results

Of the 20 patients 12 (60%) underwent lower extremity amputation, of which 9 had major limb amputation (3 above knee and 6 below knee) and 3 had minor limb amputation. 7 (35%) underwent debridement only and 1 patient was managed conservatively with antibiotics only. Table 2 shows a comparison of data from patients treated with lower extremity amputation and those treated conservatively.

TABLE 1

WAGNER CLASSIFICATION

Wagner class	Description
0	No ulcer in a high-risk foot
1	Superficial ulcer involving full skin thickness but not underlying tissues
2	Deep ulcer penetrating down to ligaments and muscles but no bone involvement or abscess formation
3	Deep ulcer with cellulitis or abscess formation often with osteomyelitis
4	Localized gangrene
5	Extensive gangrene involving the whole foot

TABLE 2

COMPARISON OF DATA FROM PATIENTS TREATED WITH LOWER EXTREMITY AMPUTATION AND THOSE TREATED CONSERVATIVELY

Variable	Lower extremity amputation (n = 12)	Conservative (n = 8)
Gender:		
Male	5	5
Female	7	3
Age (years):		
Median	53.5	65.5
Range	44-70	45-79
HbA1c (%):		
Median	13.4	9
Range	9.4-14	6.1-11.2
Wagner class 1-5:		
Median	3	2
Range	2-5	1-3
White cell count (x10 ⁶ /l):		
Median	18,100	12,000
Range	7000-34,000	6000-22,200
Haemoglobin (g/dl):		
Median	9.8	9.6
Range	7.9-11.8	4.9-12.9

Discussion

Gender was not associated with LEA, a finding similar to studies from Singapore (9), Japan (10) and Turkey (11).

In our study the median age of those having LEA was lower than that of the conservatively treated patients. This is in contrast to other studies. An American hospital survey in 1990 found that the amputation rate was 1.4 to 2.4 times higher in individuals 65-74 years old and ≥75 years old than in those below 65 years.

There was no difference between the haemoglobin (Hb) levels in our two groups but both had median levels below 10 g/dl. In a study from Singapore (9) an Hb level of <10 g/dl was associated with limb loss, and a recent European study found that an Hb of <8.2 g/dl was a strong predictor for lower limb loss (12).

Our study did not show an association between white cell count (WCC) and LEA, in contrast to the Singapore study, which found a WCC of ≥11,000 to be a good predictor of

lower limb loss.

Wagner class 3 is widely associated with an increasing rate of amputation (13) and was a significant factor for LEA in our series.

Levels of HbA1c were higher in the LEA group than in those treated conservatively. Other studies have also found an association between high levels of HbA1c and LEA (14,15).

Limitations

There are other investigations like Doppler sonography, ankle brachial index measurements and angiography that were not used in this study series before embarking on LEA.

Conclusions

The prevalence of diabetes in the PNG population is increasing rapidly and poses a major problem for the health services. Urgent attention is needed in terms of preventive

education. At the individual management level, surgeons dealing with patients with diabetic septic foot are faced with difficult decisions. Use of the Wagner ulcer scale and knowledge of the HbA1c level are helpful in making these decisions.

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A pilot study of the quality of life among cancer patients attending the Ambulatory Cancer Clinic at Port Moresby General Hospital, Papua New Guinea

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SUMMARY

45 cancer patients and 15 health care providers (HCPs) were interviewed using a specifically designed questionnaire to assess the experiences and knowledge of quality of life (QoL) dimensions in cancer care. There was widespread suffering in the domains of physical well-being, social and family well-being, emotional well-being and functional well-being. The worst quality of life was seen in total laryngectomy and permanent colostomy patients, followed by advanced head and neck cancer and amputees. Whilst both groups agreed on functional well-being and social and family well-being as important there were differences of views on the other domains. Interestingly the patient group did not think their relationship with their doctors and nurses was overly important whereas the HCPs did think so. There is considerable suffering from disease and treatment-related aspects of cancer care that needs to be addressed. HCPs also need to be realigned to the needs of the patients more and use more effective organ-preserving palliative care treatments earlier in the course of the disease.

Introduction

Measurement of treatment outcomes is based on directly observable events such as morbidity and mortality. Quality of life (QoL) is a new concept, yet will remain an important consideration for as long as there are diseases around. The reluctance to use it has been due to its lack of conceptualization and inability to convert to a measurable event (1). Many attempt to organize what are abstract domains such as symptoms, social and family well-being, emotional and functional well-being and last but not least spiritual concerns. These span the totality of a person's life experience that contributes to quality of life. With improvements in statistical methods (2) these QoL concerns can now achieve some usefulness in clinical outcome studies. The disadvantage is that it takes time to complete the questions and therefore the reluctance to use the QoL concept may yet continue for

some time.

Palliative care is closely related to cancer management and other chronic diseases. When the disease burden overwhelms any therapeutic efforts then palliative care is given. This is to assuage the many fears that afflict the dying patient such as pain, family acceptance, emotional problems and life after death issues. It is now recognized that rather than be given late, palliative care should be integrated with definitive care earlier on. This has led to better outcomes with quality of life as well as disease-free survivals (3,4).

In Papua New Guinea (PNG), quality of life studies have not been done. Most of what may be considered palliative care may fail to achieve its aims for the majority of patients. A few get referred to centres that can offer meaningful treatment, albeit considered palliative whatever the modality. Doctors

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and nurses who treat such diseases amass considerable experience but may not improve disease-free or recurrence-free survival. There are as yet the inaccessible, the ignorant and the dispossessed patients, who are what has aptly been termed the 'hidden burden of cancer' (5), who die in their misery out there somewhere.

This study was done to see if indeed there were QoL concerns that needed to be addressed and also to gauge the views of health care providers (HCPs) to see if they were similar or otherwise to those of the cancer sufferers.

Methods and Materials

The study was conducted at the Cancer Ward of the Port Moresby General Hospital (PMGH) from December 2000 to March 2001. 45 new patients were recruited consecutively from those referred for medical or ongoing postoperative care, without restrictions. The questionnaires were pretested with the interviewees and some patients preferred to answer the questions on their own at home. They were allowed to do so because it is a very personal matter. Also 15 HCPs who were known to routinely deal with cancer patients were asked to complete the same forms. There were no exclusion criteria.

We used the European Organization for Research and Treatment of Cancer Questionnaire (EORTC QLQ-C30) in its two formats: a) Functional Assessment of Cancer Therapy – General (FACT-G) and b) FACT-H&N for head and neck cancer. There were a total of 46 questions and each response was scored from 0 (not at all) to 4 (very much) for every domain and an analogue score from 1 to 10 as a summary for every domain. The scores were adjusted using a weighted score and the sum total multiplied by the number of items and divided by the number of responses. Finally they were added to get a final score for each domain. The reader may look these questions up for further information (2). The responses were then compared using the χ^2 test where applicable.

The domains are written thus: physical well-being (PWB); social and family well-being (SFWB); relationship with doctor (RWD); emotional well-being (EWB); functional well-being (FWB); and head and neck cancer

concerns (HNC).

Results

Of the patients, there were 24 males and 21 females whose ages ranged from 15 to 70 years with a mean of 48 years. There were 16 oral cancers, 12 breast cancers, 5 skin cancers, 3 colorectal cancers, 3 laryngeal/hypopharyngeal cancers and 2 oesophageal cancers and 1 each of cancer of the ear, eye and maxilla and non-Hodgkin's lymphoma (NHL). The FACT-G scores of the patients in order of worst scores were: SFWB 811.3/1260, PWB 807.6/1260, FWB 716.3/1260, EWB 605.5/900 and RWD 178/355. Head and neck cancer subdomain (FACT-H&N) was 659/960 (Table 1).

Of the HCPs, there were 8 doctors, 4 nurses and 3 social workers who were based at the hospital. Their responses are as follows in order of preferences of importance: FWB 88/399, EWB 83/399, RWD 79/399, SFWB 76/399 and PWB 73/399.

Table 2 shows the results of patients and HCPs ranking the domains as <5 or ≥ 5 . Overall patients and HCPs had opposite perceptions. Though the perceptions for SFWB and FWB were similar in both groups they diverged significantly in the PWB, RWD and EWB domains with p values of 0.02 or 0.05. The 22 patients with HNC and the HCPs scored similarly in their QoL concerns.

Individual responses show that total laryngectomy patients with permanent tracheostomy, permanent colostomy patients and advanced head and neck cancer patients had the worst scores. Some were tearful and depressed and preferred the privacy of their homes to complete the questions.

Discussion

In this study we have found a disturbingly high level of suffering in all domains contributing to poor quality of life. The areas of particular concern are in domains relating to personal dignity and worth. The physical symptoms such as pain or nausea from the disease or treatment have an additive effect on family carers and loss of self-esteem in the patient. It is also remarkable that patients can be so stoical in the face of mounting hopelessness. Coping with illness is shown to be poor with an EWB score of 605.5 and a high degree of

TABLE 1

TOTAL NUMBER OF RESPONSES GENERATED FOR EACH QUALITY OF LIFE CONCERN

Quality of life concern	Patients n = 45 Score (% of worst possible score)	Health care providers n = 15 Score (% of worst possible score)	Total
Physical well-being (PWB)	807.6 (64)	73 (18)	880.6
Social and family well-being (SFWB)	811.3 (64)	76 (19)	887.3
Relationship with doctor (RWD)	178 (50)	79 (66 [†])	257
Emotional well-being (EWB)*	605.5 (67)	83 (21)	688.5
Functional well-being (FWB)	716.3 (57)	88 (22)	804.3
Head and neck cancer (HNC) concerns**	659 (69)	88 (57)	747

[†]Best possible score

*EWB with denominator of 5

**Additional HNC scores for 22 patients

TABLE 2

NUMBER OF RANKINGS FOR EACH DOMAIN USING AN ANALOGUE SCALE

Quality of life domain	Patients (n = 45)		Health care providers (n = 15)		p value
	Number ranked <5 [†]	Number ranked ≥5	Number ranked <5	Number ranked ≥5	
Physical well-being	27	18	6	8	0.05
Social and family well-being	22	23	6	9	0.95
Relationship with doctor	31	14	4	10	0.02
Emotional well-being	27	18	4	11	0.02
Functional well-being	23	22	6	9	0.99
Head and neck cancer	9	13	5	9	0.99
Total	139	108	31	56	

[†]<5 less important and ≥5 more important

negative emotions (67%). Certain patients with colostomies and permanent tracheostomy cope extremely poorly: patients had a problem speaking or the need to always be 'colostomy conscious' prevented free association with people. Anecdotal experiences show that patients are labelled 'sick' and therefore an object of pity, worsening the situation. We have spent many years treating these patients and are not surprised at the large number who have admitted to unrelieved symptoms and suffering. We believe the main reasons would be 1) irregular and inadequate supply of drugs, 2) advanced stage of the diseases, 3) poor stoma care and rehabilitation, 4) lack of an irradiation facility in PMGH and 5) lack of knowledge of the care of dying patients.

The 22 patients with HNC excluding 2 oesophageal cancer patients have a high cumulative score of 659 and the worst functional impairment of 69%. This concerns basic vegetative functions such as breathing, eating and communicating. Patients with cancer in other sites remote from the head and neck region score lower than those with HNC and have better QoL than the HNC patients. This study shows too that HCPs have a better perception of an HNC patient's needs than of those for patients with cancers in other sites. The hypothesis that there may be a difference did not prove significant on statistical testing. We believe that this improved perception may be due to 1) the life-preserving functions of head and neck structures, 2) the fact that HNC is exposed and 3) HCP professionals knowing more about it because HNC is common in Papua New Guinea.

Health care providers, however, were quite emphatic that they played an important role in a cancer patient's life (Table 1 – 66%, Table 2: 10 – p value 0.02). Patients did not reflect the same sentiments and half of the scores suggested that HCPs could do better. This suggests that HCPs need to spend more time with complex patients such as cancer sufferers and those with end-stage systemic diseases.

There are some notable omissions from our study population such as patients with gynaecological cancers and childhood cancers and post-irradiation patients. These patients attend different clinics and the radiation facility is in Lae, Morobe Province. The EORTC questionnaire (QLQ-C30) also does not include a spiritual domain, which is

important for Papua New Guinean patients who are either Christian or from an animist background. Furthermore the government has not acted on the recommendation of the International Society of Palliative Care Physicians to make morphine accessible for cancer pain control. These factors may have an impact on the high level of suffering we believe is prevalent in the community.

The study was done more than a decade ago and we may add that the conditions prevailing then are still the same now. It has, however, given us an opportunity to discuss the issues in light of the current progress in the field. It has become clear that the fight against cancer has just begun. The genome project is almost complete and with it the promise of mapping out almost all the known human diseases. On the palliation front we should aim to integrate palliative care as early as possible to get better responses and outcomes.

Our findings in this study show that in Papua New Guinea our services fall short of four cardinal principles practised in the care of cancer sufferers (6). They are: 1) respect the patient as a person; 2) do good; 3) minimize harm; and 4) make fair use of available resources. These principles underpin the universally held views on the sanctity of life and the inevitability of death. In PNG we lack data on the seriousness of this problem, which may explain in part our poor management of this group of patients. Recently efforts from Australian international aid and the International Society of Palliative Care Physicians alerted the Health Department to the scale of the problem. They updated the *Guidelines for the Treatment of Cancer in Papua New Guinea* and conducted workshops on cancer pain management. Like all fields in medicine palliative care is evolving; however, locally we need to do simple things well before we embrace difficult things. An ethical and humane form of treatment where the organ is preserved as much as possible should be the treatment of choice in PNG (5). That in short means palliative irradiation and the use of surgery sparingly for advanced diseases whilst using medical palliation concurrently. Recent findings (3,4) suggest that palliative care must be integrated into early definitive treatment to get the best results.

Our study also suggests that the health system may be in danger of 'dumping' gravely

ill patients on the traditional extended family system. Certainly the family system absorbs the family member who is dying but there is no reason why he or she should die in misery. A society is measured by its attitude to its women and children and its sick and dying, and therefore this indeed is a societal problem. These are huge challenges but let us take one step at a time until we get mastery over our burden of suffering in the community. No one will do it for us.

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Herbal products utilization among patients with HIV/AIDS in East Sepik Province, Papua New Guinea: a pilot survey to determine the prevalence

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SUMMARY

HIV (human immunodeficiency virus) infection remains a major public health problem globally including Papua New Guinea. This is despite the introduction of highly active antiretroviral drug therapy. HIV-infected people often seek complementary and/or alternative therapies, among which traditional herbal medicinal products have become common in Africa and other developing countries. In an effort to understand whether herbal medicine is used in Papua New Guinea, we conducted a pilot survey in two HIV clinics in East Sepik Province to determine the prevalence of herbal product access and use among people with HIV infection. 55 HIV patients consented to be surveyed. Of 54 patients who responded 39 (72%; 16 males, 23 females) reported taking herbal products, of whom 27 (50%) did so with antiretroviral therapy (ART) and 12 (22%) without ART. Only 15 patients (28%; 11 males, 4 females) indicated that they had been taking only ART. Interestingly, relatively more women than men were accessing and using herbal products that were available in the local areas. Of the patients who were taking herbal products 49% informed their health care providers that they were doing so, and 79% reported experiencing some benefit from the herbs. Although the study was limited to two sites in one province, the findings should be of concern to health care providers, clinicians and policy makers because of the profound clinical and policy implications for HIV treatment in Papua New Guinea. Efforts should be directed at generating more data to determine the scope and depth of these practices across the country.

Introduction

HIV (human immunodeficiency virus) infection has become a pandemic that has engulfed the world. It is one of the three most deadly infectious diseases which are recognized for their high mortality worldwide (1), the other two being malaria and tuberculosis. Deaths due to HIV infections are attributed to AIDS (acquired immunodeficiency syndrome), a syndromic disease characterized by a low CD4 lymphocyte count (<200/ μ l of blood) and opportunistic infections (2-4). Although the use of highly active antiretroviral therapy (HAART or ART) has positively

impacted on the disease progression with marked improvement in survival rate and the quality of life for many patients with HIV (1,5) it has definitely been unsuccessful in curing HIV infection. The HAART is based on triple or quadruple combinations of antiretroviral drugs; however, while reducing HIV to very low levels, this combination treatment fails to eliminate the viraemia completely (6-10). To achieve complete viral eradication and to provide cure, the cells bearing a latent population of viruses (viruses that are lying dormant and are refractory to ART) must be targeted and eliminated (9-11). Unfortunately, no anti-HIV agents that are available today can

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be used for that purpose, but development of such anti-HIV agents from natural sources are in progress (12,13).

Although HIV infection was first reported in Papua New Guinea (PNG) in 1987, the magnitude of the epidemic still remains a significant health issue, and the number of HIV-infected individuals in need of care is increasing. An estimated 32,297 people (0.54% of the population of 6 million) were living with HIV in PNG at the end of 2013, and the figure was projected to increase by 0.03% to 33,948 by the end of 2015 (14). The antiretroviral drug therapies are the only recommended treatment for HIV/AIDS as part of a comprehensive HIV/AIDS management program including treatment of people with HIV/AIDS in PNG. The HIV/AIDS policy guidelines do not include options for alternative treatment modalities that could provide choices for the use of traditional herbal medicines and/or natural health products. The implication of such policy has yet to be assessed in terms of ART adherence and whether people with HIV/AIDS are strictly on conventional therapies. It has been estimated, however, from various studies across Africa that approximately 30% of people living with HIV and on ART utilize some form of traditional herbal/plant medicines/products (15-18). Many governments in African countries recognize and support the use of traditional herbal medicines/remedies and natural health products alongside ART (19). In PNG, it has always been recognized that traditional herbal remedies are easily accessible in rural areas and it would not be surprising if some of these herbal products could easily find their way into HIV/AIDS treatments. There are no empirical data to suggest otherwise, so in an effort to understand if herbal products (defined as extracted products derived from herbs or parts of plants or a combination of both) were accessed and used by HIV/AIDS patients, we conducted a pilot survey among HIV/AIDS patients attending two HIV/AIDS clinics in East Sepik Province (ESP) to determine the use and the prevalence.

Study methodology

Study design and setting

A descriptive cross-sectional survey was conducted among HIV/AIDS patients at Wasaie and Sepik Centre of Hope Clinics from June to December 2013. The two clinics

were staffed by trained HIV/AIDS health care professionals who provide supervision, voluntary counselling and monitoring of treatment for people with HIV/AIDS living in ESP. Both clinics are located in an urban township which is the commercial/business hub of the province and the clinics receive referrals of HIV patients from rural health facilities across the province.

Participant recruitment

The clinics were conveniently selected and participants were selected using a convenience sampling technique. Each participant was approached individually as they came to the clinic and was provided with necessary information including description of the purpose and objectives of the study. The participants were eligible if their HIV status was known to be positive and they had registered at the clinic of study, if they were aged 18 years and above, and if they had provided written consent to participate in the study. Participants were also informed that the survey was conducted on a voluntary basis, and anyone who wished to participate must sign a consent form; those who did not wish to participate in the survey were free to go and the services provided by the health care providers at the clinics were not denied to them. All selected participants meeting the inclusion criteria were enrolled. Participants were excluded if they did not wish to participate or refused to give written informed consent.

Data collection

Participants' data were collected using a pilot-tested self-administered semi-structured questionnaire developed specifically for the survey. The data were collected by three trained research assistants under the direct supervision of the principal investigator. The main outcome measure was herbal products use. This referred to someone who had ever used or was currently using herbal products intended for the treatment of HIV infection. Participants were asked when and why they started using herbal products, what herbal products they were using, and what they experienced when taking herbal products. Participants were also asked whether the use of herbal products was disclosed to their health care providers.

The questionnaire was also designed to collect demographic characteristics of

the participants including age, sex, level of education attained, and marital and employment status. The questionnaire was either self-administered or, in the case of those who needed assistance, a trained research assistant was assigned to assist the participants. Questionnaire forms were available in both English and Tok Pisin (local lingua franca), providing choices for the participating patients.

Data and statistical analysis

The collected data were entered into Microsoft Excel and stored on multiple computers and password protected. The 'sort and filter' function was used to clean and validate the data before computing basic statistics. Data analysis was restricted to quantitative data and was summarized by descriptive statistics. Due to the nature of the study design and small sample size obtained, descriptive statistics were used predominantly, without further statistical exploration of associations or causality for certain variables.

Ethical considerations

The study protocol was approved by the PNG National AIDS Council Research Advisory Committee and Divine Word University Research Ethics Committee. Permission to conduct the study at the two centres was granted by the East Sepik Provincial HIV/AIDS Committee. We ensured that each participant was recruited on a voluntary basis and that each one signed a written informed consent form; each one was informed that they could leave the study anytime during the study. We also ensured confidentiality of the participants' information using a coding system instead of participants' names.

Results

Demographics

55 HIV-confirmed participants participated in the survey. The mean age of the participants was 36.9 ± 10.1 (mean \pm SD) years. There were 28 males (51%) and 27 females (49%) with a mean age of 38.6 ± 9.5 and 36.4 ± 9.6 years, respectively. The age range of the male participants was 24 to 62 years and for the female participants 19 to 48 years. The sociodemographic characteristics of the participants are shown in Table 1.

Married participants accounted for 83%, and 94% of the participants had formal education. Of the 52 participants who responded 31 (60%) indicated being employed, 23 of whom were working for government departments or private organizations and were on regular salaries while 8 were self-employed.

The number of participants on herbal products and ART are shown in Table 2. Interestingly, more female participants (85%) reported taking herbal products in general than their male counterparts (59%). Herbal product use among male (48%) and female (52%) participants on ART was similar.

Prevalence and types of herbal products used

39 (16 males, 23 females) of the 54 participants who responded reported that they were taking some forms of herbal product, giving an overall prevalence of 72%. 27 participants (50%) were taking a herbal product in conjunction with ART, 12 participants (22%) were taking only herbal products while 15 participants (28%) were taking only ART (Table 2).

Participants were taking a wide variety of herbal products that included Gawi herbal juice, Noni juice, Pangwi herbs, Tiens products, Balagam herbs, Kire herbs and others including self-produced herbal products (Table 3). Most of these herbal products have not been scientifically validated or identified nor have these products been approved, even as traditional herbal medicines, for HIV treatment. Thus, in the present study, efforts were directed at understanding why people living with HIV/AIDS are resorting to using these herbal products. Table 4 provides the time-line for when ART and/or herbal products were commenced after diagnosis and for what reasons. Of the 39 participants taking herbal products, 19 (49%) were taking herbal products with the knowledge of their health care providers at the study sites.

Valued perception of the herbal products

The valued perception in this context is defined as *opinion and thoughts that users hold in regard to the use of herbal products*. The participants provided a variety of reasons as to why they had chosen to use ART and/or herbal products (Table 4). A total of 31 participants (79%) of the 39 taking herbal

TABLE 1

SUMMARY OF THE BASIC SOCIODEMOGRAPHIC CHARACTERISTICS OF THE CONSENTED PARTICIPANTS

Characteristics	Male n (%) 28 (50.9)	Female n (%) 27 (49.1)	Total n (%) 55 (100)
Education level	N = 27	N = 27	N = 54
No schooling	2 (7.4)	1 (3.7)	3 (5.6)
Primary schooling	7 (25.9)	7 (25.9)	14 (25.9)
Secondary schooling	13 (48.1)	17 (63.0)	30 (55.6)
Tertiary education	5 (18.5)	2 (7.4)	7 (13.0)
No response	1	0	1
Marital status	N = 26	N = 26	N = 52
Never married	3 (11.5)	6 (23.1)	9 (17.3)
Married or cohabitation	23 (88.5)	20 (76.9)	43 (82.7)
No response	2	1	3
Employment status	N = 27	N = 25	N = 52
Employed	13 (48.1)	10 (40.0)	23 (44.2)
Unemployed	13 (48.1)	8 (32.0)	21 (40.4)
Self-employed	1 (3.7)	7 (28.0)	8 (15.4)
Unspecified	1	2	3

TABLE 2

SUMMARY OF RESPONSES BY THE HIV/AIDS PATIENTS TO THE USE OF HERBAL PRODUCTS AND ANTIRETROVIRAL THERAPY

Types of treatment	Male n (%) N = 28	Female n (%) N = 27	Total n (%) N = 55
Use of herbs	N = 27		N = 54
Yes	16 (59.3)	23 (85.2)	39 (72.2)
No	11 (40.7)	4 (14.8)	15 (27.8)
Invalid	1	0	1
Current treatment	N = 27		N = 54
ART only	11 (40.7)	4 (14.8)	15 (27.8)
Herbs only	3 (11.1)	9 (33.3)	12 (22.2)
ART and herbs	13 (48.1)	14 (51.9)	27 (50.0)
Invalid	1	0	1

ART = antiretroviral therapy

TABLE 3

SUMMARY OF THE DIFFERENT TYPES OF HERBAL PRODUCTS SOME PATIENTS WITH HIV/AIDS WERE TAKING

Type of herbal products taken by 26 of the patients	Biological name	n (%) N = 26
Gawi herbal juice	A mixture of several herbs administered as concoction	12 (46.2)
Noni juice	<i>Morinda citrifolia</i> juice	6 (23.1)
Pangwi herbs	A mixture of several herbs administered as concoction	4 (15.4)
Tiens products	A mixture of several herbs administered as concoction	2 (7.7)
Balagam herbs	A mixture of several herbs administered as concoction	1 (3.8)
Kire herbs	A mixture of several herbs administered as concoction	1 (3.8)

products reported experiencing some forms of positive response: 15 (38%) experienced increased appetite and weight gain, 10 (26%) experienced restoration of their strength and 6 (15%) reported minor health benefits. Of these 31 participants, 20 were taking ART and herbal products simultaneously, while 11 participants were exclusively taking herbal products (not included in the table).

Discussion

The results of the pilot survey show that herbal products were being accessed and used by some of the participating patients with HIV/AIDS at the two survey sites. Of the 54 participants with valid responses, 39 (72%) were taking herbal products, and of these 27 (50%) were taking herbal products with ART. This latter group of participants would be of concern, considering the potential impact of herbal products on HIV treatment with ART. It is therefore important that herbal medicines/products use in any form should be regulated and, when used, should be monitored for any herbal-ART interactions, and/or for prevention of emergence of ART resistance in the country (20,21). Although the prevalence of herbal products use obtained in the present survey is high, it is nonetheless in general agreement with findings in other similar studies across

Africa (16-18,22,23) and elsewhere (24-27).

Interestingly, women were more frequently engaged in herbal products use than men. Although the survey was limited in its design in eliciting possible explanations for the gender differences, similar trends have also been observed across several larger studies (19,22,23,25,27-30) and in non-HIV/AIDS health care studies (31,32). It is possible that gender difference observed across different studies may only reflect differences in sociodemographic determinants (age, education and household income). However, it may also reflect the greater neglect of women's health care needs than those of men in the public health care system, prompting women to turn to non-conventional therapies including traditional herbal medicines/products. Further studies may be needed to explore gender biases and differences in health-care-seeking behaviour and the accessibility to health services pertaining to HIV/AIDS.

In the present survey, 19 (49%) of the 39 participants reported taking herbal products were doing so with the knowledge of the health care providers at the study sites. The health care providers' awareness of herbal products use is crucial, not only

TABLE 4

SUMMARY OF THE TIME PROFILE OF THE COMMENCEMENT OF ART AND HERBAL USE AND REASONS FOR THEIR USE BY PARTICIPANTS

	Male n (%)	Female n (%)	Total n (%)
Start of ART after HIV diagnosis in 40 of the 55 patients	N = 23	N = 17	N = 40
Within 3 months	5 (21.7)	5 (29.4)	10 (25.0)
At 12 months	9 (39.1)	5 (29.4)	14 (35.0)
At 24 months	6 (26.1)	2 (11.8)	8 (20.0)
More than 24 months	3 (13.0)	5 (29.4)	8 (20.0)
Reasons for taking ART in 41 patients	N = 23	N = 18	N = 41
Available on demand	2 (8.7)	1 (5.6)	3 (7.3)
Easily accessible	1 (4.3)	0	1 (2.4)
Trust drugs to work	9 (39.1)	6 (33.3)	15 (36.6)
Easily accessible and trust drugs to work	0	2 (11.1)	2 (4.9)
All elements (availability, accessibility, trust drugs to work)	11 (47.8)	8 (44.4)	19 (46.3)
Recommended by doctor	0	1 (5.6)	1 (2.4)
Start of herbal products after HIV diagnosis for 35 patients	N = 14	N = 21	N = 35
Before knowing HIV status	3 (21.4)	2 (9.5)	5 (14.3)
Within 3 months	4 (28.6)	7 (33.3)	11 (31.4)
At 12 months	3 (21.4)	4 (19.0)	7 (20.0)
At 24 months	3 (21.4)	4 (19.0)	7 (20.0)
More than 24 months	1 (7.1)	4 (19.0)	5 (14.3)
Reasons for taking herbal products in 32 patients	N = 14	N = 18	N = 32
Available on demand	1 (7.1)	0	1 (3.1)
Easily accessible	1 (7.1)	1 (5.6)	2 (6.3)
Trust herbs to work	3 (21.4)	7 (38.9)	10 (31.3)
Available on demand and easily accessible	2 (14.3)	1 (5.6)	3 (9.4)
Easily accessible and trust herbs to work	2 (14.3)	1 (5.6)	3 (9.4)
All elements (availability, accessibility, trust herbs to work)	5 (35.7)	5 (27.8)	10 (31.3)
Other reasons	0	3 (16.6)	3 (9.4)

ART = antiretroviral therapy

to optimize patient care (22), but also to minimize the potential for negative impact on the quality of life when both ART and herbal products are used simultaneously (30). Concurrent administration of herbal products and antiretroviral drugs do impact on adverse effects (30), including the potency of antiretroviral drugs (33). The health care providers were aware of herbal practices by the participants at the study sites, but chose to remain complaisant, preferring not to discourage attendance. This survey revealed a need to better understand the factors involved in a patient's HIV management choices, including treatment.

A good number of patients reported some form of therapeutic benefit, such as weight gains and improvements in strength, with the use of herbal products. The reports of health benefits from herbal use were subjective and it is uncertain whether the use of herbal products alone provided the therapeutic benefits. However, plants/herbal products do have therapeutic benefits and examples from history have provided us with effective antimalarials (34,35) and anti-cancer drugs (36). Even some of the earliest forms of protease inhibitors were derived from natural products (37), and currently more are being investigated (12,13,15,38-40). Further efforts through systematic research and clinical trials will be needed to understand which herbal products used alongside ARTs could provide therapeutic benefits to patients.

Conclusions

To the best of our knowledge, this is the first survey addressing the use of herbal products by those with HIV/AIDS living in ESP, PNG. The results show that unknown herbal products were being accessed and used in conjunction with ART. Further studies involving several sites with adequate sampling size is suggested.

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Wandering spleen with torsion of the pedicle: a case report

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SUMMARY

Wandering spleen is an uncommon condition characterized by laxity or absence of splenic ligaments. Patients with torsion of the wandering spleen may have acute, chronic or intermittent symptoms. We report a case of wandering spleen with torsion of the pedicle in an 18-month-old child who presented as a case of bowel obstruction. To our knowledge, this is the first case of wandering spleen reported in Papua New Guinea.

Case Report

An 18-month-old male child presented to our care on 15 October 2015 with a history of nausea, vomiting, intermittent colicky abdominal pain and constipation for 3 days. He had a temperature of 37.5°C, respiratory rate of 36 per minute and a pulse rate of 147 beats per minute. On abdominal examination, he had abdominal distension without guarding or rebound tenderness. There was a fixed and tender mass in the lower right quadrant. Per rectum examination was unremarkable. His haematological parameters were normal. A nasogastric tube decompression revealed bile-stained aspirate. His urine output was normal. An exploratory laparotomy was planned with a diagnosis of ruptured appendicitis with subsequent bowel obstruction in mind.

Operation

At laparotomy through a small midline incision extending from 3 cm above the umbilicus down to just above the symphysis pubis the small bowel was delivered and an attempt made to deliver the mass from the right lower quadrant. To our surprise, the mass was the spleen with a 90-degree torsion of the pedicle (Figure 1). The splenic pedicle was abnormally long. To exclude accessory spleen, we extended the incision superiorly to visualize the left upper quadrant and to give us good access. There was no spleen in the left upper quadrant but the left lobe of the liver

extended to the left upper quadrant. There was omental attachment from the splenic pedicle to the right paracolic gutter (Figure 2). The pancreatic body and the tail were also attached to the splenic pedicle inferiorly (Figure 3). The omental attachments were released and the splenic pedicle was detorsioned. The spleen was viable by its colour and pulsation in the splenic vessels. A splenopexy was employed, with the placement of the spleen in the posterolateral position in the left upper quadrant with a double suture to the posterior wall. The child made an uneventful recovery and was discharged 6 days postoperatively.

Discussion

Wandering spleen is a rare condition. A 1989 review of the literature by Allen and Andrew found 35 cases of wandering spleen in children less than 10 years old (1). 18 of these patients presented as acute surgical emergencies. Of these, only 8 had a diagnosis of splenic torsion preoperatively. Children with a wandering spleen are typically between 3 months and 10 years old: the most frequent age at presentation is less than 1 year (1). Affected patients may be asymptomatic and present with an incidental mass on physical examination, may have mild abdominal pain due to vascular congestion or intermittent torsion and spontaneous detorsion, or may present with an acute abdomen due to torsion of the splenic pedicle with subsequent infarction. With acute torsion, the condition

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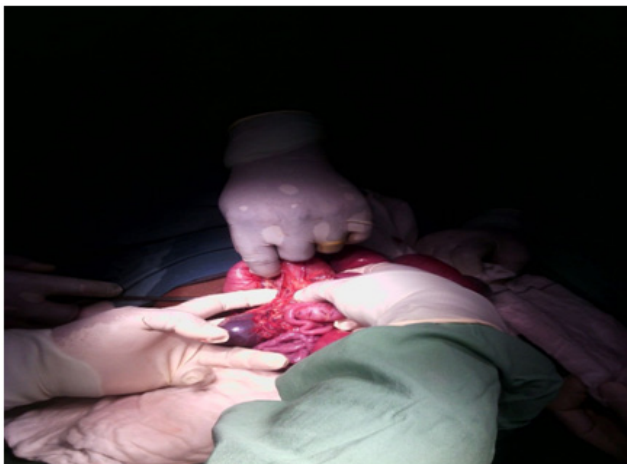


Figure 1. Showing the spleen delivered out from the right lower quadrant.



Figure 2. Showing the splenic pedicle with omental attachment to the right paracolic gutter.

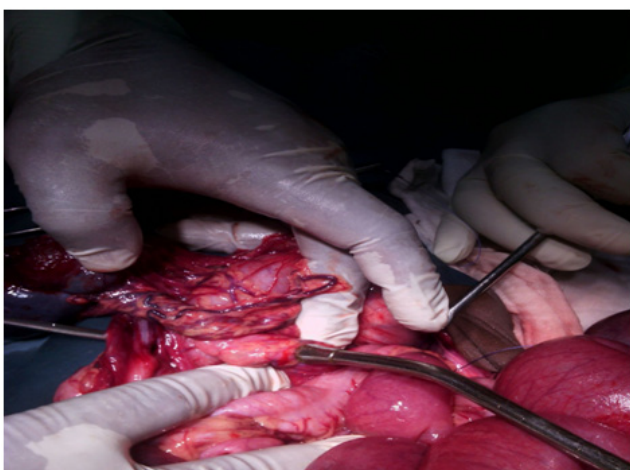


Figure 3. The suction tip pointing towards the pancreas below the splenic pedicle.

can be confused with appendicitis or ovarian torsion. Other clinical findings include nausea, vomiting, fever, leucocytosis, peritoneal signs and a palpable mass in the abdomen or pelvis. Complications of splenic torsion include gangrene, abscess formation, local peritonitis, intestinal obstruction and necrosis of the pancreatic tail (2).

In adults, particularly in women of childbearing age, splenic torsion has usually been attributed to acquired abnormalities such as ligamentous laxity, splenomegaly, trauma and hormonal effects of pregnancy (2). Splenic torsion in children is believed to be congenital and due to abnormal development of the dorsal mesogastrium (2). Normally the dorsal mesogastrium gives rise to the spleen and its supporting structures, the lienorenal and gastrosplenic ligaments (3). The most important ligament is the lienorenal ligament, which arises after fusion of the posterior leaf of the dorsal mesogastrium with the parietal peritoneum in front of the left kidney. This ligament attaches the spleen to the posterior body wall and contains the splenic artery. The lienorenal and gastrosplenic ligaments allow some mobility of the spleen normally, but prevent its displacement from a position posterior to the stomach and anterior to the left kidney. Incomplete fusion or formation of the dorsal mesogastrium results in an abnormally mobile spleen with a long vascular pedicle that is predisposed to torsion. The dorsal pancreatic bud also develops within the dorsal mesogastrium. When the parietal peritoneum and posterior leaf of the dorsal mesogastrium fuse, the pancreas becomes a retroperitoneal organ. If the dorsal mesogastrium is incomplete or fails to fuse with the parietal peritoneum, portions of the pancreatic tail may be intraperitoneal or can be involved in the splenic torsion (3). This occurred in our case.

Multiple imaging techniques have been used to diagnose wandering spleen (4). Plain radiographs of the abdomen usually have non-specific findings, but they can suggest a mass in conjunction with the absence of

a splenic shadow in the left upper quadrant. Barium enema findings may be normal or can show displacement by an extrinsic mass. Sonography and CT (computerized tomography) are able to show the typical comma shape of the spleen in an ectopic position and lack of splenic tissue in the left upper quadrant. CT is not degraded by bowel gas and has an added advantage of being able to establish the presence or absence of perfusion. Angiography can provide evidence of torsion but it is invasive and no longer indicated for diagnosis (5).

Conclusion

Splenic torsion can be recognized as a differential diagnosis of an acute abdomen in children. Splenectomy is the treatment of choice in acute splenic torsion with infarction. Splenopexy can be performed in patients who have chronic or intermittent symptoms and without infarction. By the end of the 1990s laparoscopic splenectomy and splenopexy were being performed with favourable outcomes (6).

ACKNOWLEDGEMENT

We thank Dr D. Aisi and Dr W. Pakalu for their help in managing this case.

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LETTER TO THE EDITOR

Microscopic observation of *Rodentolepis nana* eggs in a faecal specimen

Necator americanus, *Ascaris lumbricoides* and *Trichuris trichiura* are endemic throughout Papua New Guinea (1,2). *Strongyloides fuelleborni* subspecies *kellyi* is another helminth infection that is endemic in Papua New Guinea, but with a restricted distribution (2). In recent years, there has been a growing awareness throughout the world of the public health significance of these enteric parasitic diseases, particularly their detrimental effect on childhood development including malnutrition, decreased fitness and decreased cognitive ability. We report here what we believe are the eggs (n = 10) of *Rodentolepis nana* (*Hymenolepis nana*) observed in a routine microscopic examination of a faecal specimen obtained from an adult Papua New Guinean food handler. A sample photograph of a *Rodentolepis nana* egg as seen under light microscopy (40 x magnification) and captured on a Leica ICC50 camera using a Leica microscope is presented (Figure 1).

R. nana (a dwarf tapeworm) may not be the only hymenolepidid species found in humans (3); it does occur, however, wherever humans and rodents live. It can be found throughout the world but is usually most common in warm and temperate zones and in remote communities where poor sanitation

and poor public health practices prevail (3,4). It commonly affects children but the infection usually remains asymptomatic. It is one of a few enteric parasites that can cause autoinfection which can persist for years. *R. (H.) nana* infection has been described as fairly rare in Papua New Guinea by Ewers and Jeffrey (5) and, to our knowledge, there has been no published photograph of its occurrence here. We report our microscopic finding so that laboratory technicians may be aware of it when examining faecal specimens.

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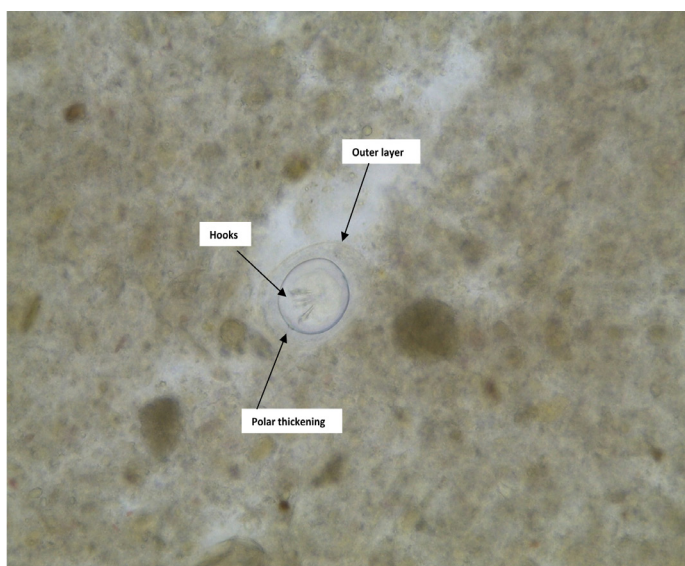


Figure 1. Photograph of a *Rodentolepis* (*Hymenolepis*) *nana* egg captured on a Leica ICC50 camera with a Leica microscope. 40X

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OBITUARY

Dr Regina Wangnapi – going above and beyond the call of duty

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The untimely death of our much cherished and admired colleague Dr Regina Wangnapi in February 2016 not only leaves a huge gap in the lives of her family, friends and colleagues, but is also a tremendous loss to science and health care in Papua New Guinea and beyond.

As an aspiring research clinician Dr Wangnapi (Figure 1) supervised a number of important studies conducted at the Papua New Guinea Institute of Medical Research (PNGIMR), two of which are published in this edition of the Journal (1,2). I had the honour to work alongside Dr Regina Wangnapi during the completion phase of the IPTp (Intermittent Preventive Treatment in Pregnancy) trial in Madang Province (3), which included a key sub-study on sexually transmitted infections in pregnancy conducted by Dr Wangnapi (4) (Figure 2).

It was during this time that I recognized Dr Wangnapi's enormous clinical, scientific and leadership potential. Always going above and beyond the call of duty, she gave everything to ensure the well-being of our patients and team members and the smooth running of the study, which all too often meant staying on late to complete the tasks at hand. Any hurdle was taken with great patience, diligence, transparency, scientific integrity, kindness, and an astonishing selflessness, the latter being her most defining characteristic.

At the forefront of her work was a deep passion for improving the health of Papua New Guineans and to support the professional development of local scientists in the context of continuing international collaboration. In addition to her scientific contribution she leaves us with a legacy of hope, optimism



Figure 1. Dr Regina Wangnapi, December 2012.



Figure 2. Dr Wangnapi at the IPTp study office in Madang, reviewing trial case report forms.

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and human warmth. When facing challenging clinical or scientific situations myself I often try to imagine what Regina would have done, and take guidance from my personal experience of working alongside this colleague and friend. *"In the long run, persons appreciate the ones who help them to grow, not the ones upon whom we have become dependent"* (5). Dr Wangnapi's mentorship and friendship is greatly missed, yet will continue to resonate within us.

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OBITUARY

In memory of Regina Alice Wangnapi-Taput

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She was known as Alice by her family, as Regie by her friends and as Dr Regina or Dr Wangnapi-Taput by her colleagues, patients and the general public who knew her (Figure 1).

I knew of Regina during my training at Kavieng Hospital in 2006, where I worked with her parents, Dr Wangnapi and Sr Wangnapi, but did not know her personally until May 2009 when she came to work on the same research projects that I was working on at the Papua New Guinea Institute of Medical Research (PNGIMR) in Madang. Since then, she became not only my colleague but also a best friend and the sister I never had.

Regina and I worked in a team of three research clinicians supporting our senior research clinician in coordinating and supervising the implementation of two large pregnancy trials (PREGVAX and IPTp) conducted in Madang by PNGIMR between 2008 and 2013 (Figure 2). Regina proved

to be a natural leader who led her team with honesty and respect. Despite the demanding workload from these two trials, Regina took on an extra challenge by undertaking her Master's degree, which was investigating the prevalence and risk factors of sexually transmitted infections (STIs) in pregnant women in Madang Province. By 2013, she had not only completed the two trials successfully but had also successfully completed her Master's degree.

For a person who worked closely with Regina for 5 years, this was never considered impossible. Regina was a very intelligent woman and was very committed to her work and determined to get her tasks completed. Running the two trials at the same time demanded a lot and I would often feel stressed about it all but Regina was always calm and went about her work without a fuss. She was so committed that she would come to work even while she was sick and on strict observations or on intravenous medications. Since our office was close to the hospital, she would come and find something to do and return to the hospital when it was time for medications and observations. She would just laugh it off if I scolded her about it. In 2013, she presented her research work at the Medical Symposium and received an award for the best oral presentation. Following that, in 2014 she published her research work on STIs and contributed to many other papers.

Regina was a very loving, kind and caring person to everyone that she came across and worked with. She had so much respect for everyone, no matter who they were and where they came from. This is why she had so many friends. She could sit next to a stranger in a PMV bus and by the time she got off the bus, she had made that stranger her friend. She



Figure 1. Regina Alice Wangnapi-Taput.

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Figure 2. The IPTp and PREGVAX study team.

made people feel at ease when around her and feel that they could trust her as a friend.

She had so many beautiful qualities that will be greatly missed by all who knew her. Of these there were four things I found overwhelming: her endless kindness, her deepest love for her family, her commitment to her belief in God and her commitment to her work as a clinician and a researcher. She gave to anyone who was in need and never expected anything in return. She took in friends and made them her family and cared for them like her own family. At work, she always made time to help a colleague in need of help in their work or provide training

for staff. She was a great leader, intelligent teacher and a very caring doctor.

To me personally, Regina was a very patient, respectful, kind, loving and supportive friend and a sister who held my hand when I was upset, cried with me when I cried, celebrated with me when I achieved something and always provided encouragement (Figure 3). I would leave my daughter with her and know that she would take good care of her and keep her safe and happy. I was so privileged to have known Regina and I will miss her dearly, but I am comforted to know that this is only a brief parting.



Figure 3. Regina Wangnapi and Maria Ome-Kaius.

OBITUARY

Dr Regina Wangnapi

LEANNE ROBINSON¹

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At the Papua New Guinea Institute of Medical Research (PNGIMR), as medical researchers from all different places in Papua New Guinea (PNG) and around the world, we come together to try and find answers to difficult and challenging questions. Sadly, we know that sometimes things do not make sense and there are no answers to some difficult questions.

The passing of Dr Regina Wangnapi in early 2016 was an enormous personal loss not only for her family, friends and colleagues who had the great privilege of working alongside her, but also for the PNGIMR and the medical community throughout the country. Regina was a natural clinician with the care of patients and study participants always her top priority. She also recognized that through her work in research she could potentially contribute to improvements in health outcomes for millions of her fellow Papua New Guineans. Regina was integral to the success of a large study investigating the burden of *Plasmodium vivax* malaria in pregnancy and to the first-ever trial of intermittent preventive malaria treatment during pregnancy conducted in PNG. Together with her dear friends and colleagues Dr Maria Ome-Kaius, Dr Sarah Hanieh and Dr Holger Unger, Regina led a large team of health workers to enrol more than 2000 women in a trial which clearly demonstrated that this intervention improved the health of mothers and their newborn babies.

At the same time, Regina successfully obtained her Master's degree, her research revealing a high burden of asymptomatic but potentially harmful sexually transmitted infections in women in Madang Province. The

data from this study have been instrumental in PNGIMR obtaining further research funding to investigate a possible way to reduce this high burden of STIs in PNG women through a trial of point-of-care testing and treating. Most recently, Regina made an invaluable contribution to the Partnership in Health program of demographic and health surveillance.

Regina's 18 published manuscripts in leading health and medical research journals are a testament to the impact her work has already had and a lasting legacy of her contribution to research. Regina not only had the ability to supervise, mentor and lead her fellow colleagues, but she was able to partner with international collaborators, communicate her research at international meetings, and both learn from her colleagues and at the same time teach them so much about health issues in her country. In doing so she earned an extremely high level of respect and admiration from a large number of international collaborators, who could see the immense contribution Regina made and the capabilities she possessed. They mourn with us today and send their deepest sympathies to all of her family.

We will always remember Regina as a beautifully generous, warm, caring, thoughtful, motivated and hard-working doctor, researcher, colleague and, most importantly, friend. She always put others first, never hesitating to help in whatever way she could, even when it was to her own expense. And she knew how much good she could do with only her smile. She quietly motivated and inspired us and, while we will deeply

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miss working with her, Regina's memory will continue to inspire us. We grieve because we have been denied the chance of seeing Regina ever reach her full potential and getting to enjoy the full life with her family that she so truly deserved, but we take comfort

from the fact that Regina spent her whole life helping others and that was something she loved. Our job is to protect Regina's legacy and continue the work that she started and to never forget how she went about it.

Peer reviewers

The *Papua New Guinea Medical Journal*, like all peer-reviewed journals, is dependent on the voluntary contributions of its reviewers for their critical assessments of every manuscript that is submitted to the Editors for publication. The reviewers also act as referees and offer their opinion as to whether a manuscript should be accepted or not. For this reason we on the editorial staff, when we compile indexes to the papers published in the Journal in the preceding 3 years, provide a list of the referees who have helped us over this period. We always include a proviso that some referees may not have come to our attention because of the practice of including focus issues where the responsibility for obtaining reviews and judging acceptability is given to a guest editor. The list of Referees for 2012-2014 was published in the *Papua New Guinea Medical Journal* in 2015 (*PNG Med J* 2015 Mar-Dec;58(1-4):145). During this period we were, unusually, provided by the Guest Editors of the Focus Issue on Malaria with the full list of their reviewers/referees. Unfortunately we omitted to include them in the published list. For this we sincerely apologize. We append the names here. Only the names of the editors were included among those acknowledged in the original list in 2015 and for completeness we have added their names also to the following list.

Editorial Staff

Sandra Alba	Jeffrey Hii	Ivo Mueller
Jo-an Atkinson	Harin Karunajeewa	Pie Mueller
Ingrid Felger	Christian Lengeler	Anna Rosanas
Andrew Greenhill	Jutta Marfurt	Tanya Russell
Manuel Hetzel	Sarah Moore	Nicolas Senn

List of Medical Research Projects in Papua New Guinea

Approved or Noted

By the Medical Research Advisory Committee in 2015

Sexual, reproductive and maternal health (SRMH) related vulnerabilities for young women in the Autonomous Region of Bougainville

Mr Morgan Garcia (Manager, Sexual, Reproductive and Maternal Health, Care International in PNG, PO Box 1157, Goroka, Eastern Highlands Province, Papua New Guinea)

Determinants influencing demand and delivery of health services for women in Papua New Guinea

Ms Ellen Kulumbu (PhD Candidate, State, Society and Governance in Melanesia, Coral Bell School of Asia Pacific Affairs, Australian National University College of Asia and the Pacific, ACT 2601, Australia)

Papua New Guinea (2015): HMM evaluation and ICCM needs assessment: mixed methods study on stated case management of common childhood illness and perceptions of available treatment options

Ms Hinabokiole Kama (Research Manager, Population Services International/PNG, PO Box 327, Port Moresby, National Capital District, Papua New Guinea)

Severe malaria surveillance

Dr Moses Laman (Papua New Guinea Institute of Medical Research, PO Box 378, Madang, Madang Province, Papua New Guinea)

Factors contributing to loss to follow-up of women commenced on Option B+ through preventative parent-to-child transmission of HIV (PPTCT) programs in Papua New Guinea

Angela Kelly (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province, Papua New Guinea)

Donor funding to the PNG health sector: how much, where it comes from, and where it is spent

Mr Ali Kevin (Curtin University, GPO Box U1987, Perth, Western Australia 6845, Australia)

Impact of Free Primary Health Care Policy (FPHCP) in PNG: an interrupted time series analysis (2004-2014) on utilization rates of outpatient, antenatal care and supervised delivery services

Ms Anna Maalsen (PO Box 127, Waigani, National Capital District, Papua New Guinea)

Formative evaluation of the rural health services delivery project

Ms Emma Field (Abt JTA, PO Box 753, Waigani, National Capital District, Papua New Guinea)

Investigation into gut microbiome of Papua New Guinea people and the potential impacts on health

Dr Paul Horwood, Dr Masahiro Umezaki and Dr Andrew Greenhill (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province, Papua New Guinea)

Midline evaluation of the CMCA Middle and South Fly Health Program

Ms Emma Field (Abt JTA, PO Box 753, Waigani, National Capital District, Papua New Guinea)

Reduced HIV infection and increased survival among HIV-exposed infants using two newly developed point-of-care tests in Myanmar, Papua New Guinea and China: accelerating ART initiation among mothers and infants (AAMI)

A/Prof. Stanley Luchters, Prof. Xiang-Sheng Chen, A/Prof. Andrew Vallely and Dr Hla Htay (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province, Papua New Guinea)

KP IBBS: respondent driven sampling

study of female sex workers and men who have sex with men and transgender in Papua New Guinea (Kauntim Mi Tu)

Dr Angela Kelly-Hanku (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province, Papua New Guinea)

Understanding the effects of 'Planim save strongpela'

Dr Anik Gevers, Dr Angela Kelly and Sister Lorraine Garasu (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province, Papua New Guinea)

Electrocardiographic safety evaluation of monthly dihydroartemisinin-piperaquine for use in mass treatment campaigns to block malaria transmission in Lihir Islands, PNG

Dr Leanne Robinson, Dr Harin Karunajeewa, Dr Oriol Mitjà, Prof. Ivo Mueller, Prof. Pedro L. Alonso and Dr Quique Bassat (Papua New Guinea Institute of Medical Research, PO Box 378, Madang, Madang Province, Papua New Guinea)

Assessing mobile phone usage and availability among rural health professionals of the Eastern Highlands on health service delivery

Ms Magdelene Libab (74 Hanson Lane, Canterbury Village, Christchurch 8041, New Zealand)

Longitudinal study of midwifery graduates: outcomes and experiences of midwifery graduates from 2012 and 2013 Papua New Guinea Bachelor of Midwifery Programs

Prof. Caroline Homer (Faculty of Health, University of Sydney, Building 10, 235-253 Jones St, Ultimo, NSW 2007, Australia)

In-hospital risk factors and prevalence of childhood malnutrition in Papua New Guinea: a prospective case-control study

Dr Moses Laman, Dr Jimmy Aipit, Dr Leanne Robinson, Sr Susan Aipit and Prof. Peter Siba (Papua New Guinea Institute of Medical Research, PO Box 378, Madang, Madang Province, Papua New Guinea)

PNG pneumonia and meningitis aetiology

study of the pneumococcal conjugate vaccine in hospitalized children with pneumonia and meningitis

Dr Christopher Blyth, A/Prof. Fiona Russell, Dr William Pomat and A/Prof. Deborah Lehmann (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province, Papua New Guinea)

Evaluating knowledge, attitude and practices related to mass drug administration and lymphatic filariasis in villages in East Sepik and West Sepik Provinces of Papua New Guinea

Dr Daniel Tisch (Papua New Guinea Institute of Medical Research, PO Box 400, Maprik, East Sepik Province, Papua New Guinea)

Mapping trachoma in Papua New Guinea as part of the Global Trachoma Mapping Project

Dr Jambi Garap (National Department of Health, PO Box 807, Waigani, National Capital District, Papua New Guinea)

Evaluation of the National Malaria Control Program, 2015-2017

Dr Justin Pulford, Dr Manuel W. Hetzel and Prof. Peter M. Siba (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province, Papua New Guinea)

Note:

These projects have been examined and cleared by the MRAC but they have not all started, nor is there any guarantee that they all will, since in many cases this still depends on funding. It should be noted that the project funds for the MRAC were deleted from the Health Budget from 1997 to 2015.

Information about these projects may be obtained from the investigators or from the Chairperson of the Medical Research Advisory Committee (Director of Research and Monitoring, Department of Health, PO Box 807, Waigani, National Capital District, Papua New Guinea).

MEDLARS BIBLIOGRAPHY

PUBLICATIONS OF RELEVANCE TO PAPUA NEW GUINEA AND MELANESIA

Bibliographic Citation List generated from MEDLARS

- 1 **Aia P, Kal M, Lavu E, John LN, Johnson K, Coulter C, Ershova J, Tosas O, Zignol M, Ahmadova S, Islam T.**
The burden of drug-resistant tuberculosis in Papua New Guinea: results of a large population-based survey.
PLoS One 2016 Mar 22;11(3):e0149806. doi: 10.1371/journal.pone.0149806. eCollection 2016.
BACKGROUND: Reliable estimates of the burden of multidrug-resistant tuberculosis (MDR-TB) are crucial for effective control and prevention of tuberculosis (TB). Papua New Guinea (PNG) is a high TB burden country with limited information on the magnitude of the MDR-TB problem. METHODS: A cross-sectional study was conducted in four PNG provinces: Madang, Morobe, National Capital District and Western Province. Patient sputum samples were tested for rifampicin resistance by the Xpert MTB/RIF assay and those showing the presence of resistance underwent phenotypic susceptibility testing to first- and second-line anti-TB drugs including streptomycin, isoniazid, rifampicin, ethambutol, pyrazinamide, ofloxacin, amikacin, kanamycin and capreomycin. RESULTS: Among 1,182 TB patients enrolled in the study, MDR-TB was detected in 20 new (2.7%; 95% confidence interval [CI] 1.1-4.3%) and 24 previously treated (19.1%; 95%CI: 8.5-29.8%) TB cases. No case of extensively drug-resistant TB (XDR-TB) was detected. Thirty percent (6/20) of new and 33.3% (8/24) of previously treated cases with MDR-TB were detected in a single cluster in Western Province. CONCLUSION: In PNG the proportion of MDR-TB in new cases is slightly lower than the regional average of 4.4% (95%CI: 2.6-6.3%). A large proportion of MDR-TB cases were identified from a single hospital in Western Province, suggesting that the prevalence of MDR-TB across the country is heterogeneous. Future surveys should further explore this finding. The survey also helped strengthening the use of smear microscopy and Xpert MTB/RIF testing as diagnostic tools for TB in the country.
- 2 **Alba S, Bakker MI, Hatta M, Scheelbeek PF, Dwiyantri R, Usman R, Sultan AR, Sabir M, Tandirogang N, Amir M, Yasir Y, Pastoor R, van Beers S, Smits HL.**
Risk factors of typhoid infection in the Indonesian Archipelago.
PLoS One 2016 Jun 9;11(6):e0155286. doi: 1371/journal.pone.0155286. eCollection 2016.
BACKGROUND: Knowledge of risk factors and their relative importance in different settings is essential to develop effective health education material for the prevention of typhoid. In this study, we examine the effect of household level and individual behavioural risk factors on the risk of typhoid in three Indonesian islands (Sulawesi, Kalimantan and Papua) in the Eastern Indonesian archipelago encompassing rural, peri-urban and urban areas. METHODS: We enrolled 933 patients above 10 years of age in a health facility-based case-control study between June 2010 and June 2011. Individuals suspected of typhoid were tested using the typhoid IgM lateral flow assay for the serodiagnosis of typhoid fever followed by blood culture testing. Cases and controls were defined post-recruitment: cases were individuals with a culture or serology positive result (n = 449); controls were individuals negative to both serology and culture, with or without a diagnosis other than typhoid (n = 484). Logistic regression was used to examine the effect of household level and individual level behavioural risk factors and we calculated the population attributable fraction (PAF) of removing each significant independent behavioural risk factor. RESULTS: Washing hands at critical moments of the day and washing hands with soap were strong independent protective factors for typhoid (OR = 0.38 95% CI 0.25 to 0.58 for each unit increase in hand washing frequency score with values between 0 = Never and 3 = Always; OR = 3.16 95% CI = 2.09 to 4.79 comparing washing hands with soap sometimes/never vs. often). These effects were independent of levels of access to water and sanitation. Up to two-thirds of cases could be prevented by compliance to these practices (hand washing PAF = 66.8 95% CI 61.4 to 71.5; use of soap PAF = 61.9 95%CI 56.7 to 66.5). Eating food out in food stalls or restaurant was an important risk factor (OR = 6.9 95%CI 4.4 to 10.8 for every unit increase in frequency score). CONCLUSIONS: Major gains could potentially be achieved in reducing the incidence of typhoid by ensuring adherence to adequate hand-washing practices alone. This confirms that there is a pivotal role for 'software' related interventions to encourage behaviour change and create demand for goods and services, alongside development of water and sanitation infrastructure.
- 3 **Atwell JE, Thumar B, Robinson LJ, Tobby R, Yambo P, Ome-Kaius M, Siba PM, Unger HW, Rogerson SJ, King CL, Karron RA.**
Impact of placental malaria and hypergammaglobulinemia on transplacental transfer of respiratory syncytial virus antibody in Papua New Guinea.
J Infect Dis 2016 Feb 1;213(3):423-431. doi: 10.1093/infdis/jiv401. Epub 2015 Aug 3.
BACKGROUND: Passively acquired respiratory syncytial virus (RSV) neutralizing antibody protects against RSV-associated lower respiratory infections, but placental malaria (PM) and maternal hypergammaglobulinemia might interfere with transplacental immunoglobulin transport. METHODS: We measured RSV plaque-reduction neutralization (PRN) antibody in 300 full-term maternal/cord serum pairs in 2 cohorts in malaria-endemic Papua New Guinea: Alexishafen (2005-2008) and the Fetal Immunity Study (FIS) (2011-2013). We defined impaired transport as a cord-to-maternal titer ratio <1.0 and a protective

RSV PRN titer (PRNT) as ≥ 200 . RESULTS: PM and hypergammaglobulinemia occurred in 60% and 54% of Alexishafen mothers versus 8% and 9% of FIS mothers, respectively. 34% of Alexishafen and 32% of FIS pairs demonstrated impaired transport. Multivariate modeling revealed significant associations between increasing maternal IgG (log_e) and impaired transport (adjusted OR, Alexishafen: 2.68 [1.17-6.14], FIS: 6.94 [1.94-24.8]) but no association with PM. 34% of Alexishafen and 31% of FIS cord PRNTs were < 200 . CONCLUSIONS: Impaired RSV antibody transport was observed in approximately one-third of maternal/cord pairs. Hypergammaglobulinemia, but not PM, was associated with impaired transport, particularly among women with low RSV PRNT. Detection of RSV PRNT < 200 in one-third of cord sera confirms the need to increase levels of RSV neutralizing antibody in pregnant women through maternal immunization.

- 4 **Badman SG, Vallely LM, Toliman P, Kariwiga G, Lote B, Pomat W, Holmer C, Guy R, Luchters S, Morgan C, Garland SM, Tabrizi S, Whitley D, Rogerson SJ, Mola G, Wand H, Donovan B, Causer L, Kaldor J, Vallely A.**

A novel point-of-care testing strategy for sexually transmitted infections among pregnant women in high-burden settings: results of a feasibility study in Papua New Guinea.

BMC Infect Dis 2016 Jun 6;16(1):250. doi: 10.1186/s12879-016-1573-4.

BACKGROUND: Sexually transmitted and genital infections in pregnancy are associated with an increased risk of adverse maternal and neonatal health outcomes. High prevalences of sexually transmitted infections have been identified among antenatal attenders in Papua New Guinea. Papua New Guinea has amongst the highest neonatal mortality rates worldwide, with preterm birth and low birth weight major contributors to neonatal mortality. The overall aim of our study was to determine if a novel point-of-care testing and treatment strategy for the sexually transmitted and genital infections *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG), *Trichomonas vaginalis* (TV) and bacterial vaginosis (BV) in pregnancy is feasible in the high-burden, low-income setting of Papua New Guinea. **METHODS:** Women attending their first antenatal clinic visit were invited to participate. CT/NG and TV were tested using the GeneXpert platform (Cepheid, USA), and BV tested using BVBlue (Gryphus Diagnostics, USA). Participants received same-day test results and antibiotic treatment as indicated. Routine antenatal care including HIV and syphilis screening were provided. **RESULTS:** Point-of-care testing was provided to 125/222 (56%) of women attending routine antenatal care during the three-month study period. Amongst the 125 women enrolled, the prevalence of CT was 20.0%; NG, 11.2%; TV, 37.6%; and BV, 17.6%. Over half (67/125, 53.6%) of women had one or more of these infections. Most women were asymptomatic (71.6%; 47/67). Women aged 24 years and under were more likely to have one or more STI than older women (odds ratio 2.38; 95% CI: 1.09-5.21). Most women with an STI received treatment on the same day (83.6%; 56/67). HIV prevalence was 1.6% and active syphilis 4.0%. **CONCLUSION:** Point-of-care STI testing and treatment using a combination of novel, newly available assays was feasible during

routine antenatal care in this setting. This strategy has not previously been evaluated in any setting and offers the potential to transform STI management in pregnancy and to prevent their associated adverse health outcomes.

- 5 **Carter K, Tovv V, Langati JT, Buttsworth M, Dingley L, Calo A, Harrison G, Rao C, Lopez AD, Taylor R.**

Causes of death in Vanuatu.

Popul Health Metr 2016 Mar 15;14:7. doi: 10.1186/s12963-016-0074-4. eCollection 2016.

BACKGROUND: The population of the Pacific Melanesian country of Vanuatu was 234,000 at the 2009 census. Apart from subsistence activities, economic activity includes tourism and agriculture. Current completeness of vital registration is considered too low to be usable for national statistics; mortality and life expectancy (LE) are derived from indirect demographic estimates from censuses/surveys. Some cause of death (CoD) data are available to provide information on major causes of premature death. **METHODS:** Deaths 2001-2007 were coded for cause (ICDv10) for ages 0-59 years from: hospital separations (HS) (n=636), hospital medical certificates (MC) of death (n=1,169), and monthly reports from community health facilities (CHF) (n=1,212). Ill-defined causes were 3% for hospital deaths and 20% from CHF. Proportional mortality was calculated by cause (excluding ill-defined) and age group (0-4, 5-14 years), and also by sex for 15-59 years. From total deaths by broad age group and sex from 1999 and 2009 census analyses, community deaths were estimated by deduction of hospital deaths MC. National proportional mortality by cause was estimated by a weighted average of MC and CHF deaths. **RESULTS:** National estimates indicate main causes of deaths < 5 years were: perinatal disorders (45%) and malaria, diarrhea, and pneumonia (27%). For 15-59 years, main causes of male deaths were: circulatory disease 27%, neoplasms 13%, injury 13%, liver disease 10%, infection 10%, diabetes 7%, and chronic respiratory disease 7%; and for females: neoplasms 29%, circulatory disease 15%, diabetes 10%, infection 9%, and maternal deaths 8%. Infection included tuberculosis, malaria, and viral hepatitis. Liver disease (including hepatitis and cancer) accounted for 18% of deaths in adult males and 9% in females. Non-communicable disease (NCD), including circulatory disease, diabetes, neoplasm, and chronic respiratory disease, accounted for 52% of premature deaths in adult males and 60% in females. Injuries accounted for 13% in adult males and 6% in females. Maternal deaths translate into an annual maternal mortality ratio of 130/100,000 for the period. **CONCLUSION:** Vanuatu manifests a double burden of disease with significant proportional mortality from perinatal disorders and infection/pneumonia < 5 years and maternal mortality, coupled with significant proportional mortality in adults (15-59 years) from cardiovascular disease (CVD), neoplasms, and diabetes.

- 6 **Cella E, Gabrielli I, Zehender G, Giovanetti M, Lo Presti A, Lai A, Dicuonzo G, Angeletti S, Salemi M, Ciccozzi M.**

Phylogeny of Murray Valley encephalitis virus in Australia and Papua New Guinea.

Asian Pac J Trop Med 2016 Apr;9(4):385-389. doi: 10.1016/j.apjtm.2016.03.006. Epub 2016 Mar 9.

OBJECTIVE: To study the genetic diversity of Murray Valley encephalitis virus (MVEV) in Australia and Papua New Guinea. **METHODS:** MVEV envelope gene sequences were aligned using Clustal X and manual editing was performed with Bioedit. ModelTest v. 3.7 was used to select the simplest evolutionary model that adequately fitted the sequence data. Maximum likelihood analysis was performed using PhyML. The phylogenetic signal of the dataset was investigated by the likelihood mapping analysis. The Bayesian phylogenetic tree was built using BEAST. **RESULTS:** The phylogenetic trees showed two main clades. The clade I included eight strains isolated from West Australia. The clade II was characterized by at least four epidemic entries, three of which localized in Northern West Australia and one in Papua New Guinea. The estimated mean evolutionary rate value of the MVEV envelope gene was 0.407×10^{-3} substitution/site/year (95% HPD: 0.623×10^{-4} - 0.780×10^{-3}). Population dynamics defines a relatively constant population until the year 2000, when a reduction occurred, probably due to a bottleneck. **CONCLUSIONS:** This study has been useful in supporting the probable connection between climate changes and viral evolution, also by the vector point of view; multidisciplinary monitoring studies are important to prevent new viral epidemics inside and outside new endemic areas.

- 7 **Chaidir L, Sengstake S, de Beer J, Oktavian A, Krismawati H, Muhapril E, Kusumadewi I, Annisa J, Anthony R, van Soelingen D, Achmad TH, Marzuki S, Alisjahbana B, van Crevel R.**

Predominance of modern *Mycobacterium tuberculosis* strains and active transmission of Beijing sublineage in Jayapura, Indonesian Papua. *Infect Genet Evol* 2016 Apr;39:187-193. doi: 10.1016/j.meegid.2016.01.019. Epub 2016 Jan 26.

Mycobacterium tuberculosis genotype distribution is different between West and Central Indonesia, but there are no data on the most Eastern part, Papua. We aimed to identify the predominant genotypes of *M. tuberculosis* responsible for tuberculosis in coastal Papua, their transmission, and the association with patient characteristics. A total of 199 *M. tuberculosis* isolates were collected. Spoligotyping was applied to describe the population structure of *M. tuberculosis*, lineage identification was performed using a combination of lineage-specific markers, and genotypic clusters were identified using a combination of 24-locus-MIRU-VNTR and spoligotyping. A high degree of genetic diversity was observed among isolates based on their spoligopatterns. Strains from modern lineage 4 made up almost half of strains (46.9%), being more abundant than the ancient lineage 1 (33.7%) and modern lineage 2 (19.4%). Thirty-five percent of strains belonged to genotypic clusters, especially strains in the Beijing genotype. Previous TB treatment and mutations associated with drug resistance were more common in patients infected with strains of the Beijing genotype. Papua shows a different distribution of *M. tuberculosis* genotypes compared to other parts of Indonesia. Clustering and drug resistance of modern strains recently introduced to Papua may contribute to the high tuberculosis burden in this region.

- 8 **Challacombe SJ.**
Global oral inequalities in HIV infection.

Oral Dis 2016 Apr;22 Suppl 1:35-41. doi: 10.1111/odi.12408.

Analysis of the prevalence and incidence of HIV infection globally reveals striking variances with regard to continent, country, region and gender. Of the global total of 33 million people infected with HIV, approximately 65% are in sub-Saharan African countries and 15% in South and South-East Asia with the remaining 20% spread over the rest of the world. As a percentage of the population, the Caribbean at 1.1% is second only to sub-Saharan Africa (5.5%). The majority of the world's HIV is in women. Deaths from HIV are twenty-fold greater in Africa than in Europe or the USA. Individual countries in sub-Saharan Africa show huge variances in the HIV+ prevalence with most West African countries having a rate of less than 2% whilst southern African countries including Swaziland and Botswana have rates of around 25%. Environment, education and social habits all contribute to the HIV infection rates. Similar variations between countries are seen in SE Asia with Cambodia and Papua New Guinea having rates three times greater than Pakistan. One of the most striking examples of inequality is in life years added to HIV populations as a result of antiretroviral therapy. UN AIDS figures over 1996-2008 suggest an average of 2.88 added years in the USA and Europe, but only 0.1 in sub-Saharan Africa, a thirty-fold difference largely due to accessibility to ART. ART leads to a reduction in oral lesions but it is estimated that some 10 million HIV+ subjects do not have access to oral care. Thus, inequalities exist both for HIV infection and for the associated oral lesions, mainly related to ART access. HIV infection and oral mucosal lesions both appear to be related to general social determinants of health. Oral HCW must be part of mainstream healthcare teams to address these inequalities.

- 9 **Charlton KE, Russell J, Gorman E, Hanich Q, Delisle A, Campbell B, Bell J.**

Fish, food security and health in Pacific island countries and territories: a systematic literature review. *BMC Public Health* 2016 Mar 24;16(1):285. doi: 10.1186/s12889-016-2953-9.

BACKGROUND: Pacific island countries and territories (PICTs) face a double burden of disease, with a high prevalence of household food insecurity and childhood micronutrient deficiencies, accompanied by a burgeoning increase in adult obesity, diabetes and heart disease. **METHODS:** A systematic literature review was undertaken to assess whether increased availability of, and access to, fish improves a) household food security and b) individual nutritional status. **RESULTS:** A total of 29 studies were reviewed. Fourteen studies identified fish as the primary food source for Pacific islanders and five studies reported fish/seafood as the primary source of dietary protein. Fish consumption varied by cultural sub-region and Pacific island countries and territories. Fish consumption and nutritional status was addressed in nine studies, reporting moderate iodine deficiency in Vanuatu where only 30% of participants consumed mostly fresh fish. Similarly, the degree to which Pacific islanders depended on fishing for household income and livelihood varied between and within PICTs. For more economically developed countries, household income was derived increasingly from salaried work and dependency on fishing activities has been

declining. **CONCLUSIONS:** Fishing remains a major contributor to food security in PICTs, through subsistence production and income generation. However, there is a paucity of research aimed at assessing how maintaining and/or improving fish consumption benefits the diets and health of Pacific islanders as they contend with the ongoing nutrition transition that is characterised by an increasing demand for packaged imported foods, such as canned meats, instant noodles, cereals, rice, and sugar-sweetened beverages, with subsequent decreased consumption of locally produced plants and animals.

- 10 **Cooley GM, Mitjà O, Goodhew B, Pillay A, Lammie PJ, Castro A, Moses P, Chen C, Ye T, Ballard R, Martin DL.**

Evaluation of multiplex-based antibody testing for use in large-scale surveillance for yaws: a comparative study. *J Clin Microbiol* 2016 May;54(5):1321-1325. doi: 10.1128/JCM.02572-15. Epub 2016 Mar.

WHO has targeted yaws for global eradication by 2020. The program goals are to interrupt the transmission in countries where yaws is endemic and to certify countries as yaws free where yaws was endemic in the past. No new rapid plasmin reagin (RPR) seroreactivity in young children is required for certification of elimination at a country level. We sought to evaluate whether antibody responses to specific treponemal antigens measured in a high-throughput multiplex bead array (MBA) assay differentiate past versus current infection and whether a nontreponemal lipoidal antigen test can be incorporated into the MBA. Serum and dried blood spot specimens collected for yaws surveillance projects in Ghana, Vanuatu, and Papua New Guinea (PNG) were run on MBA to measure antibodies against recombinant p17 (rp17) and treponemal membrane protein A (TmpA) treponemal antigens. Results were compared to standard treponemal laboratory (TPPA or TPHA [TPP(H)A]) and quantitative RPR test data. Of 589 specimens, 241 were TPP(H)A(+)/RPR(+), 88 were TPP(H)A(+)/RPR(-), 6 were TPP(H)A(-)/RPR(+), and 254 were negative for both tests. Compared to TPP(H)A, reactive concordance of rp17 was 93.7%, while reactive concordance of TmpA was only 81.9%. TmpA-specific reactivity showed good correlation with RPR titers ($R^2 = 0.41$; $p < 0.0001$). IgG responses to the lipoidal antigen used in RPR testing (cardiolipin) were not detected in the MBA. Our results suggest that TmpA can be used as a treponemal antigen marker for recent or active infection and potentially replace RPR in a high-throughput multiplex tool for large-scale yaws surveillance.

- 11 **Cooper MG, Wake PB, Morriss WW, Cargill PD, McDougall RJ.**

Global safe anaesthesia and surgery initiatives: implications for anaesthesia in the Pacific region. *Anaesth Intensive Care* 2016 May;44(3):420-424.

In 2015 three major events occurred for global anaesthesia and surgery. In January, the World Bank published Disease Control Priorities 3rd edition (DCP 3rd edition). This volume, Essential Surgery, highlighted the cost-effective role of anaesthesia and surgery in global health. In April, the Lancet Commission on Global Surgery released its report "Global Surgery 2030: Evidence

and solutions for achieving health, welfare, and economic development". The report focuses on five key areas to promote change including: access to timely surgery, surgical workforce and procedural capability, surgical volume, data collection such as perioperative mortality rate, and financial protection. In May, the 68th World Health Assembly (WHA) voted in favour of Resolution A68/31: Strengthening emergency and essential surgical and anaesthesia care as a component of universal health coverage. The resolution was passed unanimously and it is the first time that surgery and anaesthesia have received such prominence at WHA level. These three events all have profound implications for the provision and access of safe anaesthesia and surgery in the Pacific region in the next 15 years. This article considers some of the regional factors that affect these five key areas, especially with regard to anaesthetic specialist workforce density in different parts of the region. There are many challenges to improve anaesthesia access, safety, and workforce density in the Pacific region. Future efforts, initiatives and support will help address these problems.

- 12 **Crainey JL, Ribeiro da Silva TR, Luz SL.**

Historic accounts of *Mansonella* parasitaemias in the South Pacific and their relevance to lymphatic filariasis elimination efforts today.

Asian Pac J Trop Med 2016 Mar;9(3):205-210. doi: 10.1016/j.apjtm.2016.01.040. Epub 2016 Jan 11.

There are two species of filarial parasites with sheathless microfilariae known to commonly cause parasitaemias in humans: *Mansonella perstans* and *Mansonella ozzardi*. In most contemporary accounts of the distribution of these parasites, neither is usually considered to occur anywhere in the Eastern Hemisphere. However, Sir Patrick Manson, who first described both parasite species, recorded the existence of sheathless sharp-tailed *Mansonella ozzardi*-like parasites occurring in the blood of natives from New Guinea in each and every version of his manual for tropical disease that he wrote before his death in 1922. Manson's reports were based on his own identifications and were made from at least two independent blood sample collections that were taken from the island. Pacific region *Mansonella perstans* parasitaemias were also later (in 1923) reported to occur in New Guinea and once before this (in 1905) in Fiji. Although *Mansonella* parasitaemias are generally regarded as benign, they are thought to be of public health importance because they can affect the epidemiological monitoring of other filarial diseases. In this article, we reviewed the historic literature concerning Pacific-origin *Mansonella* parasitaemias in an attempt to explain how, despite repeated reports of Pacific-region *Mansonella* parasitaemias, by as early as the 1970s, the WHO had arrived at the present-day view that *Wuchereria bancrofti* is the only cause of filarial parasitaemias in Papua New Guinea. We have also evaluated the evidence supporting the contemporary existence of Pacific-area parasitaemia-causing *Mansonella* parasites and assessed the relevance such parasites could have for present-day lymphatic filariasis elimination efforts in the region.

- 13 **Dare AJ, Lee KC, Bleicher J, Elobu AE, Kamara TB, Liko O, Luboga S, Danlop A, Kune G, Hagander L, Leather AJ, Yamey G.**
- Prioritizing surgical care on national health agendas:

a qualitative case study of Papua New Guinea, Uganda, and Sierra Leone.

PLoS Med 2016 May 17;13(5):e1002023. doi: 10.1371/journal.pmed.1002023. eCollection 2016.

BACKGROUND: Little is known about the social and political factors that influence priority setting for different health services in low- and middle-income countries (LMICs), yet these factors are integral to understanding how national health agendas are established. We investigated factors that facilitate or prevent surgical care from being prioritized in LMICs. **METHODS AND FINDINGS:** We undertook country case studies in Papua New Guinea, Uganda, and Sierra Leone, using a qualitative process-tracing method. We conducted 74 semi-structured interviews with stakeholders involved in health agenda setting and surgical care in these countries. Interviews were triangulated with published academic literature, country reports, national health plans, and policies. Data were analyzed using a conceptual framework based on four components (actor power, ideas, political contexts, issue characteristics) to assess national factors influencing priority for surgery. Political priority for surgical care in the three countries varies. Priority was highest in Papua New Guinea, where surgical care is firmly embedded within national health plans and receives significant domestic and international resources, and much lower in Uganda and Sierra Leone. Factors influencing whether surgical care was prioritized were the degree of sustained and effective domestic advocacy by the local surgical community, the national political and economic environment in which health policy setting occurs, and the influence of international actors, particularly donors, on national agenda setting. The results from Papua New Guinea show that a strong surgical community can generate priority from the ground up, even where other factors are unfavorable. **CONCLUSIONS:** National health agenda setting is a complex social and political process. To embed surgical care within national health policy, sustained advocacy efforts, effective framing of the problem and solutions, and country-specific data are required. Political, technical, and financial support from regional and international partners is also important.

14 **Datta SS, Ropa B, Sui GP, Khattar R, Krishnan RS, Okayasu H.**

Using short-message-service notification as a method to improve acute flaccid paralysis surveillance in Papua New Guinea.

BMC Public Health 2016 May 17;16(1):409. doi: 10.1186/s12889-016-3062-5.

BACKGROUND: High quality acute flaccid paralysis (AFP) surveillance is required to maintain polio-free status of a country. Papua New Guinea (PNG) is considered as one of the highest risk countries for polio re-importation and circulation in the Western Pacific Region (WPRO) of the World Health Organization due to poor healthcare infrastructure and inadequate performance in AFP surveillance. The Government of PNG, in collaboration with WHO, piloted the introduction of short-message-service (SMS) to sensitize pediatricians and provincial disease control officers on AFP and to receive notification of possible AFP cases to improve surveillance quality in PNG. **METHODS:** Ninety-six health care professionals were registered to receive SMS reminders to report any case of acute flaccid paralysis. Fourteen SMS messages were sent to

each participant from September 2012 to November 2013. The number of reported AFP cases were compared before and after the introduction of SMS. **RESULTS:** 253 unique responses were received with an overall response rate of 21%. More than 80% of responses were reported within 3 days of sending the SMS. The number of reported AFP cases increased from 10 cases per year in 2009-2012 to 25 cases per year during the study period and correlated with provincial participation of the health care professionals. **CONCLUSIONS:** Combined with improved sensitization of health care professionals on AFP reporting criteria and sample collection, SMS messaging provides an effective means to increase timely reporting and improve the availability of epidemiologic information on polio surveillance in PNG.

15 **Dawson A, Kililo M, Geita L, Mola G, Brodie PM, Rumsey M, Copeland F, Neill A, Homer CS.**

Midwifery capacity building in Papua New Guinea: key achievements and ways forward.

Women Birth 2016 Apr;29(2):180-188. doi: 10.1016/j.wombi.2015.10.007. Epub 2015 Nov 10.

BACKGROUND: Papua New Guinea has some of the poorest health outcomes in the Asia-Pacific region. Maternal mortality is unacceptably high and there is a severe midwifery shortage requiring a quadrupling of the workforce. **AIM:** This paper outlines the findings of an evaluation of the Maternal Child Health Initiative (MCHI) (2012-2013) to determine key factors contributing to maternal health workforce strengthening. **METHOD:** A descriptive mixed methods study was undertaken. Data were gathered through interviews, focus group discussions and surveys with clinicians, midwifery students and staff from nursing and midwifery schools and National Department of Health staff. Documentation from stakeholder meetings and regular site reports were reviewed. Each data set was analysed separately and meta-inferences were drawn across all data. **FINDINGS:** Learning opportunities were found to have increased for midwifery educators and improvements were described in midwifery educators teaching capacity and student clinical education experience. There was an increase in the number of midwifery graduates and improvements were noted in the working environment and skills of clinical staff. Education challenges were described including the lack of clinical preceptoring and limited continuing education for clinical educators. Participants recommended increasing clinical education hours and extending the length of the midwifery program. Ongoing efforts to accredit the midwifery curricula and regulate midwifery graduates were noted. **CONCLUSION:** The MCHI has contributed to strengthening the midwifery workforce nationally. However, scaling-up and sustaining these achievements requires leadership and funding commitments from the midwifery schools and government alongside the accreditation of midwifery curricula and regulation of new graduates.

16 **Duff E.**

Maternal mortality remains high in Papua New Guinea.

Midwifery 2016 Feb;33:7-8.

17 **Duffy MF, Noviyanti R, Tsuboi T, Feng ZP, Trianty L, Sebayang BF, Takashima E, Sumardy F, Lampah DA, Turner L, Lavstsen T, Fowkes FJ,**

Siba P, Rogerson SJ, Theander TG, Marfurt J, Price RN, Anstey NM, Brown GV, Papenfuss AT. Differences in PfEMP1s recognized by antibodies from patients with uncomplicated or severe malaria. *Malar J* 2016 May 5;15(1):258. doi: 10.1186/s12936-016-1296-4.

BACKGROUND: *Plasmodium falciparum* erythrocyte membrane protein 1 (PfEMP1) variants are encoded by var genes and mediate pathogenic cytoadhesion and antigenic variation in malaria. PfEMP1s can be broadly divided into three principal groups (A, B and C) and they contain conserved arrangements of functional domains called domain cassettes. Despite their tremendous diversity there is compelling evidence that a restricted subset of PfEMP1s is expressed in severe disease. In this study antibodies from patients with severe and uncomplicated malaria were compared for differences in reactivity with a range of PfEMP1s to determine whether antibodies to particular PfEMP1 domains were associated with severe or uncomplicated malaria. **METHODS:** Parts of expressed var genes in a severe malaria patient were identified by RNAseq and several of these partial PfEMP1 domains were expressed together with others from laboratory isolates. Antibodies from Papuan patients to these parts of multiple PfEMP1 proteins were measured. **RESULTS:** Patients with uncomplicated malaria were more likely to have antibodies that recognized PfEMP1 of group C type and recognized a broader repertoire of group A and B PfEMP1s than patients with severe malaria. **CONCLUSION:** These data suggest that exposure to a broad range of group A and B PfEMP1s is associated with protection from severe disease in Papua, Indonesia.

- 18 **Duke T.** Decoding vital signs during triage: pulse pressure in children – author's reply. *Lancet* 2016 May 21;387(10033):2092. doi: 10.1016/S0140-6736(16)30542-6.
- 19 **Duke T, Graham H, Peel D, Izadnegahdar R, Duke C.** Solar powered health care. *Int J Tuberc Lung Dis* 2016 May;20(5):572-573. doi: 10.5588/ijtld.16.0210.
- 20 **Duke T.** New WHO guidelines on emergency triage assessment and treatment. *Lancet* 2016 Feb 20;387(10020):721-724. doi: 10.1016/S0140-6736(16)00148-3. Epub 2016 Feb 18.
- 21 **Duke T, Yano E, Hutchinson A, Hwaihwanje I, Aipit J, Tovilu M, Uluk T, Rongap T, Vetuna B, Lagani W, Amini J; Paediatric Society of Papua New Guinea.** Large-scale data reporting of paediatric morbidity and mortality in developing countries: it can be done. *Arch Dis Child* 2016 Apr;101(4):392-397. doi: 10.1136/archdischild-2015-309353. Epub 2015 Oct 21.

Although the WHO recommends all countries use International Classification of Diseases (ICD)-10 coding for reporting health data, accurate health facility data are rarely available in developing or low and middle income countries. Compliance with ICD-10 is extremely resource intensive, and the lack of real data seriously undermines evidence-based

approaches to improving quality of care and to clinical and public health program management. We developed a simple tool for the collection of accurate admission and outcome data and implemented it in 16 provincial hospitals in Papua New Guinea over 6 years. The program was low cost and easy to use by ward clerks and nurses. Over 6 years, it gathered data on the causes of 96,998 admissions of children and 7128 deaths. National reports on child morbidity and mortality were produced each year summarising the incidence and mortality rates for 21 common conditions of children and newborns, and the lessons learned for policy and practice. These data informed the National Policy and Plan for Child Health and triggered the implementation of a process of clinical quality improvement and other interventions to reduce mortality in the neediest areas, focusing on diseases with the highest burdens. It is possible to collect large-scale data on paediatric morbidity and mortality, to be used locally by health workers who gather it, and nationally for improving policy and practice, even in very resource-limited settings where ICD-10 coding systems such as those that exist in some high-income countries are not feasible or affordable.

- 22 **França CT, Hostetler JB, Sharma S, White MT, Lin E, Kiniboro B, Waltmann A, Darcy AW, Li Wai Suen CS, Siba P, King CL, Rayner JC, Fairhurst RM, Mueller I.**

An antibody screen of a *Plasmodium vivax* antigen library identifies novel merozoite proteins associated with clinical protection.

PLoS Negl Trop Dis 2016 May 16;10(5):e0004639. doi: 10.1371/journal.pntd.0004639. eCollection 2016.

BACKGROUND: Elimination of *Plasmodium vivax* malaria would be greatly facilitated by the development of an effective vaccine. A comprehensive and systematic characterization of antibodies to *P. vivax* antigens in exposed populations is useful in guiding rational vaccine design. **METHODOLOGY/PRINCIPAL FINDINGS:** In this study, we investigated antibodies to a large library of *P. vivax* entire ectodomain merozoite proteins in 2 Asia-Pacific populations, analysing the relationship of antibody levels with markers of current and cumulative malaria exposure, and socioeconomic and clinical indicators. 29 antigenic targets of natural immunity were identified. Of these, 12 highly immunogenic proteins were strongly associated with age and thus cumulative lifetime exposure in Solomon Islanders ($p < 0.001-0.027$). A subset of 6 proteins, selected on the basis of immunogenicity and expression levels, were used to examine antibody levels in plasma samples from a population of young Papua New Guinean children with well-characterized individual differences in exposure. This analysis identified a strong association between reduced risk of clinical disease and antibody levels to P12, P41, and a novel hypothetical protein that has not previously been studied, PVX_081550 (IRR 0.46-0.74; $p < 0.001-0.041$). **CONCLUSION/SIGNIFICANCE:** These data emphasize the benefits of an unbiased screening approach in identifying novel vaccine candidate antigens. Functional studies are now required to establish whether PVX_081550 is a key component of the naturally acquired protective immune response, a biomarker of immune status, or both.

- 23 **Gangaiah D, Marinov GK, Roberts SA, Robson J, Spinola SM.**

Draft whole-genome sequence of *Haemophilus ducreyi* strain AUSPNG1, isolated from a cutaneous ulcer of a child from Papua New Guinea.

Genome Announc 2016 Feb 4;4(1). pii: e01661-15. doi: 10.1128/genomeA.01661-15.

Haemophilus ducreyi has recently emerged as a leading cause of cutaneous ulcers in the yaws-endemic areas of Papua New Guinea and other South Pacific islands. Here, we report the draft genome sequence of the *H. ducreyi* strain AUSPNG1, isolated from a cutaneous ulcer of a child from Papua New Guinea.

- 24 **Hanandita W, Tampubolon G.**

Geography and social distribution of malaria in Indonesian Papua: a cross-sectional study.

Int J Health Geogr 2016 Apr 12;15:13. doi: 1186/s12942-016-0043-y.

BACKGROUND: Despite being one of the world's most affected regions, only little is known about the social and spatial distributions of malaria in Indonesian Papua. Existing studies tend to be descriptive in nature; their inferences are prone to confounding and selection biases. At the same time, there remains limited malaria-cartographic activity in the region. Analysing a subset (N = 22,643) of the National Basic Health Research 2007 dataset (N = 987,205), this paper aims to quantify the district-specific risk of malaria in Papua and to understand how socio-demographic/economic factors measured at individual and district levels are associated with individual's probability of contracting the disease. **METHODS:** We adopt a Bayesian hierarchical logistic regression model that accommodates not only the nesting of individuals within the island's 27 administrative units but also the spatial autocorrelation among these locations. Both individual and contextual characteristics are included as predictors in the model; a normal conditional autoregressive prior and an exchangeable one are assigned to the random effects. Robustness is then assessed through sensitivity analyses using alternative hyperpriors. **RESULTS:** We find that rural Papuans as well as those who live in poor, densely forested, lowland districts are at a higher risk of infection than their counterparts. We also find age and gender differentials in malaria prevalence, if only to a small degree. Nine districts are estimated to have higher-than-expected malaria risks; the extent of spatial variation on the island remains notable even after accounting for socio-demographic/economic risk factors. **CONCLUSIONS:** Although we show that malaria is geography-dependent in Indonesian Papua, it is also a disease of poverty. This means that malaria eradication requires not only biological (proximal) interventions but also social (distal) ones.

- 25 **Herrera M, de Cássia de O Collaço R, Villalta M, Segura Á, Vargas M, Wright CE, Paiva OK, Matainaho T, Jensen SD, León G, Williams DJ, Rodrigues-Simioni L, Gutiérrez JM.**

Neutralization of the neuromuscular inhibition of venom and taipoxin from the taipan (*Oxyuranus scutellatus*) by F(ab')₂ and whole IgG antivenoms.

Toxicol Lett 2016 Jan 22;241:175-183. doi: 10.1016/j.toxlet.2015.11.020. Epub 2015 Nov 24.

The neuromuscular junction activity of *Oxyuranus scutellatus* venom and its presynaptic neurotoxin, taipoxin, and their neutralization by

two antivenoms were examined in mouse phrenic nerve-diaphragm preparations. The action of taipoxin was also studied at 21°C. The efficacy of the antivenoms was also assessed in an in vivo mouse model. Both antivenoms were effective in neutralizing the neuromuscular blocking activity in preincubation-type experiments. In experiments involving independent addition of venom and antivenoms, neutralization depended on the time interval between venom addition and antivenom application. When taipoxin was incubated for 5, 10 or 20 min at 21°C, and antivenom added and temperature increased to 37°C, neutralization was achieved only when the toxin was incubated for 5 or 10 min. The neutralization by the two antivenoms in an in vivo model showed that both whole IgG and F(ab')₂ antivenoms were effective in neutralizing lethality. Our findings highlight the very rapid action of taipan venom at the nerve terminal, and the poor capacity of antivenoms to revert neurotoxicity as the time interval between venom or taipoxin application and antivenom addition increased. Additionally the disparity between molecular masses of the active substances of the two antivenoms did not result in differences in neutralization.

- 26 **Hetzel MW, Reimer LJ, Gideon G, Koimbu G, Barnadas C, Makita L, Siba PM, Mueller I.**

Changes in malaria burden and transmission in sentinel sites after the roll-out of long-lasting insecticidal nets in Papua New Guinea.

Parasit Vectors 2016 Jun 14;9(1):340. doi: 10.1186/s13071-016-1635-x.

BACKGROUND: Papua New Guinea exhibits a complex malaria epidemiology due to diversity in malaria parasites, mosquito vectors, human hosts, and their natural environment. Heterogeneities in transmission and burden of malaria at various scales are likely to affect the success of malaria control interventions, and vice versa. This manuscript assesses changes in malaria prevalence, incidence and transmission in sentinel sites following the first national distribution of long-lasting insecticidal nets (LLINs). **METHODS:** Before and after the distribution of LLINs, data collection in six purposively selected sentinel sites included clinical surveillance in the local health facility, household surveys and entomological surveys. Not all activities were carried out in all sites. Mosquitoes were collected by human landing catches. Diagnosis of malaria infection in humans was done by rapid diagnostic test, light microscopy and PCR for species confirmation. **RESULTS:** Following the roll-out of LLINs, the average monthly malaria incidence rate dropped from 13/1,000 population to 2/1,000 (incidence rate ratio=0.12; 95% CI: 0.09-0.17; p<0.001). The average population prevalence of malaria decreased from 15.7% pre-LLIN to 4.8% post-LLIN (adjusted odds ratio=0.26; 95% CI: 0.20-0.33; p<0.001). In general, reductions in incidence and prevalence were more pronounced in infections with *P. falciparum* than with *P. vivax*. Additional morbidity indicators (anaemia, splenomegaly, self-reported fever) showed a decreasing trend in most sites. Mean *Anopheles* man biting rates decreased from 83 bites/person/night pre-LLIN to 31 post-LLIN (p=0.008). *Anopheles* species composition differed between sites but everywhere diversity was lower post-LLIN. In two sites, post-LLIN *P. vivax* infections in anophelines had decreased but *P. falciparum* infections had increased despite the

opposite observation in humans. **CONCLUSIONS:** LLIN distribution had distinct effects on *P. falciparum* and *P. vivax*. Higher resilience of *P. vivax* may be attributed to relapses from hypnozoites and other biological characteristics favouring the transmission of *P. vivax*. The effect on vector species composition varied by location, which is likely to impact on the effectiveness of LLINs. In-depth and longer-term epidemiological and entomological investigations are required to understand when and where residual transmission occurs and whether observed changes are sustained.

- 27 **Jones FK, Ko AI, Becha C, Joshua C, Musto J, Thomas S, Ronse A, Kirkwood CD, Sio A, Aumua A, Nilles EJ.**

Increased rotavirus prevalence in diarrheal outbreak precipitated by localized flooding, Solomon Islands, 2014.

Emerg Infect Dis 2016 May;22(5):875-879. doi: 10.3201/eid2205.151743.

Flooding on 1 of the Solomon Islands precipitated a nationwide epidemic of diarrhea that spread to regions unaffected by flooding and caused >6,000 cases and 27 deaths. Rotavirus was identified in 38% of case-patients tested in the city with the most flooding. Outbreak potential related to weather reinforces the need for global rotavirus vaccination.

- 28 **Joshua IB, Passmore PR, Sunderland BV.**

An evaluation of the essential medicines list, standard treatment guidelines and prescribing restrictions, as an integrated strategy to enhance quality, efficacy and safety of and improve access to essential medicines in Papua New Guinea.

Health Policy Plan 2016 May;31(4):538-546. doi: 10.1093/heapol/czv083. Epub 2015 Sep 15.

The World Health Organization (WHO) has advocated the development and use of country specific Standard Treatment Guidelines (STGs) and Essential Medicines Lists (EML) as strategies to promote the rational use of medicines. When implemented effectively STGs offer many health advantages. Papua New Guinea (PNG) has official STGs and a Medical and Dental Catalogue (MDC) which serves as a national EML for use at different levels of health facilities. This study evaluated consistency between the PNG Adult STGs (2003 and 2012) and those for children (2005 and 2011) with respect to the MDCs (2002, 2012) for six chronic and/or acute diseases: asthma, arthritis, diabetes, hypertension, pneumonia and psychosis. Additionally, the potential impact of prescriber-level restrictions on rational medicines use for patients living in rural areas, where no medical officer is present, was evaluated. Almost all drugs included in the STGs for each disease state evaluated were listed in the MDCs. However, significant discrepancies occurred between the recommended treatments in the STGs with the range of related medicines listed in the MDCs. Many medicines recommended in the STGs for chronic diseases had prescriber-level restrictions hindering access for most of the PNG population who live in rural and remote areas. In addition many more medicines were listed in the MDCs which are commonly used to treat arthritis, high blood pressure and psychosis than were recommended in the STGs, contributing to inappropriate prescribing. We recommend that the public health and rational use of medicines deficiencies associated with these findings are

addressed, requiring: reviewing prescriber-level restrictions; updating the STGs; aligning the MDC to reflect recommendations in the STGs; establishing the process where the MDC would automatically be updated based on any changes made to the STGs; and developing STGs for higher levels of care.

- 29 **Kaptigau WM, Rosenfeld JV, Kevau I, Watters DA.** The establishment and development of neurosurgery services in Papua New Guinea.

World J Surg 2016 Feb;40(2):251-257.

BACKGROUND: Papua New Guinea (PNG) is a developing Pacific nation of 7.3 million people. Although neurosurgery training was introduced to PNG in the year 2000, it was in 2003 that a neurosurgery service was established. Prior to this time, neurosurgery in PNG was performed by general surgeons, with some assistance from visiting Australian neurosurgeons. Neurosurgical training was introduced to PNG in 2000. The model involved a further 3 years of training for a surgeon who had already completed 4 years of general surgical training. We aim to review the output, outcomes and impact achieved by training the first national neurosurgeon. **METHODS:** The data on activity (output) and outcomes were collected prospectively from 2003 to 2012. Ongoing mentoring and continuing professional development were provided through annual neurosurgical visits from Australia. There were serious limitations in the provision of equipment, with a lack of computerized tomographic or MR imaging, and adjuvant oncological services. **RESULTS:** There were 1618 neurosurgery admissions, 1020 neurosurgical procedures with a 5.74% overall mortality. Seventy percent of cases presented as emergencies. There were improved outcomes, particularly for head injuries, whilst hydrocephalus was managed with an acceptable morbidity and revision rate. **CONCLUSIONS:** The training of a neurosurgeon resulted in PNG patients receiving a better range of surgical services, with a lower mortality. The outcomes able to be delivered were limited by late presentations of patients and lack of resources including imaging. These themes are familiar to all low- and middle-income countries (LMICs) and this may serve as a model for other LMIC neurosurgical services to adopt as they consider whether to establish and develop neurosurgical and other sub-specialist surgical services.

- 30 **Kashima E, Williams D, Mark Ellison T, Schokkin D, Escudero P.**

Uncovering the acoustic vowel space of a previously undescribed language: the vowels of Nambo.

J Acoust Soc Am 2016 Jun;139(6):EL252. doi: 10.1121/1.4954395.

This study presents the first acoustic description of the vowel space of a Papuan language – Nambo, spoken in southern Papua New Guinea – based on duration and first and second formant measurements from 19 adult male and female speakers across three age groups (young, middle-aged, senior). Phonemically, Nambo has six full vowels /i, e, æ, a, o, u/ and a reduced vowel tentatively labeled /ə/. Unlike the full vowels, the quality of /ə/ showed great variation: seniors' and young females' realizations tended to be more open and retracted than those by young males, while middle-aged speakers' productions fell between these two variants.

- 31 **Kenangalem E, Karyana M, Burdarm L, Yeung S,**

Simpson JA, Tjitra E, Anstey NM, Poespoprodjo JR, Price RN, Douglas NM.

Plasmodium vivax infection: a major determinant of severe anaemia in infancy.

Malar J 2016 Jun 16;15:321. doi: 10.1186/s12936-016-1373-8.

BACKGROUND: Most malarious countries outside of Africa are co-endemic for *Plasmodium falciparum* and *Plasmodium vivax*. The comparative burden of anaemia in the community caused by these two species is incompletely characterized. **METHODS:** A three-stage, cross-sectional, community survey was used to determine the proportion of moderate or severe anaemia (haemoglobin <7 g/dL) attributable to patent *P. vivax*, *P. falciparum* and mixed parasitaemia in Papua, Indonesia. Adjusted population-attributable fractions were calculated from multivariable logistic regression models. Eight hundred and twenty-five households were surveyed with a total of 5255 occupants, 3890 (74%) of whom were present and provided a blood sample. *Plasmodium falciparum* parasitaemia was present in 8.1% (n = 315) of participants, *P. vivax* in 6.4% (n = 250) and mixed infections in 1.9% (n = 72). Overall, *P. falciparum* was associated with a mean reduction in haemoglobin of 1.16 g/dL compared to those without patent parasitaemia [95% confidence interval (95% CI) 0.91-1.41 g/dL]. The corresponding values for *P. vivax* and mixed infections were 0.66 g/dL (95% CI 0.35-0.96) and 1.25 g/dL (0.71-1.80), respectively. Overall, 16.7% (95% CI 8.52-24.2%) of haemoglobin concentrations <7 g/dL in the community were estimated to be attributable to patent parasitaemia. The fractions for infants and 1-5 years old were 34.4% (95% CI -3.30-58.3%) and 23.2% (95% CI 3.34-39.0%), respectively. *Plasmodium vivax* was associated with a greater than threefold higher attributable fraction of anaemia in infants compared with *P. falciparum* [27.6% (95% CI -3.20-49.2%) versus 7.94% (-5.87-20.0%)]. **CONCLUSION:** Despite comparatively low-level endemicity, malaria is associated with a significant proportion of all cases of community anaemia in southern Papua. Contrary to its benign reputation, *P. vivax* is an important and preventable risk factor for anaemia during infancy – a probable consequence of relapsing disease prior to the development of immunity.

32 **Kho S, Marfurt J, Handayani I, Pava Z, Noviyanti R, Kusuma A, Piera KA, Burdam FH, Kenangalem E, Lampah DA, Engwerda CR, Poespoprodjo JR, Price RN, Anstey NM, Minigo G, Woodberry T.**

Characterization of blood dendritic and regulatory T cells in asymptomatic adults with sub-microscopic *Plasmodium falciparum* or *Plasmodium vivax* infection.

Malar J 2016 Jun 21;15:328. doi: 10.1186/s12936-016-1382-7.

BACKGROUND: *Plasmodium falciparum* and *Plasmodium vivax* infections compromise dendritic cell (DC) function and expand regulatory T (Treg) cells in both clinical disease (malaria) and experimental human sub-microscopic infection. Conversely, in asymptomatic microscopy-positive (patent) *P. falciparum* or *P. vivax* infection in endemic areas, blood DCs increase or retain HLA-DR expression and Treg cells exhibit reduced activation, suggesting that DC and Treg cells contribute to the control of patent asymptomatic infection. The effect of sub-microscopic (sub-patent) asymptomatic

Plasmodium infection on DC and Treg cells in malaria-endemic area residents remains unclear. **METHODS:** In a cross-sectional household survey conducted in Papua, Indonesia, 162 asymptomatic adults were prospectively evaluated for DC and Treg cells using field-based flow cytometry. Of these, 161 individuals (99%) were assessed retrospectively by polymerase chain reaction (PCR), 19 of whom had sub-microscopic infection with *P. falciparum* and 15 with sub-microscopic *P. vivax* infection. Flow cytometric data were re-analysed after re-grouping asymptomatic individuals according to PCR results into negative controls, sub-microscopic and microscopic parasitaemia to examine DC and Treg cell phenotype in sub-microscopic infection. **RESULTS:** Asymptomatic adults with sub-microscopic *P. falciparum* or *P. vivax* infection had DC HLA-DR expression and Treg cell activation comparable to PCR-negative controls. Sub-microscopic *P. falciparum* infection was associated with lower peripheral CD4(+) T cells and lymphocytes; however, sub-microscopic *Plasmodium* infection had no apparent effect on DC sub-set number or Treg cell frequency. **CONCLUSIONS:** In contrast to the impairment of DC maturation/function and the activation of Treg cells seen with sub-microscopic parasitaemia in primary experimental human *Plasmodium* infection, no phenotypic evidence of dysregulation of DC and Treg cells was observed in asymptomatic sub-microscopic *Plasmodium* infection in Indonesian adults. This is consistent with DC and Treg cells retaining their functional capacity in sub-microscopic asymptomatic infection with *P. falciparum* or *P. vivax* in malaria-endemic areas.

33 **Kim J, Kim JH, Cheong HK, Kim H, Honda Y, Ha M, Hashizume M, Kolam J, Inape K.**

Effect of climate factors on the childhood pneumonia in Papua New Guinea: a time-series analysis.

Int J Environ Res Public Health 2016 Feb 15;13(2):213. doi: 10.3390/ijerph13020213.

This study aimed to assess the association between climate factors and the incidence of childhood pneumonia in Papua New Guinea quantitatively and to evaluate the variability of the effect size according to their geographic properties. The pneumonia incidence in children under five years and meteorological factors were obtained from six areas, including monthly rainfall and the monthly average daily maximum temperatures during the period from 1997 to 2006, from national health surveillance data. A generalized linear model was applied to measure the effect size of local and regional climate factor. The pooled risk of pneumonia in children per every 10 mm increase of rainfall was 0.24% (95% confidence interval: -0.01%-0.50%), and risk per every 1°C increase of the monthly mean of the maximum daily temperatures was 4.88% (95% CI: 1.57-8.30). Southern oscillation index and dipole mode index showed an overall negative effect on childhood pneumonia incidence, -0.57% and -4.30%, respectively, and the risk of pneumonia was higher in the dry season than in the rainy season (pooled effect: 12.08%). There was a variability in the relationship between climate factors and pneumonia which is assumed to reflect distribution of the determinants of and vulnerability to pneumonia in the community.

34 **Kong Z, Fang Y, Zhang M, Hong J, Tan Z, Yuan Z,**

Zhu F, Mao X, Jin Z, Zhu Y, Chen J.

Melioidosis acquired by a traveller from Papua New Guinea.

Travel Med Infect Dis 2016 May-Jun;14(3):267-270. doi: 10.1016/j.tmaid.2015.12.010. Epub 2016 Jan 20.

Melioidosis is an infectious disease caused by *Burkholderia pseudomallei*. Melioidosis is of public health importance in endemic areas, particularly in tropical and sub-tropical areas. We describe a case of melioidosis contracted by a man with diabetes from Papua New Guinea that was evaluated using multi-locus sequence typing and whole genome sequencing.

35 Korzeniewski K, Juszczak D, Zwolińska E.

Zika - another threat on the epidemiological map of the world.

Int Marit Health 2016;67(1):31-37. doi: 10.5603/IMH.2016.0007

Zika fever is an acute infectious disease caused by the Zika virus (ZIKV) of the *Flaviviridae* family and *Flavivirus* genus. It is transmitted by day-time active *Aedes* mosquitoes, and potentially by sexual contacts, blood transfusion, and from mother to foetus (resulting in microcephaly in a child). ZIKV was first isolated from a macaque monkey in the Zika forest in Uganda in 1947. The first case of the Zika fever in a human was recorded in Nigeria in 1954. Until 2007 only 14 cases of the disease were confirmed worldwide. In 2007, there was an outbreak of the Zika fever in Micronesia (Yap Island) with an estimated 5,000 cases. Between 2013 and 2015 a further outbreak of the disease occurred in the Pacific islands: in French Polynesia, New Caledonia, Cook Islands, Easter Island, and Solomon Islands. In 2015, the Zika fever spread to Brazil and more than 20 other countries in South and Central America. Until March 2016, an estimated 1.6 million autochthonous cases of Zika have been reported globally, with approximately 1.5 million cases recorded in Brazil. Typically, 80% of Zika infections are asymptomatic. The most common symptoms of the disease include fever, maculopapular rash, muscle and joint pain, conjunctivitis. Zika fever can be diagnosed on the basis of clinical signs (it must be differentiated from dengue, chikungunya); ZIKV identification is also possible by the application of polymerase chain reaction in acutely ill patients and the detection of specific IgM and IgG antibodies to ZIKV. Until today, there is no effective antiviral treatment or an effective vaccine against Zika fever (in case of an infection only symptomatic treatment is applied). In August 2016 in Rio de Janeiro (Brazil) the Summer Olympic Games will take place, attracting thousands of athletes and spectators. The fight against the Zika fever and the race against time have gained momentum.

36 Logue K, Keven JB, Cannon MV, Reimer L, Siba P, Walker ED, Zimmerman PA, Serre D.

Unbiased characterization of *Anopheles* mosquito blood meals by targeted high-throughput sequencing. *PLoS Negl Trop Dis* 2016 Mar 10;10(3):e0004512. doi: 10.1371/journal.pntd.0004512. eCollection 2016.

Understanding mosquito host choice is important for assessing vector competence or identifying disease reservoirs. Unfortunately, the availability of an unbiased method for comprehensively evaluating the composition of insect blood meals is very limited,

as most current molecular assays only test for the presence of a few pre-selected species. These approaches also have limited ability to identify the presence of multiple mammalian hosts in a single blood meal. Here, we describe a novel high-throughput sequencing method that enables analysis of 96 mosquitoes simultaneously and provides a comprehensive and quantitative perspective on the composition of each blood meal. We validated in silico that universal primers targeting the mammalian mitochondrial 16S ribosomal RNA genes (16S rRNA) should amplify more than 95% of the mammalian 16S rRNA sequences present in the NCBI nucleotide database. We applied this method to 442 female *Anopheles punctulatus* s. l. mosquitoes collected in Papua New Guinea (PNG). While human (52.9%), dog (15.8%) and pig (29.2%) were the most common hosts identified in our study, we also detected DNA from mice, one marsupial species and two bat species. Our analyses also revealed that 16.3% of the mosquitoes fed on more than one host. Analysis of the human mitochondrial hypervariable region I in 102 human blood meals showed that 5 (4.9%) of the mosquitoes unambiguously fed on more than one person. Overall, analysis of PNG mosquitoes illustrates the potential of this approach to identify unsuspected hosts and characterize mixed blood meals, and shows how this approach can be adapted to evaluate inter-individual variations among human blood meals. Furthermore, this approach can be applied to any disease-transmitting arthropod and can be easily customized to investigate non-mammalian host sources.

37 Lokuge K, Verputten M, Ajakali M, Tolboom B, Joshy G, Thurber KA, Plana D, Howes S, Wakon A, Banks E.

Health services for gender-based violence: Médecins Sans Frontières experience caring for survivors in urban Papua New Guinea.

PLoS One 2016 Jun 10;11(6):e0156813. doi: 10.1371/journal.pone.0156813. eCollection 2016.

BACKGROUND: Levels of gender-based violence in Papua New Guinea (PNG) are high; health services for survivors are limited. Evidence from the few existing health services for survivors can inform improvements in care in this and similar settings. **METHODS:** Médecins Sans Frontières supported health services for survivors in Lae, PNG from 2008 to 2013. Routine monitoring data from August 2010-April 2013 were used to describe patient and service characteristics. **RESULTS:** 5,892 individuals received care over 6,860 presentations, the majority self-referred or referred by friends and family. Presentations were attributed to intimate partner violence (62%), non-partner sexual violence (15%), other forms of violence (3%), and past (but not current) violence (21%). 97% were female; an estimated 4.9% (95%CI:4.8-5.0%) of females resident in the catchment area presented to the programme during the 2.8 years analysed. Of presentations for non-partner sexual violence, 79% knew their abuser and 50% were children <16 years. 92% of presentations reporting current violence received medical treatment for injuries. The majority of patients who received multiple counselling sessions reported improved functioning and decreased severity of psycho-social complaints. **CONCLUSIONS:** Community awareness of the availability of free, best-practice, accessible, confidential medical and counselling services for

sexual and gender-based violence in Lae, PNG resulted in many survivors presenting for care. High levels of ongoing intimate partner violence and child sexual abuse by known abusers indicates that alongside comprehensive medical care, access to effective services in non-health sectors such as policing, protection and legal services are needed if survivors are to escape the cycle of violence.

- 38 **Manning L, Cutts J, Staniscic DI, Laman M, Carmagnac A, Allen S, O'Donnell A, Karunajeewa H, Rosanas-Urgell A, Siba P, Davis TM, Michon P, Schofield L, Rockett K, Kwiatkowski D, Mueller I.** A Toll-like receptor-1 variant and its characteristic cellular phenotype is associated with severe malaria in Papua New Guinean children.

Genes Immun 2016 Jan-Feb;17(1):52-59. doi: 10.1038/gene.2015.50. Epub 2015 Dec 3.

Genetic factors are likely to contribute to low severe malaria case fatality rates in Melanesian populations, but association studies can be underpowered and may not provide plausible mechanistic explanations if significant associations are detected. In preparation for a genome-wide association study, 29 candidate single-nucleotide polymorphisms (SNPs) with minor allele frequencies >5% were examined in a case-control study of 504 Papua New Guinean children with severe malaria. In parallel, an immunological substudy was performed on convalescent peripheral blood mononuclear cells (PBMCs) from cases and controls. Following stimulation with a Toll-like receptor (TLR) 1/2 agonist, effector cytokines and chemokines were assayed. The only significant genetic association observed involved a nonsynonymous SNP (TLR1rs4833095) in the TLR1 gene. A recessive (TT) genotype was associated with reduced odds of severe malaria of 0.52 (95% confidence interval 0.29-0.90, $p = 0.006$). Concentrations of pro-inflammatory cytokines interleukin-1 β and tumour necrosis factor α were significantly higher in severe malaria cases compared with healthy controls, but lower in children with the protective recessive (TT) genotype. A genetic variant in TLR1 may contribute to the low severe malaria case fatality rates in this region through a reduced pro-inflammatory cellular phenotype.

- 39 **Marks M, Bottomley C, Tome H, Pitakaka R, Butcher R, Sokana O, Kako H, Solomon AW, Mabey DC.**

Mass drug administration of azithromycin for trachoma reduces the prevalence of genital *Chlamydia trachomatis* infection in the Solomon Islands.

Sex Transm Infect 2016 Jun;92(4):261-265. doi: 10.1136/sextrans-2015-052439. Epub 2016 Feb 17.

OBJECTIVES: *Chlamydia trachomatis* is the most common bacterial sexually transmitted infection and is frequently asymptomatic; ocular *C. trachomatis* strains cause trachoma. Mass drug administration (MDA) of azithromycin for trachoma might also reduce the prevalence of genital *C. trachomatis*. In a survey conducted in the Solomon Islands in 2014, prior to MDA, the prevalence of genital *C. trachomatis* was 20.3% (95% CI 15.9% to 25.4%). We conducted a survey to establish the impact of MDA with azithromycin on genital *C. trachomatis*. **METHODS:** Women attending three community outpatient clinics, predominantly for antenatal care, 10 months after MDA with azithromycin given

for trachoma elimination, were enrolled in this survey. Self-taken high vaginal swabs were for *C. trachomatis* and *Neisseria gonorrhoeae* using the BD Probetec strand displacement assay. **RESULTS:** 298 women were enrolled. *C. trachomatis* infection was diagnosed in 43 women (14.4%, 95% CI 10.6% to 18.9%) and *N. gonorrhoeae* in 9 (3%, 95% CI 1.4% to 5.7%). The age-adjusted OR for *C. trachomatis* infection was consistent with a significant decrease in the prevalence of *C. trachomatis* following MDA (OR 0.58, 95% CI 0.37 to 0.94, $p = 0.027$). There was no change in the prevalence of *N. gonorrhoeae* following MDA (OR 0.51, 95% CI 0.22 to 1.22, $p = 0.13$). **CONCLUSIONS:** This study demonstrated a 40% reduction in the age-adjusted prevalence of genital *C. trachomatis* infection following azithromycin MDA for trachoma elimination.

- 40 **Mason DS, Marks M, Sokana O, Solomon AW, Mabey DC, Romani L, Kaldor J, Steer AC, Engelman D.**

The prevalence of scabies and impetigo in the Solomon Islands: a population-based survey.

PLoS Negl Trop Dis 2016 Jun 27;10(6):e0004803. doi: 10.1371/journal.pntd.0004803. eCollection 2016

BACKGROUND: Scabies and impetigo are common, important and treatable skin conditions. Reports from several Pacific island countries show extremely high prevalence of these two conditions, but for many countries, including the Solomon Islands, there is a paucity of epidemiological data. **METHODOLOGY:** Ten rural villages in the Western Province of the Solomon Islands were included in the study, chosen so that data collection could be integrated with an existing project investigating clinical and serological markers of yaws. All residents were eligible to participate, and 1908 people were enrolled. Participants were interviewed and examined by a paediatric registrar, who recorded relevant demographic information, and made a clinical diagnosis of scabies and/or impetigo, severity and distribution. **PRINCIPAL FINDINGS:** The total unweighted prevalence of scabies was 19.2% (95% confidence interval [CI] 17.5-21.0), and age and gender weighted prevalence 19.2% (95%CI 16.7-21.9). The adult prevalence of scabies was 10.4% (95%CI 8.2-13.2), and the highest prevalence was found in infants <1 year of age (34.1%, adjusted odds ratio [AOR] compared with adults: 3.6, 95%CI 2.2-6.0) and children aged 1-4 years (25.7%, AOR 2.6, 95%CI 1.7-3.9). Scabies affected two or more body regions in 80.9% of participants, and 4.4% of scabies cases were classified as severe. The total unweighted prevalence of active impetigo was 32.7% (95%CI 30.6-34.8), and age and gender weighted prevalence 26.7% (95%CI 24.2-29.5). The highest prevalence was found in children aged 1-4 years (42.6%, AOR compared with adults: 4.1, 95%CI 2.9-5.8). Scabies infestation was associated with active impetigo infection (AOR 2.0, 95%CI 1.6-2.6), with 41.1% of active impetigo cases also having scabies. **CONCLUSIONS AND SIGNIFICANCE:** Scabies and impetigo are very common in the rural Western Province of the Solomon Islands. Scabies infestation is strongly associated with impetigo. Community control strategies for scabies may reduce the burden of both conditions and their downstream complications.

- 41 **McCall C.**

In Papua New Guinea, HIV/AIDS-related stigma is

still rife.

Lancet 2016 Jan 16;387(10015):215-216. doi: 10.1016/S0140-6736(16)00095-7. Epub 2016 Jan 15.

- 42 **Menegon M, Bardaji A, Martínez-Espinosa F, Bôto-Menezes C, Ome-Kaius M, Mueller I, Betuela I, Arévalo-Herrera M, Kochar S, Kochar SK, Jaju P, Hans D, Chitnis C, Padilla N, Castellanos ME, Ortiz L, Sanz S, Piqueras M, Desai M, Mayor A, Del Portillo H, Menéndez C, Severini C.**

Microsatellite genotyping of *Plasmodium vivax* isolates from pregnant women in four malaria endemic countries.

PLoS One 2016 Mar 24;11(3):e0152447. doi: 10.1371/journal.pone.0152447. eCollection 2016.

Plasmodium vivax is the most widely distributed human parasite and the main cause of human malaria outside the African continent. However, the knowledge about the genetic variability of *P. vivax* is limited when compared to the information available for *P. falciparum*. We present the results of a study aimed at characterizing the genetic structure of *P. vivax* populations obtained from pregnant women from different malaria endemic settings. Between June 2008 and October 2011 nearly 2000 pregnant women were recruited during routine antenatal care at each site and followed up until delivery. A capillary blood sample from the study participants was collected for genotyping at different time points. Seven *P. vivax* microsatellite markers were used for genotypic characterization on a total of 229 *P. vivax* isolates obtained from Brazil, Colombia, India and Papua New Guinea. In each population, the number of alleles per locus, the expected heterozygosity and the levels of multilocus linkage disequilibrium were assessed. The extent of genetic differentiation among populations was also estimated. Six microsatellite loci on 137 *P. falciparum* isolates from three countries were screened for comparison. The mean value of expected heterozygosity per country ranged from 0.839 to 0.874 for *P. vivax* and from 0.578 to 0.758 for *P. falciparum*. *P. vivax* populations were more diverse than those of *P. falciparum*. In some of the studied countries, the diversity of *P. vivax* population was very high compared to the respective level of endemicity. The level of inter-population differentiation was moderate to high in all *P. vivax* and *P. falciparum* populations studied.

- 43 **Michael E, Singh BK.**

Heterogeneous dynamics, robustness/fragility trade-offs, and the eradication of the macroparasitic disease, lymphatic filariasis.

BMC Med 2016 Jan 28;14:14. doi: 10.1186/s12916-016-0557-y.

BACKGROUND: The current WHO-led initiative to eradicate the macroparasitic disease, lymphatic filariasis (LF), based on single-dose annual mass drug administration (MDA), represents one of the largest health programs devised to reduce the burden of tropical diseases. However, despite the advances made in instituting large-scale MDA programs in affected countries, a challenge to meeting the goal of global eradication is the heterogeneous transmission of LF across endemic regions, and the impact that such complexity may have on the effort required to interrupt transmission in all socioecological settings. **METHODS:** Here, we apply a Bayesian computer simulation procedure to fit transmission models of LF to field data assembled

from 18 sites across the major LF endemic regions of Africa, Asia and Papua New Guinea, reflecting different ecological and vector characteristics, to investigate the impacts and implications of transmission heterogeneity and complexity on filarial infection dynamics, system robustness and control. **RESULTS:** We find firstly that LF elimination thresholds varied significantly between the 18 study communities owing to site variations in transmission and initial ecological parameters. We highlight how this variation in thresholds leads to the need for applying variable durations of interventions across endemic communities for achieving LF elimination; however, a major new result is the finding that filarial population responses to interventions ultimately reflect outcomes of interplays between dynamics and the biological architectures and processes that generate robustness/fragility trade-offs in parasite transmission. Intervention simulations carried out in this study further show how understanding these factors is also key to the design of options that would effectively eliminate LF from all settings. In this regard, we find how including vector control into MDA programs may not only offer a countermeasure that will reliably increase system fragility globally across all settings and hence provide a control option robust to differential locality-specific transmission dynamics, but by simultaneously reducing transmission regime variability also permit more reliable macroscopic predictions of intervention effects. **CONCLUSIONS:** Our results imply that a new approach, combining adaptive modelling of parasite transmission with the use of biological robustness as a design principle, is required if we are to both enhance understanding of complex parasitic infections and delineate options to facilitate their elimination effectively.

- 44 **Mita T, Culleton R, Takahashi N, Nakamura M, Tsukahara T, Hunja CW, Win ZZ, Htike WW, Marma AS, Dysoley L, Ndonga M, Dzodzomenyo M, Akhwale WS, Kobayashi J, Uemura H, Kaneko A, Hombhanje F, Ferreira MU, Björkman A, Endo H, Ohashi J.**

Little polymorphism at the K13 propeller locus in worldwide *Plasmodium falciparum* populations prior to the introduction of artemisinin combination therapies.

Antimicrob Agents Chemother 2016 May 23;60(6):3340-3347. doi: 10.1128/AAC.02370-15. Print 2016 Jun.

The emergence and spread of artemisinin-resistant *Plasmodium falciparum* is of huge concern for the global effort toward malaria control and elimination. Artemisinin resistance, defined as a delayed time to parasite clearance following administration of artemisinin, is associated with mutations in the *Pfkelch13* gene of resistant parasites. To date, as many as 60 nonsynonymous mutations have been identified in this gene, but whether these mutations have been selected by artemisinin usage or merely reflect natural polymorphism independent of selection is currently unknown. To clarify this, we sequenced the *Pfkelch13* propeller domain in 581 isolates collected before (420 isolates) and after (161 isolates) the implementation of artemisinin combination therapies (ACTs), from various regions of endemicity worldwide. Nonsynonymous mutations were observed in 1% of parasites isolated prior to the introduction of ACTs. Frequencies of mutant isolates, nucleotide diversity, and haplotype diversity were significantly higher in the parasites isolated

from populations exposed to artemisinin than in those from populations that had not been exposed to the drug. In the artemisinin-exposed population, a significant excess of dN compared to dS was observed, suggesting the presence of positive selection. In contrast, pairwise comparison of dN and dS and the McDonald and Kreitman test indicate that purifying selection acts on the *Pfkelch13* propeller domain in populations not exposed to ACTs. These population genetic analyses reveal a low baseline of *Pfkelch13* polymorphism, probably due to purifying selection in the absence of artemisinin selection. In contrast, various *Pfkelch13* mutations have been selected under artemisinin pressure.

- 45 **Moore BR, Laman M, Salman S, Batty KT, Page-Sharp M, Hombhanje F, Manning L, Davis TME.** Naphthoquine: an emerging candidate for artemisinin combination therapy. *Drugs* 2016 May;76(7):789-804. doi: 10.1007/s40265-016-0572-5.

Naphthoquine is a 4-aminoquinoline antimalarial drug first synthesised in China in 1986 but which was not developed for clinical use until the late 1990s. Early in vitro parasite sensitivity and in vivo efficacy data, together with a long terminal elimination half-life (up to 23 days), suggested that it could be used as monotherapy for uncomplicated falciparum and vivax malaria, but is now marketed as a single-dose, fixed co-formulation with artemisinin in a milligram per kilogram ratio of 1:2.5. This form of artemisinin combination therapy (ACT) has also shown high cure rates, especially in two randomised trials in which, consistent with World Health Organization recommendations for all ACTs, it was administered daily for 3 days rather than as single dose for *Plasmodium falciparum* and *P. vivax* infections (28-day adequate clinical and parasitological response $\geq 98.4\%$). Although detailed safety monitoring has been performed in a minority of subjects, >4000 healthy volunteers and patients with malaria have been exposed to naphthoquine without any documented significant toxicity. As with other 4-aminoquinolines, naphthoquine is associated with prolongation of the electrocardiographic QT interval but not with cardiac or neurological events. It has been administered to children as young as 4 months of age but, due to a lack of pharmacokinetic, efficacy and toxicity data in young infants and in pregnant/lactating women, it should not be used in these vulnerable patient groups. With the emergence of parasite resistance to other ACTs, naphthoquine partnered with a potent artemisinin derivative may prove a viable alternative treatment for uncomplicated malaria.

- 46 **Nagle N, Ballantyne KN, van Oven M, Tyler-Smith C, Xue Y, Taylor D, Wilcox S, Wilcox L, Turkalov R, van Oorschot RA, McAllister P, Williams L, Kayser M, Mitchell RJ; Genographic Consortium.** Antiquity and diversity of Aboriginal Australian Y-chromosomes. *Am J Phys Anthropol* 2016 Mar;159(3):367-381. doi: 10.1002/ajpa.22886. Epub 2015 Oct 30.

OBJECTIVE: Understanding the origins of Aboriginal Australians is crucial in reconstructing the evolution and spread of *Homo sapiens* as evidence suggests they represent the descendants of the earliest group to leave Africa. This study analyzed a large sample of Y-chromosomes to answer questions relating to the migration routes of

their ancestors, the age of Y-haplogroups, date of colonization, as well as the extent of male-specific variation. **METHODS:** Knowledge of Y-chromosome variation among Aboriginal Australians is extremely limited. This study examined Y-SNP and Y-STR variation among 657 self-declared Aboriginal males from locations across the continent. 17 Y-STR loci and 47 Y-SNPs spanning the Y-chromosome phylogeny were typed in total. **RESULTS:** The proportion of non-indigenous Y-chromosomes of assumed Eurasian origin was high, at 56%. Y lineages of indigenous Sahul origin belonged to haplogroups C-M130*(xM8,M38,M217,M347) (1%), C-M347(19%), K-M526*(xM147,P308,P79,P261,P256,M231,M175,M45,P202) (12%), S-P308 (12%), and M-M186 (0.9%). Haplogroups C-M347, K-M526*, and S-P308 are Aboriginal Australian-specific. Dating of C-M347, K-M526*, and S-P308 indicates that all are at least 40,000 years old, confirming their long-term presence in Australia. Haplogroup C-M347 comprised at least three sub-haplogroups: C-DYS390.1del, C-M210, and the unresolved paralog C-M347*(xM347,xM347.1del,M210). **CONCLUSIONS:** There was some geographic structure to the Y-haplogroup variation, but most haplogroups were present throughout Australia. The age of the Australian-specific Y-haplogroups suggests New Guineans and Aboriginal Australians have been isolated for over 30,000 years, supporting findings based on mitochondrial DNA data. Our data support the hypothesis of more than one route (via New Guinea) for males entering Sahul some 50,000 years ago and give no support for colonization events during the Holocene, from either India or elsewhere.

- 47 **NCD Risk Factor Collaboration (NCD-RisC).** Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4.4 million participants. *Lancet* 2016 Apr 9;387(10027):1513-1530. doi: 10.1016/S0140-6736(16)00618-8. Epub 2016 Apr 6.

BACKGROUND: One of the global targets for non-communicable diseases is to halt, by 2025, the rise in the age-standardised adult prevalence of diabetes at its 2010 levels. We aimed to estimate worldwide trends in diabetes, how likely it is for countries to achieve the global target, and how changes in prevalence, together with population growth and ageing, are affecting the number of adults with diabetes. **METHODS:** We pooled data from population-based studies that had collected data on diabetes through measurement of its biomarkers. We used a Bayesian hierarchical model to estimate trends in diabetes prevalence – defined as fasting plasma glucose of 7.0 mmol/L or higher, or history of diagnosis with diabetes, or use of insulin or oral hypoglycaemic drugs – in 200 countries and territories in 21 regions, by sex and from 1980 to 2014. We also calculated the posterior probability of meeting the global diabetes target if post-2000 trends continue. **FINDINGS:** We used data from 751 studies including 4,372,000 adults from 146 of the 200 countries we make estimates for. Global age-standardised diabetes prevalence increased from 4.3% (95% credible interval 2.4-7.0) in 1980 to 9.0% (7.2-11.1) in 2014 in men, and from 5.0% (2.9-7.9) to 7.9% (6.4-9.7) in women. The number of adults with diabetes in the world increased from 108 million in 1980 to 422 million in 2014 (28.5% due to the rise in prevalence, 39.7% due to population growth and ageing, and 31.8% due to interaction of

these two factors). Age-standardised adult diabetes prevalence in 2014 was lowest in northwestern Europe, and highest in Polynesia and Micronesia, at nearly 25%, followed by Melanesia and the Middle East and north Africa. Between 1980 and 2014 there was little change in age-standardised diabetes prevalence in adult women in continental western Europe, although crude prevalence rose because of ageing of the population. By contrast, age-standardised adult prevalence rose by 15 percentage points in men and women in Polynesia and Micronesia. In 2014, American Samoa had the highest national prevalence of diabetes (>30% in both sexes), with age-standardised adult prevalence also higher than 25% in some other islands in Polynesia and Micronesia. If post-2000 trends continue, the probability of meeting the global target of halting the rise in the prevalence of diabetes by 2025 at the 2010 level worldwide is lower than 1% for men and is 1% for women. Only nine countries for men and 29 countries for women, mostly in western Europe, have a 50% or higher probability of meeting the global target. INTERPRETATION: Since 1980, age-standardised diabetes prevalence in adults has increased, or at best remained unchanged, in every country. Together with population growth and ageing, this rise has led to a near quadrupling of the number of adults with diabetes worldwide. The burden of diabetes, both in terms of prevalence and number of adults affected, has increased faster in low-income and middle-income countries than in high-income countries.

- 48 **Norton HL, Hanna M, Werren E, Friedlaender J.** The rs387907171 SNP in TYRP1 is not associated with blond hair color on the island of Bougainville. *Am J Hum Biol* 2016 May;28(3):431-435. doi: 10.1002/ajhb.22795. Epub 2015 Oct 9.

OBJECTIVES: The aims of this study are to characterize the frequency of the derived allele at rs387907171 in populations from the islands of New Britain and Bougainville in Northern Island Melanesia, to confirm its association with lighter hair color, and to refine hypotheses regarding its evolutionary history. METHODS: rs387907171 was genotyped in 93 individuals from New Britain and 101 from Bougainville for whom quantitative assessments of skin and hair pigmentation were available. Combining these with existing data from other Melanesian islands we tested for differences in allele frequencies between islands and for associations with skin and hair pigmentation using ANOVA, including sex, age, and island affiliations as covariates. RESULTS: The derived allele at rs387907171 was observed in a single copy in the New Britain and Bougainville populations genotyped here. Its frequency differs significantly among islands in the region ($\chi^2 = 206.5$, $df=3$, $p<0.001$). rs387907171 remains significantly, although weakly, associated with lighter hair pigmentation ($F = 10.28$, $R^2 = 0.0125$, $p=0.0014$). This association increases when sex and age ($F = 20.68$, $R^2 = 0.074$, $p<7.92 \times 10^{-13}$) are included as covariates. CONCLUSIONS: The rs387907171 SNP exhibits strong allele frequency differences among islands in Northern Island Melanesia. Its absence from Bougainville, as well as the weak association with decreased hair color, indicates that additional alleles contribute to the blondism phenotype. Its geographic distribution suggests that a Lapita-mediated model for the dispersal of the derived allele at rs387907171

remains a viable evolutionary scenario.

- 49 **Park JW, Cheong HK, Honda Y, Ha M, Kim H, Kolam J, Inape K, Mueller I.**

Time trend of malaria in relation to climate variability in Papua New Guinea.

Environ Health Toxicol 2016 Feb 25;31:e2016003. doi: 10.5620/eh.t.2016003. eCollection 2016.

OBJECTIVES: This study was conducted to describe the regional malaria incidence in relation to the geographic and climatic conditions and describe the effect of altitude on the expansion of malaria over the last decade in Papua New Guinea. METHODS: Malaria incidence was estimated in five provinces from 1996 to 2008 using national health surveillance data. The time trend of malaria incidence was compared with rainfall and minimum/maximum temperature. In the Eastern Highlands Province, the time trend of malaria incidence over the study period was stratified by altitude. The spatio-temporal pattern of malaria was analyzed. RESULTS: Nationwide, malaria incidence was stationary. Regionally, the incidence increased markedly in the highland region (292.0/100000/yr, $p = 0.021$), and remained stationary in the other regions. Seasonality of the malaria incidence was related with rainfall. Decreasing incidence of malaria was associated with decreasing rainfall in the southern coastal region, whereas it was not evident in the northern coastal region. In the Eastern Highlands Province, malaria incidence increased in areas below 1700 m, with the rate of increase being steeper at higher altitudes. CONCLUSIONS: Increasing trend of malaria incidence was prominent in the highland region of Papua New Guinea, while long-term trend was dependent upon baseline level of rainfall in coastal regions.

- 50 **Rafiei N, Hajkowicz K, Redmond A, Taylor C.**

First report of Zika virus infection in a returned traveller from the Solomon Islands.

Med J Aust 2016 Mar 21;204(5):186.

- 51 **Rehan R, Jones PD, Abdeen H, Rowas H, Dhaliwal J.**

The dangers to children from coconut tree trauma, in Kirakira, Solomon Islands: a retrospective clinical audit.

Arch Public Health 2016 Apr 11;74:14. doi: 10.1186/s13690-016-0125-0.

BACKGROUND: Kirakira is small community of 3,000 people and is the capital of Makira-Ulawa Province in Solomon Islands. Kirakira is an impoverished community with a small 30-bed hospital with limited resources. This audit was conducted by final year students from Bond University as part of a selective clinical placement. METHODS: The audit included admissions to the hospital from 2011 to 2014. Trauma-related admissions were identified and classified according to the patient's age, sex, description of injury, mechanism of injury and whether they were transferred to the National Referral Hospital (NRH) in Honiara for further treatment. Injuries due to coconut tree trauma were classified as being due to falls from the tree, or trauma from either falling branches or falling coconut fruit. RESULTS: There were 3455 admissions and 23 (0.7%) non-neonatal deaths over the 3 year period. 126 (3.6%) admissions were referred on to the NRH for further treatment. 277 (8.02%) admissions were trauma-related with 57 (21%)

of these referred on to the NRH. 142 (55%) of the trauma admissions involved children. Coconut tree trauma was the commonest cause of a traumatic admission to hospital. There were 49 coconut tree trauma admissions including 35 from falls, 12 from falling branches and two from falling coconuts. 80% of coconut tree trauma involved males and the median age of those injured was 13. Primary school age children aged 6-14 years were most at risk for coconut tree trauma. 15 (31%) of the coconut tree trauma admissions were referred to NRH for further treatment. **CONCLUSIONS:** Coconut tree trauma is common in Kirakira and is an important preventable cause of serious injury that particularly affects primary school age boys in Kirakira, Solomon Islands. A public education campaign that focuses on this at-risk age group warning of the dangers of climbing coconut trees should be considered.

- 52 **Reimer LJ, Thomsen EK, Koimbu G, Keven JB, Mueller I, Siba PM, Kazura JW, Hetzel MW, Zimmerman PA.**

Malaria transmission dynamics surrounding the first nationwide long-lasting insecticidal net distribution in Papua New Guinea.

Malar J 2016 Jan 12;15:25. doi: 10.1186/s12936-015-1067-7.

BACKGROUND: The major malaria vectors of Papua New Guinea exhibit heterogeneities in distribution, biting behaviour and malaria infection levels. Long-lasting, insecticide-treated nets (LLINs), distributed as part of the National Malaria Control Programme, are the primary intervention targeting malaria transmission. This study evaluated the impact of LLINs on anopheline density, species composition, feeding behaviour, and malaria transmission. **METHODS:** Mosquitoes were collected by human landing catch in 11 villages from East Sepik Province and Madang Province. Mosquitoes were collected for 3 years (1 year before distribution and 2 years after), and assayed to determine mosquito species and *Plasmodium* spp. infection prevalence. The influence of weather conditions and the presence of people and animals on biting density was determined. Determinants of biting density and sporozoite prevalence were analysed by generalized estimating equations (GEE). **RESULTS:** Mosquito biting rates and entomological inoculation rates decreased significantly after the distribution. *Plasmodium falciparum* and *P. vivax* sporozoite prevalence decreased in year 2, but increased in year 3, suggesting the likelihood of resurgence in transmission if low biting rates are not maintained. An earlier shift in the median biting time of *Anopheles punctulatus* and *An. farauti* s.s. was observed. However, this was not accompanied by an increase in the proportion of infective bites occurring before 2200 hours. A change in species composition was observed, which resulted in dominance of *An. punctulatus* in the Dreikikir region, but a decrease in *An. punctulatus* in the Madang region. When controlling for village and study year, *An. farauti* s.s., *An. koliensis* and *An. punctulatus* were equally likely to carry *P. vivax* sporozoites. However, *An. punctulatus* was significantly more likely than *An. farauti* s.s. (OR 0.14; $p = 0.007$) or *An. koliensis* (OR 0.27; $p < 0.001$) to carry *P. falciparum* sporozoites. **CONCLUSIONS:** LLINs had a significant impact on malaria transmission, despite exophagic and crepuscular feeding behaviours of dominant vectors. Changes in species composition and feeding

behaviour were observed, but their epidemiological significance will depend on their durability over time.

- 53 **Ross A, Koepfli C, Schoepfli S, Timinao L, Siba P, Smith T, Mueller I, Felger I, Tanner M.**

The incidence and differential seasonal patterns of *Plasmodium vivax* primary infections and relapses in a cohort of children in Papua New Guinea.

PLoS Negl Trop Dis 2016 May 4;10(5):e0004582. doi: 10.1371/journal.pntd.0004582. eCollection 2016.

Plasmodium vivax has the ability to relapse from dormant parasites in the liver weeks or months after inoculation, causing further blood-stage infection and potential onward transmission. Estimates of the force of blood-stage infections arising from primary infections and relapses are important for designing intervention strategies. However, in endemic settings their relative contributions are unclear. Infections are frequently asymptomatic, many individuals harbor multiple infections, and while high-resolution genotyping of blood samples enables individual infections to be distinguished, primary infections and relapses cannot be identified. We develop a model and fit it to longitudinal genotyping data from children in Papua New Guinea to estimate the incidence and seasonality of *P. vivax* primary infection and relapse. The children, aged one to three years at enrolment, were followed up over 16 months with routine surveys every two months. Blood samples were taken at the routine visits and at other times if the child was ill. Samples positive by microscopy or a molecular method for species detection were genotyped using high-resolution capillary electrophoresis for *P. vivax* MS16 and msp1F3, and *P. falciparum* msp2. The data were summarized as longitudinal patterns of success or failure to detect a genotype at each routine time-point (eg 001000001). We assume that the seasonality of *P. vivax* primary infection is similar to that of *P. falciparum* since they are transmitted by the same vectors and, because *P. falciparum* does not have the ability to relapse, the seasonality can be estimated. Relapses occurring during the study period can be a consequence of infections occurring prior to the study: we assume that the seasonal pattern of primary infections repeats over time. We incorporate information from parasitological and entomology studies to gain leverage for estimating the parameters, and take imperfect detection into account. We estimate the force of *P. vivax* primary infections to be 11.5 (10.5-12.3) for a three-year-old child per year and the mean number of relapses per infection to be 4.3 (4.0-4.6) over 16 months. The peak incidence of relapses occurred in the two month interval following the peak interval for primary infections: the contribution to the force of blood-stage infection from relapses is between 71% and 90% depending on the season. Our estimates contribute to knowledge of the *P. vivax* epidemiology and have implications for the timing of intervention strategies targeting different stages of the life cycle.

- 54 **Rubiang-Yalambing L, Arcot J, Greenfield H, Holford P.**

Aibika (*Abelmoschus manihot* L.): genetic variation, morphology and relationships to micronutrient composition.

Food Chem 2016 Feb 15;193:62-68. doi: 10.1016/j.foodchem.2014.08.058. Epub 2014 Aug 23.

Aibika (*Abelmoschus manihot* L.) is believed to be a good source of micronutrients. However, although

many varieties of aibika are commonly consumed in Papua New Guinea, their micronutrient content is unknown. Therefore, the mineral (Ca, Fe, K, Mg, Mn, Na, Zn & Cu), folate composition and the genetic variation of 23 aibika accessions from the collection at the National Agricultural Research Institute were studied over a 3-year period to provide data for nutritional studies and to inform breeding programs. The data showed that aibika is, potentially, a crop of high nutritional value with the potential to boost the micronutrient status of local PNG communities. However, there were substantial differences in the micronutrient concentrations of the accessions from year to year and accessions that had the highest concentration of a particular mineral in 1 year did not have the high concentrations in other years. Clusters determined using the unweighted pair group method with arithmetic mean analysis (UPGMA) of the micronutrient contents differed in each of the 3 years. Genetic analysis made using random amplification of polymorphic DNA and directed amplification of minisatellite region DNA placed the accessions into five groups. There was no correlation between these groups and leaf morphology, nor were there correlations with the clusters determined from the UPGMA analyses. There appears to be considerable interaction between genotype and environmental factors determining micronutrient composition and environmental factors may play a greater role than genotype in influencing micronutrient composition.

- 55 **Russell TL, Beebe NW, Bugoro H, Apairamo A, Collins FH, Cooper RD, Lobo NF, Burkot TR.**

Anopheles farauti is a homogeneous population that blood feeds early and outdoors in the Solomon Islands.

Malar J 2016 Mar 9;15(1):151. doi: 10.1186/s12936-016-1194-9.

BACKGROUND: In the 1970s, *Anopheles farauti* in the Solomon Islands responded to indoor residual spraying with DDT by increasingly feeding more outdoors and earlier in the evening. Although long-lasting insecticidal nets (LLINs) are now the primary malaria vector control intervention in the Solomon Islands, only a small proportion of *An. farauti* still seek blood meals indoors and late at night where they are vulnerable to being killed by contact with the insecticides in LLINs. The effectiveness of LLINs and indoor residual spraying (IRS) in controlling malaria transmission where the vectors are exophagic and early biting will depend on whether the predominant outdoor or early biting phenotypes are associated with a subpopulation of the vectors present. **METHODS:** Mark-release-recapture experiments were conducted in the Solomon Islands to determine if individual *An. farauti* repeat the same behaviours over successive feeding cycles. The two behavioural phenotypes examined were those on which the WHO-recommended malaria vector control strategies, LLINs and IRS, depend: indoor and late night biting. **RESULTS:** Evidence was found for *An. farauti* being a single population regarding time (early evening or late night) and location (indoor or outdoor) of blood feeding. Individual *An. farauti* did not consistently repeat behavioural phenotypes expressed for blood feeding (eg, while most mosquitoes fed early and outdoors, and would repeat those behaviours, some fed late at night or indoors in the next feeding cycle). **CONCLUSIONS:** The finding that *An. farauti* is a homogeneous population is significant, because during the multiple feeding

cycles required to complete the extrinsic incubation period, many individual female anophelines will enter houses late at night and be exposed to the insecticides used in LLINs or IRS. This explains, in part, the control that LLINs and IRS have exerted against a predominantly outdoor feeding vector, such as *An. farauti*. These findings may be relevant to many of the outdoor feeding vectors that dominate transmission in much of the malaria endemic world and justifies continued use of LLINs. However, the population-level tendency of mosquitoes to feed outdoors and early in the evening does require complementary interventions to accelerate malaria control towards elimination.

- 56 **Russell TL, Burkot TR, Bugoro H, Apairamo A, Beebe NW, Chow WK, Cooper RD, Collins FH, Lobo NF.**

Larval habitats of the *Anopheles farauti* and *Anopheles lungae* complexes in the Solomon Islands.

Malar J 2016 Mar 15;15(1):164. doi: 10.1186/s12936-016-1196-7.

BACKGROUND: There is an urgent need for vector control tools to supplement long-lasting insecticidal nets (LLINs) and indoor residual spraying, particularly in the Solomon Islands, where the primary vector, *Anopheles farauti*, is highly anthropophilic and feeds mainly outdoors and early in the evening. Currently, the only supplementary tool recommended by the World Health Organization is larval source management (LSM). The feasibility and potential effectiveness of LSM requires information on the distribution of anophelines, the productivity of larval habitats and the potential impacts of larval control on adult fitness. **METHODS:** The distribution of anophelines in Central and Western Provinces in the Solomon Islands was mapped from cross-sectional larval habitat surveys. The composition and micro-distribution of larval instars within a large permanent river-mouth lagoon was examined with a longitudinal survey. Density-dependent regulation of *An. farauti* larvae was investigated by longitudinally following the development and survival of different densities of first instars in floating cages in a river-mouth lagoon. **RESULTS:** Five anopheline species were molecularly identified from a range of fresh and brackish water habitats: *An. farauti* s.s., *An. hinesorum*, *An. lungae*, *An. nataliae* and *An. solomonis*. The most common habitats used by the primary malaria vector, *An. farauti*, were coastal lagoons and swamps. In the detailed study of lagoon micro-productivity, *An. farauti* was non-uniformly distributed with highest densities found at collection sites most proximal and distal to the mouth of the lagoon. The survival of *An. farauti* larvae was more than twofold lower when larvae were held at the highest experimental density (1 larva per 3.8 cm²) when compared with the lowest density (1 larva per 38 cm²). **CONCLUSIONS:** The only documented major malaria vector collected in larval surveys in both Central and Western Provinces was *An. farauti*. Lagoons and swamps, the most common, largest and (potentially) most productive larval sites of this malaria vector, were 'few, fixed and findable' and theoretically, therefore, amenable to successful LSM. However, the immense scale and complexity of these ecosystems in which *An. farauti* larvae are found raises questions regarding the ability to effectively control the larvae, as incomplete larviciding could trigger density dependent effects resulting in increased larval survivorship. While

LSM has the potential to significantly contribute to malaria control of this early and outdoor biting vector, more information on the distribution of larvae within these extensive habitats is required to maximize the effectiveness of LSM.

- 57 **Russell TL, Beebe NW, Bugoro H, Apairamo A, Chow WK, Cooper RD, Collins FH, Lobo NF, Burkot TR.**

Frequent blood feeding enables insecticide-treated nets to reduce transmission by mosquitoes that bite predominately outdoors.

Malar J 2016 Mar 10;15(1):156. doi: 10.1186/s12936-016-1195-8.

BACKGROUND: The effectiveness of vector control on malaria transmission by long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS) depends on the vectors entering houses to blood feed and rest when people are inside houses. In the Solomon Islands, significant reductions in malaria have been achieved in the past 20 years with insecticide-treated bed nets, IRS, improved diagnosis and treatment with artemisinin combination therapies, despite the preference of the primary vector, *Anopheles farauti*, to feed outdoors and early in the evening and thereby avoid potential exposure to insecticides. Rational development of tools to complement LLINs and IRS by attacking vectors outdoors requires detailed knowledge of the biology and behaviours of the target species. **METHODS:** Malaria transmission in Central Province, Solomon Islands was estimated by measuring the components comprising the entomological inoculation rate (EIR) as well as the vectorial capacity of *An. farauti*. In addition, the daily and seasonal biting behaviour of *An. farauti* was examined and the duration of the feeding cycle was estimated with a mark-release-recapture experiment. **RESULTS:** *Anopheles farauti* was highly exophagic with 72% captured by human landing catches (HLC) outside of houses. Three-quarters (76%) of blood feeding on humans was estimated to occur before 21.00 h. When the hourly location of humans was considered, the proportion of exposure to mosquito bites on humans occurring indoors (π) was only 0.130 ± 0.129 . Peak densities of host seeking *An. farauti* occurred between October and January. The annual EIR was estimated to be 2.5 for 2012 and 33.2 for 2013. The length of the feeding cycle was 2.1 days. **CONCLUSIONS:** The short duration of the feeding cycle by this species offers an explanation for the substantial control of malaria that has been achieved in the Solomon Islands by LLINs and IRS. *Anopheles farauti* is primarily exophagic and early biting, with 13% of mosquitoes entering houses to feed late at night during each feeding cycle. The two-day feeding cycle of *An. farauti* requires females to take 5-6 blood meals before the extrinsic incubation period (EIP) is completed, and this could translate into substantial population-level mortality by LLINs or IRS before females would be infectious to humans with *Plasmodium falciparum* and *Plasmodium vivax*. Although *An. farauti* is primarily exophagic, the indoor vector control tools recommended by the World Health Organization (LLINs and IRS) can still provide an important level of control. Nonetheless, elimination will likely require vector control tools that target other bionomic vulnerabilities to suppress transmission outdoors and that complement the control provided by LLINs and IRS.

- 58 **Russell TL, Beebe NW, Bugoro H, Apairamo A, Cooper RD, Collins FH, Lobo NF, Burkot TR.**

Determinants of host feeding success by *Anopheles farauti*.

Malar J 2016 Mar 10;15(1):152. doi: 1186/s12936-016-1168-y.

BACKGROUND: The proportion of blood meals that mosquitoes take from a host species is a function of the interplay of extrinsic (abundance and location of potential hosts) and intrinsic (innate preference) factors. A mark-release-recapture experiment addressed whether host preference in a population of *Anopheles farauti* was uniform or if there were anthropophilic and zoophilic subpopulations. The corresponding fitness associated with selecting different hosts for blood meals was compared by measuring fecundity. **METHODS:** The attractiveness of humans for blood meals by *An. farauti* in the Solomon Islands was compared to pigs using tent traps. Host fidelity was assessed by mark-release-recapture experiments in which different colour dusts were linked to the host to which the mosquito was first attracted. Outdoor resting *An. farauti* were captured on barrier screens and the human blood index (HBI) as well as the feeding index were calculated. The fecundity of individual *An. farauti* after feeding on either humans or pigs was assessed from blood-fed mosquitoes held in individual oviposition chambers. **RESULTS:** *Anopheles farauti* were more attracted to humans than pigs at a ratio of 1.31:1.00. The mark-release-recapture experiment found evidence for *An. farauti* being a single population regarding host preference. The HBI of outdoor resting *An. farauti* was 0.93 and the feeding index was 1.29. *Anopheles farauti* that fed on a human host laid more eggs but had a longer oviposition time compared to *An. farauti* that had blood fed on a pig. **CONCLUSIONS:** One of the strongest drivers for host species preference was the relative abundance of the different host species. Here, *An. farauti* have a slight preference for humans over pigs as blood meal sources. However, the limited availability of alternative hosts relative to humans in the Solomon Islands ensures a very high proportion of blood meals are obtained from humans, and thus the transmission potential of malaria by *An. farauti* is high.

- 59 **Santos C, Phillips C, Fondevila M, Daniel R, van Oorschot RA, Burchard EG, Schanfield MS, Souto L, Uacyisrael J, Via M, Carracedo A, Lareu MV.**

Pacifiplex: an ancestry-informative SNP panel centred on Australia and the Pacific region.

Forensic Sci Int Genet 2016 Jan;20:71-80. doi: 10.1016/j.fsigen.2015.10.003. Epub 2015 Oct 20.

The analysis of human population variation is an area of considerable interest in the forensic, medical genetics and anthropological fields. Several forensic single nucleotide polymorphism (SNP) assays provide ancestry-informative genotypes in sensitive tests designed to work with limited DNA samples, including a 34-SNP multiplex differentiating African, European and East Asian ancestries. Although assays capable of differentiating Oceanian ancestry at a global scale have become available, this study describes markers compiled specifically for differentiation of Oceanian populations. A sensitive multiplex assay, termed Pacifiplex, was developed and optimized in a small-scale test applicable to forensic analyses. The Pacifiplex assay comprises 29 ancestry-informative marker SNPs (AIM-SNPs)

selected to complement the 34-plex test that in a combined set distinguish Africans, Europeans, East Asians and Oceanians. Nine Pacific region study populations were genotyped with both SNP assays, then compared to four reference population groups from the HGDP-CEPH human diversity panel. STRUCTURE analyses estimated population cluster membership proportions that aligned with the patterns of variation suggested for each study population's currently inferred demographic histories. Aboriginal Taiwanese and Philippine samples indicated high East Asian ancestry components, Papua New Guinean and Aboriginal Australian samples were predominantly Oceanian, while other populations displayed cluster patterns explained by the distribution of divergence amongst Melanesians, Polynesians and Micronesians. Genotype data from Paciflex and 34-plex tests are particularly well suited to analysis of Australian Aboriginal populations and when combined with Y and mitochondrial DNA variation will provide a powerful set of markers for ancestry inference applied to modern Australian demographic profiles. On a broader geographic scale, Paciflex adds highly informative data for inferring the ancestry of individuals from Oceanian populations. The sensitivity of Paciflex enabled successful genotyping of population samples from 50-year-old serum samples obtained from several Oceanian regions that would otherwise be unlikely to produce useful population data. This indicates that tests primarily developed for forensic ancestry analysis also provide an important contribution to studies of populations where useful samples are in limited supply.

- 60 **Small ST, Reimer LJ, Tisch DJ, King CL, Christensen BM, Siba PM, Kazura JW, Serre D, Zimmerman PA.**

Population genomics of the filarial nematode parasite *Wuchereria bancrofti* from mosquitoes. *Mol Ecol* 2016 Apr;25(7):1465-1477. doi: 10.1111/mec.13574. Epub 2016 Mar 15.

Wuchereria bancrofti is a parasitic nematode and the primary cause of lymphatic filariasis – a disease specific to humans. *W. bancrofti* currently infects over 90 million people throughout the tropics and has been acknowledged by the World Health Organization as a vulnerable parasite. Current research has focused primarily on the clinical manifestations of disease and little is known about the evolutionary history of *W. bancrofti*. To improve upon knowledge of the evolutionary history of *W. bancrofti*, we whole genome sequenced 13 *W. bancrofti* larvae. We circumvent many of the difficulties of multiple infections by sampling larvae directly from mosquitoes that were experimentally inoculated with infected blood. To begin, we used whole genome data to reconstruct the historical population size. Our results support a history of fluctuating population sizes that can be correlated with human migration and fluctuating mosquito abundances. Next, we reconstructed the putative pedigree of *W. bancrofti* worms within an infection using the kinship coefficient. We deduced that there are full-sib and half-sib relationships residing within the same larval cohort. Through combined analysis of the mitochondrial and nuclear genomes we concluded that this is likely a result of polyandrous mating, the first time reported for *W. bancrofti*. Lastly, we scanned the genomes for signatures of natural selection. Annotation of putative selected

regions identified proteins that may have aided in a parasitic life style or may have evolved to protect against current drug treatments. We discuss our results in the greater context of understanding the biology of an animal with a unique life history and ecology.

- 61 **St Laurent B, Supratman S, Asih PB, Bretz D, Mueller J, Miller HC, Baharuddin A, Shinta, Surya A, Ngai M, Laihad F, Syafruddin D, Hawley WA, Collins FH, Lobo NF.**

Behaviour and molecular identification of *Anopheles* malaria vectors in Jayapura District, Papua Province, Indonesia.

Malar J 2016 Apr 8;15(1):192. doi: 10.1186/s12936-016-1234-5.

BACKGROUND: Members of the *Anopheles punctulatus* group dominate Papua, Indonesia and Papua New Guinea (PNG), with a geographic range that extends south through Vanuatu. *An. farauti* and *An. punctulatus* are the presumed major vectors in this region. Although this group of species has been extensively studied in PNG and the southern archipelagoes within their range, their distribution, ecology and vector behaviours have not been well characterized in eastern Indonesia. **METHODS:** Mosquitoes were collected in five villages in Jayapura District, Papua, Indonesia using human-landing collections, animal-baited tents and backpack aspirators. Mosquitoes were morphologically typed and then molecularly distinguished based on ribosomal ITS2 sequences and tested for *Plasmodium falciparum* and *P. vivax* infection using circumsporozoite ELISA and PCR. **RESULTS:** The presence and vector status of *An. farauti* 4 in Papua, Indonesia is confirmed here for the first time. The data indicate that this species is entering houses at a rate that increases its potential to come into contact with humans and act as a major malaria vector. *An. farauti* 4 was also abundant outdoors and biting humans during early evening hours. Other species collected in this area include *An. farauti* 1, *An. hinesorum*, *An. koliensis*, *An. punctulatus*, and *An. tessellatus*. Proboscis morphology was highly variable within each species, lending support to the notion that this characteristic is not a reliable indicator to distinguish species within the *An. punctulatus* group. **CONCLUSIONS:** The vector composition in Papua, Indonesia is consistent with certain northern areas of PNG, but the behaviours of anophelines sampled in this region, such as early and indoor human biting of *An. farauti* 4, may enable them to act as major vectors of malaria. Presumed major vectors *An. farauti* and *An. punctulatus* were not abundant among these samples. Morphological identification of anophelines in this sample was often inaccurate, highlighting the importance of using molecular analysis in conjunction with morphological investigations to update keys and training tools.

- 62 **Tanimia H, Jayaratnam S, Mola GL, Amoa AB, de Costa C.**

Near-misses at the Port Moresby General Hospital: a descriptive study.

Aust NZ J Obstet Gynaecol 2016 Apr;56(2):148-153. doi: 10.1111/ajo.12430. Epub 2016 Feb 3.

BACKGROUND: The World Health Organization (WHO) defines 'maternal near-miss' as 'a woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of her pregnancy'. With declining

rates of maternal mortality, near-miss analysis is being examined in both developed and developing country settings for the assessment of obstetric care. AIMS: Over a 15-month period, details of cases that could be classified as 'near-misses' were collected at Port Moresby General Hospital (PMGH) to assess the practicality of collecting such data routinely and determine near-miss rates for the hospital. MATERIALS AND METHODS: Information about all cases that fitted the WHO definition of 'near-miss' was collected prospectively. RESULTS: During the audit period, there were 13 338 live births at PMGH; 131 women presented with a life-threatening condition of whom 122 met WHO criteria for 'maternal near-miss'; there were nine maternal deaths. The maternal mortality ratio was 67.5/100 000 live births, the maternal near-miss index ratio 9.1/1000 live births and the combination of maternal deaths and near-misses gave a severe maternal outcome ratio of 9.8/1000 live births. Main causes of the 'near-misses' were obstetric haemorrhage, hypertensive disorders and infections. Grandmultiparity, nulliparity, no antenatal attendance and age beyond 30 years were associated with maternal near-misses. CONCLUSION: Assessment of near-misses equivalent to that provided in developed countries is possible in less well-resourced settings such as PMGH. Knowledge of causes of near-misses will assist health professionals to anticipate or prevent devastating maternal morbidities and thereby improve maternal and perinatal outcomes.

63 **Tay AK, Rees S, Kareth M, Silove D.**

Associations of adult separation anxiety disorder with conflict-related trauma, ongoing adversity, and the psychosocial disruptions of mass conflict among West Papuan refugees.

Am J Orthopsychiatry 2016 Mar;86(2):224-235. doi: 10.1037/ort0000126. Epub 2016 Jan 11.

Refugees commonly experience traumatic events that threaten the self and close others, suggesting the possibility that they may experience overlapping symptoms of posttraumatic stress disorder (PTSD) and separation anxiety disorder (SAD). We examine this possibility among West Papuan refugees (n = 230) displaced to Port Moresby, Papua New Guinea. We also examine associations between the combined PTSD-SAD construct and indices of past trauma exposure, ongoing adversity, and the psychosocial disruptions caused by mass conflict and displacement. We applied culturally adapted interview modules to assess symptoms of PTSD, SAD, traumatic events (TEs), ongoing adversity, and 5 psychosocial dimensions. Latent class analysis identified a PTSD class (23%), a posttraumatic (PT) SAD class (22%), and a low-symptom class (55%). Compared with the low-symptom class, both the PTSD and PT-SAD classes endorsed higher levels of exposure to all domains of TEs (conflict-related trauma, witnessing murder, childhood related adversities, traumatic losses, and health stress) and ongoing adversity (access to health care, displacement/separation, safety in the community, and access to basic needs), but the 2 comorbid groups did not differ on these indices. The PT-SAD class alone scored higher than the low-symptom reference class in relation to disruptions to the psychosocial domains (safety/security, bonds/network, access to justice, roles/identities, existential meaning) and higher than the PTSD class on safety/security, justice and roles/identities. Our findings

suggest that the PT-SAD pattern may represent a response to the most severe forms of psychosocial disruptions of mass conflict among refugees. A focus on separation anxiety may enhance psychotherapies designed to treat PTSD in refugees.

64 **Tay AK, Rees S, Chen J, Kareth M, Silove D.**

Factorial structure of complicated grief: associations with loss-related traumatic events and psychosocial impacts of mass conflict amongst West Papuan refugees.

Soc Psychiatry Psychiatr Epidemiol 2016 Mar;51(3):395-406. doi: 10.1007/s00127-015-1099-x.

INTRODUCTION: Definitions of complicated grief vary across diagnostic systems, being represented as persistent complex bereavement (PCB) in DSM-5 and prolonged grief disorder (PGD) in the proposed revision of the ICD system. A past study in a high-income country has identified a six-factor structure for complicated grief, but there are no data testing this or any other model across cultures. The present study reports findings from a survey amongst West Papuan refugees (n = 230, response rate = 92%) residing in Port Moresby, Papua New Guinea. MATERIALS AND METHODS: We applied culturally adapted measures of conflict-related traumatic events (TEs) (drawing specifically on domains of conflict and loss), symptoms of complicated grief adapted and modified to the culture, and a multidimensional psychosocial index of the broader effects of conflict and displacement. RESULTS: Confirmatory factor analysis yielded a single higher order construct of complicated grief comprising six factors of yearning/preoccupation; shock/disbelief; anger/negative appraisal; behavioural change; estrangement from others/impairment; and a novel dimension of confusion/diminished identity. In contrast, our analysis failed to support DSM or ICD models of PCB or PGD. A Multiple Indicators Multiple Causes (MIMIC) model revealed that traumatic loss and the sense of injustice each were associated with the unitary construct of complicated grief and its subdomains of yearning/preoccupation; shock/disbelief; anger/negative appraisal (exclusive to injustice); and estrangement from others/social impairment (exclusive to TE domain of conflict and loss). CONCLUSIONS: Conflict and loss associated with feelings of injustice may be especially pathogenic in generating the anger/negative appraisal component of complicated grief amongst refugees.

65 **Thomsen EK, Sanuku N, Baea M, Satofan S, Maki E, Lombore B, Schmidt MS, Siba PM, Weil GJ, Kazura JW, Fleckenstein LL, King CL.**

Efficacy, safety, and pharmacokinetics of coadministered diethylcarbamazine, albendazole, and ivermectin for treatment of bancroftian filariasis. *Clin Infect Dis* 2016 Feb 1;62(3):334-341. doi: 10.1093/cid/civ882. Epub 2015 Oct 20.

BACKGROUND: Available treatments for lymphatic filariasis (LF) are limited in their longterm clearance of microfilaria from the blood. The safety and efficacy of a single-dose triple-drug therapy of the antifilarial drugs diethylcarbamazine (DEC), ivermectin (IVM), and albendazole (ALB) for LF are unknown. METHODS: We performed a pilot study to test the efficacy, safety, and pharmacokinetics of single-dose DEC, IVM, and ALB in *Wuchereria bancrofti*-infected Papua New Guineans. Adults

were randomized into 2 treatment arms, DEC 6 mg/kg + ALB 400 mg (N = 12) or DEC 6 mg/kg + ALB 400 mg + IVM 200 µg/kg (N = 12), and monitored for microfilaria, parasite antigenemia, adverse events (AEs), and serum drug levels. **RESULTS:** Triple-drug therapy induced >2-log reductions in microfilaria levels at 36 and 168 hours after treatment compared with approximately 1-log reduction with 2 drugs. All 12 individuals who received 3 drugs were microfilaria negative 1 year after treatment, whereas 11 of 12 individuals in the 2-drug regimen were microfilaria positive. In 6 participants followed 2 years after treatment, those who received 3 drugs remained microfilaria negative. AEs, particularly fever, myalgias, pruritus, and proteinuria/hematuria, occurred in 83% vs 50% of those receiving triple-drug compared to 2-drug treatment respectively (p = 0.021); all resolved within 7 days after treatment. No serious AEs were observed in either group. There was no significant effect of IVM on DEC or ALB drug levels. **CONCLUSIONS:** Triple-drug therapy is safe and more effective than DEC + ALB for bancroftian filariasis and has the potential to accelerate elimination of lymphatic filariasis.

66 **Tierney D, Bolton P, Matanu B, Garasu L, Barnabas E, Silove D.**

The mental health and psychosocial impact of the Bougainville Crisis: a synthesis of available information.

Int J Ment Health Syst 2016 Mar 3;10:18. doi: 10.1186/s13033-016-0054-x. eCollection 2016.

BACKGROUND: The Bougainville Crisis (1988-1997) was the largest armed conflict in the Pacific since WW-II. Despite this, there has been no assessment of the mental health and psychosocial (MHPS) impact of the war. The aim of this paper is to summarize the available data regarding the longer-term MHPS impact of the Bougainville Crisis. **METHODS:** A literature review and a sequence of consultations in Bougainville were conducted to identify the MHPS impact of the Bougainville Crisis and the capacity within Bougainville to address these issues. **RESULTS:** The Bougainville Crisis resulted in violence-related deaths; the displacement of more than half of the population; widespread human rights abuses; far-reaching societal impacts including undermining of the traditional authority of elders and women and damage to cultural values and relationships; property damage; and significant impacts on education and the economy. Conflict-related experiences continue to impact on mental health in the form of trauma-related symptoms, anger, complicated grief, alcohol and substance abuse, domestic violence including sexual assault, excessive alcohol use and a lack of engagement in purposeful activities. Other impacts include an increase in other forms of gender-based violence (including sexual assault), population displacement, and adverse trans-generational effects on children exposed to disturbed parental behaviours attributable to conflict exposure. In spite of the evident needs, there is limited capacity within Bougainville to address these pressing MHPS issues. **CONCLUSIONS:** The Bougainville Crisis has had a significant MHPS impact at multiple levels in the society. There is a strong interest within Bougainville to draw on external expertise to build local capacity to address MHPS issues. Preliminary recommendations are made to assist the process of building the capacity in Bougainville to address

MHPS needs.

67 **Trauer JM, Denholm JT, Waseem S, Ragonnet R, McBryde ES.**

Scenario analysis for programmatic tuberculosis control in Western Province, Papua New Guinea. *Am J Epidemiol* 2016 Jun 15;183(12):1138-1148. doi: 10.1093/aje/kwv323. Epub 2016 May 19.

Tuberculosis (TB) and multidrug-resistant TB (MDR-TB) are major health problems in Western Province, Papua New Guinea. While comprehensive expansion of TB control programs is desirable, logistical challenges are considerable, and there is substantial uncertainty regarding the true disease burden. We parameterized our previously described mathematical model of *Mycobacterium tuberculosis* dynamics in Western Province, following an epidemiologic assessment. Five hypothetical scenarios representing alternative programmatic approaches during the period from 2013 to 2023 were developed with local staff. Bayesian uncertainty analyses were undertaken to explicitly acknowledge the uncertainty around key epidemiologic parameters, and an economic evaluation was performed. With continuation of existing programmatic strategies, overall TB incidence remained stable at 555 cases per 100,000 population per year (95% simulation interval (SI): 420-807), but the proportion of incident cases attributable to MDR-TB increased from 16% to 35%. Comprehensive, province-wide strengthening of existing programs reduced incidence to 353 cases per 100,000 population per year (95% SI: 246-558), with 46% being cases of MDR-TB, while incorporating programmatic management of MDR-TB into these programs reduced incidence to 233 cases per 100,000 population per year (95% SI: 198-269) with 14% MDR-TB. Most economic costs were due to hospitalization during the intensive treatment phase. Broad scale-up of TB control activities in Western Province with incorporation of programmatic management of MDR-TB is vital if control is to be achieved. Community-based treatment approaches are important to reduce the associated economic costs.

68 **Umezaki M, Naito YI, Tsutaya T, Baba J, Tadokoro K, Odani S, Morita A, Natsuhara K, Phuanukoonnon S, Vengiau G, Siba PM, Yoneda M.**

Association between sex inequality in animal protein intake and economic development in the Papua New Guinea highlands: the carbon and nitrogen isotopic composition of scalp hair and fingernail.

Am J Phys Anthropol 2016 Jan;159(1):164-173. doi: 10.1002/ajpa.22844. Epub 2015 Sep 2.

OBJECTIVES: People in the Papua New Guinea Highlands consume sweet potatoes as their dietary staple; consumption of animal protein is limited. In such societies with marginal protein intake, the intra-household allocation of animal protein in terms of sex or age is of importance. The objective of this study was to investigate how the allocation pattern of protein-rich foods by sex and age is associated with economic development in the Papua New Guinea Highlands. **METHODS:** The carbon and nitrogen isotopic compositions of fingernails, collected in 1995 in two areas (Tari and Port Moresby [the national capital where Tari migrants resided]), and of scalp hair, collected in 2007, 2012, and 2013 in three areas of different degree of economic development

(Levani, Tari and Goroka), were analyzed. RESULTS: Analysis of fingernail samples showed that $\delta^{15}\text{N}$ was lower in rural communities than in the urban migrant community, while a sex difference in $\delta^{15}\text{N}$ (higher in males than in females) was found in the former but not in the latter community. Age was not associated with either $\delta^{15}\text{N}$ or $\delta^{13}\text{C}$ values. The analysis of scalp hair samples showed that $\delta^{15}\text{N}$ values were lowest in Levani, the least developed area. Furthermore, there were statistically significant sex differences in $\delta^{15}\text{N}$ values in Levani but not in Tari and Goroka. Age was not associated with either $\delta^{15}\text{N}$ or $\delta^{13}\text{C}$ values. DISCUSSION: The sex inequality in animal protein consumption seems to have decreased as the communities in the Papua New Guinea Highlands have experienced economic development.

- 69 **Valentin F, Détoit F, Spriggs MJ, Bedford S.** Early Lapita skeletons from Vanuatu show Polynesian craniofacial shape: implications for Remote Oceanic settlement and Lapita origins. *Proc Natl Acad Sci USA* 2016 Jan 12;113(2):292-297. doi: 10.1073/pnas.1516186113. Epub 2015 Dec 28.

With a cultural and linguistic origin in Island Southeast Asia the Lapita expansion is thought to have led ultimately to the Polynesian settlement of the east Polynesian region after a time of mixing/integration in north Melanesia and a nearly 2,000-y pause in West Polynesia. One of the major achievements of recent Lapita research in Vanuatu has been the discovery of the oldest cemetery found so far in the Pacific at Teouma on the south coast of Efate Island, opening up new prospects for the biological definition of the early settlers of the archipelago and of Remote Oceania in general. Using craniometric evidence from the skeletons in conjunction with archaeological data, we discuss here four debated issues: the Lapita-Asian connection, the degree of admixture, the Lapita-Polynesian connection, and the question of secondary population movement into Remote Oceania.

- 70 **Vallely LM, Homiehombo P, Walep E, Moses M, Tom M, Kelly-Hanku A, Vallely A, Nataraye E, Ninnes C, Mola GD, Morgan C, Kaldor JM, Wand H, Whittaker A, Homer CS.**

Feasibility and acceptability of clean birth kits containing misoprostol for self-administration to prevent postpartum hemorrhage in rural Papua New Guinea.

Int J Gynaecol Obstet 2016 Jun;133(3):301-306. doi: 10.1016/j.ijgo.2015.10.018. Epub 2016 Feb 24.

OBJECTIVE: To determine the feasibility and acceptability of providing clean birth kits (CBKs) containing misoprostol for self-administration in a rural setting in Papua New Guinea. METHODS: A prospective intervention study was conducted between April 8, 2013 and October 24, 2014. Eligible participants were women in the third trimester of pregnancy who attended a prenatal clinic in Unggai Bena. Participants received individual instruction and were then given a CBK containing 600µg misoprostol tablets for self-administration following an unsupervised birth if they could demonstrate their understanding of correct use of items in the CBK. Data regarding the use and acceptability of the CBK and misoprostol were collected during postpartum follow-up. RESULTS: Among 200 participants, 106

(53.0%) had an unsupervised birth, and 99 (93.4%) of these women used the CBK. All would use the CBK again and would recommend it to others. Among these 99 women, misoprostol was self-administered by 98 (99.0%), all of whom would take the drug again and would recommend it to others. CONCLUSION: The findings strengthen the case for community-based use of misoprostol to prevent postpartum hemorrhage in remote communities. Large-scale interventions should be planned to further evaluate impact and acceptability.

- 71 **Vernot B, Tucci S, Kelso J, Schraiber JG, Wolf AB, Gittelman RM, Dannemann M, Grote S, McCoy RC, Norton H, Scheinfeldt LB, Merriwether DA, Koki G, Friedlaender JS, Wakefield J, Pääbo S, Akey JM.**

Excavating Neandertal and Denisovan DNA from the genomes of Melanesian individuals.

Science 2016 Apr 8;352(6282):235-239. doi: 10.1126/science.aad9416. Epub 2016 Mar 17.

Although Neandertal sequences that persist in the genomes of modern humans have been identified in Eurasians, comparable studies in people whose ancestors hybridized with both Neandertals and Denisovans are lacking. We developed an approach to identify DNA inherited from multiple archaic hominin ancestors and applied it to whole-genome sequences from 1523 geographically diverse individuals, including 35 previously unknown Island Melanesian genomes. In aggregate, we recovered 1.34 gigabases and 303 megabases of the Neandertal and Denisovan genome, respectively. We use these maps of archaic sequences to show that Neandertal admixture occurred multiple times in different non-African populations, characterize genomic regions that are significantly depleted of archaic sequences, and identify signatures of adaptive introgression.

- 72 **Wellsh BM, Kuzma JM.**

Ultrasound-guided pediatric forearm fracture reductions in a resource-limited ED.

Am J Emerg Med 2016 Jan;34(1):40-44. doi: 10.1016/j.ajem.2015.09.013. Epub 2015 Sep 21.

BACKGROUND: Pediatric forearm fractures are a common presentation in emergency departments in Papua New Guinea. Often these children undergo 'blind' closed reduction with reduction adequacy assessed by standard radiographs. This study aims to demonstrate the safety and efficacy of ultrasound (US) in guiding closed reduction of pediatric forearm fractures in a resource-limited setting. METHODS: We recruited consecutive children with closed forearm fractures requiring reduction. A US scanner was used to visualize and aid fracture reductions. The outcome measures were the rate of successful reductions (ie, adequate alignment without the need for a second procedure or further surgical intervention), length of stay in hospital, and adverse events during each procedure and at follow-up after 6 weeks. RESULTS: Of 47 children recruited, there were 44 (94%) successful reductions, whereas 3 (6%) required repeated reduction. The mean (SD) length of stay in hospital of the successful cases was 8.77 (3.66) hours. Two patients had tight plaster casts during early follow-up which were immediately addressed. Of the 44 successful cases, only 38 were retrieved for the final review. No further adverse events were observed in the latter. CONCLUSIONS: This small-scale study has demonstrated the safe

and efficacious use of US-guided closed reduction of pediatric forearm fractures in a low-resource setting. Using US, real-time visualization of reduction efforts can reassure the clinician in decision-making, thus reducing the rate of repeated reductions and allowing shorter hospital stay.

- 73 **Wen S, Harvard KE, Gueye CS, Canavati SE, Chancellor A, Ahmed BN, Leaburi J, Lek D, Namgay R, Surya A, Thakur GD, Whittaker MA, Gosling RD.**

Targeting populations at higher risk for malaria: a survey of national malaria elimination programmes in the Asia Pacific.

Malar J 2016 May 10;15(1):271. doi: 10.1186/s12936-016-1319-1.

BACKGROUND: Significant progress has been made in reducing the malaria burden in the Asia Pacific region, which is aggressively pursuing a 2030 regional elimination goal. Moving from malaria control to elimination requires national malaria control programmes (NMCPs) to target interventions at populations at higher risk, who are often not reached by health services, highly mobile and difficult to test, treat, and track with routine measures, and if undiagnosed, can maintain parasite reservoirs and contribute to ongoing transmission. **METHODS:** A qualitative, free-text questionnaire was developed and disseminated among 17 of the 18 partner countries of the Asia Pacific Malaria Elimination Network (APMEN). **RESULTS:** All 14 countries that responded to the survey identified key populations at higher risk of malaria in their respective countries. Thirteen countries engage in the dissemination of malaria-related Information, Education, and Communication (IEC) materials. Eight countries engage in diagnostic screening, including of mobile and migrant workers, military staff, and/or overseas workers. Ten countries reported distributing or recommending the use of long-lasting insecticide-treated nets (LLINs) among populations at higher risk, with fewer countries engaging in other prevention measures such as indoor residual spraying (IRS) (two countries), spatial repellents (four countries), chemoprophylaxis (five countries), and mass drug administration (MDA) (three countries). Though not specifically tailored to populations at higher risk, 11 countries reported using mass blood surveys as a surveillance tool and ten countries map case data. Most NMCPs lack a monitoring and evaluation structure. **CONCLUSION:** Countries in the Asia Pacific have identified populations at higher risk and targeted interventions to these groups but there is limited information on the effectiveness of these interventions. Platforms like APMEN offer the opportunity for the sharing of protocols and lessons learned related to finding, targeting and successfully clearing malaria from populations at higher risk. The sharing of programme data across borders may further strengthen national and regional efforts to eliminate malaria. This exchange of real-life experience is invaluable to NMCPs when scarce scientific evidence on the topic exists to aid decision-making and can further support NMCPs to develop strategies that will deliver a malaria-free Asia Pacific by 2030.

- 74 **Wiesen E, Lagani W, Sui G, Arava J, Reza S, Diorditsa S, Lin YC.**

Assessment of the hepatitis B birth dose vaccination

program, Papua New Guinea, 2014.

Vaccine 2016 Jan 12;34(3):367-372. doi: 10.1016/j.vaccine.2015.11.044. Epub 2015.

INTRODUCTION: Papua New Guinea (PNG) implemented hepatitis B birth dose (BD) vaccination in 2005 yet since that time coverage has remained low, allowing mother-to-child transmission to occur. We conducted a field assessment of the BD vaccination program to develop strategies for improving the BD coverage. **METHODS:** We selected five provinces with higher hepatitis B prevalence and five with lower prevalence based on the results of a 2013 hepatitis B serological survey. Within each province, we interviewed district and provincial health officers, health workers, village volunteers, and caregivers from ten randomly selected health facilities. Data were collected on knowledge, practice, vaccine management and data recording/reporting. To identify enabling factors and barriers, we compared health facilities with higher BD coverage with those with lower coverage, and compared caregivers whose children received BD with those whose children did not. **RESULTS:** Overall timely BD coverage was 31% and BD vaccination was taking place in 81% of sampled health facilities. Lack of cold chain and vaccine were the major reasons for not providing the BD. Insufficiencies in supervision, vaccine management, community outreach, and data management were identified as obstacles to achieving high timely hepatitis B BD coverage. Good supervision, knowledge of hepatitis B and hepatitis B vaccination, antenatal care including information about the hepatitis B BD, provision of vaccine refrigerators in maternity wards, and outreach vaccination for home deliveries were associated with higher timely BD coverage. **DISCUSSION:** Several steps will likely be effective in improving BD coverage: strengthening training and supervision among health workers and officers, educating caregivers on the benefits of the BD and delivery in health facilities, improving vaccine management, and improving data quality. Considerable effort and leadership will be needed to achieve these steps.

- 75 **Williams DE, Izard F, Arnould S, Dalisay DS, Tantapakul C, Maneerat W, Matainaho T, Julien E, Andersen RJ.**

Structures of nahuic acids B-E produced in culture by a *Streptomyces* sp. isolated from a marine sediment and evidence for the inhibition of the histone methyl transferase SETD8 in human cancer cells by nahuic acid A.

J Org Chem 2016 Feb 19;81(4):1324-1332. doi: 10.1021/acs.joc.5b02569. Epub 2016 Feb 1.

Nahuic acids A-E (1-5) have been isolated from laboratory cultures of a *Streptomyces* sp. obtained from a tropical marine sediment. The structures of the new polyketides 2-5 were elucidated by analysis of spectroscopic data of the natural products and the chemical derivatives 6 and 7. Nahuic acids 1-5 are in vitro inhibitors of the histone methyltransferase SETD8, and nahuic acid A (1) and its pentaacetate derivative 8 inhibit the proliferation of several cancer cell lines in vitro with modest potency. At the IC₅₀ for cancer cell proliferation, nahuic acid A (1) showed selective inhibition of SETD8 in U2OS osteosarcoma cells that reflect its selectivity against a panel of pure histone methyl transferases. A cell cycle analysis revealed that the cellular toxicity of nahuic acid A (1)

is likely linked to its ability to inhibit SETD8 activity.

76 **Wirth KE.**

Alternative forms of penile foreskin cutting and HIV infection in Papua New Guinea.

Sex Transm Infect 2016 May;92(3):193. doi: 10.1136/sextrans-2015-052317.

77 **Yang YM, Hsiao SH, Chou FH, Hou L, Lee SL, Lin YH.**

Health care providers' perceptions of maternal health concerns in the Solomon Islands.

J Transcult Nurs 2016 Jan;27(1):49-56. doi: 10.1177/1043659614526256. Epub 2014 May 20.

PURPOSE: The objective of this study was to explore the maternal health risk factors and sentinel events among women in the Solomon Islands, from the viewpoints of health care providers in the Solomon Islands. **DESIGN AND METHOD:** Three focus group interviews were conducted in July and August 2011 at a secondary referral hospital in an

urban area. The study consisted of 10 registered nurses and 11 skilled birth assistants. Thematic analysis was used for this qualitative data analysis. **FINDINGS:** Six major themes emerged from the data: (a) environmental hazard: malaria, (b) malnutrition: iron deficiency anemia, (c) adolescent pregnancy, (d) betel nut chewing, (e) cultural beliefs influencing women's health, and (f) difficulty accessing health care services. **CONCLUSIONS AND IMPLICATIONS FOR PRACTICE:** The results of this study provide a useful first step toward identifying specific maternal health risks among women in the Solomon Islands. The findings may assist the health sector and midwives/antenatal educators to better understand the health risks and reduce the disease burden among pregnant women in South Pacific countries. The results may also contribute to the development of policies to improve maternal health and to accelerate progress toward the fifth target goal of UNICEF's Millennium Development Goals.

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- 4 **Cochrane RG.** A critical appraisal of the present position of leprosy. In: Lincicome DP, ed. *International Review of Tropical Medicine*. New York: Academic Press, 1961:1-42.

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CONTENTS

EDITORIAL

- A case for the introduction of a rotavirus vaccine in Papua New Guinea *A.R. Greenhill, M.H. Danchin, W. Pomat and P.F. Horwood* 129

Neglected Diseases

ORIGINAL ARTICLES

- Challenges of diagnosing leprosy in a rural low-endemic setting in Papua New Guinea
K. Yaku, N. Berry, C. Asuak, J. Kumai and R.A. Wangnapi 134
- Towards elimination of yaws in Papua New Guinea *W. Houinej, R.A. Wangnapi, J. Wangi, M.Y. Abdad, M. Marks, L.N. John, S.V. Bieb and O. Mitjà* 137
- Shigellosis: a truly neglected disease in Papua New Guinea *E. Malau, J. Mosse, P.F. Horwood and A.R. Greenhill* 147

ORIGINAL ARTICLES

- Bacterial profile and antimicrobial susceptibility patterns in primary surgical infections at Modilon Hospital, Papua New Guinea *J.M. Kuzma, F.W. Hombhanje, J. Pawiying and M.V. Hombhanje* 155
- "I have a heart to help the mothers": 25 years of the Village Birth Attendant Program in Milne Bay Province, Papua New Guinea *L.M. Vallety, R. Paul, B. Naidi, J. Morewaya, G. Kariwiga, A. Vallety, C. Morgan and C.S.E. Homer* 164
- Sociocultural barriers to access and utilization of birth delivery services in a rural area of Papua New Guinea *N. Ipi, J.D. Vince and G.L. Mola* 178
- Factors associated with lower extremity amputation in patients presenting with diabetic septic foot: a prospective case series *J.G. Nuli, C. Breria, K. Lapu and I. Kevau* 187
- A pilot study of the quality of life among cancer patients attending the Ambulatory Cancer Clinic at Port Moresby General Hospital, Papua New Guinea *G. Gende and S. Mwadede* 191
- Herbal products utilization among patients with HIV/AIDS in East Sepik Province, Papua New Guinea: a pilot survey to determine the prevalence *C. Manineng, M. Baigry, E. Trowalle and F.W. Hombhanje* 196

CASE REPORT

- Wandering spleen with torsion of the pedicle: a case report *J.G. Nuli and K. Lapu* 204

LETTER TO THE EDITOR

- Microscopic observation of *Rodentolepis nana* eggs in a faecal specimen *F.W. Hombhanje, M.V. Hombhanje and J. Pawiying* 207

OBITUARY – TRIBUTES TO DR REGINA WANGNAPI

- Dr Regina Wangnapi – going above and beyond the call of duty *H.W. Unger* 209
- In memory of Regina Alice Wangnapi-Taput *M. Ome-Kaius* 211
- Dr Regina Wangnapi *L. Robinson* 213

PEER REVIEWERS

MEDICAL RESEARCH PROJECTS IN PAPUA NEW GUINEA

MEDLARS BIBLIOGRAPHY

215

216

218