ISSN 0031-1480

PAPUA NEW GUINEA MEDICAL JOURNAL

VOL. 55, NO 1-4, MARCH-DECEMBER 2012

Medical Society of Papua New Guinea

Executive 2012

President:	Nakapi Tefuarani
Vice-President:	Nicholas Mann
Secretary:	Sylvester Lahe
Treasurer:	Glen Mola
Executive Member:	Evelyn Lavu

ACKNOWLEDGEMENT

We are grateful to the Government of Australia through AusAID for providing funding for the publication of this issue of the Journal.

The Editors

Australian Government
AusAID

Published quarterly by the Medical Society of Papua New Guinea

Papua New Guinea Medical Journal

ISSN 0031-1480

March-December 2012, Volume 55, Number 1-4

Email: pngmedj@pngimr.org.pg
Web page: http://www.pngimr.org.pg

* Registered at GPO, Port Moresby for transmission by Post as a Qualified Publication.

* Printed by Moore Printing for the Medical Society of Papua New Guinea.

* Authors preparing manuscripts for publication in the Journal should consult 'Information for Authors' inside back cover.

CONTENTS

PNG Med J 2012 Mar-Dec;55(1-4):1-4

EDITORIAL

The crisis of tuberculosis in Papua New Guinea – the role of older strategies for public health disease control

Tuberculosis (TB) in Papua New Guinea (PNG) is not under control. At the PNG Medical Symposium in 2012 we heard that the prevalence of active tuberculosis disease in some areas is as high as 1.5% of the population. Published studies show that rates of multidrug-resistant (MDR) TB are high: 5.2% was reported from Madang (1); 25% was reported among patients from Western Province treated in Cairns (2); and there are now at least 6 known cases of extensive-drug-resistant (XDR) TB in Western Province. TB is a major cause of mortality and long-term morbidity across the age spectrum. PNG paediatricians from all regions of the country see many children with multisystem tuberculosis, severe meningitis, abdominal or miliary tuberculosis and bronchiectasis (3). These children die, or survive with severe morbidity: neurological disability including cerebral palsy and cognitive impairment, chronic lung disease, crippling spinal deformity or severe malnutrition. Many of these children have had treatment commenced earlier for milder forms of pulmonary TB or suspected TB meningitis, have been discharged within a month, have not adhered to medicines and have relapsed. Such patients represent missed opportunities for effective treatment, a long-term loss of human potential, an individual, family and community burden and false economy in health service provision.

The reasons behind this alarming situation are several and complex. Some are challenging to address for now, but other fundamental structural changes to the TB program, albeit against conventional international recommendations, may be needed. Below we explain four reasons for this dire situation, each with a proposed solution.

Lack of TB drug supplies

The model for the TB program in the last 10 years has been heavily driven by international donors. The Stop TB initiative of the World Health Organization (WHO) has been remarkably successful in other countries by the implementation of the DOTS (Directly Observed Treatment, Short course) strategy (4). The foundtion of the DOTS strategy is the use of community treatment partners – responsible members of the community who supervise the treatment of TB patients on a voluntary basis. Linked to the DOTS strategy by the Stop TB program has been the provision of fixed-dose combination (FDC) therapy drugs, aimed at reducing the number of tablets a patient has to take each day (the 'pill burden'), and reducing the chances of multidrug resistance by eliminating the use of monotherapy (5). Within the Stop TB program developing countries are supplied with high-quality TB drugs from prequalified suppliers as long as the DOTS strategy is implemented. TB patients receive a kit of TB drugs which contains their whole treatment course, and this follows them to their community, where a community treatment partner ensures adherence. The DOTS strategy was adopted by PNG in the early 2000s, but the implementation has been slow and fragmented. DOTS is reportedly successful in Daru, where large resources have been put into combating the MDR problem and Torres Strait TB issues between PNG and Queensland. However, DOTS does not seem to be working elsewhere in PNG. With the limitations of the national TB program, DOTS is still a work in progress. Directly observed treatment in the community will be effective in some locations for some patients, and will work better if there is national commitment to all the components of the WHO Stop TB program. However, the end result of progress – where directly observed therapy with volunteer community treatment partners provides for all TB treatment in the country – is not in sight.

The single biggest factor in TB drug resistance is non-adherence; there should be no mistaking this fact. The origins of non-adherence are complex, but include early discharge from hospital while patients are still vulnerable to relapse and not adequately

educated about the duration of treatment and the importance of adherence, the absence of TB drugs in health facilities, and the absence of a structure for supervision of TB patients in the community.

To understand why this has happened one needs to review the history of TB drug supplies and how the health centres receive medicines. Formerly health centres were supplied with single (loose) TB drugs in the same way as they were supplied with amoxycillin or chloroquine tablets, through the pharmaceutical distribution system. Supplies were sometimes inadequate, but at least there was a clear mechanism by which health centres could access TB drugs. Since the change to fixed-dose combination therapy the flow of FDC drugs is managed by the national TB program, rather than the routine pharmaceutical system. FDC drugs are available in most hospitals now, but not at health centres. At the recent Paediatric Symposium, the health centres in every province where paediatricians were represented were said not to have the FDC therapy appropriate for children. Although the TB drugs are supposed to 'go with the patients' from the place where they are diagnosed and registered, this is not always the case. Children are referred from the hospital where the diagnosis is made back to their health centres for ongoing treatment supplied with some drugs, but these run out and the health centre does not have supplies to continue. This has the effect of increasing non-adherence and defaulting, and creating lack of confidence in the health centres as being places where ongoing TB care can be given effectively, close to a patient's community. At the Symposium, there were many stories of children who defaulted, relapsing with more severe forms of TB, and with the consequent increase in the risk of multidrug resistance. We also heard stories of two and three patients sharing the one FDC kit because the supplies were low.

The recent changes to the way health centres receive all their drugs and commodities provide an opportunity to correct this major problem and improve access of patients who are referred to a community level to obtain TB medicines. If a supply of FDC kits for both adults and children could be included in the 'Health Centre 100% Kits' then patients who run out of TB drugs after being referred back to their health centre would not go without until they had the funds to travel back to the main hospital. The primary strategy of having TB drugs go with the patient would not change, but this would provide a safety net when supplies ran short. It would increase confidence in the health centres, and they would start to understand the FDC therapy concept. Then, for easy-to-diagnose cases, in remote areas, health centres could function as they are supposed to and make clinical diagnoses and start treatment. Without drug supplies of their own they will never be familiar with the changes that have been made to the TB program and never function as basic management units for TB.

The arguments against this by international authorities include that it leads to drug wastage, that it increases the risk of resistance if the drugs are used poorly, that health centre staff do not know how to use the drugs, and that this is against the DOTS roll-out plan. This counter argument states that TB FDC kits should only be in health centres trained in DOTS as basic management units. However, in PNG almost *every* health centre has patients in their catchment area with TB. The lack of knowledge about FDC therapy drugs is not a reason to deny access to a high proportion of health centres to drugs that are needed by their patients. It is a reason to increase training for health centre staff. The situation is particularly problematic for childhood TB, as FDC therapy is more complicated, and training has been more limited. TB FDC treatment is in the Standard Treatment Manuals for Children and Adults, and these manuals are distributed to health centres. Without access to TB drugs and training, health centres will be impotent in the treatment of TB in their community.

Too early discharge

Early discharge is often the seed of non-adherence. Sometimes doctors discharge patients early and sometimes patients or parents insist on leaving or abscond. Although it sounds radical in the context of international recommendations, we believe it is time to make a 2-month policy, which states that every TB patient should be encouraged and supported to remain in hospital for the full 2 months of the intensive phase, as TB drug adherence achieved through voluntary community treatment partners is not yet working. This was the strategy when short-course chemotherapy for TB was first introduced in PNG (6). This should be the standard position, with exceptions only

where a DOTS provider is reliable and can be supervised. This would reduce the risk of children relapsing with worse forms of TB, and reduce selection pressure for drug resistance. The challenge for this is the pressure on beds, especially in busy hospitals like Port Moresby General Hospital. In most provincial and district hospitals this 2-month inpatient recommendation should be achievable, at least for children. However, long-term stay in hospital has social, and sometimes financial, consequences and a further challenge is to provide a pleasant environment and reasonable support and encouragement for the parents, families and patients. The introduction of such a policy will not eliminate the problems of defaulting and relapse, but should reduce it. Even with effective short-course treatment a proportion of the patients will relapse: in an earlier study in PNG the relapse rate among those who had completed TB treatment was 2% (6).

Lack of formal supervision in the community

In most provinces the Provincial Disease Control Officers (PDCOs) are nominally responsible for TB patients once they are discharged into the community. However, they are also responsible for other disease outbreaks (typhoid, cholera etc), and from consistent reports over many years most PDCOs have limited liaison with hospitals. When the DOTS strategy and FDC therapy were introduced, there were also plans to employ specific TB officers in all provinces. However, the evidence that this has happened in most provinces is minimal. With questions over the effectiveness of volunteer community partners, there is an urgent need for better formal treatment supervision. Previously there were TB outreach nurses, who would identify patients in the hospital, ensure the patients were registered, take them home after the intensive phase of treatment, link them to a health centre and supervise their treatment. Indeed, even in areas where DOTS strategy is effective in PNG, such outreach TB nurses are still essential.

Lack of implementation of isoniazid preventive therapy

Most children with TB disease have a parent with TB. Many of these parents have been diagnosed in hospitals, and managed at hospital clinics, but their children have never been screened for TB, and have not been on isoniazid preventive therapy. If a young child is exposed to smear-positive TB, they are at high risk of developing TB. This can be prevented by 6 months of isoniazid. A Cochrane review concluded that the protective efficacy of isoniazid preventive therapy is about 60% (7).

Maybe it is time to return to these fundamental pillars of TB treatment:

- A Department of Health policy of keeping patients in hospital for the full duration of their intensive phase treatment (2 months) whenever feasible
- Have outreach TB nurses follow patients from hospital wards to home and supervise their care
- Ensure TB drug availability in all health centres, by including a supply of FDC kits for different age groups in the Health Centre Drug Supply Kits (100% Kits) and train health staff in their use
- Ensure that in all adult TB clinics a nurse screens exposed children and starts isoniazid preventive therapy if the child does not have symptoms of TB.

Other things will be needed, including a comprehensive review of the effectiveness of community-partner directly observed therapy in the varied PNG contexts of urban settlements and remote rural areas. Paying community treatment partners for assisting with treatment has been tried in Daru. More extensive use of the new molecular Gene X-pert testing would help increase diagnosis and recognition of MDR cases. A rethink is needed, and not all ideas will be new. While we should adopt DOTS and the Stop TB program strategy wherever it is appropriate, we should not at the same time discard older, effective forms of public health disease control. For the crisis that is TB in PNG in 2012, we need to be open to all strategies that may work in the PNG context, and critically analyse their effectiveness.

James Amini
Chief Paediatrician
Port Moresby General Hospital
Private Mail Bag
Boroko
National Capital District 111
Papua New Guinea

Harry Poka
Papua New Guinea Institute of Medical Research
PO Box 60
Goroka
Eastern Highlands Province 441
Papua New Guinea

Joe Kumbu
Paediatrician
Port Moresby General Hospital
Private Mail Bag
Boroko
National Capital District 111
Papua New Guinea

Naomi Pomat
Paediatrician
Modilon (Madang) General Hospital
PO Box 2030
Madang
Madang Province 511
Papua New Guinea

Paulus Ripa
Senior Lecturer in Medical Education
School of Medicine and Health Sciences
University of Papua New Guinea
PO Box 5623
Boroko
National Capital District 111
Papua New Guinea

Nakapi Tefuarani
Professor of Child Health
School of Medicine and Health Sciences
University of Papua New Guinea
PO Box 5623
Boroko
National Capital District 111
Papua New Guinea

John D. Vince
Deputy Dean
School of Medicine and Health Sciences
University of Papua New Guinea
PO Box 5623
Boroko
National Capital District 111
Papua New Guinea

Trevor Duke
Centre for International Child Health
University of Melbourne
Royal Children's Hospital
Parkville
Victoria 3052
Australia
trevor.duke@rch.org.au

REFERENCES

1 **Ballif M, Harino P, Ley S, Coscolla M, Niemann S, Carter R, Coulter C, Borrell S, Siba P, Phuanukoonnon S, Gagneux S, Beck HP.** Drug resistance-conferring mutations in *Mycobacterium tuberculosis* from Madang, Papua New Guinea. *BMC Microbiol* 2012 Sep 4;12:191. doi:10.1186/1471-2180-12-191

2 **Simpson G, Coulter C, Weston J, Knight T, Carter R, Vincent S, Robertus L, Konstantinos A.** Resistance patterns of multidrug-resistant tuberculosis in Western Province, Papua New Guinea. *Int J Tuberc Lung Dis* 2011;15:551-552.

3 **Law I, Poka H, Vince J, Mokela D, Ripa P, Sorensen E, Yadav R, Patel M, Graham S, Duke T.** The burden of childhood tuberculosis in Papua New Guinea: 2005-2006. Abstract PS-81260-18 in Abstract Book of the Thirty-ninth World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The Union), Paris, 16-20 Oct 2008. *Int J Tuberc Lung Dis* 2008;12(11,Suppl 2):S96.

4 **World Health Organization.** The Stop TB Strategy: DOTS. Geneva: World Health Organization, 2012. http://www.who.int/tb/strategy/stop_tb_strategy/en/index.html

5 **Blomberg B, Spinaci S, Fourie B, Laing R.** The rationale for recommending fixed-dose combination tablets for treatment of tuberculosis. *Bull World Health Organ* 2001;79:61-68.

6 **Biddulph J.** Short course chemotherapy for childhood tuberculosis. *Pediatr Infect Dis J* 1990;9:794-801.

7 **Smieja MJ, Marchetti CA, Cook DJ, Smaill FM.** Isoniazid for preventing tuberculosis in non-HIV infected persons. *Cochrane Database Syst Rev* 2000;(2):CD001363.

PNG Med J 2012 Mar-Dec;55(1-4):5-11

Bloodstream infections caused by resistant bacteria in surgical patients admitted to Modilon Hospital, Madang

Henao Asa[1], Moses Laman[2,3], Andrew R. Greenhill[2], Peter M. Siba[2], Timothy M.E. Davis[3], John Maihua[1] and Laurens Manning[3,4]

Modilon General Hospital, Madang, Papua New Guinea, Papua New Guinea Institute of Medical Research, Madang and School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Australia

SUMMARY

In view of the dearth of information relating to antibiotic resistance in community- and hospital-acquired bacterial infections in Papua New Guinea (PNG), we carried out a prospective, hospital-based observational study of surgical patients between October 2008 and October 2009. In a sample of 115 patients (median age 30 years; 55% males) suspected of having a bloodstream infection, blood cultures were positive in 11 (10%) and a significant pathogen was isolated in 9 (8%). *Staphylococcus aureus* was isolated in 4 patients (44%) and 3 were methicillin resistant; all these isolates were considered community acquired because cultures were performed within 48 hours of admission. Of the remaining 5 isolates, 4 were Gram-negative organisms with at least intermediate resistance to chloramphenicol that were grown from blood taken >48 hours post-admission and thus considered nosocomially acquired. These data suggest two distinct patterns of bacterial infection in PNG surgical inpatients that have implications for national antibiotic prescription guidelines.

Introduction

In many developing countries, diagnostic microbiology facilities for invasive bacterial infections are not given priority due to their cost, a shortage of trained laboratory staff and the heavy burden of other diseases such as HIV/AIDS (human immunodeficiency virus/ acquired immune deficiency syndrome), malaria and tuberculosis (1,2). In some of these countries, empiric use of broad-spectrum antibiotics is widespread and paralleled by high rates of infections caused by multiresistant organisms. One pertinent example is the recent report of the dissemination of a metallo-beta-lactamase (NDM-1) carried by a *Klebsiella pneumoniae* from India. Bacteria that acquire NDM-1 are resistant to all but the last line of antibiotics (3). Methicillin-resistant *Staphylococcus aureus* (MRSA) is another multiresistant organism that causes skin, soft tissue, bone, joint and bloodstream infections (2) and is a leading cause of morbidity and mortality worldwide, including tropical countries (4-6).

In Papua New Guinea (PNG), reports of MRSA are limited to a single case report (7) and a mortality audit which identified only two infected children (8). Similarly, to the best of our knowledge, there have been only two studies within the last 15 years describing the local epidemiology of multiresistant Gram-negative bacteria in PNG (9,10). In view of unregulated antibiotic use in the community and the lack of hospital laboratory facilities that are needed to identify and thus help restrict the spread of resistant bacteria, we hypothesized that community-acquired MRSA (CA-MRSA) and Gram-negative infections resistant to currently used antibiotics might be important causes of infection in hospitalized

1 Modilon General Hospital, PO Box 2030, Madang, Madang Province 511, Papua New Guinea

2 Papua New Guinea Institute of Medical Research, PO Box 378, Madang, Madang Province 511, Papua New Guinea

3 School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, PO Box 480, Fremantle, Western Australia 6959, Australia

4 Corresponding author
laurens.manning@uwa.edu.au

surgical patients in PNG.

Patients and Methods

We performed a prospective, hospital-based observational study of surgical patients at Modilon General Hospital, the referral hospital in Madang Province. Patients were recruited over a 12-month period between October 2008 and October 2009, and were considered eligible for inclusion if they were suspected of having bloodstream infections on clinical grounds including an axillary temperature >37.5°C. Patients were classified as having i) a community-acquired bloodstream infection if a positive blood culture was obtained within 48 hours of admission, and ii) a nosocomial infection if the positive culture was from blood taken more than 48 hours after admission (11).

Venous blood samples were drawn for blood culture, full blood count (Coulter Ac•T diff, Beckman Coulter, Brea, USA) and malaria microscopy. For adults, blood (5-10 ml) was placed into commercially prepared aerobic and anaerobic blood culture bottles whilst, for children, a single paediatric bottle (2-3 ml) was used. After incubation in an automated blood culture system (Bactec 9050 Becton-Dickinson, Franklin, New Jersey, USA), isolates were inoculated on to either chocolate agar plates or, for Gram-negative organisms, MacConkey agar and further incubated in a candle jar under 5% CO_2 for 72 hours as previously described (12). Gram's stain, catalase, coagulase and oxidase tests were performed for preliminary identification of organisms. Bacterial isolates were then stored in skim milk broth at -80°C until formal identification and antibiotic susceptibility testing could be performed at a reference laboratory. Antibiotic susceptibility testing was undertaken by the Kirby-Bauer disc diffusion method using antibiotic-impregnated discs (Oxoid, UK) and minimum inhibitory concentrations (MICs) were determined using e-tests (AB Biodisk, Sweden). All susceptibility break points were defined using standard guidelines (13). Coagulase-negative staphylococci, bacillus species and corynebacteria species were considered contaminants.

This study was conducted as part of good-quality clinical care and bacteriology investigations were done concurrently with a severe illness study of Papua New Guinean children at Modilon Hospital (MRAC 08.13). Written informed consent was obtained from individual patients before participation. Clinical data were entered into case report forms that included demographic information, examination findings, surgical diagnosis, investigations and outcome. Data were analysed using Stata (version 8). Univariate comparisons between patients with positive and negative blood cultures were performed using Mann-Whitney U and chi-squared tests for continuous and categorical variables, respectively. A level of significance of $p \leq 0.05$ was used throughout.

Results

Blood cultures were performed on 115 surgical patients suspected of having a bloodstream infection. The median age was 30 years (interquartile range [IQR] 28-34) and 55% were male. Trauma was the leading cause of admission, accounting for 40 patients (35%). Soft tissue injury (10 patients), fractures (10 patients), knife wounds (8 patients), head injury (4 patients), penetrating abdominal wounds (2 patients) and animal bites (2 patients) accounted for the majority of trauma cases. Other causes of admission included appendicitis (21%), malignancy (12%), abscesses (6%), burns (6%), ulcers (5%), other focal infections (5%), paraplegia (3%), hernia (3%) and others (4%).

Blood cultures were positive in 11 patients (10%) and a significant pathogen was isolated in 9 (8%); 2 contaminants (2%, both coagulase-negative staphylococci) were identified during the study. These data are summarized in Figure 1. The clinical features, risk factors and outcomes of patients with and without bloodstream infections are shown in Table 1. Prior use of antibiotics and malignancy were significantly associated with a higher risk of a positive blood culture. Mortality was also significantly higher in patients with a positive blood culture (33% versus 6.7%, $p = 0.012$).

The organisms isolated and their antibiotic susceptibility patterns are shown in Figure 1 and Table 2, respectively. *Staphylococcus aureus* was isolated in 4 patients (44%) and 3 of these were MRSA. Whilst the MRSA isolates were resistant to oxacillin and therefore methicillin and flucloxacillin, they remained sensitive to second-line antibiotics including chloramphenicol. All *S. aureus* isolates were considered community acquired

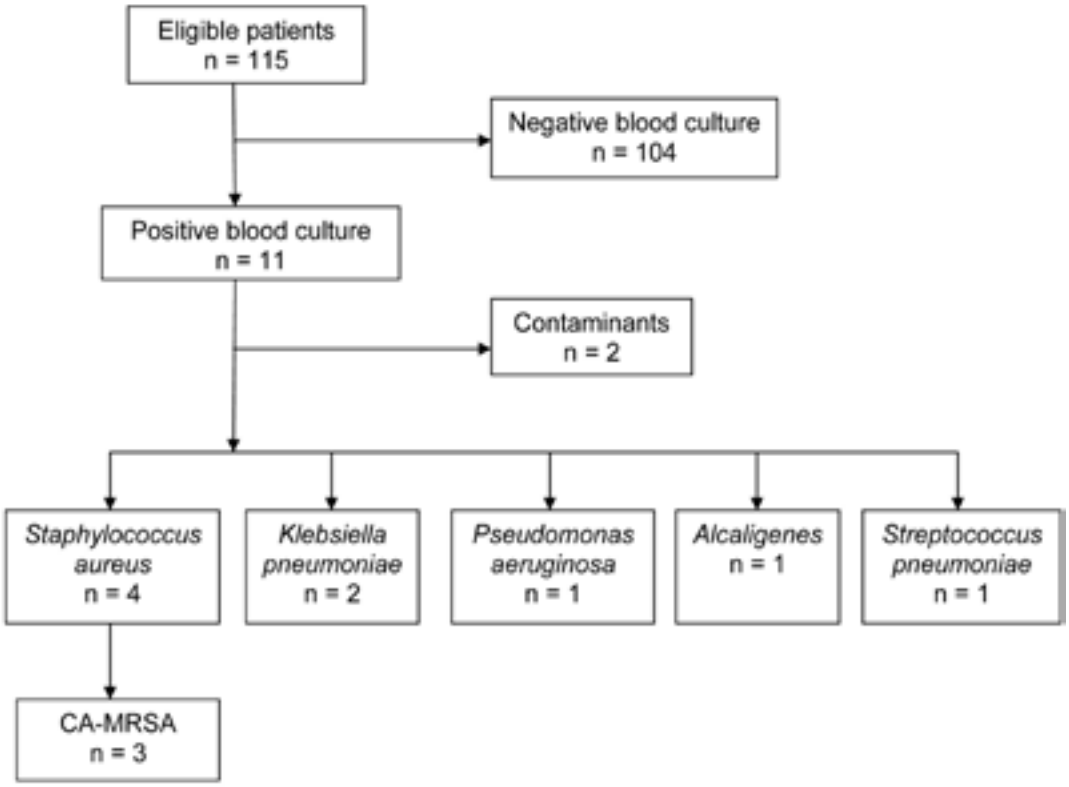


Figure 1. Consort diagram outlining study recruitment and positive blood culture results.
CA-MRSA = community-acquired methicillin-resistant *Staphylococcus aureus*

because blood cultures were performed within 48 hours of admission. 2 of the 3 patients with CA-MRSA were admitted with abscesses and the other had septic arthritis. Two were treated with flucloxacillin and one with flucloxacillin plus chloramphenicol and one patient had surgical debridement. All patients with CA-MRSA survived. One patient absconded during recovery thereby precluding follow-up.

Of the remaining 5 isolates, 4 were Gram-negative and considered nosocomial infections. They included *Klebsiella pneumoniae* (2 isolates), *Pseudomonas aeruginosa* (1 isolate) and *Alcaligenes* spp. (1 isolate). The final isolate was identified as *Streptococcus pneumoniae* that was cultured 6 days after the patient's admission following ear trauma. Although this patient was likely to have had prior carriage of *Streptococcus pneumoniae,* he was also considered to have a nosocomial infection.

Of the 4 Gram-negative organisms, all showed resistance or intermediate resistance to tetracycline, 3 to chloramphenicol, 3 to cotrimoxazole, 2 to gentamicin and 1 to ciprofloxacin. Formal screening for extended-spectrum beta-lactamases was not performed, nor was the susceptibility to ceftriaxone determined. None of the 5 patients with Gram-positive infections died compared with 3 of the 4 patients with Gram-negative nosocomial infections (Fisher's exact test, p = 0.048)

Discussion

This study demonstrates that multiresistant organisms are prevalent in PNG and that they cause severe community- and hospital-acquired surgical infections. In addition, two broad patterns of invasive bacterial disease emerged. First, there was a predominance of CA-MRSA in invasive *S. aureus* infections. Second, nosocomial infections were mostly caused by Gram-negative bacteria that were resistant to chloramphenicol (CMP).

Despite the small size of the present study and the possibility of ascertainment bias due to recruitment of patients who had

TABLE 1

Clinical and laboratory features, risk factors and outcome in surgical patients who had blood cultures performed. Data are presented as median [interquartile range] or percent (%)

	Positive blood culture (n = 9)	Negative blood culture (n = 106)*	p value**
Age (years)	28 [10.6-39.7]	30 [28-34]	0.5
Male sex (%)	50	65	0.46
Prior antibiotic use (%)	60	23.8	0.014
Blood culture performed <48 hours (%)	44.4	50	1.00
Axillary temperature (°C)	38.8 [38.1-39.2]	38.5 [38.5-38.7]	0.48
Pulse rate (/minute)	100.5 [75.5-122.1]	100 [98-101]	0.90
Respiratory rate (/minute)	20 [16.6-28]	19 [18-20]	0.49
Risk factors:			
Malignancy (%)	20	4.8	0.05
Recent surgery (%)	50	32.4	0.26
Intravenous catheter in situ (%)	70	75.2	0.72
Indwelling urinary catheter in situ (%)	20	17.1	0.82
Haemoglobin (g/l)	94.5 [78.9-131.1]	98 [87-105]	0.51
Leukocyte count ($x10^9$/l)	10.8 [4.2-13.6]	8.5 [7.8-8.9]	0.46
Platelet count ($x10^9$/l)	226 [15.5-325.8]	199 [172.4-248.6]	0.45
Positive malaria blood slide (%)	0	8.6	0.34
Length of admission (days)	15 [6-37]	11 [8-14]	0.45
Deaths (%)	33	6.7	0.012

*Includes 2 contaminants

**Mann-Whitney test or chi-squared test was used for comparison between positive and negative blood cultures

failed antibiotic treatment in the community, our data highlight that CA-MRSA is likely to be an important emerging disease in PNG and probably other developing countries with similar sociodemographic and health care circumstances (4,5,14,15). This finding has major implications for the empiric antibiotic treatment of severe soft tissue and orthopaedic infections because parenteral antibiotics such as vancomycin, lincomycin, linezolid and daptomycin that are normally used for severe MRSA infections in high-income countries have previously been unavailable in PNG and are very expensive. As a response to the preliminary results of this study and the wider appreciation of the likely country-wide importance of CA-MRSA, intravenous lincomycin has now been included in the drafts of the 6th edition of the PNG Adult Standard Treatment Guidelines for use in empiric therapy for severe skin, soft tissue and orthopaedic infections when MRSA is suspected (16).

Based on antibiotic susceptibility profiles, the CA-MRSA isolates could be examples

TABLE 2

ANTIMICROBIAL SUSCEPTIBILITY OF ISOLATES TO COMMONLY USED ANTIBIOTICS

Organism	AMP [a]	MET [b]	ERY [c]	TET [d]	GEN [e]	COT [f]	CIP [g]	CMP [h]
Staphylococcus aureus *(3/4)								
Isolate 1	R	R	S	S	S	-	-	S
Isolate 2	R	R	S	S	S	S	-	S
Isolate 3	R	R	S	S	S	S	-	S
Klebsiella pneumoniae (2/2)								
Isolate 1	R	-	-	R	S	R	S	R
Isolate 2	R	-	-	R	R	R	S	R
Alcaligenes species (1/1)	R	-	-	R	IR	S	IR	S
Pseudomonas aeruginosa (1/1)	R	-	-	R	S	R	S	R
*Streptococcus pneumoniae**	-	-	-	-	-	-	-	-

*Antimicrobial susceptibility testing was not done (1 *S. aureus*; 1 *Streptococcus pneumoniae*)
[a]Ampicillin
[b]Methicillin
[c]Erythromycin
[d]Tetracycline
[e]Gentamicin
[f]Cotrimoxazole
[g]Ciprofloxacin
[h]Chloramphenicol
R = resistant; S = susceptible; IR = shows intermediate resistance

of either the Queensland Clone (multilocus sequence typing [ST]-93) or the Western Samoan CA-MRSA (ST-30) subtype (17). Both subtypes are prevalent in Australia, carry the same resistance cassette, and harbour the Panton-Valentine Leukocidin (PVL) gene which encodes a virulence factor thought to be associated with severe infections (17). Intercontinental transfer of MRSA clones has been reported in the Western Pacific (18). Alternatively, the MRSA strain observed in this study could have arisen spontaneously in a manner similar to dominant clones in other regions of Australia (18). Further studies are underway aimed at identifying the dominant strain of CA-MRSA in PNG and the rate of nasal carriage of CA-MRSA in healthy community-dwelling adults. It is anticipated that this new study will provide additional insights into the local epidemiology of this important infection.

The second broad pattern identified in the present study is that of nosocomial infections caused by Gram-negative organisms such as *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Alcaligenes* spp. Risk factors for infection, such as prior antibiotic use and malignancy, and the increased mortality we observed are similar to those seen in hospitalized patients in developed countries (19) and highlight the need for local microbiology diagnostic facilities that can assist in patient management.

A major concern was the high rate of chloramphenicol resistance in patients with Gram-negative sepsis. Both *Klebsiella* isolates and the *Pseudomonas aeruginosa* isolate were resistant to CMP. Chloramphenicol has been the recommended treatment for most severe infections in PNG for the last 3 decades (20), but has recently been superseded by the third generation cephalosporin, ceftriaxone. Recently published data in PNG children with acute bacterial meningitis showing that all *Haemophilus influenzae* type b isolates were CMP resistant together with rising *Streptococcus pneumoniae* MICs to CMP (21), and the prominence of CMP resistance in Gram-negative organisms isolated in the present study imply that widespread use of CMP in the community is responsible for increasing resistance in organisms across many different genera.

Considering the limited antibiotic options available and the lack of diagnostic microbiology facilities in PNG, our findings have important implications for antibiotic guidelines including empiric therapy. The incorporation of intravenous lincomycin for severe *S. aureus* infections thought to be CA-MRSA into proposed standard treatment guidelines is an appropriate response to the emergence of CA-MRSA. However, widespread access to broader spectrum antibiotics may have detrimental effects through promoting even greater antibiotic resistance in a country where health care spending and infrastructure are already under tremendous pressure. Such concerns are not hypothetical as demonstrated in a recent study of neonates admitted to Port Moresby General Hospital Special Care Nursery, where rising resistance to ceftriaxone and amikacin has been found in bloodstream isolates of *Klebsiella pneumoniae* (9). For the moment, we recommend ongoing structured sentinel surveillance for CA-MRSA and resistant Gram-negative organisms from selected hospitals in PNG. To achieve this, local laboratory facilities should be scaled up and combined with data management infrastructure that ensures reporting of resistant organisms to the PNG National Department of Health. This strategy would ensure a cost-effective approach to the identification of clinically significant bacterial antibiotic resistance and the timely modification of treatment protocols.

ACKNOWLEDGEMENTS

We thank Audrey Michael at the PNG Institute of Medical Research (PNGIMR) Microbiology Unit in Goroka for antimicrobial susceptibility testing. We also thank the PNGIMR/MalariaGEN staff at Modilon Hospital, the nursing staff of Modilon Hospital Surgical Ward and the patients and their families for participation. Financial support for purchase of blood culture bottles was obtained from a National Health and Medical Research Council grant (#513782) held by TMED.

REFERENCES

1 **Peacock SJ, Newton PN.** Public health impact of establishing the cause of bacterial infections in rural Asia. *Trans R Soc Trop Med Hyg* 2008;102:5-6.

2 **Forrest APM, Carter DC, Macleod IB.** Principles and Practice of Surgery: A Surgical Supplement to Davidson's Principles and Practice of Medicine. Second edition. Edinburgh: ELBS with Churchill Livingstone, 1990.

3 **Walsh TR, Weeks J, Livermore DM, Toleman MA.** Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human

health: an environmental point prevalence study. *Lancet Infect Dis* 2011;11:355-362.

4 **Nickerson EK, Hongsuwan M, Limmathurotsakul D, Wuthiekanun V, Shah KR, Srisomang P, Mahavanakul W, Wacharaprechasgul T, Fowler VG, West TE, Teerawatanasuk N, Becher H, White NJ, Chierakul W, Day NP, Peacock SJ.** *Staphylococcus aureus* bacteraemia in a tropical setting: patient outcome and impact of antibiotic resistance. *PLoS One* 2009;4:e4308.

5 **Nickerson EK, West TE, Day NP, Peacock SJ.** *Staphylococcus aureus* disease and drug resistance in resource-limited countries in south and east Asia. *Lancet Infect Dis* 2009;9:130-135.

6 **Turnidge JD, Kotsanas D, Munckhof W, Roberts S, Bennett CM, Nimmo GR, Coombs GW, Murray RJ, Howden B, Johnson PD, Dowling K; Australia New Zealand Cooperative on Outcomes in Staphylococcal Sepsis**. *Staphylococcus aureus* bacteraemia: a major cause of mortality in Australia and New Zealand. *Med J Aust* 2009;191:368-373.

7 **Brian MJ, Michael A**. Community-acquired infection with methicillin-resistant *Staphylococcus aureus* in Papua New Guinea. *Pediatr Infect Dis J* 1989;8:807-808.

8 **Duke T, Michael A, Mgone J, Frank D, Wal T, Sehuko R.** Etiology of child mortality in Goroka, Papua New Guinea: a prospective two-year study. *Bull World Health Organ* 2002;80:16-25.

9 **Lithgow AE, Kilalang C.** Outbreak of nosocomial sepsis in the Special Care Nursery at Port Moresby General Hospital due to multiresistant *Klebsiella pneumoniae*: high impact on mortality. *PNG Med J* 2009;52:28-34.

10 **Duke T, Michael A.** Increase in sepsis due to multi-resistant enteric gram-negative bacilli in Papua New Guinea. *Lancet* 1999;353:2210-2211.

11 **Steinberg JP, Clark CC, Hackman BO.** Nosocomial and community-acquired *Staphylococcus aureus* bacteremias from 1980 to 1993: impact of intravascular devices and methicillin resistance. *Clin Infect Dis* 1996;23:255-259.

12 **Laman M, Manning L, Hwaiwhange I, Vince J, Aipit S, Mare T, Warrel J, Karunajeewa H, Siba P, Mueller I, Davis TM.** Lumbar puncture in children from an area of malaria endemicity who present with a febrile seizure. *Clin Infect Dis* 2010;51:534-540.

13 **Clinical and Laboratory Standards Institute.** Performance standards for antimicrobial susceptibility testing: Nineteenth informational supplement (CLSI document M100-S19). Wayne, Pennsylvania: Clinical and Laboratory Standards Institute, 2009.

14 **Nagaraju U, Bhat G, Kuruvila M, Pai GS, Jayalakshmi, Babu RP.** Methicillin-resistant *Staphylococcus aureus* in community-acquired pyoderma. *Int J Dermatol* 2004;43:412-414.

15 **Baranwal AK, Singh M, Marwaha RK, Kumar L.** Empyema thoracis: a 10-year comparative review of hospitalised children from south Asia. *Arch Dis Child* 2003;88:1009-1014.

16 **Physicians Society of Papua New Guinea.** Standard Treatment Guidelines for Adult Medicine in Papua New Guinea. Sixth edition. Port Moresby: Physicians Society of Papua New Guinea, 2011.

17 **Nimmo GR, Coombs GW, Pearson JC, O'Brien FG, Christiansen KJ, Turnidge JD, Gosbell IB, Collignon P, McLaws ML.** Methicillin-resistant *Staphylococcus aureus* in the Australian community: an evolving epidemic. *Med J Aust* 2006;184:384-388.

18 **Coombs GW, Monecke S, Pearson JC, Tan HL, Chew YK, Wilson L, Ehricht R, O'Brien FG, Christiansen KJ.** Evolution and diversity of community-associated methicillin-resistant *Staphylococcus aureus* in a geographical region. *BMC Microbiol* 2011;11:215.

19 **Karchmer AW.** Nosocomial bloodstream infections: organisms, risk factors, and implications. *Clin Infect Dis* 2000;31(Suppl 4):S139-S143.

20 **Shann F, Barker J, Poore P.** Chloramphenicol alone versus chloramphenicol plus penicillin for bacterial meningitis in children. *Lancet* 1985;2:681-684.

21 **Manning L, Laman M, Greenhill AR, Michael A, Siba P, Mueller I, Davis TM.** Increasing chloramphenicol resistance in *Streptococcus pneumoniae* isolates from Papua New Guinean children with acute bacterial meningitis. *Antimicrob Agents Chemother* 2011;55:4454-4456.

PNG Med J 2012 Mar-Dec;55(1-4):12-15

The bacterial flora of acute appendicitis at the Port Moresby General Hospital in Papua New Guinea

Damien J. Hasola[1,2], Ray Dutta[3], Cecil Darrell[3], George Gende[1], William Kaptigau[1], Osborne Liko[1] and Ikau Kevau[1]

Surgery Department and Pathology and Microbiology Department, Port Moresby General Hospital, Papua New Guinea

SUMMARY

Acute appendicitis is a common cause of acute abdomen requiring an emergency appendicectomy. Complications such as perforation and peritoneal contamination leading to peritonitis can result from delay in presentation and an emergency operation. This study prospectively recruited 101 patients diagnosed with acute appendicitis to correlate the bacterial flora with the severity of appendicitis. The results show that 90 patients had acutely inflamed or gangrenous appendicitis and 11 had perforated appendicitis. The ages ranged from 6 to 49 years with a median of 20 years. There were 59 females and 42 males. The commonest isolates were aerobic bacteria such as *Escherichia coli*, Group D streptococci and *Klebsiella pneumoniae*. Mixed infection with anaerobes such as *Bacteroides fragilis* was seen only in perforated appendicitis. The best choices of antibiotic were a fluoroquinolone, cephalosporin and aminoglycoside for aerobic organisms and metronidazole for anaerobes.

Introduction

Appendicitis is a disease of antiquity but acquired prominence when it was recognized as a clinical and pathological entity requiring surgical therapy in 1886. Before this in the 16th century it was known as perityphlitis, a 'fatal suppurative disease of the caecal region' (1).

The basic pathological process in appendicitis is obstruction, usually by a faecolith. The progressive nature of the inflammation results from a sudden rise in intraluminal hydrostatic pressure with vascular obstruction and bacterial invasion of the appendicular wall. Perforation occurs at the weakest point, which is at the antimesenteric border. There are other intriguing causes such as orange seeds, ascarids and pins that have lodged themselves in the caecal appendix but they are extremely rare. The equivalent of the Peyer's patches in the appendix has been suggested as the place where the process initiates but at present this is only speculative (1).

It was only as recently as 1938 that bacterial infection was documented by Altemeier in appendicitis (2). Since then it is known that from 4 to 10 different species which act in synergism can be isolated. Most studies (2-5) show that bacterial invasion is secondary and that the isolates are mainly *Escherichia coli*, streptococci groups and *Bacteroides fragilis*.

In Papua New Guinea no such study has been done to date to establish the microbiology of appendicitis. The aim of this study was to establish the bacterial profile in acute appendicitis and the antibiotic susceptibilities of the bacteria and to correlate these findings with the severity of the disease.

Materials and Methods

101 patients with clinical and histologically proven acute appendicitis were recruited into

1 Surgery Department, Port Moresby General Hospital, Free Mail Bag, Boroko, National Capital District 111, Papua New Guinea

2 Present address: Department of General Surgery, Buka General Hospital, Autonomous Region of Bougainville tsitonx@yahoo.co.nz

3 Pathology and Microbiology Department, Port Moresby General Hospital, Free Mail Bag, Boroko, National Capital District 111, Papua New Guinea

the study. All patients were operated on at the Port Moresby General Hospital from March to December 2009. Before operation antibiotics effective against both aerobic and anaerobic organisms were routinely given. Under general anaesthesia, the appendicectomies were mainly done through a Lanz incision except for patients with peritonitis who had lower midline laparotomies. Once the abdomen had been opened the diseased appendix was amputated and any pus or fibrin sucked out. The peritoneal cavity was copiously irrigated with normal saline and the wound repaired in layers. The layers of skin were approximated loosely or left open if pus was present and closed by secondary intention.

Specimen procurement

The appendix was divided into halves without entering the lumen. One half was sent for histological diagnosis and the other for bacteriological culture. The tissue for culture was mashed using a sterile plate. Immediately it was placed in Robertson's cooked medium (enriched medium) and sealed with an air-tight cap. In the laboratory the samples were incubated at 36-37°C for 48 hours under aerobic and anaerobic conditions with anaerobic gas pack for another 48 hours. Positive colonies were Gram stained and any Gram-negative rods were tested against metronidazole and gentamicin discs. The first subculture after 48 hours on to MacConkey agar was incubated in an aerobic environment at 35-37°C for 18-48 hours. Positive colonies were Gram stained and tested using the Analytical Profile Index (API – Oxide bioMérieux Inc, USA) to identify the different isolates.

Results

Of the 101 patients 59 were females and 42 were males. The youngest was 6 years old and the oldest 49 years with a median of 20 years. The duration of illness to the day of operation ranged from 2 to 6 days with an average of 3 days. 50 patients had acutely inflamed appendicitis, 40 had gangrenous appendicitis and 11 had perforated appendicitis (Table 1). There were no deaths in this series; however, one patient had a residual abscess that was drained and improved.

TABLE 1

Aerobic and anaerobic bacteria cultured from early, gangrenous and perforated appendicitis

Bacteria	Early appendicitis n = 50	Gangrenous appendicitis n = 40	Perforated appendicitis n = 11	Total
Aerobic (123)				
Escherichia coli	29	40	11	80
Group D streptococci	3	7	10	20
Klebsiella pneumoniae	3	3	5	11
Citrobacter freundii	1	1	6	8
Proteus mirabilis	1	1	2	4
Anaerobic (3)				
Bacteroides fragilis	0	0	3	3

TABLE 2

THE ANTIBIOTIC SUSCEPTIBILITY PATTERNS OF ISOLATES FROM ACUTE APPENDICITIS AT PORT MORESBY GENERAL HOSPITAL IN 2009

Bacteria	Number of strains	Amoxycillin	Chloramphenicol	Gentamicin	Ceftriaxone	Ciprofloxacin	Metronidazole
Aerobic (123)							
Escherichia coli	80	33/80 (41%)	61/80 (76%)	76/80 (95%)	78/80 (98%)	80/80 (100%)	
Group D streptococci	20	15/20 (75%)	19/20 (95%)	15/20 (75%)	19/20 (95%)	20/20 (100%)	
Klebsiella pneumoniae	11	2/11 (18%)	8/11 (73%)	11/11 (100%)	11/11 (100%)	11/11 (100%)	
Citrobacter freundii	8	7/8 (88%)	7/8 (88%)	8/8 (100%)	8/8 (100%)	8/8 (100%)	
Proteus mirabilis	4	2/4 (50%)	3/4 (75%)	3/4 (75%)	3/4 (75%)	4/4 (100%)	
Anaerobic (3)							
Bacteroides fragilis	3	nt	nt	0/3 (0%)	nt	nt	3/3 (100%)
Total	126						

nt = not tested

The 126 bacterial isolates showed an upward trend in colonization both qualitatively and quantitatively as the disease worsened. *Escherichia coli*, Group D streptococci and *Klebsiella pneumoniae* accounted for 90% of aerobic isolates whereas *Bacteroides fragilis* was isolated from 3 patients with perforated appendicitis (Table 1).

Bacterial susceptibilities showed a variable pattern of resistance to commonly used antibiotics ranging from 0 to 82% (Table 2) in the aerobic pathogens group. All aerobic organisms were susceptible to ciprofloxacin. In the anaerobic group, *B. fragilis* was completely susceptible to metronidazole.

Discussion

This study showed that a mixed infection exists, with aerobic bacteria predominating in early infection and anaerobic bacteria appearing in late complicated appendicitis. *E. coli*, Group D streptococci, *K. pneumoniae* and *Citrobacter freundii* accounted for 97% of aerobic bacteria in early acute appendicitis. This study affirms the position of *B. fragilis* in perforated appendicitis.

The antibiotics of first choice are a fluoroquinolone, cephalosporin and aminoglycoside for aerobic organisms and metronidazole for anaerobes. Although there was no mortality in this study, 1 case of post-appendicectomy residual abscess in a perforated appendicitis was seen. Complications were reduced because of a tendency to early operation, copious peritoneal saline wash and antibiotic therapy including metronidazole (6). Community-acquired appendicitis from *E. coli*, *K. pneumoniae* and streptococci had a high level of resistance to the commonly used antibiotics such as chloramphenicol and penicillins. This may be due to indiscriminate prescription patterns in Papua New Guinea.

The emergence of multiple drug resistance in bacteria appears to be a formidable challenge to our hospitals. Our findings are supported by other studies in both the qualitative and quantitative nature of the bacteria isolated; however, they differ with respect to the antibiotics used (3,4,6). It is probable that the use of clindamycin and gentamicin as the antibiotics of choice is a reflection of lengthy exposure to many antibiotics over time (7). Metronidazole has been shown to reduce mortality and morbidity from appendicitis and has become the main prophylactic antibiotic in appendicitis. The further isolation of *Bacteroides* species depends on the laboratory's capacity to culture and identify them. *Pseudomonas* species were not seen in our study but were predominant in western studies, which is hard to explain. Our findings suggest that there are serious levels of resistance against commonly used antibiotics in the community. Since this is the first study for our hospital it will need to be repeated in the future to monitor resistance levels for site-specific diseases such as appendicitis, osteomyelitis and pyelonephritis.

In conclusion, a cephalosporin or gentamicin combined with metronidazole should be the first choice for antibiotic therapy in appendicitis. Ciprofloxacin should be reserved for cases not responding to cephalosporin or an aminoglycoside. The emergency operation should be done the same day by a trained surgeon to get optimum results in our setting. It is also important to have a hospital policy so that there is a protocol for prescribing antibiotics that is based on the organisms likely to be found and their antibiotic resistance levels rather than 'best guess'.

REFERENCES

1 **Williams NS, Bulstrode CJK, O'Connell PR, eds.** Bailey and Love's Short Practice of Surgery. Twenty-fifth edition. London: Hodder Arnold, 2008.

2 **Altemeier WA.** The bacterial flora of acute perforated appendicitis with peritonitis: a bacteriologic study based upon one hundred cases. *Ann Surg* 1938;107:517-528.

3 **Bennion RS, Baron EJ, Thompson JE Jr, Downes J, Summanen P, Talan DA, Finegold SM.** The bacteriology of gangrenous and perforated appendicitis – revisited. *Ann Surg* 1990;211:165-171.

4 **Roberts JP.** Quantitative bacterial flora of acute appendicitis. *Arch Dis Child* 1988;63:536-540.

5 **Brook I.** Bacterial studies of peritoneal cavity and postoperative surgical wound drainage following perforated appendix in children. *Ann Surg* 1980;192:208-212.

6 **Pinto DJ, Sanderson PJ.** Rational use of antibiotic therapy after appendicectomy. *Br Med J* 1980;280:275–277.

7 **Berne TV, Yellin AE, Appleman MD, Gill MA, Chenella FC, Heseltine PN.** Surgically treated gangrenous or perforated appendicitis: a comparison of aztreonam and clindamycin versus gentamicin and clindamycin. *Ann Surg* 1987;205:133-137.

PNG Med J 2012 Mar-Dec;55(1-4):16-23

Validation of the Roche Amplicor HIV DNA test version 1.5 for early infant diagnosis of HIV in Papua New Guinea

B. John[1,2], T. Lupiwa[1,3], P. Toliman[1], E. Lavu[4], P. Zimmerman[5], P.M. Siba[1] and J. Markby[4,6]

Papua New Guinea Institute of Medical Research, Goroka, Central Public Health Laboratory, Port Moresby, Papua New Guinea, The Center for Global Health and Diseases, Case Western Reserve University, Cleveland, USA and Virology Department and Centre for International Health, Burnet Institute, Melbourne, Australia

SUMMARY

Human immunodeficiency virus (HIV) is a significant public health issue in Papua New Guinea (PNG). After heterosexual transmission (90%), the second most common route of transmission is vertically from mother to child (3.5%). Before the introduction of molecular methods of HIV testing in PNG, diagnosing exposed infants was problematic because there were no reliable assays available for accurate early infant HIV detection. This study aimed to validate and assess a global gold standard for virological early infant HIV diagnosis in PNG: the AMPLICOR® HIV DNA v1.5 assay (Roche) using dried blood spot (DBS) specimens. The assay was validated in three ways: by testing well-characterized DBS and kit controls and by blinded retesting of 42 patient specimens. The assay was further investigated by comparison with a serological assay. The results indicated that the assay was robust and highly reproducible using DBS and kit controls, with 100% sensitivity and specificity. Of the 42 infant DBS specimens that were retested blindly, 100% of the test results were concordant with diagnostic results. Among the 42 infant specimens tested with the Amplicor HIV DNA v1.5 assay we found that 33% of infants (n = 14) were HIV PCR positive and 67% (n = 28) negative. The earliest point of HIV detection established for this study was three months of age. This pilot study indicates that HIV-infected infants in PNG can be effectively diagnosed using virological testing and can thus be started earlier on treatment than was previously possible with serological testing.

Introduction

Human immunodeficiency virus (HIV) is a significant public health issue in Papua New Guinea (PNG) and after heterosexual transmission (90%) the second most common route is through perinatal transmission (3.5%) (1). The progression to AIDS (acquired immune deficiency syndrome) in infants is rapid owing largely to the immature status of the immune system. Due to an immature immune system and other HIV-related illness many infants die before the age of one year. However, life expectancy for HIV-seropositive infants can now be prolonged, as shown by the Children with HIV Early Antiretroviral Therapy (CHER) study, with a mortality rate reduced by 76% and HIV progression by 75% (2). The

1 Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea

2 Present address: Clinton Health Access Initiative, PO Box 8312, Boroko, National Capital District 111, Papua New Guinea
banganjohn@gmail.com

3 Present address: Sensen Consultancy Firm Ltd, PO Box 714, Port Moresby, National Capital District 121, Papua New Guinea

4 Central Public Health Laboratory, Port Moresby General Hospital, Private Mail Bag 1, Boroko, National Capital District 111, Papua New Guinea

5 The Center for Global Health and Diseases, Biomedical Research Building 4th Floor, Case Western Reserve University, 10900 Euclid Ave LC: 4983, Cleveland, OH 44106-7286, USA

6 Virology Department and Centre for International Health, Burnet Institute, PO Box 2284, Melbourne, Victoria 2001, Australia

improvement in the survival and quality of life for infants in this study was due to the use of virological assays and resulted in obtaining accurate HIV data to signal early initiation of anti-HIV treatment. HIV serological assays cannot be accurately used in infants under 18 months of age due to the potential presence of maternal anti-HIV antibodies, which can cause false positive serological results. Therefore molecular or virological assays should be used to allow for more accurate diagnosis since they directly detect virus particles. Many virological assays use the polymerase chain reaction (PCR) for detecting HIV ribonucleic acid (RNA), and studies done in both developed and developing country settings show that this is very sensitive and specific, accurate and affordable (3-8). The AMPLICOR® HIV DNA PCR version 1.5 (AMPLICOR® v1.5 kit, AU$36 per test) is one of the assays that has been used extensively in other studies and has proven to be highly sensitive and specific; it has been used as the gold standard assay for early infant diagnosis of HIV (9-12). The Amplicor v1.5 kit has been validated using dried blood spot (DBS) specimens, and has been shown to be highly efficient, cheap and logistically easier than other tests, especially for resource-poor settings (13-19) such as PNG. In PNG, the unreliability of electricity supply and delays in freighting of specimens mean that samples such as whole blood may deteriorate before reaching the referral laboratory for testing; this is much less likely with DBS specimens. The present investigation was designed to assess the accuracy of the Amplicor v1.5 kit and to pave the way for further studies relating to HIV and infants in PNG using this assay as a sensitive tool for early infant diagnosis. In addition, in light of the fact that this assay has been newly used for early infant diagnosis (EID) in PNG it is important to subject the assay to validation in the country as no such study has previously been carried out. Early diagnosis of infants born to HIV-seropositive women is important because the early detection of infection means that infants can be registered for antiretroviral therapy to reduce their mortality and morbidity.

This small study will provide pilot data for a larger study to more stringently evaluate this assay in PNG settings and provide insight into its effectiveness and feasibility for use in diagnostic programs in PNG. This will be done through validating the Amplicor v1.5 PCR kit in PNG, determining the status of infants born to HIV-seropositive women and demonstrating that the PCR kit can detect HIV infection much earlier than serology in infants. Furthermore, since August 2008 it has been implemented into the national health program of PNG.

Methods

Before the commencement of the study ethical approval number 08/19 was obtained from the Medical Research Advisory Committee (MRAC) of PNG.

Patients

The DBS specimens studied were obtained sequentially from patients enrolled in the Early Infant Diagnosis Program in PNG who attended Port Moresby General Hospital (PMGH) Well Baby Clinic, the Nine Mile Clinic, Port Moresby and the Goroka General Hospital (GGH). There were 47 DBS specimens in total that were collected, of which 42 were tested. These 42 DBS specimens were from infants whose mothers had confirmed antibody HIV-positive status, while the other 5 were from mothers with unknown HIV status and therefore excluded from the study. The infants in the study were aged between 4 and 56 weeks. Infants aged less than 4 weeks and greater than 18 months were excluded from the study. Of the 42 DBS specimens, 20 were from infants at the GGH, 21 were from the PMGH Well Baby Clinic and 1 was from the Nine Mile Clinic.

Dried blood spot specimens

The specimens for the study were obtained by pricking the heel or big toe of the infant with a 2 mm safety lancet and collecting the single drops of blood (approximately 50 µl) on to Whatman (S&S) 903 grade filter paper cards. At least three single drops were collected per patient and air-dried for at least three hours before being stored at -20°C in individual ziplock plastic bags with desiccant sachets and humidity indicator cards. DBS specimens that contained insufficient blood or appeared layered, crusty, clotted or wetted were discarded.

DBS controls were obtained from the United States government Centers for Disease Control and Prevention (US-CDC), made by spotting healthy HIV-negative patient blood on to Whatman S&S 303 filter paper.

Positive DBS controls were prepared at CDC by infecting healthy blood with cultured HIV before aliquots were applied on to the filter paper.

Polymerase chain reaction

To determine the HIV infection status of infants a PCR assay – the Roche Amplicor HIV-1 DNA assay, version 1.5 (Roche Molecular Systems Inc, Branchburg, NJ) – was employed. The assay was performed using DBS specimens and controls as outlined above and was carried out according to the manufacturer's instructions. One whole blood spot (approximately 50 µl) was completely excised from the Whatman 903 card, using a 6 mm diameter punch to cut out discs from the centre of the DBS, and transferred using sterile forceps to 1.5 ml Starstedt cryovial tubes. Proviral DNA was extracted from the DBS using the Roche kit extraction reagents following the manufacturer's instructions. PCR and post-amplification detection steps were performed according to the manufacturer's instructions.

Negative results were determined if the optical density (OD) reading was less than 0.2 at 450 nm and positive if the OD reading was greater than 2.5. Results between 0.2 and 2.5 were deemed to be equivocal and were repeated. Positive results were also repeated to reduce the likelihood of false positivity.

Serology

The Vironostika® HIV Microelisa System Assay (Vironostika, bioMérieux, France) was modified and optimized to incorporate the elution of serum from DBS specimens. The DBS specimens were equilibrated to room temperature and then the DBS discs were punched. Stainless steel, hand-held, 6 mm diameter punches were used to punch a disc from the centre of the DBS. In order to elute the serum from the DBS, one DBS disc was used per well in a sterile, flat-bottomed, 96-well microtitre plate. 200 µl of elution buffer was added (phosphate-buffered saline (PBS), Tween 20 (0.05%) and 5% dried skim milk powder). The DBS discs were submerged in the elution buffer and eluted overnight in the fridge at 6-8ºC. The dilution of the serum resulted in 5 µl of the eluate from each 6 mm DBS disc. Eluates were used for the Vironostika assay the following morning and were discarded before 5 days. The Vironostika assay was completed according to manufacturer's instructions.

Data analysis

The data collected were managed and analysed using Microsoft Excel, Fox Pro Version 9.0 and Intercool Stata Version 8.0.

Results and Discussion

Validation of Roche assay using CDC and Roche controls

The Amplicor v1.5 PCR kit was validated firstly by testing 13 well-characterized CDC controls as mentioned previously. The Amplicor v1.5 PCR kit demonstrated a 100% concordance with the CDC controls (Table 1), with 7 positive results and 6 negative results. These CDC controls were tested repeatedly and we were able to replicate the same

TABLE 1

VALIDATION OF AMPLICOR V1.5 PCR KIT WITH CDC CONTROLS

		CDC controls		
		Positive	**Negative**	**Concordance (%)**
Amplicor v1.5 PCR kit	**Positive**	7	0	
	Negative	0	6	
				100 (n = 13)

PCR = polymerase chain reaction
CDC = Centers for Disease Control and Prevention

results.

Assay reproducibility was assessed by validating 8 manufacturer's controls, 4 of which were positive and 4 negative. The Amplicor v1.5 PCR kit was able to reproduce the 4 known positive and 4 negative (Table 2). This demonstrated that the Amplicor v1.5 PCR kit has a 100% concordance with the manufacturer's controls.

The validation was conducted in a purposely built laboratory in PNG's major general hospital. When testing the CDC and Roche controls the HIV DNA PCR showed a specificity and sensitivity of 100%. Thus these results agreed with the findings from the meeting that the World Health Organization (WHO) and CDC conducted to review the performance of laboratory virological methods, particularly the Amplicor v1.5 PCR kit, which concluded that it is an accurate method for correct identification of HIV-1 (13-19) and can be applied even in resource-limited settings. This supports the use of this HIV DNA PCR kit to be used in PNG for future and ongoing studies.

Validation by blinded retesting of clinical specimens

Thirdly, validation was performed through testing and blinded retesting of the clinical specimens. The results of the 42 DBS specimens obtained and tested by technician one were compared to those by technician two (Table 3). The Amplicor v1.5 PCR kit results of technician two agreed with those of technician one. Of the 42 samples 33% (n = 14) were positive and 67% (n = 28) were negative. Thus, the Amplicor v1.5 PCR kit in this set of validations demonstrated robustness, in so far as it can be performed by different technicians without variation in results. Furthermore, the accuracy of the blinded retesting of the 42 DBS specimens by the different technicians indicates that the conditions used for the assay result in reproducible results from assay to assay. This means that detection and diagnosing of infants can be done in different sites by trained technicians. Additionally, that would reduce the cost of sending samples from around the country to only one site.

Comparison of PCR with serology

As the final part of the investigation, the Amplicor v1.5 PCR kit was compared with a serological assay, since serology was at the time the only form of detection of HIV for children in the country. Of the total 42 DBS specimens 4 were exhausted and could not be tested using serology. Thus, only 38 DBS specimens were tested to compare the results between the Amplicor v1.5 PCR kit and Vironostika assay. The results from the two assays were concordant for 24 and discordant for 14 samples (Table 4). Of the discordant results, 2 samples were positive by PCR but negative by serology and 12 samples were negative by PCR and positive by serology.

The 2 DBS specimens that were found to be positive by PCR but negative by serology may be due to a recent HIV infection in which seroconversion had not yet taken place. Another possibility is that the serology test results were false negatives; alternatively, the PCR results may be incorrect. The

TABLE 2

VALIDATION OF AMPLICOR V1.5 PCR KIT WITH ROCHE CONTROLS

		Roche controls		
		Positive	**Negative**	**Concordance (%)**
Amplicor v1.5 PCR kit	**Positive**	4	0	
	Negative	0	4	
				100 (n = 8)

PCR = polymerase chain reaction

TABLE 3

BLIND RETESTING OF CLINICAL SPECIMENS WITH THE AMPLICOR V1.5 PCR KIT

		Technician 2		
		Positive	**Negative**	**Concordance (%)**
Technician 1	**Positive**	14	0	
	Negative	0	28	
				100 (n = 42)[1]

[1]Demonstration of robustness and reproducibility of the PCR kit

TABLE 4

COMPARING AMPLICOR V1.5 PCR KIT TO SEROLOGICAL ASSAY

		Serological assay[1]		
		Positive	**Negative**	**Concordance (%)**
Amplicor v1.5 PCR kit	**Positive**	11	2	
	Negative	12	13	
				63 (24/38)

PCR = polymerase chain reaction
[1]A comparison of the PCR kit against the serological assay that is used in Papua New Guinea

latter appears less likely in light of a body of evidence indicating a very low frequency of false positive results for a first Roche PCR test and 0% for retesting of initially positive results. For example, in Uganda a 0.4% false positive rate for the initial HIV PCR test was subsequently 0% of false positives for retested specimens (20), with similar findings in other studies in other African countries. Therefore, because of the established high sensitivity and specificity of PCR, any PCR false positives are unlikely.

For the 12 samples that were negative for PCR but positive for serology, it is likely that the anti-HIV maternal antibodies were detected by serology in infants that were not infected and therefore negative for viral particle DNA. This demonstrates why serological tests are not reliable for diagnosing HIV infection in infants less than 18 months of age because of the positive results generated by the maternal antibodies present in the infant's blood. The PCR and serological assays had a 63% concordance due principally to maternal anti-HIV antibodies without infant HIV infection, and this demonstrates the value of PCR as a direct method of HIV detection.

Infant HIV PCR status

Of the 42 women with confirmed HIV positive status, 14 (33%) of their infants were HIV PCR positive and 28 (67%) were HIV PCR negative (Table 5). Although the sample size is low the result is important and an analysis of the national data collected for EID would be valuable in order to understand more

comprehensively the vertical HIV transmission rates in PNG. This rate of 33% is higher than in other studies, for example in South Africa, where the mother-to-child transmission (MTCT) rate is 25% (21), but falls within the expected range of 20-45% reported by others for transmission rates without a prevention of parent-to-child transmission (PPTCT) intervention (22). Furthermore, of the 14 HIV PCR-positive infants the youngest was 12 weeks of age. Although only one infant had HIV detected at 12 weeks it demonstrates that the Amplicor v1.5 PCR kit can detect HIV much earlier than 18 months. As reported in other studies, the earliest it can detect HIV is at six weeks, with a sensitivity of 100% and specificity of 99.6% (15).

These results demonstrate that infants under the age of 18 months can now be tested using this assay in the PNG setting. Previously, in the country it was not possible to determine the HIV status of infants under the age of 18 months born to seropositive mothers since only conventional serological assays were available for use. The findings demonstrate that infants can be diagnosed accurately and much earlier. Thus treatment can also be administered earlier. A study done recently showed that early diagnosis reduces mortality and HIV progression in infants (2), as previously noted. Furthermore, the ability of the Roche HIV PCR to determine the status of infants means that PNG can monitor and collect valuable information on infants that are infected each year.

Study limitations and prospective studies

The present study had some limitations that affected the extent to which the assay could be validated and prompts further validation. The main limitations in the study were delays in the sourcing of DBS test specimens and procurement of the test assays and other laboratory consumables. These impediments contributed to the late commencement of the laboratory component of the present study, the small sample size studied and the limited time frame that the study was conducted in.

Ideally, the Roche assay could have been compared to one or more other virological assays to compare sensitivity and specificity. For example, Fisher et al. evaluated the Roche assay by comparison to a nested PCR in-house assay and observed 100% sensitivity and 98% specificity from DBS specimens using the Roche assay (17). Others have made similar comparisons to RNA viral load assays such as total nucleic acid real-time reverse transcriptase PCR (23), or ultra-sensitive HIV p24 assays (12).

Future studies will compare the Roche assay with an in-house reverse transcriptase (RT) HIV PCR developed at the PNG Institute of Medical Research for HIV surveillance. Such a comparison was not possible in the present study due to limited specimen availability as well as limited funding for assay reagents. Since whole blood for use with other PCR methods was not available from the

TABLE 5

COMPARING MOTHER* AND INFANT HIV STATUS

HIV status of infants by Amplicor v1.5 PCR kit	
Positive	14 (33%)
Negative	28 (67%)
Total	42

*All 42 mothers were HIV positive
HIV = human immunodeficiency virus
PCR = polymerase chain reaction

cohort of infants studied, methodologies that were optimized for testing DBS specimens were evaluated. In the future, low-cost viral load technologies that test from DBS will also be evaluated in PNG.

Conclusion

The study demonstrated that the Roche Amplicor HIV-1 DNA assay is reproducible under the conditions used for this study and reliable under the controlled conditions of the laboratory. It showed that this DNA assay can be used for determining the HIV status of infants exposed to HIV. The earliest detection in this study was in a 12-week-old infant, demonstrating that this assay can accurately detect infection much earlier than serological assays. The implications, as highlighted by this small pilot study, are that HIV-infected infants can be accurately diagnosed before 18 months and as early as 3 months and thus started earlier on treatment than was previously possible with serological testing. It would be valuable to determine whether accurate virological testing can be carried out as early as 4 or 6 weeks of age. Furthermore, in PNG, this assay provides an excellent tool for PPTCT incidence surveillance and for evaluating the efficacy of PPTCT programs.

REFERENCES

1 **Papua New Guinea Department of Health.** The 2008 HIV and AIDS Six Monthly Surveillance Report. Port Moresby: Department of Health, 2008.

2 **Violari A, Cotton MF, Gibb DM, Babiker AG, Steyn J, Madhi SA, Jean-Philippe P, McIntyre JA; for the CHER Study Team.** Early antiretroviral therapy and mortality among HIV-infected infants. *N Engl J Med* 2008;359:2233-2244.

3 **Young NL, Shaffer N, Chaowanachan T, Chotpitayasunondh T, Vanparapar N, Mock PA, Waranawat N, Chokephaibulkit K, Chuachoowong R, Wasinrapee P, Mastro TD, Simonds RJ; Bangkok Collaborative Perinatal HIV Transmission Study Group.** Early diagnosis of HIV-1-infected infants in Thailand using RNA and DNA PCR assays sensitive to non-B subtypes. *J Acquir Immune Defic Syndr* 2000;24:401-407.

4 **Dunn DT, Brandt CD, Krivine A, Cassol SA, Roques P, Borkowsky W, De Rossi A, Denamur E, Ehrnst A, Loveday C.** The sensitivity of HIV-1 DNA polymerase chain reaction in the neonatal period and the relative contributions of intra-uterine and intra-partum transmission. *AIDS* 1995;9:F7-F11.

5 **Nelson RP Jr, Price LJ, Halsey AB, Graven SN, Resnick L, Day NK, Lockey RF, Good RA.** Diagnosis of pediatric human immunodeficiency virus infection by means of a commercially available polymerase chain reaction gene amplification. *Arch Pediatr Adolesc Med* 1996;150:40-45.

6 **Nolan ML, Greenberg AE, Fowler MG.** A review of clinical trials to prevent mother-to-child HIV-1 transmission in Africa and inform rational intervention strategies. *AIDS* 2002;16:1991-1999.

7 **Benjamin DK Jr.** Integration of statistical theory and practical clinical expertise. Polymerase chain reaction testing of the HIV-exposed infant. *Minerva Pediatr* 2002;54:105-111.

8 **Mrus JM, Yi MS, Eckman MH, Tsevat J.** The impact of expected HIV transmission rates on the effectiveness and cost of ruling out HIV infection in infants. *Med Decis Making* 2002;22(5 Suppl):S38-S44.

9 **Dunn DT, Simonds RJ, Bulterys M, Kalish LA, Moye J Jr, de Maria A, Kind C, Rudin C, Denamur E, Krivine A, Loveday C, Newell ML.** Interventions to prevent vertical transmissions of HIV-1: effect on viral detection rate in early infant samples. *AIDS* 2000;14:1421-1428.

10 **Sherman GG, Jones SA, Coovadia AH, Urban MF, Bolton KD.** PMTCT from research to reality – results from a routine service. *S Afr Med J* 2004;94:289-292.

11 **Sherman GG, Stevens G, Stevens WS.** Affordable diagnosis of human immunodeficiency virus infection in infants by p24 antigen detection. *Pediatr Infect Dis J* 2004;23:173-176.

12 **Patton JC, Sherman GG, Coovadia AH, Stevens WS, Meyers TM.** Ultrasensitive human immunodeficiency virus type 1 p24 antigen assay modified for use on dried whole-blood spots as a reliable, affordable test for infant diagnosis. *Clin Vaccine Immunol* 2006;13:152-155.

13 **Driver GA, Patton JC, Moloi J, Stevens WS, Sherman GG.** Low risk of contamination with automated and manual excision of dried blood spots for HIV DNA PCR testing in the routine laboratory. *J Virol Methods* 2007;146:397-400.

14 **Creek T, Tanuri A, Smith M, Seipone K, Smit M, Legwaila K, Motswere C, Maruping M, Nkoane T, Ntumy R, Bile E, Mine M, Lu L, Tebele G, Mazhani L, Davis MK, Roels TH, Kilmarx PH, Shaffer N.** Early diagnosis of human immunodeficiency virus in infants using polymerase chain reaction on dried blood spots in Botswana's national program for prevention of mother-to-child transmission. *Pediatr Infect Dis J* 2008;27:22-26.

15 **Sherman GG, Stevens G, Jones SA, Horsfield P, Stevens WS.** Dried blood spots improve access to HIV diagnosis and care for infants in low-resource settings. *J Acquir Immune Defic Syndr* 2005;38:615-617.

16 **Sherman GG, Cooper PA, Coovadia AH, Puren AJ, Jones SA, Mokhachane M, Bolton KD.** Polymerase chain reaction for diagnosis of human immunodeficiency virus infection in infancy in low resource settings. *Pediatr Infect Dis J* 2005;24:993-997.

17 **Fischer A, Lejczak C, Lambert C, Servais J, Makombe N, Rusine J, Staub T, Hemmer R, Schneider F, Schmit JC, Arendt V.** Simple DNA extraction method for dried blood spots and comparison of two PCR assays for diagnosis of vertical human immunodeficiency virus type 1 transmission in Rwanda. *J Clin Microbiol* 2004;42:16-20.

18 **Patton JC, Akkers E, Coovadia AH, Meyers TM, Stevens WS, Sherman GG.** Evaluation of dried whole blood spots obtained by heel or finger stick as an alternative to venous blood for diagnosis of human immunodeficiency virus type 1 infection in vertically exposed infants in the routine diagnostic laboratory. *Clin Vaccine Immunol* 2007;14:201-203.

19 **Stevens W, Sherman G, Downing R, Parsons LM, Ou CY, Crowley S, Gershy-Damet GM, Fransen K, Bulterys M, Homsy J, Lu L, Finkbeiner T,**

Nkengasong JN. Role of the laboratory in ensuring global access to ARV treatment for HIV-infected children: consensus statement on the performance of laboratory assays for early infant diagnosis. *Open AIDS J* 2008;2:17-25.

20 **Ou CY, Yang H, Balinandi S, Sawadogo S, Shanmugam V, Tih PM, Adje-Toure C, Tancho S, Ya LK, Bulterys M, Downing R, Nkengasong JN.** Identification of HIV-1 infected infants and young children using real-time RT PCR and dried blood spots from Uganda and Cameroon. *J Virol Methods* 2007;144:109-114.

21 **De Zulueta P.** Randomised placebo-controlled trials and HIV-infected pregnant women in developing countries. Ethical imperialism or unethical exploitation? *Bioethics* 2001;15:289-311.

22 **De Cock KM, Fowler MG, Mercier E, de Vincenzi I, Saba J, Hoff E, Alnwick DJ, Rogers M, Shaffer N.** Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. *JAMA* 2000;283:1175-1182.

23 **Balinandi S, Downing R.** Evaluation of total nucleic acid (TNA) real-time PCR for detection of HIV-1 infection in infants. WHO/CDC Informal Consultation to Review the Performance of the DNA PCR Assay for Early HIV-1 Diagnosis in PMTCT Programs in Different Countries with Diverse HIV-1 Subtypes. Entebbe, Uganda: World Health Organization and Centers for Disease Control and Prevention, 2006.

PNG Med J 2012 Mar-Dec;55(1-4):24-34

'Because it is a joyful thing to carry a baby': involving men in reproductive, maternal and newborn health in East New Britain, Papua New Guinea

W. Holmes[1], G. Wambo[2], R. Gabong[2], E. Kavang[2], S. Luana[2], A. Sawa[2], H. Supsup[2], J.C. Reeder[1], S. Cassidy[2] and L.J. Natoli[1,3]

Centre for International Health, Burnet Institute for Medical Research and Public Health, Melbourne, Australia and East New Britain Sexual Health Improvement Project, Kokopo, Papua New Guinea

SUMMARY

***Background*: There are many benefits to involving expectant fathers in maternal and newborn health, including reducing vulnerability to HIV (human immunodeficiency virus) and sexually transmitted infections (STIs). Women are at risk of HIV infection and other STIs during pregnancy and breastfeeding and in Papua New Guinea (PNG) a number of complex factors interact to enhance this vulnerability. PNG health policies do support men's involvement in maternal and newborn health, but currently there is limited understanding of appropriate or effective ways by which this could be achieved. *Aims*: The aims of this research were to gather information to inform strategies to enable the greater involvement of men in maternal and newborn health services and to explore the factors that contribute to STI and HIV vulnerability among pregnant women in East New Britain Province. *Methods*: Between June 2011 and February 2012 we conducted a total of 14 focus group discussions with pregnant women, expectant fathers, older men and older women. Ten in-depth interviews were conducted with health workers and staff within the provincial administration. *Key findings*: Expectant fathers were concerned for the health of their wife and baby both during and after pregnancy. They had many questions about pregnancy, childbirth and the care of their baby and were eager for information. Protecting their family is viewed as an important role for men and could be a useful way of engaging with them. Misconceptions about the safety of sex during pregnancy are one reason that couples are often sexually abstinent for long periods. This may contribute to the likelihood that either partner will seek sex outside marriage during pregnancy or postpartum, and increase a pregnant woman's risk of contracting STIs and HIV. We heard that it is common for men as well as women to have extramarital sex at this time. Currently, male involvement in maternal and child health care is uncommon and community attitudes are mixed. Some significant barriers to involving men relate to traditional customs and feelings of shame and embarrassment. Others can be attributed to health service factors, such as a lack of privacy and the attitudes of health care workers. Various community channels for reaching expectant fathers were suggested.**

Introduction

Family planning, pregnancy, childbirth and newborn care have great cultural and social significance. They are seen as 'women's business', yet are often governed by men. Men make decisions about family planning and the prevention of sexually transmitted infections (STIs). When their wife is pregnant they influence attendance at antenatal, delivery and postnatal care, her diet, workload, sense of security and happiness, and infant feeding

1 Centre for International Health, Burnet Institute for Medical Research and Public Health, 85 Commercial Road, Melbourne, Victoria 3004, Australia

2 East New Britain Sexual Health Improvement Project, PO Box 1458, Kokopo, East New Britain 613, Papua New Guinea

3 Corresponding author
lisan@burnet.edu.au

(1-4). However, maternal and newborn health care services focus on women, and men often lack the information they need to make informed decisions. There have been many calls for greater involvement of men in reproductive, maternal and newborn health care, and for research to better understand men's behaviours and motivations (5-7). The benefits of involving men include improved maternal and perinatal survival through encouraging antenatal care, better preparation for birth and recognition of the danger signs of complications (8-11). Involving men can help to prevent women becoming infected with HIV (human immunodeficiency virus) during and after pregnancy, increase the uptake of interventions to reduce the risk of mother-to-child transmission of HIV (12), and improve the use of postpartum family planning (10,13). Men's support can help to prevent maternal depression (14) and reduce the risk of violence, which is often more common during pregnancy (15).

In Papua New Guinea (PNG), uptake of family planning is low and rates of maternal and perinatal deaths and STI prevalence are high. HIV continues to be a serious concern. Key policy documents support greater involvement of men, including the PNG National HIV and AIDS Strategy 2011-2015 (16) and the Operational Plan 2010-2015 for Prevention of Parent to Child Transmission of HIV and Paediatric AIDS in PNG (17). Moreover, there is strong evidence for a 'family-centred' approach to HIV prevention and care (18). However, there is limited understanding of the most appropriate and effective ways to achieve greater male involvement in the specific cultural context of PNG.

Since 2007, the Burnet Institute has partnered with the East New Britain (ENB) Provincial Government through the East New Britain Sexual Health Improvement Project (ENBSHIP). Over the course of ENBSHIP, the need to engage men and the likely benefits of their involvement with maternal and child health services have become increasingly clear. This, and the need to explore women's vulnerability to STIs and HIV in the pregnant and postpartum period, were motivations for this research.

Methods

This was an exploratory qualitative study. A team from the Burnet ENBSHIP staff, the Provincial AIDS Council and local health services participated in a five-day training and planning workshop during which question guides were developed. After obtaining informed consent, the team conducted a total of 14 focus group discussions (FGDs) with pregnant women, expectant fathers, older men and older women between June 2011 and February 2012. A purposive sample was identified from the communities around four health facilities: Gelagela Health Centre (Rabaul District), Butuwin Urban Clinic (Kokopo District), Warangoi Rural Hospital (Pomio District) and Rabaul Urban Clinic (Rabaul District). Ten in-depth interviews were also undertaken with health workers and staff within the provincial administration. The FGDs were gender sensitive, with male researchers facilitating FGDs for male participants and female researchers for female participants. An expatriate volunteer worked with facilitators and note-takers after each FGD and interview to consolidate the field notes and translate data from Tok Pisin to English. Interviews were tape-recorded with the informed consent of participants.

Thematic analysis was used to identify recurrent themes in the data and differences across the various FGDs and interviews. Interpretations were checked through a participatory process involving local counterparts. Discussions ('tok save') were held with the communities who participated in the research to share the findings and stimulate discussion.

Ethical considerations

Ethical approval for the study was received from the Research Advisory Committee of the National AIDS Council Secretariat (NACS) in Papua New Guinea and the Alfred Hospital Human Research Ethics Committee, Melbourne. We were studying sensitive issues so team training included particular emphasis on issues such as the informed consent process, avoiding causing offence or distress, and maintaining confidentiality of data.

Findings

Pregnancy and antenatal care

Antenatal care (ANC) was generally viewed as beneficial and a helpful source of information. However, some women do not

attend ANC and most of those who do, attend late in the pregnancy. Reasons included the need to travel long distances and a lack of support from husband or parents: *"Sampela gutpela papa save givim moni long meri, sampela nogat."* (Some good fathers give money to their wives but others do not) [Older man]. Some women mentioned that when they attended early in the pregnancy they were told to return later by health workers. Shame or embarrassment were also commonly reported barriers, and these feelings related to being illiterate, young, unmarried, having many children, being a sex worker, or being pregnant as a result of incest. Some women fear being diagnosed with HIV or another STI and their confidentiality being breached. Fear of being told off by health workers, for example, for having too many children or becoming pregnant again too soon, was another reason given for not attending ANC.

Many expectant fathers expressed concern for the health of their wife and baby. They worried about the baby being born prematurely or dying, or being in the wrong position for birth, or the mother getting an STI, or whether she would get to the clinic in time for the birth. They showed concern that their wife may work too hard during the pregnancy or not get the necessary medication if sick. They worried about how to help their wife with labour pains, and feared that she may die during childbirth: *"Mi no slip inap mi harim meri bilong mi karim."* (I could not sleep until my wife delivered) [Expectant father].

Expectant fathers wanted information. They have questions about fertility, conception and contraception. They wanted to know about their wife working during pregnancy, how to keep her healthy, when she should go to the clinic, whether it is safe to have sex, and how to know when the baby would be born. They also had many questions about how to feed and care for the baby: *"Mi laik save long lukautim pikinini na bai noken kisim sik."* (I want to know how to look after my baby so it doesn't get sick) [Expectant father]. Another said: "*We just leave it to the mother to breastfeed the baby. I would like to know what food the baby should first eat and when is the right time to stop breastfeeding. What kind of signs do you see that it's time to give food to the baby?*" [Expectant father]. Men also want to know why some babies are born early, are stillborn or have disabilities.

Attitudes towards involving men in maternal and newborn health care

Traditionally men have not been involved in pregnancy and childbirth and currently very few expectant fathers attend ANC. Some accompany their partner to the clinic but are not included in the consultation. But we heard that they may show support by providing a bus fare, asking to look at the health book and encouraging their wife to take her medicines.

Attitudes towards men's participation in maternal health care were mixed. Several mentioned that it would cause shame; one older woman said: *"Ol hailans, ol ino save sem. ….. ol meri tu ol i save sem long ol man go wantaim long klinik."* (It would be OK in the highlands where they would not be embarrassed, but not in East New Britain… women here feel ashamed to have their husbands accompany them to a clinic); and a health worker said: *"Ol save sem, ol man na bai ol ino inap bihainim meri bilong ol."* (Men feel ashamed because normally men don't go with their wives to the clinic). However, many men, women and some older people were positive about the idea, feel that customs could change, and that there would be benefits. For example, one pregnant woman said: "*Gutpela long kisim advais….. em gutpela long lukautim ol meri bilong em. Ol meri bai amamas long dispela."* (It would be good for men to get advice and be able to look after their wife. Women would be happy about this); and an older man said: *"Yumi sud senisim ol kastom. Gavamen sud putim lo dat man mas go wantaim meri igo long haus sik bikos man bai kisim skul wanem ol hevi mama i kisim o gat."* (We should change the custom. The government should make a law that the man must go to the clinic with his wife to learn about her problems). Participants suggested that men could learn about how to care for their wife, and to be aware of danger signs during pregnancy, and would then be more likely to share in the responsibility of child care. Health workers noted that attending ANC would enable men to have the same knowledge as their wives, and that couples could be tested and treated for STIs together, and learn about family planning together. It was also felt that involving partners could strengthen couples' relationships, reduce the likelihood of extramarital sex, and help mothers to feel happy and supported.

Overcoming barriers to greater involvement of expectant fathers

Although many of the expectant fathers were willing to be more involved in ANC, we heard that community norms and beliefs about gender roles and relations would need to be addressed. For example, one pregnant woman said: *"Ol man isi kirap long kamapim pikinini na ino inap karim na helpim igo long klinik."* (Men are keen to make the baby but not to help with going to the clinic). There is also a belief that: *"Yu noken bihainim meri tumas. Ol bikman bai korosim yu long bihainim em*." (You shouldn't follow your wife around too much. If you do, the village elders will scold you) [Expectant father]. We also heard the belief that men's activities might be harmed if they take an interest in pregnancy. For example, one older man said: *"Meri gat bel na papa go wantaim em long klinik bai daunim strong bilong painim pis."* (If you spend time with your pregnant wife you won't be able to catch fish). Local Tolai custom forbids mothers-in-law and sons-in-law from speaking directly to each other. Because mothers often accompany daughters to ANC, this was also a concern for some expectant fathers. FGD participants suggested that men attending ANC might fear drawing attention to themselves and get teased for being too young, too old, a first-time parent, unmarried, or for having many or closely spaced children. Some expectant fathers mentioned a reluctance to attend ANC with their pregnant wives because they would prefer other women to think that they are single and 'available'. One older woman noted: "*Ol i sem bikos ol narapela girlpren bai lukim ol igo wantaim long klinik."* (He might feel shame because his other girlfriends might see him at the clinic with his wife). Men also feared that they might get diagnosed with HIV or another STI at ANC.

Health-service-related barriers were also discussed. The clinic environment is seen as not 'male friendly' – it is unusual to see other men there, and there is nothing specific for men to do. Lack of space and privacy were commonly reported concerns. We were told that health workers may send men away, tease or scold them for having too many children, make them feel inadequate because of illiteracy or accuse them of 'just wanting to have sex'. However, one health official said: *"Mind bilong ol man tasol, maybe, olsem. Mi no lukim wanpela barrier long health facility."* (The mentality of men is the only problem. I don't see any barrier with the health facility). Another health official, though, spoke of improvements which could be made with health worker attitudes and behaviour: "*Health workers can build it or break it (the inclusion of men). The health workers should be trained so that they can approach this in a more sensitive manner. Men are different, some can be very angry, some can be very shy, some can be very nervous and so these people, health workers, they must be taught, maybe, ways of handling the situation."*

Other barriers mentioned include work commitments, lack of money, fear of being seen by police and uncertainty about being the father (Figure 1).

Suggestions to make health services more welcoming to men included: privacy for couples; having something specific for men to do so they feel involved; attending as a group; having a male staff member to talk to; providing a regular service (currently ANC is available once a week); offering a mobile/ outreach service; training health workers in counselling skills; educating officers-in-charge so that they are supportive; and extending an invitation via the wife and reinforcing this on clinic days. One health official commented: *"The nurse or health worker needs to change their attitude a little. They have to welcome them, smile at them and 'win their hearts'…. Smile and say, 'thank you for coming with your wife'. Our culture makes these things very difficult. Maybe we can put in a TV, DVD player. We had these before; they were bought by AusAID. There was one at the Butuwin clinic and it showed health-related videos. Plenty of men came. It was for health promotion."*

Improving community awareness of men's role in caring for their wives and babies was considered to be very important. It was suggested that ward councillors, church leaders and health workers could play a role in this, and that gender-specific outreach would be important. This might occur through churches, workplaces, cultural or sporting activities, the Tumbuan Society (secret men's society) or the new Community Learning Centres. One health official commented: *"We can use the cultural institutions. In the Tumbuan Society we congregate as men, there are no women there, the* tereiu *or meeting place is the best place to deliver this. We should use existing cultural institutions to*

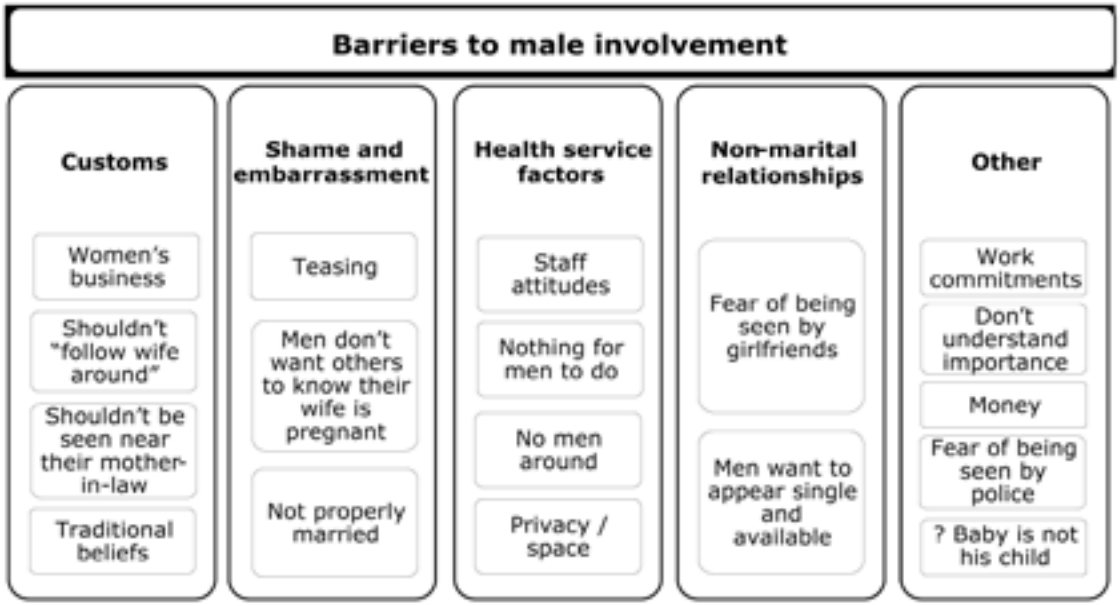


Figure 1. Summary of the barriers to male involvement.

our advantage. They will receive it with mixed feelings but at the end of the day the message will certainly be relayed. But, we have to be careful not to break taboos." The church was considered to have an important role in community awareness, as one health official pointed out: "*In ENB all people, all Christian people, plenty of people go to church. So that's where we can reach them. But first we need to educate the clergy, the pastors, so that they know about pregnancy and birth, otherwise it will be hard for them to provide information to men and they will just relay their own beliefs. We need to give them good information first and strengthen our relationship with them."*

A number of participants felt it important to appeal to men's role as head of the family: "*Tell men that they are the head of the family. They have to feel important, that it's their role. Tell couples they must work together and love each other. Men must understand that the clinic is important*." [Older woman].

Other opportunities to involve men

When women deliver in a clinic or hospital the time of discharge was mentioned as a time to engage fathers. Unfortunately a postnatal visit is not part of routine care in PNG, but the baby's first immunization is another opportunity to involve men. A health worker noted that: "*Man tu mas karimaut wok bilong mama. Ino mama tasol bai wokim wok."* (It is important that men too should be involved in assisting the mother with her work, like taking the baby for immunization. It's not only her responsibility). A male health worker supported the idea of involving men in the first immunization: *"because it is a joyful thing to carry a baby"*. It was also mentioned that there is a men's health clinic in ENB's Five Year Implementation Plan, and that this would provide a further opportunity to involve men in maternal and newborn health in the future.

Sexual beliefs and behaviour during pregnancy and breastfeeding

Varied and sometimes conflicting beliefs were reported. Some believe sex should be avoided altogether during pregnancy. Some believe sex is safe in the first six months, but should be avoided in the last trimester, while others consider sex only to be safe in the middle trimester. Health workers often share these beliefs, with some advising against sex in the first three to five months, whilst others suggest sex in the first six months is safe, but recommend abstinence in the last trimester.

Participants worried that sex would affect the health of the mother or baby. Concerns for the mother included pain or discomfort, weakness, cancer, bleeding, prolonged labour and even death. Concerns for the

baby included bone fractures or limb damage, miscarriage, damage to the head and death. Several participants said: *"Mi ting olsem nogut kok bai bagarapim het long pikinini."* (I think it's not good because the penis can damage the head of the baby) [Expectant father]. There are also fears that during breastfeeding semen can cause the baby to suffer diarrhoea or vomiting and to become weak and malnourished. There was awareness that men could pass STIs on to the mother and that these could be transmitted to the baby, and of the potential for another pregnancy when sex takes place during the breastfeeding period. Some mentioned that having sex with his pregnant wife could reduce the likelihood of the man having sex with someone else. One participant said that relations with 'tambu' (in-laws) could be damaged if they know the man is having sex with his wife while she is pregnant.

In East New Britain, traditionally men and women would sleep in separate houses for approximately three months after the birth, but this is now rarely the case, even in rural areas. While most participants suggested abstinence periods of between one to six months, reported resumption of postpartum sex ranged from immediately after discharge from hospital to up to four years postpartum. Common concerns about postpartum sex relate to maternal health, healing of perineal tears and associated discomfort, and fears of becoming pregnant again. Some spoke of resuming sex after bleeding has ceased and wounds have healed, or when the woman resumes menstruation. Others talked about waiting until the 'semen is ready' or when there is a particular moon in the sky. As mentioned above, there are also fears for the baby related to semen mixing with the breastmilk. For some the husband makes the decision to resume sex: "*Mipela ino ownim mipela, sapos boss itok den mipela koap tasol."* (We don't own ourselves, if the 'boss' says so, then we have sex) [Pregnant woman].

Occasionally pregnant women ask health workers if it is safe to have sex and, if so, at what gestational age and in which positions it is safe. However, most ANC health workers said that if they are not asked about the topic of sex they don't bring it up themselves. Some health workers felt that they lacked the knowledge and confidence to raise the topic, but that this could be improved with further training, support of other staff and dedicated time to spend on the topic, for example during ANC education sessions. Women said they would be relieved if sensitive topics like sex during pregnancy were spoken about, but would otherwise be too embarrassed to ask. Women felt that if they raised such questions the health worker would wonder why they were asking. They also feared being teased if others were to overhear.

Due to taboos and misconceptions about the safety of sex during pregnancy and postpartum, couples may be subject to long periods of sexual abstinence. This may contribute to the likelihood of either partner seeking sex outside marriage. FGD participants were asked how likely it is that men in their community have sex with women outside marriage while their partner is pregnant or breastfeeding. The group was shown the diagram (Figure 2, left), given ten stones and asked to distribute them according to the group's perceptions of male partner sexual practices during pregnancy. Findings for the different FGD sites are shown in the table on the right of the figure.

Extramarital sex is obviously common and we heard that the use of condoms is rare. One said that men don't use condoms because they are sleeping with former girlfriends so they think they are safe from STIs. When men were asked whether they thought those men engaging in extramarital sex would use a condom with their wife, they said that it would be unlikely.

Pregnant women were also asked about the likelihood of pregnant women in their community having sex with men outside marriage during pregnancy and breastfeeding (Figure 3).

Female health officials suggested that while expectant couples may abstain from sex with each other, pregnancy is often a time when women may satisfy their own sexual needs with, or cement the support of, another long-term partner, who they may believe is the father of their child. This support may be practical and financial and therefore important to the pregnant woman.

When pregnant women and expectant fathers were asked about the possible consequences of extramarital sex they mentioned the wife being infected with STIs or committing suicide, domestic violence or

divorce. It was also believed that the wife may experience delayed second stage labour and that the baby might experience shortness of breath, malaria or stunted growth.

When use of condoms in the postpartum period was discussed it was clear that it is unlikely that condoms would be used within marriages, for reasons related to questioning trust and lack of access to condoms. We heard that many men and women would not tell their spouse if they had an STI for fear that their spouse would accuse them of being unfaithful, would be physically violent, or would leave them. Barriers to STI treatment-seeking include fear of gossip, shame and concerns about health workers breaching confidentiality.

Sources of information for men about maternal and newborn health

Older people were commonly mentioned as sources of advice and information about reproduction, pregnancy, childbirth and care of the newborn: *"My bubu (*grandparents) *would talk to me, but not my parents. People used to do that (speak to their grandchildren but not their children), that's the cultural practice."* [Health official]. However, their advice was not always well informed. It is important to try to reach older people with health messages about reproductive and maternal health, as well as young people.

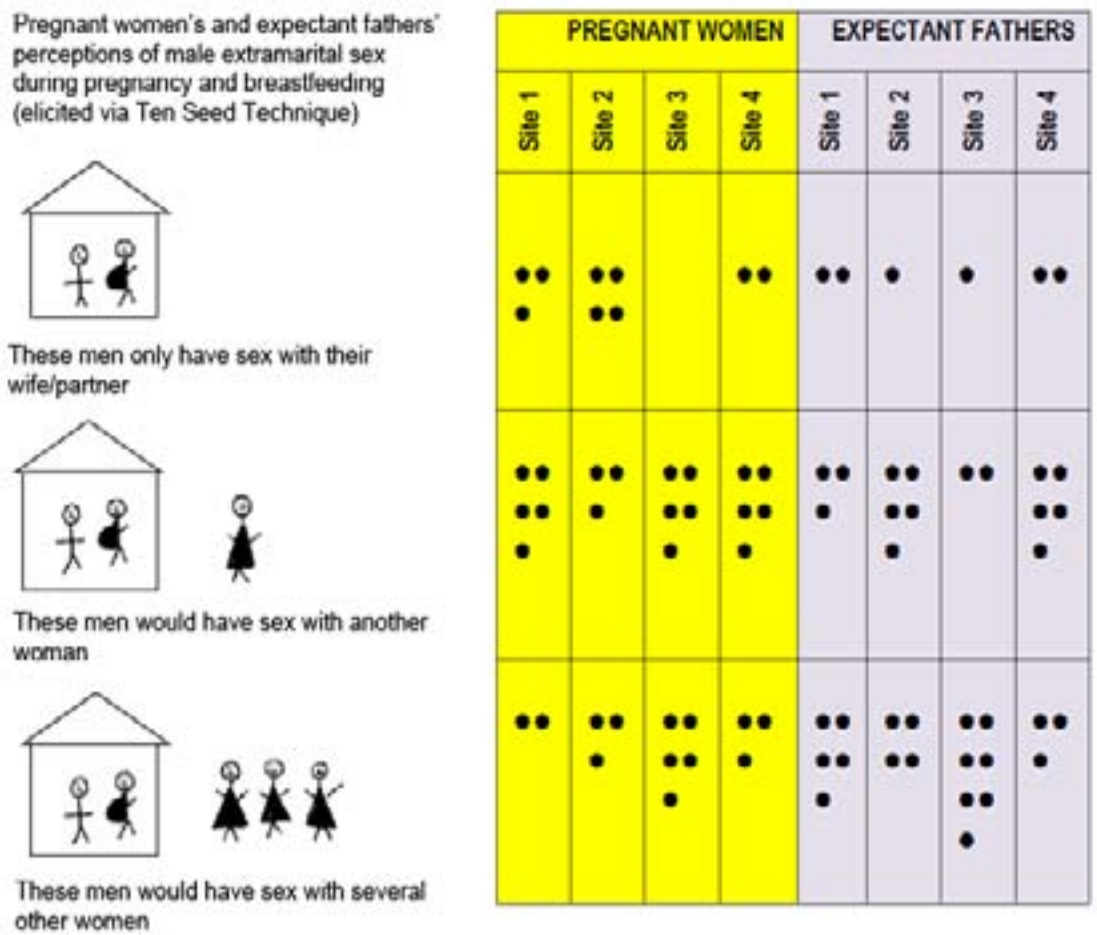


Figure 2. Pregnant women's and expectant fathers' perceptions of male extramarital sex during pregnancy and breastfeeding (elicited via Ten Seed Technique).

Expectant couples also obtain information from health workers, church and community leaders, friends and 'stret tokers' (locals who peer educate on sexual health). Radio, books, television, movies, newspapers and workshops conducted by non-government organizations (NGOs) were also mentioned as sources of information. When expectant fathers were asked about their preferred ways of receiving information about pregnancy they mentioned their parents, the aid post, the church (eg, through men's retreats) and community leaders through the community hall.

Discussion

Despite the sensitive nature of the topics discussed, the local facilitators were able to stimulate discussion to provide a wealth of data about the range of relevant beliefs and behaviours to inform policy and planning for greater involvement of men in maternal and newborn health in East New Britain, and more broadly in PNG. Although this goes against traditional cultural beliefs, many participants could see potential benefits and welcomed the idea.

Expectant fathers showed concern for their wives and babies and a real desire for knowledge. It will clearly be important to appeal to men's sense of responsibility and their traditional gender role of protecting their family. There is evidence that programs that promote gender-equitable relationships

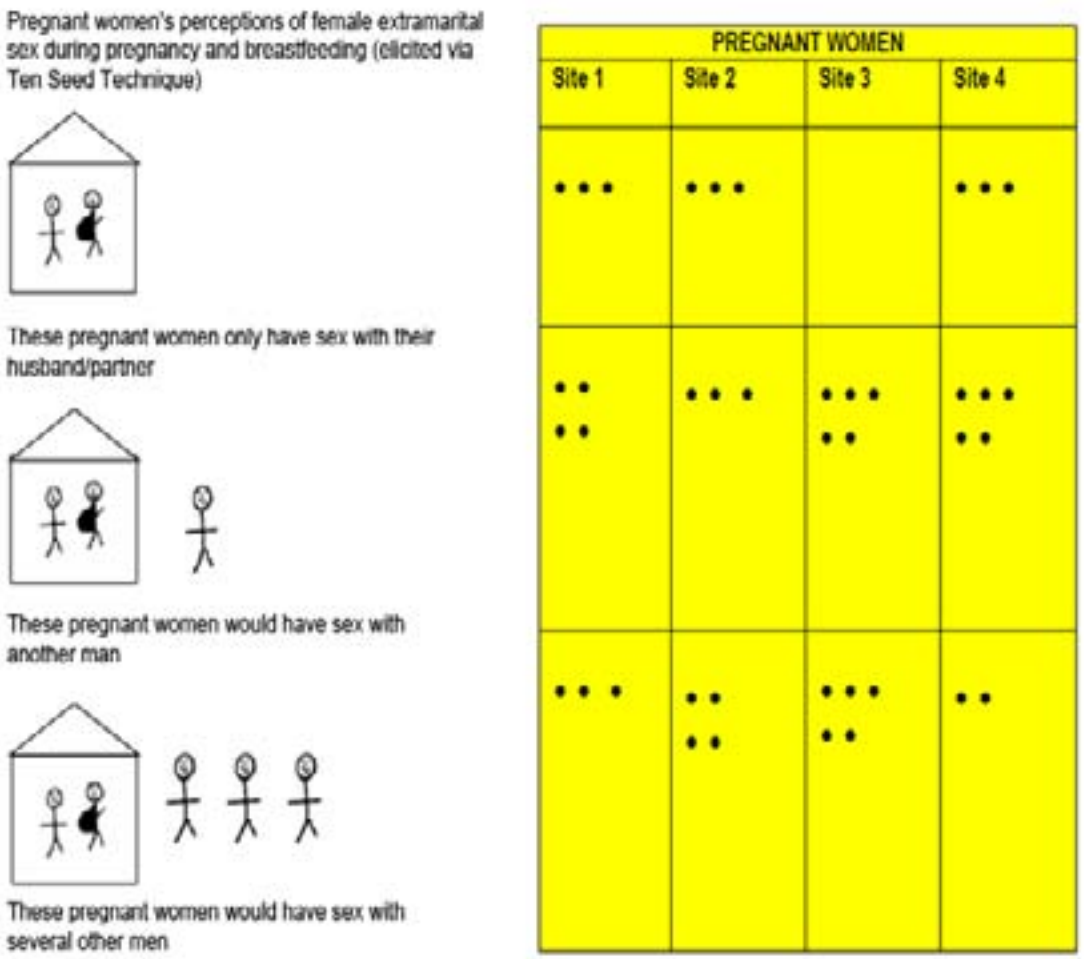


Figure 3. Pregnant women's perceptions of female extramarital sex during pregnancy and breastfeeding (elicited via Ten Seed Technique).

and address social context are effective in producing behaviour change among men (19), and there are many accounts of progress in achieving male participation in sexual and reproductive health (20). Experience in Lao People's Democratic Republic (PDR), Cambodia, India, South Africa and Indonesia shows that when expectant fathers are encouraged to attend ANC they are keen to do so (10,13,21).

There are many examples in the research literature of how health care provider attitudes and behaviour can affect ANC attendance by both men and women (22,23), including a study from PNG (24). Health care providers often work in difficult conditions and will need training in communication skills (25), as well as guidelines to give them confidence in talking to couples, expectant fathers and fathers. The lack of privacy in the ANC is a problem worth addressing for the sake of pregnant women, but becomes an even more important issue when men are present. This relates both to enabling conversations to be private and to ensuring that women are not examined in front of men. The infrastructure of many health facilities needs upgrading but it is possible to make clinics more welcoming to men by arranging a sheltered waiting place (which need not be inside the clinic), having posters and information materials relevant to men, and arranging better privacy through the use of curtains (26). ANC clinic times may need to be modified to better fit with men's work commitments.

Our finding that women as well as men commonly have sex with one or more partners outside marriage during pregnancy is significant and further research is needed about the reasons and circumstances. This behaviour increases the vulnerability of women and their babies to STIs and HIV infection, and also increases the vulnerability of their partners. Women are more susceptible to infection with HIV during pregnancy and HIV-positive women are more likely to transmit HIV to men when pregnant (27). Women who become infected during pregnancy or breastfeeding have a much higher risk of transmission to the baby (28). A significant proportion of HIV infection in children is the result of new maternal infections during pregnancy and breastfeeding (29), so it is important that both men and women are aware of this risk. Men may be more likely to have sex with someone else because they avoid sex with their pregnant partner out of concern for the safety of the baby, so they need to know that sex with their partner is safe throughout a normal pregnancy. Simply testing expectant fathers for HIV without providing them with information and treatment services is insufficient (30). Condoms must be more widely available to both men and women, and women need access to contraception postpartum so that they do not fear another pregnancy.

In addition to a routine couple antenatal visit (31), there are a variety of models for reaching men with information about reproductive, maternal and newborn health. A program in Migende, PNG, has shown that holding a separate weekly clinic for men can attract men for HIV and syphilis testing, and for couple counselling (32). The clinic is publicized through public announcements in churches, through community leaders and public awareness campaigns, through invitation to wives at ANC and via peers. In Lao PDR expectant fathers have been enthusiastic participants in group discussions at ANC with a male member of staff about safer sex during pregnancy and protecting the health of their partners (33). Other possibilities are holding meetings of young men and expectant fathers at the Tumbuan Society or other male-only community meetings, in the workplace and at churches. Older people are influential and should be included in health education efforts. A brochure about the safety of sex during pregnancy and the postpartum period should be provided to all pregnant women during the first ANC visit, and health workers need to be informed about the safety of sex during pregnancy so that they are able to provide evidence-based advice about this to antenatal women. We have developed some communication materials and guidelines for health care providers informed by our findings (available from the Burnet Institute).

Conclusions

There is a strong rationale for involving men in maternal and newborn health, and men have a right to the information they need to make decisions to protect their own health and that of their family. Just as pregnancy provides an opportunity for contact with preventive health care services for women, men's own future health, as well as their families' health, could benefit from contact with health services at this time. Pregnancy is a time when expectant

fathers feel responsible and are more likely to be open to health messages. It is important to understand context-specific cultural beliefs and norms, and also to be aware that these can change. We need to bear in mind that new public health strategies, such as vaccination, or malaria bednets, took time to become established and accepted.

In 2009, a technical review of the PNG Prevention of Parent to Child Transmission (PPTCT) of HIV and Paediatric HIV Care and Treatment strategy reinforced the need for greater involvement of men (34). The review explicitly referred to the gendered nature of ANC services and how they act as a barrier to male involvement, and the insufficient focus paid to 'family-centred' HIV counselling and testing. This study provides useful guidance to national and district level planners, and we hope that it will stimulate progress in involving men more in reproductive, maternal and newborn health care.

ACKNOWLEDGEMENTS

This research was funded through the PNG National AIDS Council. We are grateful to the East New Britain women, men and health workers who gave so generously of their time to take part in discussions and interviews and to the Burnet Institute team in ENB and the provincial and district government partners who supported this research and assisted with data collection. We acknowledge the valuable contribution and support of: ENB Provincial Health Office; ENB PAC – Steven Auri; Simone Cassidy and Geoff Chan (Burnet Institute); Leo Ono (Rabaul District HIV Coordinator); Jack Melki (Nonga Base Hospital); Elsie Buka (Rabaul Urban Clinic); Rosemarie Luluai (Warangoi Rural Hospital); Junias Tenaen (Raluana Local Level Government); Rison Holde (Tapo Health Centre); William Nitting (PNG Family Health); Elsie Penaia; Robert Wasobon; Stephanie Lusby. The original idea for the Ten Seed diagram came from Norbu Drumdui (Tibet). We gratefully acknowledge the contribution to this work of the Victorian Operational Infrastructure Support Program received by the Burnet Institute.

REFERENCES

1 **Greene ME, Mehta M, Pulerwitz J, Wulf D, Bankole A, Singh S.** Involving men in reproductive health: contributions to development. New York: United Nations Millennium Project, 2004. www.unmillenniumproject.org/documents/Greene_et_al-final.pdf

2 **Langen TT.** Gender power imbalance on women's capacity to negotiate self-protection against HIV/AIDS in Botswana and South Africa. *Afr Health Sci* 2005;5:188-197.

3 **Roth DM, Mbizvo MT.** Promoting safe motherhood in the community: the case for strategies that include men. *Afr J Reprod Health* 2001;5:10-21.

4 **Bhandari N, Kabir AK, Salam MA.** Mainstreaming nutrition into maternal and child health programmes: scaling up of exclusive breastfeeding. *Matern Child Nutr* 2008;4(Suppl 1):5-23.

5 **Mbizvo MT, Bassett MT.** Reproductive health and AIDS prevention in sub-Saharan Africa: the case for increased male participation. *Health Policy Plan* 1996;11:84-92.

6 **Rivers K, Aggleton P.** Men and the HIV Epidemic, Gender and the HIV Epidemic. New York: HIV and Development Programme, United Nations Development Programme, 1999. www.undp.org/hiv/publications/gender/mene.htm

7 **O'Farrell N.** Enhanced efficiency of female-to-male HIV transmission in core groups in developing countries: the need to target men. *Sex Transm Dis* 2001;28:84-91.

8 **World Health Organization.** Engaging men and boys in changing gender-based inequity in health: evidence from programme interventions. Geneva: World Health Organization, 2007.

9 **Mullick S, Kunene B, Wanjiru M.** Involving men in maternity care: health service delivery issues. In: Agenda: Special Focus on Gender, Culture and Rights. New York: Population Council, 2005:124-135. www.popcouncil.org/pdfs/frontiers/journals/Agenda_Mullick05.pdf - 2005-08-31

10 **Shefner-Rogers CL, Sood S.** Involving husbands in safe motherhood: effects of the SUAMI SIAGA campaign in Indonesia. *J Health Commun* 2004;9:233-258.

11 **Turan JM, Nalbant H, Bulut A, Sahip Y**. Including expectant fathers in antenatal education programmes in Istanbul, Turkey. *Reprod Health Matters* 2001;9:114-125.

12 **Farquhar C, Kiarie JN, Richardson BA, Kabura MN, John FN, Nduati RW, Mbori-Ngacha DA, John-Stewart GC.** Antenatal couple counseling increases uptake of interventions to prevent HIV-1 transmission. *J Acquir Immune Defic Syndr* 2004;37:1620-1626.

13 **Varkey LC, Mishra A, Das A, Ottolenghi E, Huntington D, Adamchak S, Khan ME, Homan F.** Involving men in maternity care in India. Frontiers in Reproductive Health Program. New Delhi: Population Council, 2004.

14 **Fisher J, Cabral de Mello M, Patel V, Rahman A, Tran T, Holton S, Holmes W.** Prevalence and determinants of common perinatal mental disorders in women in low- and lower-middle-income countries: a systematic review. *Bull World Health Organ* 2012;90:139G-149G.

15 **Cook J, Bewley S.** Acknowledging a persistent truth: domestic violence in pregnancy. *J R Soc Med* 2008;101:358-363.

16 **National AIDS Council of Papua New Guinea.** Papua New Guinea: National HIV and AIDS Strategy 2011-2015. Port Moresby: National AIDS Council of Papua New Guinea, 2010.

17 **Papua New Guinea National Department of Health.** Operational Plan 2011-2015: Prevention of Parent to Child Transmission of HIV and Paediatric AIDS in Papua New Guinea. Port Moresby: National Department of Health, 2010.

18 **Betancourt TS, Abrams EJ, McBain R, Fawzi MC.** Family-centred approaches to the prevention of mother to child transmission of HIV. *J Int AIDS Soc* 2010;13(Suppl 2):S2.

19 **Barker G, Ricardo C, Nascimento M, Olukoya A, Santos C.** Questioning gender norms with men to improve health outcomes: evidence of impact. *Glob Public Health* 2010;5:539-553.

20 **Sternberg P, Hubley J.** Evaluating men's involvement as a strategy in sexual and reproductive health promotion. *Health Promot Int* 2004;19:389-396.

21 **Kunene B, Beksinska M, Zondi S, Mthembu N, Mullick S, Ottolenghi E, Kleinschmidt I, Adamchak S, Janowitz B, Cuthbertson C.** Involving men in maternity care: South Africa. New York: Population Council, Oct 2004. http://www.popcouncil.org/pdfs/FRONTIERS/FR_FinalReports/SA_MIM.pdf

22 **Bowser D, Hill K.** Exploring evidence for disrespect and abuse in facility-based childbirth. Report of a landscape analysis. USAID-TRAction Project. Bethesda: United States Agency for International Development, 20 Sep 2010.

23 **Govender V, Penn-Kekana L.** Gender biases and discrimination: a review of health care interpersonal interactions. Background paper prepared for the Women and Gender Equity Knowledge Network of the WHO Commission on Social Determinants of Health. Geneva: World Health Organization, Jun 2007. www.who.int/social_determinants/ resources/gender_biases_and_discrimination_wgkn_2007.pdf

24 **Larsen GL, Lupiwa S, Kave HP, Gillieatt S, Alpers MP.** Antenatal care in Goroka: issues and perceptions. *PNG Med J* 2004;47:202-214.

25 **World Health Organization.** Counselling for maternal and newborn health care: a handbook for building skills. Geneva: World Health Organization, 2010.

26 **Raju S, Leonard A, eds.** Men as supportive partners in reproductive health: moving from rhetoric to reality. New Delhi: Population Council South and East Asia Regional Office, 2000.

27 **Mugo NR, Heffron R, Donnell D, Wald A, Were EO, Rees H, Celum C, Kiarie JN, Cohen CR, Kayintekore K, Baeten JM; Partners in Prevention HSV/HIV Transmission Study Team.** Increased risk of HIV-1 transmission in pregnancy: a prospective study among African HIV-1-serodiscordant couples. *AIDS* 2011;25:1887-1895.

28 **Humphrey JH, Marinda E, Mutasa K, Moulton LH, Iliff PJ, Ntozini R, Chidawanyika H, Nathoo KJ, Tavengwa N, Jenkins A, Piwoz EG, Van de Perre P, Ward BJ; ZVITAMBO Study Group.** Mother to child transmission of HIV among Zimbabwean women who seroconverted postnatally: prospective cohort study. *BMJ* 2010;341:c6580.

29 **Johnson LF, Stinson K, Newell ML, Bland RM, Moultrie H, Davies MA, Rehle TM, Dorrington RE, Sherman GG.** The contribution of maternal HIV seroconversion during late pregnancy and breastfeeding to mother-to-child transmission of HIV. *J Acquir Immune Defic Syndr* 2012;59:417-425.

30 **Sherr L, Croome N.** Involving fathers in prevention of mother to child transmission initiatives – what the evidence suggests. *J Int AIDS Soc* 2012;15(Suppl 2):17378.

31 **Holmes W.** Effective provision of antenatal care. *Lancet* 2001;358:928.

32 **Prasanna ST.** Together, we can: the success of the Mingende practice model for preventing parent-to-child transmission of HIV in Papua New Guinea. Bangkok: UNICEF East Asia and Pacific Regional Office, Mar 2011. www.unicef.org/eapro/Together_We_Can_updated26July11.pdf

33 **Natoli L, Holmes W, Chanlivong N, Chan G, Toole MJ.** Promoting safer sexual practices among expectant fathers in the Lao People's Democratic Republic. *Glob Public Health* 2012;7:299-311.

34 **Inter-Agency Task Team.** PNG Prevention of Parent to Child Transmission (PPTCT) and Paediatric HIV Care and Treatment Review, March 9-16th, 2009. Joint Mission Report and Recommendations. New York: UNICEF, 2009.

PNG Med J 2012 Mar-Dec;55(1-4):35-44

Arboviruses of human health significance in Papua New Guinea

Marinjho H. Jonduo[1], Grace Bande[1] and Paul F. Horwood[1,2]

Papua New Guinea Institute of Medical Research, Goroka

SUMMARY

Arboviruses (arthropod-borne viruses) are important emerging pathogens in many tropical and developing countries of the world. The Southeast Asian and Western Pacific regions have recently experienced large outbreaks of dengue, Japanese encephalitis and chikungunya fever. In Papua New Guinea (PNG) serological surveys and mosquito isolation experiments suggest that arboviruses are prevalent throughout the country. However, the lack of surveillance and clinical reporting means that the distribution and prevalence of these diseases is unknown. In this paper we review the most important arboviruses with regard to human health in the PNG region.

Introduction

The word arbovirus is an ecological term that is used to define the heterogeneous collection of viruses which are transmitted by haematophagous arthropods. The term is a contraction of the phrase 'arthropod-borne virus' and thus has no taxonomic significance. The arboviruses include a wide variety of virus taxa, representing eight family groups and 14 genera (1). However, most arboviruses of human health significance belong to only three RNA viral families: *Flaviviridae*, *Togaviridae* and *Bunyaviridae*. The Centers for Disease Control (International Catalogue for Arboviruses) have registered over 530 viruses. However, only approximately 130 of these viruses have been associated with human disease and a much smaller number implicated in serious illnesses (2,3).

Arboviruses are among the most common agents of febrile illnesses worldwide and are important emerging pathogens. The last three decades have seen a dramatic increase in the incidence of epidemics due to arboviruses, in particular dengue virus (DENV), chikungunya virus (CHIKV), yellow fever virus (YFV), Japanese encephalitis virus (JEV) and West Nile virus. The reasons behind the emergence (or re-emergence) of these diseases are complex and multifactorial, yet aspects such as increased international travel, habitat destruction and global climate change probably play an important role (4). Countries worldwide are becoming more aware of the increased threat that emerging arboviral diseases present to the health of their people.

This paper will review the impact of arboviral diseases in Papua New Guinea (PNG) and surrounding regions and discuss the possible threat from exotic arboviruses.

Clinical disease

Arboviral infections cause a broad range of disease, including asymptomatic infections and acute self-limiting febrile illnesses. Some viruses are also associated with severe secondary conditions such as meningoencephalitis and haemorrhagic fever which may result in disabling sequelae and death. Generally, arboviral infections can be classified into four main clinical syndromes (Table 1): 1) acute, undifferentiated fever; 2) meningoencephalitis; 3) haemorrhagic fever; and 4) polyarthritis (3,5). Arboviral infections are commonly confused with other illnesses such as malaria, typhoid and dysentery due to their non-specific clinical symptoms and therefore remain undiagnosed in many developing countries (6).

Transmission and life cycles

Arboviruses are transmitted between

1 Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea

2 Corresponding author
paul.horwood@hotmail.com

TABLE 1

ARBOVIRAL SPECIES OF POSSIBLE HUMAN HEALTH SIGNIFICANCE IN PAPUA NEW GUINEA

Virus name	Distribution	Disease	Principal vectors	Vertebrate host
Flaviviridae				
Dengue virus 1-4 (DENV1-4)	Worldwide tropics and subtropics	FI, HF	*Ae. aegypti*	Humans, primates
Japanese encephalitis virus (JEV)	Asia and Australasia	FI, ME	*Cx. tritaeniorhynchus, Cx. annulirostris*	Birds, pigs
Murray Valley encephalitis virus (MVEV)	Australia, New Guinea, Indonesia	FI, ME	*Cx. annulirostris*	Birds
Kunjin virus (KUNV)	Australia, New Guinea, Indonesia	FI, ME, PA	*Cx. annulirostris*	Birds
Sepik virus (SEPV)	New Guinea	FI	*Ficalbia* spp.	Unknown
Togaviridae				
Ross River virus (RRV)	Australia, New Guinea	FI, PA	*Cx. annulirostris, Ae. vigilax, Ae. camptorhynchus*	Marsupials
Chikungunya virus (CHIKV)	Africa, Asia	FI, PA, HF	*Ae. aegypti, Ae. albopictus*	Humans, primates

FI = febrile illness
HF = haemorrhagic fever
ME = meningoencephalitis
PA = polyarthritis
Ae. = *Aedes*
Cx. = *Culex*

vertebrate hosts through the bite of haematophagous, or blood-sucking, arthropods. Mosquitoes are the primary vectors associated with arbovirus transmission, although other biting arthropods such as ticks, sandflies and midges may also transmit viruses. All known arbovirus transmission occurring in PNG and the surrounding region is through mosquito vectors, and therefore this review will focus on mosquito-borne arboviruses of public health significance in the region.

Arboviruses display several types of life cycle, but generally most arboviruses can be classified into two main transmission cycles (Figure 1). In the sylvatic cycle (also called the enzootic or jungle cycle), the virus in transmitted from mosquitoes to a wild vertebrate host, with humans usually being a dead-end host when infected. In the urban (or epidemic) cycle, the virus cycles between humans and mosquitoes; the mosquito vector in the urban cycle is usually *Aedes aegypti*, which lives in close association with humans. Some viruses such as DENV, YFV and CHIKV are maintained in both sylvatic and urban cycles (7).

The majority of arboviruses are maintained in a sylvatic cycle between mosquitoes and a wild vertebrate host, and are therefore regarded as zoonotic diseases when humans are infected (8). The natural vertebrate host for arboviruses varies greatly between viral species. However, in terms of human arboviral diseases the most important primary hosts are birds, rodents and non-human primates; but many other species such as pigs, horses and marsupials may also play an important role as primary hosts for specific arboviruses (1).

Arthropod hosts become infected after a blood meal on a viraemic vertebrate host and

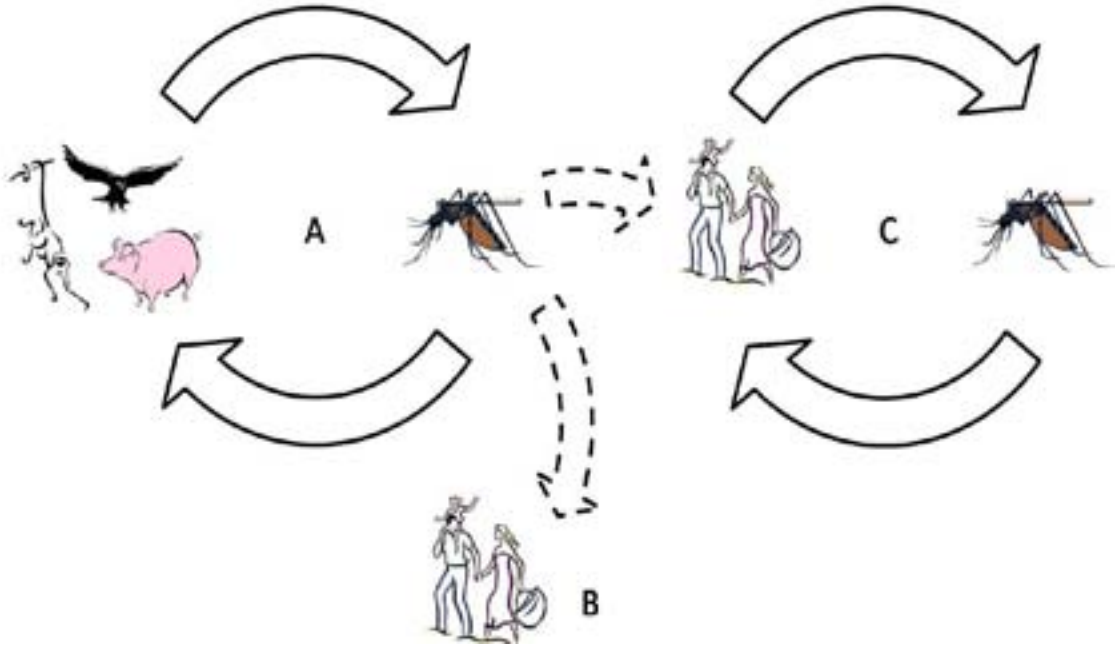


Figure 1. Arboviral transmission cycles.
A Sylvatic/enzootic cycle – most arboviral transmission occurs in an enzootic cycle between mosquitoes and wild animals such as birds, rodents and non-human primates. However, some arbovirus transmission may include domesticated animals such as pigs and horses.
B Humans are usually a dead-end host when infected with viruses that are maintained in an enzootic cycle (eg, JEV, MVEV, KUNV).
C Urban/epidemic cycle – some arboviruses have adapted to an urban cycle where transmission occurs between mosquitoes and humans (DENV, CHIKV). These viruses may also be maintained in a sylvatic cycle with wild animals.

JEV = Japanese encephalitis virus
MVEV = Murray Valley encephalitis virus
KUNV = Kunjin virus
DENV = Dengue virus
CHIKV = Chikungunya virus

after a period of replication in the arthropod tissues the virus can be transmitted during subsequent feedings. The arthropod host usually remains infectious throughout the rest of its life (6). If the vertebrate host cannot act as a reservoir or sufficiently replicate the virus for the reinfection of other vectors, this vertebrate becomes a dead-end host. This happens when the vertebrate is not the normal host, resulting in a low viraemia, and consequently transmission chances are very low (3,9). The infection of a dead-end host can often lead to more severe clinical disease (10). Humans are dead-end hosts for almost all arboviruses except for DENV, YFV and CHIKV (11-13).

Epidemiology of arboviral infections

Despite the increased incidence of large outbreaks of arboviral diseases and the public health impact in many tropical countries, little is known about the geographical distribution, risk factors and disease burden associated with these diseases. This is particularly pertinent in many developing countries such as PNG. It is clear that the health risks of arboviral infections are significant and the factors that influence the transmission and emergence of arboviruses need to be elucidated. Social and economic factors play an important role in the incidence and prevalence of arboviral diseases. For instance, industrialized countries are better able to prevent the transmission of many arboviruses through proper window screens, treated mosquito nets, air conditioning and safe water supplies (14). In developing countries poor housing and living conditions are the major cause of disease outbreaks. In

addition, better health services can reduce or eliminate mortality associated with many of these illnesses (14,15).

Historically, the geographical distribution and existence of arboviruses was determined by the ecological parameters governing their transmission cycles. The majority of arboviruses are found in the tropical regions, where the climatic conditions are highly favourable, allowing year-round transmission (3). However, global demographic and societal changes have influenced and thus facilitated the expansion of these diseases beyond their natural (historical) boundaries. Increased population density, urbanization, socioeconomic development, increased travelling made possible by modern transportation, increased animal husbandry and climate change are some of the leading factors that have also influenced arboviral distribution (3,4).

Arboviral activity within the PNG region

Over 65 arboviruses have been reported in the Australasian region alone (16), which is approximately 12% of the viruses registered in the International Catalogue of Arboviruses. However, only a few of these viruses are of medical importance. In Southeast Asia and Western Pacific, the most significant arboviral species include DENV types 1-4 (DENV1-4), JEV, Murray Valley encephalitis virus (MVEV), kunjin virus (KUNV), CHIKV, Ross River virus (RRV) and Barmah Forest virus (BFV) (16-18).

A number of studies have been conducted over the years which have indicated that there is a high prevalence of arboviral infections in PNG (19-21). Although research in this area has been limited, serological evidence and mosquito isolations suggest that there are two groups of arboviruses in PNG: the flaviviruses, including DENV1-4, JEV, MVEV, KUNV, Sepik virus (SEPV) and kokobera virus; and the togaviruses, including RRV. Thus far, there are no data available on the detection of bunyaviruses in PNG, simply because little or no research has been done on this group of arboviruses, their vectors and activities in the region. Trevett and Sanders (22) in their paper on arbovirus disease in PNG explained that in all of the areas where surveys have been carried out, antibodies to both flaviviruses and togaviruses were prevalent, mostly among inhabitants of lowland regions, with the disappearance of antibodies 1500 m above sea level. However, the absence of flavivirus and togavirus activity in the highland plateau does not necessarily rule out the introduction of these viruses from the coastal lowlands (23).

A large variety of mosquito species are known to be present in PNG. Of particular concern are the species which are commonly associated with arboviral transmission such as *Aedes aegypti*, *Culex annulirostris*, *Ae. vigilax*, *Ae. albopictus*, *Ae. camptorhynchus* and many other species that have been implicated as efficient vectors for arboviruses (24). The large lowland swamps, abundant birdlife and year-round tropical temperatures indicate that arboviral activity may be very high in PNG.

Below we will review some of the most important arboviruses that are known to circulate in PNG and also discuss some of the important viral species that may be a threat to PNG in the future.

Dengue virus

Dengue is currently considered the most important arboviral infection in the world in terms of morbidity and mortality. The worldwide incidence of dengue has increased dramatically in recent decades. Thus more than half of the world's population (3.5 billion people) are at risk of the disease and up to 100 million cases occur each year (15,25,26). This virus is distributed throughout most of the tropical regions of the world and presents serious public health problems in Southeast Asia, Africa, the Caribbean, Pacific Islands and Latin America (27). Dengue is endemic throughout many countries in Southeast Asia and the Western Pacific, including Papua New Guinea, Indonesia, Malaysia, The Philippines, Thailand, Cambodia and Vietnam (28,29).

Dengue fever (DF) is caused by any of 4 antigenically distinct serotypes of DENV, which display only 62-67% amino acid sequence similarity (26). Nonetheless, the four viruses are nearly identical in terms of epidemiology and clinical presentation. Infection with DENV provides life-long protection to that particular serotype, but does not provide cross-protective immunity against the other serotypes (27). DF is manifested as a sudden onset of fever with headache, myalgia and arthralgia, with or without retro-orbital pain and rash (15).

Classical DF lasts for about two to seven days and milder cases are often misdiagnosed for influenza or other viral infections. In more severe cases, DENV infections may proceed to dengue haemorrhagic fever (DHF), which is characterized by haemorrhaging and thrombocytopenia that may lead to dengue shock syndrome (DSS) as a result of excessive plasma leakage (30,31). DHF and DSS are potentially deadly complications, but early and appropriate treatment can greatly reduce the mortality rate associated with these diseases (28). The factors that influence the progression of disease to DHF and DSS are currently unknown. Many hypotheses have been proposed, which include immunological, host genetic and viral virulence factors (32-34).

The principal vector of dengue is the mosquito *Ae. aegypti*, which is highly adapted to the urban environment and breeds in water-filled containers. The widespread tropical distribution of dengue is attributed to the gradual invasion of *Ae. aegypti* throughout the world (35). DENV can be maintained in both sylvatic and urban cycles. In some African and Southeast Asian countries the virus is transmitted between mosquitoes and non-human primates in a sylvatic cycle. However, the virus can also be maintained in an urban cycle between *Ae. aegypti* mosquitoes and humans. Distinct genetic differences between sylvatic and urban strains of dengue suggest that the two cycles are now epidemiologically independent (30).

Dengue is believed to be endemic in PNG. However, information about the distribution and prevalence of these viruses is limited. The first major outbreak to be documented in this country was in Rabaul in 1971. Over a 5-month period over 1100 cases of dengue-like illness were recorded, with DENV2 identified as the causative agent (36). Further outbreaks were recorded in PNG in 1976 and 1983 (37). Thus the presence of DENV in PNG is evident from the reported clinical cases yet very little information is known about its epidemiology in the country. A recent study at Modilon Hospital, Madang Province detected DENV in 8% of febrile cases enrolled into the study (38), thus confirming that DENV is an important pathogen in PNG.

Although DHF is a leading cause of hospitalization and death in children in Southeast Asia (27), there have only been rare reports of DHF in PNG. However, three cases of DHF were reported in Vanimo in February 2011 (unpublished data). The lack of DHF and DSS cases in PNG is interesting due to the high level of infection believed to occur in PNG and the presence of multiple serotypes. Host susceptibility or viral virulence factors may play a role in the low numbers of cases observed in this country. Alternatively, the paucity of DHF reports in PNG may be an indication of the lack of surveillance and reporting rather than a true absence of cases.

Japanese encephalitis virus

JEV is the most important cause of human encephalitis in Southeast Asia, with an estimated 175,000 cases occurring in this region annually (39). Japanese encephalitis (JE) is characterized by a variety of neurological symptoms including headaches, convulsions, seizures, photophobia, reduced levels of consciousness and coma (40,41). Clinical cases of JE are fatal in approximately 25% of cases and severe disabling sequelae occur in up to 50% of cases. However, the majority of JEV infections are asymptomatic with only between 1 in 50 and 1 in 1000 infections resulting in clinical encephalitis (39). JEV may also be an under-appreciated cause of undifferentiated fever in Southeast Asia and other endemic areas. A study in Thailand found that infections with JEV were the apparent cause of fever in 14% of acute febrile cases (42).

Culex species of mosquito, in particular *Culex tritaeniorhynchus*, are the major vectors of JEV. The principal vector in PNG and the Torres Strait region of Australia is thought to be *Cx. annulirostris* (24). The natural vertebrate hosts for JEV are the ardeid wading birds, such as egrets and herons. However, over 90 species of wild and domestic birds have been reported with JEV seroconversion or viraemia (39). Pigs also play an important role as amplifying hosts for JEV, and most epidemics occur where there is a high pig population. Pigs are the main vertebrate species that are associated with transmission cycles with respect to human infections due to the close association of pigs with human settlements in JEV-endemic areas and the high viraemia that results in porcine infections (39). Humans are considered a dead-end host for JEV transmission because they do not develop high levels of viraemia sufficient to infect a mosquito for subsequent transmission of the

virus (43).

JE was first reported in PNG from 3 cases in the upper Fly area of Western Province between 1997 and 1998 (17). Subsequent serological studies have shown that JEV has been present in Western Province since at least 1989 (44). Human and porcine serological evidence suggests that JEV is now endemic across much of this area (44). In addition, numerous isolations of JEV from *Culex* species of mosquitoes have been made from a wide area of Western Province (24) and the nearby Torres Strait (45,46). There are concerns that JEV is spreading across a wider region of PNG with human seroconversion detected in the Gulf and Southern Highlands Provinces of the country (17). Clinical cases of JE have also been reported from Normanby Island and Alotau and a case was imported from the Port Moresby region to Australia (18,47). A recent study into the aetiology of febrile encephalopathy at Port Moresby General Hospital detected IgM antibodies to JEV in the cerebrospinal fluid of three patients (48).

Murray Valley encephalitis virus

Murray Valley encephalitis (MVE) is characterized by symptoms similar to JE. The clinical presentation of MVE may be variable but features such as sudden onset of fever, headache, nausea and vomiting may be observed, followed by neurological symptoms such as drowsiness, confusion and seizures (49). MVE is fatal in approximately 25% of cases, with a further 25% of cases resulting in severe disabling sequelae. Similarly to JEV, only a small proportion of infections with MVEV are symptomatic (<1 in 1000) and mild febrile illnesses are also common (17).

Although MVEV antibodies have been detected in many species of birds and mammals, the main vertebrate hosts are believed to be the ardeid wading birds (8). The major mosquito vector of MVEV is *Cx. annulirostris*, but many other species may be involved in transmission cycles (49). Serological evidence suggests that MVEV has an enzootic focus in north-western Australia, with epidemic activity occurring throughout much of northern Australia (50). MVEV is also found in PNG (51) and probably in the eastern islands of the Indonesian archipelago (16). One case of MVE was reported in PNG in 1956, and this case was confirmed after MVEV was isolated from the brain tissue of the deceased patient (52). In 1960, a second case from Dutch New Guinea (West Papua) was confirmed serologically (53). MVEV was also detected in mosquitoes collected from the Balimo area in 1998 (24). Sequence analysis of MVEV isolates has revealed that four distinct lineages of the virus exist in Australasia; lineages 1 and 2 have been detected in Australia, and lineages 1, 3 and 4 in PNG (54-56).

Kunjin virus

KUNV is very similar to MVEV in terms of vectors, vertebrate hosts and distribution (17). However, kunjin encephalitis is generally milder and non-life-threatening. Similarly to MVEV and JEV infections, KUNV infections are often asymptomatic. Acute febrile illness with polyarthralgia has also been associated with infections from this virus (57). KUNV antibodies have been detected in humans from Australia, PNG, Indonesia, Malaysia, Thailand, Laos and Cambodia (8,21,58). Although neither kunjin encephalitis nor febrile illness have been reported in PNG, this is probably due to the non-specific nature and low severity of the illnesses.

Sepik virus

SEPV was first isolated from several species of mosquitoes in the Sepik area in 1966 (59). Subsequently, the virus was isolated from a pool of *Culex sitiens* subgroup mosquitoes in Balimo, Western Province (24). The geographical and temporal distance between these two isolations suggests that SEPV may have a wide distribution around PNG. High neutralizing antibody titres have been detected in the blood of a patient recovering from a febrile illness, which suggests that SEPV is a potential human pathogen (59). To date, SEPV has only been detected in PNG (60).

Ross River virus

Ross River fever is the most frequently reported arboviral disease in Australia, with approximately 5000 cases occurring in the country every year (61). The disease is also endemic in PNG (20,21,62,63), but the distribution and prevalence is unknown due to the lack of surveillance in this country. In 1979 a large outbreak of Ross River fever spread

throughout many Pacific island nations, including Fiji, New Caledonia, Samoa and the Cook Islands. This epidemic was the largest outbreak of Ross River fever ever recorded with more than 50,000 people infected (17,64).

The symptoms of Ross River fever (or epidemic polyarthritis) include headache, fever, lethargy, maculopapular rash, arthralgia and arthritis (65,66). Although most patients make a rapid recovery from the infection, a significant proportion of people report arthritic symptoms lasting more than a year and in some cases symptoms have been reported to persist for up to three years (67). The arthritic symptoms observed in cases of Ross River fever are thought to be due to viral replication in the joint tissues and evidence to support this has been provided by antigen staining and RT-PCR (68). Interestingly, clinical disease is only rarely reported in children, which is probably due to their reduced ability to produce arthrogenic cytokines (TNF-α and TNF-γ) and therefore lower susceptibility to immune-induced damage to the synovial joints (69).

RRV has been detected in at least 30 species of mosquito from six genera. However, three species are considered the major vectors for this virus: *Cx. annulirostris*, *Ae. vigilax* and *Ae. camptorhynchus* (17,49). Many other species may be involved in transmission cycles and vector importance seems to be closely linked to environmental conditions. Various marsupials such as kangaroos and wallabies are believed to be the major vertebrate hosts for RRV. However, many other species of marsupial and placental mammals have been identified as competent hosts for the virus (70-73). Indeed, during the large Pacific islands outbreak much of the transmission was thought to be between mosquitoes and humans alone (16).

Although it is generally accepted that RRV is widely distributed and endemic in PNG, only limited research and reports of clinical disease have been published. Tesh and associates (20) conducted a comprehensive serological survey for various arboviruses throughout the Pacific island and Southeast Asian regions. RRV antibodies were detected in adult populations across most of PNG, including Southern Highlands, Eastern Highlands, Sepik, New Britain, Louisiade Archipelago, Bougainville, Port Moresby, Morobe and New Ireland. In some areas, such as Sepik and Port Moresby, neutralizing antibodies to RRV were detected in over 60% of samples. More recent mosquito trapping studies have also detected RRV virus in Western Province (24). The role of RRV in cases of infectious arthritis in PNG was confirmed by Scrimgeour et al. (62) with serological confirmation of infection in three cases of polyarthritis from Port Moresby. The same authors also attributed 14% (182 patients) of arthritis cases at Port Moresby General Hospital, Goroka Base Hospital and Nonga Base Hospital (Rabaul) between 1977 and 1982 to RRV infection (63). Hii and associates (23) detected RRV antibodies in 59% of people tested in the Southern Highlands. This study found that antibody prevalence increased with age, which suggests that RRV is endemic in this region. Unfortunately, no recent studies have been conducted to investigate the distribution and clinical importance of RRV in PNG.

Chikungunya virus

Historically, chikungunya fever was known as an enzootic and endemic disease of tropical Africa and Asia. However, since 2004 widespread outbreaks of the disease have occurred throughout the Indian Ocean and in Italy, India, Malaysia, Indonesia, East Timor, Thailand and New Caledonia (74-78). Chikungunya fever is characterized by high fever, maculopapular rash on the trunk and limbs, painful arthritis in the extremities (79) and in some severe cases haemorrhagic manifestations and encephalitis (75). A major contribution to the sudden, widespread outbreaks of CHIKV is a recent mutation in the E1 envelope glycoprotein which has enhanced the replication and transmission of the virus in *Ae. albopictus* mosquitoes (4). Although chikungunya fever has not so far been reported in PNG, two serological studies conducted in the 1970s found a wide distribution of CHIKV antibodies throughout PNG (20) and West Papua (21). Considering the widespread distribution of this virus throughout the region it is likely that chikungunya is already present in PNG, but has not been identified due to similarities with the clinical presentation of Ross River fever, dengue and malaria.

Conclusions

It is evident that arboviruses and their associated diseases are common and widespread throughout PNG. However, the absence of surveillance and clinical reporting,

coupled with the non-specific symptoms of many arboviral diseases, has resulted in limited data being available for these viruses. Serological evidence suggests that the distributions of DENV, JEV and RRV are widespread throughout the country. Less is known about other pathogens of potential significance in PNG such as MVEV, KUNV, SEPV and CHIKV.

Identification of the prevalence and distribution of arboviruses in PNG will not alter the treatment of these diseases. The benefit will be at the population level with the realization that febrile illnesses can be caused by pathogens other than malaria and typhoid. Control strategies that are in line with the current bednet distribution programs taking place for malaria may have a positive effect on the impact and distribution of many arboviruses. However, for some arboviruses such as dengue, which are transmitted by day-biting mosquitoes, the impact may not be as extensive.

PNG is rapidly changing in terms of agriculture, increased urbanization and habitat destruction. These activities may allow endemic and exotic arboviruses to spread and establish in new geographical areas. Unfortunately, PNG does not have an active arboviral disease surveillance program linked to specialized laboratories with the capacity to detect these viruses.

REFERENCES

1 **Gubler DJ.** The global emergence/resurgence of arboviral diseases as public health problems. *Arch Med Res* 2002;33:330-342.

2 **Centers for Disease Control and Prevention, Division of Vector-Borne Infectious Diseases.** International Catalogue of Arboviruses. Atlanta, Georgia: Centers for Disease Control and Prevention, 2011. http://wwwn.cdc.gov/arbocat/index.asp

3 **Gubler DJ.** Human arbovirus infections worldwide. *Ann NY Acad Sci* 2001;951:13-24.

4 **Gould EA, Higgs S.** Impact of climate change and other factors on emerging arbovirus diseases. *Trans R Soc Trop Med Hyg* 2009;103:109-121.

5 **Alatoom A, Payne D.** An overview of arboviruses and bunyaviruses. *LabMedicine* 2009;40:237-240.

6 **Sang RC, Dunster LM.** The growing threat of arbovirus transmission and outbreaks in Kenya: a review. *East Afr Med J* 2001;78:655-661.

7 **Ciota AT, Kramer LD.** Insights into arbovirus evolution and adaptation from experimental studies. *Viruses* 2010;2:2594-2617.

8 **Mackenzie JS, Williams DT.** The zoonotic flaviviruses of Southern, South-Eastern and Eastern Asia, and Australasia: the potential for emergent viruses. *Zoonoses Public Hlth* 2009;56:338-356.

9 **Gubler DJ.** The global resurgence of arboviral diseases. *Trans R Soc Trop Med Hyg* 1996;90:449-451.

10 **Forshey BM, Guevara C, Laguna-Torres VA, Cespedes M, Vargas J, Gianella A, Vallejo E, Madrid C, Aguayo N, Gotuzzo E, Suarez V, Morales AM, Beingolea L, Reyes N, Perez J, Negrete M, Rocha C, Morrison AC, Russell KL, Blair PJ, Olson JG, Kochel TJ; NMRCD Febrile Surveillance Working Group.** Arboviral etiologies of acute febrile illnesses in Western South America, 2000-2007. *PLoS Negl Trop Dis* 2010;4:e787.

11 **Guillaumot L.** Arboviruses and their vectors in the Pacific – status report. *Pac Health Dialog* 2005;12:45-52.

12 **Pfeffer M, Dobler G.** Emergence of zoonotic arboviruses by animal trade and migration. *Parasit Vectors* 2010;3:35.

13 **Vasilakis N, Weaver SC.** The history and evolution of human dengue emergence. *Adv Virus Res* 2008;72:1-76.

14 **LaBeaud AD.** Why arboviruses can be neglected tropical diseases. *PLoS Negl Trop Dis* 2008;2:e247.

15 **Guha-Sapir D, Schimmer B.** Dengue fever: new paradigms for a changing epidemiology. *Emerg Themes Epidemiol* 2005;2:1.

16 **Mackenzie JS, Lindsay MD, Coelen RJ, Broom AK, Hall RA, Smith DW.** Arboviruses causing human disease in the Australasian zoogeographic region. *Arch Virol* 1994;136:447-467.

17 **Mackenzie JS, Broom AK, Hall RA, Johansen CA, Lindsay MD, Phillips DA, Ritchie SA, Russell RC, Smith DW.** Arboviruses in the Australian region, 1990 to 1998. *Commun Dis Intell* 1998;22:93-100.

18 **Mackenzie JS, Chua KB, Daniels PW, Eaton BT, Field HE, Hall RA, Halpin K, Johansen CA, Kirkland PD, Lam SK, McMinn P, Nisbet DJ, Paru R, Pyke AT, Ritchie SA, Siba P, Smith DW, Smith GA, van den Hurk AF, Wang LF, Williams DT.** Emerging viral diseases of Southeast Asia and the Western Pacific. *Emerg Infect Dis* 2001;7(3 Suppl):497-504.

19 **Wisseman CL Jr, Gajdusek DC, Schofield FD, Rosenzweig EC.** Arthropod-borne virus infections of Aborigines indigenous to Australasia. A preliminary report. *Bull World Health Organ* 1964;30:211-219.

20 **Tesh RB, Gajdusek DC, Garruto RM, Cross JH, Rosen L.** The distribution and prevalence of group A arbovirus neutralizing antibodies among human populations in Southeast Asia and the Pacific Islands. *Am J Trop Med Hyg* 1975;24:664-675.

21 **Kanamitsu M, Taniguchi K, Urasawa S, Ogata T, Wada Y, Wada Y, Saroso JS.** Geographic distribution of arbovirus antibodies in indigenous human populations in the Indo-Australian Archipelago. *Am J Trop Med Hyg* 1979;28:351-363.

22 **Trevett AJ, Sanders RC.** Arbovirus disease in Papua New Guinea. *PNG Med J* 1994;37:116-124.

23 **Hii J, Dyke T, Dagoro H, Sanders RC.** Health impact assessments of malaria and Ross River virus infection in the Southern Highlands Province of Papua New Guinea. *PNG Med J* 1997;40:14-25.

24 **Johansen CA, van den Hurk AF, Ritchie SA, Zborowski P, Nisbet DJ, Paru R, Bockarie MJ, Macdonald J, Drew AC, Khromykh TI, Mackenzie JS.** Isolation of Japanese encephalitis virus from mosquitoes (Diptera: Culicidae) collected in the Western Province of Papua New Guinea, 1997-1998. *Am J Trop Med Hyg* 2000;62:631-638.

25 **Hemungkorn M, Thisyakorn U, Thisyakorn C.** Dengue infection: a growing global health threat. *Biosci Trends* 2007;1:90-96.

26 **Kyle JL, Harris E.** Global spread and persistence of

dengue. *Annu Rev Microbiol* 2008;62:71-92.
27 **Gubler DJ.** Dengue and dengue hemorrhagic fever. *Clin Microbiol Rev* 1998;11:480-496.
28 **Ooi EE, Gubler DJ.** Dengue in Southeast Asia: epidemiological characteristics and strategic challenges in disease prevention. *Cad Saúde Pública* 2009;25(Suppl 1):S115-S124.
29 **Arima Y, Matsui T.** Epidemiologic update of dengue in the Western Pacific Region, 2010. *Western Pac Surveill Response J* 2011;2:4-8.
30 **Weaver SC, Vasilakis N.** Molecular evolution of dengue viruses: contributions of phylogenetics to understanding the history and epidemiology of the preeminent arboviral disease. *Infect Genet Evol* 2009;9:523-540.
31 **Chaturvedi UC, Nagar R.** Dengue and dengue haemorrhagic fever: Indian perspective. *J Biosci* 2008;33:429-441.
32 **Kuno G.** Emergence of the severe syndrome and mortality associated with dengue and dengue-like illness: historical records (1890 to 1950) and their compatibility with current hypotheses on the shift of disease manifestation. *Clin Microbiol Rev* 2009;22:186-201.
33 **Martina BEE, Koraka P, Osterhaus ADME.** Dengue virus pathogenesis: an integrated view. *Clin Microbiol Rev* 2009;22:564-581.
34 **Noisakran S, Perng GC.** Alternate hypothesis on the pathogenesis of dengue hemorrhagic fever (DHF)/ dengue shock syndrome (DSS) in dengue virus infection. *Exp Biol Med (Maywood)* 2008;233:401-408.
35 **Diallo M, Ba Y, Sall AA, Diop OM, Ndione JA, Mondo M, Girault L, Mathiot C.** Amplification of the sylvatic cycle of dengue virus type 2, Senegal, 1999–2000: entomologic findings and epidemiologic considerations. *Emerg Infect Dis* 2003;9:362-367.
36 **Zigas V, Doherty RL.** An outbreak of dengue in the Rabaul community. *PNG Med J* 1973;16:42-45.
37 **Kiedrzynski T, Souarès Y, Stewart T.** Dengue in the Pacific: an updated story. *Pacific Health Dialog* 1998;5:129-136.
38 **Senn N, Luang-Suarkia D, Manong M, Siba PM, McBride WJH.** Contribution of dengue fever to the burden of acute febrile illnesses in Papua New Guinea: an age-specific prospective study. *Am J Trop Med Hyg* 2011;85:132-137.
39 **van den Hurk AF, Ritchie SA, Mackenzie JS.** Ecology and geographic expansion of Japanese encephalitis virus. *Annu Rev Entomol* 2009;54:17-53.
40 **Hanna JN, Ritchie SA, Phillips DA, Shield J, Bailey MC, Mackenzie JS, Poidinger M, McCall BJ, Mills PJ.** An outbreak of Japanese encephalitis in the Torres Strait, Australia, 1995. *Med J Aust* 1996;165:256-260.
41 **Ghosh D, Basu A.** Japanese encephalitis – a pathological and clinical perspective. *PLoS Negl Trop Dis* 2009;3:e437.
42 **Watt G, Jongsakul K.** Acute undifferentiated fever caused by infection with Japanese encephalitis virus. *Am J Trop Med Hyg* 2003;68:704-706.
43 **Solomon T.** Flavivirus encephalitis. *N Engl J Med* 2004;351:370-378.
44 **Johansen C, Ritchie S, van den Hurk A, Bockarie M, Hanna J, Phillips D, Melrose W, Poidinger M, Scherret J, Hall R, Mackenzie J.** The search for Japanese encephalitis virus in the Western Province of Papua New Guinea, 1996. *Arbovirus Res Aust* 1997;7:131-136.
45 **Johansen CA, van den Hurk AF, Pyke AT, Zborowski P, Phillips DA, Mackenzie JS, Ritchie SA.** Entomological investigations of an outbreak of Japanese encephalitis virus in the Torres Strait, Australia, in 1998. *J Med Entomol* 2001;38:581-588.
46 **Johansen CA, Nisbet DJ, Foley PN, van den Hurk AF, Hall RA, Mackenzie JS, Ritchie SA.** Flavivirus isolations from mosquitoes collected from Saibai Island in the Torres Strait, Australia, during an incursion of Japanese encephalitis virus. *Med Vet Entomol* 2004;18:281-287.
47 **Hanson JP, Taylor CT, Richards AR, Smith IL, Boutlis CS.** Japanese encephalitis acquired near Port Moresby: implications for residents and travellers to Papua New Guinea. *Med J Aust* 2004;181:282-283.
48 **Anga G, Barnabas R, Kamaniel O, Tefuarani N, Vince J, Ripa P, Riddell M, Duke T.** The aetiology, clinical presentations and outcome of febrile encephalopathy in children in Papua New Guinea. *Ann Trop Paediatr* 2010;30:109-118.
49 **Russell RC.** Arboviruses and their vectors in Australia: an update on the ecology and epidemiology of some mosquito-borne arboviruses. *Rev Med Vet Entomol* 1995;83:141-158.
50 **Spencer JD, Azoulas J, Broom AK, Buick TD, Currie B, Daniels PW, Doggett SL, Hapgood GD, Jarrett PJ, Lindsay MD, Lloyd G, Mackenzie JS, Merianos A, Moran RJ, Ritchie SA, Russell RC, Smith DW, Stenhouse FO, Whelan PI.** Murray Valley encephalitis virus surveillance and control initiatives in Australia. National Arbovirus Advisory Committee of the Communicable Diseases Network Australia. *Commun Dis Intell Q Rep* 2001;25:33-47.
51 **Anderson SG, Price AVG, Nanadai-Koia, Slater K.** Murray Valley encephalitis in Papua and New Guinea. II. Serological survey, 1956-1957. *Med J Aust* 1960;47:410-413.
52 **French EL, Anderson SG, Price AVG, Rhodes FA.** Murray Valley encephalitis in New Guinea. 1. Isolation of a Murray Valley encephalitis virus from the brain of a fatal case of encephalitis occurring in a Papuan native. *Am J Trop Med Hyg* 1957;6:827-834.
53 **Essed WCAH, Van Tongeran HAE.** Arthropod-borne virus infections in Western New Guinea. 1. Report of a case of Murray Valley encephalitis in a Papuan woman. *Trop Geogr Med* 1965;1:52-55.
54 **Lobigs M, Marshall ID, Weir RC, Dalgarno L.** Murray Valley encephalitis virus field strains from Australia and Papua New Guinea: studies on the sequence of the major envelope protein gene and virulence for mice. *Virology* 1988;165:245-255.
55 **Coelen RJ, Mackenzie JS.** Genetic variation of Murray Valley encephalitis virus. *J Gen Virol* 1988;69:1903-1912.
56 **Johansen CA, Susai V, Hall RA, Mackenzie JS, Clark DC, May FJ, Hemmerter S, Smith DW, Broom AK.** Genetic and phenotypic differences between isolates of Murray Valley encephalitis virus in Western Australia, 1972-2003. *Virus Genes* 2007;35:147-154.
57 **Hall RA, Broom AK, Smith DW, Mackenzie JS.** The ecology and epidemiology of Kunjin virus. *Curr Top Microbiol Immunol* 2002;267:253–269.
58 **Scherret JH, Poidinger M, Mackenzie JS, Broom AK, Deubel V, Lipkin WI, Briese T, Gould EA, Hall RA.** The relationships between West Nile and Kunjin viruses. *Emerg Infect Dis* 2001;7:697-705.
59 **Woodroofe GM, Marshall ID.** Arboviruses from the Sepik district of New Guinea. In: The John Curtin School of Medical Research Annual Report. Canberra: Australian National University, 1971:90-91.

60 **Hawkes RA, Boughton CR, Naim HM, Wild J, Chapman B.** Arbovirus infections of humans in New South Wales. Seroepidemiology of the flavivirus group of togaviruses. *Med J Aust* 1985;143:555-561.

61 **Carver S, Bestall A, Jardine A, Ostfeld RS.** Influence of hosts on the ecology of arboviral transmission: potential mechanisms influencing dengue, Murray Valley encephalitis, and Ross River virus in Australia. *Vector Borne Zoonotic Dis* 2009;9:51-64.

62 **Scrimgeour EM, Aaskov JG, Matz LR.** Ross River virus arthritis in Papua New Guinea. *Trans R Soc Trop Med Hyg* 1987;81:833-834.

63 **Scrimgeour EM, Matz LR, Aaskov JG.** A study of arthritis in Papua New Guinea. *Aust NZ J Med* 1987;17:51-54.

64 **Aaskov JG, Mataika JU, Lawrence GW, Rabukawaqa V, Tucker MM, Miles JA, Dalglish DA.** An epidemic of Ross River virus infection in Fiji, 1979. *Am J Trop Med Hyg* 1981;30:1053-1059.

65 **Suhrbier A, La Linn M.** Clinical and pathologic aspects of arthritis due to Ross River virus and other alphaviruses. *Curr Opin Rheumatol* 2004;16:374-379.

66 **Harley D, Sleigh A, Ritchie S.** Ross River virus transmission, infection, and disease: a cross-disciplinary review. *Clin Microbiol Rev* 2001;14:909-932.

67 **Fraser JR.** Epidemic polyarthritis and Ross River virus disease. *Clin Rheum Dis* 1986;12:369-388.

68 **Soden MH, Vasudevan H, Roberts B, Coelen R, Hamlin G, Vasudevan S, La Brooy J.** Detection of viral ribonucleic acid and histologic analysis of inflamed synovium in Ross River virus infection. *Arthritis Rheum* 2000;43:365-369.

69 **Rulli NE, Melton J, Wilmes A, Ewart G, Mahalingam S.** The molecular and cellular aspects of arthritis due to alphavirus infections: lesson learned from Ross River virus. *Ann NY Acad Sci* 2007;1102:96-108.

70 **Doherty RL, Standfast HA, Domrow R, Wetters EJ, Whitehead RH, Carley JG.** Studies of the epidemiology of arthropod-borne virus infections at Mitchell River Mission, Cape York Peninsula, North Queensland. IV. Arbovirus infections of mosquitoes and mammals, 1967–1969. *Trans R Soc Trop Med Hyg* 1971;65:504-513.

71 **Gard G, Marshall ID, Woodroofe GM.** Annually recurrent epidemic polyarthritis and Ross River virus activity in a coastal area of New South Wales. II. Mosquitoes, viruses and wildlife. *Am J Trop Med Hyg* 1973;22:551-560.

72 **Pascoe RR, St George TD, Cybinski DH.** The isolation of a Ross River virus from a horse. *Aust Vet J* 1978;54:600.

73 **Ryan PA, Martin L, Mackenzie JS, Kay BH.** Investigation of gray-headed flying foxes (*Pteropus poliocephalus*) (Megachiroptera: Pteropodidae) and mosquitoes in the ecology of Ross River virus in Australia. *Am J Trop Med Hyg* 1997;57:476-482.

74 **Cavrini F, Gaibani P, Pierro AM, Rossini G, Landini MP, Sambri V.** Chikungunya: an emerging and spreading arthropod-borne viral disease. *J Infect Dev Ctries* 2009;3:744-752.

75 **Tandale BV, Sathe PS, Arankalle VA, Wadia RS, Kulkarni R, Shah SV, Shah SK, Sheth JK, Sudeep AB, Tripathy AS, Mishra AC.** Systemic involvements and fatalities during Chikungunya epidemic in India, 2006. *J Clin Virol* 2009;46:145-149.

76 **Laras K, Sukri NC, Larasati RP, Bangs MJ, Kosim R, Djauzi, Wandra T, Master J, Kosasih H, Hartati S, Beckett C, Sedyaningsih ER, Beecham HJ 3rd, Corwin AL.** Tracking the re-emergence of epidemic chikungunya virus in Indonesia. *Trans R Soc Trop Med Hyg* 2005;99:128-141.

77 **Rianthavorn P, Prianantathavorn K, Wuttirattanakowit N, Theamboonlers A, Poovorawan Y.** An outbreak of chikungunya in southern Thailand from 2008 to 2009 caused by African strains with A226V mutation. *Int J Infect Dis* 2010;14(Suppl 3):e161-e165.

78 **ProMED-mail.** Chikungunya (06): New Caledonia. ProMED 2011 Mar 8. http://www.promedmail.org Archive Number: 20110308.0759.

79 **Solignat M, Gay B, Higgs S, Briant L, Devaux C.** Replication cycle of chikungunya: a re-emerging arbovirus. *Virology* 2009;393:183-197.

PNG Med J 2012 Mar-Dec;55(1-4):45-54

The use of complementary and alternative medicine in children admitted to Angau Memorial Hospital, Lae, Papua New Guinea

R. Kipalan[1], T. Rongap[1], P. Ripa[2] and J.D. Vince[2,3]

Department of Paediatrics, Angau Memorial Hospital, Lae, Papua New Guinea and School of Medicine and Health Sciences, University of Papua New Guinea, Port Moresby

SUMMARY

There is considerable overlap between traditional medicine (TM) and complementary and alternative medicine (CAM). Although the use of CAM, often regarded as TM, is recognized to be widespread in Papua New Guinea (PNG) there are few if any studies of its use in children. This study assessed the use of CAM in 300 children admitted to the children's wards of Angau Memorial Hospital between April and July in 2010 and the same time period in 2011. 54% of the children had been treated with some form of CAM. The use of CAM did not appear to depend on socioeconomic indices. Children with chronic illness were twice as likely to have received CAM as those with acute illness. 116 (72% of the 161 children who had received CAM and 39% of the total sample) had received alternative medicine prior to commencing conventional treatment. Of these, 72 (62%) used plant-derived medication, 29 (25%) sought spiritual/religious help, 12 (10%) admitted to having accessed the help of sorcerers and 3 had used minerals. 43 (37%) were using some form of CAM whilst in hospital. The commonest reasons for using alternative medicine were previous use with perceived good effect (50, 43%), belief that it was a cure for the disease or symptom (28, 24%) and belief that the disease was due to a nonmedical or spiritual cause (14, 12%). Belief in spiritual or nonmedical causation of illness was strongly associated with delay in accessing conventional treatment. When CAM was used only in the outpatient setting plant-based treatment was more commonly used than mind-body medicine, whereas mind-body medicine – mainly religious activity – was used more commonly in the inpatient setting. CAM was given to 12 of the 35 outpatient user only group because of a perception that conventional treatment was not working whilst 13 carers gave it to assist in healing. The large majority of CAM treatments were free but in two cases (one the use of purported electromagnetic field with Biodisc^{R} and one religious activity) the cost had been more than 100 kina. The study demonstrates that the use of CAM for the treatment of childhood illness is common in PNG. Whilst most forms of CAM were in themselves not harmful, potential for harm exists, particularly when its use results in significant delay in accessing conventional treatment.

Introduction

Complementary and alternative medicine (CAM) refers to the use of substances or modalities normally regarded as outside the domain of established western medical practice. As defined by the US Office of Alternative Medicine CAM Research Methodology group, a definition also used by the Cochrane Collaboration, "Complementary and alternative medicine (CAM) is a broad domain of healing resources that encompasses all health care systems, modalities, practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period. CAM includes all such practices and ideas self-defined by their users as preventing or treating illness or promoting health and well-

1 Department of Paediatrics, Angau Memorial Hospital, PO Box 457, Lae, Morobe Province 411, Papua New Guinea

2 School of Medicine and Health Sciences, University of Papua New Guinea, PO Box 5255, Boroko, National Capital District 111, Papua New Guinea

3 Corresponding author
johndvince@gmail.com

being. Boundaries within CAM and between the CAM domain and that of the dominant system are not always sharp or fixed." (1).

Within CAM the term 'alternative medicine' refers to treatment methods that are not used in conjunction with conventional or western medicine, whilst 'complementary medicine' implies methods used in conjunction with conventional medical practice.

Traditional medicine (TM) is defined by the World Health Organization (WHO) as: "the sum total of knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures that are used to maintain health, as well as to prevent, diagnose, improve or treat physical and mental illnesses" (2).

From the two definitions CAM and traditional medicine clearly overlap and complementary medicine (CM), as defined by the National Institute of Complementary Medicine, is inclusive of traditional medicine (3).

The US National Institutes of Health National Center for Complementary and Alternative Medicine subdivides CAM into the following groups, noting that some treatments fall into more than one category (4):

- *Natural products* such as minerals, vitamins, probiotics and other substances derived from plants or animals
- *Mind-body medicine* such as meditation, yoga, relaxation techniques and acupuncture
- *Manipulative and body-based practices* such as massage and spinal manipulation (chiropractic)
- *Other CAM practices* such as movement therapies, traditional Chinese medicine, Ayurvedic medicine, homeopathy, bioelectric magnetic-based interventions and energy fields.

The use of CAM is widespread in the developed world. A recent survey by the National Institutes of Health found that 38% of Americans use some form of CAM (5). In African and Asian countries 80% of the population use traditional medicine as their primary care (2). Western medicine is a recent introduction to Papua New Guinea (PNG), a country with a rich variety of traditional medicines and practices, providing a rich source of knowledge on indigenous medicinal plant species (6-8). There is a strong belief in traditional medicine and even when access to modern health facilities is possible many people will seek traditional remedies. In many areas with no or nonfunctional health services traditional medicine is the only form available. Official recognition of the widespread use and belief in traditional medicine in PNG led to a national workshop in 2004 (9), which led to the launching of a National Policy on Traditional Medicine in 2007.

Whilst medical practitioners are well aware that their patients may have used CAM before or are still using CAM during their conventional treatment there is very little documentation of the types of CAM used and the prevalence of this practice in children in Papua New Guinea.

The aim of this study was to investigate the use of complementary and alternative medicine among children admitted to the Angau Memorial Hospital.

The objectives were to determine:

- the type of CAM used in children
- the source of parents' information on CAM
- reasons for the use of CAM
- costs, and
- if the use of CAM had resulted in delayed presentation at a health facility.

Methods

This was a descriptive study using a questionnaire to obtain information from parents or guardians of children admitted to the Paediatric Unit of Angau Memorial Hospital. Convenience sampling was used. The purpose of the study was explained to the parents or guardians before seeking their consent for inclusion in the study. The first form of CAM mentioned by the parent or caregiver was recorded and used in the analysis.

Data, including sociodemographic indicators and information relating to the use

of CAM, were entered in SPSS version 10 and Excel 2003. Odds ratios with 95% confidence intervals, or chi-squared tests for proportional differences, were used to assess differences between patients using and those not using CAM. The odds ratio was used to assess difference in the use of CAM between those presenting with acute and those with chronic conditions, and Fisher's exact test was used to determine the relationship between given reasons for the use of CAM and delay in accessing conventional treatment.

Results

No parent or guardian refused to be interviewed. 176 (59%) of the 300 children whose parents or guardians were interviewed were male. The median age of the children was 7 months with an interquartile range of 3-22 months.

161 (54%) of the children had received CAM as alternative or complementary medicine or both during the current illness.

No differences were found in the assessed sociodemographic indicators between those using and those not using CAM (Table 1).

CAM was twice more likely to be used in children with chronic than with acute conditions (Table 2): the odds ratio for children with tuberculosis and malnutrition (chronic) versus those with pneumonia/bronchiolitis, malaria, diarrhoea and meningitis (acute) was 2.21(95% CI 1.28-3.49).

The use of CAM in relation to the current illness is shown in Table 3, and the types of CAM used are shown in Table 4.

Alternative medicine

116 (72% of the 161 children who had received CAM and 39% of the total sample) had received alternative medicine prior to commencing conventional treatment. Of these, 72 (62%) used plant-derived medication, 29 (25%) sought spiritual/religious help, 12 (10%) admitted to having accessed the help of sorcerers and 3 had used minerals. 43 (37%) were using some form of CAM whilst in hospital.

Reasons for the use of alternative medicine and the time taken to access conventional treatment are shown in Table 5. 50 (43%) of the 116 patients used alternative medicine because they had used it before and thought it had worked, 28 (24%) believed it to be a cure for the disease or symptom and 14 (12%) thought the disease was due to a nonmedical or spiritual cause. 10 patients used it because of transport difficulties, 7 because of inaccessible health facilities, 5 for financial reasons and 2 for other reasons. Just over half of the patients (63) waited for 1-3 days, 15 for 3-5 days, 6 for 5-7 days and 32 for more than a week prior to accessing a health facility. Parents who believed that the disease was due to spiritual and nonmedical causes were much more likely to delay accessing a health facility for more than a week than those who had other reasons (Fisher's exact test, $p < 0.0001$).

The majority of the 116 parents had obtained their information from relatives or friends (60 and 12, respectively), 5 had obtained information from books, 4 from health workers and 3 from street sellers. The remaining 32 indicated their own religious belief as their rationale.

The large majority (106/116) of alternative treatments were free; 2 had cost less than 10 kina, 6 between 11 and 50 kina, 1 between 50 and 100 kina and 1 in excess of 100 kina.

Complementary medicine

101 (63%) of the 161 patients who used CAM used some form of complementary medicine. Of these, 56/101 also used alternative medicine. 35 patients used complementary medicine as an outpatient, 40 as an inpatient and 26 in both situations (Table 4).

34 used biologically based complementary medicine, 64 used mind-body medicine, 1 used chiropractic and 2 used 'electromagnetic' medicine (Biodisc^{R}). There was a highly significant difference between the use of biologically based and mind-body-based CAM between the outpatient (OP) and inpatient (IP) settings, with plant-based treatment more commonly used in the outpatient setting (22/35 OP vs 12/66 IP) and mind-body medicine (predominantly religious activity) more commonly used in the inpatient setting (12/35 OP vs 52/66 IP) (Table 4). 3 uses of witchcraft were recorded in the OP and 1 in the IP settings. The consumption of animal blood was recorded in 1 outpatient use of

TABLE 1

SOCIODEMOGRAPHIC FACTORS AND THE USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) IN CHILDREN

	The use of CAM by parents		Odds ratio (95% CI)
	Yes	**No**	**p value**
Employment status of father			
Employed	81	70	1.0 (0.62-1.61)
Unemployed	80	69	
Employment status of mother			
Employed	24	15	1.45 (0.69-3.05)
Unemployed	137	124	
Education status of father			
Educated	137	111	1.49 (0.79-2.82)
Uneducated	24	29	
Unknown	7	2	
Education status of mother			
Educated	120	100	1.14 (0.65-1.98)
Uneducated	39	37	
Unknown	2	2	
Residential area			
City	17	18	p = 0.22
Settlement	79	43	
Village	65	43	
Number of children in the family			
1 child	41	38	p = 0.54
2-3 children	64	60	
4-5 children	45	29	
>5 children	11	12	

CAM. 12 of the 35 carers who used CAM only in the outpatient setting felt that conventional medicine was not working and 13 gave it to assist in healing. 52 of the 66 carers using CAM in the inpatient setting did so in the belief that it assisted healing.

Complementary medicine was free in 78 cases, cost less than 10 kina in 10, between 10 and 49 kina in 10 and between 50 and 100 kina in 1. The cost was greater than 100 kina in 2 instances, one involving the purchase of Biodisc^{R} and the other for religious activity.

TABLE 2

DIAGNOSIS AND THE USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM)

Diagnosis	Use of CAM		Number of patients
	Yes	No	
Pneumonia/Bronchiolitis	36	52	88
Malaria	7	10	17
Diarrhoea	11	16	27
Meningitis	26	16	42
Tuberculosis	45	17	62
Malnutrition	34	27	61
Others	2	1	3
Total	161	139	300

Odds ratio for tuberculosis and malnutrition vs pneumonia/bronchiolitis, malaria, diarrhoea and meningitis 2.21 (95% CI 1.28-3.49)

TABLE 3

USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE DURING CURRENT ILLNESS

Use of complementary and alternative medicine	Number (%)*
Alternative:	
No complementary	60 (37.3)
Plus complementary as outpatient	13 (8.1)
Plus complementary as inpatient	28 (17.4)
Plus complementary as outpatient and inpatient	15 (9.3)
Total	116 (72)
Complementary only:	
As outpatient	22 (13.7)
As inpatient	12 (7.5)
As outpatient and inpatient	11 (6.8)
Total	45 (28)

*Percentage of total number using complementary and/or alternative medicine – 161

TABLE 4

TYPES OF ALTERNATIVE AND COMPLEMENTARY MEDICINE USED

Use of complementary and alternative medicine	Natural products	Mind-Body		Manipulative/ body-based	Other	Total
		Religion Spiritual Witchcraft Meditation	Sorcery			
Alternative	75	29	12			116
Complementary outpatient only	22	6	6		1	35
Complementary inpatient only	8	27	3	1	1	40
Complementary outpatient and inpatient	4	21	1			26
Total	109	83	22	1	2	217*

*Note: 56 of the 101 patients using complementary medicine also used alternative medicine

Relatives and friends were the main source of information for those using CAM only in the outpatient setting. In the inpatient setting prayer and religious activity was the main type of CAM, with friends and relatives being sources of information for the natural products.

Outcome

19 of the 300 children studied died. 5 were among the 60 who had received alternative medicine, but in only one of these had there been a delay in seeking conventional medical assistance of more than 7 days.

Discussion

The study showed that 54% of the children had been treated with some form of CAM. The use of CAM did not appear to depend on socioeconomic indices. Children with chronic illness were twice as likely to have received CAM as those with acute illness – a finding consistent with studies from other parts of the world (5). This may well relate to the duration of symptoms rather than the specific disease, but our study design did not allow for further interpretation of the data in this regard. 39% of the children had received alternative therapy. Important was the finding that belief in spiritual or nonmedical causation of illness was associated with delay in accessing conventional treatment.

Whilst the use of CAM is in some instances related to the difficulty in accessing conventional treatment, its widespread use in PNG is also related to beliefs about causation of illness. Hamnett and Connell in their study of traditional practitioners in the North Solomons described 3 different cultural classes of diseases in PNG which affected treatment-seeking behaviour (10). These were ‘sik bilong ples’ – related to village problems, sorcery, family disputes; ‘sik nating’ – not really sick at all or sick without apparent cause; and ‘sik bilong waitman’ – illness associated with white people. Whilst this study was done some 30 years ago, belief in village customs and power of witchcraft and sorcery is deep rooted and prevalent across large sections of the community (11). A recent study of treatment-seeking behaviour among the Nasioi people of the Autonomous Region of Bougainville reported that people subscribe to both traditional and western approaches to illness and treatment and that western medical concepts “have been assimilated but have not displaced traditional understanding of illness” (12). CAM is not limited to societies with poor

TABLE 5

REASONS FOR THE USE OF ALTERNATIVE MEDICINE AND DELAY IN SEEKING CONVENTIONAL TREATMENT

Number of days before conventional treatment	Used before and it worked	Transport difficulties	Inaccessible health services	Financial constraints	Heal the disease	Spiritual and nonmedical causes	Others	Total
1-3 days	29	8	4	4	16	1	1	63
4-7 days	11	0	0	0	7	2	1	21
>7 days	10	2	3	1	5	11*	0	32
Total	50	10	7	5	28	14	2	116

* 6 using religious prayer, 5 using spiritual witchcraft

access to conventional medicine. 38% of Americans were shown in a recent study to use some form of CAM (5) and a survey of paediatricians in America found that 87% had been asked by a patient or parent about one or more CAM therapies (13).

Although CAM is widely used throughout the world, hard evidence for its effectiveness is hard to find. A recent overview of systematic reviews of different forms of CAM in children found that whilst there is some evidence for the beneficial effects of some forms in specific conditions (for example, the use of acupuncture for postoperative nausea and pain) the claims for effectiveness of many forms of CAM are not supported by adequate evidence (14).

Holistic medicine is described as "the art and science of healing that addresses care of the whole person – body, mind, and spirit. The practice of holistic medicine integrates conventional and complementary therapies to promote optimal health, and prevent and treat disease by addressing contributing factors." (15). Put succinctly it treats 'the person with the disease' rather than the 'disease in a person'. Many forms of traditional medicine have a holistic view of pathology and treatment that includes social, spiritual, environmental and cultural factors. The holistic approach is an important feature of many forms of CAM, and unfortunately is often lacking in the way in which conventional western medicine is administered. It is certainly acknowledged within the PNG health system that uncaring and unwelcoming attitudes of health staff and rushed consultations may deter patients from seeking treatment (16,17).

The study found that plant products, a common form of CAM worldwide, are used extensively in Papua New Guinea. It is pertinent to any discussion of the use of plant-based treatments to remember that many of the medicines in everyday use are derived from plants (digitalis and artemether to name but two). There is considerable interest in the extraction of novel medicinal products from PNG indigenous plants (7) and it is important to keep an open mind about the use of plant-derived CAM products.

Religious activity – and prayer in particular – is an important form of CAM although the border between family members praying in the normal way for a sick relative and more intensely focused prayer activity is blurred. Religious activity accounted for 25% of alternative therapies in the present study. As a form of CAM it was used more frequently in inpatients than in outpatients – 47/66 vs 12/35; OR 4.74 (95% CI 1.97-11.41) – probably reflecting the families' perceptions of the degree of illness severity.

Sorcery accounted for 10% of alternative therapies and 10% of complementary therapies. Reluctance to admit to the use of sorcery may well have resulted in underreporting.

In considering the relationship between CAM and conventional medicine it is important to distinguish between therapies used as alternative medicine and those used as complementary medicine. CAM therapies themselves fall into three categories:

- they may be harmful (for example severe dietary restriction),
- they may, as far as is known, be ineffective but harmless (electromagnetic fields), and
- there may be weak evidence of benefit in some situations (14).

The use of alternative medicine may delay access to appropriate conventional care and this may in some situations be a cause of morbidity and even mortality. The issue of possible interaction with conventional medications – either adverse or beneficial – is also important.

Our information did not allow for an estimation of the proportion of CAM treatments that were potentially harmful. The drinking of animal blood certainly has the potential for harm, but specific details of what was done or given in all the cases of sorcery were not determined. The types and quantities of plant-based treatment and thus their potential for harm in young children and neonates were also not determined. This is an important issue and one which requires further study.

Conflicts may occasionally arise between carers and health workers in relation to the use of CAM; these involve important and complex ethical issues, including that of autonomy, and legal issues such as child protection sometimes arise. For example, parents using

CAM for their children may delay conventional treatment in life-threatening situations or may decide to stop conventional treatment when the consequences will almost certainly be deleterious. Although such issues are not common, the increasing use of CAM has led to discussions and proposals for paediatric guidelines (18). "Paediatric use of CAM therapies raises complex issues at the borderland of medicine, law and public policy. Although some parental choices endanger children, others simply clash with those of clinicians, raising differences in outlook, lifestyle and health care preferences." (19)

This was a small preliminary study on an important but sensitive topic and it has several limitations. The information was collected by means of face-to-face interviews. It is quite possible that those interviewed gave incorrect answers, perhaps being afraid to give accurate information for fear of ridicule or of being thought primitive or uneducated. It is at least possible that parents were reluctant to discuss the use of sorcery and that the reported figure of 10% for its use as a form of alternative medicine may well be lower than the true figure. Individuals may have given 'expected' rather than genuine answers. Only one form of CAM was recorded for each patient – and it is quite possible that more than one form was utilized in many cases. Information was collected via a structured questionnaire. More accurate information might have been obtained using qualitative methods – more open-ended questions and the use of focus groups. Since participation in the study was based on the availability of parents for interview, some selection bias may have occurred. The study has, nevertheless, given valuable insight into a previously unexamined area of patient care, and should form a baseline for further exploration of this important area.

ACKNOWLEDGEMENTS

We thank the caregivers of the children for their willingness to participate in this study. We gratefully acknowledge the support of Dr Francesca Feiling, Dr Alphonse Rongap and Prof. Nakapi Tefuarani during the course of the study.

REFERENCES

1 **Alternative Therapies in Health and Medicine.** Defining and describing complementary and alternative medicine. CAM Research Methodology Conference, April 1995 Panel on Definition and Description. *Altern Ther Health Med* 1997;3(2):49-57.

2 **World Health Organization.** Traditional Medicine. Fact Sheet No 134. Geneva: World Health Organization, Dec 2008. www.who.int/mediacentre/factsheets/fs134/en/

3 **National Institute of Complementary Medicine**. Definition of complementary medicine. Sydney: NICM, Jan 2009. www.nicm.edu.au/content/view/31/35/

4 **National Center for Complementary and Alternative Medicine.** Complementary, alternative, or integrative health: what's in a name? Bethesda, Maryland: NCCAM, Oct 2008. www.nccam.nih.gov/health/whatiscam/

5 **Barnes PM, Bloom B, Nahin RL.** Complementary and alternative medicine use among adults and children: United States, 2007. National Health Statistics Reports No 12. Hyattsville, MD: National Center for Health Statistics, Dec 2008. www.cdc.gov/nchs/data/nhsr/nhsr012.pd

6 **Waruruai J, Sipana B, Koch M, Barrows LR, Matainaho TK, Rai PP.** An ethnobotanical survey of medicinal plants used in the Siwai and Buin districts of the Autonomous Region of Bougainville. *J Ethnopharmacol* 2011;138:564-577.

7 **Barrows LR, Matainaho TK, Ireland CM, Miller S, Carter GT, Bugni T, Rai P, Gideon O, Manoka B, Piskaut P, Banka R, Kiapranis R, Noro JN, Pond CD, Andjelic CD, Koch M, Harper MK, Powan E, Pole AR, Jensen JB.** Making the most of Papua New Guinea's biodiversity: establishment of an integrated set of programs that link botanical survey with pharmacological assessment in "The Land of the Unexpected". *Pharm Biol* 2009;47:795-808.

8 **Rai P, Matainaho T, Saulei S, Ambihaipahar U, Cordell G, eds.** Medicinal Plants in Papua New Guinea. Manila: World Health Organization Regional Office for the Western Pacific, 2009.

9 **Rai PP, ed.** Traditional Medicine in Papua New Guinea: Proceedings of the National Workshop on Policy and Practices, 28-30 Jul 2004. Port Moresby: Papua New Guinea Department of Health, 2004.

10 **Hamnett MP, Connell J.** Diagnosis and cure: the resort to traditional and modern medical practitioners in the North Solomons, Papua New Guinea. *Soc Sci Med B* 1981;15:489-498.

11 **Macfarlane J.** Common themes in the literature on traditional medicine in Papua New Guinea. *PNG Med J* 2009;52:44-53.

12 **Macfarlane JE, Alpers MP.** Treatment-seeking behaviour among the Nasioi people of Bougainville: choosing between traditional and western medicine. *Ethn Health* 2009;14:147-168.

13 **Kemper KJ, O'Connor KG.** Paediatricians' recommendations for complementary and alternative medical (CAM) therapies. *Ambul Pediatr* 2004;4:482-487.

14 **Hunt K, Ernst E.** The evidence-base for complementary medicine in children: a critical overview of systematic reviews. *Arch Dis Child* 2011;96:769-776.

15 **American Holistic Medicine Association.** About holistic medicine. Woodmere, Ohio: American Holistic Medicine Association. www.holisticmedicine.org/content.asp?pl=2&sl=43&contentid=43

16 **Larsen GL, Lupiwa S, Kave HP, Gillieatt S, Alpers MP.** Antenatal care in Goroka: issues and perceptions. *PNG Med J* 2004;47:202-214.

17 **Namuigi P, Phuanukoonnon S.** Barriers to measles immunization: the beliefs and attitudes of caregivers in Goroka, Eastern Highlands Province, Papua New Guinea. *PNG Med J* 2005;48:183-187.
18 **Gilmour J, Harrison C, Cohen MH, Vohra S.** Pediatric use of complementary and alternative medicine: legal, ethical and clinical issues in decision-making. *Pediatrics* 2011;128(Suppl 4):S149-S154.
19 **Cohen MH, Kemper KJ, Stevens L, Hashimoto D, Gilmour J.** Pediatric use of complementary therapies: ethical and policy choices. *Pediatrics* 2005;116:e568-e575.

PNG Med J 2012 Mar-Dec;55(1-4):55-60

A technique of a one-stage repair of soft tissues in severe bilateral cleft lip without presurgical orthodontics or lip adhesion

G.Gende[1]

Surgery Department, Port Moresby General Hospital, Papua New Guinea

SUMMARY

The repair of severe bilateral cleft lip is usually done electively at three months after orthodontic appliances have pushed back the protuberant premaxilla to its expected position in the dental arch shelves. Historically the premise that the repair will break down or that the premaxilla will not recede has been challenged. This paper describes a technique that the author has used as a one-stage 'putting it all together' repair without presurgical orthodontics or lip adhesion. The results have been favourable and may bring about a rethink on the tissues' inherent plasticity, the need for early orthodontics and the effect of a muscular strut as an effective substitute for artificial appliances.

Introduction

For a long time repair of very wide bilateral clefts of the lips and palate has been considered difficult and the results half as good as unilateral cleft lips (1). Over the last decade continued improvements in techniques and centralization of multidisciplinary cleft teams in the United Kingdom and Scandinavia have resulted in improved results (2). A child who had a bilateral cleft can enjoy a near normal appearance, speech and facial growth just as his milder unilateral cleft lip kin.

Surgical repair of cleft lips and palates has three main goals: 1) restore a near normal appearance, 2) improve speech, and 3) allow for normal facial growth. Restoration of appearance is usually achieved during the primary repair of soft tissues ensuring symmetry of nasolabial structures such as nasal floor and sill, upper lip Cupid's bow, pout, a pleasing vermillion and vertical height. There are so many techniques but the method used by Ralph Millard (3) has been found to be so versatile that it is the method of first choice now.

Secondary surgery is usually to realign a rotated maxillary segment with its accompanying teeth and/or to improve nose projection by columella lengthening or nasal tip augmentation by the age of 9 years.

Most centres around the world agree that a wide or very wide bilateral cleft lip and palate should be done in two stages. From birth till 5 months an orthodontic appliance is used to push back the protuberant premaxilla and push out the collapsed dental arches in the mouth. Once the normal horseshoe shape is achieved, usually by 5 months, then the surgeon repairs and restores the nasolabial relationships including the anterior palate. The soft palate is repaired by 9 months.

In Papua New Guinea (PNG) cleft lip and palate combined has an incidence of 1:640 live births. Repair of clefts in Port Moresby General Hospital (PMGH) was the commonest non-obstetric operation until it was overtaken by appendicectomy during the 1990s. PMGH does not have a dedicated cleft team and patients do not usually return for follow-up and therefore a pleasing result must be achieved during the primary surgery. I report here a technique locally named as the *Port Moresby technique* that can be done without presurgical orthodontics or lip adhesion.

Selection of patients

The patients considered suitable are:

- all types and severity of bilateral cleft

1 Surgery Department, Port Moresby General Hospital, Free Mail Bag, Boroko, National Capital District 111, Papua New Guinea

lip and palate, and

- very wide unilateral cleft lip and palate.

Relative contraindications to operation are anaemia, malnutrition or an intercurrent respiratory infection incident or secondary to a coexisting congenital heart problem. These conditions should be corrected before surgery.

Anaesthesia

General anaesthesia is given ensuring that the Ray's endotracheal tube is well centred and secured firmly in place. Airway security is rechecked after the surgeon repositions the head before the operation. A throat pack completes the anaesthetic preparations. A prophylactic antibiotic is always given before the incision and I prefer crystalline penicillin in most situations.

Operative procedure

1. The repair of the anterior palate using the vomerian flaps and palatal mucoperiosteum is easier in a severe bilateral cleft because of the cleft itself. This will help prevent fistulas and facilitate later repair of the posterior palate at 9 months.

2. For the cleft lip the straight line closure described by Veau in 1921 is used with a slight modification to accommodate a tiny triangular flap to simulate the Cupid's bow (Figure 1: 1 and 3).

3. Local infiltration of 0.5% lignocaine with 1:200,000 adrenaline to a maximum of 2 ml is always given.

4. Cuts are made as shown in Figure 1: 5. All three layers of skin, orbicularis oris muscle (OOM) and mucosa are variously mobilized taking care to advance only 1 cm laterally on the lip margin. This safeguards arterial supply to the OOM from the labial artery. The OOM is completely dissected off the superomedial aspects of the lip and nose. The muscle is then split along its length for 2 cm, leaving a fork of muscle of two sizes, the upper flap half as wide as the lower.

5. The prolabium is incised along the white roll or the mucocutaneous junction and lifted superiorly. This flap must have a generous padding of subcutaneous tissue. The dissection must stop short of the base of the columella to preserve a tenuous blood supply to the flap.

6. The upper lip sulcus is incised medially and extended laterally for a short distance using a blunt instrument (the base of a scalpel handle serves this purpose well). The whole of the cheek is mobilized in the loose areolar supraperiosteal plane (Figure 1: 5 shaded area). The superior extent is to the orbital margin and laterally as far as the malar cheek.

7. Then the lateral nasal alae are mobilized.

8. The suturing starts with the upper lip sulci in such a manner as to advance it medially. The mucosa and the new sulcus is created by suturing the lateral segments to the prolabial mucosa.

9. At this point I find that suturing the columella or nasal base makes subsequent repair somewhat easier.

10. Then the OOM flaps are approximated with vicryl sutures using mattress stitch across the virgin territory of the prolabium. It amazes me as it reaches out to its fellow as to a long-lost friend. The assistant may sometimes help gathering the cheeks medially.

11. The prolabial skin is trimmed down and draped over the muscle and matched to its fellow point by point including the small triangular flaps to its slot on the prolabium. The vermillion flaps are quite redundant and can be sutured either overlaid to each other or trimmed and matched for symmetry. The prolabial mucosa is finally sutured to the lower vermillion border.

12. Finally two retention sutures are inserted to suspend the splayed lateral nasal cartilages through the nasal sill and tied over a tiny ball of gauze as in Figure 2c.

13. A small dressing is applied and no Logan's bow was used in any of the patients.

Postoperative care

Blood loss is made good. All the patients are back on fluid diet as soon as they demand it and usually get discharged the next day.

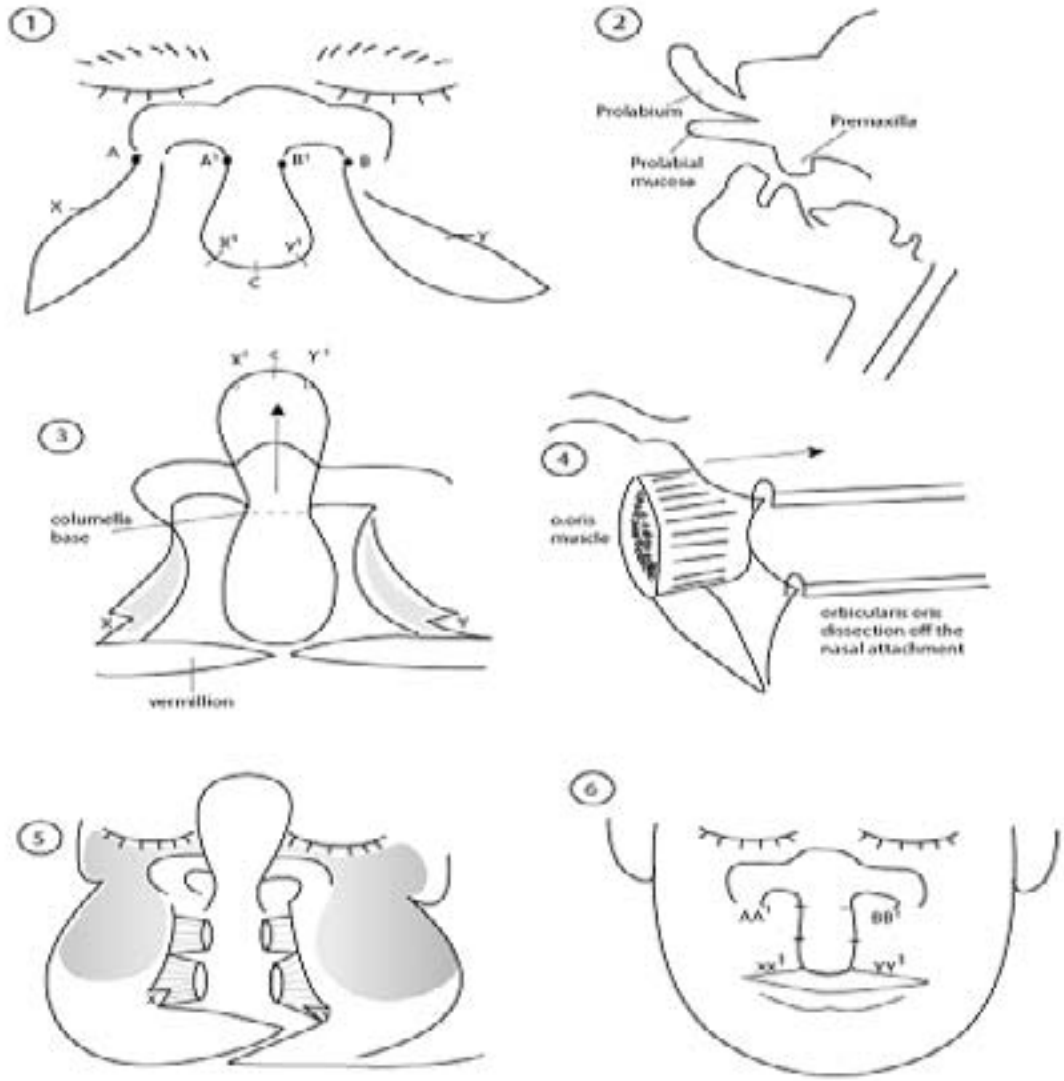


Figure 1. Schematic diagram of the *Port Moresby technique* of the repair of severe bilateral cleft lip and palate.

Our practice has been to continue penicillin for 5 days and sutures are removed after 7 days.

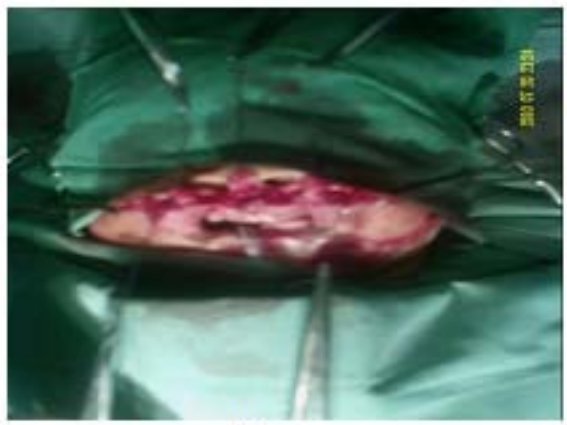
Second-stage operation

This is to close the posterior palate at 9 months. A Veau/Langenbech's two-flap procedure or Wardill's four flaps are used to achieve push back of deficient palatal tissue in the anterior-posterior axis. The closure is in two layers, ie, nasal and oral layers, with reconstitution of the tensor velli palatine muscle. Adequate mobilization is vital to get a tensionless closure.

Results

Of a total of 200 cases, only 25 severe bilateral cleft lips and 1 very wide unilateral cleft will be discussed. All had 18 mm or greater cleft defects and 8 cases had defects measuring between 30 and 35 mm. Various combinations of clefts of the palate were seen associated with the cleft lips. The youngest of the 26, who had severe bilateral cleft lip and palate, was 3 months of age and the oldest was 4 years. The commonest problems seen

a



b

c

Figure 2. Shows (a) a severe lip defect of 35 mm, (b) the lip after repair, and (c) postoperative view.

are listed in Table 1, of which the commonest overall was anterior palatal fistulae. Prominent scars were seen in 2 cases and 1 disruption was seen in a 4-year-old and only at the midline vermillion suture from an infection. Rotated premaxilla was seen in 1 patient. No deaths occurred for the entire 200 patients.

Discussion

I have shown that a one-stage primary repair of soft tissues in severe bilateral cleft lip and palate is possible thanks to the elasticity of tissues of the lip. A tensionless closure of all the three layers is possible even when the defect is as wide as 35 mm. The OOM acts as a better strut to push back the premaxilla to its fellows. This small series of 25 patients attests to that fact and challenges the view that tissue dehiscence is a real risk. During follow-up one wound breakdown was seen and was related to infection at the vermillion suture. It healed with antibiotics and the defect was tidied up at a later time when the tissues were healed. The sulcus was of sufficient depth and the upper lip was full and supple. The outcomes of prominent scar, loss of prolabium and wide central lip are amendable through increased experience and finesse in technique. The misaligned teeth and anterior palatal fistulae can be reduced by the use of orthodontic appliances, which ought to be used early when available. Follow-up of a few of the patients until age 8 showed that they had normal mid-face growth.

A noticeable benefit has been the relief and appreciation of the family immediately after the repair. I believe this is important for the well-being and future of the child as a normal person growing up in a traditional society.

Most surgeons have abandoned the idea of doing any soft tissue repair for defects of 18 mm or more (4) and have opted for presurgical orthodontic appliances instead. In 1984, Dr Black (5) reported a technique in a paper that reflected the sentiments echoed in this article but then he also used presurgical orthodontics. Moreover, many surgeons today feel that lip adhesion should not be used because of the unnatural thinness of the lip, and rightly so. There is no longer any controversy regarding the repair of the OOM to improve function and appearance of the upper lip. In the words of John Mulliken, an American cleft surgeon, “it is clear that the initial nasolabial and palatal repairs are the critical determinant of outcome in terms of appearance, speech and facial growth” (6). This is only possible with good presurgical orthodontic treatment. It would be interesting to read reports of fellow surgeons working in developing countries whose papers may not get published in top echelon journals. I hope that the technique described in this paper will be of use to them.

TABLE 1

Complications of one-stage repair of severe bilateral cleft lip and palate in 26 cases*

Complication	Number
Prominent scar lip	2
Anterior palatal fistulae	2
Rotated premaxilla with misaligned teeth	1
Dehiscence after an infection	1
Partial loss of prolabium	1
Wide prolabium giving poor aesthetic lip	1
Referred to Australia at family’s request	1

*Includes one case with very wide unilateral cleft

This paper reports on the experiences of one surgeon without the benefits of orthodontic expertise and speech therapy. The follow-up of patients is another problem in our setting. Despite these problems the results are acceptable, implying that some long-held views about wound disruptions, premaxillary recession using the fully corrected lip and facial growth are challenged. It is my view that defects greater than 18 mm can be repaired without the use of orthodontic appliances and lip adhesion techniques.

ACKNOWLEDGEMENTS

My special thanks to all the doctors and nurses who have contributed to the care of cleft children. I thank Dr J. Ollapallil for inspiration with his own patients before he left for Australia in 2000 and Mr T. Vincent of the Medical Learning Resources Unit for his help with Figure 1.

REFERENCES

1 **Theogaraj SD.** Bilateral cleft lip. In: Sinha RN, Gupta JL, Ganguli AC, eds. A Textbook of Plastic Surgery in the Tropics. New Delhi: Orient Longman, 1976:286-302.

2 **Cutting CB.** Primary bilateral cleft lip and nose repair. In: Aston SJ, Beasley RW, Thorne CHM, eds. Grabb and Smith's Plastic Surgery. Fifth edition. Philadelphia: Lippincott-Raven, 1997:255-262.

3 **Millard DR Jr.** Closure of bilateral cleft lip and elongation of columella by two operations in infancy. *Plast Reconstr Surg* 1971:47:324-331.

4 **Sharma LK.** Management of bilateral cleft lip with protruding premaxilla. *Indian J Plast Surg* 1976;9:27.

5 **Black PW, Scheflan M.** Bilateral cleft lip repair: "putting it all together". *Ann Plast Surg* 1984;12:118-127.

6 **Mulliken JB.** The changing faces of children with cleft lip and palate. *N Engl J Med* 2004;351:745-747.

PNG Med J 2012 Mar-Dec;55(1-4):61-66

Diabetic foot ulcers in Port Moresby General Hospital 2003-2008: review of the principles of effective prevention and management of diabetic foot

Jerzy Kuzma[1,2], Damien J. Hasola[1], Tom Lino[1], Osborne Liko[1], Arnold Waine[1] and Ikau Kevau[1]

Surgery Department, Port Moresby General Hospital, Papua New Guinea

SUMMARY

***Background*: In the recent decade in Papua New Guinea and other Pacific countries there has been an increasing trend of lifestyle diseases, including obesity associated with diabetes mellitus. Foot ulceration and infection leading to amputation are common and feared complications of diabetes. Yet these are potentially the most preventable of all complications in diabetic patients. Several studies have shown that half of all diabetic foot ulcers can be prevented by education and simple foot care. The primary goal of this study was to depict the scale of the diabetic foot as a community health problem. The secondary goal was to review the current literature on diabetic foot in order to develop a more effective preventive strategy. *Methodology*: A retrospective study on the patients with diabetic foot admitted to the surgical unit at Port Moresby General Hospital (PMGH) in 2003 and 2008 was conducted. We also carried out an extensive online search on the prevention and management of diabetic foot ulcers. *Results*: Our study showed an increasing trend of diabetic foot ulcers and infections from 1.4 to 2.2% of all surgical patients at PMGH over a 5-year period. Interestingly, over that period the representation of females increased from one-third to almost half of all patients with diabetic foot. Furthermore, the patients with diabetic foot complications showed a lower average hospital stay of 35 days in 2008 compared to 54 days in 2003. The literature review showed that the introduction of a diabetic podiatric team service providing simple education to diabetic patients in the form of one teaching session and/or preventive written materials, with a short explanation of diabetic foot pathology and simple preventive measures, reduced the number of amputations by half. *Recommendation*: The introduction of a comprehensive foot care education program and organizing a specialist foot clinic for diabetic patients can reduce bed occupancy and health expenditure on diabetic patients as well as the number of amputations and subsequent disability.**

Introduction

The feet are commonly affected by the metabolic changes of diabetes mellitus. The development of a diabetic foot is a complex process involving the neurological, vascular and musculoskeletal systems. The primary underlying cause of these changes is the increased level of glucose in serum resulting in nonenzymatic glycosylation at the molecular level (1).

Although ulceration and infection of the feet are potentially the most preventable of all complications in diabetic patients, they remain common and frequently lead to amputation. Several studies have shown that half of all diabetic foot ulcers can be prevented by education and simple foot care (2,3). When foot ulceration or infection occurs, energetic and aggressive treatment may prevent amputation. In Papua New Guinea (PNG) diabetic foot disease is exacerbated by sociocultural factors such as the prevalence of walking barefoot, low education, lack of knowledge about the complications connected with diabetic foot and the low socioeconomic status of patients. Of note is the publication by Campbell et al. (4) on the treatment of diabetic patients at Port Moresby General

1 Surgical Unit, Port Moresby General Hospital, Private Mail Bag, Boroko, National Capital District 111, Papua New Guinea

2 Present address: Divine Word University, PO Box 483, Madang, Madang Province 511, Papua New Guinea jkuzma@dwu.ac.pg

Hospital (PMGH), which introduced elements of modern prevention such as advice to wear light gym shoes or thongs and wash any abrasions, and the early use of antibiotics for the wound on the diabetic foot. A report from Solomon Islands by Salini et al. (5) showed that diabetic patients constitute more than a third of all surgical patients and present a serious surgical health problem. Moreover, they showed that diabetic patients had long hospital stays and approximately half of them had more than one operation performed.

The primary goal of this study was to depict the scale of the diabetic foot as a community health problem. As diabetic foot ulceration is a highly preventable condition, our secondary goal was to review the current literature in order to develop a more effective preventive strategy for diabetic patients.

Methodology

A retrospective study on the patients with diabetic foot admitted to PMGH in 2003 and 2008 was conducted. All patients with diabetic foot treated operatively in the three surgical wards were included in the study. Patients were treated respectively by the orthopaedic and two surgical consultants while most of the operations were performed by surgical registrars. In patients with decompensated diabetes a medical team consultation was sought and the patient was usually put on a sliding scale with frequent doses of short-acting insulin. In the case of infection, the general policy was wide-spectrum antibiotic cover with early debridement. Major amputation was when the amputation level was above the ankle and minor amputation when the amputation level was below the ankle. Demographic characteristics, total length of hospital stay, type of surgical procedure and mortality due to diabetic foot sepsis were extracted from patients' records. We also carried out an extensive online search on 'diabetic foot OR diabetic foot ulcer AND prevention AND management' using the search in PubMed, HINARI and MEDSCAPE.

Results

Diabetic foot ulcers at PMGH

Our study showed an increasing trend in the incidence of diabetic foot ulcers and infections at PMGH over the 5-year study period. In 2003 and 2008 there were respectively 33 (out of 2357 surgical patients) and 42 (out of 1909*)* patients treated surgically for diabetic foot. They represent 1.4% and 2.2% respectively of all surgical patients treated at PMGH in those years. Interestingly, in 2003 females constituted one-third (33%) while in 2008 about half (48%) of all patients treated surgically for diabetic foot.

In 2003, PMGH's general mortality records from all wards showed that 3 patients with infected diabetic foot died from sepsis without operation whereas in 2008 1 died before surgery and 1 after below knee amputation was performed. In 2008 40% (17/42) of the surgically treated had more than one procedure and 19% (8/42) had more than three surgical procedures performed.

Furthermore, we recorded that the patients with diabetic foot complications had longer average hospital stay in 2003 (54 days) than in 2008 (35 days). Regarding the surgical procedures, in 2003 10 and in 2008 9 patients underwent major limb amputation.

In PMGH there is an organized diabetic clinic with trained diabetic nurses educating diabetic patients. Also in the surgical unit clinicians give some instructions to the diabetic patients regarding prevention of foot ulcers; however, a comprehensive educational program on prevention of diabetic foot ulcers has not been organized. Moreover, most of the patients were not treated by an orthopaedic surgeon, who is most qualified to address foot deformity caused by diabetic neuropathy.

Literature search

Pathophysiology of diabetic foot ulcer

The development of a diabetic foot ulcer is a multifactorial process which begins with increased serum glucose, resulting in nonenzymatic glycosylation at the molecular level. This process affects the integrity of collagen, many enzymatic reactions and the function of biological membranes. The systems most affected by these abnormalities are neurological, vascular and musculoskeletal.

Nervous system

Peripheral neuropathy in a stocking/glove pattern includes sensory, motor and autonomic nerve dysfunctions. Sensory neuropathy with

loss of protective sensation allows for episodes of repeated microtrauma. Motor neuropathy in the diabetic foot and reduced innervation to intrinsic muscles leads to clawing of the toes and further progresses to equinus and cavus foot deformity. Furthermore, glycosylation of collagen results in increased joint stiffness (6). All these abnormalities contribute to increased pressure under the metatarsal heads and subsequently to development of ulcers.

In the presence of autonomic neuropathy the foot becomes dry (anhydrosis) due to lack of sweat production. This leads to the development of thick, dry and cracked calluses in areas of increased pressure below the metatarsal heads. These skin cracks serve as portals of entry for bacterial infection.

A final stage of peripheral neuropathy with loss of protective sensation is a progressive destructive neuropathic osteoarthropathy called Charcot foot. Clinically, Charcot foot presents as a very warm, erythematous, dry, swollen and collapsing foot, and is not infrequently mistaken for osteomyelitis or cellulitis. Charcot foot often results in debilitating foot deformity and ulceration.

Vascular system

Diabetic vascular disease affecting the lower extremity can be divided into two components: macroangiopathy and microangiopathy. Macroangiopathy affects predominantly smaller arteries whereas atherosclerotic occlusion prefers the aorta and iliac arteries. Although diabetic patients have an increased incidence of atherosclerotic peripheral vascular disease, many patients with foot ulcers have palpable pulses and adequate peripheral blood flow. Contrary to the common belief, many diabetic patients with neuropathy have an increased blood flow to the foot. Only approximately 30% of foot ulcerations in diabetic patients are associated with vascular insufficiency (6). The simple palpation of both pedal pulses and popliteal pulses is the most reliable indication of arterial perfusion to the foot (6).

Microangiopathy depends on thickening of the capillary basement membranes. This thickening leads to inability to dilate in response to injury (functional ischaemia) and limits the migration of white blood cells to the site of injury (7,8).

Diabetic foot risk factors

Foot ulcers and amputations are major causes of morbidity and disability for patients with diabetes. The American Diabetes Association consensus statement (9) identified the following risk factors for developing foot ulcers in people with diabetes: 1) duration of diabetes for more than 10 years, 2) males, 3) poor glucose control, 4) present cardiovascular, renal or retinal complications.

Foot-related conditions associated with increased risk of amputation (9) are:

- Peripheral neuropathy with loss of protective sensation
- Altered biomechanics (in the presence of neuropathy)
    - Evidence of increased pressure (erythema, haemorrhage under callus)
    - Bony deformity (pes equinus, claw toes)
- Peripheral vascular disease – screening: absent pedal pulses is sufficient (6)
- History of ulcers or amputation
- Severe nail pathology.

It should be emphasized that poor glucose control and increased level of glycolized haemoglobin are positively associated with the incidence of lower extremity amputation rate (10). Other risk factors for foot ulcers in patients with diabetes include obesity, malnutrition, collagen vascular diseases, use of immunosuppressants, advanced age and use of inappropriate footwear (6). AW in his unpublished study of diabetic foot at PMGH (Clinical dynamics of amputation in diabetic patients in the surgical wards of PMGH 2008-2010) found that age over 50 years, infection and higher Wagner score of the ulcer were associated with a higher major amputation rate.

Prevention strategies

Preventive programs usually include formation of a diabetic podiatric team service providing simple education to diabetic

patients in the form of one teaching session and/or preventive written materials with short explanation of diabetic foot pathology and simple preventive measures. In a medical centre in the United States major leg amputation dropped from 85 to 37 the year after the diabetic podiatric foot service was formed (2).

Similarly Viswanathan at al. (3) recorded significantly reduced rate of amputations due to diabetic foot after implementation of a preventive program.

Having analysed the effective diabetic foot ulcer prevention programs (2,8,9) we suggest the following foot care prevention and education program, adapted to the situation in Papua New Guinea:

1. Annual foot examination in the orthopaedic specialist clinic of all patients with diabetes, which should identify 'foot at risk':
   a) Initial screening of vascular status including a history of claudication and checking on both pedal pulses;
   b) Checking for features of increased pressure and neuropathy: erythema, increased warmth, foot deformity (arch collapse, claw or hammer toes, equinus) or callus formation; and
   c) If available, checking protective sensation using 10 g monofilament.
2. Good glycaemic control, which can delay neuropathy.
3. Each diabetic patient should be given at least one education session (for instance by a trained nurse) and/or written materials on diabetic foot care.

Patient education

The education of a diabetic patient regarding foot care should include:

1. Patient with neuropathy and evidence of increased pressure (erythema, increased warmth, callus) should:
   a) have well-fitting, padded walking shoes (soft and comfortable gym shoes or thongs);
   b) be instructed to break in new shoes gradually to minimize the risk of blisters and ulcer formation; and
   c) be convinced not to walk barefoot.
2. Instruction to the patient how to inspect the feet daily after washing.
   a) a patient's spouse or family member, or a mirror can help to check the soles of the feet; and
   b) web spaces should be checked for fissures and moisture.
3. Education of the patient about proper foot care:
   a) to use moisturizers (eg, coconut oil) for dry skin; and
   b) to treat tinea (fungal infection) to prevent deterioration of skin condition.
4. In the case of any new findings – such as the slightest scratch, minor wound, swelling, heat blister, excoriation, discomfort – the patient should immediately visit the clinic for dressing and antibiotic treatment.
5. Advice on weight control for overweight patients.
6. Advice on cessation of smoking, which reduces the risk of vascular disease.

Kucan and Robson (11) found shoe-related diabetic foot ulceration secondary to repetitive pressure in 36% of their cases. This finding emphasizes the importance of appropriate protective footwear monitored by an orthopaedic surgeon or physiotherapist. They noted also that about half of all diabetic patients who present with foot infections will have an infection in the contralateral foot within 18 months unless protective footwear and daily foot inspection are implemented (11).

Current management of diabetic foot ulcers

The best results in diabetic foot care in

terms of avoiding amputation are achieved by a team approach (1,2). The basic principle of this approach is to provide complete foot care for diabetic patients, ranging from education and prevention to aggressive treatment and follow-up. The orthopaedic surgeon has a primary role in the team approach to the diabetic foot. With an expertise in foot surgery, understanding of the biomechanical function of the extremity in gait, and the ability to prescribe footwear, orthoses and prosthetics, the orthopaedist is qualified to act as a leader of the diabetic foot team (1).

Successful treatment of diabetic foot ulcers consists of addressing four basic issues: 1) debridement; 2) pressure off-loading; 3) infection control; and 4) good blood glucose control (12). The first three of these will be dealt with here.

Debridement

In case of abscess, early incision and drainage are essential. Treating deep infection with antibiotics without drainage and debridement leads to the spread of infection and failure resulting in amputation. Conversely, many feet have been saved by timely drainage and debridement procedures. There are hundreds of dressings on the market, and most of them render similar results. Of note is that few randomized trials have shown that honey can improve healing of the ulcer (8,12).

Pressure off-loading

The simplest and most effective methods of off-loading the affected foot are bed rest or non-weight-bearing walking with crutches or having the patient in a wheelchair. Off-loading measures should continue (usually not shorter than 3 months) until the infection settles or the ulcer heals and the temperature of the affected foot does not differ more than 2^{o}C from the good foot (8).

Although total contact cast (TCC) is an optimal method of off-loading regarding effectiveness (shown to heal 70-100% of ulcers), weekly application of TCC is work consuming and requires high skills (eg, an orthopaedic surgeon) otherwise it may lead to the formation of new ulcers. TCC is contraindicated for patients with severe vascular compromise, morbid obesity, discharging wounds or poor compliance (8,12). It is advised that casting is continued for about 3 weeks after healing to allow the newly epithelialized wound to mature (13).

Selected patients may benefit from so-called internal off-loading, which includes surgical procedures such as resection of metatarsal heads or correction of foot deformity (eg, equinus deformity).

Administration of biphosphonates in preventing bony destruction is giving early promising results (8).

Infection control

Typically in three-quarters of cases of diabetic foot the infection is polymicrobial, including such pathogens as *Staphylococcus aureus* (30% methicillin resistant), β-haemolytic streptococci, *Pseudomonas aeruginosa,* enterococci and anaerobes (12).

Before the result of the cultures is available a broad-spectrum antibiotic best covering the Gram-positive and Gram-negative spectrum is prescribed. A specimen should be taken for antibiotic susceptibilities; however, culturing the surface of the ulcer base has been proven to be of small value, because most of the wounds are secondarily colonized, so this practice leads to over-prescribing of antibiotics. Signs of infection should be noted and culture obtained from purulent discharge or from deep tissue after debridement.

For patients with mild infections ambulatory treatment with oral antibiotics such as cephalexin, amoxycillin with potassium clavulanate (Augmentin), clindamycin or ciprofloxacin is sufficient (12). In PNG clindamycin can be substituted by chloramphenicol. For severe infection patients should be hospitalized and treated with intravenous (IV) broad-spectrum antibiotics such as chloramphenicol or flucloxacillin or cephalexin IV plus metronidazole orally. Another treatment option for severe infection is quadruple therapy: IV amoxycillin or crystalline penicillin (for *Streptococcus*), flucloxacillin (for *Staphylococcus*), metronidazole (for anaerobes) and ceftazidime or gentamicin (for Gram-negative organisms) (8).

Conservative surgery without local or high-level amputation is successful in almost half of the cases of diabetic foot osteomyelitis (14).

The optimal duration of antibiotic therapy is unknown, although soft-tissue infections usually require 2 weeks of therapy whereas osteomyelitis requires 4 to 6 weeks (15). Discontinuation of antibiotics should be considered when signs and symptoms of infection have resolved even if the ulceration has not completely healed (16).

Successful outcomes in patients with diabetic foot ulcers are the joint responsibility of the caregivers (including primary care physicians, surgeons and other paramedical personnel), the patients and their families. The surgeon's role in treating the problem wound in a patient with diabetes is a keystone of this joint responsibility.

Conclusions and Recommendations

The introduction of a comprehensive foot care education program for diabetic patients can reduce bed occupancy and health expenditure on diabetic patients as well as the number of amputations and subsequent disability.

A further step towards improving quality care for patients with diabetic foot could be setting up a diabetic foot care team consisting of a medical specialist, surgeon (preferably orthopaedic) and nurse responsible for patients' education. There is also a need to organize a specialist diabetic foot clinic, run best by an orthopaedist.

The effectiveness of educational interventions on diabetic foot care could be evaluated in a further study.

REFERENCES

1 **Laughlin RT, Calhoun JH, Mader JT.** The diabetic foot. *J Am Acad Orthop Surg* 1995;3:218-225.

2 **Boegel WA.** Expert diabetic foot care for the primary care physician. *Clinical Diabetes* 1999;17:37-41.

3 **Viswanathan V, Madhavan S, Rajasekar S, Chamukuttan S, Ambady R.** Amputation prevention initiative in South India: positive impact of foot care education. *Diabetes Care* 2005;28:1019-1021.

4 **Campbell I, Quinn E, Martin FIR.** Experience in the treatment of diabetes at Port Moresby General Hospital. *PNG Med J* 1978;21:343-346.

5 **Salini G, Baerodo D, Kevau I, Liko O, Pickacha D.** A review of surgical management of diabetic foot ulcers at the National Referral Hospital, Honiara. Abstract 11 in Program and Abstracts of the Forty-sixth Annual Medical Symposium of the Medical Society of Papua New Guinea, Wewak, 29 Aug-3 Sep 2010:60.

6 **Frykberg RG.** Diabetic foot ulcers: pathogenesis and management. *Am Fam Physician* 2002;66:1655-1662.

7 **Strauss MB, Aksenov IV.** Evaluation of diabetic wound classifications and a new wound score. *Clin Orthop Relat Res* 2005;439:79-86.

8 **Watkins PJ.** The diabetic foot. *Br Med J* 2003;326:977-979.

9 **American Diabetes Association.** Preventive foot care in people with diabetes. *Diabetes Care* 2002;25(Suppl 1):S69-S70.

10 **Lepore G, Maglio ML, Cuni C, Dodesini AR, Nosari I, Minetti B, Trevisan R.** Poor glucose control in the year before admission as a powerful predictor of amputation in hospitalized patients with diabetic foot ulceration. *Diabetes Care* 2006;29:1985.

11 **Kucan JO, Robson MC.** Diabetic foot infections: fate of the contralateral foot. *Plast Reconstr Surg* 1986;77:439-441.

12 **Kruse I, Edelman S.** Evaluation and treatment of diabetic foot ulcers. *Clinical Diabetes* 2006;24:91-93.

13 **Robinson AHN, Pasapula C, Brodsky JW.** Surgical aspects of the diabetic foot. *J Bone Joint Surg Br* 2009;91:1-7.

14 **Aragón-Sánchez FJ, Cabrera-Galván JJ, Quintana-Marrero Y, Hernández-Herrero MJ, Lázaro-Martínez JL, García-Morales E, Beneit-Montesinos JV, Armstrong DG.** Outcomes of surgical treatment of diabetic foot osteomyelitis: a series of 185 patients with histopathological confirmation of bone involvement. *Diabetologia* 2008;51:1962-1970.

15 **Nalini R.** Anti-infective therapy for foot ulcers in patients with diabetes. *Clin Orthop Relat Res* 2005;439:87-90.

16 **Bader MS.** Diabetic foot infection. *Am Fam Physician* 2008;78:71-79.

PNG Med J 2012 Mar-Dec;55(1-4):67-75

Management of difficult airways in surgical patients at the Port Moresby General Hospital operating theatre and intensive care unit

G. Gende[1,2], Yang Xing[3,4], Jianhu Wen[1,3], J. Raymond[5], E. Laim[5], V. Konga[5], L. Dimugu[5], J. Maihua[1], M. Garo[1], J. Goswammi[4], H. Paiva[4], L. Sogoromo[4] and M. Pole[4]

Port Moresby General Hospital, Papua New Guinea and Chongqing Three Gorges Central Hospital, China

SUMMARY

We report on the results of a retrospective audit of airway management in patients presenting to the Port Moresby General Hospital from 1998 to 2009. Safe and secure airway management can be challenging in the operating room during head and neck surgery. These challenges continue into the postoperative period and can present significant issues to intensive care staff. This series includes many patients with upper airway and upper gastrointestinal malignancy, head and neck trauma, head and neck infections, thyroid pathology and cleft palate. This series highlights the importance of anticipating the possibility of difficult airway preoperatively and modifying the airway management appropriately. We consider that all members of the operating team including surgeons, anaesthetists, intensive care physicians and nursing staff should cooperate and communicate effectively to optimize outcomes for these potentially difficult cases. A proposed airway management algorithm is presented to guide surgical teams performing head and neck surgery in Papua New Guinea and similar regions.

Introduction

Difficult airway is a clinical scenario where a trained anaesthetist experiences difficulty with mask ventilation, tracheal intubation or both. Difficult airway can contribute to dental damage, airway injury and hypoxaemia. Hypoxaemia can lead to the dreaded complications of hypoxic encephalopathy and death. Furthermore, adverse events relating to the airway occur in up to 20% of critical incidents in intensive care units (1). Difficult mask ventilation (DMV) is a condition in which it is not possible for the anaesthetist to provide adequate face mask ventilation because of one or more of the following problems: a) inadequate mask seal, b) excessive gas leak, and 3) excessive resistance to the ingress and egress of gas.

Methods to improve the airway patency include the triple airway manoeuvre (TAM) (T = head tilt, A = advance mandible and M = mouth open), as well as insertion of oral and nasal airways. Various studies have shown that DMV occurs in 2-8% of patients (2,3). Tracheal intubation is described as difficult when it requires multiple attempts in the presence or absence of tracheal pathology. The incidence of DMV and difficult tracheal intubation (DTI) is highly variable amongst reported studies. This reflects differences in the definitions of DMV and DTI.

Several clinical predictors of difficult intubation have been proposed; unfortunately they all have a low positive predictive value. As a result many airways predicted to be difficult by such tests are straightforward.

1 Surgery Department, Port Moresby General Hospital, Free Mail Bag, Boroko, National Capital District 111, Papua New Guinea

2 g_gende@yahoo.com

3 Department of Anaesthesia, Chongqing Three Gorges Central Hospital, Jian Kang Road 1, Yu Zhong District, Chongqing 400014, China

4 Anaesthesia Department, Port Moresby General Hospital, Free Mail Bag, Boroko, National Capital District 111, Papua New Guinea

5 Nursing Division, Port Moresby General Hospital, Free Mail Bag, Boroko, National Capital District 111, Papua New Guinea

Mallampati and colleagues described a clinical scale (4) which on its own has a low predictive value. When considered together with other dependent variables such as inter-incisor distance and short thyromental distance, the predictive value increases. There are also other important factors that can influence the success or failure of tracheal intubation. These include the experience of the operator, correct positioning of the head and neck ('sniffing the wind' position) and the quality of equipment used. Considering that the overall difficult intubation rate varies, a preplanned strategy is central to the safe management of difficult airways when they do occur.

The incidence of DTI and adverse events is not known in Papua New Guinea (PNG). It is reasonable to assume that the incidence is higher in PNG than that cited in the western anaesthetic literature. Factors that might contribute to this include: 1) a shortage of experienced anaesthetists in PNG, 2) the late presentation of patients with advanced pathology, 3) limited preoperative imaging, and 4) limited access to equipment to allow alternative airway management strategies.

This paper reports on one general surgery unit's experience with managing difficult airways over a period of 10 years. The lessons learned can be useful to others faced with similar challenges with their patients.

Materials and Methods

This is a retrospective study looking at the instances of DMV and DTI. All patients admitted to the Port Moresby General Hospital (PMGH) for surgery of the head and neck region and requiring general anaesthesia were included. They were admitted through the general surgery unit with special interest in plastic and reconstructive surgery. The period of study was from 1998 to 2009, excluding 1999 when the principal author (GG) was overseas: a study period of 10 years within an 11-year span. Cases were identified by manual review of the theatre registry books. A single investigator who had primary responsibility for all the cases collated and analysed all data to minimize observer errors and duplications. When there was uncertainty regarding the data in the theatre registry, patient medical records were obtained to ensure that relevant cases were included.

Many patients with DMV and DTI would naturally follow on with a surgical airway such as cricothyroidotomy. In the event that a preoperative assessment had identified concerns regarding the patient's airway then the appropriateness of fibre optic intubation (FOI) or other adjunctive techniques would be considered. However, patients with severe jaw ankylosis and/or trismus went straight to tracheostomy under local anaesthesia.

There were no exclusion criteria related to patients or diseases. The only indications to abort an operation were 1) where the case failed to meet the 'World Health Organization (WHO) Safe Surgery Checklist' and 2) where there were more than 4 attempts at tracheal intubation.

Table 1 lists the techniques of tracheal intubation used during the 11-year period under review.

Operating theatre procedure

For all patients undergoing elective or emergency surgery on any upper aero-digestive tract area where a real or possible difficult airway situation exists, all concerned team members must be present. This includes the surgeon, senior anaesthetist and nurse with a full retinue of support staff during the airway access phase until ventilation is safely delivered. The anaesthetic management is fully explained to the team and all necessary adjuncts such as tracheostomy trays are always available in the room. The surgeon must not leave the room at any time during this interval. Since 2009 the WHO Safe Surgery Checklist (Table 2) was trialed in this unit. This extends from the arrival in the operating room to the completion of the operation and on to the recovery room. The planned procedure is aborted in elective cases if the WHO Safe Surgery Checklist is not met in full (5).

Non-surgical tracheal intubations

The standard techniques for non-surgical tracheal intubations as described in specialist texts should be administered by senior anaesthetists, who should physically be in attendance during the procedure. We advise that the techniques must be taught and mastered and would encourage referrals of all potentially difficult airways. Inadvertent use of the techniques by novices can result in more harm than good.

TABLE 1

Techniques used for tracheal intubation in difficult airways at Port Moresby General Hospital, Papua New Guinea, 1998-2009

Gas induction and intubation whilst spontaneously breathing
Awake fibre optic intubation (FOI)
Retrograde intubation (RI)
Stylet-assisted and gum elastic bougie-assisted intubation
Cricothyroidotomy
Tracheostomy (Bjork)

TABLE 2

World Health Organization Safe Surgery Checklist

Before induction of anaesthesia
- Patient verifies name, procedure, site and consent
- Surgical site is marked or not applicable
- Pulse oximeter is on the patient and functioning
- All members of team are aware of patient allergy, if any
- The patient's airway and risk of aspiration have been evaluated and appropriate corrective equipment is available

Before skin incision – verbally
- Confirm that all team members have been introduced by name and role
- Confirm patient's identity, surgical site and procedure
- Review the anticipated critical events by surgeon, anaesthetist and nurse
- Confirm that prophylactic antibiotics have been administered ≤60 minutes before incision or not indicated
- Confirm that all imaging results for correct patient are displayed in operating room

Before patient leaves operating room
- Nurse final check aloud with team
- Name of procedure as recorded
- That the needle, sponge and instrument counts are complete (or not applicable)
- That the specimen (if any) is correctly labelled including patient's name
- Whether there are any issues with equipment to be addressed

- The team review aloud any key concerns for the recovery room management

Awake fibre optic intubation is a well-validated technique that is widely used for management of the difficult airway. The success of this technique is highly operator dependent and also requires that equipment be in good working order. Awake FOI is unlikely to achieve safe and secure airway access in a difficult airway scenario if the operator lacks experience with the technique. Medical staff involved in the management of difficult airways should train themselves to perform awake FOI, including the performance

of many intubations in patients with normal airway anatomy. The equipment required for FOI is costly and delicate. Special care is required in handling such equipment. Damage to the optical bundles or the case of the instrument often mandates replacement, which is a costly exercise.

Surgical tracheal intubation

Cricothyroidotomy

Cricothyroidotomy is indicated as a rescue technique for the 'can't intubate, can't ventilate' situation. Cricothyroidotomy can be performed by either a cannula or surgical technique. We advocate a surgical approach that does not rely on potentially unfamiliar or unavailable equipment.

Equipment:

- Scalpel with number 15 blade
- Small (eg, 6 or 7 mm) cuffed endotracheal tube

Steps:

i. Identify the cricothyroid membrane.

ii. Stab incision through skin and membrane. Start with scalpel tip in midline and blade lateral. Turn scalpel through 180 degrees and repeat.

iii. Enlarge wound with scalpel handle or forceps.

iv. Insert tube and inflate cuff.

v. Verify tube position and ventilation.

Tracheostomy

Tracheostomy is indicated when conditions of difficult intubation exist and as an adjunctive procedure to assist in postoperative care. It can be done under local anaesthesia or under general anaesthesia. Bjork's method of tracheostomy is used as the method of choice except for burns to the airways when a slit tracheostomy is used.

Steps:

The detailed steps can be learned from any standard textbook. However, it is relevant for this paper to bring out the salient points that will make the procedure smooth, safe and less of a drama in the operating theatre.

i. Take time to explain the procedure to the patient and ask for his cooperation.

ii. Extend the neck and use local anaesthesia with adrenaline.

iii. A crease incision is better and after separating the muscles the thyroid isthmus is divided and tied or retracted upward.

iv. An inverted 'U' is made in the 2-3 tracheal rings and the tracheostomy tube inserted. The base of the flap must be slightly wider than the tip to make it springier (Figure 1).

v. The skin is approximated with two stitches and the tube secured to the neck.

Airway management in the Intensive Care Unit (ICU)

Airway management in ICU patients with tracheal intubation aims to ensure adequate oxygenation and ventilation, avoid tube displacements and extubate successfully. Nursing care must be judicious to avoid tube displacements during patient repositioning and ensure that the patient is well sedated. Almost all our patients had sedation using morphine infusion or fentanyl/midazolam and after a successful leak test the tracheal tube is removed. Some problem cases may have an 'airway exchange catheter' (AEC) introduced through the endotracheal tube (ETT) and held in place while the ETT is removed. Through this AEC, oxygen can be delivered by means of jet ventilation or oxygen insufflations. Patients with Bjork-type tracheostomy were nursed in the surgical high-dependency unit (HDU), the next step downward after ICU, as long as their condition was stable after the operation.

Results

We found that 115 months out of a total of 132 months from 1998 to 3009 were available for the study. Anaesthetic records did not state the techniques used to access difficult airways but stated the length of anaesthetic induction time and made only brief remarks.

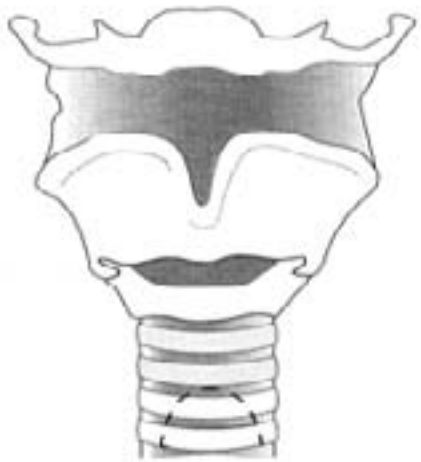


Figure 1. Bjork flap tracheostomy.

Patients' anaesthetic records in the medical charts may give details, but this study did not look at them. Nursing records were very particular in recording time in theatre but did not show any other objective information.

There were a total of 602 major operations for which there existed a real or an apparent difficult tracheal intubation risk (Table 3). Of these, 168 were for cancers of the oropharyngeal cavity and/or lips, 110 for thyroid diseases and 52 for salivary gland diseases. Cleft lip and palate operations totalled 181, accounting for 30% of cases. There was only one death, in a 28-year-old man with a massive colloid goitre who died from a possible obstruction from a late haematoma or tracheomalacia. No post-mortem examination was done since relatives refused. There were no perioperative deaths directly related to airway access interventions during the study period.

The commonest surgical airway was Bjork's flap tracheostomy, of which 62 were performed, both at preinduction under local anaesthesia and as an adjunctive procedure while under general anaesthesia (Table 4). There was only one suspected tube displacement, which could not be verified with a flexible bronchoscope. The patient was well after suction. Two patients had basal atelectasis without fever and were on crystalline penicillin. Only one perinatal patient had failed intubation and a vertical slit tracheostomy was done under local anaesthetic infiltration.

One cricothyroidotomy was performed in a patient presenting with a massive left pleomorphic adenoma. After the induction the anaesthetist was unable to intubate or ventilate the patient with a mask. This is a rate of 0.2% of all the cases considered to be a difficult airway.

No specific data were available for stylet-assisted or gum elastic bougie-assisted intubation but one patient had significant airways haemorrhage and there was one postoperative death in a patient with massive colloid goitre. The complication rate was highest at 1.8% when intubating thyroid cases.

Fibre optic, retrograde and awake intubations were successfully done by one of the authors (YX). The failed attempts at FOI were made by colleagues other than the authors and were converted to tracheostomies under local anaesthesia. The failure rate with FOI was high and operator dependent.

Discussion

We have found that it is rare to encounter failed intubation and failed ventilation, which

TABLE 3

Major surgical operations with apparent or real difficult airways undertaken in this study

Cancer resections	168
Thyroid operations	110
Salivary gland operations	52
Trauma (including burns)	15
Orofacial clefts	181
Others	76
Total	602

TABLE 4

Difficult tracheal intubations and complications encountered in this study

Technique	Number	Complications	Remarks
Tracheostomy	63	3	1 possible displaced tube 2 atelectasis without fever 62 Bjork and 1 vertical slit tracheostomy in a PRS baby
Cricothyroidotomy	1	-	Fail to intubate and fail to ventilate
Stylet- and bougie-assisted intubation	NA	2	1 airways haemorrhage 1 post-thyroidectomy death at day 3
Retrograde intubation	1	-	Requires expert operator
Fibre optic intubation	5	-	3 failed and converted to tracheostomy Requires expert operator
Awake intubation	2	-	1 converted Requires expert operator

PRS = Pierre-Robin Sequence
NA = data not available

in our series of 602 patients had a rate of 0.2%. The single patient that developed this adverse event did not have anything wrong with the larynx but had some limitation with the mouth opening due to a very large left parotid tumour. The patient was quickly salvaged because the full team was there and a cricothyroidotomy was done and a size 5 ETT inserted. There was always a readiness to do tracheostomy as soon as the anaesthetic colleague suggested it or there was marked trismus. Bjork tracheostomy was used because it provides an easy access for changing tubes without the need for bedside trays for emergency reintubations. It also prevents infection because of the wide stoma facilitating expectoration of mucus. It is also noteworthy that when a healed Bjork tracheostomy is reopened the flap is back flush with the trachea with a slight forward bossing from scarring at the incision site. Re-entry is easy. All skin fistulas had healed very well. Future risk of tracheal stenosis at the tracheostomy site is minimized because of the increased luminal diameter with a Bjork flap. Our practice was to decannulate after day 6 in the ward.

A Bjork-type tracheostomy is best suited to our setting where there is lack of adequate nursing care and frequent shortages of consumables. With ease of care and the low complication rate we have come to advocate its use in every situation where tracheostomy is indicated (Figure 1). Over the study period there was only 1 Pierre-Robin Sequence baby that had failed airway access and had a vertical slit tracheostomy. It is speculative at this stage whether a vertical slit or a flap technique should be used. Animal studies and some reviews (6,7) suggest that a flap tracheostomy is possibly safer in children under 16 years of age.

Our experience is in agreement with the reports of others (5,8), who estimate impossible intubation and ventilation in about 0.5%. It is the practice to immediately institute mask ventilation and consider other intubating options. In our setting we advise strongly to do cricothyroidotomy at the first instance when mask ventilation is not possible or poses difficulty. It is also worth considering that an operation can be postponed to another day, allowing for a planned tracheostomy performed under local anaesthesia when everyone will be better prepared for it. This we believe is not a failure but a wise and prudent clinical decision. It is also difficult to define what would constitute a failed intubation and how many attempts one would say is enough. Our low threshold for tracheostomy under local anaesthesia has been a path that is well worn and therefore we have seen less of failed intubations, particularly with oropharyngeal cancers. However, we have encountered difficulty with some congenital orofacial clefts in intubations but almost always the ETT has been eventually placed under better controlled conditions. It remains for another study perhaps to investigate this problem and offer some explanations.

Our experience with thyroid patients is important to note when reports from other centres are conflicting. Voyagis and Kyriakos (9) and Wakeling et al. (10) suggest that airway difficulty is present whereas Amathieu et al. (11), Bouaggad et al. (12) and Shaha et al. (13) found only marginally increased difficulty. It is well known that a large goitre can apply pressure on the trachea, affect the recurrent laryngeal nerve, erode the wall and soften the tracheal ring cartilage from long-standing pressure. The complication of haemorrhage in Table 4 was due to the use of a metal stylet rather than the gum elastic bougie. The single death in a patient who had undergone total thyroidectomy occurred on day 3 in the ward and may not be related to the bougie-assisted intubation. We maintain that anecdotal experiences do suggest that intubation difficulty can occur in a thyroid case.

Other methods of intubation (fibre optic, retrograde and awake intubation) are seldom employed unless the operator is well versed in their use. Their use can increase the scope of an anaesthetist's armamentarium, but they are by no means without disadvantages (14), not to mention the patient's discomfort. We suggest that they be used only by an experienced operator.

A drawback of this paper is that 17 months of records were missing and the anaesthetic and nursing records were unsuitable for use. We also did not apply the WHO Safe Surgery Checklist (15) until 2009, after it had been introduced at PMGH. The lack of standardization of difficult airways is a problem that may affect the interpretation of results in any investigations in this area.

We believe this is the first paper that audits

one unit's results from the perspective of the team effort involving nurses and doctors in a theatre and ICU/HDU setting. The paper has reaffirmed the well-known adage that good outcomes are possible when all concerned work as a team. The identification of the team leader (usually the surgeon) who will have the ultimate right to proceed or abort an operation must be established from the outset. From induction of anaesthesia to the recovery room open dialogue and total commitment are imperative. This has been emphasized by the introduction of the WHO Safe Surgery Checklist (Table 2) – an instrument that has been rigorously validated in a multicentre trial (6,15). It has been found to significantly reduce the morbidity and mortality from surgical operations by as much as 36%.

Figure 2 shows an algorithm reflecting our experience at the Port Moresby General Hospital. It can only work when a surgeon

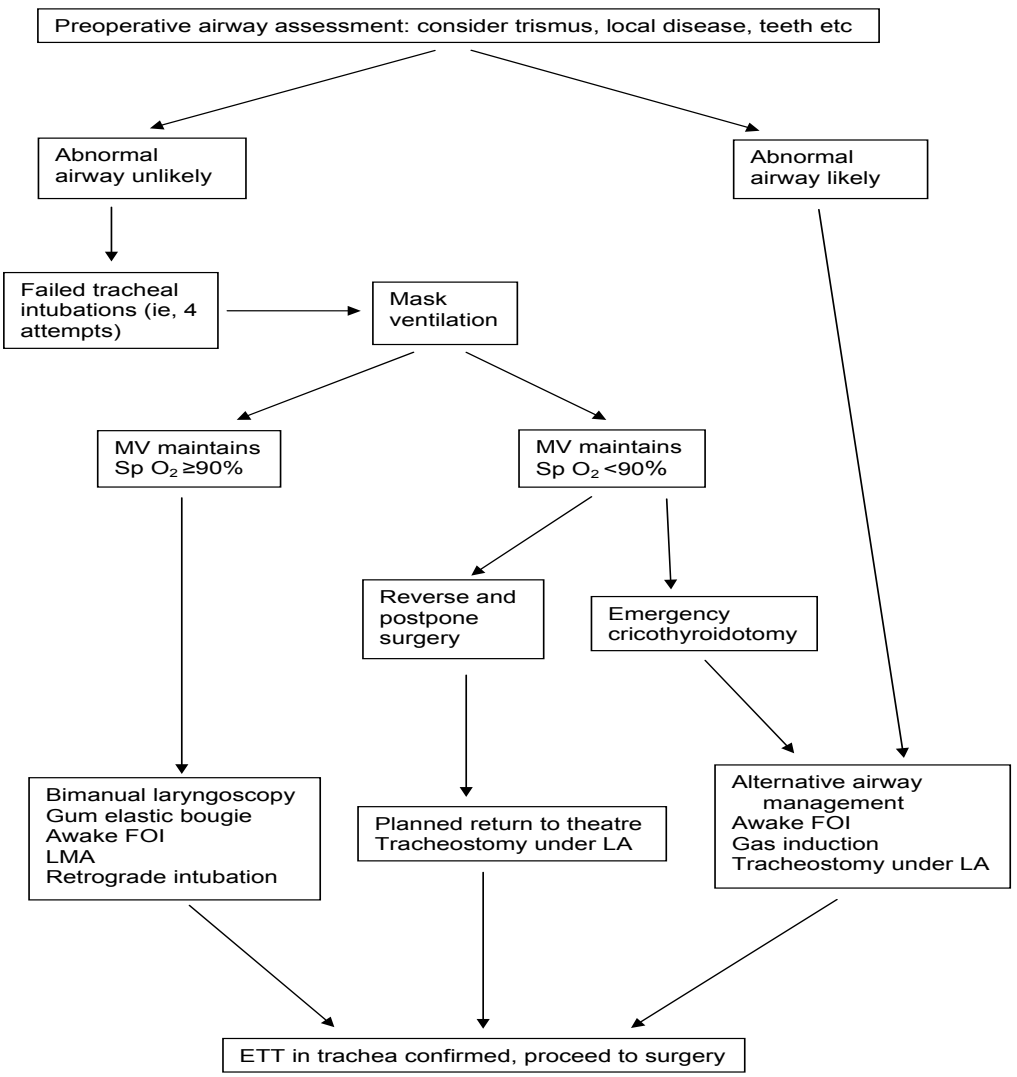


Figure 2. Failed intubation algorithm based on experience at Port Moresby General Hospital.
Sp = saturation percentage
FOI = fibre optic intubation
LMA = laryngeal mask airway
LA = local anaesthesia
ETT = endotracheal tube

has the primary responsibility and is ably supported by a good anaesthetist. The flow chart is simple and our own data suggest that it can be used safely. Though based on our own experience it is similar to flow charts recommended by others. We will welcome any suggestions to improve its validity in the country.

ACKNOWLEDGEMENTS

We thank Mr T. Vincent from the Medical Learning Resources Unit at the School of Medicine and Health Sciences, University of Papua New Guinea for his help with Figure 1. We also thank the Interplast Australia teams, comprising anaesthetists, surgeons and nurses, who helped during their visits with some of the patients. We thank the many trainee doctors who rotated through the yellow unit from 1998 to 2009. We acknowledge the input of David Daly, visiting consultant anaesthetist and consultant anaesthetist at the Alfred Hospital, Melbourne, who helped review and revise our paper.

REFERENCES

1 **American Society of Anesthesiologists Task Force on Management of the Difficult Airway.** Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology* 2003;98:1269-1277.

2 **Kheterpal S, Han R, Tremper KK, Shanks A, Tait AR, O'Reilly M, Ludwig TA.** Incidence and predictors of difficult and impossible mask ventilation. *Anesthesiology* 2006;105:885-891.

3 **Langeron O, Masso E, Huraux C, Guggiari M, Bianchi A, Coriat P, Riou B.** Prediction of difficult mask ventilation. *Anesthesiology* 2000;92:1229-1236.

4 **Mallampati SR, Gatt SP, Gugino LD, Desai SP, Waraksa B, Freiberger D, Liu PL.** A clinical sign to predict difficult tracheal intubation: a prospective study. *Can Anaesth Soc J* 1985;32:429-434.

5 **Rose DK, Cohen MM.** The airway: problems and predictions in 18,500 patients. *Can J Anaesth* 1994;41:372-383.

6 **Haynes AB, Weiser TG, Berry WR, Lipsitz SR, Breizat AH, Dellinger EP, Herbosa T, Joseph S, Kibatala PL, Lapitan MC, Merry AF, Moorthy K, Reznick RK, Taylor B, Gawande AA; Safe Surgery Saves Lives Study Group**. A surgical safety checklist to reduce morbidity and mortality in a global population. *N Engl J Med* 2009:360:491-499.

7 **Miller FR, Guay ME, Bauer T, Tucker HM.** Long-term flap tracheostomy in a pediatric animal model. *Arch Otolaryngol Head Neck Surg* 1995;21:743-748.

8 **Caplan RA, Posner KL, Ward RJ, Cheney FW.** Adverse respiratory events in anesthesia: a closed claims analysis. *Anesthesiology* 1990;72:828-833.

9 **Voyagis GS, Kyriakos KP.** The effect of goiter on endotracheal intubation. *Anesth Analg* 1997;84:611-612.

10 **Wakeling HG, Ody A, Ball A.** Large goiter causing difficult intubation and failure to intubate using the intubating laryngeal mask airway: lessons for next time. *Br J Anaesth* 1998;81:979-981.

11 **Amathieu R, Smail N, Catineau J, Poloujadoff MP, Samii K, Adnet F.** Difficult intubation in thyroid surgery: myth or reality*? Anesth Analg* 2006;103:965-968.

12 **Bouaggad A, Nejmi SE, Bouderka MA, Abbassi O.** Prediction of difficult tracheal intubation in thyroid surgery. *Anesth Analg* 2004;99:603-606.

13 **Shaha AR, Burnett C, Alfonso A, Jaffe BM.** Goiters and airway problems. *Am J Surg* 1989;158:378-380.

14 **Shaw IC, Welchew EA, Harrison BJ, Michael S.** Complete airway obstruction during awake fiberoptic intubation. *Anaesthesia* 1997;52:582-585.

15 **Gawande A, Weiser T, eds.** World Alliance for Patient Safety. World Health Organization Guidelines for Safe Surgery. Geneva: World Health Organization, 2008.

PNG Med J 2012 Mar-Dec;55(1-4):76-87

Knowledge of cardiopulmonary resuscitation among doctors at the Port Moresby General Hospital

Taita Kila[1,2] and Sam Yockopua[1]

Department of Emergency Medicine, Port Moresby General Hospital, Papua New Guinea

SUMMARY

This descriptive questionnaire-based study carried out between 16 June and 30 September 2010 aimed to assess the knowledge among doctors at Port Moresby General Hospital of basic life support and cardiopulmonary resuscitation (CPR) for children and adults, based on Australian Resuscitation Council Guidelines. 87 (81%) of 107 questionnaires were returned from 15 consultants (17% of respondents), 51 registrars (59%) – of whom 39 (45%) were in training – and 21 resident medical officers (24%). The respondents were based in internal medicine, surgery, emergency medicine, anaesthetics, obstetrics and gynaecology, paediatrics and smaller disciplines (ear, nose and throat, ophthalmology, intensive care, radiology, psychiatry and pathology). Knowledge of CPR in this study population was uneven and overall inadequate. Only 51 respondents (59%) knew that basic CPR was a priority over intubation. 72 (83%) knew the correct compression:ventilation ratio for children but only 38 (44%) knew this for adults. 33 (38%) knew the correct compression rate for children and 29 (33%) for adults. 40 (46%) knew the correct compression depth for children and 35 (40%) for adults. 60 (69%) knew the sites for defibrillator pads. Knowledge of types of defibrillator and shockable rhythms was poor: 21 (24%) gave two correct arrhythmias for defibrillation and 44 (51%) gave one. Medical officers in training appeared to have better knowledge than their colleagues in postgraduate training programs. As a group, doctors working in emergency medicine, anaesthetics and intensive care had better knowledge of adult resuscitation than their counterparts in the other adult disciplines and had similar knowledge of paediatric resuscitation to that of their paediatric counterparts, although overall knowledge was incomplete in all groups. Basic life support (BLS) and advanced life support (ALS) flow charts for both children and adults should be highly visible throughout the hospital and there is a need for regular training in CPR.

Introduction

Sudden cardiac arrest (SCA) is a leading cause of death in adults in western countries. In Europe SCA affects 700,000 adults a year (1). The exponential rise in the prevalence of non-communicable disease in Papua New Guinea (PNG) has resulted in SCA being a common event in Papua New Guinean adults.

At the time of the first heart rhythm analysis about 40% of adult SCA victims have ventricular fibrillation (VF) (2-5). It is likely that many more victims have VF or rapid ventricular tachycardia (VT) at the time of collapse but by the time the first electrocardiogram (ECG) is recorded their rhythm has deteriorated to asystole (6-7). In children the majority of arrests are due to hypoxia and hypotension – and are categorized as arrests from asphyxia. In such arrests the usual electrocardiographic finding is severe bradycardia or asystole.

The individual who collapses or has cardiorespiratory arrest is managed in four stages, provided each preceding stage is successful.

1 Department of Emergency Medicine, Port Moresby General Hospital, Free Mail Bag, Boroko, National Capital District 111, Papua New Guinea

2 taita.kila@gmail.com

1. The initial response and basic life support.
2. Advanced life support.
3. Post-resuscitation care (if above is successful).
4. Long-term management.

The initial life support and basic resuscitation can be performed by doctors, nurses, paramedical personnel and trained lay persons. Basic life support (BLS) is intended to maintain organ perfusion until definitive measures or interventions are done. It involves maintaining airway patency and supporting breathing and circulation without use of equipment other than a device to protect against transmission of infection via oral secretions. BLS is done by coordinated chest compressions and expired air ventilation.

Early bystander cardiopulmonary resuscitation (CPR) doubles or triples survival from VF SCA and has been adopted by the European Resuscitation Council as part of their concept of a chain of survival as vital steps for successful resuscitation (8-11). Immediate CPR provides a small but critical blood flow and increases the likelihood that a defibrillation shock will terminate a VF. Studies have shown that for every minute without CPR, survival from witnessed VF decreases by 7-10% (8). When bystander CPR is provided, the decline in survival is more gradual and averages 3-4%/min (8,11,12).

During the first few minutes after non-asphxial cardiac arrest, the blood oxygen content remains high and myocardial and cerebral oxygen delivery is limited, more reduced by cardiac output than lack of oxygen in the lungs (13). Ventilation is therefore less important than chest compression in the first few minutes. CPR must be continued without interruption for adequate perfusion of vital organs. Animal studies have shown that chest compressions only may be effective in the first few minutes after non-asphxial arrests.

In developed countries BLS now includes the use of semi-automated external defibrillators (SAED), if available. These are sensitive and specific for correct diagnosis of VF and VT and simple for bystanders to use with minimal training (14,15).

Advanced life support (ALS) is almost always necessary to produce return of spontaneous circulation after circulatory arrest. ALS is intended to achieve adequate ventilation, control cardiac arrhythmias, stabilize the haemodynamic status and restore organ perfusion. Endotracheal intubation is the gold standard for advanced management of the airway during cardiac arrest. It provides a clear and secure airway allowing ventilation, oxygenation, suction and administration of medication if indicated. Immediate defibrillation and cardioversion may precede intubation and intravenous line insertion in VF and VT. The speed at which defibrillation and cardioversion are carried out is important for successful resuscitation (14,15).

There has to be good knowledge of CPR for it to be appropriately, safely and effectively performed. Studies have shown that there are significant problems surrounding CPR amongst health workers; for example, a study done in Saimaniya Medical Complex in Manama, Bahrain found that of a sample of 82 nurses only 7% of the responders passed the knowledge test in CPR (16).

This study aimed to determine the knowledge of CPR among doctors at Port Moresby General Hospital (PMGH).

Methods

In this cross-sectional descriptive study of doctors at PMGH carried out from 16 June to 30 September 2010 a questionnaire was used to assess knowledge of BLS and ALS protocols for adults and children based on Australian Resuscitation Council Guidelines (Figure 1).

The questionnaires were distributed to resident medical officers, medical officers and consultants across the range of medical specialty. Selection was opportunity based. Data were analysed using SPSS software. Where appropriate chi-squared tests using Epi Info Statcalc were calculated for composite scores (the overall proportion of the sum of correct responses) obtained by specific groups of respondents.

Results

87 (81%) of the 107 questionnaires were returned. Only the results from questions on BLS were analysed.

QUESTIONNAIRE

Some questions require more than one correct answer.
[Correct answers are in bold face.]

Basic Life Support

1. Adult resuscitation

1 a) How far down the anterior posterior diameter of the chest is the compression depth?
⅓ ½ ¼ Not sure

1 b) What is the compression rate per minute?
30 60 **100** >100

1 c) What is the compression:ventilation ratio?
15:2 **30:2** 30:5 60:5

1 d) Where is the site of compression?
- Middle ½ of the sternum
- Apex
- Upper ⅓ of the sternum
- **Lower ⅓ of the sternum**

2. Paediatric resuscitation excluding the newborn

2 a) How far down the anterior posterior diameter of the chest is the compression depth?
⅓ ½ ¼ Not sure

2 b) What is the compression rate per minute?
30 60 **100** >100

2 c) What is the compression:ventilation ratio?
15:2 **30:2** 30:5 60:5

3. Intubation and use of defibrillators

3 a) Is intubating a patient a priority over the cycle of CPR?
Yes **No**

3 b) Which of these are types of defibrillators?
- **Monophasic**
- Phasic
- **Semi automated external defibrillators (SAED)**

- Not sure

3 c) What are the indications for defibrillation in an arrest?
- Asystole
- **Pulseless ventricular tachycardia (VT)**
- **Ventricular fibrillation (VF)**
- Pulseless electrical activity (PEA)

3 d) Where are the defibrillator pads applied?
- **One paddle placed to the right of the sternum below the clavicle and the other in the position of the cardiac apex**
- One paddle to the right of the sternum and the other to the left of the sternum just below the clavicle
- **One paddle over the cardiac apex and the other in the back in the left infrascapular region**
- Not sure

3 e) Do you defibrillate a witnessed arrest?
Yes **No**

Figure 1. Questionnaire used to assess knowledge of basic life support protocols for adults and children based on Australian Resuscitation Council Guidelines.

39 (45%) of the respondents were medical officers in postgraduate training programs. 10 of the 12 not in training were posted at the Emergency Department (ED) and 2 at the Children's Outpatient Department.

Overall reported knowledge on CPR is shown for adults and children in Tables 1-3. Knowledge of basic CPR was poor. Knowledge of paediatric resuscitation appeared to be better than for adults although it should be noted that both 30:2 and 15:2 compression:ventilation ratios were accepted as correct for children. Correct answers were recorded for more than 50% of responders only for compression:ventilation ratios in children, the priority of CPR over intubation, the site of defibrillator pads and knowledge of one shockable rhythm. For only two of the questions – compression:ventilation ratio in children and knowledge of 1 defibrillator pad site – were the correct response rates more than 60%. Many respondents left questions unanswered. The highest correct score was for the compression:ventilation ratio for children at 83%. Questions on adults' compression depth, compression rates for children and adults and defibrillator types were answered poorly.

Knowledge by level of training of respondents is shown in Tables 4-6. Knowledge appeared to be very uneven both across the categories of training from resident medical officer to specialist medical officer and across the spectrum of question topics. Service medical officers (not in a postgraduate training program) appeared to have the best knowledge overall, whilst the knowledge of medical officers in training programs was disappointing.

No respondent answered all questions correctly and none answered all incorrectly. 5 respondents (an anaesthetist, an anaesthetic trainee, an obstetrics and gynaecology trainee, a paediatric trainee and an ED medical officer not in training) answered all questions in the adult and paediatric CPR sections correctly. 2 respondents answered all questions in these sections incorrectly. No respondent answered all questions on the section relating to intubation and defibrillation correctly.

CPR knowledge by specialty grouping (excluding residents) is shown in Tables 7-9. The specialties of emergency medicine, anaesthetics and intensive care are combined and compared with the other adult disciplines

TABLE 1

Overall knowledge of basic cardiopulmonary resuscitation in adults

	Correct No (%)	Incorrect No (%)	Not sure No (%)	No answer No (%)
Compression depth	35 (40)	32 (37)	19 (22)	1 (1)
Compression rate	29 (33)	53 (61)	4 (5)	1 (1)
Compression:ventilation ratio	38 (44)	46 (53)	2 (2)	1 (1)
Site of compression	40 (46)	45 (52)	1 (1)	1 (1)

TABLE 2

Overall knowledge of cardiopulmonary resuscitation in children

	Correct No (%)	Incorrect No (%)	Not sure No (%)	No answer No (%)
Compression depth	40 (46)	28 (32)	18 (21)	1 (1)
Compression rate	33 (38)	49 (56)	3 (3)	2 (2)
Compression:ventilation ratio	72 (83)	11 (13)	1 (1)	3 (3)

in Table 7 and with the paediatric respondents in Table 8. This 'front line' group appeared to have better knowledge of basic CPR than their counterparts in the other adult disciplines ($p = 0.0008$) and overall knowledge at least comparable with their paediatric colleagues. Knowledge of the other components of resuscitation did not appear to differ between the 'front line' group and other doctors. 4 doctors in this group reported that they would (incorrectly) defibrillate in a witnessed arrest and only 14 (67%) reported that CPR takes precedence over intubation.

Specialties with most correct answers for individual questions were:

- Paediatric compression depth – paediatrics 75%.
- Compression:ventilation ratio for adults – emergency medicine 92%.
- Compression:ventilation ratio for children – emergency medicine 85%; paediatrics 75%.
- CPR in a witnessed arrest – surgery 78%.
- CPR as priority over intubation in an arrest – paediatrics and anaesthetics, 75% each.

Discussion

In many western countries, health workers undergo certification training in CPR conducted by their country's Resuscitation Council in accordance with their guidelines. In PNG there is no such body to ensure standard knowledge and practice of both BLS and ALS.

TABLE 3

Overall knowledge of cardiopulmonary resuscitation (CPR), intubation and defibrillation

	Correct No (%)	Incorrect No (%)	Not sure No (%)	No answer No (%)
CPR priority over intubation	51 (59)	34 (39)	2 (2)	0
Defibrillator types:				
One	30 (35)	3 (3)	49 (56)	
Two	5 (6)			
Defibrillator rhythms:				
One	44 (51)	18 (21)	4 (5)	
Two	21 (24)			
Defibrillator pad sites:				
One	57 (66)	3 (3)	24 (28)	
Two	3 (3)			
Defibrillate a witnessed arrest	31 (36)	46 (53)	10 (11)	

TABLE 4

Correct answers given by different levels of training – adult CPR

	Resident MO n = 21 No (%)	MO not in training n = 12 No (%)	MO in training n = 39 No (%)	Specialist n = 15 No (%)
Compression depth	9 (43)	6 (50)	17 (44)	3 (20)
Compression rate	7 (33)	7 (58)	14 (36)	1 (7)
Compression:ventilation ratio	7 (33)	11 (92)	16 (41)	4 (27)
Site of compression	7 (33)	7 (58)	19 (49)	7 (47)

CPR = cardiopulmonary resuscitation
MO = medical officer

TABLE 5

CORRECT ANSWERS GIVEN BY DIFFERENT LEVELS OF TRAINING – PAEDIATRIC CPR

	Resident MO n = 21 No (%)	MO not in training n = 12 No (%)	MO in training n = 39 No (%)	Specialist n = 15 No (%)
Compression depth	11 (52)	6 (50)	13 (33)	10 (67)
Compression rate	7 (33)	7 (58)	14 (36)	5 (33)
Compression:ventilation ratio	18 (86)	9 (75)	32 (82)	13 (87)

CPR = cardiopulmonary resuscitation
MO = medical officer

TABLE 6

CORRECT ANSWERS GIVEN BY DIFFERENT LEVELS OF TRAINING

	Resident MO n = 21 No (%)	MO not in training n = 12 No (%)	MO in training n = 39 No (%)	Specialist n = 15 No (%)
CPR priority over intubation	14 (67)	8 (67)	22 (56)	7 (47)
Defibrillator types:				
One	6 (29)	5 (42)	14 (36)	5 (33)
Two	1 (5)	2 (17)	1 (3)	1 (7)
Defibrillator rhythms:				
One	10 (48)	6 (50)	20 (51)	8 (53)
Two	4 (19)	6 (50)	7 (18)	4 (27)
Defibrillator pad sites:				
One	9 (43)	12 (100)	26 (67)	10 (67)
Two	1 (5)	0	2 (5)	0
Defibrillate a witnessed arrest	7 (33)	2 (17)	17 (44)	5 (33)

CPR = cardiopulmonary resuscitation
MO = medical officer

TABLE 7

CORRECT ANSWERS GIVEN BY TRAINEES AND SPECIALISTS FOR ADULT CPR

	Emergency, anaesthetics and intensive care n = 21 No (%)	Medicine, surgery, obstetrics & gynaecology and others n = 37 No (%)
Compression depth	10 (48)	13 (35)
Compression rate	11 (52)	8 (22)
Compression:ventilation ratio	15 (71)	13 (35)
Site of compression	12 (57)	16 (43)

p = 0.0008
CPR = cardiopulmonary resuscitation

TABLE 8

CORRECT ANSWERS GIVEN BY TRAINEES AND SPECIALISTS FOR PAEDIATRIC CPR

	Emergency, anaesthetics and intensive care n = 21 No (%)	Paediatrics n = 8 No (%)
Compression depth	12 (57)	6 (75)
Compression rate.	13 (62)	2 (25)
Compression:ventilation ratio	19 (90)	6 (75)

p = 0.44
CPR = cardiopulmonary resuscitation

CPR has been taught to students at various stages of their training but until recently there has been no formal assessment of students' or health workers' ability and no ongoing follow-up program to ensure that adequate skills are developed and maintained. Whilst there are now courses held annually that teach CPR, for example Early Life Support (ELS) and Primary Trauma Care (PTC), there is still clearly much room for improvement. Our study, the first of its kind in Papua New Guinea, shows that there is generally inadequate knowledge of CPR among the doctors working at the country's only tertiary hospital.

At the time of the study there was only one emergency senior medical officer (SMO) at PMGH, who was supervising this project. Although most of the medical officers in the emergency group were not in training they had fair knowledge due to attending short courses and regular ED teaching sessions. This

TABLE 9

CORRECT ANSWERS GIVEN BY SPECIALISTS AND RESIDENT MEDICAL OFFICERS

	Emergency, anaesthetics and intensive care n = 21 No (%)	Medicine, surgery, paediatrics, obstetrics & gynaecology and others n = 45 No (%)
CPR priority over intubation	14 (67)	23 (51)
Defibrillator types:		
One	11 (52)	13 (29)
Two	3 (14)	1 (2)
Defibrillator rhythms:		
One	10 (48)	24 (53)
Two	8 (38)	9 (20)
Defibrillator pad sites:		
One	20 (95)	28 (62)
Two	1 (5)	1 (2)
Defibrillate a witnessed arrest	4 (19)	20 (44)

p = 0.28
CPR = cardiopulmonary resuscitation
Note: There was no emergency physician and only three emergency medicine trainees, two of whom were in the first year of training

regular on-the-job training probably explains their superior performance compared with those in postgraduate training programs in the other disciplines.

In January 2005 the consensus on science and treatment recommended a compression: ventilation ratio of 30:2 for all infants (except newborn at birth), children and adults. A ratio of 15:2 was recommended for CPR performed by two health care rescuers (17). These recommendations replaced the previous 5:1 for two-person rescue of adults, children and infants.

The rationale for a higher ratio is based on the possibility that a ratio of 5:1:

1. May provide unnecessary ventilation. Cardiac output during good CPR is only a quarter to half of normal cardiac output.
2. May obstruct venous return thereby limiting cardiac output.
3. May excessively lower blood carbon dioxide levels thereby causing cerebral vasoconstriction.
4. Frequently interrupts cardiac compression causing blood pressure to fall nearly to zero at each interruption, thereby failing to perfuse the cerebral and coronary vascular areas.

In March 2006 the American Resuscitation Council (ARC) released updated guidelines based on an extensive evaluation of resuscitation by the International Liaison Committee on Resuscitation (ICOR) (18,19). Some changes included making the compression:ventilation ratio 30:2 regardless of the number of rescuers. This was chosen to encourage uninterrupted cardiac compression

sequences and decrease unnecessary ventilation. It is also easier for all rescuers to learn, remember and perform.

However, children differ from adults. They have higher respiratory rates than adults and the prime cause of SCA in children is asphyxia. The consensus of opinion among the paediatricians who participated in the 2005 evaluation of the science of resuscitation was that ventilation should be emphasized as a prominent part of CPR for children and infants, that the ratio of 30:2 would result in insufficient ventilation and that the ratio of 15:2 should be standard for children (18,19).

In the present study the paediatric compression:ventilation ratio of either 30:2 or 15:2 was accepted and most participants answered correctly, with 41 giving a ratio of 15:2. All 8 participants in anaesthetics answered correctly.

Following SCA 40% of adults have VF at their first heart rhythm analysis (2-5). Many more may have VF or rapid ventricular tachycardia at the time of collapse but by the time the first ECG is recorded their rhythm is likely to have deteriorated to asystole (6,7). It is therefore important that all doctors involved in patient care should have some basic knowledge of the types of arrhythmia requiring defibrillation.

In an arrest defibrillation is required if the rhythm shown on a cardiac monitor is a shockable rhythm. Most of the witnessed arrests in our hospital setting are not connected to cardiac monitors at the time of arrest. The type of cardiac rhythm is therefore not known. With the type of rhythm not known the importance of early uninterrupted external chest compression is emphasized. More than half of the respondents reported that they would wrongly defibrillate a witnessed arrest. However, this result may well reflect ambiguity in the question. Had this specified the first response to a witnessed arrest, answers may have differed.

Immediate defibrillation when a defibrillator is available has been a key element in guidelines and teaching and considered to be of paramount importance for survival from VF. This concept has been challenged as evidence suggests that a period of chest compression before defibrillation may improve survival (8,20). The European Resuscitation Council (ERC) states that immediate CPR can double or triple survival from VF SCA. Studies have shown that for every minute without CPR, survival from witnessed VF decreases by 7-10% (8). When bystander CPR is provided, the decline in survival is more gradual and averages 3-4%/min (8,11,12), as noted previously. CPR must be continued without interruption for adequate perfusion of vital organs. Early defibrillation within 3-5 minutes of collapse can produce survival rates as high as 49-75% (7-11,21-32). Each minute of delay reduces the probability of survival to discharge by 10-15%. In the PNG context CPR is of paramount importance and should be started immediately, followed by defibrillation if a defibrillator is available and there is a shockable rhythm.

There are a number of limitations to the present study. The sample size was small and included a cross-section of doctors at varying levels of training. Sampling bias may have resulted from the opportunistic distribution of questionnaires. The questionnaire was in multiple choice format, and some answers may have been guesses. Some questions could have been more clearly formulated. 19% of the questionnaires were not returned. Although an 80% return for a questionnaire-based study may be regarded as providing reasonably accurate information, it is possible that inadequate knowledge may have been the reason for non-participation, adding significant bias to the results.

In conclusion, our study, though small and with the noted limitations, forms a baseline for future assessments. It clearly shows that there is inadequate knowledge of CPR for both children and adults in medical staff at the country's tertiary hospital. To improve the situation we recommend that:

- CPR should continue to be taught in the undergraduate medical curriculum and should be emphasized in the emergency medicine rotation to prepare students for residency.
- Courses focusing on CPR should be held regularly for all health workers.
- The current annual courses like ELS should be continued.
- Appropriate resuscitation charts should be easily visible in all areas of the

hospital.

- A PNG Resuscitation Group should be established.

ACKNOWLEDGEMENTS

We thank the doctors who participated in this study. We acknowledge the assistance of Prof. J. Vince in preparing the project for publication.

REFERENCES

1 **Sans S, Kesteloot H, Kromhout D.** The burden of cardiovascular diseases mortality in Europe. Task Force of the European Society of Cardiology on Cardiovascular Mortality and Morbidity Statistics in Europe. *Eur Heart J* 1997;18:1231-1248.

2 **Cobb LA, Fahrenbruch CE, Olsufka M, Copass MK.** Changing incidence of out-of-hospital ventricular fibrillation, 1980-2000. *JAMA* 2002;288:3008-3013.

3 **Rea TD, Eisenberg MS, Sinibaldi G, White RD.** Incidence of EMS-treated out-of-hospital cardiac arrest in the United States. *Resuscitation* 2004;63:17-24.

4 **Vaillancourt C, Stiell G; Canadian Cardiovascular Outcomes Research Team.** Cardiac arrest care and emergency medical services in Canada. *Can J Cardiol* 2004;20:1081-1090.

5 **Waalewijn RA, de Vos R, Koster RW.** Out-of-hospital cardiac arrests in Amsterdam and its surrounding areas: results from the Amsterdam resuscitation study (ARREST) in 'Utstein' style. *Resuscitation* 1998;38:157-167.

6 **American Journal of Emergency Medicine.** Automated external defibrillators and ACLS: a new initiative from the American Heart Association. *Am J Emerg Med* 1991:9:91-94.

7 **Waalewijn RA, Nijpels MA, Tijssen JG, Koster RW.** Prevention of deterioration of ventricular fibrillation by basic life support during out-of-hospital cardiac arrest. *Resuscitation* 2002;54:31-36.

8 **Valenzuela TD, Roe DJ, Cretin S, Spaite DW, Larsen MP.** Estimating effectiveness of cardiac arrest interventions: a logistic regression survival model. *Circulation* 1997;96:3308-3313.

9 **Holmberg M, Holmberg S, Herlitz J; Swedish Cardiac Arrest Registry.** Factors modifying the effect of bystander cardiopulmonary resuscitation on survival in out-of-hospital cardiac arrest patients in Sweden. *Eur Heart J* 2001;22:511-519.

10 **Holmberg M, Holmberg S, Herlitz J, Gårdelöv B.** Survival after cardiac arrest outside hospital in Sweden. Swedish Cardiac Arrest Registry. *Resuscitation* 1998;36:29-36.

11 **Waalewijn RA, de Vos R, Tijssen JGP, Koster RW.** Survival models for out-of-hospital cardiopulmonary resuscitation from the perspectives of the bystander, the first responder, and the paramedic. *Resuscitation* 2001;51:113-122.

12 **Resuscitation.** Recommended guidelines for uniform reporting of data from out-of-hospital cardiac arrest: the 'Utstein style'. Prepared by a Task Force of Representatives from the European Resuscitation Council, American Heart Association, Heart and Stroke Foundation of Canada, Australian Resuscitation Council. *Resuscitation* 1991;22:1-26.

13 **Kern KB, Hilwig RW, Berg RA, Sanders AB, Ewy GA.** Importance of continuous chest compressions during cardiopulmonary resuscitation: improved outcome during a simulated single lay-rescuer scenario. *Circulation* 2002;105:645-649.

14 **Cameron P, Jelinek G, Kelly AM, Murray L, Brown AFT, Heyworth J, eds.** Textbook of Adult Emergency Medicine. Second edition. London: Churchill Livingstone, 2004.

15 **Cameron P, Jelinek G, Everitt I, Browne GJ, Raftos J, eds.** Textbook of Paediatric Emergency Medicine. Second edition. London: Churchill Livingstone, 2011.

16 **Marzooq H, Lyneham J.** Cardiopulmonary resuscitation knowledge among nurses working in Bahrain. *Int J Nurs Pract* 2009;15:294-302.

17 **Nolan JP, Hazinski MF, Steen PA, Becker LB.** Controversial topics from the 2005 International Consensus Conference on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Resuscitation* 2005;67:175-179.

18 **Resuscitation.** Proceedings of the 2005 International Consensus Conference on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Resuscitation* 2005;67:157-341.

19 **International Liaison Committee on Resuscitation.** Summary of the 2005 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Circulation* 2005;112(22 Suppl):III1-III136.

20 **Cohen SE, Andes LC, Carvalho B.** Assessment of knowledge regarding cardiopulmonary resuscitation of pregnant women. *Int J Obstet Anesth* 2008;17:20-25.

21 **Page S, Meerabeau L.** Achieving change through reflective practice: closing the loop. *Nurse Educ Today* 2000;20:365-372.

22 **Cummins RO, Ornato JP, Thies WH, Pepe PE.** Improving survival from sudden cardiac arrest: the "chain of survival" concept. A statement for health professionals from the Advanced Cardiac Life Support Subcommittee and the Emergency Cardiac Care Committee, American Heart Association. *Circulation* 1991;83:1832-1847.

23 **Calle PA, Lagaert L, Vanhaute O, Buylaert WA.** Do victims of an out-of-hospital cardiac arrest benefit from a training program for emergency medical dispatchers? *Resuscitation* 1997;35:213-218.

24 **Curka PA, Pepe PE, Ginger VF, Sherrard RC, Ivy MV, Zachariah BS.** Emergency medical services priority dispatch. *Ann Emerg Med* 1993;22:1688-1695.

25 **Weaver WD, Hill D, Fahrenbruch CE, Copass MK, Martin JS, Cobb LA, Hallstrom AP.** Use of the automatic external defibrillator in the management of out-of-hospital cardiac arrest. *N Engl J Med* 1988;319:661-666.

26 **Auble TE, Menegazzi JJ, Paris PM.** Effect of out-of-hospital defibrillation by basic life support providers on cardiac arrest mortality: a metanalysis. *Ann Emerg Med* 1995;25:642-648.

27 **Stiell IG, Wells GA, De Maio VJ, Spaite DW, Field BJ 3rd, Munkley DP, Lyver MB, Luinstra LG, Ward R.** Modifiable factors associated with improved cardiac arrest survival in a multicentre basic life support/defibrillation system: OPALS Study Phase I results. Ontario Prehospital Advance Life Support. *Ann Emerg Med* 1999;33:44-50.

28 **Stiell IG, Wells GA, Field BJ, Spaite DW, De Maio**

VJ, Ward R, Munkley DP, Lyver MB, Luinstra LG, Campeau T, Maloney J, Dagnone E. Improved out-of-hospital cardiac arrest survival through the inexpensive optimization of an existing defibrillation program: OPALS Study Phase II. Ontario Prehospital Advance Life Support. *JAMA* 1999;281:1175-1181.

29 **Caffrey S.** Feasibility of public access to defibrillation. *Curr Opin Crit Care* 2002;8:195-198.

30 **O'Rourke MF, Donaldson E, Geddes JS.** An airline cardiac arrest program. *Circulation* 1997;96:2849-2853.

31 **Page RL, Hamdan MH, McKenas DK.** Defibrillation aboard a commercial aircraft. *Circulation* 1998;97:1429-1430.

32 **Valenzuela TD, Roe DJ, Nichol G, Clark LL, Spaite DW, Hardman RG.** Outcomes of rapid defibrillation by security officers after cardiac arrest in casinos. *N Engl J Med* 2000;343:1206-1209.

PNG Med J 2012 Mar-Dec;55(1-4):88-93

Seroprevalence of anti-*Toxoplasma gondii* antibodies in HIV/AIDS patients and healthy blood donors at the Port Moresby General Hospital, Papua New Guinea

L. Ninmongo John[1,2], W.J. McBride[3], J. Millan[4] and K. Wilson[5]

Internal Medicine Department, Port Moresby General Hospital, Papua New Guinea, School of Medicine and Dentistry, James Cook University, Cairns, Australia, National Department of Health, Port Moresby, Papua New Guinea and National Serology Reference Laboratory, Melbourne, Australia

SUMMARY

The findings of a seroepidemiological study into the prevalence of *Toxoplasma gondii* infection amongst normal blood donors and patients infected with HIV (human immunodeficiency virus) are presented. Of the total 301 participants, 181 were HIV antibody positive and 120 blood donors were HIV antibody negative. We used a prevalidated questionnaire, enzyme-linked immunosorbent assay (ELISA) and the Epi Info version 3.2 software plus SPSS version 10 for data analysis. The results showed an overall antibody prevalence rate of 53% in the population and a significantly higher infection rate amongst HIV-positive patients: odds ratio 2.14 (95% CI 1.30-3.53), p = 0.001. The study further showed that exposure to cats and highlands origin were independent risk factors. This study has demonstrated that in light of the current HIV/AIDS (acquired immune deficiency syndrome) epidemic, opportunistic infections such as toxoplasmosis will be a cause of considerable morbidity and mortality. It is therefore important that clinicians and public health practitioners fit these findings into overall management strategies to help control toxoplasmosis.

Introduction

Toxoplasmosis is caused by an obligate intracellular coccidian parasite, *Toxoplasma gondii* (1). It has both a feline and a non-feline cycle. Its definitive hosts are cats, where it completes its sexual cycle. During an acute infection cats may excrete as many as 100 million parasites per day (1). The oocysts are highly infectious and can remain viable for many years in the soil. The non-feline cycle takes place in an intermediate host such as humans, mammals and birds. Ingestion of infected soil or undercooked meat containing oocysts or bradyzoites (not dose-dependent) is enough to cause a lifelong infection. Sporulation in the body leads to generalized infection and encystations, particularly in the cells of the central nervous system and skeletal muscles. Transplacental transmission is also known to occur in a third of infected mothers. Uncommonly infection is also reported from blood transfusion and organ transplantation (2).

Acute toxoplasmosis can be asymptomatic and self-limiting in humans whose immune systems are intact. However, in immunocompromised patients, such as people with AIDS (acquired immune

1 Internal Medicine Department, Port Moresby General Hospital, Free Mail Bag, Boroko, National Capital District 111, Papua New Guinea

2 Present address: Disease Control Branch, National Department of Health, PO Box 807, Waigani, National Capital District 131, Papua New Guinea
lucyninmongojohn@gmail.com

3 School of Medicine and Dentistry at Cairns Clinical School, James Cook University and Cairns Base Hospital, PO Box 6811, Cairns, Queensland 4870, Australia

4 National Department of Health, PO Box 807, Waigani, National Capital District 131, Papua New Guinea

5 National Serology Reference Laboratory, Level 4, Healy Building, St Vincents Hospital, 41 Victoria Parade, Fitzroy, Victoria 3065, Australia

deficiency syndrome) and those receiving chemotherapy or immunosuppressive therapy, the infection may reactivate. It presents as lymphadenopathy and other non-specific symptoms such as fever, headache and malaise. Almost 95% of susceptible AIDS patients develop toxoplasma encephalitis when the CD4 count falls below 100 cells/mm^3, which can be rapidly fatal if not recognized and treated early (2). Toxoplasmosis is the most common opportunistic infection (OI) in AIDS patients in developed countries (3).

Previous studies done in Papua New Guinea (PNG) in the general population estimated the prevalence rate of toxoplasmosis at 14-32% (4) and 18% in an antenatal population (5). In other countries the seroprevalence rate varies considerably (6-8), from 3% in Thailand and 15% in the USA to 59% in Malaysia. Falusi and colleagues in 2002 (7) showed that there is a 30% greater risk of patients with HIV (human immunodeficiency virus) developing serious OIs such as toxoplasma encephalitis when their CD4 count falls below 100 cells/mm^3. There is currently very little information on the prevalence of anti-toxoplasma antibodies among the HIV-infected and AIDS patients in PNG's population.

This study aimed to determine the prevalence of toxoplasmosis and to ascertain whether there is indeed a difference in infection rate between HIV-positive patients and HIV-negative blood donors. It also examined various sociodemographic factors that could be linked to the infection in the community. Results from this study will provide relevant baseline data for PNG.

Materials and Methods

Population

All study participants were recruited from March 2003 to March 2005 at the Port Moresby General Hospital's Sexually Transmitted Infections Clinic, medical wards and blood bank service centre. There were 181 HIV/AIDS patients recruited from Heduru Clinic and the medical wards and 120 normal healthy blood donors. No inclusion and/or exclusion criteria were used and all were adults using these facilities during the study period.

Approval from the University of Papua New Guinea's Medical Research Advisory Committee as well as individual informed consent was obtained for the study.

Questionnaire

The proforma questionnaire was pretested on volunteers and found to be valid. The interviews were done by the principal author for every subject to reduce inter-observer error. The main sociodemographic factors looked at were ethnicity, exposure to domestic cats, meat diet, educational level and length of HIV infection in HIV-positive participants (Figure 1).

Toxoplasma gondii serology tests

A specimen of 10 ml venous blood was allowed to clot and centrifuged. The supernatant was separated as serum and stored at −20°C until it was transported on dry ice to the National Reference Laboratory in Melbourne, Australia.

The enzyme-linked immunoassay was used for the detection of IgG or IgM *Toxoplasma gondii*-specific antibodies, ETI – TOXOK – G PLUS and ETI – TOXOK – M REVERSE PLUS (DiaSorin, Italy). The sample was considered positive when antibody titres were >15 IU/ml and considered negative or poorly reactive if titres were ≤15 IU/ml. Ambiguous results or readings at or about 10% below or above the cut-off point were retested again for verification.

Statistical analysis

Chi-squared tests were used in this study. Some variables with a p value of less than 0.1 were retested again using a logistic regression model to adjust for confounding. A p value of less than 0.05 and odds ratio with 95% confidence interval (95% CI) not including 1 were considered significant.

The Epi Info version 3.2 software, Feb 2004 and SPSS version 10 were used for statistical analysis.

Results

There were 301 participants in the study, of whom 191 were males and 110 females. Their ages ranged from 15 to 59 years with a mean of 32 years. Of the group studied, 181 were positive and 120 were negative for HIV. Over half (53%) of the study population

SERO-PREVALENCE OF TOXOPLASMOSIS IN AIDS PATIENTS AT HIV CLINIC OR ADMITTED TO MEDICAL WARDS AND HEALTHY BLOOD DONORS AT PORT MORESBY GENERAL HOSPITAL, PNG, July 2003-March 2004.

PSN - ☐ ☐ ☐

Name: Surname_____ Given Name _____

Age. (Years) _____

Sex. M ☐ F ☐ Date of Birth ……/……/……

Place of Origin: Village _____ District _____ Province _____

Current Address: _____

Date of Admission…/…/… Date of Discharge. …/…. /… Other Remarks:

Able to read/write Y ☐ N ☐ If yes, indicate level of education _____

Cat as a Pet Y ☐ N ☐ If yes, for how long? _____

Eat raw or half cooked meat Y ☐ N ☐

For how long do you think you have been infected with HIV/AIDS? _____
(<1yr, 1-5yrs, 6-10yrs or > 10yrs)

Laboratory tests:

HIV antibody: (Pos/Neg) _____
Anti-Toxoplasma antibody (Reactive/Non-reactive) IgG_____ IgM _____

Figure 1. The questionnaire proforma used during the interviews.

was from the Southern Region; 34% were highlanders and others originated from both Momase and New Guinea Islands regions.

Anti-*Toxoplasma gondii* IgG antibodies were detected in 159 (53%) of all those recruited. In Figure 2 the seroprevalence in HIV-infected participants was 108 (60%) compared to 49 (41%) in the HIV-negative group ($p = 0.001$).

Exposure to domestic cats was looked at: 34/52 (65%) of those exposed had *T. gondii* IgG antibodies; by comparison, of those who were never exposed, 123/249 (49%) were IgG positive, as illustrated in Figure 3.

Table 1 shows that the rate of infection was higher in highlanders than combined coastals, with 69/103 (67%) and 88/198 (44%) respectively, and a p value of 0.0002.

Other sociodemographic and disease variables studied such as meat diet, educational levels and length of HIV infection did not demonstrate any correlation (Table 2).

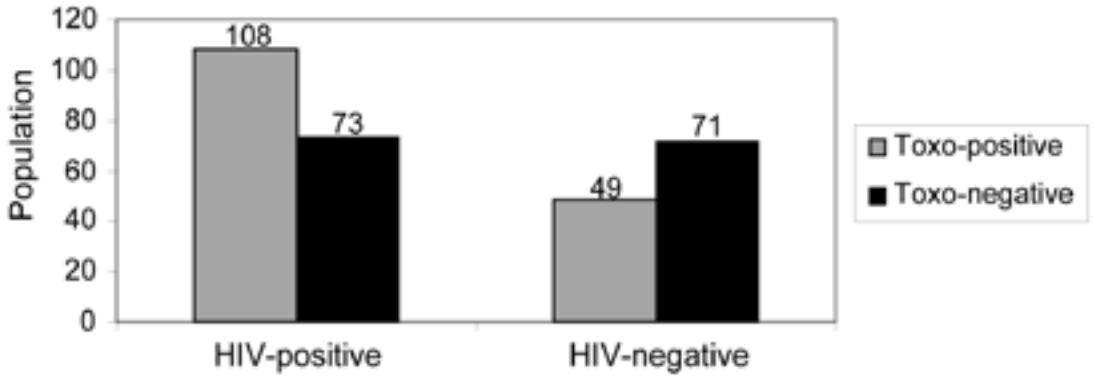


Figure 2. HIV status and presence of IgG toxoplasma antibodies.

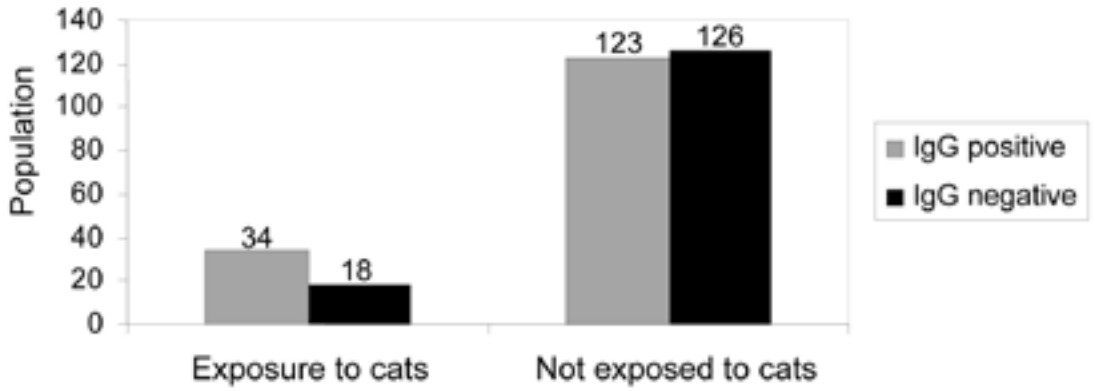


Figure 3. Exposure to cats and presence of toxoplasma IgG antibodies.

TABLE 1

REGIONAL BACKGROUND AS A RISK FACTOR FOR TOXOPLASMA INFECTION (N = 301)

Region of origin	IgG		Odds ratio (95% CI)	p value
	Positive	Negative		
Highlands	69	34		
Coast	88	110	2.54 (1.50-4.30)	0.0002

CI = confidence interval

TABLE 2

SOCIODEMOGRAPHIC FACTORS SHOWING LACK OF ASSOCIATION WITH *TOXOPLASMA GONDII* INFECTION

Variables	OR	95% CI	p value
Length of HIV infection since diagnosis:			
0-5 years	1.39	0.35-5.90	0.61
>5-10 years	1.47	0.34-6.63	0.56
>10 years	0.67	0.02-13.26	0.76
Educational level	1.37	0.74-2.53	0.28
Meat diet	1.26	0.45-3.51	0.60

OR = odds ratio
CI = confidence interval
HIV = human immunodeficiency virus

Discussion

This study showed an overall toxoplasma seroprevalence rate of 53%, one of the highest in the Asia-Pacific Region. Toxoplasma infection is relatively common in the population and HIV-infected subjects are twice as likely to have antibodies. On bivariate analysis, the relationship between HIV status and toxoplasma positivity proved to be significant (odds ratio 2.14, 95% CI 1.30-3.53, p = 0.001). The strong association implies a greater risk in HIV-positive subjects that is independent of other factors.

A similar study in Thailand (6) in the general population showed 3% seroprevalence. In the United States of America (7) they reported a seroprevalence rate of 15%, whereas in some parts of Europe it is 50%. San-Andrés and colleagues in Spain (8) demonstrated a slightly higher frequency at 30% than the rest of continental Europe with their study population of 1115 HIV-positive patients. That study showed a direct relationship of toxoplasma infection with declining CD4 cell numbers. In Nigeria (9) a comparable study into the seroprevalence found 30% in a control group and 54% in an HIV-positive group.

Our study also confirms that the rate is not influenced by the length of HIV infection (p = 0.56). However, the incidence of symptomatic OIs such as toxoplasma encephalitis can serve as a reliable proxy for the measure of advanced HIV and its management in the community (7,8). We are in agreement with San-Andrés and colleagues (8) in this case since overt OIs are directly related to the decline in CD4 T lymphocyte counts. Effective anti-retroviral therapy (ART) has been shown to reduce the incidence and severity of overt OIs (7,8) .

The seroprevalence of anti-toxoplasma IgG antibody in the 'cat exposed' subjects was 65% compared to 49% in those who were not exposed (X^2 = 3.79 with Yates correction, relative risk 1.32, 95% CI 1.05-1.67, p = 0.05). This suggests a strong association. Bivariate analysis of this study also shows that exposure to domestic cats is an independent risk factor for acquiring the infection. This contradicts the report by Wallace and colleagues (10), who reported that 1/13 HIV-infected people seroconverted with a known pet history. We suggest that this difference may be due to the different populations studied as well as the different attitudes to domestic cats. It is worth noting that HIV-positive but toxoplasma-negative subjects will need to avoid cats or handling cat's waste as a precaution. What is surprising is the high prevalence (41%) of toxoplasma infection among HIV-negative blood donors. The low overall number of people with a history of exposure to cats raises the possibility that there may be some other, as yet undefined, means of infection in PNG.

There was a tendency towards more highlanders than other ethnic groups to acquire toxoplasma antibodies (Table 1). This finding is consistent with the increased prevalence in antenatal mothers from the highlands region reported by Klufio et al. (5). The 'highlander' factor may be multifactorial, such as their dietary habits, behavioural patterns and genetics, which could be evaluated in further studies.

The limitations of this study include the inability of our laboratories to do CD4 counts at the time of the study. Historical information on length of HIV infection is not as sensitive as that of CD4 or viral load counts. Personal observations of cats as domestic pets in PNG indicate that they are not as pampered as in western societies and are normally allowed a free range. This study did not explore this further.

In PNG, where there are many competing priorities in health care, provision of ART will mainly depend on donor funding for many years to come. It is, therefore, necessary to be aware of the many presentations of OIs such as congenital toxoplasmosis, toxoplasma encephalitis, chorioretinitis and *Pneumocystis jirovecii* pneumonia. We need to strengthen our laboratory's ability to provide diagnostic tests and ensure that we have a reliable stock of drugs such as cotrimoxazole and ART to treat people living with HIV.

What this study has highlighted is the potential with which OIs will be presenting to the clinician. This is made more likely by the uncertainty of external funding for ART and the ongoing HIV epidemic in PNG. Some of these OIs such as *Pneumocystis jirovecii* pneumonia and toxoplasma encephalitis can be treated with cotrimoxazole for both clinical treatment and prophylaxis. It is certainly an attractive option to 'kill two birds with one stone'. However, it may not be as simple as 'cotrimoxazole' with the huge challenges for all stakeholders in the general fight against HIV/AIDS. What is certain though is that more emphasis is needed on basic hygiene and sanitation and healthier lifestyle choices for our people.

ACKNOWLEDGEMENTS

We thank the National HIV/AIDS Support Project (NHASP) for funding this study and Dr G. Tau and colleagues and nurses at Heduru Clinic and Port Moresby General Hospital for their assistance. We also thank Dr G. Gende for his encouragement.

REFERENCES

1 **Brooks GF, Butel JS, Ornston LN, eds.** Jawetz, Melnick and Adelberg's Medical Microbiology. Nineteenth edition. London: Appleton & Lange, 1991:353-355.

2 **Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, eds.** Harrison's Principles of Internal Medicine. Sixteenth edition. New York: McGraw-Hill Professional, 2004:1243-1248.

3 **McCabe R, Chirurgi V.** Issues in toxoplasmosis. *Infect Dis Clin North Am* 1993;7:587-604.

4 **Wallace GD, Zigas V, Gajdusek DC.** Toxoplasmosis and cats in New Guinea. *Am J Trop Med Hyg* 1974;23:8-14.

5 **Klufio CA, Delamare O, Amoa AB, Kariwiga G.** The prevalence of toxoplasma antibodies in pregnant patients attending the Port Moresby General Hospital antenatal clinic: a seroepidemiological survey. *PNG Med J* 1993;36:4-9.

6 **Maruyama S, Boonmar S, Morita Y, Sakai T, Tanaka S, Yamaguchi F, Kabeya H, Katsube Y.** Seroprevalence of *Bartonella henselae* and *Toxoplasma gondii* among healthy individuals in Thailand. *J Vet Med Sci* 2000;62:635-637.

7 **Falusi O, French AL, Seaberg EC, Tien PC, Watts DH, Minkoff H, Piessens E, Kovacs A, Anastos K, Cohen MH.** Prevalence and predictors of *Toxoplasma* seropositivity in women with and at risk for human immunodeficiency virus infection. *Clin Infect Dis* 2002;35:1414-1417.

8 **San-Andrés FJ, Rubio R, Castilla J, Pulido F, Palao G, de Pedro I, Costa JR, del Palacio A.** Incidence of acquired immunodeficiency syndrome-associated opportunistic diseases and the effect of treatment on a cohort of 1115 patients infected with human immunodeficiency virus, 1989-1997. *Clin Infect Dis* 2003;36:1177-1185.

9 **Akanmu AS, Osunkalu VO, Ofomah JN, Olowoselu FO.** Pattern of demographic risk factors in the seroprevalence of anti-*Toxoplasma gondii* antibodies in HIV infected patients at the Lagos University Teaching Hospital. *Nig Q J Hosp Med* 2010:20:1-4.

10 **Wallace MR, Rosetti JR, Olsem PE.** Cats and toxoplasmosis risk in HIV-infected adults. *JAMA* 1993;269:76-77.

PNG Med J 2012 Mar-Dec;55(1-4):94-97

Case Report

An unusual case of severe cervicofacial actinomycosis masquerading as pseudosarcomatous tumour of soft tissues of the head

G. Gende[1,2], D.J. Hasola[1], B. Dagam[1], L. Lun[1] and J. Morewaya[3]

Surgery Department and Pathology Department, Port Moresby General Hospital, Papua New Guinea

SUMMARY

An unusual case of severe facial and scalp actinomycosis is described. A Papuan man presented with an ulcerative tumour that was progressively spreading on the left face and scalp. Biopsy reported pseudotumour on two occasions and just granulation tissue once. Non-operative treatment was frustrating until a discharge of sulphur granules led to the diagnosis of actinomycosis. The final diagnosis was made histologically after a careful search. This report highlights the usual and unusual points in the diagnosis and management of a case of actinomycosis.

Case description

A Papuan male aged 39 years presented with a severe ulceronodular lesion covering the left front scalp, left forehead, orbit, cheek and neck, which he had had for 4 years. It started from a small laceration of the scalp skin sustained in a motor vehicle accident. It got infected and he sought treatment for it. It resolved but some months later he noted that a swelling persisted and later increased in size and started to ulcerate. He sought treatment for it but this time it did not go away. It continued to spread relentlessly over the neck, face and scalp. He also complained of moderate to severe pain, which was relieved by paracetamol, codeine, morphine and sometimes with carbamazepine for neuropathic pain.

He did not have any other symptoms. In previous admissions he was treated with steroids but to no avail.

The patient is a policeman by profession and left his work because of the unsightly condition. There was no family history of tuberculosis or leprosy.

On examination the patient was well nourished and not pale or jaundiced. His lesions were quite striking and extended from the left neck, cheek, orbit, forehead and scalp as far as the parietal eminence (Figure 1). The lesion in the neck was from involved lymph nodes. The ulcerations at some places were superficial and others quite deep. The superficial lesions had a serpiginous appearance and were not undermined. There was little pus but a slight serous discharge was noted. No granules were observed during the long period of hospitalization. The bridging skin had ill-defined indurations.

A biopsy of the lesion came back as pseudotumour. A second opinion suggested 'pseudoactinomycotic' features but did not confirm it. Not satisfied with this we started the patient on doxycycline for 3 weeks. The lesions began to subside but after 1 month

1 Surgery Department, Port Moresby General Hospital, Free Mail Bag, Boroko, National Capital District 111, Papua New Guinea

2 g_gende@yahoo.com

3 Pathology Department, Port Moresby General Hospital, Free Mail Bag, Boroko, National Capital District 111, Papua New Guinea

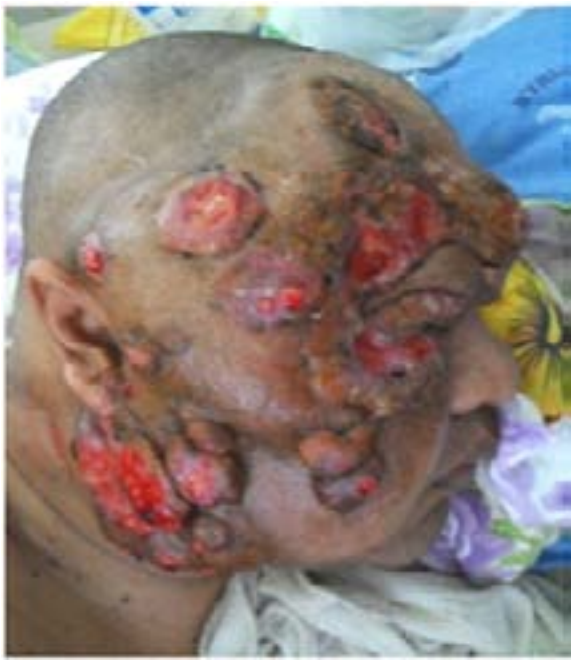


Figure 1. Undiagnosed actinomycosis.

the same lesions recurred again. A second biopsy also reported the same diagnosis of pseudotumour. A pus swab reported local infection with *Proteus mirabilis* susceptible to ceftriaxone. Other tests were normal except a white cell count of 2000/µl; however, the blood film suggested neutrophilia with moderate toxic granulation. A subsequent white blood cell count was normal. Lupus erythematosus (LE) cells were negative, HIV (human immunodeficiency virus) test non-reactive and blood sugar was normal. A short course of tuberculosis (TB) treatment was given for a month based on the endemicity of TB, appearance of slight clear discharge, superficial ulcers and nodes.

The induration softened but the ulcerations were much the same. Another biopsy of deeply situated tissue reported granulation tissue only.

At this point surgical extirpation with reconstruction was contemplated. Since we did not have tissue expanders or free tissue transfer capabilities it was going to involve staged pedicle flaps from neighbouring and distant sites. At that point the surgical registrar excitedly reported seeing what appeared to be sulphur granules. Indeed on closer inspection there were 1 mm granules with a creamy light yellowish color. We had exhausted our three local pathologists' interest but with this new finding we pressed for a further re-examination. This time the characteristic central mass of actinomyces was diagnosed in the biopsied tissue (Figure 2).

The patient was started on high-dose intravenous crystalline penicillin (10-15 million units/day) and thereafter the lesions began to heal. The granulation tissue was initially friable but it began to coalesce with hardening. When the healing stabilized he was maintained on amoxycillin for another 6-12 months (Figure 3). At this stage we are hopeful of a good outcome without the need for surgery. We do not believe that he has evidence of disseminated disease.

Discussion

Actinomycosis has an incidence of 1:300,000. When it occurs it is often cervicofacial but unusual when it mimics a pseudosarcomatous tumour of the head and neck region.

In the experience of one author (GG) 2 cases of cervicofacial actinomycosis were

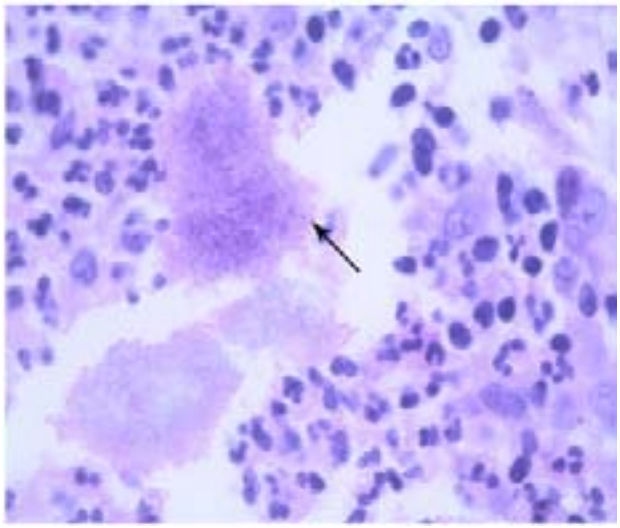


Figure 2. Haematoxylin and eosin stain of an actinomyces microgranule (arrow). The *A. israelii* filaments show as a nondescript mass with heavy stain. It requires special stains to demonstrate the filaments or coccoid forms.

Figure 3. Appearance after 6 months of amoxycillin treatment following an initial course of intravenous crystalline penicillin. (Published with the patient's permission)

seen over a 13-year period and 1 thoracic and 1 foot actinomycosis, the latter two from other colleagues in our hospital. This particular case is interesting in that it is the first such case reported from Papua New Guinea that presented as a pseudosarcoma of the face that is remote from the oral cavity.

The condition is not common and is caused by *Actinomyces israelii*, a Gram-positive filamentous anaerobic bacterium. It is found mainly in the soil and in the oral cavity of humans. The infection is diagnosed by doing a wet mount preparation of the sulphur granule showing micelles and eosinophilic bodies surrounding it. Culture is also done using thioglycolate or brain heart infusion agar but bacterial isolation usually takes up to 2 weeks. Histologically the lesion can be atypical unless sulphur granules are present. Co-infection with other oral bacteria is common. Other related bacteria such as *Actinomadura madurae* and *Streptomyces* species can cause mycetoma, a chronic infection of the

foot. *Nocardia* species are also related to actinomyces and cause infection of the lung; they do not exude sulphur granules.

Cervicofacial actinomycosis occurs in 50%, with lesions in the lungs in 20%, abdominopelvic region in 20% and other sites in 10%. Reports of other intriguing sites (1) such as pericardium, inferior vena cava syndrome and cholecystitis make interesting reading. It was even said to mimic a desmoid tumour of the chin (2).

Actinomycosis presents with a poorly defined hard swelling that can soften into abscesses and burst forming sinuses. The lesions are usually painless and can spread into contiguous structures. The discharge of sulphur granules usually suggests the diagnosis. These granules can vary from 1 to 2 mm in size; the colour is variable and may be yellow or cream or appear greenish.

It took 24 months to diagnose our patient as he meandered from one doctor to another. A Chinese report (3) cited 9 cases and an average of 13.1 months' delay in diagnosis (range 2-36 months), with 8 cures and 1 death.

It must be recognized that not all chronic swellings are cancers. Likewise, not all chronic infections with sinuses are tuberculosis. Though an uncommon disease, actinomycosis does mimic anything. The prolonged suffering and hospitalization that may occur, as in this case, make it necessary for the doctor to diagnose and treat the disease quickly.

REFERENCES

1 **Acevedo F, Baudrand R, Letelier LM, Gaete P.** Actinomycosis: a great pretender. Case reports of unusual presentations and a review of the literature. *Int J Infect Dis* 2008;12:358-362.

2 **Pant R, Marshall TL, Crosher RE.** Facial actinomycosis mimicking a desmoid tumour: case report. *Br J Oral Maxillofac Surg* 2008;46:391-393.

3 **Wang L, Liu ZY, Wang AX.** A clinical analysis of 9 cases of actinomycosis. [Ch] *Zhonghua Nei Ke Za Zhi* 2007;46:389-391.

List of Medical Research Projects in Papua New Guinea

Approved or Noted

By the Medical Research Advisory Committee in 2011

Diversity of disease and colonisation strains of *Streptococcus pneumoniae* in Papua New Guinea
Ms Celestine Aho, Prof. Gerd Pluschke, Dr Andrew Greenhill, A/Prof. Deborah Lehmann (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Does *Plasmodium vivax* cytoadhere in the brain?
Dr Anna Rosanas-Urgell (Papua New Guinea Institute of Medical Research, PO Box 378, Madang, Madang Province 511, Papua New Guinea)

A study of safety and immunogenicity of 10-valent and 13-valent pneumococcal conjugate vaccines to inform policy regarding pneumococcal vaccination in Papua New Guinean children
Dr William Pomat, Dr Andrew Greenhill, Prof. Peter Siba, A/Prof. Deborah Lehmann (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Development of molecular surveillance tools for the monitoring of cholera outbreaks and analysis of the factors that influence cholera transmission
Dr Paul Horwood, Dr Andrew Greenhill, Mr Aisak Pue, Dr Hebe Gouda (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

The characterisation of *Lactobacillus* biota and its role in human gut function in Papua New Guinea
Dr Andrew Greenhill, Prof. Peter Siba, Dr Jens Walter (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Population genomics of *Plasmodium vivax* in Papua New Guinea
Prof. Peter Siba, Dr Inoni Betuela, Dr Ivo Mueller, Prof. John Reeder and Dr Alyssa Barry (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Splenic volume changes in Papua New Guinean children with malarial anaemia
Dr Moses Laman, Dr Laurens Manning, Dr Ivo Mueller and Dr Timothy M. E. Davis (Papua New Guinea Institute of Medical Research, PO Box 378, Madang, Madang Province 511, Papua New Guinea)

Development and implementation of a Multiplex Real-Time PCR assay for the detection of viral respiratory pathogens
Dr Paul Horwood (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Surveillance and characterisation of avian influenza viruses in Papua New Guinean poultry
Dr Paul Horwood, Prof. Richard Webby, Dr Nime Kapo (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Malarial transmission potential of *Anopheles punctulatus* species complex
Dr Lisa Reimer and Prof. Peter Siba (Papua New Guinea Institute of Medical Research, PO Box 378, Madang, Madang Province 511, Papua New Guinea)

Population biology and epidemiology of two newly identified human malaria species
Dr Inoni Betuela, Dr Ivo Mueller, Dr Celine Barnadas and Dr Alyssa Barry (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

The genetic epidemiology of severe malaria in PNG children: supplementary protocol on

the host immune response to severe malaria

Dr Ivo Mueller, Dr James Beeson, Dr Louis Schofield, Dr Stephen Rogerson, Dr Laurens Manning, Dr Moses Laman, Dr Celine Barnadas and Dr Alyssa Barry (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Evolution of *Plasmodium vivax* drug resistance in Papua New Guinea

Dr Celine Barnadas, Dr Ivo Mueller, Prof. Timothy Davis and Prof. Peter Siba (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Molecular investigation into the importance of arboviruses and rickettsias in the presentation of febrile illness in Papua New Guinea

Dr Paul Horwood (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Kuru field studies in Papua New Guinea 2010-2015: concluding phase of a study ongoing since 1962

Prof. John Collinge, Prof. Michael Alpers and Prof. Peter Siba (MRC Prion Unit, University College London, The National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, England, United Kingdom)

Identification of pathogens that cause diarrhoea in Papua New Guinean populations (IPCD study): a pilot study

Dr Andrew Greenhill, Dr Masahiro Umezaki, Dr Paul Horwood and Mr Tadayuki Iwase (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

What is the epidemic overlap of HSV-2 and HIV-1 in the highlands of Papua New Guinea?

Dr Claire Ryan, Prof. Peter Siba, A/ Prof. Andrew Vallely, Dr Zure Kombati, Mr Cassey Simbiken, Prof. John Kaldor and Dr Petronia Kaima (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Human papillomavirus (HPV) infection among women attending sexual health clinics in Mt Hagen, Goroka and Port Moresby, Papua New Guinea

Dr Andrew Vallely, Dr Claire Ryan, Prof. Peter Siba and Prof. John Kaldor (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Molecular epidemiology of HIV-1 subtypes in the highlands of Papua New Guinea

Ms Janet Gare, Mr Tawarot Kurumop, Dr Justin Pulford, Dr Andrew Vallely, Dr Greg Law and Ms Serah Kurumop (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

The application of geographic information systems for the public health management of cholera in Papua New Guinea

Mr Elias Namosha (Papua New Guinea Institute of Medical Research, PO Box 7981, Boroko, NCD 111, Papua New Guinea)

Impact of vector control on human immunity to malaria and genetic complexity of *P. falciparum* and *P. vivax* in two holoendemic areas of Papua New Guinea (ICEMR) [DMID#10-0035]

Dr James Kazura and Prof. Peter Siba (Centre for Global Health & Diseases, Case Western Reserve University School of Medicine, 10900 Euclid Avenue (BRB Bldg, Room 423), Cleveland, OH 44106-7286, USA)

Feasibility and acceptability of insecticide-treated plastic sheeting (ITPS) for vector control in Papua New Guinea

Dr Justin Pulford and Dr Manuel Hetzel (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Quality of anti-malarial drugs at the provider level in Papua New Guinea

Ms Nancy Bala and Dr Manuel Hetzel (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Benefits of iron supplementation in Papua New Guinean children with malarial and non-malarial anaemia: a sub-study of Mugil Clinical Trial II

Dr Moses Laman, Dr Brioni Moore and Dr Anna Rosanas-Urgell (Papua New Guinea Institute of Medical Research, PO Box 378, Madang, Madang Province 511, Papua New

Guinea)

Women's experience of pregnancy and childbirth in Unggai-Bena District, Eastern Highlands Province, Papua New Guinea
Ms Lisa Vallely, Dr Angela Kelly, Ms Voletta Fiya, Ms Primrose Homeihombo, Dr Andrea Whittaker, Dr Andrew Vallely and Prof. John Kaldor (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

An investigation into health workers' understanding of syphilis testing in Papua New Guinea
Dr Claire Ryan, Mr Tawarot Kurumop, Dr Justin Pulford, Dr Andrew Vallely, Dr Greg Law and Ms Serah Kurumop (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Study to determine the risk factors for postpartum upper genital tract infections and to derive a simplified case management for these infections, and study of the impact of maternal chlamydial infection during labour on neonatal health [Request to send specimens to collaborators in Australia]
Dr Megan Passey (University Centre for Rural Health, PO Box 3074, Lismore, NSW 2480, Australia)

The aetiology of acute lower respiratory tract infection and meningitis in hospitalized children from the Eastern Highlands Province, Papua New Guinea
Dr Christopher Blyth and Dr Andrew Greenhill (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Knowledge, attitudes and practices on lymphatic filariasis in the East Sepik Province, Papua New Guinea
Ms Sarah E. Krier (Papua New Guinea Institute of Medical Research, PO Box 378, Madang, Madang Province 511, Papua New Guinea)

Morbidity self-management of lymphatic filariasis in Papua New Guinea
Ms Robin T. Klar (Papua New Guinea Institute of Medical Research, PO Box 378, Madang, Madang Province 511, Papua New Guinea)

Spontaneous and induced abortion – a mixed-methods hospital-based study from 2 sites in Papua New Guinea
Ms Lisa Vallely (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Fetal immunity to malaria
Dr Christopher King and Prof. Peter Siba (Centre for Global Health & Diseases, Case Western Reserve University School of Medicine, 10900 Euclid Avenue (BRB Bldg, Room 423), Cleveland, OH 44106-7286, USA)

Cervical cancer screening using visual inspection with acetic acid (VIA) and its relationship to cervical cytology and high-risk human papillomavirus (HR-HPV) infection in women attending Well Women Clinics in Papua New Guinea
Dr Andrew Vallely (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Sik bilong bel study: meanings and beliefs of cervical cancer, its causation, prevention and treatment in Papua New Guinea
Dr Andrew Vallely (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Improving maternal health care in Papua New Guinea: capacity building in midwifery education and practice
Dr Caroline Homer (WHO Collaborating Centre for Nursing, Midwifery and Health, University of Technology Sydney, PO Box 123, Broadway, NSW 2007, Australia)

Malaria tracking results continuously (TRaC) study evaluation of net use and treatment-seeking behaviours among caregivers of children younger than age 5 in Papua New Guinea
Ms Barbara Kepa (PSI-PNG, PO Box 327, Port Moresby, National Capital District 121, Papua New Guinea)

Evaluating the ART reporting component of the (STI, HIV/AIDS) Surveillance Unit at the National Department of Health
Ms Charlotte Polly (School of Medicine and Health Sciences, University of Papua New Guinea, PO Box 5623, Boroko, National

Capital District 111, Papua New Guinea)

Preliminary clinical dose-finding and safety evaluation of a new antivenom for the treatment of Papuan taipan (*Oxyuranus scutellatus*) envenoming in Papua New Guinea

Dr David Williams (AVRU-UPNG Snakebite Research Project, School of Medicine and Health Sciences, University of Papua New Guinea, PO Box 5623, Boroko, National Capital District 111, Papua New Guinea)

Scoping low vision and rehabilitation services in Papua New Guinea

Ms Eileen Tugum (PNG Eye Care, PO Box 913, Boroko, National Capital District 111, Papua New Guinea)

Improving methods to measure mortality by cause in Papua New Guinea

Dr Ian Riley and Dr Hebe Gouda (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea)

Optimization of mass drug administration with existing drug regimens for lymphatic filariasis: efficacy of ongoing treatment programs in Papua New Guinea

Dr Christopher King and Prof. Peter Siba (Centre for Global Health & Diseases, Case Western Reserve University School of Medicine, Wolstein Research Building, Room 4-125, 2103 Cornwell Road, Cleveland, Ohio 44106-7286, USA)

Pharmacodynamics and pharmacokinetics studies for triple drug therapy to treat human lymphatic filariasis (LF): diethylcarbamazine (DEC), albendazole (ALB) and ivermectin (IVM)

Dr Christopher King and Prof. Peter Siba (Centre for Global Health & Diseases, Case Western Reserve University School of Medicine, Wolstein Research Building, Room 4-125, 2103 Cornwell Road, Cleveland, Ohio 44106-7286, USA)

Strengthen control of vector-borne diseases to lessen the impact of climatic change in Papua New Guinea – project evaluation plan

Dr Manuel Hetzel and Dr Inoni Betuela (Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, 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 2011.

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, NCD 131).

MEDLARS BIBLIOGRAPHY

PUBLICATIONS OF RELEVANCE TO PAPUA NEW GUINEA AND MELANESIA

Bibliographic Citation List generated from MEDLARS

1 **Allibone R, Cronin SJ, Charley DT, Neall VE, Stewart RB, Oppenheimer C.**
Dental fluorosis linked to degassing of Ambrym volcano, Vanuatu: a novel exposure pathway.
Environ Geochem Health 2012 Apr;34(2):155-170.

Ambrym in Vanuatu is a persistently degassing island volcano whose inhabitants harvest rainwater for their potable water needs. The findings from this study indicate that dental fluorosis is prevalent in the population due to fluoride contamination of rainwater by the volcanic plume. A dental survey was undertaken of 835 children aged 6-18 years using the Dean's Index of Fluorosis. Prevalence of dental fluorosis was found to be 96% in the target area of West Ambrym, 71% in North Ambrym, and 61% in Southeast Ambrym. This spatial distribution appears to reflect the prevailing winds and rainfall patterns on the island. Severe cases were predominantly in West Ambrym, the most arid part of the island, and the most commonly affected by the volcanic plume. Over 50 km downwind, on a portion of Malakula Island, the dental fluorosis prevalence was 85%, with 36% prevalence on Tongoa Island, an area rarely affected by volcanic emissions. Drinking water samples from West Ambrym contained fluoride levels from 0.7 to 9.5 ppm F (average 4.2 ppm F, n = 158) with 99% exceeding the recommended concentration of 1.0 ppm F. The pathway of fluoride-enriched rainwater impacting upon human health as identified in this study has not previously been recognised in the aetiology of fluorosis. This is an important consideration for populations in the vicinity of degassing volcanoes, particularly where rainwater comprises the primary potable water supply for humans or animals.

2 **Aruhuri B, Tarivonda L, Tenet V, Sinha R, Snijders PJ, Clifford G, Pang J, McAdam M, Meijer CJ, Frazer IH, Franceschi S.**
Prevalence of cervical human papillomavirus (HPV) infection in Vanuatu.
Cancer Prev Res (Phila) 2012 May;5(5):746-753.

To provide information on human papillomavirus (HPV) prevalence and the distribution of individual HPV types in Pacific Islands, we conducted a population-based survey in Vanuatu, South Pacific. Nine hundred and eighty-seven women between 18 and 64 years of age were included. GP5(+)/6(+)-mediated PCR assay was used for HPV testing. The prevalence of 44 HPV types was 28.4% corresponding to an age (world)-standardized prevalence of 25.0% [95% confidence interval (CI), 21.9%-28.0%]. The prevalence of high-risk (HR) HPV types was 21.7% (age-standardized prevalence of 19.2%; 95% CI, 16.4%-22.0%). Among 840 women with adequate cytologic results, 13.6% showed cervical abnormalities, including 3.6% with high-grade squamous intraepithelial lesions (HSIL) and 0.8% with invasive cervical carcinoma. HPV prevalence declined from 46.1% in women aged ≤21 to 15.3% in those ≥45 years. Being single was significantly associated with HPV positivity. HR HPV findings by PCR assay and hybrid capture 2 (HC2; conducted in Vanuatu) were moderately correlated (κ test = 0.59). The positive predictive values of HR HPV positivity for HSIL or worse were 27.6% for PCR and 35.2% for HC2 among women aged ≥30. Nearly half of screening-positive women could not be reevaluated mainly on account of the difficulty to trace back women. The availability of a rapid HPV testing method that allows see-and-treat approaches at the same visit would be, therefore, essential. On account of their high cumulative burden of cervical lesions, also women older than 40 years should be included in at least the first screening round in unscreened populations.

3 **Asante A, Roberts G, Hall J.**
A review of health leadership and management capacity in the Solomon Islands.
Pac Health Dialog 2012 Apr;18(1):166-177.

ACCESS AND UTILISATION OF HEALTH CARE: The armed conflict that engulfed the Solomon Islands between 1998 and 2003 significantly disrupted the provision of health care especially in rural and remote areas. There is one doctor for 3,300 people and approximately 13 nurses and midwives for 10,000 people. Despite limitations 87% of people seek health care when sick. FINANCING THE HEALTH SYSTEM: The SIG placed a series of reservations on ministerial goods and services budgets that effectively reduced the budget by 33%, severely impacting provincial budgets and resulting in acquired debts. Shortfalls have been addressed by allocating Health Sector Support Program funds to the provinces to allow services to continue, a strategy that will likely recur, but by which donor support replaces government provision. Provincial health accountants have received training in MYOB in 2009 but acquittal systems require higher level accounting skills for reports to be submitted on time to permit the release of subsequent funding tranches. HUMAN RESOURCES FOR HEALTH: The shortage of doctors and specialists is a key challenge. As at December 2010, there were a total of 2,728 health workers in the public sector in Solomon Islands. Staff costs consume on average 55% of provincial health grants. Filled Public Service Division staff establishments and budgetary reservations have reduced the ability to meet the salary and wage costs of new graduates. Solomon Islands is currently negotiating to assist Vanuatu in filling its nursing staff vacancies with its surplus. The return of 75 Cuban trained medical officers from 2013 presents the management challenge of accessing budget provisions for so many new positions and in funding the infrastructure needed to house, equip and maintain them in service. HEALTH MANAGEMENT STRUCTURE: Provincial health managers are operationally responsive to local needs, managerially responsible to provincial governments, while being concerned with adherence to central MHMS policy and to Ministry of Finance and Public Service Division

regulations. The delineation of central and provincial health authorities' responsibilities requires guidelines in a changing system, where both population-based and targeted vertical programs are implemented at local levels. NUMBER AND DISTRIBUTION OF MANAGERS: Nine of the 10 positions of Provincial Health Director have experienced high turnover, which reportedly occurs without adequate handover to incoming appointees, most of whom are recent clinical graduates. Health services in the Honiara urban area are provided through the Honiara City Council. Church health services are staffed by government employees. COMPETENCE OF DISTRICT HEALTH MANAGERS: Management skills are reportedly weak at the provincial level. The Regional Assistance Mission to Solomon Islands provides governance training inputs to provincial government staff. Provincial health departments have limited financial and human resource management capacity. They also have clinical backgrounds and no training in public health planning or health services management, other than that provided by donors, the Regional Assistance Mission itself and the MHMS. MANAGEMENT WORKING ENVIRONMENT: Provincial health directors have limited control over health staff. Little supportive supervision in management is provided to new provincial health directors. No performance management systems are in place to ensure that staff are properly assessed and supported to do their best. Large numbers of non-government organisations working at the provincial level in youth and women's programs require coordination by provincial health directors to avoid duplication or implementation of programs that will require ongoing funding, but this is not done. FUNCTIONING OF MANAGEMENT SUPPORT SYSTEMS: Management support systems for budgeting and finance, management information and procurement and supply do not function adequately to support provincial health directors to manage effectively. THE SOCIO-CULTURAL CONTEXT: Socio-cultural issues such as favouritism based on kinship, discrimination against women and the big-man culture have implications for effective management and strong health leadership. These cultural features create situations where a manager may be reluctant to discipline a member of their clan, or where a person with cultural influence may be able to distort systems.

4 **Asante AD, Negin J, Hall J, Dewdney J, Zwi AB.**
Analysis of policy implications and challenges of the Cuban health assistance program related to human resources for health in the Pacific.
Hum Resour Health 2012 May 6;10(1):10.

BACKGROUND: Cuba has extended its medical cooperation to Pacific Island Countries (PICs) by supplying doctors to boost service delivery and offering scholarships for Pacific Islanders to study medicine in Cuba. Given the small populations of PICs, the Cuban engagement could prove particularly significant for health systems development in the region. This paper reviews the magnitude and form of Cuban medical cooperation in the Pacific and analyses its implications for health policy, human resource capacity and overall development assistance for health in the region. METHODS: We reviewed both published and grey literature on health workforce in the Pacific including health workforce plans and human resource policy documents. Further information was gathered through discussions with key stakeholders involved in health workforce development in the region. RESULTS: Cuba formalised its relationship with PICs in September 2008 following the first Cuba-Pacific Islands ministerial meeting. Some 33 Cuban health personnel work in Pacific Island Countries and 177 Pacific island students are studying medicine in Cuba in 2010 with the most extensive engagement in Kiribati, the Solomon Islands, Tuvalu and Vanuatu. The cost of the Cuban medical cooperation to PICs comes in the form of countries providing benefits and paying allowances to in-country Cuban health workers and return airfares for their students in Cuba. This has been seen by some PICs as a cheaper alternative to training doctors in other countries. CONCLUSIONS: The Cuban engagement with PICs, while smaller than engagement with other countries, presents several opportunities and challenges for health system strengthening in the region. In particular, it allows PICs to increase their health workforce numbers at relatively low cost and extends delivery of health services to remote areas. A key challenge is that with the potential increase in the number of medical doctors, once the local students return from Cuba, some PICs may face substantial rises in salary expenditure which could significantly strain already stretched government budgets. Finally, the Cuban engagement in the Pacific has implications for the wider geo-political and health sector support environment as the relatively few major bilateral donors, notably Australia (through AusAID) and New Zealand (through NZAID), and multilaterals such as the World Bank will need to accommodate an additional player with whom existing links are limited.

5 **Atkinson JA, Johnson ML, Wijesinghe R, Bobogare A, Losi L, O'Sullivan M, Yamaguchi Y, Kenilorea G, Vallely A, Cheng Q, Ebringer A, Bain L, Gray K, Harris I, Whittaker M, Reid H, Clements A, Shanks D.**
Operational research to inform a sub-national surveillance intervention for malaria elimination in Solomon Islands.
Malar J 2012 Mar 30;11:101. doi: 10.1186/1475-2875-11-101.

BACKGROUND: Successful reduction of malaria transmission to very low levels has made Isabel Province, Solomon Islands, a target for early elimination by 2014. High malaria transmission in neighbouring provinces and the potential for local asymptomatic infections to cause malaria resurgence highlights the need for sub-national tailoring of surveillance interventions. This study contributes to a situational analysis of malaria in Isabel Province to inform an appropriate surveillance intervention. METHODS: A mixed method study was carried out in Isabel Province in late 2009 and early 2010. The quantitative component was a population-based prevalence survey of 8,554 people from 129 villages, which were selected using a spatially stratified sampling approach to achieve uniform geographical coverage of populated areas. Diagnosis was initially based on Giemsa-stained blood slides followed by molecular analysis using polymerase chain reaction (PCR). Local perceptions and practices related to management of fever and treatment-seeking that would impact a surveillance intervention were also explored using qualitative research methods. RESULTS: Approximately 33% (8,554/26,221) of the population of Isabel Province participated in the survey. Only one subject was found to be infected with *Plasmodium falciparum* (*Pf*) (96 parasites/μL) using Giemsa-stained blood films, giving a prevalence

of 0.01%. PCR analysis detected a further 13 cases, giving an estimated malaria prevalence of 0.51%. There was a wide geographical distribution of infected subjects. None reported having travelled outside Isabel Province in the previous three months suggesting low-level indigenous malaria transmission. The qualitative findings provide warning signs that the current community vigilance approach to surveillance will not be sufficient to achieve elimination. In addition, fever severity is being used by individuals as an indicator for malaria and a trigger for timely treatment-seeking and case reporting. In light of the finding of a low prevalence of parasitaemia, the current surveillance system may not be able to detect and prevent malaria resurgence. CONCLUSION: An adaption to the malERA surveillance framework is proposed and recommendations made for a tailored provincial-level surveillance intervention, which will be essential to achieve elimination, and to maintain this status while the rest of the country catches up.

6 **Au L.**
Successes and failures of using the cell phone as a main mode of communication between participants and facilitators from a distance: an innovative method of training rural health facility managers in Papua New Guinea.
Stud Health Technol Inform 2012;182:19-26.

Rural Health Facility Management Training is a training program developed by the National Department of Health in collaboration with AusAID through the office of the Capacity Building Service Centre. The purpose of the training is to train officers-in-charge who did not acquire knowledge and skills of managing a health facility. As part of this study, it is essential to assess whether the cell phone is a better mode of communication between the participants and the facilitators compared with other modes of communication from a distance. The study used the cross-sectional method to collect 160 samples from 12 provinces and the statistical software Stata (version 8) was used to analyse the data. The results showed that mobile coverage is not very effective in most rural areas, though it is efficient and accessible. Furthermore, it is expensive to make a call compared with sending text messages. In spite of the high cost involved, most health managers prefer to use the cell phone compared to normal post, email, or fax. This clearly shows that the mobile phone is a better device for distant learning in rural Papua New Guinea compared to other modes of communication.

7 **Batty KT, Salman S, Moore BR, Benjamin J, Lee ST, Page-Sharp M, Pitus N, Ilett KF, Mueller I, Hombhanje FW, Siba P, Davis TM.**
Artemisinin-naphthoquine combination therapy for uncomplicated pediatric malaria: a pharmacokinetic study.
Antimicrob Agents Chemother 2012 May;56(5):2472-2484. doi: 10.1128/AAC.06250-11. Epub 2012 Feb 13.

Artemisinin-naphthoquine (ART-NQ) is a coformulated antimalarial therapy marketed as a single-dose treatment in Papua New Guinea and other tropical countries. To build on limited knowledge of the pharmacokinetic properties of the components, especially the tetra-aminoquinoline NQ, we studied ART-NQ disposition in Papua New Guinea children aged 5 to 12 years with uncomplicated malaria, comparing a single dose (15 and 6 mg/kg of body weight) administered with water (group 1; n =13), a single dose (22 and 9 mg/kg) with milk (group 2) (n = 17), and two daily doses of 22 and 9 mg/kg with water (group 3; n = 16). The plasma NQ concentration was assayed by high-performance liquid chromatography, and the plasma ART concentration was assayed using liquid chromatography-mass spectrometry. Population-based multicompartment pharmacokinetic models for NQ and ART were developed. NQ disposition was best characterized by a three-compartment model with a mean absorption half-life (t(1/2)) of 1.0 h and predicted median maximum plasma concentrations that ranged as high as 57 μg/liter after the second dose in group 3. The mean NQ elimination t(1/2) was 22.8 days; clearance relative to bioavailability (CL/F) was 1.1 liters/h/kg; and volume at steady state relative to bioavailability (V(ss)/F) was 710 liters/kg. Administration of NQ with fat (8.5 g; 615 kJ) versus water was associated with 25% increased bioavailability. ART disposition was best characterized by a two-compartment model with a mean CL/F (4.1 liters/h/kg) and V/F (21 liters/kg) similar to those of previous studies. There was a 77% reduction in the bioavailability of the second ART dose (group 3). NQ has pharmacokinetic properties that confirm its potential as an artemisinin partner drug for treatment of uncomplicated pediatric malaria.

8 **Bauze AE, Tran LN, Nguyen KH, Firth S, Jimenez-Soto E, Dwyer-Lindgren L, Hodge A, Lopez AD.**
Equity and geography: the case of child mortality in Papua New Guinea.
PLoS One 2012;7(5):e37861. doi: 10.1371/journal.pone.0037861. Epub 2012 May 25.

BACKGROUND: Recent assessments show continued decline in child mortality in Papua New Guinea (PNG), yet complete subnational analyses remain rare. This study aims to estimate under-five mortality in PNG at national and subnational levels to examine the importance of geographical inequities in health outcomes and track progress towards Millennium Development Goal (MDG) 4. METHODOLOGY: We performed retrospective data validation of the Demographic and Health Survey (DHS) 2006 using 2000 Census data, then applied advanced indirect methods to estimate under-five mortality rates between 1976 and 2000. FINDINGS: The DHS 2006 was found to be unreliable. Hence we used the 2000 Census to estimate under-five mortality rates at national and subnational levels. During the period under study, PNG experienced a slow reduction in national under-five mortality from approximately 103 to 78 deaths per 1,000 live births. Subnational analyses revealed significant disparities between rural and urban populations as well as inter- and intra-regional variations. Some of the provinces that performed the best (worst) in terms of under-five mortality included the districts that performed worst (best), with district-level under-five mortality rates correlating strongly with poverty levels and access to services. CONCLUSIONS: The evidence from PNG demonstrates substantial within-province heterogeneity, suggesting that under-five mortality needs to be addressed at subnational levels. This is especially relevant in countries, like PNG, where responsibility for health services is devolved to provinces and districts. This study presents the first comprehensive estimates of under-five mortality at the district level for PNG. The results demonstrate that for countries that rely on few data sources even greater importance must be given to the quality of future population surveys and to the exploration of

alternative options of birth and death surveillance.

9 **Benjamin J, Moore B, Lee ST, Senn M, Griffin S, Lautu D, Salman S, Siba P, Mueller I, Davis TM.**
Artemisinin-naphthoquine combination therapy for uncomplicated pediatric malaria: a tolerability, safety, and preliminary efficacy study.
Antimicrob Agents Chemother 2012 May;56(5):2465-2471. doi: 10.1128/AAC.06248-11. Epub 2012 Feb 13.

Artemisinin-naphthoquine (ART-NQ) is a fixed-dose coformulated antimalarial therapy recommended as a single-dose treatment and marketed in Papua New Guinea among other tropical countries. We conducted a tolerability, safety, and efficacy study of ART-NQ for Papua New Guinean children aged 5 to 12 years with uncomplicated malaria, comparing single-dose ART-NQ (15 and 6 mg/kg of bodyweight) given with water (group 1; n = 15), single-dose ART-NQ (22 and 9 mg/kg) given with milk (group 2; n = 17), or two daily doses of 22 and 9 mg/kg given with water (group 3; n = 16). Of the 48 children (45 with *Plasmodium falciparum* malaria, 2 with *Plasmodium vivax* malaria, and 1 with mixed-species malaria), 2 in group 2 did not attend all follow-up assessments. All regimens were well tolerated, with no serious adverse events. There were no clinically significant changes in pulse, blood pressure, rate-corrected electrocardiographic QT, routine biochemistry/hematology, or hearing after treatment. Fever clearance was prompt. Mean 50% parasite clearance times were 4, 4, and 5 h for groups 1, 2, and 3, respectively. One group 1 patient had PCR-confirmed *P. falciparum* recrudescence at day 23; four had PCR-confirmed *P. falciparum* reinfections on day 28 or 42; and three had *P. vivax* infections detected on day 42. The only recurrent parasitemia in groups 2 and 3 occurred in a group 2 child who developed a *P. vivax* infection on day 42. Day 14 gametocyte positivity levels were 20%, 27%, and 9% in groups 1, 2, and 3, respectively. The lower single ART-NQ dose was associated with relatively frequent recurrence of parasitemia, but the prolonged gametocytemia in all three groups has implications for the transmission of malaria.

10 **Benton D.**
Advocating globally to shape policy and strengthen nursing's influence.
Online J Issues Nurs 2012 Jan 31;17(1):5.

The International Council of Nurses is a federation of national nursing associations that works to enable nurses to speak with one voice so as to influence health policy and advance the profession of nursing. In this article the author highlights how nurses can advocate for the nursing profession by coordinating nursing actions to develop both public and healthcare-service policies. He addresses issues that are common in many parts of the world and provides examples drawn from real-life experiences that illustrate how nurses in El Salvador, Rwanda, Paraguay, Papua New Guinea, and Iran have worked in their countries to coordinate their actions and advocate for public and/or healthcare service policies within their countries. He concludes by noting that all nurses must do their part and use a wide range of opportunities creatively, and with clarity of intent, to improve the profession and the lives of the millions of people who depend upon us.

11 **Betuela I, Bassat Q, Kiniboro B, Robinson LJ, Rosanas-Urgell A, Stanisic D, Siba PM, Alonso PL, Mueller I.**
Tolerability and safety of primaquine in Papua New Guinean children 1 to 10 years of age.
Antimicrob Agents Chemother 2012 Apr;56(4):2146-2149. doi: 10.1128/AAC.05566-11. Epub 2012 Jan 17.

Primaquine is currently the only drug available for radical cure of *Plasmodium vivax* and *P. ovale* liver infection stages, but limited safety data exist for children <10 years of age. Detailed daily assessments of side effects in glucose-6-phosphate dehydrogenase (G6PD)-normal children treated with 14 days of primaquine plus chloroquine (3 days; n = 252) or artesunate (7 days; n = 141) (0.5 mg/kg of body weight) showed that both treatments are well tolerated, do not lead to reductions in hemoglobin levels, and can thus safely be used in children 1 to 10 years of age.

12 **Carter KL, Rao C, Lopez AD, Taylor R.**
Mortality and cause-of-death reporting and analysis systems in seven Pacific Island countries.
BMC Public Health 2012 Jun 13;12:436. doi: 10.1186/1471-2458-12-436.

BACKGROUND: Mortality statistics are essential for population health assessment. Despite limitations in data availability, Pacific Island countries are considered to be in epidemiological transition, with non-communicable diseases increasingly contributing to premature adult mortality. To address rapidly changing health profiles, countries would require mortality statistics from routine death registration given their relatively small population sizes. METHODS: This paper uses a standard analytical framework to examine death registration systems in Fiji, Kiribati, Nauru, Palau, Solomon Islands, Tonga and Vanuatu. RESULTS: In all countries, legislation on death registration exists but does not necessarily reflect current practices. Health departments carry the bulk of responsibility for civil registration functions. Medical cause-of-death certificates are completed for at least hospital deaths in all countries. Overall, significantly more information is available than perceived or used. Use is primarily limited by poor understanding, lack of coordination, limited analytical skills, and insufficient technical resources. CONCLUSION: Across the region, both registration and statistics systems need strengthening to improve the availability, completeness, and quality of data. Close interaction between health staff and local communities provides a good foundation for further improvements in death reporting. System strengthening activities must include a focus on clear assignment of responsibility, provision of appropriate authority to perform assigned tasks, and fostering ownership of processes and data to ensure sustained improvements. These human elements need to be embedded in a culture of data sharing and use. Lessons from this multi-country exercise would be applicable in other regions afflicted with similar issues of availability and quality of vital statistics.

13 **Cassar O, Charavay F, Bassot S, Plancoulaine S, Grangeon JP, Laumond-Barny S, Martin PM, Chanteau S, Gessain A.**
Divergent KSHV/HHV-8 subtype D strains in New Caledonia and Solomon Islands, Melanesia.
J Clin Virol 2012 Mar;53(3):214-218. doi: 10.1016/j.jcv.2011.12.016. Epub 2012 Jan 11.

BACKGROUND: KSHV/HHV-8 is the etiological agent of Kaposi's sarcoma, primary effusion lymphoma and most multicentric Castleman's

disease cases. KSHV exhibits a high genetic variability comprising five genotypes (A-E). Few data are yet available concerning the situation of KSHV, its genetic variability and the associated diseases in Melanesia. OBJECTIVES: We performed a study on 626 native Melanesians from New Caledonia and Vanikoro Island to evaluate KSHV seroprevalence and characterize molecularly the viral strains. STUDY DESIGN: Plasma from 343 males and 283 females (age range: 15-86 years, mean age: 60) were tested for KSHV latent antibodies by an immunofluorescence assay (IFA) using BC-3 cells. DNAs extracted from peripheral blood buffy-coat of KSHV seropositive individuals were amplified to obtain a 737-bp fragment of the ORF-K1 gene. Phylogenetic analyses were then performed. RESULTS: Among 626 samples, 148 were IFA positive (dilution ≥1:80). The overall seroprevalence was 23.6% (25.2% in New Caledonia, 17.5% in Vanikoro). Fifteen (8 men and 7 women, mean age 69 years) out of 148 DNA samples were found PCR positive. All ORF-K1 sequences belonged to KSHV genotype D. A geographic clustering according to the island of origin of KSHV infected persons was clearly observed with sequences from New Caledonia clustering with most Vanuatu strains. CONCLUSIONS: New Caledonia and Vanikoro are endemic for KSHV with a high diversity of genotype D variants. These strains were probably introduced into New Caledonia during multiple waves of migrations of Melanesian and Polynesian individuals that have colonized this archipelago.

14 **Chan CW, Spathis R, Reiff DM, McGrath SE, Garruto RM, Lum JK.**
Diversity of *Plasmodium falciparum* chloroquine resistance transporter (*pfcrt*) exon 2 haplotypes in the Pacific from 1959 to 1979.
PLoS One 2012;7(1):e30213. doi: 10.1371/journal.pone.0030213. Epub 2012 Jan 17.

Nearly one million deaths are attributed to malaria every year. Recent reports of multi-drug treatment failure of falciparum malaria underscore the need to understand the molecular basis of drug resistance. Multiple mutations in the *Plasmodium falciparum* chloroquine resistance transporter (*pfcrt*) are involved in chloroquine resistance, but the evolution of complex haplotypes is not yet well understood. Using over 4,500 archival human serum specimens collected from 19 Pacific populations between 1959 and 1979, the period including and just prior to the appearance of chloroquine treatment failure in the Pacific, we PCR-amplified and sequenced a portion of the *pfcrt* exon 2 from 771 *P. falciparum*-infected individuals to explore the spatial and temporal variation in falciparum malaria prevalence and the evolution of chloroquine resistance. In the Pacific, the prevalence of *P. falciparum* varied considerably across ecological zones. On the island of New Guinea, the decreases in prevalence of *P. falciparum* in coastal, high-transmission areas over time were contrasted by the increase in prevalence during the same period in the highlands, where transmission was intermittent. We found 78 unique *pfcrt* haplotypes consisting of 34 amino acid substitutions and 28 synonymous mutations. More importantly, two *pfcrt* mutations (N75D and K76T) implicated in chloroquine resistance were present in parasites from New Hebrides (now Vanuatu) eight years before the first report of treatment failure. Our results also revealed unexpectedly high levels of genetic diversity in *pfcrt* exon 2 prior to the historical chloroquine resistance selective sweep, particularly in areas where disease burden was relatively low. In the Pacific, parasite genetic isolation, as well as host acquired immune status and genetic resistance to malaria, were important contributors to the evolution of chloroquine resistance in *P. falciparum*.

15 **Conrad MD, Gorman AW, Schillinger JA, Fiori PL, Arroyo R, Malla N, Dubey ML, Gonzalez J, Blank S, Secor WE, Carlton JM.**
Extensive genetic diversity, unique population structure and evidence of genetic exchange in the sexually transmitted parasite *Trichomonas vaginalis*.
PLoS Negl Trop Dis 2012;6(3):e1573. doi: 10.1371/journal.pntd.0001573. Epub 2012 Mar 27.

BACKGROUND: *Trichomonas vaginalis* is the causative agent of human trichomoniasis, the most common non-viral sexually transmitted infection world-wide. Despite its prevalence, little is known about the genetic diversity and population structure of this haploid parasite due to the lack of appropriate tools. The development of a panel of microsatellite markers and SNPs from mining the parasite's genome sequence has paved the way to a global analysis of the genetic structure of the pathogen and association with clinical phenotypes. METHODOLOGY/PRINCIPAL FINDINGS: Here we utilize a panel of *T. vaginalis*-specific genetic markers to genotype 235 isolates from Mexico, Chile, India, Australia, Papua New Guinea, Italy, Africa and the United States, including 19 clinical isolates recently collected from 270 women attending New York City sexually transmitted disease clinics. Using population genetic analysis, we show that *T. vaginalis* is a genetically diverse parasite with a unique population structure consisting of two types present in equal proportions world-wide. Parasites belonging to the two types (type 1 and type 2) differ significantly in the rate at which they harbor the *T. vaginalis* virus, a dsRNA virus implicated in parasite pathogenesis, and in their sensitivity to the widely used drug, metronidazole. We also uncover evidence of genetic exchange, indicating a sexual life-cycle of the parasite despite an absence of morphologically distinct sexual stages. CONCLUSIONS/SIGNIFICANCE: Our study represents the first robust and comprehensive evaluation of global *T. vaginalis* genetic diversity and population structure. Our identification of a unique two-type structure, and the clinically relevant phenotypes associated with them, provides a new dimension for understanding *T. vaginalis* pathogenesis. In addition, our demonstration of the possibility of genetic exchange in the parasite has important implications for genetic research and control of the disease.

16 **Dancause KN, Vilar M, Chan C, DeHuff C, Wilson M, Soloway LE, Tarivonda L, Regenvanu R, Kaneko A, Garruto RM, Lum JK.**
Patterns of childhood and adolescent overweight and obesity during health transition in Vanuatu.
Public Health Nutr 2012 Jan;15(1):158-166. doi: 10.1017/S1368980011001662. Epub 2011 Aug 11.

OBJECTIVE: Rapid economic development and subsequent changes in lifestyle and disease burdens ('health transition') is associated with increasing prevalence of obesity among both adults and children. However, because of continued infectious diseases and undernutrition during the early stages of transition, monitoring childhood obesity has not been prioritized in many countries and the scope of the problem is unknown. Therefore we sought to characterize

patterns of childhood overweight and obesity in an early transitional area, the South Pacific archipelago of Vanuatu. DESIGN: We completed an anthropometric survey among children from three islands with varying levels of economic development, from rural areas (where adult obesity prevalence is low) to urban areas (where adult obesity prevalence is high). SETTING: The islands of Ambae (rural), Aneityum (rural with tourism) and Efate (urban). SUBJECTS: Boys and girls (n 513) aged 6-17 years. RESULTS: Height-, weight- and BMI-for-age did not vary among islands, and prevalence of overweight/obesity based on BMI was low. However, girls from Aneityum – a rural island where the tourism industry increased rapidly after malaria eradication – had increased central adiposity compared with girls from the other islands. This is contrary to adult patterns, which indicate higher obesity prevalence in urban areas. Multiple factors might contribute, including stunting, biological responses after malaria control, sleeping patterns, diet and physical activity levels. CONCLUSIONS: Measures of central adiposity highlight an emerging obesity risk among girls in Vanuatu. The data highlight the synergistic relationship among infectious diseases, undernutrition and obesity during the early stages of health transition.

17 **Daoni E, Kitur U, Parunga A, Ndenzako F, Lloyd A, Yu D.**
Experience in piloting HIV drug resistance early warning indicators to improve the antiretroviral program in Papua New Guinea.
Clin Infect Dis 2012 May;54 Suppl 4:S303-S305. doi: 10.1093/cid/cir994.

In 2009, World Health Organization human immunodeficiency virus drug resistance early warning indicator monitoring was piloted at 2 large antiretroviral therapy (ART) clinics in Papua New Guinea: Heduru Clinic in Port Moresby and Tininga Clinic in Mount Hagen. Results demonstrated that both Heduru and Tininga clinics met internationally suggested targets for prescribing appropriate first-line ART regimens in accordance with national ART guidelines, retention on first-line ART at 12 months, and drug supply continuity. However, both clinics failed to achieve suggested targets for rates of loss to follow-up and on-time pill pickup. Reasons for poor clinic performance on loss to follow-up and on-time pill pickup were explored, and appropriate corrective actions were implemented.

18 **Delfin F, Myles S, Choi Y, Hughes D, Illek R, van Oven M, Pakendorf B, Kayser M, Stoneking M.**
Bridging near and remote Oceania: mtDNA and NRY variation in the Solomon Islands.
Mol Biol Evol 2012 Feb;29(2):545-564. doi: 10.1093/molbev/msr186. Epub 2011 Jul 18.

Although genetic studies have contributed greatly to our understanding of the colonization of Near and Remote Oceania, important gaps still exist. One such gap is the Solomon Islands, which extend between Bougainville and Vanuatu, thereby bridging Near and Remote Oceania, and include both Austronesian-speaking and Papuan-speaking groups. Here, we describe patterns of mitochondrial DNA (mtDNA) and nonrecombining Y chromosome (NRY) variation in over 700 individuals from 18 populations in the Solomons, including 11 Austronesian-speaking groups, 3 Papuan-speaking groups, and 4 Polynesian Outliers (descended via back migration from Polynesia). We find evidence for ancient (pre-Lapita) colonization of the Solomons in old NRY paragroups as well as from M2-M353, which probably arose in the Solomons ~9200 years ago and is the most frequent NRY haplogroup there. There are no consistent genetic differences between Austronesian-speaking and Papuan-speaking groups, suggesting extensive genetic contact between them. Santa Cruz, which is located in Remote Oceania, shows unusually low frequencies of mtDNA and NRY haplogroups of recent Asian ancestry. This is in apparent contradiction with expectations based on archaeological and linguistic evidence for an early (~3,200 years ago), direct colonization of Santa Cruz by Lapita people from the Bismarck Archipelago, via a migration that 'leapfrogged' over the rest of the Solomons. Polynesian Outliers show dramatic island-specific founder events involving various NRY haplogroups. We also find that NRY, but not mtDNA, genetic distance is correlated with the geographic distance between Solomons groups and that historically attested spheres of cultural interaction are associated with the recent genetic structure of Solomons groups, as revealed by mtDNA HV1 sequence and Y-STR haplotype diversity. Our results fill an important lacuna in human genetic studies of Oceania and aid in understanding the colonization and genetic history of this region.

19 **Errington F, Fujikura T, Gewertz D.**
Instant noodles as an antifriction device: making the BOP with PPP in PNG.
Am Anthropol 2012;114(1):19-31.

Focusing primarily, but not exclusively, on urban and periurban Papua New Guinea (PNG), we discuss the significance of instant ramen noodles to those now known as the "bottom of the pyramid" (BOP). Although instant noodles are remarkable in that they are eaten by virtually everyone in the world, albeit in different amounts and for different reasons, they are marketed in PNG specifically as a "popularly positioned product" (PPP) for the BOP. Cheap, convenient, tasty, filling, and shelf stable, they are a modern addition to Sidney Mintz's classic "proletarian hunger killers" of sugar, tea, and coffee. But, we argue, instant noodles have a distinctive contemporary role: they do more than sustain the poor; they transform them into the aspiring consumers of the BOP. As such, instant noodles can be viewed as an antifriction device, greasing the skids of capitalism as it extends its reach.

20 **Eves R.**
Resisting global AIDS knowledges: born-again Christian narratives of the epidemic from Papua New Guinea.
Med Anthropol 2012;31(1):61-76. doi: 10.1080/01459740.2011.594122.

The recognition that HIV prevention materials need to be adapted to local cultures is not often sufficiently understood and applied. Counter discourses and determined disputation about the best means of HIV prevention show that success is not simply a matter of mindfully translating globally sanctioned knowledge and presenting it to receptive audiences. Beliefs contrary to global AIDS knowledges will not be displaced inevitably by scientific facts. As this study of born-again Christians in Papua New Guinea shows, there is incommensurability between the globalized approach preferred by the government and the approach of these Christians. The answer may lie in two words: respect and dialogue.

21 **Geuze RH, Schaafsma SM, Lust JM, Bouma A, Schiefenhövel W, Groothuis TG.**
Plasticity of lateralization: schooling predicts hand preference but not hand skill asymmetry in a non-industrial society.
Neuropsychologia 2012 Apr;50(5):612-620. doi: 10.1016/j.neuropsychologia.2011.12.017. Epub 2012 Jan 3.

Considerable variation in the frequency of left-handedness between cultures has been reported, ranging from 0.5 to 24%. This variation in hand preference may have evolved under natural or cultural selection. It has been suggested that schooling affects handedness but as in most human societies only a selected and minor part of the population does not attend school this is difficult to test. We investigated to what extent schooling affects both hand preference and asymmetry in hand skill in a non-industrial population in the highlands of New Guinea. This provided unique opportunities because of the relatively recent establishment of a primary school in this population, and where people still live a non-industrial traditional life reflecting conditions in which handedness may have evolved. We interviewed 620 inhabitants (aged 5-70 y) to collect demographic data and school history, tested hand preference on 10 ecologically relevant activities, and measured performance of each hand on three tasks (pegboard, grip force, ball throwing). Schooled individuals were overall faster in fine motor performance, had greater grip strength and greater throwing accuracy. This suggests that there is implicit selection on the fitter part of the population to enter school. Schooling is associated with hand preference, as schooled individuals were more likely to be extremely right-handed and less likely to be strongly right-handed, but not with asymmetry of hand skill (controlled for sex and age). Developmental plasticity in hand preference but not skill asymmetry, and the weak correlations between hand preference and hand skill asymmetry indicate that they represent different aspects of brain lateralization. Furthermore, the weak correlations between hand preference and hand skill asymmetry leave room for moderating factors such as schooling, sex and age to have a differential effect on hand preference and hand skill, and each needs to be studied in its own right.

22 **Henry-Halldin CN, Nadesakumaran K, Keven JB, Zimmerman AM, Siba P, Mueller I, Hetzel MW, Kazura JW, Thomsen E, Reimer LJ, Zimmerman PA.**
Multiplex assay for species identification and monitoring of insecticide resistance in *Anopheles punctulatus* group populations of Papua New Guinea.
Am J Trop Med Hyg 2012 Jan;86(1):140-151. doi: 10.4269/ajtmh.2012.11-0503.

Anopheles punctulatus sibling species (*An. punctulatus* s.s., *Anopheles koliensis*, and *Anopheles farauti* species complex [eight cryptic species]) are principal vectors of malaria and filariasis in the Southwest Pacific. Given significant effort to reduce malaria and filariasis transmission through insecticide-treated net distribution in the region, effective strategies to monitor evolution of insecticide resistance among *An. punctulatus* sibling species is essential. Mutations in the voltage-gated sodium channel (VGSC) gene have been associated with knock-down resistance (kdr) to pyrethroids and DDT in malarious regions. By examining VGSC sequence polymorphism we developed a multiplex assay to differentiate wild-type versus *kdr* alleles and query intron-based polymorphisms that enable simultaneous species identification. A survey including mosquitoes from seven Papua New Guinea provinces detected no *kdr* alleles in any *An. punctulatus* species. Absence of VGSC sequence introgression between species and evidence of geographic separation within species suggests that *kdr* must be monitored in each *An. punctulatus* species independently.

23 **Herman J, Ameratunga S, Jackson R.**
Burden of road traffic injuries and related risk factors in low- and middle-income Pacific Island countries and territories: a systematic review of the scientific literature (TRIP 5).
BMC Public Health 2012 Jun 25;12:479. doi: 10.1186/1471-2458-12-479.

BACKGROUND: In Pacific Island countries and territories, the burden of road traffic injuries and their attendant risks are considered significant but are poorly quantified. As with other low- and middle-income countries, understanding the epidemiology of road traffic injuries in Pacific countries is critical to informing sustainable research and policy initiatives aimed at reducing this burden. METHODS: We undertook a systematic review and critical appraisal of the relevant epidemiological literature between January 1980 and December 2010, using key search strings for incidence and aetiological studies focusing on RTIs in less resourced Pacific countries. RESULTS: Nineteen studies were identified. The majority were descriptive and were unable to provide population-based estimates of the burden of road crash injury, or reliable information on risk factors using well-designed aetiological research methods. All studies were published more than 10 years ago, and all but three reported on data from Papua New Guinea, thereby limiting the generalisability of findings to the current status in the region. Studies undertaken in Papua New Guinea suggested that RTIs were more frequent among young males, with head injuries the most common cause of death or hospital admission. Two-thirds of fatalities occurred at the crash site or soon after admission. Most road crash victims were passengers or pedestrians. Factors postulated to influence the risk of RTIs were travel in open-back utility vehicles, utility vehicle overcrowding, and alcohol. CONCLUSIONS: This review suggests that, despite increasing awareness of the importance of addressing road safety among stakeholders in less resourced Pacific Island countries, road traffic injuries have not been a research priority with little relevant current evidence from the region to inform policy. Robust epidemiological research that can assess the magnitude and key determinants of road traffic injuries in these settings is essential to determine context-specific road safety initiatives that are relevant and affordable. Greater attention to harnessing routinely collected data (e.g., hospital information systems and police crash statistics) to inform policy is also required.

24 **Herrera M, Fernández J, Vargas M, Villalta M, Segura Á, León G, Angulo Y, Paiva O, Matainaho T, Jensen SD, Winkel KD, Calvete JJ, Williams DJ, Gutiérrez JM.**
Comparative proteomic analysis of the venom of the taipan snake, *Oxyuranus scutellatus*, from Papua New Guinea and Australia: role of neurotoxic and procoagulant effects in venom toxicity.
J Proteomics 2012 Apr 3;75(7):2128-2140. doi:

10.1016/j.jprot.2012.01.006. Epub 2012 Jan 14.

The venom proteomes of populations of the highly venomous taipan snake, *Oxyuranus scutellatus*, from Australia and Papua New Guinea (PNG), were characterized by reverse-phase HPLC fractionation, followed by analysis of chromatographic fractions by SDS-PAGE, N-terminal sequencing, MALDI-TOF mass fingerprinting, and collision-induced dissociation tandem mass spectrometry of tryptic peptides. Proteins belonging to the following seven protein families were identified in the two venoms: phospholipase A(2) (PLA(2)), Kunitz-type inhibitor, metalloproteinase (SVMP), three-finger toxin (3FTx), serine proteinase, cysteine-rich secretory proteins (CRISP), and coagulation factor V-like protein. In addition, C-type lectin/lectin-like protein and venom natriuretic peptide were identified in the venom of specimens from PNG. PLA(2)s comprised more than 65% of the venoms of these two populations. Antivenoms generated against the venoms of these populations showed a pattern of cross-neutralization, corroborating the immunological kinship of these venoms. Toxicity experiments performed in mice suggest that, at low venom doses, neurotoxicity leading to respiratory paralysis represents the predominant mechanism of prey immobilization and death. However, at high doses, such as those injected in natural bites, intravascular thrombosis due to the action of the prothrombin activator may constitute a potent and very rapid mechanism for killing prey.

25 **Hetzel BS.**
Commentary: from iodine deficiency in Papua New Guinea to a global programme of prevention.
Int J Epidemiol 2012 Jun;41(3):595-598. doi: 10.1093/ije/dys057. Epub 2012 May 13.

26 **Hetzel MW, Gideon G, Lote N, Makita L, Siba PM, Mueller I.**
Ownership and usage of mosquito nets after four years of large-scale free distribution in Papua New Guinea.
Malar J 2012 Jun 10;11:192. doi: 10.1186/1475-2875-11-192.

BACKGROUND: Papua New Guinea (PNG) is a highly malaria endemic country in the South-West Pacific with a population of approximately 6.6 million (2009). In 2004, the country intensified its malaria control activities with support from the Global Fund. With the aim of achieving 80% ownership and usage, a country-wide campaign distributed two million free long-lasting insecticide-treated nets (LLINs). METHODS: In order to evaluate outcomes of the campaign against programme targets, a country-wide household survey based on stratified multi-stage random sampling was carried out in 17 of the 20 provinces after the campaign in 2008/09. In addition, a before-after assessment was carried out in six purposively selected sentinel sites. A structured questionnaire was administered to the heads of sampled households to elicit net ownership and usage information. RESULTS: After the campaign, 64.6% of households owned a LLIN, 80.1% any type of mosquito net. Overall usage by household members amounted to 32.5% for LLINs and 44.3% for nets in general. Amongst children under five years, 39.5% used a LLIN and 51.8% any type of net, whereas 41.3% of pregnant women used a LLIN and 56.1% any net. Accessibility of villages was the key determinant of net ownership, while usage was mainly determined by ownership. Most (99.5%) of the household members who did not sleep under a net did not have access to a (unused) net in their household. In the sentinel sites, LLIN ownership increased from 9.4% to 88.7%, ownership of any net from 52.7% to 94.1%. Usage of LLINs increased from 5.5% to 55.1%, usage of any net from 37.3% to 66.7%. Among children under five years, usage of LLINs and of nets in general increased from 8.2% to 67.0% and from 44.6% to 76.1%, respectively (all $p \leq 0.001$). CONCLUSIONS: While a single round of free distribution of LLINs significantly increased net ownership, an insufficient number of nets coupled with a heterogeneous distribution led to overall low usage rates. Programme targets were missed mainly as a result of the distribution mechanism itself and operational constraints in this very challenging setting.

27 **Hickson RI, Mercer GN, Lokuge KM.**
A metapopulation model of tuberculosis transmission with a case study from high to low burden areas.
PLoS One 2012;7(4):e34411. doi: 10.1371/journal.pone.0034411. Epub 2012 Apr 4.

Tuberculosis (TB) is a growing problem worldwide, especially with the emergence and high prevalence of multidrug-resistant strains. We develop a metapopulation model for TB spread, which is particularly suited to investigating transmission between areas of high and low prevalence. A case study of cross-border transmission in the Torres Strait region of Australia and Papua New Guinea (PNG) is considered and a sensitivity analysis is conducted. We find that only 6 of the 50 parameters analysed are important to the cumulative number of clinically active TB patients in the entire region. Of these, only the detection rate in PNG is found to be an important intervention parameter. We therefore give insight into the extent the area with the high burden of TB (PNG in the case study) is dominating the TB dynamics of the entire region. Furthermore, the sensitivity analysis results give insight into the data that are most important to collect and refine, which is found to be data relating to the PNG parameters.

28 **Jackson KJ, Wang Y, Gaeta BA, Pomat W, Siba P, Rimmer J, Sewell WA, Collins AM.**
Divergent human populations show extensive shared *IGK* rearrangements in peripheral blood B cells.
Immunogenetics 2012 Jan;64(1):3-14. doi: 10.1007/s00251-011-0559-z. Epub 2011 Jul 26.

We have analysed the transcribed immunoglobulin kappa (*IGK*) repertoire of peripheral blood B cells from four individuals from two genetically distinct populations, Papua New Guinean and Australian, using high-throughput DNA sequencing. The depth of sequencing data for each individual averaged 5548 high-quality *IGK* reads, and permitted genotyping of the inferred *IGKV* and *IGKJ* germline gene segments for each individual. All individuals were homozygous at each *IGKJ* locus and had highly similar inferred *IGKV* genotypes. Preferential gene usage was seen at both the *IGKV* and *IGKJ* loci, but only *IGKV* segment usage varied significantly between individuals. Despite the differences in *IGKV* gene utilisation, the rearranged *IGK* repertoires showed extensive identity at the amino acid level. Public rearrangements (those shared by two or more individuals) made up 60.2% of the total sequenced *IGK* rearrangements. The total diversity of *IGK* rearrangements of each individual was estimated to range from just 340 to 549 unique amino acid sequences. Thus, the repertoire of unique expressed *IGK* rearrangements is dramatically less

than previous theoretical estimates of *IGK* diversity, and the majority of expressed *IGK* rearrangements are likely to be extensively shared in individual human beings.

29 **Jayasuriya R, Whittaker M, Halim G, Matineau T.**
Rural health workers and their work environment: the role of inter-personal factors on job satisfaction of nurses in rural Papua New Guinea.
BMC Health Serv Res 2012 Jun 12;12:156. doi: 10.1186/1472-6963-12-156.

BACKGROUND: Job satisfaction is an important focal attitude towards work. Understanding factors that relate to job satisfaction allows interventions to be developed to enhance work performance. Most research on job satisfaction among nurses has been conducted in acute care settings in industrialized countries. Factors that relate to rural nurses are different. This study examined inter-personal, intra-personal and extra-personal factors that influence job satisfaction among rural primary care nurses in a Low and Middle Income Country (LMIC), Papua New Guinea. METHODS: Data were collected using self administered questionnaires from rural nurses attending a training program from 15 of the 20 provinces. Results of a total of 344 nurses were available for analysis. A measure of overall job satisfaction and measures for facets of job satisfaction were developed in the study based on literature and a qualitative study. Multi-variate analysis was used to test prediction models. RESULTS: There was significant difference in the level of job satisfaction by age and years in the profession. Higher levels of overall job satisfaction and intrinsic satisfaction were seen in nurses employed by Church facilities compared to government facilities ($p < 0.01$). Ownership of facility, work climate, supervisory support and community support predicted 35% ($R2 = 0.35$) of the variation in job satisfaction. The factors contributing most were work climate (17%) and supervisory support (10%). None of these factors were predictive of an intention to leave. CONCLUSIONS: This study provides empirical evidence that inter-personal relationships – work climate and supportive supervision – are the most important influences of job satisfaction for rural nurses in an LMIC. These findings highlight that the provision of a conducive environment requires attention to human relations aspects. For PNG this is very important as this critical cadre provides the frontline of primary health care for more than 70% of the population of the country. Many LMIC are focusing on rural health, with most of the attention given to aspects of workforce numbers and distribution. Much less attention is given to improving the aspects of the working environment that enhances intrinsic satisfaction and work climate for rural health workers who are currently in place if they are to be satisfied in their job and productive.

30 **Jayawardena N, Subhi R, Duke T.**
The Western Pacific Regional Child Survival Strategy: progress and challenges in implementation.
J Paediatr Child Health 2012 Mar;48(3):210-219. doi:10.1111/j.1440-1754.2010.01926.x. Epub 2010 Dec 29.

The Regional Child Survival Strategy (RCSS) was launched by the World Health Organization and United Nations Children's Fund in 2006. This initially involved the six highest mortality burden countries in the region (Cambodia, China, Laos PDR, Papua New Guinea, Philippines and Vietnam). This paper aimed to describe the experiences of countries in the region in adopting and implementing the RCSS, and to identify factors that promote and impede progress. Child mortality has fallen substantially since 1990, and the region as a whole is on track to achieve the Millennium Development Goal 4 (MDG-4) targets. Some countries have made slower progress and are struggling. There is an urgent need to support countries that have, until now, not been included in the RCSS, particularly smaller Pacific Island nations, and to provide greater support to the poorest countries if MDG-4 targets for the region are to be achieved.

31 **John E, Christiansen FT, Mueller I, Schofield L, Senitzer D, Siba P, Witt CS.**
Distinct distribution of killer-cell immunoglobulin-like receptor genes in the Mugil and Ilaita areas of Papua New Guinea.
Tissue Antigens 2012 Apr;79(4):263-271. doi: 10.1111/j.1399-0039.2012.01848.x. Epub 2012 Feb 9.

The frequency of the killer-cell immunoglobulin-like receptor (KIR) genes and transmembrane alleles of *KIR2DL4* were studied in coastal (Mugil community) and inland (Ilaita community) communities in Papua New Guinea. Linkage disequilibria between KIR genes and between alleles of *KIR2DL4* and the KIR genes were similar to those found in other populations suggesting conservation of the usual gene order in Papua New Guinean haplotypes. Significant differences in the frequency of KIR genes were found between the two populations despite being separated by only 300 km. Examples of individuals who lacked the *KIR2DL4* gene and others whose *KIR2DL4* allele appeared to have 11 adenines in the polyadenine tract in exon 6 were identified. A relatively low frequency of the KIR A haplotype was found in both populations and particularly in the inland community. The KIR gene frequencies were consistent with the inland Ilaita community being closely related to Australian Aborigines and southern Indians, whereas the KIR gene frequencies of the coastal Mugil community appeared to have been influenced either by recent or ancient admixture from populations with a higher frequency of the KIR A haplotype.

32 **Karthikeyan P, Ramalingam KP.**
Meningitis: is it a major cause of disability amongst Papua New Guinea children?
Disabil Rehabil 2012;34(18):1585-1588. doi: 10.3109/09638288.2011.651190. Epub 2012 Jan 19.

PURPOSE: This article is intended to focus on the need for the use of rehabilitation services, for children with meningitis in Papua New Guinea, which is one of largest developing countries in the Pacific with diverse culture and landscape. Meningitis is the fifth leading disease that results in disability in the country. The first line of treatment is usually antibiotics; administration of vaccination is also recommended. Currently community-based rehabilitation workers and physiotherapists offer the rehabilitation services. There is a need for other rehabilitation professionals and appropriate education for the CBR workers and caregivers for providing effective rehabilitation. METHOD: Articles related to meningitis were recruited through various electronic databases such as Ovid SP, MEDLINE, CINHAL, Google Scholar and HINARI and EBSCO host for full text. The search included journal articles, editorials, research reports, systematic reviews and books. RESULTS: The neurological sequelae

resulting from meningitis are increasing. There is a need for Hib vaccination to reduce the rate of mortality. Physiotherapists are new professionals that emerged since 2006 and are assisting in reducing the motor and neurological disability. CONCLUSIONS: A multidisciplinary approach is required to manage the child with meningitis. Adequate knowledge, resources and assistance about the condition among health professionals, carers and teachers would enable the children to achieve the best quality of life.

33 **Kazura JW, Siba PM, Betuela I, Mueller I.**
Research challenges and gaps in malaria knowledge in Papua New Guinea.
Acta Trop 2012 Mar;121(3):274-280. doi: 10.1016/j.actatropica.2011.08.002. Epub 2011 Aug 27.

Taking into consideration the relative number of people living in Papua New Guinea the burden of malaria in this country is among the highest in Asia and the Pacific region. This article summarizes the research questions and challenges being undertaken by the Southwest Pacific International Center of Excellence for Malaria Research in the context of the epidemiology, transmission and pathogenesis of *Plasmodium falciparum* and *P. vivax* at the present time and the recent past. It is hoped that the research accomplished and local infrastructure strengthened by this effort will help inform regional and national policy with regard to the control and ultimately elimination of malaria in this region of the world.

34 **Kelly A, Kupul M, Fitzgerald L, Aeno H, Neo J, Naketrumb R, Siba P, Kaldor JM, Vallely A; Male Circumcision Acceptability and Impact Study (MCAIS) team.**
"Now we are in a different time; various bad diseases have come." Understanding men's acceptability of male circumcision for HIV prevention in a moderate prevalence setting.
BMC Public Health 2012 Jan 22;12:67. doi: 10.1186/1471-2458-12-67.

BACKGROUND: Adult male surgical circumcision (MC) has been shown to reduce HIV acquisition in men and is recommended by the WHO for inclusion in comprehensive national HIV prevention programs in high prevalence settings. Only limited research to date has been conducted in countries experiencing moderate burden epidemics, where the acceptability, operational feasibility and potential epidemiological impact of MC remain unclear. METHODS: A multi-method qualitative research study was conducted at four sites in Papua New Guinea (PNG), with 24 focus group discussions and 65 in-depth interviews carried out among 276 men. RESULTS: The majority of men were in favour of MC being introduced for HIV prevention in PNG and considered improved genital hygiene, enhanced sexual pleasure and cultural appropriateness key factors in the acceptability of a future intervention. A minority of men were against the introduction of MC, primarily due to concerns regarding sexual risk compensation and that the intervention went against prevailing cultural and religious beliefs. CONCLUSION: This is one of the first community-based MC acceptability studies conducted in a moderate prevalence setting outside of Africa. Research findings from this study suggest that a future MC program for HIV prevention would be widely accepted by men in PNG.

35 **Kenny EE, Timpson NJ, Sikora M, Yee MC, Moreno-Estrada A, Eng C, Huntsman S, Burchard EG, Stoneking M, Bustamante CD, Myles S.**
Melanesian blond hair is caused by an amino acid change in TYRP1.
Science 2012 May 4;336(6081):554. doi: 10.1126/science.1217849.

Naturally blond hair is rare in humans and found almost exclusively in Europe and Oceania. Here, we identify an arginine-to-cysteine change at a highly conserved residue in tyrosinase-related protein 1 (TYRP1) as a major determinant of blond hair in Solomon Islanders. This missense mutation is predicted to affect catalytic activity of TYRP1 and causes blond hair through a recessive mode of inheritance. The mutation is at a frequency of 26% in the Solomon Islands, is absent outside of Oceania, represents a strong common genetic effect on a complex human phenotype, and highlights the importance of examining genetic associations worldwide.

36 **Kep JK.**
Reflecting on 34 years nursing in Papua New Guinea.
Aust Nurs J 2012 Jun;19(11):38-39.

37 **Kitur U.**
Health information challenges for Papua New Guinea.
Pac Health Dialog 2012 Apr;18(1):29-31.

38 **Kwon S, Kingham TP, Kamara TB, Sherman L, Natuzzi E, Mock C, Kushner A.**
Development of a surgical capacity index: opportunities for assessment and improvement.
World J Surg 2012 Feb;36(2):232-239. doi: 10.1007/s00268-011-1385-z.

BACKGROUND: Significant gaps exist in the provision of surgical care in low- and middle-income countries (LMICs). The purpose of this study was to develop a metric to monitor surgical capacity in LMICs. METHODS: The World Health Organization developed a survey called the Tool for Situational Analysis to Assess Emergency and Essential Surgical Care. Using this tool, we developed a surgical capacity scoring index and assessed its usefulness with data from Sierra Leone, Liberia, and the Solomon Islands. RESULTS: There were data from 10 hospitals in Sierra Leone, 16 hospitals in Liberia, and 9 hospitals in the Solomon Islands. The levels of surgical capacity were created using our scoring index based on a possible 100 points: level 1 for hospitals with <50 points, level 2 with 50-70 points, level 3 with 70-80 points, and level 4 with >80 points. In Sierra Leone, 40% of the hospitals had a surgical capacity rating of level 1, 50% level 2, and 10% level 3. In Liberia, 37.5% of the hospitals had a surgical capacity rating of level 1, 56.3% level 2, and only one hospital level 3. For Sierra Leone and Liberia, two factors – infrastructure and personnel – had the greatest deficits. In the Solomon Islands, 44.4% of the hospitals had their surgical capacity rated at level 1, 22.2% at level 2, 11.1% at level 3, and 22.2% at level 4. CONCLUSIONS: Pending pilot testing for reliability and validity, it appears that a systematic hospital surgical capacity index can identify areas for improvement and provide an objective measure for monitoring changes over time.

39 **Laman M, Manning L, Greenhill AR, Mare T, Michael A, Shem S, Vince J, Lagani W, Hwaiwhanje I, Siba PM, Mueller I, Davis TM.**
Predictors of acute bacterial meningitis in children from a malaria-endemic area of Papua New Guinea.

Am J Trop Med Hyg 2012 Feb;86(2):240-245. doi: 10.4269/ajtmh.2012.11-0312.

Predictors of acute bacterial meningitis (ABM) were assessed in 554 children in Papua New Guinea 0.2-10 years of age who were hospitalized with culture-proven meningitis, probable meningitis, or non-meningitic illness investigated by lumbar puncture. Forty-seven (8.5%) had proven meningitis and 36 (6.5%) had probable meningitis. Neck stiffness, Kernig's and Brudzinski's signs and, in children <18 months of age, a bulging fontanel had positive likelihood ratios (LRs) ≥4.3 for proven/probable ABM. Multiple seizures and deep coma were less predictive (LR = 1.5-2.1). Single seizures and malaria parasitemia had low LRs (≤0.5). In logistic regression including clinical variables, Kernig's sign and deep coma were positively associated with ABM, and a single seizure was negatively associated (p ≤0.01). In models including microscopy, neck stiffness and deep coma were positively associated with ABM and parasitemia was negatively associated with ABM (p ≤0.04). In young children, a bulging fontanel added to the model (p <0.001). Simple clinical features predict ABM in children in Papua New Guinea but malaria microscopy augments diagnostic precision.

40 **Leow JJ, Groen RS, Bae JY, Adisa CA, Kingham TP, Kushner AL.**
Scarcity of healthcare worker protection in eight low- and middle-income countries: surgery and the risk of HIV and other bloodborne pathogens.
Trop Med Int Health 2012 Mar;17(3):397-401. doi:10.1111/j.1365-3156.2011.02909.x. Epub 2011 Oct 31.

OBJECTIVE: In view of the substantial incidence of bloodborne diseases and risk to surgical healthcare workers in low- and middle-income countries (LMICs), we evaluated the availability of eye protection, aprons, sterile gloves, sterilizers and suction pumps. METHODS: Review of studies using the WHO Tool for the Situational Analysis of Access to Emergency and Essential Surgical Care. RESULTS: Eight papers documented data from 164 hospitals: Afghanistan (17), Gambia (18), Ghana (17), Liberia (16), Mongolia (44), Sierra Leone (12), Solomon Islands (9) and Sri Lanka (31). No country had a 100% supply of any item. Eye protection was available in only one hospital in Sri Lanka (4%) and most abundant in Liberia (56%). The availability of sterile gloves ranged from 24% in Afghanistan to 94% in Ghana. CONCLUSION: Substantial deficiencies of basic protective supplies exist in low- and middle-income countries.

41 **Lewis IR.**
At risk: the relationship between experiences of child sexual abuse and women's HIV status in Papua New Guinea.
J Child Sex Abus 2012;21(3):273-294. doi: 10.1080/10538712.2012.668265.

Child sexual abuse in Papua New Guinea is a human rights issue as well as an indicator of HIV risk in women. This study aimed to develop knowledge about the link between violence experienced by women and their HIV status. The study used a mixed method approach to collect quantitative and qualitative data through structured interviews with a sample of 415 women across four provinces of Papua New Guinea: National Capital District, Western Highlands, Western, and Morobe. Participants were asked about violence they had experienced as children and in their adult relationships and the impact of the violence. The quantitative data were analyzed using SPSS, and qualitative data were coded using a thematic approach. Child sexual abuse was reported by 27.5% of the sample (n = 114). Women reporting child sexual abuse were more likely to live in violent relationships, be HIV positive, and have a higher number of sexual partners.

42 **Li J, Menard V, Benish RL, Jurevic RJ, Guillemette C, Stoneking M, Zimmerman PA, Mehlotra RK.**
Worldwide variation in human drug-metabolism enzyme genes *CYP2B6* and *UGT2B7*: implications for HIV/AIDS treatment.
Pharmacogenomics 2012 Apr;13(5):555-570. doi: 10.2217/pgs.11.160.

AIM: Hepatic enzymes, CYP2B6 and UGT2B7, play a major role in the metabolism of the widely used antiretroviral drugs efavirenz, nevirapine and zidovudine. In the present study, we provide a view of UGT2B7 haplotype structure, and quantify the genetic diversity and differentiation at both *CYP2B6* and *UGT2B7* genes on a worldwide scale. MATERIALS & METHODS: We genotyped one intronic and three promoter SNPs, and together with three nonsynonymous SNPs, inferred *UGT2B7* alleles in North American (n = 326), West African (n = 133) and Papua New Guinean (n = 142) populations. We also included genotype data for five *CYP2B6* and six *UGT2B7* SNPs from an additional 12 worldwide populations (n = 629) analyzed in the 1000 Genomes Project. RESULTS: We observed significant differences in certain SNP and allele frequencies of *CYP2B6* and *UGT2B7* among worldwide populations. Diversity values were higher for *UGT2B7* than for *CYP2B6*, although there was more diversity between populations for *CYP2B6*. For both genes, most of the genetic variation was observed among individuals within populations, with the Papua New Guinean population showing the highest pairwise differentiation values for *CYP2B6*, and the Asian and European populations showing higher pairwise differentiation values for *UGT2B7*. CONCLUSION: These new genetic distinctions provide additional insights for investigating differences in antiretroviral pharmacokinetics and therapy outcomes among ethnically and geographically diverse populations.

43 **Liberski PP, Sikorska B, Lindenbaum S, Goldfarb LG, McLean C, Hainfellner JA, Brown P.**
Kuru: genes, cannibals and neuropathology.
J Neuropathol Exp Neurol 2012 Feb;71(2):92-103. doi:10.1097/NEN.0b013e3182444efd.

Kuru was the first human transmissible spongiform encephalopathy (TSE) or prion disease identified, occurring in the Fore linguistic group of Papua New Guinea. Kuru was a uniformly fatal cerebellar ataxic syndrome, usually followed by choreiform and athetoid movements. Kuru imposed a strong balancing selection on the Fore population, with individuals homozygous for the 129 Met allele of the gene (*PRNP*) encoding for prion protein (PrP) being the most susceptible. The decline in the incidence of kuru in the Fore has been attributed to the exhaustion of the susceptible genotype and ultimately by discontinuation of exposure via cannibalism. Neuropathologically, kuru-affected brains were characterized by widespread degeneration of neurons, astroglial and microglial proliferation, and the presence of amyloid plaques. These early findings have been confirmed and extended by recent immunohistochemical studies for the detection of the

TSE-specific PrP (PrP). Confocal laser microscopy also showed the concentration of glial fibrillary acidic protein-positive astrocytic processes at the plaque periphery. The fine structure of plaques corresponds to that described earlier by light microscopy. The successful experimental transmission of kuru led to the awareness of its similarity to Creutzfeldt-Jakob disease and Gerstmann-Sträussler-Scheinker disease and formed a background against which the recent epidemics of iatrogenic and variant Creutzfeldt-Jakob disease could be studied.

44 **Liberski PP, Sikorska B, Brown P.**
Kuru: the first prion disease.
Adv Exp Med Biol 2012;724:143-153. doi: 10.1007/978-1-4614-0653-2_12.

Kuru disease is linked with the name of D. Carleton Gajdusek and he was the first to show that this human neurodegenerative disease can be transmitted to chimpanzees and subsequently classified as a transmissible spongiform encephalopathy (TSE), or slow unconventional virus disease. It was first reported to the Western world in 1957 by Gajdusek and Vincent Zigas (1,2) and in 1975 a complete bibliography of kuru was published by Alpers et al. (3). "Kuru" in the Fore language in Papua New Guinea means to shiver from fever and cold. The disease has been found to spread through ritualistic cannibalism and is an invariably fatal cerebellar ataxia accompanied by tremor, choreiform and athetoid movements. Neuropathologically, kuru is characterized by the presence of amyloid "kuru" plaques.

45 **Lisciandro JG, Prescott SL, Nadal-Sims MG, Devitt CJ, Pomat W, Siba PM, Holt PG, Strickland D, van den Biggelaar AH.**
Comparison of neonatal T regulatory cell function in Papua New Guinean and Australian newborns.
Pediatr Allergy Immunol 2012 Mar;23(2):173-180. doi:10.1111/j.1399-3038.2011.01242.x. Epub 2011 Dec 23.

BACKGROUND: Environmental changes, including declining microbial exposure, have been linked with the rising incidence of allergic and autoimmune diseases in 'western' populations. This potentially occurs by altering early development of immuno-regulatory pathways including T regulatory cells (T(reg)). There is now increasing evidence that such conditioning begins in utero. METHODS: We compared neonatal T(reg) from children born under typical western conditions (Australia, AUS) with those of neonates born under more traditional conditions of high microbial burden (Papua New Guinea, PNG). RESULTS: The frequency of neonatal T(reg), defined as CD4(+) Foxp3(+) CD127(-) CD25(+/high) was found to be higher in the cord blood of AUS compared to PNG newborns. However, cord T(reg) suppressive function in a small subset of children was qualitatively similar between PNG and AUS newborns in both a T(reg) depletion assay and a T(reg) supplementation assay. CONCLUSIONS: These findings do not support the hypothesis that living in a 'western' versus more traditional environment leads to poor induction or suppressive function of neonatal T(reg). However, environmentally induced immuno-regulation may potentially occur via alternative mechanisms in PNG newborns that should now be investigated further.

46 **Lisciandro JG, Prescott SL, Nadal-Sims MG, Devitt CJ, Pomat W, Siba PM, Tulic MC, Holt PG, Strickland D, van den Biggelaar AH.**
Ontogeny of Toll-like and NOD-like receptor-mediated innate immune responses in Papua New Guinean infants.
PLoS One 2012;7(5):e36793. doi: 10.1371/journal.pone.0036793. Epub 2012 May 23.

Studies addressing the ontogeny of the innate immune system in early life have reported mainly on Toll-like receptor (TLR) responses in infants living in high-income countries, with little or even no information on other pattern recognition receptors or on early life innate immune responses in children living under very different environmental conditions in less-developed parts of the world. In this study, we describe whole blood innate immune responses to both Toll-like and nucleotide-binding oligomerization domain (NOD)-like receptor agonists including the widely used vaccine adjuvant 'alum' in a group of Papua New Guinean infants aged 1-3 (n = 18), 4-6 (n = 18), 7-12 (n = 21) and 13-18 (n = 10) months. Depending on the ligands and cytokines studied, different age-related patterns were found: alum-induced IL-1β and CXCL8 responses were found to significantly decline with increasing age; inflammatory (IL-6, IL-1β, IFN-γ) responses to TLR2 and TLR3 agonists increased; and IL-10 responses remained constant or increased during infancy, while TNF-α responses either declined or remained the same. We report for the first time that whole blood innate immune responses to the vaccine adjuvant alum decrease with age in infancy, a finding that may imply that the adjuvant effect of alum in pediatric vaccines could be age-related. Our findings further suggest that patterns of innate immune development may vary between geographically diverse populations, which in line with the 'hygiene hypothesis' particularly involves persistence of innate IL-10 responses in populations experiencing higher infectious pressure.

47 **Malloy KL, Suyama TL, Engene N, Debonsi H, Cao Z, Matainaho T, Spadafora C, Murray TF, Gerwick WH.**
Credneramides A and B: neuromodulatory phenethylamine and isopentylamine derivatives of a vinyl chloride-containing fatty acid from cf. *Trichodesmium* sp. nov.
J Nat Prod 2012 Jan 27;75(1):60-66. doi: 10.1021/np200611f. Epub 2011 Dec 12.

Credneramides A (1) and B (2), two vinyl chloride-containing metabolites, were isolated from a Papua New Guinea collection of cf. *Trichodesmium* sp. nov. and expand a recently described class of vinyl chloride-containing natural products. The precursor fatty acid, credneric acid (3), was isolated from both the aqueous and organic fractions of the parent fraction as well as from another geographically and phylogenetically distinct cyanobacterial collection (Panama). Credneramides A and B inhibited spontaneous calcium oscillations in murine cerebrocortical neurons at low micromolar concentrations (1, IC(50) 4.0 μM; 2, IC(50) 3.8 μM).

48 **Malloy KL, Choi H, Fiorilla C, Valeriote FA, Matainaho T, Gerwick WH.**
Hoiamide D, a marine cyanobacteria-derived inhibitor of p53/MDM2 interaction.
Bioorg Med Chem Lett 2012 Jan 1;22(1):683-688. doi: 10.1016/j.bmcl.2011.10.054. Epub 2011 Oct 24.

Bioassay-guided fractionation of two cyanobacterial extracts from Papua New Guinea has yielded hoiamide D in both its carboxylic acid and

conjugate base forms. Hoiamide D is a polyketide synthase (PKS)/non-ribosomal peptide synthetase (NRPS)-derived natural product that features two consecutive thiazolines and a thiazole, as well as a modified isoleucine residue. Hoiamide D displayed inhibitory activity against p53/MDM2 interaction (EC(50)=4.5 μM), an attractive target for anticancer drug development.

49 **Manning L, Rosanas-Urgell A, Laman M, Edoni H, McLean C, Mueller I, Siba P, Davis TM.**
A histopathologic study of fatal paediatric cerebral malaria caused by mixed *Plasmodium falciparum*/*Plasmodium vivax* infections.
Malar J 2012 Apr 3;11:107. doi: 10.1186/1475-2875-11-107.

Microvascular sequestration of *Plasmodium falciparum* underlies cerebral malaria. Despite suggestive ex vivo evidence, this phenomenon has not been convincingly demonstrated in coma complicating *Plasmodium vivax* malaria. Severely ill Papua New Guinean children with mixed *P. falciparum*/*P. vivax* infections are more likely to develop cerebral malaria and die than those with *P. falciparum* alone, possibly reflecting *P. vivax* sequestration. Nested PCR was performed on post mortem brain tissue from three such children dying from cerebral malaria due to mixed-species infections. No *P. vivax* DNA was detected. These findings do not support the hypothesis that *P. vivax* sequestration occurs in human brain.

50 **Mead S, Uphill J, Beck J, Poulter M, Campbell T, Lowe J, Adamson G, Hummerich H, Klopp N, Rückert IM, Wichmann HE, Azazi D, Plagnol V, Pako WH, Whitfield J, Alpers MP, Whittaker J, Balding DJ, Zerr I, Kretzschmar H, Collinge J.**
Genome-wide association study in multiple human prion diseases suggests genetic risk factors additional to *PRNP*.
Hum Mol Genet 2012 Apr 15;21(8):1897-1906. doi: 10.1093/hmg/ddr607. Epub 2011 Dec 30.

Prion diseases are fatal neurodegenerative diseases of humans and animals caused by the misfolding and aggregation of prion protein (PrP). Mammalian prion diseases are under strong genetic control but few risk factors are known aside from the PrP gene locus (*PRNP*). No genome-wide association study (GWAS) has been done aside from a small sample of variant Creutzfeldt-Jakob disease (CJD). We conducted GWAS of sporadic CJD (sCJD), variant CJD (vCJD), iatrogenic CJD, inherited prion disease, kuru and resistance to kuru despite attendance at mortuary feasts. After quality control, we analysed 2000 samples and 6015 control individuals (provided by the Wellcome Trust Case Control Consortium and KORA-gen) for 491032-511862 SNPs in the European study. Association studies were done in each geographical and aetiological group followed by several combined analyses. The *PRNP* locus was highly associated with risk in all geographical and aetiological groups. This association was driven by the known coding variation at rs1799990 (*PRNP* codon 129). No non-*PRNP* loci achieved genome-wide significance in the meta-analysis of all human prion disease. SNPs at the *ZBTB38-RASA2* locus were associated with CJD in the UK (rs295301, $p = 3.13 \times 10^{-8}$; odds ratio (OR), 0.70) but these SNPs showed no replication evidence of association in German sCJD or in Papua New Guinea-based tests. A SNP in the *CHN2* gene was associated with vCJD ($p = 1.5 \times 10^{-7}$; OR, 2.36), but not in UK sCJD (p = 0.049; OR, 1.24), in German sCJD or in PNG groups. In the overall meta-analysis of CJD, 14 SNPs were associated ($p < 10^{-5}$): two at *PRNP*, three at *ZBTB38-RASA2*, nine at nine other independent non-*PRNP* loci, more than would be expected by chance. None of the loci recently identified as genome-wide significant in studies of other neurodegenerative diseases showed any clear evidence of association in prion diseases. Concerning common genetic variation, it is likely that the *PRNP* locus contains the only strong risk factors that act universally across human prion diseases. Our data are most consistent with several other risk loci of modest overall effects which will require further genetic association studies to provide definitive evidence.

51 **Mendez FL, Watkins JC, Hammer MF.**
Global genetic variation at *OAS1* provides evidence of archaic admixture in Melanesian populations.
Mol Biol Evol 2012 Jun;29(6):1513-1520. doi: 10.1093/molbev/msr301. Epub 2012 Jan 16.

Recent analysis of DNA extracted from two Eurasian forms of archaic human shows that more genetic variants are shared with humans currently living in Eurasia than with anatomically modern humans in sub-Saharan Africa. Although these genome-wide average measures of genetic similarity are consistent with the hypothesis of archaic admixture in Eurasia, analyses of individual loci exhibiting the signal of archaic introgression are needed to test alternative hypotheses and investigate the admixture process. Here, we provide a detailed sequence analysis of the innate immune gene *OAS1*, a locus with a divergent Melanesian haplotype that is very similar to the Denisova sequence from the Altai region of Siberia. We resequenced a 7-kb region encompassing the *OAS1* gene in 88 individuals from six Old World populations (San, Biaka, Mandenka, French Basque, Han Chinese, and Papua New Guineans) and discovered previously unknown and ancient genetic variation. The 5' region of this gene has unusual patterns of diversity, including 1) higher levels of nucleotide diversity in Papuans than in sub-Saharan Africans, 2) very deep ancestry with an estimated time to the most recent common ancestor of >3 myr, and 3) a basal branching pattern with Papuan individuals on either side of the rooted network. A global geographic survey of >1,500 individuals showed that the divergent Papuan haplotype is nearly restricted to populations from eastern Indonesia and Melanesia. Polymorphic sites within this haplotype are shared with the draft Denisova genome over a span of ~90 kb and are associated with an extended block of linkage disequilibrium, supporting the hypothesis that this haplotype introgressed from an archaic source that likely lived in Eurasia.

52 **Mirabal S, Herrera KJ, Gayden T, Regueiro M, Underhill PA, Garcia-Bertrand RL, Herrera RJ.**
Increased Y-chromosome resolution of haplogroup O suggests genetic ties between the Ami aborigines of Taiwan and the Polynesian Islands of Samoa and Tonga.
Gene 2012 Jan 25;492(2):339-348. doi: 10.1016/j.gene.2011.10.042. Epub 2011 Nov 3.

The Austronesian expansion has left its fingerprint throughout two-thirds of the circumference of the globe reaching the island of Madagascar in East Africa to the west and Easter Island, off the coast of Chile, to the east. To date, several theories exist to explain the current genetic distribution of Austronesian

populations, with the “slow boat” model being the most widely accepted, though other conjectures (i.e., the “express train” and “entangled bank” hypotheses) have also been widely discussed. In the current study, 158 Y chromosomes from the Polynesian archipelagos of Samoa and Tonga were typed using high resolution binary markers and compared to populations across Mainland East Asia, Taiwan, Island Southeast Asia, Melanesia and Polynesia in order to establish their patrilineal genetic relationships. Y-STR haplotypes on the C2 (M38), C2a (M208), O1a (M119), O3 (M122) and O3a2 (P201) backgrounds were utilized in an attempt to identify the differing sources of the current Y-chromosomal haplogroups present throughout Polynesia (of Melanesian and/or Asian descent). We find that, while haplogroups C2a, S and K3-P79 suggest a Melanesian component in 23%-42% of the Samoan and Tongan Y chromosomes, the majority of the paternal Polynesian gene pool exhibits ties to East Asia. In particular, the prominence of sub-haplogroup O3a2c* (P164), which has previously been observed at only minimal levels in Mainland East Asians (2.0-4.5%), in both Polynesians (ranging from 19% in Manua to 54% in Tonga) and Ami aborigines from Taiwan (37%) provides, for the first time, evidence for a genetic connection between the Polynesian populations and the Ami.

53 **Mitjà O, Hays R, Van Straten C, Robson J, Koka M, Bassat Q.**
Mycetoma caused by *Nocardia yamanashiensis*, Papua New Guinea.
Am J Trop Med Hyg 2012 Jun;86(6):1043-1045. doi: 10.4269/ajtmh.2012.11-0670.

We report the first documented case of a mycetoma caused by *Nocardia yamanashiensis* after the initial description of this species. The 16S-rRNA gene sequence analysis was used to identify the novel species, which showed a similarity of 99.9% to the gene sequence of the type strain. The case showed both clinical non-response and reduced susceptibility in vitro to amoxycillin plus clavulanate, and it was treated successfully with trimethoprim-sulfamethoxazole and doxycycline. Given antibiotic resistance concerns, we suggest that antimicrobial susceptibility testing should be done for the majority of *Nocardia* species without well-established resistance patterns.

54 **Mitjà O, Hays R, Ipai A, Penias M, Paru R, Fagaho D, de Lazzari E, Bassat Q.**
Single-dose azithromycin versus benzathine benzylpenicillin for treatment of yaws in children in Papua New Guinea: an open-label, non-inferiority, randomized trial.
Lancet 2012 Jan 28;379(9813):342-347. doi: 10.1016/S0140-6736(11)61624-3. Epub 2012 Jan 11.

BACKGROUND: Yaws – an endemic treponematosis and, as such, a neglected tropical disease – is re-emerging in children in rural, tropical areas. Oral azithromycin is effective for syphilis. We assessed the efficacy of azithromycin compared with intramuscular long-acting penicillin to treat patients with yaws. METHODS: We did an open-label, non-inferiority, randomised trial at Lihir Medical Centre, Papua New Guinea, between Sep 1, 2010, and Feb 1, 2011. Children aged 6 months to 15 years with a serologically confirmed diagnosis of yaws were randomly allocated, by a computer-generated randomisation sequence, to receive either one 30 mg/kg oral dose of azithromycin or an intramuscular injection of 50,000 units per kg benzathine benzylpenicillin. Investigators were masked to group assignment. The primary endpoint was treatment efficacy, with cure rate defined serologically as a decrease in rapid plasma reagin titre of at least two dilutions by 6 months after treatment, and, in participants with primary ulcers, also by epithelialisation of lesions within 2 weeks. Non-inferiority was shown if the upper limit of the two-sided 95% CI for the difference in rates was lower than 10%. The primary analysis was per protocol. This trial is registered with ClinicalTrials.gov, number NCT01382004. FINDINGS: We allocated 124 patients to the azithromycin group and 126 to the benzathine benzylpenicillin group. In the per-protocol analysis, after 6 months of follow-up, 106 (96%) of 110 patients in the azithromycin group were cured, compared with 105 (93%) of 113 in the benzathine benzylpenicillin group (treatment difference -3.4%; 95% CI -9.3 to 2.4), thus meeting prespecified criteria for non-inferiority. The number of drug-related adverse events (all mild or moderate) was similar in both treatment groups (ten [8%] in the azithromycin group vs eight [7%] in the benzathine benzylpenicillin group). INTERPRETATION: A single oral dose of azithromycin is non-inferior to benzathine benzylpenicillin and avoids the need for injection equipment and medically trained personnel. A change to the simpler azithromycin treatment regimen could enable yaws elimination through mass drug administration programmes. FUNDING: International SOS and Newcrest Mining.

55 **Mueller I, Schoepflin S, Smith TA, Benton KL, Bretscher MT, Lin E, Kiniboro B, Zimmerman PA, Speed TP, Siba P, Felger I.**
Force of infection is key to understanding the epidemiology of *Plasmodium falciparum* malaria in Papua New Guinean children.
Proc Natl Acad Sci USA 2012 Jun 19;109(25):10030-10035. doi:10.1073/pnas.1200841109. Epub 2012 Jun 4.

Genotyping *Plasmodium falciparum* parasites in longitudinal studies provides a robust approach to estimating force of infection (FOI) in the presence of superinfections. The molecular parameter (mol) FOI, defined as the number of new *P. falciparum* clones acquired over time, describes basic malaria epidemiology and is suitable for measuring outcomes of interventions. This study was designed to test whether (mol)FOI influenced the risk of clinical malaria episodes and how far (mol)FOI reflected environmental determinants of transmission, such as seasonality and small-scale geographical variation, or effects of insecticide-treated nets (ITNs). Two hundred sixty-four children 1-3 y of age from Papua New Guinea were followed over 16 mo. Individual parasite clones were tracked longitudinally by genotyping. On average, children acquired 5.9 (SD 9.6) new *P. falciparum* infections per child per y. (mol) FOI showed a pronounced seasonality, was strongly reduced in children using ITNs (incidence rate ratio, 0.49; 95% confidence interval, [0.38-0.61]), increased with age, and significantly varied within villages ($p = 0.001$). The acquisition of new parasite clones was the major factor determining the risk of clinical illness (incidence rate ratio, 2.12; 95% confidence interval, [1.93-2.31]). Adjusting for individual differences in (mol)FOI completely explained spatial variation, age trends, and the effect of ITN use. This study highlights the suitability of (mol)FOI as a measure

of individual exposure and its central role in malaria epidemiology. It has substantial advantages over entomological measures in studies of transmission patterns, and could be used in analyses of host variation in susceptibility, in field efficacy trials of novel interventions or vaccines, and for evaluating intervention effects.

56 **Mulyanto, Pancawardani P, Depamede SN, Wahyono A, Jirintai S, Nagashima S, Takahashi M, Nishizawa T, Okamoto H.**
Identification of four novel subgenotypes (C13-C16) and two inter-genotypic recombinants (C12/G and C13/B3) of hepatitis B virus in Papua Province, Indonesia.
Virus Res 2012 Jan;163(1):129-140. doi: 10.1016/j.virusres.2011.09.002. Epub 2011 Sep 8.

Four novel subgenotypes (C6, C11, C12, and D6) of hepatitis B virus (HBV) were identified in Papua, a multiethnic province of Indonesia. To characterize the HBV strains in Papua, serum samples collected from 515 indigenous inhabitants (mean age: 26.6±9.6 years) in a previously unexamined area, Nabire, located in northern Papua, were used in the present study. Among 46 samples whose 1.6-kilobase (kb) HBV DNA sequence was amplified, 38 (83%) were typeable into known subgenotypes [B3 (n = 4), C1 (n = 2), C5 (n = 1), C6 (n = 5), C12 (n = 13), and D6 (n = 13)]. An analysis of the full-length sequence of the eight remaining HBV/C isolates whose sequence was either unclassifiable or uncertain within the 1.6-kb sequence showed no significant evidence of recombination in six isolates, and inter-genotypic recombination in two isolates (NAB20 and NAB46). By pairwise comparisons and a maximum-likelihood phylogenetic analysis, six non-recombinant isolates were considered significantly remote from known HBV/C isolates of subgenotypes C1-C12, and were classifiable into four novel subgenotypes (tentatively designated C13-C16). NAB20 and NAB46 were hybrids of C13/B3 and C12/G, respectively, displaying recombination breakpoints in the 5'-terminus of the P gene. Notably, the distribution of presumably indigenous subgenotypes C11-C16 was associated with particular language speakers in Papua.

57 **Negin J, Martiniuk A.**
Sector wide approaches for health in small island states: lessons learned from the Solomon Islands.
Glob Public Health 2012;7(2):137-148. doi: 10.1080/17441692.2011.584326. Epub 2011 Jul 8.

Sector Wide Approaches (SWAps) have increasingly been implemented in countries around the world as a mechanism for effective delivery of health sector funding from various sources. Despite the global focus on aid effectiveness, SWAps have been under-examined. In 2007, the Solomon Islands and development partners began discussing a health SWAp making the Solomon Islands one of the first fragile states globally to adopt a SWAp. This paper explores the establishment and implementation of a health SWAp in the Solomon Islands as a specific case study with lessons learned for the region as well as for aid architecture in fragile states more generally. Tensions between donors and the government impeded agreement and early implementation and country ownership of the SWAp idea was muted. Since mid-2009, however, the Solomon Islands SWAp has made strong progress with greater government ownership and with more focus on partnership and harmonisation rather than on funding mechanisms. The SWAp mechanism has been a challenge for the capacity-constrained Solomon Islands health sector and for development partners familiar with other aid modalities, but current momentum suggests that the SWAp will have a positive impact on adherence to agreed aid effectiveness principles.

58 **Nunnery JK, Engene N, Byrum T, Cao Z, Jabba SV, Pereira AR, Matainaho T, Murray TF, Gerwick WH.**
Biosynthetically intriguing chlorinated lipophilic metabolites from geographically distant tropical marine cyanobacteria.
J Org Chem 2012 May 4;77(9):4198-4208. doi: 10.1021/jo300160e. Epub 2012 Apr 19.

Five new vinylchlorine-containing metabolites, the lipoamides janthielamide A and kimbeamides A-C and the ketide-extended pyranone kimbelactone A, have been isolated from collections of marine cyanobacteria made in Curaçao and Papua New Guinea. Both janthielamide A and kimbeamide A exhibited moderate sodium channel blocking activity in murine Neuro-2a cells. Consistent with this activity, janthielamide A was also found to antagonize veratridine-induced sodium influx in murine cerebrocortical neurons. These lipoamides represent the newest additions to a relatively rare family of marine cyanobacterial-derived lipoamides and a new structural class of compounds exhibiting neuromodulatory activities from marine cyanobacteria.

59 **Núñez R, Cooperrider K, Wassmann J.**
Number concepts without number lines in an indigenous group of Papua New Guinea.
PLoS One 2012;7(4):e35662. doi: 10.1371/journal.pone.0035662. Epub 2012 Apr 25.

BACKGROUND: The generic concept of number line, which maps numbers to unidimensional space, is a fundamental concept in mathematics, but its cognitive origins are uncertain. Two defining criteria of the number line are that (i) there is a mapping of each individual number (or numerosity) under consideration onto a specific location on the line, and (ii) that the mapping defines a unidimensional space representing numbers with a metric – a distance function. It has been proposed that the number line is based on a spontaneous universal human intuition, rooted directly in brain evolution, that maps number magnitude to linear space with a metric. To date, no culture lacking this intuition has been documented. METHODOLOGY/PRINCIPAL FINDINGS: By means of a number line task, we investigated the universality proposal with the Yupno of Papua New Guinea. Unschooled adults did exhibit a number-to-space mapping (criterion i) but, strikingly, despite having precise cardinal number concepts, they located numbers only on the endpoints, thus failing to use the extent of the line. The produced mapping was bi-categorical and metric-free, in violation of criterion ii. In contrast, Yupnos with scholastic experience used the extent of the segment according to known standards, but they did so not as evenly as western controls, exhibiting a bias towards the endpoints. CONCLUSIONS/SIGNIFICANCE: Results suggest that cardinal number concepts can exist independently from number line representations. They also suggest that the number line mapping, although ubiquitous in the modern world, is not universally spontaneous, but rather seems to be learned through – and continually reinforced by – specific cultural practices.

60 **Pharoah P, Buttfield IH, Hetzel BS.**

Neurological damage to the fetus resulting from severe iodine deficiency during pregnancy.
Int J Epidemiol 2012 Jun;41(3):589-592. doi: 10.1093/ije/dys070. Epub 2012 May 13.

Endemic cretinism is characterised by multiple neurological defects including deaf-mutism, diplegia, squint, and mental deficiency. The condition is widely prevalent in the Highlands of New Guinea in association with severe iodine deficiency. Previous studies have shown that iodised oil provides a very satisfactory correction of severe iodine deficiency in New Guinea. A controlled trial on the use of intramuscular iodised oil in the prevention of endemic cretinism was carried out in the Western Highlands of New Guinea and involved a population of approximately 8000. Subsequent follow-up over four years revealed 26 endemic cretins out of a total of 534 children born to mothers who had not received iodised oil; the mothers of 5 of these cretins were pregnant at the start of the trial. In comparison, 7 cases of endemic cretinism occurred among 498 children born to mothers who had been treated with iodised oil; in 6 of these 7 cases, the mother was pregnant when the trial commenced. It is concluded that intramuscular iodised oil is effective in the prevention of endemic cretinism and that, for it to be effective, it should be given prior to conception. This suggests that severe iodine deficiency in the mother produces neurological damage during fetal development.

61 **Piarroux R, Faucher B.**
Cholera epidemics in 2010: respective roles of environment, strain changes, and human-driven dissemination.
Clin Microbiol Infect 2012 Mar;18(3):231-238. doi: 10.1111/j.1469-0691.2012.03763.x. Epub 2012 Jan 31.

The cholera burden has grown strikingly during the past 4 years, and has spread to countries previously spared by this disease. The current spread has proved especially violent, as illustrated by the recent deadly epidemics around the Lake Chad Basin, in East Africa, and in Haiti. This onset of severe cholera epidemics is part of the overall dynamic of the current seventh cholera pandemic, composed of successive epidemic waves. The current wave is attributable to new atypical El Tor strains, which spread from the Bay of Bengal to Papua in the east, Africa and the Caribbean Sea in the west, and caused hundreds of thousands of cases and thousands of deaths during each of the last 4 years. The particular severity of the resulting epidemics is partially attributable to the specific characteristics of the atypical El Tor strain involved. Besides the ability of El Tor to spread easily, this strain is associated with more severe clinical findings, because of elevated levels of toxin secretion resulting from a genetic content originating from classical strains. Conversely, recent studies of these deadly outbreaks raised hope by illustrating their relationship with human-borne dissemination rather than with the resurgence of environmental strains. As human-borne dissemination can be more easily targeted than ubiquitous environmental contamination, accurate and comprehensive epidemiological studies are essential to better understand the dynamics of the disease and to optimize future cholera responses.

62 **Prescott TA, Kiapranis R, Maciver SK.**
Comparative ethnobotany and in-the-field antibacterial testing of medicinal plants used by the Bulu and inland Kaulong of Papua New Guinea.
J Ethnopharmacol 2012 Jan 31;139(2):497-503. doi: 10.1016/j.jep.2011.09.058. Epub 2011 Nov 30.

ETHNOPHARMACOLOGICAL RELEVANCE: The island of New Britain in Papua New Guinea is an area of great floristic and cultural diversity that has received little attention from ethnobotanists. Here we present the results of a comparative medicinal ethnobotanical survey of the Bulu and inland Kaulong, two distinct people groups inhabiting lowland rainforest on different sides of the island. A high proportion of species are used in the treatment of bacterial infections and plants with antibacterial activity were identified in the field using a specially developed antibacterial assay kit. Follow-up testing with human pathogens was used to evaluate active plant material in more detail. MATERIALS AND METHODS: Rapid appraisal techniques were used to survey both people groups with all data corroborated by three or more separate sources. Plants from both groups were tested in-the-field with a portable antibacterial test kit based on the agar diffusion assay, using a pressure cooker to sterilise glassware and media. Follow-up laboratory-based tests were carried out using standardised agar dilution protocols for drug resistant and drug sensitive strains of *Staphylococcus aureus* and *Streptococcus pneumoniae*. RESULTS: We find surprisingly little overlap in the plant species used by the two people groups with only 1 out of 70 species used for the same purpose. There is also a difference in emphasis in the conditions treated, with 53% of Kaulong medicinal plants dedicated to treating tropical ulcers compared with only 8% in the Bulu group. In-the-field testing identified *Garcinia dulcis* bark (a Kaulong tropical ulcer treatment) to have antibacterial activity and follow-up tests against a drug resistant strain of *Staphylococcus aureus* (a pathogen implicated in tropical ulcer pathogenesis) revealed the crude bark extract to be potently active with an MIC of just 1 mg/ml. CONCLUSIONS: The results demonstrate extreme differences in medicinal plant use between two people groups living a mere 100 km apart and suggests the two medicinal plant systems have developed in isolation from one another. In-the-field antibacterial testing of plant extracts was found to be a valuable technique that enabled early identification of active plant material.

63 **Pulford J, Mueller I, Siba PM, Hetzel MW.**
Malaria case management in Papua New Guinea prior to the introduction of a revised treatment protocol.
Malar J 2012 May 7;11:157. doi: 10.1186/1475-2875-11-157.

BACKGROUND: This study aimed to document malaria case management practices in Papua New Guinea prior to the introduction of a revised national malaria treatment protocol. The revised protocol stipulates routine testing of malaria infection by rapid diagnostic test or microscopy, anti-malarial prescription to test-positive cases only, and the introduction of a new artemisinin-based first-line anti-malarial. Findings presented in this paper primarily focus on diagnostic, prescription and treatment counselling practices. METHODS: In a national cross-sectional survey of 79 randomly selected health facilities, data were collected via non-participant observation of the clinical case management of patients presenting with fever or a recent history of fever. Data were recorded on a structured clinical observation instrument. RESULTS: Overall, 15% of observed fever patients (n = 468) were tested for malaria infection by rapid diagnostic test and a further 3.6% were tested via

microscopy. An anti-malarial prescription was made in 96.4% (451/468) of cases, including 100% (17/17) of test-positive cases and 82% (41/50) of test-negative cases. In all, 79.8% of anti-malarial prescriptions conformed to the treatment protocol current at the time of data collection. The purpose of the prescribed medication was explained to patients in 63.4% of cases, dosage/regimen instructions were provided in 75.7% of cases and the possibility of adverse effects and what they might look like were discussed in only 1.1% of cases. CONCLUSION: The revised national malaria treatment protocol will require a substantial change in current clinical practice if it is to be correctly implemented and adhered to. Areas that will require the most change include the shift from presumptive to RDT/microscopy confirmed diagnosis, prescribing (or rather non-prescribing) of anti-malarials to patients who test negative for malaria infection, and the provision of thorough treatment counselling. A comprehensive clinician support programme, possibly inclusive of 'booster' training opportunities and regular clinical supervision, will be needed to support the change.

64 **Punjabi NH, Taylor WR, Murphy GS, Purwaningsih S, Picarima H, Sisson J, Olson JG, Baso S, Wangsasaputra F, Lesmana M, Oyofo BA, Simanjuntak CH, Subekti D, Corwin AL, Richie TL.** Etiology of acute, non-malaria, febrile illnesses in Jayapura, northeastern Papua, Indonesia.
Am J Trop Med Hyg 2012 Jan;86(1):46-51. doi: 10.4269/ajtmh. 2012.10-0497.

We conducted a prospective, inpatient fever study in malaria-endemic Papua, Indonesia to determine non-malaria fever etiologies. Investigations included malaria blood films, blood culture, and paired serologic samples analysis for dengue, Japanese encephalitis, leptospirosis, scrub typhus, murine typhus, and spotted fever group rickettsia. During 1997-2000, 226 patients (127 males and 99 females) 1-80 years of age (median age = 25 years) were enrolled. Positive blood cultures (n = 34, 15%) were obtained for *Salmonella typhi* (n = 13), *Escherichia coli* (n = 8), *Streptococcus pneumoniae* (n = 6), *Staphylococcus aureus* (n = 5), *Streptococcus pyogenes* (n = 1), and *Klebsiella pneumoniae* (n = 1). Twenty (8.8%) patients were positive for leptospirosis by polymerase chain reaction. Eighty (35.4%) of 226 patients had ≥1 positive serology, diagnostic for 15 rickettsial and 9 dengue cases. Acid-fast bacilli-positive sputum was obtained from three patients. Most common confirmed (81 of 226, 35.8%)/suspected diagnoses were typhoid fever (n = 41), pneumonia (n = 29), leptospirosis (n = 28), urinary tract infections (n = 20), rickettsioses (n = 19), dengue (n = 17), and meningitis/encephalitis (n = 15). There were 15 deaths; 7 (46.7%) were caused by meningitis/encephalitis. Multiple positive serologic results and few confirmed diagnoses indicate the need for improved diagnostics.

65 **Ramesh A, Small ST, Kloos ZA, Kazura JW, Nutman TB, Serre D, Zimmerman PA.** The complete mitochondrial genome sequence of the filarial nematode *Wuchereria bancrofti* from three geographic isolates provides evidence of complex demographic history.
Mol Biochem Parasitol 2012 May;183(1):32-41. doi:10.1016/j.molbiopara.2012.01.004. Epub 2012 Feb 1.

Mitochondrial (mt) genome sequences have enabled comparison of population genetics and evolution for numerous free-living and parasitic nematodes. Here we define the complete mt genome of *Wuchereria bancrofti* through analysis of isolates from Papua New Guinea, India and West Africa. Sequences were assembled for each isolate and annotated with reference to the mt genome sequence for *Brugia malayi*. The length of the *W. bancrofti* mt genome is approximately 13,637 nucleotides; it contains 2 ribosomal RNAs (rrns), 22 transfer RNAs (trns) and 12 protein-coding genes, and is characterized by a 74.6% AT content. The *W. bancrofti* mt gene order is identical to that reported for *Onchocerca volvulus*, *Dirofilaria immitis*, *Setaria digitata* and *B. malayi*. In addition to using translational start codons identified previously in the mt protein-coding genes of other filarial nematodes, *W. bancrofti* appears to be unique in using TGT as a translational start codon. Similarly, use of incomplete stop codons in mt protein-coding genes appears to be more common in *W. bancrofti* than in other human filarial parasites. The complete mt genome sequence reported here provides new genetic markers for investigating phylogenetic and geographic relationships between isolates, and assessing population diversity within endemic regions. The sequence polymorphism enables new strategies to monitor the progress of public health interventions to control and eliminate this important human parasite. We illustrate the utility of this sequence and single nucleotide polymorphisms by inferring the divergence times between the three *W. bancrofti* isolates, suggesting predictions into their origin and migration.

66 **Rijken MJ, McGready R, Boel ME, Poespoprodjo R, Singh N, Syafruddin D, Rogerson S, Nosten F.** Malaria in pregnancy in the Asia-Pacific region.
Lancet Infect Dis 2012 Jan;12(1):75-88. doi: 10.1016/S1473-3099(11)70315-2.

Most pregnant women at risk of infection with *Plasmodium vivax* live in the Asia-Pacific region. However, malaria in pregnancy is not recognised as a priority by many governments, policy makers, and donors in this region. Robust data for the true burden of malaria throughout pregnancy are scarce. Nevertheless, when women have little immunity, each infection is potentially fatal to the mother, fetus, or both. WHO recommendations for the control of malaria in pregnancy are largely based on the situation in Africa, but strategies in the Asia-Pacific region are complicated by heterogeneous transmission settings, coexistence of multidrug-resistant *Plasmodium falciparum* and *Plasmodium vivax* parasites, and different vectors. Most knowledge of the epidemiology, effect, treatment, and prevention of malaria in pregnancy in the Asia-Pacific region comes from India, Papua New Guinea and Thailand. Improved estimates of the morbidity and mortality of malaria in pregnancy are urgently needed. When malaria in pregnancy cannot be prevented, accurate diagnosis and prompt treatment are needed to avert dangerous symptomatic disease and to reduce effects on fetuses.

67 **Salman S, Page-Sharp M, Batty KT, Kose K, Griffin S, Siba PM, Ilett KF, Mueller I, Davis TM.** Pharmacokinetic comparison of two piperaquine-containing artemisinin combination therapies in Papua New Guinean children with uncomplicated malaria.
Antimicrob Agents Chemother 2012 Jun;56(6):3288-3297. doi: 10.1128/AAC.06232-11. Epub 2012 Apr 2.

Pharmacokinetic differences between piperaquine (PQ) base and PQ tetraphosphate were investigated in 34 Papua New Guinean children aged 5 to 10 years treated for uncomplicated malaria with artemisinin-PQ (ART-PQ) base or dihydroartemisinin-PQ (DHA-PQ) tetraphosphate. Twelve children received ART-PQ base (two daily doses of 3 mg of ART and 18 mg of PQ base as granules/kg of body weight) as recommended by the manufacturer, with regular clinical assessment and blood sampling over 56 days. PQ concentrations in plasma samples collected from 22 children of similar ages with malaria in a previously published pharmacokinetic study of DHA-PQ tetraphosphate (three daily doses of 2.5 mg of ART and 20 mg of PQ tetraphosphate as tablets/kg of body weight) were available for comparison. The disposition of ART was also assessed in the 12 children who received ART-PQ base. Plasma PQ was assayed by high-performance liquid chromatography with UV detection, and ART was assayed using liquid chromatography-mass spectrometry. Multicompartment pharmacokinetic models for PQ and ART were developed using a population-based approach. ART-PQ base was well tolerated, and initial fever abatement and parasite clearance were prompt. There were no differences between the two treatments in the values for the PQ area under the concentration-time curve from time zero to infinity (AUC(0-∞)), with medians of 49,451 (n = 12) and 44,556 (n = 22) μg • h/liter for ART-PQ base and DHA-PQ tetraphosphate, respectively. Recurrent parasitemia was associated with lower PQ exposure. Using a two-compartment ART model, the median AUC(0-∞) was 1,652 μg • h/liter. There was evidence of autoinduction of ART metabolism (relative bioavailability for the second dose, 0.27). These and previously published data suggest that a 3-day ART-PQ base regimen should be further evaluated, in line with World Health Organization recommendations for all artemisinin combination therapies.

68 **Senn N, Rarau P, Manong D, Salib M, Siba P, Robinson LJ, Reeder J, Rogerson S, Mueller I, Genton B.**
Rapid diagnostic test-based management of malaria: an effectiveness study in Papua New Guinean infants with *Plasmodium falciparum* and *Plasmodium vivax* malaria.
Clin Infect Dis 2012 Mar 1;54(5):644-651. doi: 10.1093/cid/cir901. Epub 2011 Dec 23.

BACKGROUND: In malaria-endemic areas it is recommended that febrile children be tested for malaria by rapid diagnostic test (RDT) or blood slide (BS) and receive effective malaria treatment only if results are positive. However, RDTs are known to perform less well for *Plasmodium vivax*. We evaluated the safety of withholding antimalarial drugs from young Papua New Guinean children with negative RDT results in areas with high levels of both *Plasmodium falciparum* and *P. vivax* infections. METHODS: Longitudinal prospective study of children aged 3-27 months visiting outpatient clinics for fever. RDT was administered at first visit. RDT and microscopy were performed if children returned because of persistent symptoms. Outcomes were rates of reattendance and occurrence of severe illnesses. RESULTS: Of 5670 febrile episodes, 3942 (70%) involved a negative RDT result. In 133 cases (3.4%), the children reattended the clinic within 7 days for fever, of whom 29 (0.7%) were parasitemic by RDT or microscopy. Of children who reattended, 24 (0.7%) presented with a severe illness: 2 had lower respiratory tract infections (LRTIs) with low-density *P. vivax* on BS; 2 received a diagnosis of *P. vivax* malaria on the basis of RDT but BSs were negative; 16 had LRTIs; 3 had alternative diagnoses. Of these 24, 22 were cured at day 28. Two children died of illnesses other than malaria and were RDT and BS negative at the initial and subsequent visits. CONCLUSION: Treatment for malaria based on RDT results is safe and feasible even in infants living in areas with moderate to high endemicity for both *P. falciparum* and *P. vivax* infections.

69 **Senn N, Rarau P, Stanisic DI, Robinson L, Barnadas C, Manong D, Salib M, Iga J, Tarongka N, Ley S, Rosanas-Urgell A, Aponte JJ, Zimmerman PA, Beeson JG, Schofield L, Siba P, Rogerson SJ, Reeder JC, Mueller I.**
Intermittent preventive treatment for malaria in Papua New Guinean infants exposed to *Plasmodium falciparum* and *P. vivax*: a randomized controlled trial. *PLoS Med* 2012;9(3):e1001195. doi: 10.1371/journal.pmed.1001195. Epub 2012 Mar 27.

BACKGROUND: Intermittent preventive treatment in infants (IPTi) has been shown in randomized trials to reduce malaria-related morbidity in African infants living in areas of high *Plasmodium falciparum* (*Pf*) transmission. It remains unclear whether IPTi is an appropriate prevention strategy in non-African settings or those co-endemic for *P. vivax* (*Pv*). METHODS AND FINDINGS: In this study, 1,121 Papua New Guinean infants were enrolled into a three-arm placebo-controlled randomized trial and assigned to sulfadoxine-pyrimethamine (SP) (25 mg/kg and 1.25 mg/kg) plus amodiaquine (AQ) (10 mg/kg, 3 d, n = 374), SP plus artesunate (AS) (4 mg/kg, 3 d, n = 374), or placebo (n = 373), given at 3, 6, 9 and 12 mo. Both participants and study teams were blinded to treatment allocation. The primary end point was protective efficacy (PE) against all episodes of clinical malaria from 3 to 15 mo of age. Analysis was by modified intention to treat. The PE (compared to placebo) against clinical malaria episodes (caused by all species) was 29% (95% CI, 10-43, p ≤0.001) in children receiving SP-AQ and 12% (95% CI, -11 to 30, p = 0.12) in those receiving SP-AS. Efficacy was higher against *Pf* than *Pv*. In the SP-AQ group, *Pf* incidence was 35% (95% CI, 9-54, p = 0.012) and *Pv* incidence was 23% (95% CI, 0-41, p = 0.048) lower than in the placebo group. IPTi with SP-AS protected only against *Pf* episodes (PE = 31%, 95% CI, 4-51, p = 0.027), not against *Pv* episodes (PE = 6%, 95% CI, -24 to 26, p = 0.759). Number of observed adverse events/serious adverse events did not differ between treatment arms (p >0.55). None of the serious adverse events were thought to be treatment-related, and the vomiting rate was low in both treatment groups (1.4%-2.0%). No rebound in malaria morbidity was observed for 6 mo following the intervention. CONCLUSIONS: IPTi using a long half-life drug combination is efficacious for the prevention of malaria and anemia in infants living in a region highly endemic for both *Pf* and *Pv*.

70 **Shapira Y, Poratkatz BS, Gilburd B, Barzilai O, Ram M, Blank M, Lindeberg S, Frostegård J, Anaya JM, Bizzaro N, Jara LJ, Damoiseaux J, Shoenfeld Y, Levin NA.**
Geographical differences in autoantibodies and anti-infectious agents antibodies among healthy adults.
Clin Rev Allergy Immunol 2012 Apr;42(2):154-163. doi: 10.1007/s12016-010-8241-z.

Much is known about the geoepidemiology of

defined autoimmune diseases (AD); however, there is currently limited data regarding the prevalence of autoantibodies among healthy populations of different geographical areas. The aim of this study was to evaluate a large profile of autoantibodies in healthy adults from distinct global regions as well as the prevalence of anti-infectious agents antibodies in those regions. Sera samples from 557 healthy donors were obtained at six centers located in different countries (i.e., Italy, Netherlands, Israel, Mexico, Columbia, Papua New Guinea (Kitavans)). Sera were tested for the presence of antinuclear antibodies (ANA) and autoantibodies associated with thrombophilia, vasculitis, and gastrointestinal (GI) disease. Sera samples were also screened for antibodies against infectious agents (i.e., EBV, CMV, HBV, *Helicobacter pylori*, *Treponema pallidum*, and *Toxoplasma gondii*). Tests were performed using the BioPlex 2200 or ELISA kits (Bio-Rad Laboratories, USA). We found a significant gradient of ANA positivity among the groups: 45% of Columbians, 38% of Kitavans, 26% of Mexicans, 12% of Italians, 12% of Dutch, and 11% of Israelis were ANA positive. Geographical differences were also observed regarding the prevalence of specific autoantibodies, namely ANA: anti-dsDNA, chromatin, SmRNP, Ro/SSA, La/SSB, Scl70; GI associated: antigliadin; and thrombophilia-associated: anti-β2GP1 and prothrombin. Additionally, significant differences were observed regarding serological markers of all infectious agents screened. The observed variance between healthy ethno-geographical distinct populations in prevalence of autoantibodies may represent different genetic or environmental (e.g., prior exposure to infection) influences and thus may illuminate possible causes of geoepidemiological differences in AD.

71 **Sikorska B, Liberski PP.**
Human prion diseases: from kuru to variant Creutzfeldt-Jakob disease.
Subcell Biochem 2012;65:457-496. doi: 10.1007/978-94-007-5416-4_17.

Transmissible spongiform encephalopathies (TSEs) or prion diseases are the names given to the group of fatal neurodegenerative disorders that includes kuru, Creutzfeldt-Jakob disease (CJD), Gerstmann-Sträussler-Scheinker disease (GSS), sporadic and familial fatal insomnia and the novel prion disease variable protease-sensitive prionopathy (PSPr) in humans. Kuru was restricted to natives of the Foré linguistic group in Papua New Guinea and spread by ritualistic endocannibalism. CJD appears as sporadic, familial (genetic or hereditary) and infectious (iatrogenic) forms. Variant CJD is a zoonotic CJD type and of major public health importance, which resulted from transmission from bovine spongiform encephalopathy (BSE) through ingestion of contaminated meat products. GSS is a slowly progressive hereditary autosomal dominant disease and the first human TSE in which a mutation in a gene encoding for prion protein (PrP) was discovered. The rarest human prion disease is fatal insomnia, which may occur in genetic and sporadic form. More recently a novel prion disease, variable protease-sensitive prionopathy (PSPr), was described in humans. TSEs are caused by a still incompletely defined infectious agent known as a 'prion' which is widely regarded to be an aggregate of a misfolded isoform (PrP(Sc)) of a normal cellular glycoprotein (PrP(c)). The conversion mechanism of PrP(c) into PrP(Sc) is still not certain.

72 **Suwamaru JK.**
An SMS-based HIV/AIDS education and awareness model for rural areas in Papua New Guinea.
Stud Health Technol Inform 2012;182:161-169.

Access to basic healthcare in many parts of Papua New Guinea (PNG) remains a challenge partly because the majority of the population is thinly scattered across a geographically rugged country. The major health problems in PNG pertain to malaria, tuberculosis and diarrheal diseases while HIV has reached epidemic levels. The proliferation of the mobile phone technology in PNG has been unprecedented since the introduction of competition in the sector in July 2007. Users in rural areas now access the mobile phone signal making it their preferred form of modern communications medium. This paper introduces an SMS-based HIV/AIDS education, awareness and information dissemination model for a predominantly rural-based PNG society.

73 **Tabone T, Garland SM, Mola G, O'Connor M, Danielewski J, Tabrizi SN.**
Prevalence of human papillomavirus genotypes in women with cervical cancer in Papua New Guinea.
Int J Gynaecol Obstet 2012 Apr;117(1):30-32. doi: 10.1016/j.ijgo.2011.11.022. Epub 2012 Feb 10.

OBJECTIVE: Prophylactic human papillomavirus (HPV) vaccines are currently not available in Papua New Guinea. Prior to introducing these vaccines, knowledge about the HPV genotypes present in cervical cancer in this region is necessary to determine whether the types covered by the 2 commercially licensed vaccines are the same as those in other regions of the world. METHODS: Fresh, frozen cervical biopsies from 70 women with cervical cancer in Papua New Guinea were collected over a 3-year period from 2006 to 2009. HPV genotypes were detected using the Genera PapType assay. RESULTS: Overall, 100% of the specimens were HPV DNA positive, with HPV types 16 and 18 being the most prevalent at 57.1% and 25.7% (95% CI, 0.45-0.68 and 0.17-0.37) respectively, followed by HPV 33 (10%; 95% CI, 0.05-0.19) and HPV 31 (4.3%; 95% CI, 0.01-0.12). Multiple genotypes were identified in 6 women (8.6%), with all biopsies containing HPV 16 and 1 other high-risk type. CONCLUSION: The 2 most prevalent HPV types identified in women with cervical cancer in Papua New Guinea correspond to global data. This suggests that the currently available HPV vaccines could potentially reduce the burden of HPV-related cervical cancer in Papua New Guinea significantly.

74 **Takahashi N, Tanabe K, Tsukahara T, Dzodzomenyo M, Dysoley L, Khamlome B, Sattabongkot J, Nakamura M, Sakurai M, Kobayashi J, Kaneko A, Endo H, Hombhanje F, Tsuboi T, Mita T.**
Large-scale survey for novel genotypes of *Plasmodium falciparum* chloroquine-resistance gene *pfcrt*.
Malar J 2012 Mar 28;11:92. doi: 10.1186/1475-2875-11-92.

BACKGROUND: In *Plasmodium falciparum*, resistance to chloroquine (CQ) is conferred by a K to T mutation at amino acid position 76 (K76T) in the *P. falciparum* CQ transporter (PfCRT). To date, at least 15 *pfcrt* genotypes, which are represented by combinations of five amino acids at positions 72-76, have been described in field isolates from various

endemic regions. To identify novel mutant *pfcrt* genotypes and to reveal the genetic relatedness of *pfcrt* genotypes, a large-scale survey over a wide geographic area was performed. METHODS: Sequences for exon 2 in *pfcrt*, including known polymorphic sites at amino acid positions 72, 74, 75 and 76, were obtained from 256 *P. falciparum* isolates collected from eight endemic countries in Asia (Bangladesh, Cambodia, Lao P.D.R., the Philippines and Thailand), Melanesia (Papua New Guinea and Vanuatu) and Africa (Ghana). A haplotype network was constructed based on six microsatellite markers located -29 kb to 24 kb from *pfcrt* in order to examine the genetic relatedness among mutant *pfcrt* genotypes. RESULTS: In addition to wild type (CVMNK at positions 72-76), four mutant *pfcrt* were identified: CVIET, CVIDT, SVMNT and CVMNT. Haplotype network revealed that there were only three mutant *pfcrt* lineages, originating in Indochina, Philippines and Melanesia. Importantly, the Indochina lineage contained two mutant *pfcrt* genotypes, CVIET (n = 95) and CVIDT (n = 14), indicating that CVIDT shares a common origin with CVIET. Similarly, one major haplotype in the Melanesian lineage contained two *pfcrt* genotypes: SVMNT (n = 71) and CVMNT (n = 3). In Africa, all mutant *pfcrt* genotypes were the CVIET of the Indochina lineage, probably resulting from the intercontinental migration of CQ resistance from Southeast Asia. CONCLUSIONS: The number of CQ-mutant lineages observed in this study was identical to that found in previous studies. This supports the hypothesis that the emergence of novel CQ resistance is rare. However, in the mutant *pfcrt* genotypes, amino acid changes at positions 72, 74 and 75 appear to have recently been generated at least several times, producing distinct *pfcrt* mutant genotypes. The occurrence of new mutations flanking K76T may yield stronger resistance to CQ and/or a higher fitness than the original *pfcrt* mutant.

75 **van den Biggelaar AH, Pomat WS, Phuanukoonnon S, Michael A, Aho C, Nadal-Sims MA, Devitt CJ, Jacoby PA, Hales BJ, Smith WA, Mitchell T, Wiertsema S, Richmond P, Siba P, Holt PG, Lehmann D.**
Effect of early carriage of *Streptococcus pneumoniae* on the development of pneumococcal protein-specific cellular immune responses in infancy.
Pediatr Infect Dis J 2012 Mar;31(3):243-248. doi: 10.1097/INF.0b013e318245a5a8.

BACKGROUND: The aim of this study was to examine the relationship between nasopharyngeal pneumococcal colonization in early life and the subsequent development of pneumococcal-specific T cell responses. METHODS: Pernasal swabs were collected from Papua New Guinean infants at the ages of 1 and 2 weeks (n = 279). At 9 months, in vitro cellular immune responses to choline-binding protein A (n = 132), pneumococcal surface protein A (n = 132), pneumolysin (n = 99), and the pneumococcal conjugate vaccine carrier CRM197 were determined. Responses were compared based on the children's carriage status within the first 2 weeks of life. RESULTS: Within the first 2 weeks of life, 40% of the study children carried *Streptococcus pneumoniae*. Early carriage was associated with lower interferon-γ and interleukin 10 responses to pneumococcal proteins at age 9 months when children had not received pneumococcal conjugate vaccines during the study period. CONCLUSIONS: Early pneumococcal carriage may result in enhanced disease susceptibility and suboptimal vaccine responses by modulating the development of pneumococcal immune responses.

76 **Van Itterbeeck J, van Huis A.**
Environmental manipulation for edible insect procurement: a historical perspective.
J Ethnobiol Ethnomed 2012 Jan 21;8:3. doi: 10.1186/1746-4269-8-3.

Throughout history humans have manipulated their natural environment for an increased predictability and availability of plant and animal resources. Research on prehistoric diets increasingly includes small game, but edible insects receive minimal attention. Using the anthropological and archaeological literature we show and hypothesize about the existence of such environmental manipulations related to the procurement of edible insects. As examples we use eggs of aquatic Hemiptera in Mexico which are semi-cultivated by water management and by providing egg laying sites; palm weevil larvae in the Amazon Basin, tropical Africa, and New Guinea of which the collection is facilitated by manipulating host tree distribution and abundance and which are semi-cultivated by deliberately cutting palm trees at a chosen time at a chosen location; and arboreal, foliage consuming caterpillars in sub-Saharan Africa for which the collection is facilitated by manipulating host tree distribution and abundance, shifting cultivation, fire regimes, host tree preservation, and manually introducing caterpillars to a designated area. These manipulations improve insect exploitation by increasing their predictability and availability, and most likely have an ancient origin.

77 **Wand H, Lote N, Semos I, Siba P.**
Investigating the spatial variations of high prevalences of severe malnutrition among children in Papua New Guinea: results from geoadditive models.
BMC Res Notes 2012 May 11;5:288. doi: 10.1186/1756-0500-5-228.

BACKGROUND: Papua New Guinea (PNG) is one of the nutritionally vulnerable countries with a high death rate in children without showing a sign of improvement in the last two decades. The current study investigated the prevalences of stunting and wasting among a cohort of children in PNG and described the spatial features of these outcomes at the province and district levels. OBJECTIVE: To determine the prevalences of stunting and wasting among a cohort of children in PNG and to describe the spatial features of these outcomes at the province and district levels. METHODS: The health and nutritional status of 683 children aged less than five years was assessed using a cross-sectional multi-stage household survey conducted in the Eastern Highlands and Madang Provinces of PNG during the period of 2003-2004. Growth z-scores such as height-for-age and weight-for-age were generated using World Health Organization classifications. RESULTS: The prevalences of stunting (height-for-age z-score less than -2.0) were 59% and 49% in the Eastern Highlands and Madang respectively (p = 0.019). The prevalences of wasting (weight-for-height z-score less than -2.0) were 14% and 22% in Eastern Highlands and Madang respectively (p = 0.039); overall, only 21% of the children had completed all their scheduled vaccines and 95% of the caregivers had less than primary school education. Our statistical maps showed considerable spatial variations (province- and district-levels) with regard to stunting, wasting and other key factors within a relatively small geographical region.

CONCLUSIONS: The current study determined one of the highest prevalences of stunting among children in PNG. The impact of geographical locations on the risk factors must be recognized as it affects the epidemiology and intervention coverage.

78 **Wardlow H.**
The task of the HIV translator: transforming global AIDS knowledge in an awareness workshop.
Med Anthropol 2012;31(5):404-419. doi: 10.1080/01459740.2012.661002.

The globalization of standardized knowledge about HIV and AIDS depends in part on local AIDS awareness educators who receive training from national and international organizations and then, ideally, disseminate what they have learned. In this article I analyze textual and observational data from a five-day introductory AIDS awareness workshop in rural Papua New Guinea. Although the instructor adhered to the handbook provided by the National AIDS Council for much of the information, she departed from it significantly when informing participants about the "root causes" of HIV's spread and in giving them advice about prevention. I explicate where her extratextual knowledge came from as well as its overall message to target audiences. I suggest that textual silences in AIDS awareness handbooks can motivate local HIV translators to embark on a kind of semiosis – the ongoing production of new, hybrid knowledge about HIV.

79 **Westcott M, Martiniuk AL, Fowler RA, Adhikari NK, Dalipanda T.**
Critical care resources in the Solomon Islands: a cross-sectional survey.
BMC Int Health Hum Rights 2012 Mar 1;12:1. doi: 10.1186/1472-698X-12-1.

BACKGROUND: There are minimal data available on critical care case-mix, care processes and outcomes in lower and middle income countries (LMICs). The objectives of this paper were to gather data in the Solomon Islands in order to gain a better understanding of common presentations of critical illness, available hospital resources, and what resources would be helpful in improving the care of these patients in the future. METHODS: This study used a mixed methods approach, including a cross sectional survey of respondents' opinions regarding critical care needs, ethnographic information and qualitative data. RESULTS: The four most common conditions leading to critical illness in the Solomon Islands are malaria, diseases of the respiratory system including pneumonia and influenza, diabetes mellitus and tuberculosis. Complications of surgery and trauma less frequently result in critical illness. Respondents emphasised the need for basic critical care resources in LMICs, including equipment such as oximeters and oxygen concentrators; greater access to medications and blood products; laboratory services; staff education; and the need for at least one national critical care facility. CONCLUSIONS: A large degree of critical illness in LMICs is likely due to inadequate resources for primary prevention and healthcare; however, for patients who fall through the net of prevention, there may be simple therapies and context-appropriate resources to mitigate the high burden of morbidity and mortality. Emphasis should be on the development and acquisition of simple and inexpensive tools rather than complicated equipment, to prevent critical care from unduly diverting resources away from other important parts of the health system.

INDEX TO THE PAPUA NEW GUINEA MEDICAL JOURNAL

2010-2011 (Vol. 53-54)

AUTHOR INDEX

(* = Editorial)

SUBJECT AND PLACE-NAME INDEX

2010-2011 (Vol. 53-54)

(* = Editorial)

REFEREES 2010-2011

To maintain its standards the Journal is dependent on the willingness and dedication of its referees, colleagues who review all papers submitted to the Editor for publication and make the Journal's peer review system a reality.

We on the editorial staff recognize that we could not function without our referees (or reviewers). Some papers submitted to the Journal are accepted with little change and some are rejected (but only after 2 referees have independently concurred in this opinion). However, the majority of papers are made acceptable only after considerable revision, following the reports of the referees. In most cases this entails a great deal of work on the part of each referee. On occasions, other colleagues are consulted about specific matters related to a submitted paper, to improve or correct it before publication.

We acknowledge the help of the following colleagues who have contributed reports on papers which were published in the Journal - or rejected - during the period 2010-2011. Many have undertaken this task more than once, some many times. We thank them all for their essential contribution to the Journal. We apologize for any omissions: since each year we have a focus issue with a guest editor, the work of some referees may not have come to our attention.

Editorial Staff

Michael Alpers
Apeawusu Amoa
Trevor Duke
Manuel Hetzel
Francis Hombhanje
John Kaldor
Jerzy Kuzma
William Lagani
Deborah Lehmann
Glen Mola
William Pomat
Stephen Rogerson
Wila Saweri
Goa Tau
Nakapi Tefuarani
Victor Temple
Andrew Vallely
John Vince
David Watters
Maxine Whittaker
Tony Williams
Peter Zimmerman

Papua New Guinea Institute of Medical Research Monograph Series

ISSN 0256 2901

1. Growth and Development in New Guinea. A Study of the Bundi People of the Madang District.
   L.A. Malcolm. ISBN 9980 71 000 4, 1970, 105p.
2. Endemic Cretinism.
   B.S. Hetzel and P.O.D. Pharoah, Editors. ISBN 9980 71 001 2, 1971, 133p.
3. Essays on Kuru.
   R.W. Hornabrook, Editor. ISBN 9980 71 002 0 (also 0 900848 95 2), 1976, 150p.
4. The People of Murapin.
   P.F. Sinnett. ISBN 9980 71 003 9 (also 0 900848 87 1), 1977, 208p.
5. A Bibliography of Medicine and Human Biology of Papua New Guinea.
   R.W. Hornabrook and G.H.F. Skeldon, Editors. ISBN 9980 71 004 7, 1977, 335p. (with 1976 Supplement, 36p.)
6. Pigbel. Necrotising Enteritis in Papua New Guinea.
   M.W. Davis, Editor. ISBN 9980 71 005 5, 1984, 118p.
7. Cigarette Smoking in Papua New Guinea.
   D.E. Smith and M.P. Alpers, Editors. ISBN 9980 71 006 3, 1984, 83p.
8. Village Water Supplies in Papua New Guinea.
   D.E. Smith and M.P. Alpers, Editors. ISBN 9980 71 007 1, 1985, 94p.
9. The Health of Women in Papua New Guinea.
   Joy E. Gillett. ISBN 9980 71 008 X, 1990, 180p.
10. National Study of Sexual and Reproductive Knowledge and Behaviour in Papua New Guinea.
    The National Sex and Reproduction Research Team and Carol Jenkins. ISBN 9980 71 009 8, 1994, 147p.
11. Childhood in Papua New Guinea.
    H. Sheils Fenbury, Editor. ISBN 9980 71 012 8, 2009, 149p.

Monographs 1-5 are case-bound, 6-11 are paperbacks.

Monographs may be obtained from
The Librarian,
Papua New Guinea Institute of Medical Research
PO Box 60, Goroka, EHP 441,
Papua New Guinea

Cost of each Monograph is K20 plus postage.

Applications for free copies of any monograph should be sent to the Director at the above address.

	Postage and Handling (PNG Kina)			
	AIRMAIL			
	Within PNG	**Zone 1**	**Zone 3/4**	**Zone 6**
1,2,10,11	10.00	20.00	60.00	75.00
3,4,5	20.00	40.00	90.00	105.00
6,7,8,9	5.00	10.50	17.50	17.50

K=PGK=Kina. Please make payment in Kina. If payment is made in any other currency, please add sufficient funds to cover all bank charges.

THE MEDICAL SOCIETY OF PAPUA NEW GUINEA

Society Membership and Journal Subscription

Membership of the Medical Society of Papua New Guinea is open to all health workers whether resident in Papua New Guinea or overseas. Members of the Society receive four issues of the Papua New Guinea Medical Journal each year. The Society organizes an annual symposium and other activities.

Membership dues are:-

Papua New Guinea residents:
Members – K150
Associate (Student) Members – K20
Overseas residents: K200; AU$120; US$120

I wish to join the Medical Society of Papua New Guinea as a

Full Member ☐

Please indicate your category

Medical Officer	[ ]
Scientific Officer	[ ]
Pharmacist	[ ]
Health Extension Officer	[ ]
Nursing Officer	[ ]
Laboratory Technologist	[ ]
Radiographer	[ ]
Social Health Worker	[ ]
Other (Please specify)	[ ]

OR a Student Member ☐
(for full-time students)

Medical Student	[ ]
Other Student (Please specify)	[ ]

I enclose my membership fee of

K……..for the year(s)…….....

Name: …….....

Title: …….....

Address: …….....

…….....

…….....

Telephone: …….....

Fax: …….....

Email: …….....

(Forward to the Membership Secretary, Medical Society of Papua New Guinea, PO Box 60, Goroka, EHP 441, Papua New Guinea)

INFORMATION FOR AUTHORS

The Papua New Guinea Medical Journal invites submission of original papers and reviews on all aspects of medicine. Priority will be given to articles and subjects relevant to the practice of medicine in Papua New Guinea and other countries in the South Pacific.

Manuscripts are accepted for publication only with the understanding that they have not been published nor submitted for publication elsewhere. All manuscripts will be sent out for referees' comments as part of the peer review process.

Original Articles: Reports of original and new investigations or contributions.

Brief Communications and Case Reports: Contents similar to that of original articles but text should be no more than a total of 4 Journal pages including all figures and tables.

Reviews: Critical analysis of previously collected and published information.

Letters: Short reports of clinical experience or topics of interest. Text should not exceed 2 pages of the Journal.

Other types of manuscript may also be accepted for publication at the Editor's discretion.

Submitted manuscripts should conform to the instructions set out below. Manuscripts not conforming to these instructions will be returned.

MANUSCRIPTS

Submit the original with a virus-free electronic copy on disk as a word document or send by email to the Editorial Office. All sections including text, references, tables and legends should be in double spacing. Manuscripts should not be right justified. Each paper should include an informative Summary, Introduction, Patients/Materials and Methods, Results, Discussion and References. The title page should include the title, full names of all authors, names and addresses of institutions where the work has been done and full present address of the first or corresponding author.

References should be in the Vancouver style and include all authors. All references should be checked against the original source. Sample references are shown below.

3 **Garner PA, Hill G.** Brainwashing in tuberculosis management. *PNG Med J* 1985;28:291-293.

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.

ILLUSTRATIONS

Tables and figures should be prepared on separate pages. Figures should be sent as separate jpeg or tiff images. Do not paste the images into Word. Photographs should be glossy prints, either 7 cm or 14.5 cm in width. Photomicrographs should have internal scale markers. Each table should have a heading and footnotes which make it understandable without reference to the text. Each figure should have a legend; figure legends should be typed together on a separate sheet.

Abbreviations: Standard abbreviations and units should be used.

Drug Names: Generic names of drugs should be used.

Orthography: The Shorter Oxford English Dictionary is followed.

EDITORIAL MAIL

Manuscripts and other editorial communications should be forwarded to:

The Editor,
Papua New Guinea Medical Journal,
PO Box 60, Goroka, EHP 441,
Papua New Guinea
Email: pngmedj@pngimr.org.pg

SUBSCRIPTIONS AND ADVERTISEMENTS

Communications relating to advertisements or subscriptions should be addressed to the Journal as above. Matters related to the Society should be addressed to the Medical Society of Papua New Guinea, PO Box 6665, Boroko, NCD 111, Papua New Guinea.

Subscriptions: Members of the Medical Society of Papua New Guinea receive the Journal as part of their annual subscription. Others may subscribe and should contact the subscription secretary for a price.

CONTENTS