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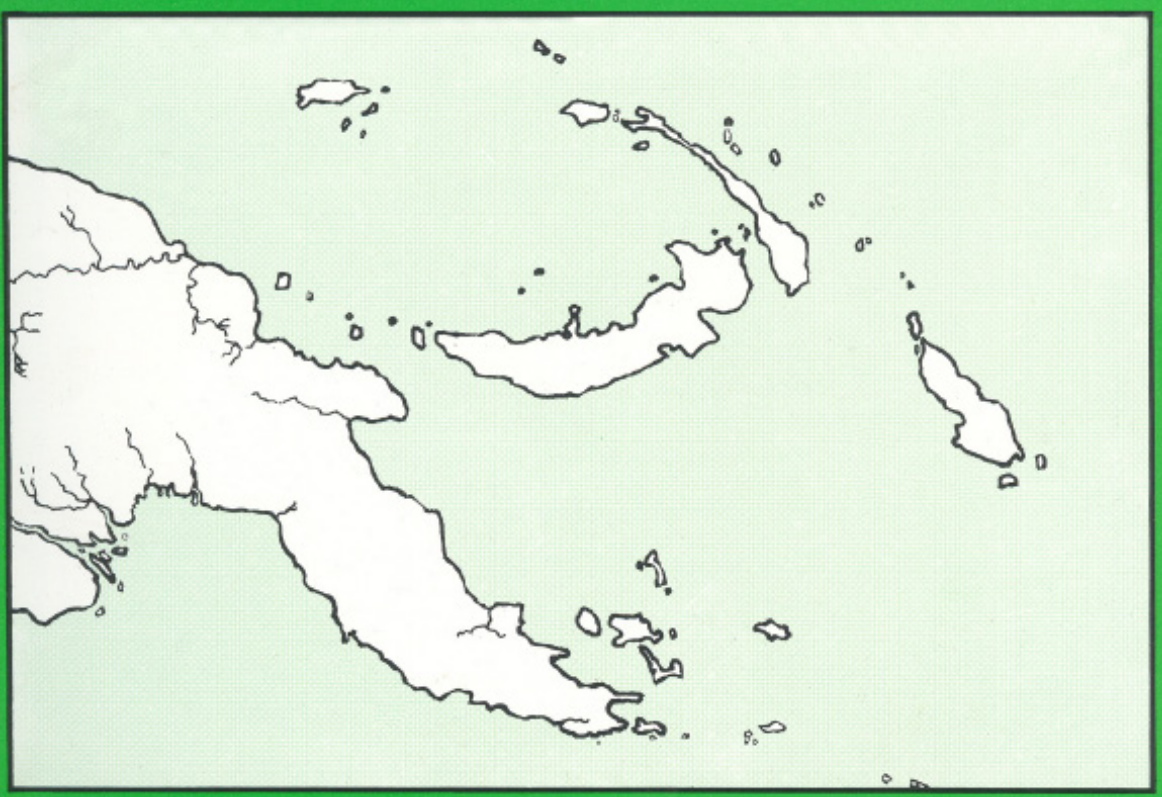

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EDITORIAL

Acute bacterial meningitis in Papua New Guinea: new treatment guidelines in response to increasing antibiotic resistance

The latest versions of the Papua New Guinea (PNG) standard treatment guidelines for children (1) and adults (2) herald a number of changes in the management of bacterial infections. A key change is a move away from chloramphenicol (CMP) to ceftriaxone, a third-generation cephalosporin, for the treatment of acute bacterial meningitis (ABM), a condition associated with substantial mortality and morbidity in PNG (3,4).

On the face of it, this seems like a reactive policy change made to counter rising CMP resistance in the organisms responsible for the majority of ABM in PNG. But such a change also highlights the benefits of PNG-specific clinical research and demonstrates the ongoing importance of functioning laboratory services both for patient care and as part of a coordinated surveillance network. Because microbiology services are not routinely available in PNG there may be some health sector risks associated with the wider availability of third-generation cephalosporins like ceftriaxone, particularly in the context of increasing antimicrobial resistance worldwide (5).

Treatment protocols for acute bacterial meningitis depend on local epidemiology, antibiotic resistance patterns, the coverage and composition of vaccination schedules and the availability and cost of antibiotics (6). In PNG, *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae* (SP) account for the majority of ABM (4,7,8). The Hib vaccine was incorporated in the expanded program of immunization (EPI) in 2008 and pneumococcal vaccination is due to be implemented within the next 5 years. Although Hib immunization has been shown to reduce ABM due to Hib in other countries, the short-term effectiveness in PNG may be diminished by poor vaccination coverage throughout much of the country. Therefore the antibiotic susceptibility patterns for these organisms will have an important influence on treatment protocols for some time yet. However, as in many other resource-poor settings, bacteriology services and data on antimicrobial susceptibility in PNG are limited.

Out with chloramphenicol, in with ceftriaxone

Based on high-quality clinical and pharmacokinetic studies performed by Frank Shann and colleagues, most PNG health facilities have used CMP as first-line treatment for ABM since the 1980s (9,10). In 2005, based on a CMP resistance rate of 21% in Hib isolates (11), the eighth edition of the PNG standard treatment guidelines incorporated ceftriaxone for treatment of young children with ABM (12). In the intervening 6 years, data from Port Moresby (unpublished – T. Duke, personal communication) and more recently Madang (13) have indicated CMP resistance in 90-100% of Hib isolates. High resistance rates clearly required a change in antibiotic protocols for Hib, but recent data from the same study site also show that the susceptibility of SP isolates to CMP has been declining over the last 15 years (13). When compared to isolates obtained in the 1990s (7), the median minimum inhibitory concentration (MIC) of SP isolates from recent studies has doubled (D. Lehmann, personal communication). Over 40% had an MIC ≥4 µg/ml, a level associated with a low chance of attaining appropriate plasma drug concentrations in the body after standard treatment doses of CMP (13).

Ceftriaxone is a third-generation cephalosporin widely used since the 1980s. Twice-daily dosing and excellent penetration into the cerebrospinal fluid (CSF) make it a good candidate for the treatment of ABM, especially since the cost has fallen to between $1-2 per day. Although all Hib and SP isolates are currently susceptible to ceftriaxone (13), this may be temporary. In countries where ceftriaxone is used, resistance occurs rarely in Hib isolates, but more commonly in SP (1-9%) (5,14). Multiresistance to antibiotics is a worldwide trend and the many factors that can promote antibiotic resistance are present in PNG, including widespread empirical use of antibiotics, counterfeit medications,

overcrowding and minimal infection control measures in health care facilities. All of these could promote the development of resistance to ceftriaxone in PNG, as recently documented in a *Klebsiella pneumoniae* outbreak at the Port Moresby General Hospital Special Care Nursery (15).

One strategy to minimize the chance of widespread ceftriaxone resistance developing would be to improve the clinical diagnosis of ABM so that treatment can be targeted to those patients most likely to have the disease. Clinical signs such as neck stiffness, Kernig's and Brudzinski's signs and bulging fontanelle in very young children have diagnostic utility for ABM (16). In addition, following a single febrile convulsion a child without any other signs of meningism has a very low likelihood of ABM and can be observed without the need for lumbar puncture or empirical ceftriaxone (8).

More importantly, adjunctive laboratory diagnostics can substantially improve diagnostic precision for ABM. Microscopic examination of thick blood films for malaria and CSF examination represent the most useful laboratory tests in a patient suspected of having ABM. Cerebrospinal fluid examination should be done whenever ABM is considered a likely diagnosis unless there are contraindications to lumbar puncture. Our recent studies (8,13,16-18) performed in coastal PNG show that, when compared to the gold standard of culture-proven ABM, a CSF white cell count >20 cells/µl has 100% sensitivity and 94% specificity. Microscopy of CSF is simple and cheap, requiring only a microscope, counting chamber and crystal violet stain, and could easily be incorporated into the training program for Rural Laboratory Assistants (RLAs) currently underway in PNG through the National Department of Health, Global Fund and Divine Word University, Madang. Diagnostic tests for malaria can also aid in the diagnosis of ABM. For example, in malaria-endemic areas, the presence of malaria parasites on microscopic examination of thick blood films suggests very strongly that ABM is not present (16). It is not yet clear, however, how rapid diagnostic tests for malaria can be incorporated into algorithms for ABM.

Finally, we believe that an up-scaled RLA program will augment surveillance networks that are necessary for effective health planning, not only to counter increasing antibiotic resistance in pathogens already known to be present in PNG but also for the inevitable arrival of pan-resistant Gram-negative organisms prevalent elsewhere in Asia (19). This eventuality will mark a major pivot point for health funders. It is not clear how the PNG health system can afford broad-spectrum and last-line antibiotics in a setting where health spending per capita on pharmaceuticals is one of the lowest worldwide. The best tools we have at the moment are to encourage the judicious use of antibiotics, standard infection control interventions and promotion of a countrywide antibiotic resistance surveillance network.

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Vitamin A status of pre-school-age children aged 6 to 59 months in the National Capital District, Papua New Guinea

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SUMMARY

Assessing the vitamin A status among pre-school-age children is essential for evaluating the magnitude and public health status of vitamin A deficiency in a population. This cross-sectional study assessed the vitamin A status of children aged 6 to 59 months resident in the National Capital District (NCD), Papua New Guinea. Children attending the Children's Outpatient Clinic at Port Moresby General Hospital participated in this study. Informed consent was obtained from parents before using blood samples from their children. Assay of plasma retinol was carried out using the 'Clin-Rep' complete kit for assay of vitamins A and E in plasma by high performance liquid chromatography (HPLC). A commercial enzyme immunoassay kit was used to assay C-reactive protein (CRP) in plasma. Of the 132 children in the study 108 (82%) had received vitamin A capsules. The median plasma retinol concentration of the 132 children was 0.98 µmol/l and the interquartile range 0.65-1.38 µmol/l. Of the 132 children, 35 (27%) had a plasma retinol concentration below 0.70 µmol/l. 75 children (57%) had normal plasma CRP levels and in 57 (43%) the CRP levels were elevated. The median plasma retinol concentration of the children with normal plasma CRP was 1.19 µmol/l and the interquartile range 0.93-1.50 µmol/l. The prevalence of vitamin A deficiency (VAD) in the children with normal plasma CRP was 11%, indicating a moderate public health problem. 74 (56%) males and 58 (44%) females were included in the study. The prevalence of VAD in the male and female children with normal plasma CRP was 14% and 8%, respectively, indicating a moderate public health problem among the male children and a mild public health problem among the female children. The prevalence of subclinical (mild to moderate) and marginal VAD among the children with and without elevated CRP strongly suggests the need for continuous monitoring of the vitamin A status of the vulnerable groups in NCD.

Introduction

Vitamin A (retinol) is required for regulation of the visual cycle and haematopoiesis, for differentiation and maintenance of the biological integrity of epithelial tissues, for mucin production, and for regulation of cell-mediated immunity and humoral antibody responses (1-4). The consequences of vitamin A deficiency (VAD) are manifold. VAD is among the 'top 10' risk factors contributing to the global burden of disease among pre-school-age children in resource-limited countries (1-6). According to recent World Health Organization (WHO) estimates, about 0.2 million deaths among pre-school-age children were due to VAD, with most occurring in children with subclinical (mild to moderate) VAD (1,2). Thus the need for continuous monitoring of this vulnerable group in the

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community cannot be overemphasized.

The vitamin A status of individuals in target populations can be assessed by quantification of their plasma retinol concentrations, using high performance liquid chromatography (HPLC) (7-10). However, the carrier protein for plasma retinol, ie, retinol-binding protein, is one of the acute phase reactants that decrease during inflammation, infection and trauma (3-6). As a consequence, plasma retinol concentrations may not accurately reflect the vitamin A status of populations with high prevalence of clinical or subclinical inflammation (3-6). One of the recommended procedures for improving the accuracy of interpreting plasma retinol data is to measure the plasma concentration of C-reactive protein (CRP), which is an indicator of both inflammation and infection (2-6,11). The plasma CRP results can then be used to stratify the plasma retinol data according to the health status of individuals in the target population (3-5).

According to the recommended cut-off points, plasma retinol concentrations below 0.70 µmol/l indicate VAD and concentrations between 0.70 and 1.05 µmol/l indicate marginal VAD (1,2,4,9,10). Furthermore, VAD can be characterized as a severe, moderate or mild public health problem, when the plasma retinol concentration is below 0.70 µmol/l in over 20%, 10% to 20% or 2% to 10% of the target population, respectively (1,2,4,9,10).

Published data on vitamin A status of pre-school-age children in Papua New Guinea (PNG) is scanty (12-14). Some studies conducted in hospitals in several provinces indicated a prevalence of clinical xerophthalmia of 0.6% to 1.0% in pre-school-age children (12-14). A mini-survey of vitamin A status of pre-school-age children in coastal and highland provinces in PNG detected no clinical signs of VAD (13,14). The authors reported a prevalence of subclinical VAD of 9.1%, 10% and 15% in children in Western Highlands, Madang and Sepik Provinces, respectively (13,14). In the National Nutrition Survey conducted between 1996 and 1998, night-blindness was reported in 0.9% of pre-school-age children (13,14). There are, however, no data to indicate the vitamin A status of pre-school-age children in the National Capital District (NCD), PNG.

In an effort to prevent VAD among pre-school-age children in PNG, the distribution of vitamin A capsules was included as part of the expanded program on immunization (EPI) in 2002 (13,14). According to the PNG National Department of Health (NDoH) protocol, the first dose of vitamin A is given together with the first measles vaccination at six months, and the second dose is given about six months later (13,14). Thus vitamin A supplementation (VAS) of pre-school-age children in PNG has been going on for several years. The NDoH protocol for supplementation includes monitoring of vitamin A status in areas already covered by supplementation programs. Recent reports from the PNG National Nutrition Survey carried out in 2005 (PNG NNS 2005) indicate a prevalence of moderate to severe VAD among pre-school-age children in the four regions of PNG (15). The PNG NNS 2005 did not provide data on the vitamin A status of pre-school-age children in the various provinces and districts in PNG (15).

The major objective of this study was to assess the vitamin A status of pre-school-age children resident in NCD, which is one of the districts in PNG that has been covered by the vitamin A supplementation program.

Subjects and Methods

Study site

The study was conducted between April and September 2008 in the NCD, which is one of the districts in the Southern Region in PNG. The NCD is the incorporated area around Port Moresby, the capital of PNG. Because of the difficulty in obtaining blood samples from healthy pre-school-age children in the households in NCD, the Children's Outpatient Clinic at Port Moresby General Hospital (PMGH) was selected as the specific study site. The PMGH is the major public general, specialist and reference hospital in NCD and PNG; it also serves as the teaching hospital for the School of Medicine and Health Sciences (SMHS), University of Papua New Guinea (UPNG).

Sample size

The sample size was calculated using a design effect of one, relative precision of 10%, and assumed prevalence rate of 20%, with a confidence level of 95% (16). The sample size of about 180 pre-school-age children

was considered adequate for a study with a predicted non-response rate of 25% (16).

Study design and sampling

This was a hospital outpatient-based cross-sectional study. All children aged between 6 and 59 months from whom blood was being collected for various reasons were enrolled in the study. Children with significant illness, those admitted to the ward and those who were not resident in NCD were excluded from the study. Further selection was by parental consent.

Collection of blood samples and data by questionnaire

About 0.3 ml of venous blood was transferred into an EDTA-coated microtainer, which was immediately put into a microtainer-box wrapped with aluminum foil for protection from light. The box was then put into a cool-box, kept at 4-8ºC in the field and during transport to the Micronutrient Laboratory (MNL) in the SMHS, UPNG. The blood samples were centrifuged, after which aliquots of plasma were kept frozen at −70ºC. A self-designed pretested questionnaire was used to collect demographic and other information, including the vitamin A supplementation history of each child.

Sample analysis and quality control

All reagents, including the internal standard, were of analytical grade and were components of the 'Clin-Rep' complete kit for assay of vitamins A and E in plasma by HPLC (17). A special reverse phase column, which was a component in the 'Clin-Rep' complete kit, was used to measure the concentration of vitamin A as retinol (17). The flow rate of the mobile phase was set at 1.5 ml/minute. The operating HPLC system used was the Waters Empower 2.0 software, configured for analysis of retinol in plasma. The wavelength of the HPLC detector was set at 325 nm (17).

The 'Levy-Jennings' charts and 'Westgard' rules were used for monitoring the internal bench quality control (QC) of the HPLC output data. Four levels of 'Clin-Chek' plasma retinol control samples were used for QC monitoring (17). The intra-assay coefficient of variation (CV) for each of the four QC samples ranged from 4.0% to 7.5%. The percent recovery of plasma retinol was 95-98.5%.

The C-reactive protein in plasma was assayed using a commercial enzyme immunoassay kit (QuikRead – 101 Orion Diagnostica, Finland) (11). Inter- and intra-assay coefficients of variation for CRP were measured, using the controls provided by the manufacturer. The intra-assay CV was 3.5% and the inter-assay CV 4.0%.

Data analysis and interpretation

Data analysis was carried out using the Statistical Package for Social Sciences (SPSS) Version 11 for Windows. The Shapiro-Wilks test was used to assess normality of data. The Wilcoxon rank sum test, Mann-Whitney U test, chi-squared (Fisher's exact test) and Student's t-test were used as appropriate. Correlations were determined by Spearman's rank correlation coefficient (ρ = rho).

For interpretation of the data in the present study, plasma retinol concentrations below 0.70 µmol/l and between 0.70 and 1.05 µmol/l were used to indicate VAD and marginal VAD, respectively (1,2,4,9,10). VAD levels of 2-10%, 10-20% and above 20% were used to indicate mild, moderate and severe public health problems, respectively (4,9,10). As recommended by the manufacturer (11), elevated CRP indicating inflammation was defined as CRP >8.0 mg/l.

Ethical clearance

Ethical clearance and approval for this study were obtained from the Ethical and Research Grant Committee in the SMHS, UPNG, the Medical Research Advisory Committee (MRAC) in the National Department of Health (MRAC No 08/28) and the PMGH. Participation was voluntary; oral and signed informed consents were obtained from the parents of each of the children. The blood samples used were only from children whose parents gave consent.

Results

Permission to include their child in the study was sought from 181 parents or guardians. Informed consent was obtained from 140, but permission to use the blood samples was obtained from only 132 (response rate 73%). This gave a non-response rate of 27%, which was higher than the predicted non-response

rate of 25% used for calculating the sample size.

Of the 132 mothers, 92 (70%) did not have their baby book with them at the time of data collection for this study. In these cases, the information obtained was based on the mother's recollection.

The median age of the study children was 16.0 months and the interquartile range (IQR) 10.3 to 24.0 months.

The distribution curve of the plasma retinol concentration for the study children was not normal, according to the Shapiro-Wilks test ($p < 0.001$, $df = 132$). Figure 1 shows the box plot of the plasma retinol concentrations. The median plasma retinol concentration was 0.98 µmol/l and the IQR was 0.65-1.38 µmol/l (Table 1).

Of the 132 children, 35 (27%) had a plasma retinol concentration below 0.70 µmol/l and 37 (28%) had a plasma retinol concentration between 0.70 and 1.05 µmol/l (Table 1). The Spearman correlation ($\rho = -0.519$) indicated a significant ($p = 0.01$) inverse relationship between the plasma retinol concentration and the plasma CRP level among the study children.

The 132 children were separated according to their plasma CRP levels. 75 (57%) of them had normal plasma CRP levels and in 57 (43%) the levels were elevated (CRP >8.0 mg/l).

The median age of the children with normal plasma CRP levels was 14.0 months (IQR = 9.0-19.0 months), while for those with elevated plasma CRP levels it was 19.0 months (IQR = 15.0-26.0 months). The difference in the mean age after log transforming the data was significant ($p = 0.018$).

The box plots in Figure 1 also represent the distributions of plasma retinol concentrations for the children with normal and elevated plasma CRP levels. The data were not normally distributed. Table 1 shows the medians and IQRs of the plasma retinol concentrations for children with normal and elevated plasma CRP levels. Statistical analysis, using the Mann-

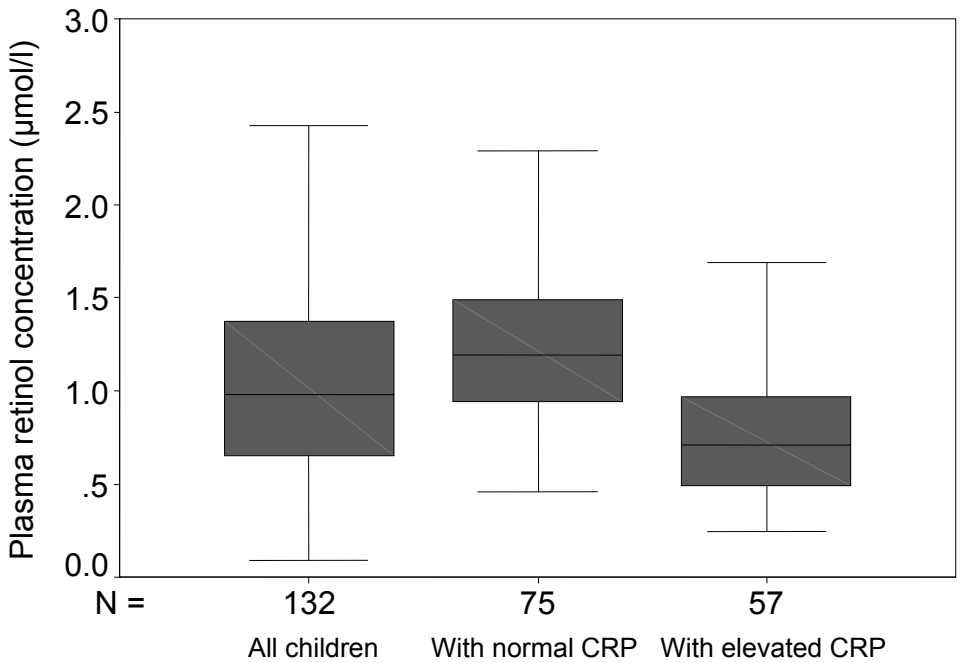

Figure 1. Box plots of plasma retinol concentration (µmol/l) for all the study children and for those with normal and elevated plasma C-reactive protein (CRP) levels.

TABLE 1

Plasma retinol concentration and percent below cut-off point that indicates vitamin A deficiency (VAD) for all the study children and for those with normal and elevated plasma C-reactive protein (CRP) levels

	All children (n = 132)	Children with normal CRP (n = 75)	Children with elevated CRP (n = 57)
Median retinol (µmol/l)	0.98	1.19	0.71
Interquartile range (µmol/l)	0.65-1.38	0.93-1.50	0.49-1.00
Mean retinol (µmol/l)	1.09	1.29	0.82
Standard deviation	0.61	0.64	0.43
95% CI (µmol/l)	0.98-1.19	1.15-1.44	0.70-0.93
Percent (number) with retinol between 0.70 and 1.05 µmol/l (marginal VAD)	28.0% (37)	26.7% (20)	29.8% (17)
Percent (number) with retinol <0.70 µmol/l (VAD)	26.5% (35)	10.7% (8)	47.4% (27)

CI = confidence interval

Whitney U test, indicated that the plasma retinol concentrations for the children with normal plasma CRP levels were significantly ($p < 0.001$) higher than for those with elevated plasma CRP levels.

The plasma retinol concentration was below 0.70 µmol/l in 11% of the 75 children with normal plasma CRP levels and 27% of them had a plasma retinol concentration between 0.70 and 1.05 µmol/l.

A significant inverse relationship ($\rho = -0.455$, $p = 0.01$) was obtained between plasma retinol concentration and plasma CRP level for children with elevated plasma CRP levels.

In order to assess the vitamin A supplementation coverage among the population in this study, each mother was asked whether their child had ever received vitamin A capsules. According to their recall, 108 (82%) of the 132 mothers responded in the affirmative, and 24 (18%) "did not remember" whether their children had ever received vitamin A capsules (Table 2). There was no significant ($p > 0.05$) difference in the plasma retinol concentrations between these two groups of children. However, the plasma retinol concentration was significantly ($p = 0.038$) higher in the children with normal CRP in the 'affirmative' group than in their counterparts in the 'did not remember' group. In addition, plasma retinol concentration was below 0.70 µmol/l in 7% of those with normal plasma CRP in the 'affirmative' group compared to 22% of their counterparts in the 'did not remember' group (Table 2).

Further analysis of the data indicated that 31 (29%) of the 108 children in the 'affirmative' group received a vitamin A capsule within the previous six months. This information was further confirmed in the baby book of each of these children. Table 2 shows the plasma retinol concentration of this group of children. The plasma retinol concentration in the children with normal plasma CRP was significantly higher ($p = 0.001$) than in those with elevated plasma CRP. In addition, 4% of the children with normal plasma CRP had a plasma retinol concentration below 0.70 µmol/l compared to 57% of their counterparts with elevated plasma CRP.

Of the 108 mothers in the 'affirmative' group 37 (34%) indicated that their children had received vitamin A capsules on two different occasions since birth. This information was

TABLE 2

PLASMA RETINOL CONCENTRATION OF STUDY CHILDREN GROUPED ACCORDING TO THEIR REPORTED HISTORY OF VITAMIN A SUPPLEMENTATION

	Affirmative, received vitamin A capsule			Did not remember ever receiving vitamin A capsule			Received vitamin A capsule within the previous 6 months			Received vitamin A capsule twice since birth		
	All	**Normal CRP**	**Elevated CRP**	**All**	**Normal CRP**	**Elevated CRP**	**All**	**Normal CRP**	**Elevated CRP**	**All**	**Normal CRP**	**Elevated CRP**
Percent (number)	81.8% (108)	52.8% (57)	47.2% (51)	18.2% (24)	75% (18)	25% (6)	28.7% (31)	77.4% (24)	22.6% (7)	34.3% (37)	73.0% (27)	27.0% (10)
Median retinol (µmol/l)	0.99	1.28	0.66	0.93	0.93	1.11	1.08	1.17	0.61	1.07	1.33	0.68
Interquartile range (µmol/l)	0.62-1.37	1.00-1.28	0.49-0.94	0.75-1.48	0.72-1.44	0.70-1.81	0.97-1.42	1.00-1.47	0.49-0.97	0.59-1.35	1.07-1.57	0.49-0.99
Mean retinol (µmol/l)	1.07	1.36	0.76	1.14	1.12	1.21	1.30	1.47	0.73	1.04	1.34	0.73
Standard deviation	0.62	0.66	0.37	0.57	0.56	0.66	0.82	0.86	0.28	0.48	0.45	0.30
95% CI (µmol/l)	0.96-1.19	1.18-1.53	0.65-0.86	0.90-1.38	0.84-1.40	0.52-1.90	1.00-1.60	1.10-1.83	0.47-0.99	0.81-1.26	1.02-1.66	0.53-0.95
Percent (number) with retinol <0.70 µmol/l (VAD)	27.8% (30)	7.0% (4)	51.0% (26)	20.8% (5)	22.2% (4)	16.7% (1)	16.1% (5)	4.2% (1)	57.1% (4)	16.2% (6)	3.7% (1)	50.0% (5)
Percent (number) marginal VAD	26.9% (29)	22.8% (13)	31.4% (16)	37.5% (9)	38.9% (7)	33.3% (2)	25.8% (8)	25.0% (6)	28.6% (2)	8.1% (3)	-	30.0% (3)

CRP = C-reactive protein; CI = confidence interval; VAD = vitamin A deficiency; marginal VAD = retinol level between 0.70 and 1.05 µmol/l

confirmed in the baby book of 9 of the 37 children. The plasma retinol concentration of this group of children is presented in Table 2. The plasma retinol concentration for those with normal plasma CRP was significantly ($p = 0.002$) higher than for those with elevated CRP.

In all instances, significant ($p < 0.05$) inverse relationships were obtained between plasma retinol concentrations and plasma CRP levels for children with elevated plasma CRP levels.

Of the 108 mothers in the 'affirmative' group, 40 (37%) could not state the exact number of times their children had received vitamin A capsules.

For further analysis of the supplementation data (Table 3), the 132 children were separated into three age groups. There were 37 (28%) in the 6 to 11 months age group, 65 (49%) in the 12 to 24 months age group and 30 (23%) in the over 24 months age group.

The results show that 29 (78%) of the 37 children in the 6 to 11 months age group had received a vitamin A capsule within the previous six months. The age range of the remaining 8 children that had not received any vitamin A capsule was 6 to 8 months (plasma CRP was elevated in these children).

Our results also show that 54 (83%) of the 65 children in the 12 to 24 months age group and 25 (83%) of the 30 children in the over 24 months age group had received a vitamin A capsule at least once. Two of the children in the 12 to 24 months age group received a vitamin A capsule within the previous six months, as was recorded in their baby books.

The plasma CRP levels were normal in 78%, 52% and 40% of the children in the 6 to 11 months, 12 to 24 months and over 24 months age groups, respectively. The plasma retinol concentration and percent below the cut-off points that indicate marginal VAD and VAD for all the children and for those with normal plasma CRP in the three age groups are presented in Table 3. The plasma retinol concentration of the children with normal plasma CRP in the over 24 months age group was significantly lower than that for the children with normal plasma CRP in the 6 to 11 months ($p = 0.035$) and 12 to 24 months ($p = 0.019$) age groups.

The plasma retinol concentrations were significantly higher ($p < 0.05$) in the children with normal plasma CRP than in their counterparts with elevated plasma CRP in the corresponding age groups.

The plasma retinol concentration was below 0.70 µmol/l in 7%, 9% and 25% of the children with normal plasma CRP in the 6 to 11 months, 12 to 24 months and over 24 months age groups, respectively.

74 (56%) of the 132 children were males with a median age of 17.0 months (IQR = 12.0-25.0 months) and 58 (44%) were females with a median age of 14.0 months (IQR = 8.8-19.0 months). The age of the male children was significantly higher ($p = 0.018$) than that of the female children.

The box plots of the plasma retinol concentrations for all the male and female children are presented in Figure 2.

The median and IQR plasma retinol concentrations for the male children were 0.93 µmol/l and 0.65-1.32 µmol/l, respectively (Table 4). The corresponding values for the female children were 1.08 µmol/l and 0.71-1.43 µmol/l. There was no significant ($p = 0.091$) difference between the plasma retinol concentrations of the male and female children. The plasma retinol concentration was below 0.70 µmol/l in 28% of the male and in 24% of the female children. The Spearman correlation indicated a significant inverse relationship between the plasma retinol concentration and plasma CRP level for the male ($\rho = -0.414$; $p = 0.01$) and the female ($\rho = -0.617$; $p = 0.01$) children.

Results for the male and female children were separated according to their plasma CRP levels. Of the 74 male children, 50% had normal and 50% had elevated plasma CRP levels. Of the 58 female children, 66% had normal and 34% had elevated plasma CRP levels. Figure 2 shows the box plots for the plasma retinol concentrations for these male and female groups. The medians and IQRs of the plasma retinol concentrations for the male and female children with normal and elevated plasma CRP levels are presented in Table 4. The table also shows the percent of children in each group with plasma retinol concentration below 0.70 µmol/l and those between 0.70 and 1.05 µmol/l.

TABLE 3

PLASMA RETINOL CONCENTRATION AND PERCENT BELOW CUT-OFF POINT THAT INDICATES VITAMIN A DEFICIENCY (VAD) FOR STUDY CHILDREN IN THE VARIOUS AGE GROUPS AND FOR THOSE WITH NORMAL PLASMA C-REACTIVE PROTEIN (CRP) LEVELS

	Children aged 6-11 months		Children aged 12-24 months		Children aged >24 months	
	All (n =37)	**Normal CRP (n = 29)**	**All (n = 65)**	**Normal CRP (n = 34)**	**All (n = 30)**	**Normal CRP (n = 12)**
Median retinol (µmol/l)	1.07	1.09	0.95	1.29	0.83	1.05
Interquartile range (µmol/l)	0.87-1.07	0.98-1.46	0.62-1.45	0.93-1.63	0.53-1.17	0.62-1.33
Mean retinol (µmol/l)	1.26	1.38	1.07	1.34	0.91	0.95
Standard deviation	0.77	0.81	0.54	0.50	0.45	0.43
95% CI (µmol/l)	1.00-1.51	1.07-1.69	0.94-1.21	1.16-1.51	0.74-1.07	0.68-1.23
Percent (number) with retinol between 0.70 and 1.05 µmol/l (marginal VAD)	32.4% (12)	34.5% (10)	24.6% (16)	23.5% (8)	33.3% (10)	25.0% (3)
Percent (number) with retinol <0.70 µmol/l (VAD)	16.2% (6)	6.9% (2)	30.8% (20)	8.8% (3)	30.0% (9)	25.0% (3)

CI = confidence interval

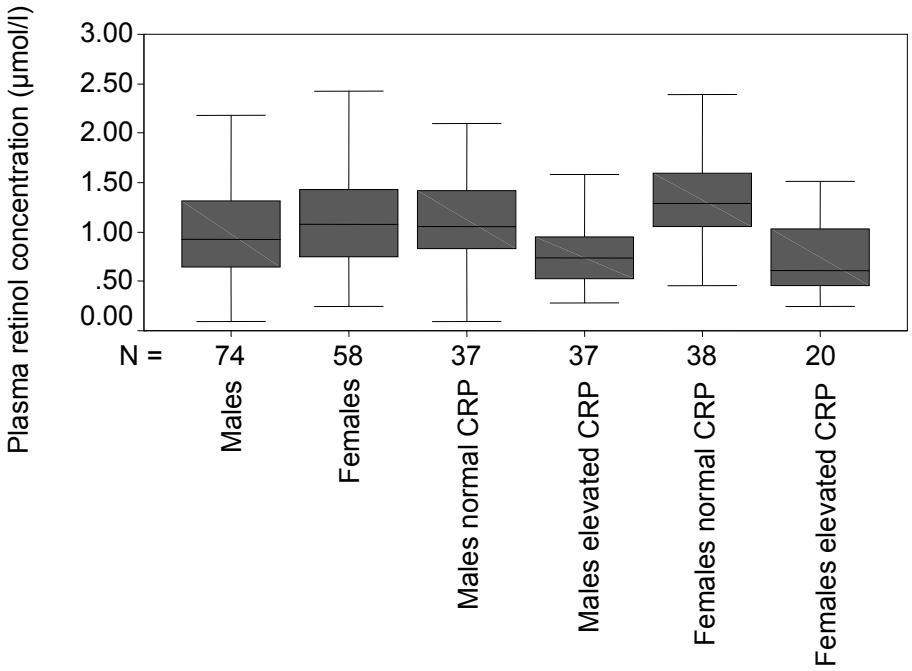

Figure 2. Box-plots of plasma retinol concentration (µmol/l) for all the male and female study children and for those with normal and elevated plasma C-reactive protein (CRP) levels.

The plasma retinol concentrations for the male children with normal plasma CRP was significantly (p = 0.001) higher than for those with elevated plasma CRP. A similar result (p = 0.001) was obtained for the female children.

No significant difference (p = 0.054) was obtained when the plasma retinol concentration for the male children with normal plasma CRP was compared with that of the females with normal plasma CRP.

Of the 37 male children with normal plasma CRP there were 14% with plasma retinol concentration below 0.70 µmol/l and 38% with plasma retinol concentration between 0.70 and 1.05 µmol/l. Of the 38 female children with normal plasma CRP only 8% had a plasma retinol concentration below 0.70 µmol/l and 16% had a plasma retinol concentration between 0.70 and 1.05 µmol/l.

The median and mean plasma retinol concentrations were higher, and the proportions with plasma retinol below 0.70 µmol/l were lower, in both the male and female children with normal plasma CRP levels than in their counterparts with elevated plasma CRP levels.

Discussion

The high non-response rate (27%) indicates some of the problems encountered by research projects that require collection of biological samples from 'apparently healthy' children. Higher non-response rates have been reported by others (18,19). Parents' awareness of the voluntary nature of their consent to the collection of biological samples from their children for the purpose of research may be one possible explanation for the negative response from some parents.

In the present study, VAD was prevalent in 27% of the study children. This was higher than the 9.1%, 10% and 15% prevalence reported respectively in children in Western Highlands, Madang and Sepik Provinces in PNG (13,14), but similar to the 25.6% prevalence recently

TABLE 4

Plasma retinol concentration and percent below cut-off point that indicates vitamin A deficiency (VAD) for all the male and female study children and for those with normal and elevated C-reactive protein (CRP) levels

	Male children			Female children		
	All (n = 74)	**Normal CRP (n = 37)**	**Elevated CRP (n = 37)**	**All (n = 58)**	**Normal CRP (n = 38)**	**Elevated CRP (n = 20)**
Median retinol (µmol/l)	0.93	1.06	0.73	1.08	1.29	0.61
Interquartile range (µmol/l)	0.65-1.32	0.82-1.44	0.52-0.96	0.71-1.43	1.05-1.61	0.43-1.08
Mean retinol (µmol/l)	0.99	1.13	0.85	1.21	1.47	0.76
Standard deviation	0.46	0.42	0.45	0.74	0.78	0.40
95% CI (µmol/l)	0.88-1.09	0.99-1.27	0.70-1.00	1.02-1.41	1.21-1.73	0.58-0.94
Percent (number) with retinol between 0.70 and 1.05 µmol/l (marginal VAD)	35.1% (26)	37.8% (14)	32.4% (12)	19.0% (11)	15.8% (6)	25.0% (5)
Percent (number) with retinol <0.70 µmol/l (VAD)	28.4% (21)	13.5% (5)	43.2% (16)	24.1% (14)	7.9% (3)	55.0% (11)

CI = confidence interval

reported for pre-school-age children in PNG (15) and within the 20.5% to 35.3% range of prevalence in the four regions of PNG (15).

The VAD prevalence in the present study was also higher than the 11.0% and 15.6% reported for pre-school-age children in Manisa and Izmir regions in Turkey (20,21), the 24.1% in Brazil (3) and the 7.8% to 15.75% in Beijing and Guizhou in China (22). However, it was lower than the 30.0%, 29.5%, 58.7%, 61.2% and 32.1% prevalence reported for pre-school-age children in Beijing, Nigeria, West Bengal in India, Republic of the Marshall Islands and Brazil, respectively (22-26).

Marginal VAD was prevalent in 28% of the study children. This was higher than the 16.8% and 23.2% reported for pre-school-age children in urban areas in Beijing, China (22), but lower than the 41.8% and 52.4% reported for the rural areas around Beijing (22).

Our results indicated a prevalence of VAD of 28% in the male and 24% in the female study children. These values were lower than the 60.3% and 62.0% prevalence of VAD reported for male and female pre-school-age children in West Bengal in India (24).

Marginal VAD was higher in the male (35%) than the female (19%) study children in NCD. Our findings support the observation by Benn et al. (27) that infant boys may be more vitamin A deficient than infant girls. These results did not reflect the plasma CRP levels in the children.

According to the recommended criteria (4,9,10), VAD should be characterized as a severe public health problem among pre-school-age children in NCD at the time of this study. However, this characterization was of concern because of the inverse correlation obtained between the plasma retinol concentration and plasma CRP level (Spearman $\rho = -0.519$, $p = 0.01$). The high percentage (43%) of study children with an elevated plasma CRP level indicates a high prevalence of subclinical infection. This figure, however, was lower than the 49.6% of pre-school-age children with an elevated plasma CRP level reported in the Republic of the Marshall Islands (25).

The prevalence of VAD in the study children with normal plasma CRP was 11%, which indicated a moderate public health problem. Children with an elevated plasma CRP had a much higher (47%) prevalence of VAD, which indicated a severe public health problem.

Our findings are consistent with recent scientific opinion, which increasingly suggests that the negative impact of subclinical infection on plasma retinol concentration may lead to overestimation of VAD (4-6).

The VAS coverage (82%) obtained in the present study was lower than the 83.1% and 96.0% reported for pre-school-age children in Ethiopia and Nepal, respectively, but higher than the 42.8% and 74.0% reported from Cambodia and the Welayta Zone in Ethiopia, respectively (28,29).

Our data indicate that the VAS coverage in NCD at the time of this study was 'on track' to achieve the WHO recommended coverage of approximately 80% of children aged 6-59 months within target populations (30). Despite this achievement, the VAS coverage (78%) among the younger (6 to 11 months) children was slightly lower than the 83% coverage obtained for the older children in the present study. This indicates the need for program planners to implement additional strategies to improve and sustain the VAS program among pre-school-age children in the NCD.

The prevalence of VAD (7%) and marginal VAD (23%) in the study children with normal plasma CRP in the VAS 'affirmative' group was significantly lower than the prevalence of VAD (22%) and marginal VAD (39%) in the study children with normal plasma CRP in the 'did not remember' VAS group. This tends to confirm the general observation that VAS is an effective intervention strategy for reducing the incidence of illness among children aged 6-59 months (3,5,28).

Our data also indicate that among the children in the VAS 'affirmative' group both VAD and marginal VAD were significantly associated with elevated plasma CRP levels.

Mild VAD was prevalent in the children with normal plasma CRP in the 6 to 11 months and 12 to 24 months age groups, comparable to the prevalence of severe VAD in the over 24 months age group. Marginal VAD was, however, more prevalent in the 6 to 11 months old children with normal plasma CRP than in the other two age groups. This indicates that the younger children are at greater risk

of developing moderate to severe VAD in the event of mild infection without a corresponding increase in the intake of vitamin A. These data underscore the need to further strengthen and expand the on-going VAS program in the NCD.

The prevalence of VAD in the male and female children with normal plasma CRP was 14% and 8%, which indicates moderate and mild public health problems, respectively.

The high prevalence of marginal VAD in the children with normal plasma CRP obtained in this study should be of concern to program planners, because, from the public health point of view, it indicates that a significant number of these children are at risk of developing VAD. This further indicates the urgent need to strongly advocate for the implementation of appropriate strategies and policies aimed at improving the vitamin A status of pre-school-age children in NCD. There is a need for intensive nutrition education, information and parental awareness campaigns, emphasizing the significance of vitamin A for children.

Our findings should be of concern to program planners involved in the VAS program in NCD. There is a need to improve and strengthen the existing monitoring of the VAS program in NCD, to ensure its efficiency, sustainability and functionality.

Although this was a hospital-based study, the prevalence of subclinical and marginal VAD in the study children with and without elevated plasma CRP strongly suggests the need for continuous monitoring of the vitamin A status of vulnerable groups (children aged 6-59 months and pregnant and lactating mothers) in NCD.

Conclusions

The prevalence of VAD in the pre-school-age children aged 6-59 months with normal plasma CRP was 11%, indicating a moderate public health problem. The prevalence of VAD in the male and female children with normal plasma CRP was 14% and 8%, which indicates moderate and mild public health problems, respectively.

The high prevalence of marginal VAD in the children with normal plasma CRP should be of concern to program planners, because, from the public health point of view, it indicates that a significant number of these children are at risk of developing VAD.

The VAS coverage in NCD is 'on track' to achieve the WHO recommended coverage of approximately 80% of children aged 6-59 months within target populations.

There is, however, a need for intensive nutrition education, information and awareness campaigns emphasizing the significance of vitamin A for pre-school-age children, and for an efficient, sustainable and functional monitoring system to strengthen and improve the VAS program in NCD.

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Zinc sulphate for treatment and prevention of diarrhoea and other conditions in children in Papua New Guinea

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SUMMARY

Over the last 10 years more than 40 randomized trials of zinc sulphate in diarrhoea have been done in developing countries throughout the world. Almost all have shown a benefit of zinc therapy for 5-10 days, if given with oral rehydration solution, in reducing the severity and duration of severe diarrhoea and preventing diarrhoea in the subsequent 3 months. Zinc has also been proven to reduce mortality in the management of children with severe malnutrition. Two studies have shown a benefit of zinc treatment on the clinical resolution of pneumonia and another study from Africa showed that zinc adjuvant treatment led to a significant reduction in mortality from pneumonia. Despite this overwhelming evidence, few countries in the Asia-Pacific region have scaled up the use of zinc in the treatment or prevention of diarrhoea or other infections. The reasons for this are several, including obstacles to incorporating new treatments into routine drug procurement and distribution mechanisms, and failure to appreciate the steps involved in the promotion of new routine treatments. A much higher priority must be given to ensuring that children with malnutrition, diarrhoea and other infections have access to zinc and oral rehydration solution – both of which are low-cost and life-saving treatments.

Introduction

Zinc is a metallic element that has many important implications for health and disease; particularly it is necessary for cellular immune function and for wound healing. Zinc deficiency results in impaired regeneration of rapidly dividing cells, particularly those of the skin and mucosa. Zinc deficiency is reflected in the 'flaky-paint' appearance of kwashiorkor, and children with congenital deficiencies of zinc have severe dermatitis.

Children with zinc deficiency are more prone to acute and chronic diarrhoea, and much research has been conducted to determine if zinc supplementation might be used to treat or prevent diarrhoea, pneumonia or other infectious diseases.

Diarrhoea

In Papua New Guinea (PNG), as in many developing countries, diarrhoea is consistently in the top 5 causes of hospital admission and death in children, and malnutrition is implicated in two-thirds of all child deaths (1,2). Effective management of diarrhoea is based on the use of oral rehydration salts (ORS), which in solution replenish water, sodium and potassium lost in diarrhoeal fluid. The development of ORS in the 1960s followed research in Bangladesh and other developing countries which found that making use of the glucose-sodium transporter channels in the small intestinal mucosa allowed one molecule of sodium to be absorbed with every molecule of glucose and that the absorption of water followed (1). Research in the last decade has identified that lower osmolarity ORS is more effective than standard osmolarity ORS; it reduces the need for intravenous fluid therapy and shortens the duration of the episode of diarrhoea (2).

Diarrhoea continues to be a major killer of children, with an estimated 1.3 million deaths worldwide annually (3). Severe dehydration

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or death from acute watery diarrhoea – most commonly caused by rotavirus – is extremely uncommon if an affected child receives appropriate amounts of ORS to maintain hydration (4,5). Other causes of diarrhoeal deaths include cholera and shigellosis – the major cause of dysentery – where deaths may occur despite ORS availability. In addition to ORS recent research has identified the value of zinc in the management of diarrhoea and malnutrition (2,6-17).

Treatment effects of zinc

Since 2000 there have been more than 40 randomized trials from many developing countries evaluating the effects of zinc on the treatment of diarrhoea and malnutrition. The following are the major findings. Zinc is effective in:

- reducing the severity and duration of acute diarrhoea (11)
- reducing the severity of cholera (13)
- decreasing mortality and improving weight gain among children with severe malnutrition (12)
- preventing diarrhoea if given to low-birthweight babies (16)
- reducing the severity and duration of dysentery (bloody diarrhoea) from shigella (14).

If given for 10-14 days to children with diarrhoea zinc shortens the length of time the child is sick, and reduces the chance of diarrhoea developing in the next 2-4 months (3,9). Therefore, even when given as treatment in hospital or health centre, zinc has an important longer-acting preventive effect. This is the really important message about zinc, but also one of the biggest challenges in its use. The uses of zinc are summarized in Table 1.

Zinc in the treatment of pneumonia

Zinc may be effective in the treatment of pneumonia, in reducing the duration of severe symptoms, if given as 20 mg per day until hospital discharge (20). This has been shown in large studies in Bangladesh (20) and in Nepal (21). Two small under-powered studies from India in 2011 failed to show any beneficial effect (22,23). These four studies from the subcontinent were in children with severe pneumonia as defined by the World Health Organization (WHO) – equivalent to moderate pneumonia in PNG. All had very low mortality rates and high rates of viral infection as manifest by wheezing or virus isolation. A study from Uganda, in a population of children with high rates of HIV (human immunodeficiency virus) infection, malnutrition and bacterial pneumonia showed a significant reduction in deaths in the zinc-treated group (24). This beneficial effect was especially strong in children with HIV infection. It is likely that in a zinc-deficient population with high rates of malnutrition, bacterial pneumonia or HIV infection, zinc would have a significant benefit in the treatment of pneumonia.

Use of zinc for infection prevention

If given weekly in the community, zinc reduces the prevalence of diarrhoea and pneumonia, and reduces mortality in children less than 2 years of age in impoverished settings (8). This has been shown to be operationally feasible in some settings (10).

Zinc is safe and effective in reducing diarrhoea prevalence in children with HIV infection (7).

Addressing low rates of ORS usage

ORS usage is low in PNG (25), as it is in many developing countries. In the 2006 Demographic and Health Survey (DHS) it was shown that only 16% of children with diarrhoea were treated with ORS (26). In many countries use of ORS is decreasing.

There is an urgent need to increase the availability and use of ORS for all children with diarrhoea. There is good evidence that when zinc sulphate tablets are available to be given with ORS, health workers are more likely to give ORS to children with diarrhoea (6). Thus the introduction of zinc is a way of addressing the low ORS usage in PNG.

Implementation of zinc

Despite the conclusive evidence that zinc is beneficial, few developing countries have systematically introduced it, or achieved high coverage (27). Zinc is a good example of how difficult it can be to go from evidence of effectiveness to widespread uptake.

TABLE 1

USES OF ZINC

Zinc sulphate comes as a dispersible 20 mg tablet.

Zinc should be given according to the PNG Standard Treatment Guidelines (18) and the WHO Pocketbook of Hospital Care for Children (19).

Acute diarrhoea/dysentery/cholera: give zinc sulphate 20 mg (one tablet) per day for 10 days. When the child is discharged home, give enough zinc to complete a 10-day course, and explain to mothers how to give it.

Malnutrition: zinc sulphate 20 mg (one tablet) per day for the duration of hospital stay and in the home until weight is >80% expected for age.

Low-birthweight babies: give zinc 10 mg per day (½ tablet) for the duration of hospital stay and in home until the baby is 6 weeks of age.

Explain to mothers the importance of ORS, zinc and continued breastfeeding in treating diarrhoea. Follow the Standard Treatment Guidelines for other management.

PNG = Papua New Guinea
WHO = World Health Organization
ORS = oral rehydration salts

No country in the Western Pacific Region has successfully introduced zinc. In Asia, Bangladesh is a useful model for other countries, while India has made a start (17,28).

The reasons for lack of introduction of zinc in most countries are multifactorial: lack of inclusion into therapeutic guidelines or the national essential medicines list; delayed endorsement of zinc as a new therapeutic agent by health departments; lack of policy outlining its use; and difficulties in finding suppliers. Lack of understanding of the evidence or delays in endorsement of zinc by professional societies seems the least important issue in most countries, reflecting the strong publicity by WHO and the United Nations Children's Fund (UNICEF) on the use of zinc.

Zinc represents an important case study of the multiple steps that are required to introduce any new, highly effective medicine, and calls for a better understanding of the exact steps involved that are specific to that country's regulations. The lack of implementation of zinc is not because of lack of funding available, but a weak understanding of the processes involved and lack of a systems approach. Table 2 lists some of the steps involved.

In Bangladesh, zinc has been introduced in a systematic way through a program called SUZY (Scaling Up Zinc for Young children), run by the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR, B) (28). The program has combined a nationwide mass media campaign to promote awareness of zinc, modelling of zinc administration by respected paediatricians, working with public physicians, private practitioners, drug vendors and unlicensed health care suppliers, and waiving of over-the-counter sales restrictions. This has been highly successful in terms of community awareness, and moderately successful in terms of coverage achieved. While awareness was between 50% (rural) and 90% (urban, non-slum areas), the use of zinc in children with diarrhoea was only 25% in urban, non-slum dwelling children and only 10% in rural children. Importantly zinc introduction was not associated with reduced utilization of ORS; on the contrary, ORS prescribing increased.

TABLE 2

SOME STEPS TO ZINC IMPLEMENTATION IN OTHER COUNTRIES

- Completion of guidelines for zinc sulphate use
- Approval of zinc by the national pharmaceutical advisory body
- Choosing the most appropriate zinc sulphate preparation and drug suppliers
- Estimation of zinc requirements: based on data of diarrhoea prevalence or ORS usage
- Promotion of awareness of zinc among paediatricians, nurses, private practitioners, drug vendors and the general public
- Linking the use of zinc with public health messages to prevent diarrhoea (hand washing, safe water, use of ORS)
- Modelling of zinc administration and use by noted paediatricians, media personalities, women's representatives
- Effective distribution of zinc to all health facilities, along with ORS and a guideline for zinc use
- Operational research to measure zinc uptake and compliance

ORS = oral rehydration salts

Further challenges in using zinc

To be most effective, particularly in the prevention of subsequent episodes of diarrhoea, zinc sulphate needs to be given daily for 10 days. Most children with acute watery diarrhoea are either treated as an outpatient or, if they are hospitalized, their length of stay is much less than 10 days. Therefore, whether parents can give zinc for the full length of treatment at home, even after the child's diarrhoea has resolved, will require monitoring and evaluation after zinc is introduced.

In PNG zinc has been made available by WHO as part of the response to cholera; 400,000 doses were purchased and sent to Lae, the location of the initial outbreak. These stocks have since been redistributed proportionately to other provinces. 400,000 zinc tablets should be sufficient zinc to treat all the children with acute watery diarrhoea presenting to all PNG provincial hospitals for 2 years. In Solomon Islands, initial stocks of zinc were brought in by Red Cross and other non-government organizations (NGOs) as part of the response to the 2007 tsunami. The stock was inconsistently distributed and quickly ran out. It is a challenge to make the most of such opportunities and to use stocks that are donated during emergencies wisely and ensure a transition to sustained routine use.

A further challenge, in times of efforts to curb drug budgets, is to convince health departments to purchase a 'new drug' which is required in large amounts and has widespread use. In the increased complexity of health programs, with many new and often expensive interventions, the simple message that ORS and zinc are very low-cost and life-saving for the treatment of diarrhoea and malnutrition must be given a very high priority.

Further trials of zinc in severe pneumonia among populations with high rates of severe

bacterial infection, malnutrition and HIV infection are needed, as zinc is likely to have a benefit on immune function and outcomes from pneumonia in these children.

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Moresby food isn't good: food security, nutritional information and adherence to antiretroviral therapy in Papua New Guinea

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SUMMARY

The relationship between HIV (human immunodeficiency virus), food security and nutrition has become increasingly important to practitioners, policy makers and people living with HIV. In this paper we describe for the first time the connection between HIV and antiretroviral therapies, the extent of nutritional counselling for HIV-positive people and food security in Papua New Guinea (PNG). A total of 374 HIV-positive people who were over the age of 16 and who had been on antiretroviral therapy (ART) for more than two weeks were recruited from six provinces, using a non-probability, convenience sampling methodology. A subsample of 36 participants also completed an in-depth qualitative interview. Participants received nutritional advice when beginning ART which focused on three main domains, of which the first two were the most frequently mentioned: what foods to avoid; what foods to eat; and how frequently to eat. 72% of the sample reported that they had experienced an increase in their appetite. Of those who reported that their appetite had increased on ART 33% reported that they did not have enough food to satisfy hunger. People who lived in the capital city, Port Moresby, within the Southern Region of PNG, had significantly more difficulty with food security than those who lived in other regions of the country. Not having enough food was the third most commonly recorded reason for non-adherence to ART. Responses to the HIV epidemic in Papua New Guinea must also begin to address the phenomenon of food insecurity for people with HIV, in particular those who are receiving antiretroviral therapies and who live in the urban areas.

Introduction

The human immunodeficiency virus (HIV) is intimately entwined with issues of food security and nutrition, with food security, poverty and HIV now understood to be major contributing factors to the devastation faced by people in sub-Saharan Africa (1-3). Food security is defined by the Food and Agriculture Organization of the United Nations (FAO) as when "all people, at all times, have physical, social and economic access to sufficient, safe and nutritious food which meets their dietary needs and food preferences for an active and healthy life" (4). FAO defines household food security as "the application of this concept to the family level, with individuals within households as the focus of concern" (4). While HIV impacts upon the nutrition status of an individual (5) it also impacts upon the food security of a household (4,6). The reverse is also true. Poor food intake negatively impacts upon immune function (7) and facilitates the progression of HIV infection while inhibiting the adequate absorption of antiretroviral therapies (8). In a Malawi study of individuals with HIV

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commencing antiretroviral therapy (ART), those who were moderately malnourished were twice as likely as those who were not malnourished to die in the first three months of treatment while those who were severely malnourished were six times more likely to die in the first three months of treatment (9). Singaporean research indicates a similar relationship between malnutrition at the time of ART commencement and death (8).

Several studies have identified the role of both poor food security and nutrition in the spread of HIV. A two-country study in Africa indicated that women who were without adequate food security were more likely to have sex without condoms and more likely to engage in practices of greater HIV risk such as the selling or exchanging of sex (10). Food insecurity has also been identified as a cofactor in the maternal transmission of HIV with HIV-positive women more likely to transmit HIV to their unborn children if they are malnourished (11,12).

In response to the concerns of food security and nutrition for people infected with HIV, nutritional programs, including guidelines on nutritional counselling, have been developed in many countries, as seen for example in Thailand and Bangladesh (13,14), although there is some contention as to whether food programs on their own achieve anything (15). With increasing emphasis on nutritional counselling for people with HIV on or commencing ART, one study suggests that people with HIV are unable to adhere to the nutritional recommendations for those on ART because of poor food security (16).

Papua New Guinea (PNG) has a generalized epidemic where over 1% of the adult population is estimated to be infected with HIV. At the time this study was undertaken the HIV prevalence estimates were over 2% but as final revisions were being made to this paper the prevalence underwent a downward revision to 0.9% based on antenatal data from Port Moresby General Hospital. In epidemics where rates of HIV are generalized, "all dimensions of food security - availability, stability, access and use of food - are affected" (1). While there is a plethora of data on food security in some developing regions such as Africa, little scholarly attention has been paid to issues of food security, nutritional beliefs and HIV in Papua New Guinea, apart from a paper on the implications of HIV for development and food security in PNG and one small-scale nutritional study of 50 people with HIV (17,18). While food security is arguably an issue that needs attention for all PNG citizens (19) it is exacerbated in the context of HIV, where food and nutrition play a critical role in the recovery of compromised immune systems and in the absorption of ART. The data for this paper are drawn from a larger study on the social experiences of ART for people living with HIV (PLHIV) in PNG (20).

Methods

The data were collected as part of a mixed-method study undertaken in six provinces of Papua New Guinea between February and July 2008. The purpose of the study was to explore the social experience of HIV-positive men and women on ART in PNG.

A total of 374 HIV-positive people who were over the age of 16 and had been on ART for more than two weeks were recruited using a non-probability, convenience sampling methodology. Participants were recruited through ART prescribing sites, PLHIV drop-in clinics and support groups in six provinces: Southern Highlands Province, National Capital District, Eastern Highlands Province, Morobe Province, Chimbu Province and Western Highlands Province. A total of 36 people with HIV who participated in the survey agreed to participate in an in-depth interview. Participants for the in-depth interview were invited to participate on the grounds of their engagement with the study and their willingness to narrate their experiences of ART in greater detail.

Participants were invited to participate in the study by health care workers or other PLHIV. All potential participants were explicitly informed that they were under no obligation to participate, and their access to ART or any form of treatment or support group would not be affected by their decision to participate or not.

After potential informants provided initial consent, they were directed to a nominated researcher. Once they had made contact, the researcher explained the purpose of the study and outlined what participation would entail. Upon providing informed consent, the participant completed an interviewer-administered questionnaire in either Tok Pisin or English.

The interviewers were Papua New Guineans undergoing an intensive HIV social research training cadetship, coordinated by the PNG Institute of Medical Research and the University of New South Wales. In addition, a person living with HIV was employed as a member of the research team and trained in the methodologies of the study.

The survey included sociodemographic information and items on knowledge and beliefs around HIV and treatment, stigma and discrimination, health and well-being, disclosure, food security, alcohol use, adherence, sexual practices and access to services. At the end of the questionnaire one qualitative question on the meaning of ART in people's lives was asked. The in-depth interview was designed to elicit further details in the areas covered by the survey.

No names were recorded on the questionnaire. All questionnaires were coded by province and recruitment site. A subsample of 36 participants also completed an in-depth qualitative interview. All participants in the in-depth interview were allocated a pseudonym and all identifiable information has been altered.

Statistical analysis

The main variables of interest for statistical analysis in this paper were appetite, hunger and ART adherence. Appetite was asked in the question: "Has your appetite changed since you started ART?" A dichotomous variable was created with 1) for those who answered that their appetite increased (n = 270), and 2) for all others who answered that their appetite was unchanged (n = 81) or decreased (n = 20) or who were missing (n = 3). Of those who answered that their appetite increased, they were then asked: "Do you have enough food to satisfy your hunger?" For hunger, those who answered 'yes' were categorized as having enough food (or not experiencing hunger) and those who answered 'no' were categorized as not having enough food (or experiencing hunger). ART adherence was categorized as for a previous paper of the same study (21). Treatment adherence was categorized into adherent (never having missed a dose) and non-adherent (missed one or more doses) in the last week. Those who were adherent were further subcategorized into perfect adherence for never having a missed or late dose in the last week and good adherence for having late dose(s) but never having missed a dose in the last week.

All categorical variables were analysed using the Pearson chi-squared test or Fisher's exact test for association. The continuous variables (ie, age, months on ART and months since HIV infection was first diagnosed) were analysed using the Mann-Whitney U test. Logistic regression was also used to further examine whether appetite and hunger were associated with ART adherence. All analyses were carried out using Stata Data Analysis and Statistical Software version 11 (StataCorp LP, College Station, TX, USA).

Thematic analysis

All in-depth interviews were transcribed, translated and then coded according to predetermined and emerging themes.

Ethical considerations

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving patients were approved by the Papua New Guinea Medical Research Advisory Committee, the Research Advisory Committee of the National AIDS Council Secretariat of Papua New Guinea, the Papua New Guinea Institute of Medical Research Internal Review Board and the University of New South Wales. Oral consent was obtained for all participants involved in the survey and written consent was obtained from all participants who agreed to participate in the in-depth interviews.

Results and Discussion

Table 1 presents the characteristics of the entire sample, according to those with an increase in appetite and those with no change or decrease in appetite. The median age of the sample was 30 years, the interquartile range was from 26 to 37 years and the range (not shown in table) was 16 to 69 years. Less than half of the sample (43%) had been diagnosed with HIV in the 12 months before the survey. Over half of all participants (60%) had commenced antiretroviral treatment in the 12 months before the survey, with no significant difference between men and women. Of the 374 study participants, 227 (61%) were women and 147 (39%) were men. Almost half the participants were married or engaged (47%) and almost a quarter widowed

TABLE 1

Characteristics of study participants living with HIV by change in appetite since starting antiretroviral therapy (ART)

	Appetite increased n = 270	Appetite unchanged or decreased n = 104*	Total n = 374	p value (χ^2 or Z)
Age[1,2]	30 (26-36)	32 (26-39)	30 (26-37)	0.290 (1.06)
Months since HIV diagnosed[1,2]	14 (6-36)	12 (7.5-24.5)	13 (6-32)	0.854 (–0.18)
Months since ART started[1,2]	9 (9-19)	10 (5-18)	9 (4-18)	0.731 (0.34)
Sex				0.055 (3.68)
Male	98 (36%)	49 (47%)	147 (39%)	
Female	172 (64%)	55 (53%)	227 (61%)	
Marital status				0.181 (4.87)
Never married	19 (7%)	6 (6%)	25 (7%)	
Married/engaged	123 (46%)	52 (50%)	175 (47%)	
Separated/divorced	55 (20%)	28 (27%)	83 (22%)	
Widowed	73 (27%)	18 (17%)	91 (24%)	
Education level				0.621 (0.95)
Never schooled	60 (22%)	19 (18%)	79 (21%)	
Elementary/primary	137 (51%)	58 (56%)	195 (52%)	
Secondary/certificate	73 (27%)	27 (26%)	100 (27%)	
Employment type				0.718 (2.09)
Garden work	116 (43%)	42 (40%)	158 (42%)	
Housework	70 (26%)	22 (21%)	92 (25%)	
Formal employment	18 (7%)	8 (8%)	26 (7%)	
Informal employment	32 (12%)	16 (15%)	48 (13%)	
Unemployed/other	34 (13%)	16 (15%)	50 (13%)	
Region of residence				0.793 (0.46)
Highlands	174 (64%)	69 (66%)	243 (65%)	
Momase	18 (7%)	5 (5%)	23 (6%)	
Southern	78 (29%)	30 (29%)	108 (29%)	
Religious affiliation				0.059 (9.09)
Pentacostal	61 (23%)	22 (21%)	83 (22%)	
Revival	63 (23%)	14 (13%)	77 (21%)	
Catholic	45 (17%)	24 (23%)	69 (18%)	
Seventh Day Adventist	39 (14%)	24 (23%)	63 (17%)	
Others[3]	62 (23%)	20 (19%)	82 (22%)	
Current physical health				<0.001 (22.6)
Extremely good - Good	181 (67%)	44 (42%)	225 (60%)	
Neutral	69 (26%)	40 (38%)	109 (29%)	

Extremely bad - Bad	19 (7%)	20 (19%)	39 (10%)	
Current mental health				0.097 (4.68)
Extremely good - Good	190 (70%)	61 (59%)	251 (67%)	
Neutral	60 (22%)	32 (31%)	92 (25%)	
Extremely bad - Bad	20 (7%)	11 (11%)	31 (8%)	
Current health satisfaction				0.047 (6.10)
Very happy - Happy	34 (13%)	7 (7%)	41 (11%)	
Neutral	32 (12%)	21 (20%)	53 (14%)	
Very unhappy - Unhappy	204 (76%)	76 (73%)	280 (75%)	
Physical strength to work since ART				0.078 (3.11)
Had enough strength	197 (73%)	85 (82%)	282 (75%)	
Did not have enough strength	73 (27%)	19 (18%)	92 (25%)	
ART adherence in the past week[4]				0.004 (11.21)
Perfect adherence	179 (66%)	53 (51%)	232 (62%)	
Good adherence	34 (13%)	27 (26%)	61 (16%)	
Non-adherence	57 (21%)	24 (23%)	81 (22%)	

HIV = human immunodeficiency virus
*Includes 3 with unknown appetite
[1]Variables with missing data: age (n = 5), months since HIV diagnosed (n = 6), months since ART started (n = 3)
[2]Median (interquartile range) and p values (Z statistics) from Mann-Whitney U test are given for age, and months since HIV diagnosed and since ART started
[3]Lutheran (n = 42), United (n = 23), Evangelical Alliance (n = 9), other religion or affiliations (n = 5), does not go to church (n = 1) and no response (n = 2)
[4]Perfect adherence = never had a missed or late dose; good adherence = had late dose(s) but never had a missed dose; non-adherence = had one or more missed dose(s)

(24%). However, of those who identified as married only 32% said that their partner lived with them in the same house. Almost three-quarters of the participants reported having never been to school (21%) or been educated only up to elementary or primary school level (52%). The majority of participants reported that garden work (42%) or housework (25%) was their primary form of employment.

A positive side-effect of ART is an increase in appetite. Since taking ART 270 (72%) of the participants reported that they had experienced an increase in their appetite (Table 1). None of the sociodemographic characteristics showed significant association with change in appetite. However, better current physical health, greater current health satisfaction and perfect ART adherence in the past week were significantly associated with increase in appetite (Table 1). This increase in appetite was a significant experience of bodily transformation in informants' narratives. As Gina shared:

> "The medicine has expanded my stomach and I want to eat plenty of food." Gina

Gina's reference here to an expanding stomach was not a reference to lipodystrophy but a description of how much hungrier she was on treatment and for her that felt like her stomach had expanded and therefore required that she eat more food. For others the increase in appetite meant that their daily routine altered. In order to satisfy their hunger they were now preparing food more frequently. Again describing the increase in appetite as both a bodily (the snake inside her body is dead) and social (cooking during the day) transformation, Betty shared the following story:

> "My sister-in-law used to say, 'Before you don't eat like that, now what's wrong and you are cooking during the day?' She will come and ask me like that. I used to say that it's because of this medicine that it's doing that. The snake that is inside is dead

and I'm always hungry." Betty

While the commencement of treatment led to an increase in appetite, the reality of food security and HIV became evident. Table 2 shows the association of hunger with other variables among those who had an increase in appetite. Of those who reported that their appetite had increased on ART 33% (n = 88) reported that they did not have enough food to satisfy hunger. There was a significant relationship between region of residence and whether people whose appetite had increased since taking ART had enough food to satisfy their hunger (χ^2 = 15.8, p <0.001). People who lived in the National Capital District – the capital city of Port Moresby – within the Southern Region of PNG had significantly more difficulty with food security than those who lived in the Highlands or Momase Regions. 51% (n = 39) of those who lived in the Southern Region reported not having enough food to satisfy their hunger compared with 28% (n = 5) of those from the Momase Region and 25% (n = 44) of those from the Highlands Region who reported having an increase in appetitie. Hunger was also associated with housework as an employment and being unemployed/other employment (eg, unpaid volunteer work). Overall, food security was an important issue for a third of those who had an increase in appetite on ART treatment, and particularly so for those who reside in urban areas (eg, the National Capital District), and for those who could not earn enough to eat. Hunger or the lack of food is in turn associated with poorer current physical health and poorer current mental health.

Exploring the challenges of food security in the in-depth interviews, a number of areas of programmatic concern are evident. Reinforcing the quantitative data that people living outside of the Highlands Region have a far greater challenge with food security, one woman shared the following account of life in Port Moresby:

> "City life is hard, we don't work. We don't work. I live with his relatives and they do not know what type of woman I am [HIV-positive]. They stay and get hungry and find food to eat. But when he goes to the village and he doesn't stay in the house or goes to another place, I do not have any support. The centres are there. So I go to the centres to get a little food to go with my medicine. When there is no food I say, 'Ah I will not die', so I drink a lot of water and take my medicine. Moresby food isn't good." Sophia

In the extract from Sophia, poverty and unemployment, city dwelling, HIV, non-disclosure of HIV status and adherence are all mutually reinforcing.

Adherence, not skipping a treatment dose and taking treatment at the prescribed time, is the most important factor for suppression of HIV and for the prevention of drug resistance. Table 3 shows the factors associated with having no missed dose(s) in the past week (Model 1: Adherence vs Non-adherence) and,

TABLE 2

BIVARIATE ASSOCIATION OF HUNGER WITH MAIN SOCIODEMOGRAPHIC FACTORS, HEALTH STATUS AND ART ADHERENCE AMONG STUDY PARTICIPANTS WHO HAD AN INCREASE IN APPETITE

	Had enough food n = 181	Did not have enough food n = 88	Total n = 269	p value (χ^2 or Z)
Age[1,2]	30 (26-36)	30 (25-36.25)	30 (26-36)	0.416 (0.8)
Sex				0.057 (3.6)
Male	73 (40%)	25 (28%)	98 (36%)	
Female	108 (60%)	63 (72%)	171 (64%)	
Marital status				0.163 (5.1)
Never married	10 (6%)	9 (10%)	19 (7%)	
Married/engaged	90 (50%)	32 (36%)	122 (45%)	
Separated/divorced	35 (19%)	20 (23%)	55 (20%)	
Widowed	46 (25%)	27 (31%)	73 (27%)	

Employment type				<0.001 (24.8)
Garden work	86 (48%)	30 (34%)	116 (43%)	
Housework	36 (20%)	33 (38%)	69 (26%)	
Formal employment	17 (9%)	1 (1%)	18 (7%)	
Informal employment	26 (14%)	6 (7%)	32 (12%)	
Unemployed/other	16 (9%)	18 (20%)	34 (13%)	
Region of residence				<0.001 (15.8)
Highlands	130 (72%)	44 (50%)	174 (65%)	
Momase	13 (7%)	5 (6%)	18 (7%)	
Southern	38 (21%)	39 (44%)	77 (29%)	
Religious affiliation				0.089 (8.1)
Pentacostal	46 (25%)	15 (17%)	61 (23%)	
Revival	33 (18%)	29 (33%)	62 (23%)	
Catholic	32 (18%)	13 (15%)	45 (17%)	
Seventh Day Adventist	26 (14%)	13 (15%)	39 (14%)	
Others[3]	44 (24%)	18 (20%)	62 (23%)	
Current physical health				0.011 (9.1)
Extremely good - Good	133 (73%)	48 (55%)	181 (68%)	
Neutral	37 (20%)	31 (36%)	68 (25%)	
Extremely bad - Bad	11 (6%)	8 (9%)	19 (7%)	
Current mental health				0.005 (10.7)
Extremely good - Good	139 (77%)	51 (58%)	190 (71%)	
Neutral	30 (17%)	29 (33%)	59 (22%)	
Extremely bad - Bad	12 (7%)	8 (9%)	20 (7%)	
Current health satisfaction				0.147 (3.8)
Very happy - Happy	143 (79%)	60 (68%)	203 (75%)	
Neutral	19 (10%)	13 (15%)	32 (12%)	
Very unhappy - Unhappy	19 (10%)	15 (17%)	34 (13%)	
Physical strength to work since ART				0.135 (2.2)
Had enough strength	137 (76%)	59 (67%)	196 (73%)	
Did not have enough strength	44 (24%)	29 (33%)	73 (27%)	
ART adherence in the past week[4]				0.116 (4.3)
Perfect adherence	126 (70%)	52 (59%)	178 (66%)	
Good adherence	18 (10%)	16 (18%)	34 (13%)	
Non-adherence	37 (20%)	20 (23%)	57 (21%)	

ART = antiretroviral therapy

[1] There were 5 missing observations on age

[2]Median (interquartile range) and p value (Z statistics) from Mann-Whitney U test are given for age

[3]Lutheran (n = 33), United (n = 17), Evangelical Alliance (n = 7), other religion or affiliations (n = 3), does not go to church (n = 1) and no response (n = 1)

[4]Perfect adherence = never had a missed or late dose; good adherence = had late dose(s) but never had a missed dose; non-adherence = had one or more missed dose(s)

TABLE 3

LOGISTIC REGRESSION MODELS ON SELF-REPORTED ART ADHERENCE IN THE PAST WEEK

	Model 1: Adherence versus Non-adherence (n = 367)[1] OR (95% CI)	Model 2: Perfect adherence versus Good adherence (n = 288)[2] OR (95% CI)
Age in years (ref: 16-25)		
26-35	1.78 (0.89-3.56)	0.74 (0.33-1.66)
36-45	1.44 (0.63-3.26)	0.95 (0.35-2.56)
over 45	2.17 (0.64-7.36)	1.82 (0.41-8.14)
Sex: Female	1.87 (0.95-3.67)	0.72 (0.33-1.57)
Marital status (ref: Married/engaged)		
Never married	0.97 (0.33-2.87)	1.08 (0.26-4.54)
Separated/divorced/widowed	0.85 (0.47-1.55)	1.12 (0.58-2.18)
Employment type (ref: Garden work)		
Housework	1.09 (0.51-2.36)	1.51 (0.64-3.57)
Paid employment	**2.81 (1.18-6.70)**	1.01 (0.43-2.38)
Other employment	2.15 (0.83-5.60)	2.65 (0.84-8.39)
Region: Highlands	**3.36 (1.75-6.46)**	0.96 (0.46-2.02)
Religion: Revival Church	**0.45 (0.24-0.83)**	**0.36 (0.17-0.76)**
Appetite and hunger (ref: Increased appetite and had enough food)		
Increased appetite but did not have enough food	1.49 (0.72-3.05)	**0.43 (0.19-0.98)**
Appetite unchanged or decreased	0.86 (0.46-1.59)	**0.21 (0.10-0.44)**

ART = antiretroviral therapy
OR = odds ratio
CI = confidence interval
[1]Model 1 fitted the predictors of never missing dose(s) for all participants with non-missing data (n = 367); adherence = never missed dose(s) in the past week; non-adherence = had one or more missed dose(s) in the past week
[2]Model 2 fitted the predictors of never having late dose(s) among those who never missed dose(s), ie, in the subset of those who reported adherence (n = 288); good adherence = had late dose(s) but never missed dose(s) in the past week; perfect adherence = never had late or missed dose(s) in the past week

in the subset (n = 288) of those with no missed dose(s), the factors associated with also having no late dose(s) in the past week (Model 2: Perfect adherence vs Good adherence). As reported in a previous paper of the same study (21), residing in the Highlands Region was significantly associated with adherence compared to residing in the Southern or Momase Regions ($p < 0.001$ in Model 1) while being a member of the Revival Church was significantly associated with non-adherence ($p = 0.010$ and 0.007 in Models 1 and 2, respectively). This association is related to the theological teachings of the Revival

Church, which emphasizes spiritual healing where people are encouraged to put trust in God's capacity to heal rather than in the ability of ART to treat. Model 1 further shows that there was no association between hunger or not having enough food and missing dose(s) in the past week; however, Model 2 shows that there was a significant association of not having enough food ($p = 0.045$) and of not having an increase in appetite ($p < 0.001$) with having late dose(s) in the past week.

Highlighting that food security is not simply an individual problem, as the research on household food security and HIV depicts, Rosa from Port Moresby details how food insecurity is a problem for couples and families:

> "Concerning food, both of us find it difficult. No food – we just drink cold water and we go to bed… No food, I take treatment without it." Rosa

The absence of food, as Rosa suggests, is forcing people to make adherence choices that are not optimal. The choice becomes one of either taking treatment without food or not taking it at all. This is counter to the information on food that the participants described that they received from their ART-prescribing health care workers, which included the need to eat regularly ("You must take food in the morning, in the sun and in the afternoon" Sasha); what foods to eat ("Fruits at the market and eating greens" Marianne); and what foods to avoid ("Not to eat greasy food. I was told to have fat-free food" Monica). Here Monica was describing being warned to avoid fatty foods such as lamb flaps rather than avocado and other healthy fats, which PLHIV are encouraged to eat. In the context of food insecurity it is important to emphasize that the participants all spoke of the need to eat before taking ART in order to increase absorption of the medication:

> "Get plenty food before medicine because it will help the medicine work inside your body." Sophia

> "I have been told by doctors that before taking ART I must eat. I must take this medication on a full stomach because this medicine is very strong." Nathaniel

> "They said you must eat a lot, and eat food from the garden. Eat a lot and then later you can take your medication. The medication will work well on your body, they said. If you don't eat and decide to just take the medication, sometimes the medicine will have bad side-effects so you have to eat properly before taking the medication so that you won't feel anything." Sasha

Of those who had an increase in appetite and who gave one or more reasons for ever having missed and/or taken a late dose, not having enough food, side-effects and/or vomiting and difficulty swallowing the pills (as reasons for not adhering) were significantly associated with hunger or not having enough food (Table 4). The top two most common reasons, forgetting to take medication (66% of those who had increased appetite from Table 4 and 65% of the whole sample, ie, inclusive of those who had unchanged or decrease in appetite) and being too busy (23% of those in Table 4 and 27% of the whole sample) were also the most common reasons cited by other studies (22-28). These were followed by not having enough food as the third most common reason for not adhering to ART medication in this sample. Despite the education that people with HIV commencing treatment receive about food and adherence, about 1 in 5 participants (18% of those in Table 4 and 22% in the whole sample) identified food insecurity as the reason for non-adherence, that is, they did not have enough food to take with the medication.

Conclusions

Although this study was not designed as a food security, nutrition and HIV project, it became apparent that these issues are of critical importance in the lives of people living with HIV in Papua New Guinea. Importantly, there appears to be discordance between the nutritional information provided and the reality of food insecurity for many of the participants in this study, particularly those in urban areas, where people are more reliant on the cash economy and where food and other costs of living are more expensive.

It appears that people with HIV are being provided with varying degrees of nutritional information which itself needs to be further examined. Although people seem aware of the importance of nutrition the reality of food insecurity remains. Reinforcing the nutritional information people with HIV in this study had received from their health care workers, Wiig and Smith (29) suggest that:

TABLE 4

Association between food availability and reasons for not adhering among study participants who had an increase in appetite and gave reasons for not adhering

	Had enough food (n = 57)	Did not have enough food (n = 46)	Overall (n = 103)	p value (χ^2)
Forgot to take medication	72% (41)	59% (27)	66% (68)	0.159 (2.0)
Too busy[1]	23% (13)	24% (11)	23% (24)	0.895 (<0.1)
Didn't have enough food	7% (4)	33% (15)	18% (19)	0.001 (11.1)
Taking medication is a reminder of HIV status	11% (6)	20% (9)	15% (15)	0.196 (1.7)
Side-effects and/or vomited	5% (3)	24% (11)	14% (14)	0.006 (7.5)
Risk disclosure when taking medicine	11% (6)	15% (7)	13% (13)	0.476 (0.5)
Limited resources[2]	9% (5)	17% (8)	13% (13)	0.190 (1.7)
Didn't believe/sought other alternatives[3]	12% (7)	9% (4)	11% (11)	0.751[4]
Too sick to take medication	4% (2)	15% (7)	9% (9)	0.074[4]
Difficult to swallow medication	2% (1)	13% (6)	7% (7)	0.043[4]
Too many pills to take at once	4% (2)	7% (3)	5% (5)	0.654[4]
Was drunk	4% (2)	0% (0)	2% (2)	0.500[4]

HIV = human immunodeficiency virus
[1]Included too busy looking after children or grandchildren, doing housework, working, getting home late and doing other things
[2]This was coded based on other reasons stated by the participant; the reasons included not having a clock or radio to know the time for taking antiretroviral medication (n = 8), transport reasons (n = 6; financial or road problems, eg, road block) and shortage of medicine at the hospital (n = 3)
[3]9 did not believe the medication was helping, of whom 3 also gave one or more of the following reasons: believed in spiritual healing (n = 2), sought herbal medicine (n = 1), sought traditional doctor (n = 1) and feared the antiretroviral medication was an experiment on him (n = 1)
[4]Fisher's exact test was performed

> "Counseling patients about the importance of maintaining adequate food intake, and education on hand-washing and safe food preparation to avoid food- and water-borne illness and opportunistic infections, are critical to HIV/AIDS patient care." (29:1012)

However, it is not as straightforward as Wiig and Smith suggest. In a context of food insecurity, nutritional guidance alone is problematic. People need to be able to satisfy their hunger before they can address the nutritional quality of their food and ensure the adequate intake of calories per day. This is evident in the only published study on nutrition amongst PLHIV in PNG, where not only do such people not meet the recommendations for energy and nutrient intake for the general population but they do not meet the higher intake recommended by the World Health Organization for PLHIV (19).

In light of the emerging and long-term issues of food insecurity, it is now argued that food security (and poverty reduction) must be an essential component of any meaningful response to HIV (1,30) because according to Mamlin, Kimaiyo, Lewis et al. (31) "responses targeting only the rapid scale-up of antiretroviral therapies are unlikely to meet the needs of the many patients they service" (31:216). Furthermore, as Gillespie and Kadiyala (32) have already argued in relation to HIV programs, "there is an urgent need

for a broader understanding of the integral role that food and nutrition security can and should play in such responses" (32:1282). A similar concern with increased appetite after commencing ART and an inability to afford the increased quantity of food required to satisfy their new hunger levels was also identified in an African study by Hardon and colleagues (33). Our data suggest that HIV responses in Papua New Guinea must also begin to address the phenomenon of food insecurity for people with HIV, in particular those who are receiving antiretroviral therapies and who live in the urban areas. Although this study does not report on the nutritional status of individuals on ART in PNG, this may well also be a research priority for PNG as it increases access to ART for its HIV-positive citizens.

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The epidemiology of malaria in the Papua New Guinea highlands: 7. Southern Highlands Province

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SUMMARY

As the last part of a program to survey the extent of malaria transmission in the Papua New Guinea highlands, a series of rapid malaria surveys were conducted in 2003-2004 and 2005 in different parts of Southern Highlands Province. Malaria was found to be highly endemic in Lake Kutubu (prevalence rate (PR): 17-33%), moderate to highly endemic in Erave (PR: 10-31%) and moderately endemic in low-lying parts (<1500 m) of Poroma and Kagua (PR: 12-17%), but was rare or absent elsewhere. A reported malaria epidemic prior to the 2004 surveys could be confirmed for the Poroma (PR: 26%) but not for the lower Kagua area. In Kutubu/Erave *Plasmodium falciparum* was the most common cause of infection (42%), followed by *P. vivax* (39%) and *P. malariae* (16%). In other areas most infections were due to *P. vivax* (63%). Most infections were of low density (72% <500/µl) and not associated with febrile illness. Overall, malaria was only a significant source of febrile illness when prevalence rates rose above 10%, or in epidemics. However, concurrent parasitaemia led to a significant reduction in haemoglobin (Hb) level (1.2 g/dl, CI_{95}: [1.1-1.4.], p <0.001) and population mean Hb levels were strongly correlated with overall prevalence of malarial infections (r = −0.79, p <0.001). Based on the survey results, areas of different malaria epidemiology are delineated and options for control in each area are discussed.

Introduction

The Southern Highlands Province (SHP) is the largest of the highlands provinces with very diverse geography. Northern, higher-lying areas (Mendi, Imbonggu, Ialibu-Pangia, Komo-Magarima, Kopiago, Kagua) are mainly mountainous or hilly with fertile volcanic slopes and fans around Mt Giluwe and Mt Yalibu and in parts of Komo and Tari. Southern, lower-lying areas such as Nipa-Kutubu, Erave and Koroba are dominated by karst and sharp limestone ridges and, with the exception of Koroba, are sparsely populated. There is little seasonality in rainfall, with rainfall >200 mm each month of the year, except in Mendi and Imbonggu Districts, where monthly rainfall exceeds 200 mm during the wet season but decreases to 100-200 mm in the dry season (July - October) (1).

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Although high prevalences of malaria infection were found in Erave, Kutubu and Tari in 1963 (2), no part of the Southern Highlands was ever included in the national malaria control program (3). During the establishment of the Hides Gas project a series of malaria surveys were conducted in the lower Tari Valley in 1990-1991. Hii et al. (4) observed that the overall malaria prevalence decreased from 49% at 1050 m to 3% at 1700 m. *Plasmodium malariae* was found to decrease in prevalence with altitude while *P. vivax* increased. Following these studies a very successful malaria control program based on indoor residual spraying with lambda-cyhalothrin was initiated and malaria virtually disappeared from the lower Tari Valley (R. Hutton, personal communication).

In all other parts of the province, the malaria situation has not been investigated for nearly 40 years and accurate and up-to-date information on malaria transmission is not available. We therefore conducted a series of malaria surveys in order to determine the current extent and nature of malaria transmission in the province and provide a baseline for the evaluation of renewed malaria control activities undertaken by the national and provincial health authorities.

Materials and Methods

Selection of survey villages

Surveying all of the potentially malarious areas in highland areas of Southern Highlands Province was not possible, due to financial and logistic constraints. It was therefore necessary to use an approach which allowed a reasonably accurate investigation of the situation in all surveyed areas with limited numbers of field surveys. This was achieved by setting up a system based on the geographical information system (GIS) for the selection of survey villages in potential malaria transmission areas. We used village coordinates from the Papua New Guinea (PNG) village gazetteer (PNG National Mapping Bureau), altitude information from the tactical pilot charts (TPC) and information on different landforms from the PNG Resource Information System (PNGRIS) (1).

In the first stage of selection, areas in the province were categorized according to their altitude as potentially non-malarious (>1800 m), of epidemic potential (1500-1800 m), and of low (1200-1500 m) and intermediate (900-1200 m) potential for stable malaria transmission. Based on this altitudinal stratification, lists of villages falling within the different categories were compiled using the PNG village gazetteer. Based on these lists, villages were randomly selected in such a way that lower-altitude areas (ie, with higher malaria transmission potential) were over-sampled and all major landforms were included. This random sample contained more villages than could feasibly be visited and a final selection of survey villages was based on further criteria such as accessibility, the prevailing local security situation and advice from local health authorities. If it was not possible to visit a selected village, then a neighbouring village was included instead.

Due to the precarious security situation at the time of the surveys, no surveys could be conducted in the Magarima, Tari and Kopiago areas. For the lower Tari Valley, the results from earlier surveys of Hii et al. (4) were thus included into an overall assessment of the malaria situation in the province. The climate in SHP is considerably less seasonal than in other parts of the highlands and thus a single survey in the late dry season of 2003 was conducted in 8 villages in the Kutubu and Erave areas (Figure 1, Table 1). These surveys were conducted in collaboration with the Community Development Initiative (CDI). As there were reports of a malaria epidemic in Poroma, lower Kagua and Erave areas of SHP just prior to the 8 surveys conducted in Imbonggu (Lower Mendi), Ialibu-Pangia, Kagua, Kewabi and Nipa areas in July-August 2004 (Figure 1, Table 2), a second round of surveys was conducted in July 2005 in order to assess year-to-year variations. These surveys were conducted in collaboration with the Catholic Health Services in Mendi.

Survey methodology

In order to achieve a sample as representative as possible of the entire village population a household-based sampling strategy was used. A number of households with a total population of approximately 140-200+ people were selected. From each selected household, every member who could be reached during the stay in the village and gave informed consent was included in the survey. In order to increase the proportion of family members sampled the survey team spent 1-2 nights in each village. If the village

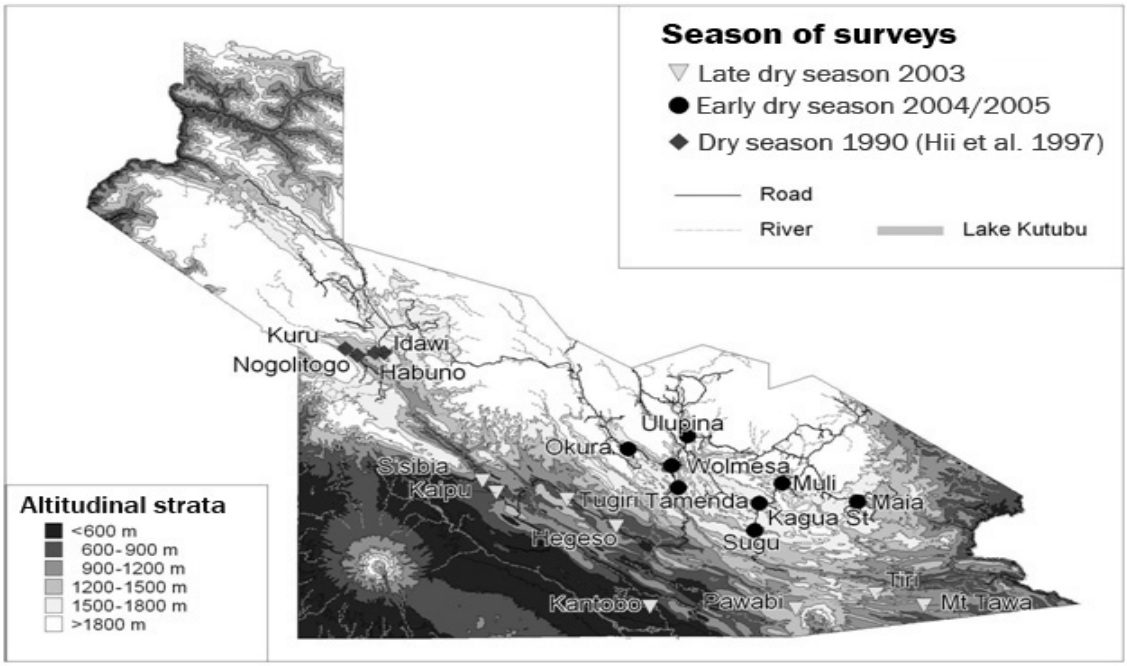

Figure 1. Locations and season of the 2003, 2004 and 2005 malaria surveys and the1990 survey by Hii et al. (4). Hii et al. surveyed in 4 villages in the dry season of 1990 (and carried out follow-up surveys in 2 villages in 1991).

had less than 200 inhabitants, sampling of every resident was attempted. This approach allowed us to sample 70-80% of all selected household members.

From each household included in the survey, the demographic data of all residents was recorded. From each individual of the household, a thick and thin blood film was prepared, the spleen palpated, the axillary temperature taken and haemoglobin (Hb) level measured. Symptomatic individuals were treated according to national guidelines with chloroquine plus Fansidar.

A short questionnaire on current symptoms, past malaria episodes and treatment, recent travel and other behaviour (ie, sleeping in garden houses, hunting, fishing and food gathering) which had been found to be related to risk of malarial infections in other parts of the highlands (5) was administered to each subject or their guardian. Further details on survey methodology are given in Mueller et al. (6).

Giemsa-stained blood films were examined microscopically for 100 thick film fields under oil immersion before being declared negative. The parasite species in positive films were identified and densities recorded as the number of parasites/200 white blood cells (WBC). Densities were converted to the number of parasites/µl of blood assuming 8000 WBC/µl. The slides were read at the PNG Institute of Medical Research (PNGIMR) in Goroka independently by two experienced microscopists.

Data entry was done at the PNGIMR in Goroka using a double-entry system. Statistical analyses were done using STATA 7.0 (Stata Corp., College Station, TX) and SPlus (Insightful Corp, Seattle, WA) statistical analysis software. Chi-squared tests and logistic regression analyses were used for categorical variables. Continuous variables were investigated using Student's t-tests, linear regression models and analyses of variance (ANOVA). Trends across age groups and levels of endemicity were tested using a non-parametric test for trends. Haemoglobin values were adjusted for age and gender effects using regression splines.

This study was approved by the PNG

TABLE 1

Summary of results of parasitology surveys in Southern Highlands Province (SHP): Lake Kutubu and Erave LLGs (SHP) and Kikori LLG (Gulf)

Village	N	Temp >37.5°C	Fever 3 days	PR (%)	Parasite species *Pf/Pv/Pm/Po*	SR (%)	Mean Hb (g/dl)	
							Male	Female
Late dry season (November-December 2003)								
Lake Kutubu and Erave								
Kaipu	191	0.5%	5.8%	23.0	16/19/14/1	22.0	12.0	11.4
Sisibia	182	0.6%	8.2%	28.6	24/24/10/2	22.0	11.7	11.0
Hegeso	178	4.5%	11.2%	32.6	26/27/9/1	18.0	12.4	11.6
Kantobo	145	3.5%	9.7%	16.6	8/13/3/1	9.0	11.8	11.1
Pawabi	179	1.1%	2.8%	9.5	9/8/2/1	1.1	13.3	12.2
Tiri	115	1.7%	13.9%	31.3	24/13/3/0	27.0	12.4	11.2
Mt Tawa	206	2.4%	15.5%	15.5	19/9/4/0	8.3	12.3	11.7
Tugiri	141	2.8%	7.1%	17.7	7/11/4/3	4.3	12.5	11.7
Kikori								
Kaiam	166	1.8%	16.0%	18.1	11/16/6/0	24.2	11.0	10.3
Kopi	178	3.4%	10.1%	9.5	4/12/1/0	13.5	11.7	10.8
Ero	188	3.7%	4.8%	5.3	2/7/1/0	1.6	12.1	12.0

LLG = Local-Level Government
N = number
Temp = temperature
PR = Overall prevalence rate of malarial infections
SR = enlarged spleen rate
Hb = Haemoglobin
Pf = Plasmodium falciparum
Pv = Plasmodium vivax
Pm = Plasmodium malariae
Po = Plasmodium ovale

Medical Research Advisory Committee (MRAC) under approval number MRAC No 00.26.

Results

A total of 3652 people were surveyed during the 24 surveys in 16 different villages in the Southern Highlands Province (Figure 1). Of all participants 54% were female and 16% were aged <5 years, 13% 5-9 years, 21% 10-19 years and 50% 20 years or over. There were comparable numbers of males and females in all age groups, except for adults (57% female).

Prevalence of *Plasmodium* infections

The examination of blood slides revealed malaria infections in all villages surveyed in 2003-2004 with mean prevalence rates ranging from 32.6% in Hegeso, Lake Kutubu (Table 1) to 2.5% in Muli, Kewabi-Ialibu (Table 2). Overall, the highest prevalence rates (>20%) were found in the Lake Kutubu, Erave and Poroma Local-Level Government (LLG) areas (Figure 2, Tables 1 and 2), while under 5% of people surveyed were infected with

TABLE 2

SUMMARY OF RESULTS OF PARASITOLOGY SURVEYS IN SOUTHERN HIGHLANDS PROVINCE: OTHER SURVEYED AREAS

Village	N	Temp >37.5°C	Fever 3 days	PR (%)	Parasite species *Pf/Pv/Pm/Po*	SR (%)	Mean Hb (g/dl)	
							Male	Female
Early dry season 2004 (July-August 2004)								
Ulupina	146	0.7%	6.9%	4.8	4/4/1/0	0.0	14.0	13.8
Wolmesa	121	0.0%	1.7%	6.6	2/7/0/0	6.6	14.3	12.7
Tamenda	201	2.0%	4.0%	26.4	19/33/5/0	22.4	12.4	11.7
Okura	50	2.0%	4.0%	10.0	1/3/1/0	2.0	15.1	13.6
Maia	149	0.7%	0.7%	2.7	1/3/0/0	0.0	14.6	13.8
Muli	201	0.0%	1.5%	2.5	1/4/1/0	0.0	14.6	13.7
Kagua Station	105	0.0%	6.7%	3.8	3/1/0/0	1.9	14.4	13.2
Sugu	107	2.8%	11.3%	16.8	6/13/1/0	6.5	13.6	12.4
Early dry season 2005 (July 2005)								
Ulupina	51	0.0%	15.2%	0.0	0/0/0/0	0.0	14.1	13.2
Wolmesa	120	1.7%	11.3%	0.8	0/1/0/0	0.0	13.2	12.8
Tamenda	186	2.7%	16.2%	12.4	8/12/4/0	3.2	13.1	12.5
Okura	66	0.0%	16.7%	1.5	1/0/0/0	0.0	14.0	13.9
Maia	155	1.3%	13.6%	3.2	4/1/0/0	0.7	13.1	12.3
Muli	218	0.0%	15.6%	4.6	1/9/1/0	0.0	14.8	13.6
Kagua Station	215	0.0%	11.6%	0.5	0/1/0/0	0.0	14.4	13.6
Sugu	224	2.7%	19.2%	13.0	4/23/2/0	0.9	14.1	13.3

N = number
Temp = temperature
PR = Overall prevalence rate of malarial infections
SR = enlarged spleen rate
Hb = Haemoglobin
Pf = Plasmodium falciparum
Pv = Plasmodium vivax
Pm = Plasmodium malariae
Po = Plasmodium ovale
Villages in italics were affected by a malaria epidemic in May-Jun 2004

Plasmodium parasites in higher-lying villages in Ialibu-Pangia, Kagua and Imbonggu. In villages with surveys in both 2004 and 2005, a significantly reduced prevalence of infections was found in the 2005 surveys (9.6% vs 5.7%, p <0.001) (Table 2), with prevalence rates between 0% in Ulupina (Lower Mendi) and 13.0% in Sugu (Kagua). This reduction in prevalence was, however, only observed in the Mendi/Poroma/Nipa villages (2004: 14.1%, 2005: 5.9%, p <0.001) and not in those in the Kagua/Kewabi/Pangia areas (2004: 5.5%, 2005: 5.5%, p >0.5).

All four human malaria species were found during the surveys. In the Kutubu and Erave surveys (November-December 2003), the most common species was *P. falciparum,*

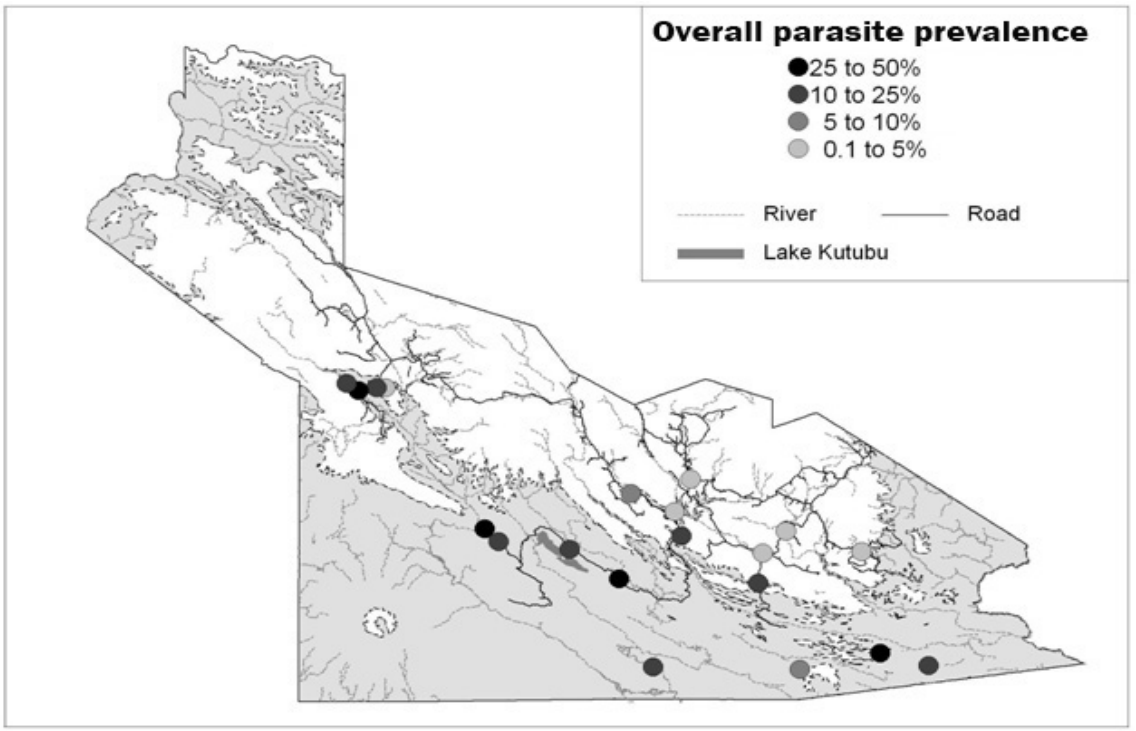

Figure 2. Overall prevalence rates of malaria infection in the 1990, 2003, 2004 and 2005 surveys.

which accounted for 42% of infections, followed by *P. vivax* (39%) and *P. malariae* (16%). *P. ovale* accounted for 3% of all infections. This species dominance was reversed in both the July-August 2004 and July 2005 surveys conducted in the higher-lying parts of the province, where *P. vivax* (62%) dominated over *P. falciparum* (30%) and *P. malariae* (8%). *P. falciparum* gametocytes were found in 0.9% of participants.

Irrespective of the survey year there was a strong association between altitude and prevalence (χ^2 = 253.6, df = 2, p <0.001), with 24.3% prevalence in villages at an altitude of <1000 m and 17.7% in villages at 1000-1499 m, but only 3.3% in villages above 1500 m. As in earlier surveys (4), the relative frequency of *P. vivax* increased with altitude (<1000 m: 46%, 1000-1499 m: 53%, ≥1500 m: 67% of all positive cases were infected with *P. vivax*, p = 0.028), while that of *P. malariae* decreased (<1000 m: 20%, 1000-1499 m: 10%, ≥1500 m: 6%, p = 0.004). *P. ovale* was found only in the Kutubu and Erave surveys and there it accounted for 3% of infections. 7.2% of all infections were mixed with no significant difference between areas.

The risk of infection was strongly age dependent (χ^2 = 173.2, df = 4, p <0.001), with infections most prevalent in 5-<10 and 2-<5 year old children (23.6% and 25.9%, respectively), followed by adolescents (10-20 years: 14.5%), infants and toddlers (<2 years: 9.5%) and adults (>20 years: 6.7%). The relative frequency of *P. vivax* significantly decreased with age (<5 years: 63%, 5-9 years: 56%, 10-19 years: 47%, ≥20 years: 40% of all positive infections, χ^2 = 14.7, df = 3, p = 0.002).

Most infections were of low density: 71.7% of infections were sparse (<500/µl), 10.6% light (500-999/µl), 14.1% moderate (1000-9999/µl) and only 3.7% were heavy (≥10,000/µl). Densities of *P. falciparum* infections were significantly higher than those of *P. vivax* and *P. malariae* infections (geometric mean 332, 183 and 187/µl, respectively, p <0.001 and p = 0.001). Mixed infections had significantly higher densities than single infections (1516 vs 216/µl, p <0.001). There were highly significant differences in intensity of infection among age groups ($F_{4,461}$ = 6.7, p <0.001). Infections were heaviest in infants and small children (607 and 430/µl, respectively) and

lightest in adolescents and adults (194 and 170/µl). For all 3 species there were no significant differences in density between areas of different altitude (p >0.2).

In line with the definition used in earlier highland studies (6-11) we used the following definitions of endemicity for further analyses: High: overall prevalence rate (PR) ≥20%; Moderate: PR 10-19%; Low: PR 5-9%; Very low: PR <5%.

Malaria-associated morbidity

The overall prevalence rates of measured fevers (axillary temperature >37.5°C) (Tables 1 and 2) were significantly correlated with the prevalence of malaria parasites in a population (r = 0.59, n = 24, p = 0.03). The prevalence of reported fevers was also significantly correlated with overall parasite prevalence in both the 2003-2004 (r = 0.59, n = 16, p = 0.02) and 2005 surveys (r = 0.70, n = 8, p = 0.06). However, in villages surveyed in both years, febrile illness was significantly more frequently reported in the 2005 survey (15.1% vs 4.2%, p <0.001).

Among the parasite-positive cases only 3.9% had a temperature >37.5°C at the time of the survey; another 10.2% reported fever in the last 3 days. There was no difference in the prevalence of simple malarial morbidity among slide-positive people at different levels of endemicity (p = 0.9). However, the occurrence of febrile symptoms was strongly affected by the intensity of infection (χ^2 = 47.0, df = 2, p <0.001): 58.8% of cases with a parasite density >10,000/µl reported being febrile, but only 9.5% of those with densities <1000/µl.

Overall, malaria accounted for 34.0% of all fevers at the time of survey and 18.4% of reported fever in the last 3 days. The risk of malaria is strongly dependent on endemicity (χ^2 = 31.1, df = 3, p <0.001). At the lowest level of transmission (PR <5%) only 7 of 117 people (6.0%) with a reported febrile illness had concurrent malarial infection compared to 20.8% at moderate (PR 11-20%) and 38.7% at high (PR >20%) transmission levels.

Mean haemoglobin levels in a village (Tables 1 and 2) were highly negatively correlated with the prevalence of malarial infections (r = −0.79, n = 24, p <0.001) and ranged from 14.6 g/dl in Okura (PR 10.0%) to 11.4 g/dl in Sisibia (PR 28.6%). Population mean Hb values were significantly lower in the remote and more malarious areas in Kutubu and Erave than in higher-lying areas (13.5 vs 11.9, t_{3647} = 23.5, p <0.001). The village mean haemoglobin level was found to decrease by 0.76 g per 10% increase in parasite prevalence rate (p <0.001). This decrease was mainly found with low and moderate parasite prevalence (−0.92 g per 10% increase, p <0.001), while at prevalences >20% no significant further decrease was observed (−0.22 g per 10% increase, p = 0.61).

Concurrent plasmodial infection was associated with a decrease in haemoglobin of 1.2 g/dl (CI_{95}: [1.1-1.4.], p <0.001). *P. falciparum* infections were associated with a larger drop in Hb than *P. vivax* infections (−1.4 vs −0.7 g/dl, p = 0.002). The (adjusted) decrease in haemoglobin is strongly dependent on levels of parasitaemia (<500/µl: −0.8, 500 – 999/µl: −1.5, 1000-9999/µl: −1.6, ≥10,000/µl: −2.9 g/dl, $F_{4,3515}$ = 58.6, p <0.001).

The prevalence of moderate-to-severe malarial anaemia (SMA) (Hb <8.0 g/dl) was independently associated with both concurrent infection (LR-test: χ^2 = 7.5, df = 1, p = 0.006) and residence in an area of moderate to high endemicity (PR >10%: LR-test: χ^2 = 13.13, df = 1, p <0.001). SMA was observed in 3.1% of participants in villages with PR >10%, compared to only 1.0% in areas with low levels of transmission. Within a population, concurrent parasitaemia was a highly significant risk factor for SMA (adjusted OR [AOR] 3.5, CI_{95} [1.9-6.5], p <0.001). The risk of SMA increases dramatically with increasing intensity of infection (<1000/µl: AOR = 1.5, 1000-10,000/µl: AOR = 9.7, >10,000/µl: AOR = 43.5; LR-test: χ^2 = 38.0, df = 3, p <0.001).

Spleen rates in the different villages ranged from 0% in villages in Imbonggu, Kagua and Ialibu-Pangia to 27% in Tiri village, Erave (Tables 1 and 2). The rate of enlarged spleen was highly correlated with the overall parasite prevalence rate (r = 0.91, n = 24, p <0.001). The average size of an enlarged spleen was 2.0 (Hackett's grade). A large spleen was highly significantly associated with a concurrent infection (18.4% vs 5.4%, p <0.001). There was no difference in this association among the different *Plasmodium* species.

Health seeking, bednet use and mobility

When people were asked whether they had had malaria recently, between 4.2% (Kaipu) and 28.3% (Sugu) of people reported having had a 'malaria' episode in the past two weeks (Table 3 and 4). The highest numbers of 'malaria' episodes were reported in 2004 in villages that were suspected to have been affected by epidemic malaria prior to the surveys (ie, Wolmesa, Tamenda, Okura and Sugu). Although still relatively high, the number of people reporting malarial illness in these areas was significantly lower in 2005 (2004: 25.0%, 2005: 14.4%, p <0.001). Of all people reporting a malaria episode, however, only 70% went to an aid post/health centre/ hospital for treatment.

Overall, reported malaria episodes were not correlated with the prevalence of infection found in a village (r = 0.12, n = 24, p = 0.6). Within surveys, a reported malaria episode in the prior two weeks was highly significantly associated with an increased risk of infection (adjusted OR = 1.83, CI_{95} [1.39-2.40], p <0.001). Of all people that reported prior antimalarial drug use, 16% had a positive blood slide in the survey, indicating the presence of drug-resistant parasites or poor compliance with antimalarial treatment.

The number of people in each village sleeping under a bednet varied greatly between regions. While 27% (range 7-52%) of people in the malaria-endemic villages of Kutubu and Erave used bednets, only 8% (range 0-22%) did so in higher-lying villages in the regions surveyed in July- August 2004 and July 2005. Most of the nets used are non-treated or non-re-treated and the reported use of bednets did not alter risk of infection with malaria (adjusted OR = 1.0, CI_{95} [0.7-1.2], p = 0.6).

The populations in Kutubu and Erave were highly mobile, and 50% (range 17-90%) of people reported that they regularly slept in

TABLE 3

SUMMARY TABLE WITH VILLAGE CHARACTERISTICS AND MALARIA-RELATED BEHAVIOUR IN SOUTHERN HIGHLANDS PROVINCE (SHP): LAKE KUTUBU AND ERAVE LLGS (SHP) AND KIKORI LLG (GULF)

Village	LLG	Altitude (m)	N	Malaria 'sickness' (%)	Antimalarial use (%)	Bednet use (%)	Slept in garden house (%)
Late dry season (November-December 2003)							
Kaipu	Lake Kutubu	920	191	4.2	3.1	31.4	23.6
Sisibia	Lake Kutubu	950	182	7.7	5.5	27.1	20.0
Hegeso	Lake Kutubu	920	178	6.2	3.9	52.3	60.7
Kantobo	Lake Kutubu	560	145	7.0	3.5	32.4	52.4
Pawabi	Erave	1350	179	5.6	3.4	15.1	16.8
Tiri	Erave	1450	115	21.7	11.3	7.0	67.8
Mt Tawa	Erave	1125	206	22.8	5.3	9.2	89.8
Tugiri	Lake Kutubu	995	141	19.9	17.7	45.4	73.1
Kaiam	Kikori (Gulf)	25	166	16.6	3.6	41.1*	24.7
Kopi	Kikori (Gulf)	10	178	11.9	8.9	87.7*	9.0
Ero	Kikori (Gulf)	40	188	5.9	2.7	67.9*	32.8

LLG = Local-Level Government
N = number
* Long-lasting insecticide-treated bednets (LLIN) distributed by health services prior to surveys

TABLE 4

Summary table with village characteristics and malaria-related behaviour in Southern Highlands Province: other surveyed areas

Village	LLG	Altitude (m)	N	Malaria 'sickness' (%)	Antimalarial use (%)	Bednet use (%)	Slept in garden house (%)
Early dry season 2004 (July-August 2004)							
Ulupina	Lower Mendi	1700	146	9.6	4.8	0.0	8.9
Wolmesa	Poroma	1580	121	25.0	15.7	0.0	0.0
Tamenda	Poroma	1420	201	22.9	19.4	22.0	0.5
Okura	Nipa	1920	50	26.0	12.0	0.0	8.2
Maia	East Pangia	1510	149	6.7	6.0	11.5	0.0
Muli	Kewabi	1680	201	14.5	10.5	3.5	0.0
Kagua Station	Kagua	1630	105	12.4	10.5	7.6	0.0
Sugu	Kagua	1440	107	28.3	26.2	6.8	0.0
Early dry season 2005 (July 2005)							
Ulupina	Lower Mendi	1700	51	7.8	0.0	0.0	9.8
Wolmesa	Poroma	1580	120	15.0	6.7	1.7	1.7
Tamenda	Poroma	1420	186	9.1	5.4	15.6	0.5
Okura	Nipa	1920	66	7.6	0.0	6.1	0.0
Maia	East Pangia	1510	155	10.3	7.1	12.3	0.0
Muli	Kewabi	1680	218	17.9	8.3	1.4	0.0
Kagua Station	Kagua	1630	215	12.1	5.6	6.1	0.0
Sugu	Kagua	1440	224	20.5	13.4	10.3	0.0

LLG = Local-Level Government
N = number

garden houses. In these villages, sleeping in a garden house was associated with a slight increased risk for malarial infection (adjusted OR = 1.3, CI_{95}[1.0-1.8], p = 0.11). Few people (1%) in the other villages slept in garden houses and doing so was not associated with an increased risk of malaria (p = 0.7).

Malaria in Kikori LLG, Gulf Province

In conjunction with the 2003 surveys in Kutubu and Erave 532 people in 3 villages in neighbouring Kikori LLG, Gulf Province were also surveyed for malarial infections. Despite their coastal/lowland location at altitudes below 40 m above sea level, the overall prevalence (range 5.3%-18.1%, Table 1) of malaria in these village was significantly lower than those observed in neighbouring Kutubu and Erave villages (10.7% vs 21.5%, p <0.001). Following a program by the Kikori health services that distributed long-lasting insecticide-impregnated bednets to surrounding villages, significantly more people in the Kikori surveys reported sleeping under a betnet than in Kutubu and Erave villages (Table 3, 66.1% vs 27.5%, p <0.001). Among people surveyed in the 2003 surveys, there was a significant reduction in the risk of malaria infection in bednet users compared to non-users (OR = 0.8, CI_{95} [0.6-1.0], p <0.05) with bednets more effective in preventing *P.*

falciparum (OR = 0.6, CI_{95} [0.4-0.9], p <0.05) than *P. viva*x infections (OR = 0.9, CI_{95} [0.6-1.3], p = 0.706). In contrast to the people in the Kutubu and Erave areas very few Kikori people slept regularly in garden houses (Table 3).

Discussion

The prevalence rates observed in the current surveys show that while areas of high transmission have remained the same, transmission levels are likely to have increased since the 1960s (2). As a result, prevalence rates of malarial infection at altitudes above 1500 m and below 1000 m are now comparable to those observed in other highlands provinces (6-11). However, at intermediate altitudes (1000-1500 m) some prevalence rates observed in these as well as earlier surveys (4) are considerably higher than those observed elsewhere in the highlands, except during epidemic outbreaks (12).

The high prevalence of malarial infection in villages in Kutubu and Erave is probably linked to both the local geography and the relatively mobile lifestyle of these populations. Up to 90% of study participants reported regularly visiting and sleeping in bush and garden areas and the altitude measured at the main village is thus only partly representative of the wider environment they live in or use. Increased malaria transmission outside the main village associated with a mobile lifestyle is a common phenomenon in remote highlands fringe communities (6-11) and may lead to malarial infections and even epidemic outbreaks being detected in villages that are situated at altitudes that would usually preclude local malaria transmission (13). Unless this high mobility is taken into account, effective malaria control will be difficult to achieve in these areas.

Four of the villages surveyed (Tamenda, Okura, Wolmesa, Sugu) in the July- August 2004 and July 2005 surveys were situated in an area that was reported to have been affected by a 'malaria' epidemic in May and June 2004. A comparison between the July 2004 and July 2005 surveys found significantly higher prevalence rates in Tamenda, Okura and Wolmesa in 2004 than in 2005, indicating that these areas were indeed affected by a malaria outbreak in 2004. However, no such increase was observed in Sugu in the lower Kagua area. The prevalence of malarial infections in Sugu and Tamenda in both 2004 and 2005 was comparable to that found at similar altitudes in Pawabi and Tiri in the Erave area or in the lower Tari Valley (4) and indicates endemic, although possibly seasonal, transmission at altitudes below 1450-1500 m in Poroma and Kagua-Erave. The geographical extent of the reported 2004 malaria epidemic in SHP was thus likely to have been significantly smaller than the areas that were later designated for spraying.

The present surveys did not allow drawing any conclusions as to the seasonality of malaria transmission in the province as no area has been surveyed in both wet and dry season. However, given that there is limited seasonality of rainfall in much of the province (1), except for the north-eastern parts, only limited seasonal variation in malaria transmission is to be expected.

A special characteristic of the surveys in SHP was the high proportion of infections caused by *P. vivax*, in particular in areas >1500 m. However, even at lower altitudes *P. vivax* prevalence was almost as high as *P. falciparum*. This differentiates these surveys from the earlier surveys of Hii et al. (4) as well as the situation in either Western Highlands Province or Simbu Province (6, 7), where *P. falciparum* is the dominant species in all but the very lowest transmission areas. The short development cycle in the mosquito, the earlier occurrence of gametocytes and the capacity to make relapses from long-lasting hypnozoites (14) all favour *P. vivax* in areas of low or variable transmission but also in small, mobile populations. On the other hand, *P. malariae*, which has the longest developmental period in the mosquito, was commonly found only in the highly endemic areas below 1000 m.

The patterns of simple malaria morbidity (ie, fever + presence of parasites) revealed two interesting facts. First, at low transmission intensities (ie, higher altitudes) very few observed and reported fevers were linked to malarial infections. However, even in these areas most episodes of fever resulted in treatment with antimalarials, thus leading to considerable over-treatment with antimalarial drugs. Secondly, as in earlier highlands surveys (6-11) most malarial infections were asymptomatic, even in areas with low transmission levels, where it is commonly thought that immunity is limited and thus

every infection should lead to an episode of malaria. The reasons for the high frequency of these low-level, asymptomatic infections in areas of low transmission are not clear. However, the decreases in prevalence rates in adolescents and adults indicate that SHP populations in malaria-endemic areas do acquire some degree of immunity to malarial infections. In addition, frequently incomplete, inadequate and/or unnecessary treatment may lead to infections becoming chronic and long lasting. Similarly, the high amount of over-treatment might act like a malarial 'prophylaxis'/intermittent treatment and, while it will not prevent new infections, it may act to suppress them to subclinical levels.

The significant drop in haemoglobin associated with malaria infections in all areas of the province and consequently the tight correlation of population mean haemoglobin levels and parasite prevalence rates corresponds to patterns observed in other PNG highlands provinces (6-11). Haemoglobin levels were lowest in low-lying, malarious villages in the remote Kutubu and Erave areas. While high-density malaria infections were associated with considerable excess risk for the development of moderate-to-severe anaemia, the overall prevalence of SMA was fortunately relatively low, even in villages with high malaria prevalence rates. Nevertheless, the present study indicates that malarial infections are an important contributor to anaemia in the province.

Overall conclusions and recommendation for control

By using data from the present and past surveys it is possible to stratify Southern Highlands Province into 3 areas with different risk of malaria (Figure 3) and therefore different needs for malaria control:

Moderate to highly endemic malaria (<1400 m)

All areas along the southern fringe of the province are clearly highly endemic for

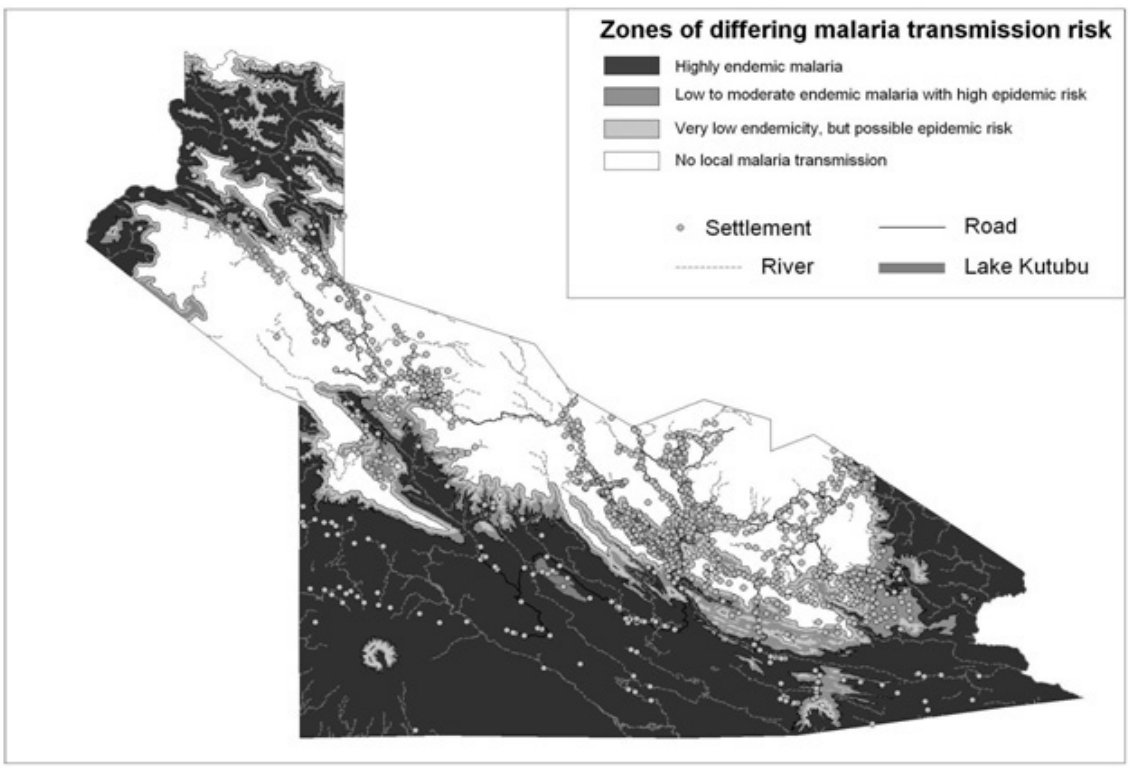

Figure 3. Zones of different malaria risk in Southern Highlands Province.

malaria. In these areas malaria transmission is intense all year round with prevalence rates reaching 10% to over 30%. Although people do develop considerable levels of immunity, malaria is a major source of illness and contributes significantly to the high levels of anaemia observed – particularly in remote communities.

The remoteness of the area and the mobility of the population as well as their limited access to health services make long-lasting insecticide-treated bednets (LLIN) the most promising control option. However, in order to be effective a LLIN distribution program needs to be accompanied by education concerning the need to use the nets both in main villages and while away in garden houses or on hunting trips. Where possible, villages should be supplied with excess nets to cover these needs. Overall, 15% of villages in Southern Highlands are situated in these areas.

Low endemic transmission with significant risk of epidemic outbreaks (1400-1600 m, locally higher)

At intermediate altitudes (1400-1700 m), transmission is generally low (PR <5-10%), but there is a considerable risk of epidemics. Most of the communities affected by the reported malaria epidemic that hit the province in the 2004 wet season are situated in this area. As seen in Tamenda and during epidemics in other provinces (12), prevalence rates at the height of the epidemic may exceed 30% and are associated with high levels of morbidity and, if uncontrolled, mortality. Depending on local geography, closeness to endemic areas and the presence of lower-lying garden and hunting areas, prevalence rates of malaria at these altitudes can vary substantially and epidemics may occur in villages up to 1700 m (13).

While indoor residual insecticide spraying (IRS) by Oil Search was effective in controlling and preventing malaria epidemics in their Hides Gas area, it may be difficult to implement IRS on a large scale in other areas due to the logistical challenges of maintaining regular IRS coverage in remote areas without reliable road access. In particular in the remoter areas, long-lasting insecticide-impregnated bednets may therefore be a more appropriate method of control. IRS in combination with mass drug administration (MDA) should, however, be the primary tool for epidemic control.

Low to non-transmission areas (above 1600-1700 m)

The majority of SHP villages (56%) and almost all densely populated areas in the northern half of the province are situated at altitudes that preclude stable local malaria transmission. In these areas prevalence rates are usually very low (<2.5%) and most malaria cases are likely to result from travel to lower-lying malarious areas both in Southern Highlands and other provinces. Consequently, malaria is only a very minor source of febrile illness and most reported 'malaria' fevers are non-malarial in origin.

Malaria control in these areas should primarily focus on prompt treatment of imported cases and education in regard to the risk associated with travel to lower-lying malarious areas, rather than on vector control. The suggested control measures in neighbouring lower-lying areas should prevent malaria epidemics from spreading into higher-lying areas; nevertheless, epidemic surveillance and, if necessary, control (using IRS and MDA) should be part of malaria control plans for these areas.

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Selective surgical management of penetrating anterior abdominal wounds at the Angau Memorial Hospital: a prospective study

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SUMMARY

Trauma is a leading cause of admissions to the surgical ward in Papua New Guinea (PNG), accounting for about 35% of cases. Of these, 15% of cases are abdominal injuries, of which 19% are penetrating injuries. Selective surgical management of patients with a low-velocity anterior abdominal wound (AAW) is beneficial in some patients. Aim: To determine if selective surgical management is a viable therapeutic option in PNG. Methods: A non-random prospective study of consecutive cases was done on 60 patients with an AAW based entirely on clinical symptoms and signs. The outcome measures were length of hospital stay, morbidity and mortality. Data were analysed using SPSS 10.0 for Windows and Microsoft Excel. Results: Immediate laparotomy was done on 24 (40%) of cases and 36 (60%) had nonoperative conservative management, of which 6 (17%) failed and went on to have laparotomy on demand. The average hospital stay was 4 days shorter (p = 0.0001) for the nonoperative group, which had significantly fewer complications (p = 0.01). No deaths were recorded in either of the two groups of patients. Conclusion: Selective nonoperative management of stable patients with an AAW with or without omental signs is a safe therapeutic option in PNG.

Introduction

A penetrating abdominal wound that breaches the peritoneum is an indication for exploratory laparotomy. The reason is that in 60% of cases there are definite injuries to solid and hollow viscera amenable to surgical repair. Furthermore there is a high price to pay for missed injuries in terms of serious morbidity and even death. However, in low-velocity injuries such as knife wounds about 5-20% of exploratory laparotomies were negative and the laparotomy was associated with longer hospital stay, significant morbidity and increased costs (1). Leading trauma centres in the world (2-5) have taken bold steps to challenge the status quo. At present it is accepted that nonoperative management of an anterior abdominal wound (AAW) can safely be practised, especially when the patient is haemodynamically stable and without peritonitis.

In Papua New Guinea (PNG) no published data exist and this study was done to see if it is indeed safe to apply nonoperative conservative management of an AAW at the Angau Memorial Hospital in Lae.

Methods

All consecutive patients admitted to the Angau Memorial Hospital in Lae between January 2009 and January 2010 with an AAW and breaches of the peritoneum were recruited into the study. The primary clinical responsibility and adherence to the study protocol rested with the lead investigator (KL) and Senior Specialist Surgeon of the Surgery Unit. Exclusion criteria included injuries to the

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back, chest or pelvis. The anterior abdominal wall is taken to mean, superiorly – the inferior costal margins, laterally – the posterior axillary line, and inferiorly – the inguinal ligament and symphysis pubis. The protocol followed for the management of penetrating anterior abdominal wounds is shown in Figure 1.

Immediate laparotomy

All patients with peritonitis or in shock with systolic blood pressure (BP) <90 and pulse rate >120 were operated on after an initial resuscitation with fluid, blood and antibiotics. The antibiotics usually depended on availability but gave an empirical broad cover against enteropathogens including *Bacteroides* species. A midline incision was always employed. Thorough exploration was done and any perforations were repaired. Copious saline washout was done. The closure was done with a single continuous en masse closure with nylon. All drip, suck and drain tubes were in place for postoperative

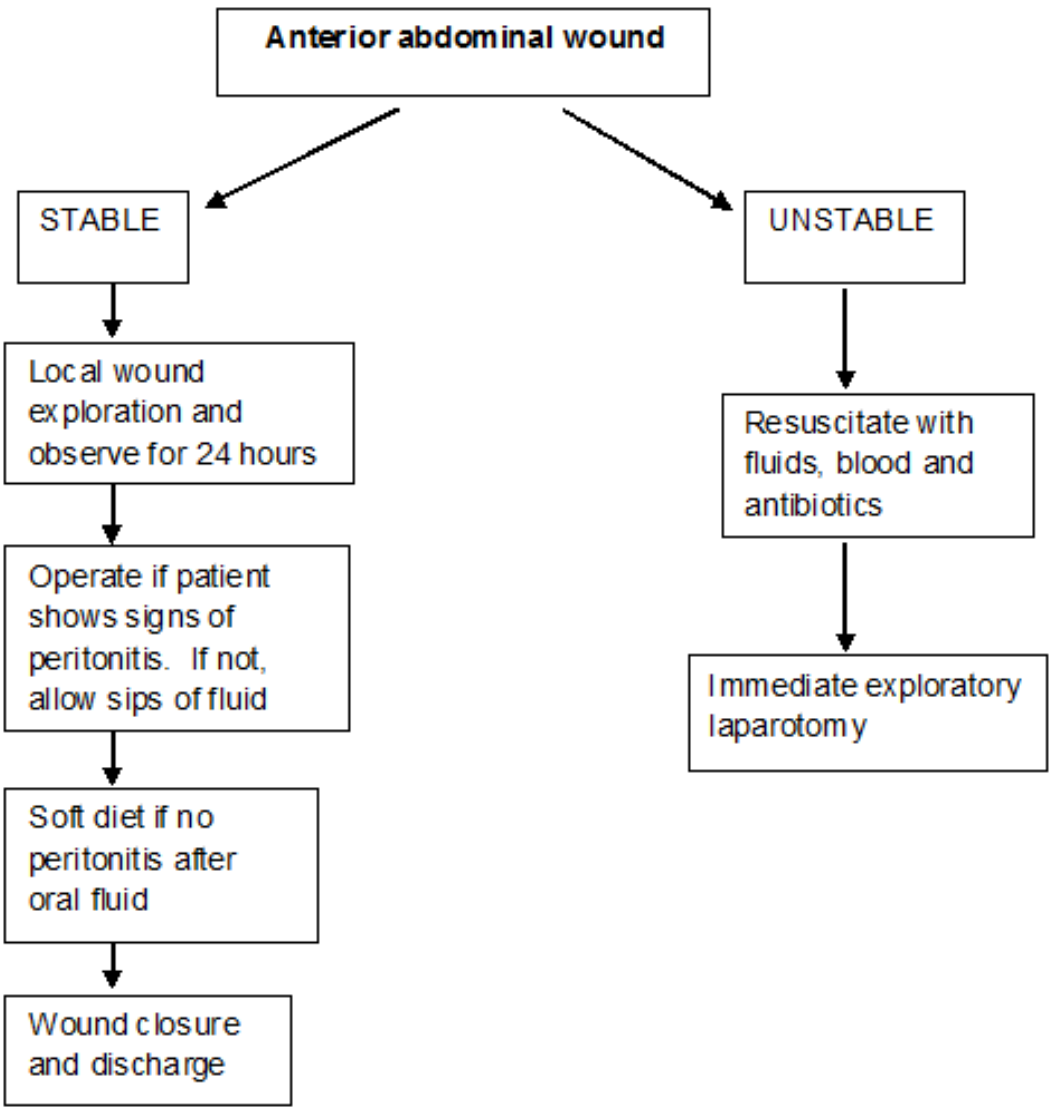

Figure 1. Protocol for the management of penetrating anterior abdominal wounds in this study.

monitoring.

Local wound exploration

All patients with a positive omental sign, bowel evisceration, local peritonism and equivocal penetration and those who were haemodynamically stable were entered into this arm. The wound was explored under local anaesthesia and may have needed some extension if necessary. Eviscerated viscera were washed with saline and returned to the abdominal cavity. Strict serial clinical examination was done every 2-4 hours for 12 hours. An oral fluid test was done after 12 hours: patient intolerance with abdominal pain and distention meant that the plan was abandoned and the patient was subjected to laparotomy. After 48-72 hours when the patient was stable the wound was repaired and the patient was discharged home.

Imaging studies

Plain X-ray, ultrasonography or an abdominal tap were an adjunct to clinical symptoms and signs, which were the main criteria for allocating patients to either arm.

Statistics

Chi (χ^2)-squared test with Yates correction and Student's t-test were used for complications and length of hospital stay, respectively.

Consent

Informed consent was obtained from all the subjects as well as relatives. The hospital chief executive officer (CEO) gave written consent as well, in view of the experimental nature of the interventions planned. The hospital did not have a research committee.

Results

The results show that 48 males and 12 females were injured and included in the study. The youngest was aged 3 years, the mean age was 27.5 years, the median 26 and the standard deviation 9.8. Almost half were due to interpersonal violence (45%); others were from domestic violence (38%) and accidental injuries (10%). The commonest weapons were of low-velocity type such as knifes, arrows and wooden sticks. There were only 3 gunshot wounds (5%). The 3-year-old child was accidentally pierced with a knife while asleep in a woven string bag.

Table 1 shows the use of clinical signs in decision-making. It shows that 36 cases (60%) were initially managed nonoperatively, of which 6 (17%) converted to laparotomy. This includes 3 negative laparotomies adjudicated on by a junior consultant outside the study protocol. These 3 cases were counted as negative laparotomy. Immediate laparotomy was done in 24 (40%).

Operative findings showed that the small intestines were commonly injured followed by large bowel and spleen. It is interesting that 8 patients (27%) in the operative group had negative findings (Table 2).

The oral fluid test was done on 36 patients,

TABLE 1

SELECTIVE MANAGEMENT OF ANTERIOR ABDOMINAL WOUNDS BASED ON CLINICAL SIGNS

Clinical signs	Nonoperative	Laparotomy on demand	Operative	Total
Peritonitis	1	6	10	17
Shock	-	-	3	3
Positive omental sign	11	-	7	18
Bowel evisceration	2	-	4	6
Local tenderness (peritonism)	15	-	-	15
Penetration equivocal	1	-	-	1
Total	30	6	24	60

TABLE 2

Operative findings of anterior abdominal wounds during exploration

Operative findings	Number	%
Small bowel	10	33
Large bowel	4	13
Spleen	4	13
Stomach	1	3
Liver	1	3
Vascular	1	3
Pancreas	1	3
Negative	8	27
Total	30	

of which 8 were positive; 6 of these patients went on to have laparotomy.

The mean length of hospital stay was 3 days for the nonoperative and 7 days for the operative group. There were 2 patients in the nonoperative group who stayed for 6 and 12 days due to wound breakdown and malaria, respectively. However, for the operative group the length of hospital stay (LOHS) ranged from 1 to 15 days with a median of 7 days.

There were 2 deaths from AAWs during the period of the study; however, they had both presented in extremis and died before entry into the study. There were 5 complications in the operative group: 3 due to paralytic ileus, 1 wound infection and 1 case of early adhesive bowel obstruction.

Student's t-test for the LOHS ($t = 5.049$, $df = 29$, $p = 0.0001$) and χ^2 test with Yates correction for complications ($\chi^2 = 5.663$, $df = 1$, $p = 0.01$) indicated that the differences between the two groups were significant.

Discussion

We have shown in this study that selective nonoperative management of AAW is a safe therapeutic option. The results have shown a significantly shorter hospital stay, significantly fewer complications and by inference reduced costs to the hospital. Except for the freakish accident involving a 3-year-old child in the sleeping bag we had a comparable age and sex profile in the two groups. In this study we did not use any of the injury severity score systems; however, the patients undergoing the new protocol were accepted on the grounds of their physiologically stable state. Our findings are also in agreement with many similar studies in leading trauma centres of the world (2-5).

However, the criteria are exacting and may impose difficulties on an understaffed surgical unit. The serial observations cannot be delegated to a community health worker (CHW), who may be the only nurse in the ward at night. It is also possible that an omental plug on a perforation may unplug after a patient is discharged. This series is too small to pick up such an event and it would require a large study to demonstrate this possibility.

An unpublished case-control study of 50 patients by Maibon (6) from 2001 to 2005 in Lae also attests to our findings. His study group was based only on a positive omental sign whereas we have broadened the criteria.

Our finding of 27% negative laparotomy is rather high given the controlled situation of the study. Three cases were adjudicated by the junior consultant outside the study protocol. Had it not been for that we would have had a rate of 17% negative laparotomy. Ponifasio et

al. (1) in a retrospective review of abdominal trauma in Port Moresby and Lae showed 7% and 20% negative laparotomy, respectively. This difference may be due to inter-observer differences or because the Port Moresby Unit relied on other adjuncts such as imaging studies. Leppäniemi and Haapiainen (4) have also shown the positive predictive power of clinical signs over imaging studies. It is our view that high rates of negative laparotomies can be reduced by judicious use of clinical signs in decision-making such as the study protocol in Figure 1. Laparoscopy may help; however, Leppäniemi et al. (3) have shown that it is weaker than exploratory laparotomy. There is also a lack of similar studies in poorer developing countries like Papua New Guinea and so we are unable to comment further on this.

Surgical practice in PNG is surgery of trauma, infections, tumours and congenital defects, mostly diseases of poverty. An innovation that is simple, directly applicable and transmissible is worthwhile. We believe that our findings will help surgeons to improve on what they have grown up with without compromising patient safety. Our greatest need yet remains, however, and that is to educate our people to prevent all the reckless and unnecessary acts of violence that plague our hospitals.

ACKNOWLEGEMENTS

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Two cases of Peutz-Jeghers syndrome presenting as bowel obstruction from intussusception

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SUMMARY

Two unusual cases of small intestinal intussusception presenting as bowel obstruction are presented. They both had freckle-like pigmentation of the perioral area, palms and soles of the feet with intestinal polyps which acted as lead points in the intussusception. Peutz-Jeghers syndrome was diagnosed. This report highlights the high risk of cancer of the intestines and extra-intestinal sites associated with this interesting but rare condition.

Case 1

A young girl aged 18 years from Enga Province presented with colicky abdominal pain with vomiting and melaena to the Port Moresby General Hospital. She had had a previous episode of abdominal pain but this time it was severe and non-remitting. Clinically she had a mobile mass in her central abdomen. She had noticeable perioral freckle-like pigmentation on her upper and lower lips. Per-rectal examination was unremarkable. Plain erect abdominal X-ray showed 'step ladder' pattern of bowel gas shadows. Ultrasound examination confirmed intussusception. In view of her X-ray findings she was subjected to laparotomy. The findings were that of an obstructed but non-gangrenous ileoileal intussusception. She had bowel resection (Figure 1) with primary intestinal anastomosis. Postoperatively her recovery was smooth and uneventful. The resected specimen had 6 pedunculated polyps ranging in size from 1 cm to 5 cm. One of the larger ones had acted as the lead point. Histological examination confirmed a benign hamartomatous polyp. Further questioning did not reveal similar skin discoloration in her other 3 siblings. The diagnosis of Peutz-Jeghers syndrome (PJS) was then made

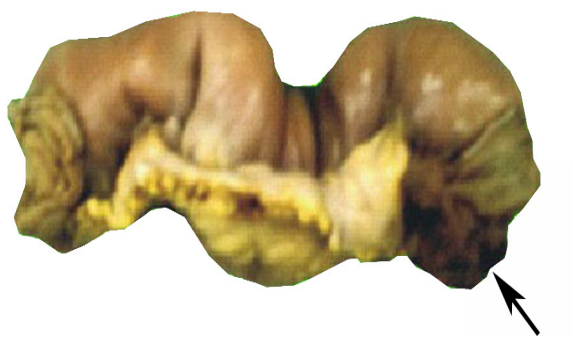

Figure 1. Resected specimen of Case 1 showing an ileoileal intussusception with an ulcerated benign polyp (arrow).

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upon the above findings.

Case 2

A 26-year-old young man from Ialibu in the Southern Highlands presented with acute bowel obstruction to the Mt Hagen Hospital. After initial resuscitation and clinical examination he was noted to have a tender and distended abdomen with reduced bowel sounds. He was also seen to have melanotic pigmentation of the perioral area, palms and feet. At laparotomy he had an obstructed ileocaecal intussusception and went on to have resection with primary ileocolic anastomosis. The resected specimen revealed multiple polyps.

Discussion

This paper presents two patients with similar presentations of abdominal pain with or without obstruction, melaena, freckle-like pigmentation of lips, palms and soles of the feet and intestinal polyposis. They fulfilled two out of the three diagnostic criteria for Peutz-Jeghers syndrome:

1) Family history consistent with autosomal dominant inheritance

2) Mucocutaneous hyperpigmentation

3) Small bowel polyposis.

We believe that the presentations of our cases are characteristic of Peutz-Jeghers syndrome (1), which occurs between the ages of 10 and 30 years. There was no family history of similar illness in the families of these patients. Between the authors' combined 23 years of surgical service that is an average of one case in 11.5 years.

PJS was first reported in 1921 and again in 1949 by J. Peutz and H. Jeghers, respectively. It has a prevalence rate of 1 in 300,000 and is thus a very rare condition. It is an autosomal dominant disorder with the gene in most families mapped to chromosome 19p13.3. Clinical manifestations are usually promoted by a second mutation on the other allele. Moreover, this is the only germ-line mutation linked to the serine-threonine kinase gene, which is believed to be a tumour suppressor gene. A few PJS phenotypes have a yet unknown locus instead of the 19p13.3 chromosome mutation.

PJS patients are at high risk of developing intestinal and extra-intestinal cancers from the third decade of life, and by 60 years 50% of patients will have had a form of cancer (2). The cancers are usually of gastrointestinal origin such as small intestine (48%), stomach (24%), colon (24%) and pancreas (5%), as well as skin, breast and gynaecological cancers. Follow-up of the original PJS family showed that mean age at death was 32 years compared to 69 years amongst unaffected families (3).

There are some related but more common conditions such as familial adenomatous polyposis (FAP), Gardner's syndrome and Turcot's syndrome which need to be excluded. None of these have the characteristic pigmentation as in our cases and PJS polyps are hamartomas whereas FAP polyps are adenomas. Prophylactic proctocolectomy is indicated in FAP because all affected patients develop cancer by age 30. Furthermore, all who are affected with polyps should be regularly followed up clinically and endoscopically for early cancer detection.

The two patients above deny similar illnesses among family members; however, follow-up and a careful search for the mucocutaneous hyperpigmentation may reveal asymptomatic affected sibs. Sporadic cases account for 30% and there is a positive family history in 70% of cases.

The patients were counselled regarding the need for cancer screening for colorectal, breast and gynaecological tumours.

NOTE

Due to the unfortunate loss of the camera containing the relevant picture of Case 1 showing perioral pigmentation, we cannot use it but a good proxy may be found in Wolfe's Colour Atlas of the Digestive System (4).

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Case report of a thermal burns patient with diabetes insipidus

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SUMMARY

We report a rare case of diabetes insipidus following fire burn injury. Meticulous fluid balance and the use of carbamazepine resulted in her survival.

Introduction

Diabetes insipidus (DI) can be either of central or renal origin. The latter is a hereditary defect in generating cAMP (cyclic adenosine 5′-phosphate) in distal tubular cells that will lead to water resorption. Central DI, in contrast, is usually acquired with tumours, infection, histiocytosis or trauma, which add their quota in that order. Almost 50% of cases are idiopathic despite exhaustive tests. Treatment will depend on the cause. Desmopressin – an analogue of vasopressin – can be used to control polyuria.

DI in burn injury is a rare complication. Only 4 cases have been reported in the literature (1-3), of which two survived. The exact mechanism is unknown but it is believed to result from hypoxic brain injury with delayed neurological sequelae. Management of this transient complication can be a challenge without laboratory support and appropriate drugs. We present an extensively burned patient who survived both the injury and the complication of DI, and discuss the possible pathophysiology.

Case history

A 23-year-old Melanesian woman from Kerema, Gulf Province was burnt after a quarrel with her husband over alleged infidelity. She had gone to the kitchen and dowsed herself with kerosene and set herself alight. She denied any past illnesses or use of psycholytics such as lithium.

On admission her vital signs were normal. She weighed 45 kg. She suffered extensive burns of her trunk, thighs and face. The total area of burn was estimated to be 65% (third degree 30%, second degree 35%). There was no evidence of airways involvement or smoke inhalation. She was resuscitated with normal saline and Hartmann's solution in the casualty department before being admitted to the ward. The subsequent fluid management (Table 1) outlines the course of her illness in the ward. Strict fluid balance was kept and excessive loss replaced together with any electrolyte imbalance.

An attempt to withhold intravenous and oral fluids failed to concentrate the urine.

Her haematological profile such as haemoglobin, haematocrit, white cell count and platelets were all within the normal range.

Since there was no vasopressin preparation nor its analogue (desmopressin) available, carbamazepine at 200 mg three times a day (t.i.d.) was given orally starting from the second week. This was reduced to 200 mg twice a day (b.i.d.) after a week. By the third week the urine began to concentrate and thereafter the daily urine volume began to contract, reaching 2000 ml at the time of discharge. Her sense of thirst was normal throughout her illness.

The wound was dressed openly with silver sulphadiazine cream and continuous saline dressings; the deep burns were grafted by the fourth week. Other supportive treatment such as tetanus toxoid, antibiotics, analgesia, cimetidine and a high-protein diet was also given.

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TABLE 1

URINE OUTPUT AND RENAL FUNCTION TESTS IN A BURNS PATIENT WITH POLYURIA

Day of admission	Volume of urine (litres/day)	Urea (mmol)	Creatinine (mmol)	Sodium (mmol)	Potassium (mmol)	Comments
6	10.5					
8	10	1.4	36	140	3.3	
10	12.03					Fluid withholding test
11	14.1					Carbamazepine started
12	14.65					
14	10.45					Weight 37 kg
16	16.6					
18	10.9	1.4	30	132	3.5	
20	8.38					Urine concentrated
22	6.79	1.8	44	135	4.5	
24	5.0					
25	5.0	1.2	43	138	3.5	Carbamazepine stopped
26	2.7					Gained weight

During the course of her hospital stay she lost 8 kg of her weight. She had one episode of wound infection due to a mixed growth of *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*, both sensitive to ceftazidime and resistant to penicillin, chloramphenicol, methicillin, Septrin and cefotaxime. Urine tests showed pH 7.5 and glucose and protein both negative but specific gravity and urine osmolality were not done due to the unavailability of the test reagents or equipment. Her electrolyte results fluctuated a little, as shown in Table 1, and our laboratory does not measure serum vasopressin levels. She started to gain weight by the second month of hospitalization and was discharged.

Discussion

A literature search produced only four reported cases of DI following burn injury (1-3). Of these one resulted from carbon monoxide (CO) poisoning and the other three from electrical burns. DI from CO poisoning is believed to result from diffuse cerebral damage and failure of antidiuretic hormone (ADH) secretion. The mechanism of DI in electrical burns is unknown. The deficit was easily corrected using vasopressin or its analogue desmopressin. There were two deaths in the reported cases unrelated to DI.

Central DI can be diagnosed when 1) there is excessive dilute urine with or without osmotic load, 2) no intrinsic renal disease is present, and 3) urine osmolality increases after vasopressin/desmopressin replacement therapy.

This case clinically fulfils the above criteria for diabetes insipidus. We can only speculate that the delayed neurological sequela of DI was due to CO poisoning inhaled during the burning process. The carboxyhaemoglobin may have led to diffuse cerebral hypoxia leading to a transient state of deficient ADH secretion from the supraoptic nuclei of the hypothalamus. Other products of incomplete combustion such as cyanide could also be involved but its role will remain speculative. It

would have been much better if the laboratory tests for arginine vasopressin (AVP), urine and plasma osmolality, urine specific gravity and carboxyhaemoglobin had been available. These tests would have helped in confirming the diagnosis and monitoring its treatment.

The use of carbamazepine was for its little-known action to prime the tubules to potentiate the action of AVP. There may be other direct action on the tubular cells but very little is known about it. Obviously where desmopressin is not available drugs such as carbamazepine and chlorpropamide could be put to good use. However, there is a chance that 11% of patients may not respond to carbamazepine (4).

This unusual case had a pleasing outcome. Such cases require a consensus management of physicians, pathologists and the primary responsible doctor. The most important aspect of management is strict fluid balance, laboratory support and hormone replacement.

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The use of a forehead flap to reconstruct the soft and hard palate after cancer excision

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SUMMARY

The successful use of a modified forehead flap technique to reconstruct an extensive defect of the soft palate after cancer resection is described. Postoperative swallowing and speech were good and nasal incontinence was short-lived. This can be an addition to the limited techniques available to surgeons working in this challenging area.

Introduction

The soft palate area constitutes the posterior part of the oral cavity and is the anterior and superior border of the nasopharynx and laryngopharynx, respectively. The lining is mainly stratified squamous cell epithelium on most of its surfaces. Several muscles traverse its substance, namely palatopharyngeus, glossopharyngeus, levator palati, tensor velli palatini and musculus uvulae. The tonsil is nestled on its lateral continuation with the pharynx between the anterior and posterior pharyngeal pillars. Its moist and smooth surface is due to many serous glands scattered within it.

It works in tandem with neighbouring structures to propel the food bolus into the aditus of the throat and prevent upward migration of food into the nasopharynx. It also helps in speech and breathing and acts as a mechanical barrier against dust and infection.

The forehead is well supplied by the frontal branch of the superficial temporalis artery as well as a recurrent branch of the posterior auricular artery. Vascular studies showed that the axial supply extends beyond the midline by two fingerbreadths. As a flap its use dates back to 1816 when Dr Carpue used it to cover a nose defect. It can be harvested as an immediate hemi-forehead or a delayed full-forehead flap for use on the face or tunnelled into the mouth. However, it has not been harvested as an immediate longer flap up to the temporal line nor has it been used to reconstruct the soft palate as described in this article (Figure 1).

Cancers of the soft palate or extension from hard palate and tonsils are unusual. Most reported series (1-5) are less than 20 patients, reflecting its low incidence. A common problem has been the lack of standardization and global experience in treating the soft palate area. Previously most defects in this area were fitted with a prosthesis and these were unwieldy and of poor function (6).

In Papua New Guinea (PNG) primary soft palate cancer accounted for 3.3% of oral cavity cancers (7). The disease in PNG is usually advanced at the time of presentation and the country lacks a dedicated team in microvascular surgery or expertise in prosthodontia. Surgical management of cancer of the soft palate is therefore fraught with great challenges if the surgeon decides to excise it.

I describe here a technique that may be useful to surgeons working in developing countries, where preparation and planning usually fall on the shoulders of a single surgeon with very limited technological support.

Case history

A65-year-old woman presented with a 10 cm x 8 cm verrucous growth overfilling the mouth and protruding from the lips over a period of 4

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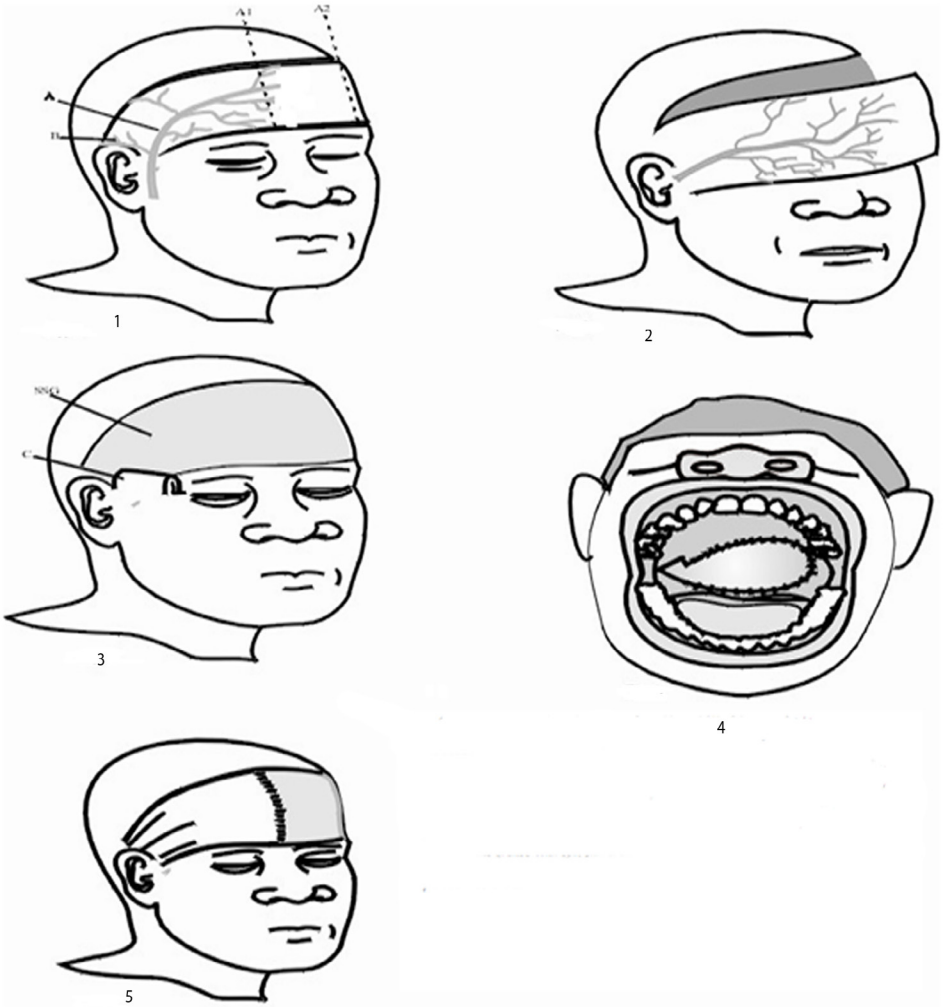

Figure 1. 1) shows normal blood supply from the frontal branch (A) of the superficial temporal artery. Additional supply comes from a branch of the posterior auricular artery (B). The dotted line A1 marks the axial supply of one side and A2 the temporal line of the forehead, a possible extended random supply. 2) shows the immediate full-forehead pedicle flap prepared and tunnelled – 3 – into the oral cavity. The donor site was grafted with a split skin graft. 4) shows the repair of the palatal defect and 5) the return of the flap three weeks later.

months. She was able to take puree food and was always in danger of accidentally chewing the cancerous growth leading to haemorrhage. She denied dyspnoea or pain. Fortunately the tongue was freely mobile and no nodes were palpable. The growth impacted the oral cavity and further assessment required anaesthesia.

Biopsy showed squamous cell carcinoma (SCC) of an intermediate differentiation. Plain X-rays of face and chest were normal as was the liver sonograph. No CT (computed tomography) or MRI (magnetic resonance imaging) was available at the time. Clinically she was staged as T4N0M0 SCC. The HIV (human immunodeficiency virus) test was non-reactive. Other routine blood tests were normal.

The airway was secured with tracheotomy under local anaesthesia. Examination under general anaesthesia showed the growth to be originating from the soft palate area extending to the right lateral pharyngeal wall. The nasopharynx and oropharynx and posterior tongue were unaffected. The lesion

was completely excised with a 1 cm margin all around including the pharynx. The full-thickness defect amounted to about 80% of the soft palate with a 5 cm defect of the lateral pharyngeal wall. No neck dissection was done since no clinically palpable nodes were felt and lymphatic drainage is usually to retropharyngeal nodes.

Reconstruction

Preparing the flap

The forehead flap based on the frontal branch of the superficial temporalis artery was chosen. The length was extended to include the temporal line for an extra 5 cm of random supply and the width included all the non-pilose skin plus some hair-bearing skin towards the base. The flap raising was easy in the avascular space above the pericranium to include the frontalis muscle. This was dissected right to the base ensuring that the feeding vessels were visualized and protected at all times. A relaxing incision of 1 cm was necessary where the incision meets the upper border of the ear. If the incision is carried further to the base of the ear it may damage an anastomotic branch from the posterior auricular artery. The flap tip was pink and bleeding.

Then a transverse cut was made on the temporalis muscle fascia just above the zygomatic arch. This area is chosen as there is less bleeding, whereas above the fascia and behind the zygoma one has to burrow through much tissue. A blunt McIndoe dissecting forceps was introduced into the infratemporal fossa onward into the oral cavity. A finger was next introduced to enlarge the tunnel in preparation for passing the flap in through to the defect.

The donor site was grafted using a split skin graft (SSG) from the thigh.

Repairing the defect

The defect had two surfaces so to meet this contingency the flap had to be folded on itself. Firstly the flap was sutured to the nasal surface with the skin facing posteriorly. Secondly the flap was folded so that the skin now faced the oral cavity. The juncture was de-epithelialized for 1 cm and the skin edges of the flap sutured to the adjacent soft palate defect. The oral defect was then completed. The pharynx was repaired by undermining and primary repair. If wider defects are created then they should be allowed to heal by secondary intention.

Inset and return of flap

After 21 days the flap was divided and the proximal end of the flap returned to the forehead and sutured back. The donor site had been covered with a split skin graft during the first operation.

Postoperative care

A nasogastric tube was left in situ for feeding. She was able to swallow well by day 27 and was decannulated. Speech was understandable by the end of 2 months. A little nasal escape of clear fluids continued for another two weeks and settled down. She was followed in the clinic for 1 year and a 1 cm x 0.5 cm recurrence was noted at the excision margin. Our radiotherapy machine had been decommissioned by then and she refused further surgery and died thereafter, maybe from other causes.

Discussion

I believe that this operation can be done expeditiously by surgeons without the need for expensive equipment. The end points for this operation were efficient swallowing without nasal incontinence, and understandable speech. She was able to achieve these on her own within 1-2 months. I have managed two primary soft palate tumours, of which one did poorly on prosthesis and the other did very well and is the case of this report.

The advantages of note of this operation are: it is simple in concept, it is a one-surgeon operation and it dispenses with SSG and local mucosal advancement, which may contract and distort the upper aero-digestive tract. However, the disadvantages are: it is a two-stage procedure, there may be donor site morbidity such as depigmentation and the inset flap is slightly bulkier than the normal soft palate. Furthermore the inset tissue is unaesthetic and may exude sebum due to the presence of sebaceous glands. The latter two have not been seen to pose any problems to the patient.

Various reports also state that primary or secondary soft palate cancers are unusual. As a result many centres do their own thing

and there is lack of agreement. Good results have been obtained with smaller defects using local myomucosal flaps (6) and a pharyngeal flap (5). It was reported that good function was achieved. However, it was added that ongoing tissue contraction would distort the upper aero-digestive tract and might require obturators. A report from Germany (8) achieved near normal pharyngeal pressure and no regurgitation using a neurovascularized infrahyoid muscle flap for partial defects. They also employed fasciocutaneous free flaps from lateral arm, radial forearm or scapula region for full-thickness defects. Sinha et al. (9) confirmed the utility of the radial forearm free flap (RFFF) for soft palate reconstruction even though two of their patients were supplemented with prosthesis. A Korean paper by Lew et al. in 2003 (10) is the first one to attempt to classify and standardize the choice and design of flaps. Their results show better swallowing and speech than with the conventional RFFF, with minimal morbidities.

The ideal choice of flap for soft palate reconstruction would now be radial forearm free fasciocutaneous flap where a dedicated unit is available. However, colleagues who live and work in third world countries may find the technique reported here a useful addition to the limited options available to us. I believe this technique is simple, requires almost nothing except stitches and gives a good functional outcome.

ACKNOWLEDGEMENT

I am thankful to Mr T. Vincent of the Medical Learning Resource Unit, University of PNG for the illustration.

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PUBLICATIONS OF RELEVANCE TO PAPUA NEW GUINEA AND MELANESIA

Bibliographic Citation List generated from MEDLARS

1 **Adhikari A, Sen A, Brumbaugh RC, Schwartz J.**
Altered growth patterns of a Mountain Ok population of Papua New Guinea over 25 years of change.
Am J Hum Biol 2011 May;23(3):325-332. doi: 10.1002/ajhb.21134. Epub 2010 Dec 22.

CONTEXT: The Mountain Ok (Mt Ok) people of Telefomin, who live at the interior of Papua New Guinea (PNG), were documented over 25 years ago to be one of the shortest populations on record, with average adult height below the fifth percentile (US). Serum growth hormone was detectable, insulin-like growth factor-1 and serum indicators of protein nutritional status fell within the normal range, suggesting that these were not primary factors for their relative short stature. OBJECTIVE: Since the Telefolmin people have experienced recent socioeconomic changes, they were re-evaluated in 2008, to examine height, weight and body mass index (BMI), for insight into relative contributions of environment and other factors that modulate stature in children and adults. STUDY DESIGN AND SETTING: Cross-sectional anthropometric data were collected from 474 individuals at Telefomin in 2008, and compared with anthropometric data from 342 individuals measured in 1983. RESULTS: The height of Telefolmin subjects, below the fifth percentile in 1983, remained below the fifth percentile in 2008. Weight and BMI of peripubertal and adult age groups increased from 1983 to 2008. Male and female heights at peripubertal ages were significantly greater in 2008. Nevertheless, final adult height did not change significantly over the 25 years. CONCLUSIONS: Recent socioeconomic changes appear to contribute to increased weight, BMI and stature at younger ages in the Mt Ok at Telefomin. In contrast, unchanging adult stature may reflect a delay in the impact of socioeconomic changes, or genetic influences that modulate responsiveness to other growth regulators.

2 **Aliota MT, Chen CC, Dagoro H, Fuchs JF, Christensen BM.**
Filarial worms reduce *Plasmodium* infectivity in mosquitoes.
PLoS Negl Trop Dis 2011 Feb 8;5(2):e963.

BACKGROUND: Co-occurrence of malaria and filarial worm parasites has been reported, but little is known about the interaction between filarial worm and malaria parasites with the same *Anopheles* vector. Herein, we present data evaluating the interaction between *Wuchereria bancrofti* and *Anopheles punctulatus* in Papua New Guinea (PNG). Our field studies in PNG demonstrated that *An. punctulatus* utilizes the melanization immune response as a natural mechanism of filarial worm resistance against invading *W. bancrofti* microfilariae. We then conducted laboratory studies utilizing the mosquitoes *Armigeres subalbatus* and *Aedes aegypti* and the parasites *Brugia malayi*, *Brugia pahangi*, *Dirofilaria immitis* and *Plasmodium gallinaceum* to evaluate the hypothesis that immune activation and/or development by filarial worms negatively impact *Plasmodium* development in co-infected mosquitoes. *Ar. subalbatus* used in this study are natural vectors of *P. gallinaceum* and *B. pahangi* and they are naturally refractory to *B. malayi* (melanization-based refractoriness). METHODOLOGY/PRINCIPAL FINDINGS: Mosquitoes were dissected and *Plasmodium* development was analyzed six days after blood feeding on either *P. gallinaceum* alone or after taking a bloodmeal containing both *P. gallinaceum* and *B. malayi* or a bloodmeal containing both *P. gallinaceum* and *B. pahangi*. There was a significant reduction in the prevalence and mean intensity of *Plasmodium* infections in two species of mosquito that had dual infections as compared to those mosquitoes that were infected with *Plasmodium* alone, and was independent of whether the mosquito had a melanization immune response to the filarial worm or not. However, there was no reduction in *Plasmodium* development when filarial worms were present in the bloodmeal (*D. immitis*) but midgut penetration was absent, suggesting that factors associated with penetration of the midgut by filarial worms are likely to be responsible for the observed reduction in malaria parasite infections. CONCLUSIONS/SIGNIFICANCE: These results could have an impact on vector infection and transmission dynamics in areas where *Anopheles* transmit both parasites, ie, the elimination of filarial worms in a co-endemic locale could enhance malaria transmission.

3 **Allison WE, Kiromat M, Vince J, Wand H, Cunningham P, Graham SM, Kaldor J.**
Development of a clinical algorithm to prioritise HIV testing of hospitalized paediatric patients in a low-resource moderate-prevalence setting.
Arch Dis Child 2011 Jan;96(1):67-72. Epub 2010 Nov 2.

OBJECTIVE: To develop a clinical algorithm to identify paediatric patients who should be offered HIV testing in a setting of moderate HIV prevalence and limited resources. METHODS: In a prospective cross-sectional study at Port Moresby General Hospital, Papua New Guinea, carers of inpatients were offered HIV testing and counseling for their children. Recruited children were tested for HIV antibodies and DNA. Standardised clinical information was collected. Multivariate regression analysis was used to ascertain independent predictors of HIV infection and these were used to develop a predictive algorithm. RESULTS: From September 2007 to October 2008, 487 children were enrolled. Overall, 55 (11%) with a median age of 7 months were found to be HIV-infected. In multivariate analysis, independent predictors of HIV infection were: persistent fever (OR = 2.05 (95% CI 1.11 to 4.68)), lymphadenopathy (OR = 2.29 (1.12 to 4.68)), oral candidiasis (OR = 3.94 (2.17 to 7.14)) and being underweight for age (OR = 2.03 (1.03 to 3.99)). The presence of any one of these conditions had a sensitivity of 96% in detecting a child with HIV infection. Using an algorithm based

on the presence of at least one of these conditions would result in around 40% of hospitalised children being offered testing. CONCLUSIONS: This clinical algorithm may be a useful screening tool for HIV infection in hospitalised children in situations where it is not feasible to offer universal HIV testing, providing guidance for HIV testing practices for increased identification and management of HIV-infected children in Papua New Guinea.

4 **Andersen F, Douglas NM, Bustos D, Galappaththy G, Qi G, Hsiang MS, Kusriastuti R, Mendis K, Taleo G, Whittaker M, Price RN, von Seidlein L.**
Trends in malaria research in 11 Asian Pacific countries: an analysis of peer-reviewed publications over two decades.
Malar J 2011 May 18;10:131.

BACKGROUND: Quantitative data are lacking on published malaria research. The purpose of the study is to characterize trends in malaria-related literature from 1990 to 2009 in 11 Asian-Pacific countries that are committed to malaria elimination as a national goal. METHODS: A systematic search was conducted for articles published from January 1990 to December 2009 in PubMed/MEDLINE using terms for malaria and 11 target countries (Bhutan, China, North Korea, Indonesia, Malaysia, Philippines, Solomon Islands, South Korea, Sri Lanka, Thailand and Vanuatu). The references were collated and categorized according to subject, *Plasmodium* species, and whether they contained original or derivative data. RESULTS: 2,700 articles published between 1990 and 2009 related to malaria in the target countries. The annual output of malaria-related papers increased linearly whereas the overall biomedical output from these countries grew exponentially. The percentage of malaria-related publications was nearly 3% (111/3741) of all biomedical publications in 1992 and decreased to less than 1% (118/12171; p <0.001) in 2009. Thailand had the highest absolute output of malaria-related papers (n = 1211), followed by China (n = 609) and Indonesia (n = 346). Solomon Islands and Vanuatu had lower absolute numbers of publications, but both countries had the highest number of publications per capita (1.3 and 2.5 papers/1,000 population). The largest percentage of papers concerned the epidemiology and control of malaria (53%) followed by studies of drugs and drug resistance (47%). There was an increase in the proportion of articles relating to epidemiology, entomology, biology, molecular biology, pathophysiology and diagnostics from the first to the second decade, whereas the percentage of papers on drugs, clinical aspects of malaria, immunology and social sciences decreased. CONCLUSIONS: The proportion of malaria-related publications out of the overall biomedical output from the 11 target Asian-Pacific countries is decreasing. The discovery and evaluation of new, safe and effective drugs and vaccines is paramount. In addition the elimination of malaria will require operational research to implement and scale up interventions.

5 **Awasthi G, Prasad GB, Das A.**
Population genetic analyses of *Plasmodium falciparum* chloroquine receptor transporter gene haplotypes reveal the evolutionary history of chloroquine-resistant malaria in India.
Int J Parasitol 2011 Jun;41(7):705-709. Epub 2011 Apr 9.

Inferring the origin and dispersal of the chloroquine-resistant (CQR) malaria parasite, *Plasmodium falciparum*, is of academic and public health importance. The Pfcrt gene of *P. falciparum* is widely known as the CQR gene and two major haplotypes of this gene (CVIET and SVMNT) occur widely across CQR-endemic regions of the globe. In India, studies to date of the Pfcrt gene have indicated the widespread prevalence of the SVMNT haplotype (prevalent in South America and Papua New Guinea), whereas the CVIET haplotype, primarily found in Southeast Asia, was not detected at a high frequency in India. This distribution pattern of the two most common CQR-*Pfcrt* haplotypes in India is quite surprising. Thus, in order to understand probable evolutionary and migration patterns of the CQR-*Pfcrt* haplotypes into India, we generated new sequence data of exon 2 of the Pfcrt gene and collected published information on the CQR-Pfcrt haplotype data from India, Papua New Guinea, Southeast Asia and South America, and performed several population and evolutionary genetic analyses. Among several interesting findings, statistically significant longitudinal clines for the CVIET and SVMNT haplotypes (in opposite directions) in India, and the clustering of India and Papua New Guinea under the SVMNT-specific clade in the phylogenetic tree, are the two most remarkable aspects of the data. It also appears that both the SVMNT and CVIET haplotypes in India have migrated from Southeast Asia. In particular, whereas the Indian CVIET haplotype has a Southeast Asian origin, the SVMNT haplotype prevalent in India seems to have originated in Papua New Guinea and entered India through Southeast Asia.

6 **Baker A, Pearson T, Price EP, Dale J, Keim P, Hornstra H, Greenhill A, Padilla G, Warner J.**
Molecular phylogeny of *Burkholderia pseudomallei* from a remote region of Papua New Guinea.
PLoS One 2011 Mar 31;6(3):e18343.

BACKGROUND: The island of New Guinea is located midway between the world's two major melioidosis-endemic regions of Australia and Southeast Asia. Previous studies in Papua New Guinea have demonstrated autochthonous melioidosis in Balimo, Western Province. In contrast to other regions of endemicity, isolates recovered from both environmental and clinical sources demonstrate narrow genetic diversity over large spatial and temporal scales. METHODOLOGY/PRINCIPAL FINDINGS: We employed molecular typing techniques to determine the phylogenetic relationships of these isolates to each other and to others worldwide to aid in understanding the origins of the Papua New Guinean isolates. Multi-locus sequence typing of the 39 isolates resolved three unique sequence types. Phylogenetic reconstruction and structure analysis determined that all isolates were genetically closer to those from Australia than those from Southeast Asia. Gene cluster analysis, however, identified a *Yersinia*-like fimbrial gene cluster predominantly found among *Burkholderia pseudomallei* derived from Southeast Asia. Higher resolution VNTR typing and phylogenetic reconstruction of the Balimo isolates resolved 24 genotypes with long branch lengths. These findings are congruent with long-term persistence in the region and a high level of environmental stability. CONCLUSIONS/SIGNIFICANCE: Given that anthropogenic influence has been hypothesized as a mechanism for the dispersal of *B. pseudomallei*, these findings correlate with limited movement of the indigenous people in the region. The palaeogeographical and anthropogenic

history of Australasia and the results from this study indicate that New Guinea is an important region for the further study of *B. pseudomallei* origins and dissemination.

7 **Becker AE, Fay KE, Agnew-Blais J, Khan AN, Striegel-Moore RH, Gilman SE.**
Social network media exposure and adolescent eating pathology in Fiji.
Br J Psychiatry 2011 Jan;198(1):43-50.

BACKGROUND: Mass media exposure has been associated with an increased risk of eating pathology. It is unknown whether indirect media exposure – such as the proliferation of media exposure in an individual's social network – is also associated with eating disorders. AIMS: To test hypotheses that both individual (direct) and social network (indirect) mass media exposures were associated with eating pathology in Fiji. METHOD: We assessed several kinds of mass media exposure, media influence, cultural orientation and eating pathology by self-report among adolescent female ethnic Fijians (n=523). We fitted a series of multiple regression models of eating pathology, assessed by the Eating Disorder Examination Questionnaire (EDE-Q), in which mass media exposures, sociodemographic characteristics and body mass index were entered as predictors. RESULTS: Both direct and indirect mass media exposures were associated with eating pathology in unadjusted analyses, whereas in adjusted analyses only social network media exposure was associated with eating pathology. This result was similar when eating pathology was operationalised as either a continuous or a categorical dependent variable (e.g. odds ratio OR=1.60, 95% CI 1.15-2.23 relating social network media exposure to upper-quartile EDE-Q scores). Subsequent analyses pointed to individual media influence as an important explanatory variable in this association. CONCLUSIONS: Social network media exposure was associated with eating pathology in this Fijian study sample, independent of direct media exposure and other cultural exposures. Findings warrant further investigation of its health impact in other populations.

8 **Brian G, Pearce MG, Ramke J.**
Refractive error and presbyopia among adults in Fiji.
Ophthalmic Epidemiol 2011 Apr;18(2):75-82.

PURPOSE: To characterize refractive error, presbyopia and their correction among adults aged ≥40 years in Fiji, and contribute to a regional overview of these conditions. METHODS: A population-based cross-sectional survey using multistage cluster random sampling. Presenting distance and near vision were measured and dilated slitlamp examination performed. RESULTS: The survey achieved 73.0% participation (n=1381). Presenting binocular distance vision ≥6/18 was achieved by 1223 participants. Another 79 had vision impaired by refractive error. Three of these were blind. At threshold 6/18, 204 participants had refractive error. Among these, 125 had spectacle-corrected presenting vision ≥6/18 ("met refractive error need"); 79 presented wearing no (n=74) or under-correcting (n=5) distance spectacles ("unmet refractive error need"). Presenting binocular near vision ≥N8 was achieved by 833 participants. At threshold N8, 811 participants had presbyopia. Among these, 336 attained N8 with presenting near spectacles ("met presbyopia need"); 475 presented with no (n=402) or under-correcting (n=73) near spectacles ("unmet presbyopia need"). Rural residence was predictive of unmet refractive error (p=0.040) and presbyopia (p=0.016) need. Gender and household income source were not. Ethnicity-gender-age-domicile-adjusted to the Fiji population aged ≥40 years, "met refractive error need" was 10.3% (95% confidence interval [CI] 8.7-11.9%), "unmet refractive error need" was 4.8% (95%CI 3.6-5.9%), "refractive error correction coverage" was 68.3% (95%CI 54.4-82.2%),"met presbyopia need" was 24.6% (95%CI 22.4-26.9%), "unmet presbyopia need" was 33.8% (95%CI 31.3-36.3%), and "presbyopia correction coverage" was 42.2% (95%CI 37.6-46.8%). CONCLUSION: Fiji refraction and dispensing services should encourage uptake by rural dwellers and promote presbyopia correction. Lack of comparable data from neighbouring countries prevents a regional overview.

9 **Brian G, Ramke J, Maher L, Page A, Fischer-Harder K, Sikivou B.**
Body mass index among Melanesian and Indian Fijians aged ≥40 years living in Fiji.
Asia Pac J Public Health 2011 Jan;23(1):34-43.

To determine the distribution and sociodemographic associations of body mass index (BMI; kg/m^2) among Melanesian and Indian Fijians aged ≥40 years living in Fiji, a population-based cross-sectional survey with multistage random sampling was conducted in 2009. Melanesians were more likely to have BMI ≥25 (odds ratio [OR] = 4.73; 95% confidence interval [CI] = 3.57-6.28; p<0.001) and BMI ≥30 (OR = 3.84; 95% CI = 2.94-5.03; p <0.001). Among Melanesians, gender and educational attainment were predictive of BMI ≥25 on multivariate analysis. Women were more likely to be overweight (OR = 2.03; 95% CI = 1.34-3.06) or obese (OR = 1.92; 95% CI = 1.43-2.59). Among Indians, gender and age were predictive of BMI ≥25. Again, women were more likely to be overweight (OR = 2.51; 95% CI = 1.69-3.73) or obese (OR = 3.71; 95% CI = 2.19-6.29). Gender-age-domicile-adjusted, and extrapolating across Fiji, 0.3%, 84.5% and 51.7% of Melanesians aged ≥40 years had BMI <18.5, ≥25 and ≥30, respectively. Among Indians, these values were 5.8%, 54.2% and 21.2%, respectively.

10 **Brian G, Ramke J, Page A, Maher L, Szetu J, Qoqonokana MQ.**
The association of diabetes and BMI among Melanesian and Indian Fijians aged ≥40 years.
Br J Nutr 2011 May;105(10):1539-1545. Epub 2011 Jan 24.

The present study examines the association of diabetes with BMI (kg/m^2) in Asian-Indian and Melanesian Fijian populations sharing a common environment. A population-based survey was used to investigate the risk of diabetes (defined by glycosylated Hb concentration ≥6.5% among participants who denied previous diagnosis of the disease by a medical practitioner) by sex, ethnicity and strata of BMI in a series of age-adjusted logistic regression models. Ethnicity and BMI interactions were compared using WHO and empirically derived BMI cut-off points. Indians had a greater risk (BMI and age adjusted) of undetected diabetes than Melanesians in both males (OR 2.99, 95% CI 1.73-5.17; p <0.001) and females (OR 2.26, 95% CI 1.56-3.28; p <0.001). BMI ≥25 to <30 and ≥30 kg/m^2 conferred a higher risk of diabetes compared with a BMI ≥18.5 to <25 kg/m^2. Risk was higher for males with a BMI ≥25 to <30 kg/m^2 (OR 2.35, 95%

CI 1.24-4.46; p = 0.007) and BMI ≥30 kg/m^2 (OR 6.08, 95% CI 3.06-12.07; p <0.001) than for females with the same BMI (OR 1.85, 95% CI 1.11-3.08; p = 0.027 and OR 2.10, 95% CI 1.28-3.44; p = 0.002, respectively). However, the threshold that appeared to differentiate higher risk varied by ethnicity and sex. For Melanesians, BMI thresholds suggested were 25 kg/m^2 for males and 32 kg/m^2 for females. For Indo-Fijians, these were 24 and 22 kg/m^2 for males and females, respectively. Disaggregating by ethnicity and sex, and applying specific evidence-based thresholds, may render BMI a more discriminating tool for assessing the risk of developing diabetes among Fiji adults.

11 **Bruce E, Bauai L, Masta A, Rooney PJ, Paniu M, Sapuri M, Keogh L, Kaldor J, Fairley CK.**
Effects of periodic presumptive treatment on three bacterial sexually transmissible infections and HIV among female sex workers in Port Moresby, Papua New Guinea.
Sex Health 2011 Jun;8(2):222-228.

BACKGROUND: Sexually transmissible infections (STI) are common in female sex workers (FSW). AIM: To determine if 3-monthly periodic presumptive treatments (PPT) would reduce the prevalence of STI in FSW. METHODS: In a cohort study conducted between November 2003 and September 2004, FSW were enrolled, counselled and interviewed. Informed consent was obtained. Testing by using polymerase chain reaction (PCR) for *Chlamydia trachomatis* (Ct), *Neisseria gonorrhoeae* (Ng) and *Trichomonas vaginalis* (Tv), and serology for HIV were performed at baseline and final follow-up visits. Each FSW received 3-monthly oral amoxycillin, probenecid, a combination of amoxycillin and clavulanic acid, and azithromycin. Tinidazole was administered once. RESULTS: The cohort consisted of 129 FSW at baseline and 71 at final follow-up visit. Of these 71 FSW, there was a significant decline in the proportion with positive PCR results for Ct from 38% to 16% (p = 0.001), Ng from 56% to 23% (p ≤0.001) and Tv from 62% to 30% (p ≤0.001) between baseline and the final follow-up visit. HIV prevalence increased from 15% to 21% (p = 0.125). CONCLUSIONS: PPT was statistically effective in reducing STI but rates rebounded rapidly. Several new HIV infections occurred. If PPT is to be very effective in FSW where the prevalence of STI is so high, then 100% condom use with clients and regular sexual partners (RSP), and high rates of notification of RSP would be required if low incidence and prevalence of STI were to be achievable.

12 **Bruce E, Bauai L, Sapuri M, Kaldor JM, Fairley CK, Keogh LA.**
HIV knowledge, risk perception, and safer sex practices among female sex workers in Port Moresby, Papua New Guinea.
Int J Womens Health 2011 Feb 15;3:53-61.

Sex workers are considered a high-risk group for sexually transmitted infections, including human immunodeficiency virus (HIV), and are often targeted by prevention interventions with safer sex messages. The purpose of this study was to explore the extent to which knowledge of HIV and perception of risk influence safer sex practices among female sex workers (FSWs) in Port Moresby, Papua New Guinea. FSWs (n = 174) were recruited from 19 sites to participate in the study. Qualitative data were collected using semistructured interviews with FSWs (n = 142) through focus group discussions and (n = 32) individual interviews. In addition, quantitative data were collected from all FSWs using a short structured, demographic questionnaire. Data were analyzed using recurring themes and calculations of confidence intervals. Despite some common misperceptions, overall, most FSWs were basically aware of the risks of HIV and informed about transmission and prevention modalities but used condoms inconsistently. Most reported using condoms 'sometimes', almost one-sixth 'never' used condoms, only a fraction used condoms 'always' with clients, and none used condoms 'always' with regular sexual partners (RSPs). Among these FSWs, being knowledgeable about the risks, transmission, and prevention of HIV did not translate into safe sex. The findings suggest that certain contextual barriers to safer sex practices exist. These barriers could heighten HIV vulnerability and possibly may be responsible for infection in FSWs. Specific interventions that focus on improving condom self-efficacy in FSWs and simultaneously target clients and RSPs with safer sex messages are recommended.

13 **Bugoro H, Cooper RD, Butafa C, Iro'ofa C, Mackenzie DO, Chen CC, Russell TL.**
Bionomics of the malaria vector *Anopheles farauti* in Temotu Province, Solomon Islands: issues for malaria elimination.
Malar J 2011 May 18;10:133.

BACKGROUND: In the Solomon Islands, the Malaria Eradication Programmes of the 1970s virtually eliminated the malaria vectors *Anopheles punctulatus* and *Anopheles koliensis*, both late night biting, endophagic species. However, the vector *Anopheles farauti* changed its behaviour to bite early in the evening outdoors. Thus, *An. farauti* mosquitoes were able to avoid insecticide exposure and still maintain transmission. Thirty years on and the Solomon Islands are planning for intensified malaria control and localized elimination; but little is currently known about the behaviour of the vectors and how they will respond to intensified control. METHODS: In the elimination area, Temotu Province, standard entomological collection methods were conducted in typical coastal villages to determine the vector, its ecology, biting density, behaviour, longevity and vector efficacy. These vector surveys were conducted pre-intervention and post-intervention following indoor residual spraying and distribution of long-lasting insecticidal nets. RESULTS: *Anopheles farauti* was the only anopheline in Temotu Province. In 2008 (pre-intervention), this species occurred in moderate to high densities (19.5-78.5 bites/person/night) and expressed a tendency to bite outdoors, early in the night (peak biting time 6-8 pm). Surveys post intervention showed that there was little, if any, reduction in biting densities and no reduction in the longevity of the vector population. After adjusting for human behaviour, indoor biting was reduced from 57% pre-intervention to 40% post-intervention. CONCLUSION: In an effort to learn from historical mistakes and develop successful elimination programmes, there is a need for implementing complementary vector control tools that can target exophagic and early biting vectors. Intensified indoor residual spraying and long-lasting insecticide net use has further promoted the early, outdoor feeding behaviour of *An. farauti* in the Solomon Islands. Consequently, the effectiveness of IRS

and the personal protection provided by bed nets is compromised. To achieve elimination, any residual transmission should be targeted using integrated vector control incorporating complementary tools such as larviciding and/or zooprophylaxis.

14 **Bulbeck D, O'Connor S.**
The Watinglo mandible: a second terminal Pleistocene *Homo sapiens* fossil from tropical Sahul with a test on existing models for the human settlement of the region.
Homo 2011 Feb;62(1):1-29. Epub 2011 Jan 8.

This paper analyses a fossil human mandible, dated to circa 10ka, from Watinglo rockshelter on the north coast of Papua New Guinea. The fossil is metrically and morphologically similar to male mandibles of recent Melanesians and Australian Aborigines. It is distinguished from Kow Swamp and Coobool Creek male mandibles (Murray Valley, terminal Pleistocene) by being smaller and having different shape characteristics, as well as smaller teeth and a slower rate of tooth wear. It pairs with the Liang Lemdubu female (Late Glacial Maximum, Aru Islands) in suggesting that the morphology of the terminal Pleistocene inhabitants of tropical Sahul was gracile compared to their contemporaries within the southern Murray drainage. An explanatory scenario for this morphological contrast is developed in the context of the *Homo sapiens* early fossil record, Australasian mtDNA evidence, terminal Pleistocene climatic variation, and the possibility of multiple entry points into Sahul.

15 **Butt L.**
Can you keep a secret? Pretences of confidentiality in HIV/AIDS counseling and treatment in Eastern Indonesia.
Med Anthropol 2011 May;30(3):319-338. doi: 10.1080/01459740.2011.560585.

A critical feature of contemporary interventions of HIV is the provision of voluntary counseling and testing. Protecting the confidentiality of the client is a lynchpin of successful counseling. This article explores the teaching and implementation of the concept of confidentiality in highlands Papua, Eastern Indonesia. Results of participant observation and in-depth interviews with clinic staff in 2009 and 2010 show that confidentiality is an ideal poorly taught and systematically violated in practice. Identifying, labeling and regulating HIV-positive persons appears more important than enacting the humanitarian and moral imperative of protecting client rights. Confidentiality becomes the means to enact dividing practices and to create categories of persons – those who choose to adhere to therapies and those who do not. The implications of this pattern are discussed with reference to wider humanitarian initiatives.

16 **Cazorla C, Guigon A, Noel M, Quilici ML, Lacassin F.**
Fatal *Vibrio vulnificus* infection associated with eating raw oysters, New Caledonia.
Emerg Infect Dis 2011 Jan;17(1):136-137.

17 **Chaves LF, Taleo G, Kalkoa M, Kaneko A.**
Spleen rates in children: an old and new surveillance tool for malaria elimination initiatives in island settings.
Trans R Soc Trop Med Hyg 2011 Apr;105(4):226-231. Epub 2011 Mar 1.

Spleen rates (SR) have been traditionally used to estimate the burden of malaria transmission. Results are presented from 51 surveys which measured SR and parasite rates (PR) in 29,962 individuals in the archipelago of Vanuatu. Indices for spleen size computed with multivariate statistical tools outperformed the WHO average spleen index and showed that spleen sizes in a population can track shifts in malaria transmission. In general, a positive linear relationship between *Plasmodium* spp. PR and SR was found for the archipelago. In the context of malaria elimination and for the specific setting of this study we found that spleen examination is a useful tool in post-malaria elimination surveillance. Finally, results highlight the value of measuring spleen sizes to rapidly assess the impact of intervention packages aimed at malaria elimination or control.

18 **Clark G, Chapman Y, Francis K.**
Understanding the context of providing HIV prevention and treatment in Papua New Guinea.
J Transcult Nurs 2011 Jan;22(1):88-94.

The HIV epidemic in Papua New Guinea is now described as a generalized epidemic; that is, more than 1% of people aged 15 to 49 years are infected with HIV. The individual behavior of people is not the single most important factor that places them at risk of infection and drives the spread of the epidemic. Rather, a diverse range of factors – biological, sociocultural, and political – makes people vulnerable to infection and dictates their access to care and treatment services. This article examines these biological, sociocultural and political influences on the HIV epidemic and on prevention and treatment strategies in Papua New Guinea.

19 **Dancause KN, Dehuff C, Soloway LE, Vilar M, Chan C, Wilson M, Tarivonda L, Regenvanu R, Kaneko A, Garruto RM, Lum JK.**
Behavioral changes associated with economic development in the South Pacific: health transition in Vanuatu.
Am J Hum Biol 2011 May;23(3):366-376. doi: 10.1002/ajhb.21146. Epub 2011 Mar 8.

Health patterns are changing in developing countries; as diet and activity patterns change with economic development, chronic disease prevalence increases, which is a characteristic of health transition. The islands of Vanuatu (South Pacific) have varying rates of economic development and provide a natural experimental model of health transition. OBJECTIVES: To characterize behavioral changes associated with modernization. METHODS: We surveyed 425 children and 559 adults on three islands varying in degree of economic development. We assessed diet (24-h dietary recall), physical activity (mode of transport, work activities and recreation), substance use and other behavioral patterns. RESULTS: Spending patterns and access to Western foods followed modernization gradients in our sample, whereas occupational patterns and ownership of technological goods were poor markers of modernization. With increasing economic development, participants consumed more animal proteins and simple carbohydrates. Physical activity levels were high; most participants were active in gardening, and sports were popular, especially in urban areas. However, urban participants spent more time in sedentary recreation. Men's use of alcohol and tobacco increased with economic development, but we observed marked differences in substance use patterns between two rural islands, one with and one without tourism. CONCLUSIONS:

Economic development in Vanuatu is accompanied by nutrition transition and increased sedentary recreation, although physical activity levels remain high. Differences in substance use patterns between rural islands with and without tourism indicate a need for more research in rural areas. These findings might inform research in other communities in the early stages of health transition.

20 **Davis WA, Clarke PM, Siba PM, Karunajeewa HA, Davy C, Mueller I, Davis TM.**
Cost-effectiveness of artemisinin combination therapy for uncomplicated malaria in children: data from Papua New Guinea.
Bull World Health Organ 2011 Mar 1;89(3):211-220. Epub 2011 Feb 1.

OBJECTIVE: To compare the cost-effectiveness of conventional antimalarial therapy with that of three artemisinin combination treatment regimens in children from Papua New Guinea aged 6 to 60 months. METHODS: An incremental cost-effectiveness analysis was performed using data from 656 children with *Plasmodium falciparum* and/or *P. vivax* malaria who participated in a large intervention trial in two clinics in northern Papua New Guinea. The children were randomized to one of the following groups: (i) conventional treatment with chloroquine plus sulfadoxine plus pyrimethamine (CQ+S+P); (ii) artesunate plus S plus P; (iii) dihydroartemisinin plus piperaquine (DHA+PQ); and (iv) artemether plus lumefantrine (A+L). For treatment outcomes, World Health Organization definitions were used. The cost of transport between home and the clinic plus direct health-care costs served as a basis for determining each regimen's incremental cost per incremental treatment success relative to CQ+S+P by day 42 and its cost per life year saved. FINDINGS: A+L proved to be the most effective regimen against *P. falciparum* malaria and was highly cost-effective at 6.97 United States dollars (US$) per treatment success (about US$ 58 per life year saved). DHA+PQ was the most effective regimen against *P. vivax* malaria and was more cost-effective than CQ+S+P. CONCLUSION: A+L and DHA+PQ are highly cost-effective regimens for the treatment of paediatric *P. falciparum* and *P. vivax* malaria, respectively, in parts of Papua New Guinea. Future research will be required to determine if these findings hold true for other territories in Asia and Oceania with similar malaria epidemiology.

21 **Deguilloux MF, Pemonge MH, Dubut V, Hughes S, Hänni C, Chollet L, Conte E, Murail P.**
Human ancient and extant mtDNA from the Gambier Islands (French Polynesia): evidence for an early Melanesian maternal contribution and new perspectives into the settlement of easternmost Polynesia.
Am J Phys Anthropol 2011 Feb;144(2):248-257. doi: 10.1002/ajpa.21398. Epub 2010 Sep 24.

Molecular anthropology has been widely used to infer the origin and processes of the colonization of Polynesia. However, there are still a lack of representative geographical studies of Eastern Polynesia and unchallenged genetic data about ancient Polynesian people. The absence of both of these elements prevents an accurate description of the demographic processes of internal dispersion within the Polynesian triangle. This study provides a twofold analysis of ancient and modern mtDNA in the eastern part of French Polynesia: the Gambier Islands. The paleogenetic analyses conducted on burials of the Temoe Atoll (14th-17th centuries) represent the first fully authenticated ancient human sequences from Polynesia. The identification of the "Melanesian" Q1 mtDNA lineage in ancient human remains substantiates the Near Oceanic contribution to the early gene pool of this region. Modern samples originate from Mangareva Island. Genealogical investigations enable us to reliably identify the conservation of the Melanesian component in Easternmost Polynesia, despite recent European colonization. Finally, the identification of rare mutations in sequences belonging to haplogroup B4a1a1a provides new perspectives to the debate on the internal peopling of the Polynesian region. Altogether, the results laid out in our study put the emphasis on the necessity of controlled sampling when discussing the internal settlement of Polynesia.

22 **Elyazar IR, Gething PW, Patil AP, Rogayah H, Kusriastuti R, Wismarini DM, Tarmizi SN, Baird JK, Hay SI.**
Plasmodium falciparum malaria endemicity in Indonesia in 2010.
PLoS One 2011;6(6):e21315. Epub 2011 Jun 29.

BACKGROUND: Malaria control programs require a detailed understanding of the contemporary spatial distribution of infection risk to efficiently allocate resources. We used model based geostatistics (MBG) techniques to generate a contemporary map of *Plasmodium falciparum* malaria risk in Indonesia in 2010. METHODS: *Plasmodium falciparum* annual parasite incidence (PfAPI) data (2006-2008) were used to map limits of *P. falciparum* transmission. A total of 2,581 community blood surveys of *P. falciparum* parasite rate (PfPR) were identified (1985-2009). After quality control, 2,516 were included into a national database of age-standardized 2-10 year old PfPR data (PfPR(2-10)) for endemicity mapping. A Bayesian MBG procedure was used to create a predicted surface of PfPR(2-10) endemicity with uncertainty estimates. Population at risk estimates were derived with reference to a 2010 human population count surface. RESULTS: We estimate 132.8 million people in Indonesia lived at risk of *P. falciparum* transmission in 2010. Of these, 70.3% inhabited areas of unstable transmission and 29.7% in stable transmission. Among those exposed to stable risk, the vast majority were at low risk (93.39%) with the remainder at intermediate (6.6%) and high risk (0.01%). More people in western Indonesia lived in unstable rather than stable transmission zones. In contrast, fewer people in eastern Indonesia lived in unstable versus stable transmission areas. CONCLUSION: While further feasibility assessments will be required, the immediate prospects for sustained control are good across much of the archipelago and medium-term plans to transition to the pre-elimination phase are not unrealistic for *P. falciparum*. Endemicity in areas of Papua will clearly present the greatest challenge. This *P. falciparum* endemicity map allows malaria control agencies and their partners to comprehensively assess the region-specific prospects for reaching pre-elimination, monitor and evaluate the effectiveness of future strategies against this 2010 baseline and ultimately improve their evidence-based malaria control strategies.

23 **Fa'alili-Fidow J.**
Ensuring economic, health, and social well-being for Papua New Guinea through trade.

Asia Pac J Public Health 2011 Jan;23(1):79-85.

The impacts of trade liberalization and open markets on global, regional, and local economies are a key consideration for those involved in government, business, and financial sectors. However, their impacts on health and social well-being of populations are not well-evidenced or acknowledged within the health sector, let alone the impact on developing countries. As free trade becomes an inevitable outcome for many developing nations, the full implications of trade on economies, environments, and population health need to be better articulated in order to ensure fully informed trade negotiations that support equitable outcomes. This article takes a broad look at the key issues for Papua New Guinea (PNG) in trade and how these translate to discrepancies in economic, health, and social benefits for its population. Despite its active trading and high GDP, only10% of the population experience better economic and social outcomes. The bulk of PNG's population lives in poverty, challenged by geographical, cultural, and political barriers to better income, education, and health. Progress needs to be made to minimize these barriers and to allow more of PNG's population to experience the economic benefits generated through trade activities. A balance needs to be maintained between the desire of developed countries to broaden their markets, and the efforts of developing countries to promote and protect the health and well-being of their populations through increasing participation in global markets. PACER Plus presents an opportunity for pursuing alternative models of trade agreements that support and develop Pacific health.

24 **Furusawa T, Furusawa H, Eddie R, Tuni M, Pitakaka F, Aswani S.**
Communicable and non-communicable diseases in the Solomon Islands villages during recovery from a massive earthquake in April 2007.
NZ Med J 2011 Apr 29;124(1333):17-28.

AIM: The major causes of mortality and morbidity have changed from infectious diseases and malnutrition conditions to non-communicable diseases (NCDs) in Melanesian societies. However, a massive earthquake and its related changes might have disturbed the patterns. This study aimed to explore which health problems were likely to be prevalent during the recovery process from the 2 April 2007 earthquake in the Solomon Islands. METHODS: Participants were recruited in Titiana, a severely damaged village located near a town; Tapurai, a severely damaged remote village; Mondo, a severely damaged, medium urban village; and Olive, a control village. Health indicators measured were classified into communicable and nutritional conditions (malaria, malnutrition, infection status and child growth) and NCDs (overweight/obesity, hypertension and diabetes). RESULTS: Titiana residents were more at risk of infectious conditions (C-reactive protein greater than or equal to 1 mg/dL) and obesity (BMI greater than or equal to 30 kg/m^2). Tapurai and Mondo residents were at risks of infectious conditions and becoming overweight (BMI greater than or equal to 25 kg/m^2), respectively. Titiana and Mondo residents complained about insufficient subsistence production. CONCLUSION: The urban communities were found to be at risks of both communicable and NCDs. Controlling urbanization as well as providing continuous support against infectious conditions during the recovery process would be beneficial.

25 **Gray RT, Zhang L, Lupiwa T, Wilson DP.**
Forecasting the population-level impact of reductions in HIV antiretroviral therapy in Papua New Guinea.
AIDS Res Treat 2011:891593. Epub 2010 Dec 1.

Papua New Guinea (PNG) recently did not secure external funding for the continuation of its antiretroviral treatment (ART) programs meaning that supplies of HIV drugs for the estimated 38,000 people living with HIV in PNG could be completely depleted during 2010. Using a mathematical model of HIV transmission calibrated to available HIV epidemiology data from PNG, we evaluated the expected population-level impact of reductions in ART availability. If the number of people on ART falls to 10% of its current level, then there could be an approximate doubling in annual incidence and an additional 12,848 AIDS-related deaths (100.7% increase) over the next 5 years; if ART provision is halved, then annual incidence would increase by ~68%, and there would be an additional ~10,936 AIDS-related deaths (85.7% increase). These results highlight that maintenance of ART and associated services through external funding is essential for the health and well-being of HIV-positive people in PNG.

26 **Grkovic T, Blees JS, Colburn NH, Schmid T, Thomas CL, Henrich CJ, McMahon JB, Gustafson KR.**
Cryptocaryols A-H, alpha-pyrone-containing 1,3-polyols from *Cryptocarya* sp. implicated in stabilizing the tumor suppressor Pdcd4.
J Nat Prod 2011 May 27;74(5):1015-1020. Epub 2011 May 3.

A high-throughput cell-based reporter assay designed to identify small-molecule stabilizers of the tumor suppressor Pdcd4 was used to screen extracts in the NCI Natural Products Repository. Bioassay-guided fractionation of an extract from a Papua New Guinea collection of the tropical tree *Cryptocarya* sp. provided a series of new 5,6-dihydro-alpha-pyrone-containing 1,3-polyols (1-8), named cryptocaryols A-H. Their structures were assigned from a combination of NMR, MS and CD studies in conjunction with NMR database comparisons. Compounds 1-8 were found to rescue Pdcd4 from TPA-induced degradation with EC50 concentrations that ranged from 1.3 to 4.9 μM.

27 **Hendra R, Ahmad S, Sukari A, Shukor MY, Oskoueian E.**
Flavonoid analyses and antimicrobial activity of various parts of *Phaleria macrocarpa* (Scheff.) Boerl fruit.
Int J Mol Sci 2011;12(6):3422-3431. Epub 2011 May 27.

Phaleria macrocarpa (Scheff.) Boerl (Thymelaceae) is commonly known as 'Crown of God', 'Mahkota Dewa' and 'Pau'. It originates from Papua Island, Indonesia and it grows in tropical areas. Empirically, it is potent in treating hypertensive, diabetic, cancer and diuretic patients. It has a long history of ethnopharmacological usage, and the lack of information about its biological activities led us to investigate the possible biological activities by characterisation of flavonoids and antimicrobial activity of various parts of *P. macrocarpa* against pathogenic bacteria and fungi. The results showed that kaempferol, myricetin, naringin and rutin were the major flavonoids present in the pericarp while naringin and quercetin were found in the mesocarp and seed. Furthermore, the antibacterial activity of

different parts of *P. macrocarpa* fruit showed a weak to moderate antibacterial activity against pathogenic tested bacteria (inhibition range: 0.93-2.17 cm) at concentration of 0.3 mg/disc. The anti-fungi activity was only found in seed extract against *Aspergillus niger* (1.87 cm) at concentration of 0.3 mg/well. From the results obtained, *P. macrocarpa* fruit could be considered as a natural antimicrobial source due to the presence of flavonoid compounds.

28 **Henrich J, Broesch J.**
On the nature of cultural transmission networks: evidence from Fijian villages for adaptive learning biases.
Philos Trans R Soc Lond B Biol Sci 2011 Apr 12;366(1567):1139-1148.

Unlike other animals, humans are heavily dependent on cumulative bodies of culturally learned information. Selective processes operating on this socially learned information can produce complex, functionally integrated, behavioral repertoires: cultural adaptations. To understand such non-genetic adaptations, evolutionary theorists propose that (i) natural selection has favoured the emergence of psychological biases for learning from those individuals most likely to possess adaptive information, and (ii) when these psychological learning biases operate in populations, over generations, they can generate cultural adaptations. Many laboratory experiments now provide evidence for these psychological biases. Here, we bridge from the laboratory to the field by examining if and how these biases emerge in a small-scale society. Data from three cultural domains – fishing, growing yams and using medicinal plants – show that Fijian villagers (ages 10 and up) are biased to learn from others perceived as more successful/knowledgeable, both within and across domains (prestige effects). We also find biases for sex and age, as well as proximity effects. These selective and centralized oblique transmission networks set up the conditions for adaptive cultural evolution.

29 **Henry-Halldin CN, Reimer L, Thomsen E, Koimbu G, Zimmerman A, Keven JB, Dagoro H, Hetzel MW, Mueller I, Siba P, Zimmerman PA.**
High throughput multiplex assay for species identification of Papua New Guinea malaria vectors: members of the *Anopheles punctulatus* (Diptera: Culicidae) species group.
Am J Trop Med Hyg 2011 Jan;84(1):166-173.

Malaria and filariasis are transmitted in the Southwest Pacific region by *Anopheles punctulatus* sibling species including *An. punctulatus*, *An. koliensis* and the *An. farauti* complex 1-8 (includes *An. hinesorum* [*An. farauti* 2], *An. torresiensis* [*An. farauti* 3]). Distinguishing these species from each other requires molecular diagnostic methods. We developed a multiplex polymerase chain reaction (PCR)-based assay specific for known species-specific nucleotide differences in the internal transcribed spacer 2 region and identified the five species most frequently implicated in transmitting disease (*An. punctulatus*, *An. koliensis*, *An. farauti* 1, *An. hinesorum* and *An. farauti* 4). A set of 340 individual mosquitoes obtained from seven Papua New Guinea provinces representing a variety of habitats were analyzed by using this multiplex assay. Concordance between molecular and morphological diagnosis was 56.4% for *An. punctulatus*, 85.3% for *An. koliensis*, and 88.9% for *An. farauti*. Among 158 mosquitoes morphologically designated as *An. farauti*, 33 were re-classified by PCR as *An. punctulatus*, 4 as *An. koliensis*, 26 as *An. farauti* 1, 49 as *An. hinesorum*, and 46 as *An. farauti* 4. Misclassification results from variable coloration of the proboscis and overlap of *An. punctulatus*, *An. koliensis* and *An. farauti* 4. This multiplex technology enables further mosquito strain identification and simultaneous detection of microbial pathogens.

30 **Henry-Halldin CN, Sepe D, Susapu M, McNamara DT, Bockarie M, King CL, Zimmerman PA.**
High-throughput molecular diagnosis of circumsporozoite variants VK210 and VK247 detects complex *Plasmodium vivax* infections in malaria endemic populations in Papua New Guinea.
Infect Genet Evol 2011 Mar;11(2):391-398. Epub 2010 Dec 13.

Malaria is endemic in lowland and coastal regions of Papua New Guinea (PNG), and is caused by *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae* and *Plasmodium ovale*. Infection by *P. vivax* is attributed to distinct strains, VK210 and VK247, which differ in the sequence of the circumsporozoite protein (pvcsp). Here, based upon sequence polymorphisms in pvcsp, we developed a post-PCR ligation detection reaction-fluorescent microsphere assay (LDR-FMA) to distinguish these *P. vivax* strains. This diagnostic assay was designed to detect the presence of both VK210 and VK247 *P. vivax* strains simultaneously in a high-throughput 96-well format. Using this assay, we analyzed human blood samples from the Wosera (n=703) and Mugil (n=986) regions to evaluate the prevalence of these *P. vivax* strains. VK210 and VK247 strains were found in both study sites. In the Wosera, single infections with VK210 strain were observed to be most common (41.7%), followed by mixed-strain (36.8%) and VK247 single-strain infections (21.5%). Similarly, in Mugil, VK210 single-strain infections were most common (51.6%), followed by mixed-strain (34.4%) and VK247 single-strain infections (14%). These results suggest that the distribution of *P. vivax* infections was similar between the two study sites. Interestingly, we observed a non-random distribution of these two *P. vivax* strains, as mixed-strain infections were significantly more prevalent than expected in both study sites (Wosera and Mugil χ^2, $p < 0.001$). Additionally, DNA sequence analysis of a subset of *P. vivax* infections showed that no individual pvcsp alleles were shared between the two study sites. Overall, our results illustrate that PNG malaria-endemic regions harbor a complex mixture of *P. vivax* strains, and emphasize the importance of malaria control strategies that would be effective against a highly diverse parasite population.

31 **Hnawia E, Hassani L, Deharo E, Maurel S, Waikedre J, Cabalion P, Bourdy G, Valentin A, Jullian V, Fogliani B.**
Antiplasmodial activity of New Caledonia and Vanuatu traditional medicines.
Pharm Biol 2011 Apr;49(4):369-376. Epub 2011 Feb 2.

CONTEXT: With the emergence of strains multiresistant to antimalarial drugs, the search for new active molecules remains a priority. Ethnopharmacology appears to be a good method of selection in such investigations. OBJECTIVE: The aim of this research work is to select plants used in Melanesian traditional medicine, in New

Caledonia and Vanuatu, which should be a promising source for the isolation of new antimalarial drugs. MATERIALS AND METHODS: Forty-seven plant extracts belonging to 12 families, traditionally used by the Melanesian people or belonging to an antimalarial known genus, were screened in vitro for antimalarial activity on *Plasmodium falciparum* chloroquine (CQ)-resistant (FcB1) and CQ-sensitive (HB3) strains. They were also tested for their inhibitory effects on a protein kinase (Pfnek) and their cytotoxicity on human breast adenocarcinoma (MCF7) cells. RESULTS: Among all extracts, four displayed strong in vitro activities against *P. falciparum*: *Gardenia urvillei* Montrouzier, *Scleria polycarpa* Boeckeler, T*erminalia catappa* L. and *Acronychia laevis* J.R. & J.G. Forster, the latter being also toxic on MCF7 cells. Except for the extracts of *S. polycarpa*, all others that were active on *P. falciparum* also possess an inhibitory effect on Pfnek. DISCUSSION AND CONCLUSION: These results confirm that ethnopharmacology is an excellent approach for such investigations. The two countries considered clearly present advantages in the field. Indeed, local populations keep their traditional knowledge alive, and their flora is exceptionally rich. In New Caledonia, the high endemicity rate (74%) ranks the island as one of the world's biodiversity hotspots. As a consequence, chances to discover new active natural compounds are also high.

32 **Joyner PM, Waters AL, Williams RB, Powell DR, Janakiram NB, Rao CV, Cichewicz RH.**
Briarane diterpenes diminish COX-2 expression in human colon adenocarcinoma cells.
J Nat Prod 2011 Apr 25;74(4):857-861. Epub 2011 Mar 25.

Exploration of a soft coral (*Briareum* sp.) from Vanuatu led to the isolation of three new briaranes, designated brialalepolides A (1), B (2) and C (3). Compounds 2 and 3 reduced the expression of COX-2 in human colon adenocarcinoma cells, as well as in murine macrophage cells. This is significant because the metabolic products of COX-2 have been implicated in the pathogenesis of colon cancer and other diseases.

33 **Juniastuti, Utsumi T, Nugrahaputra VE, Amin M, Soetjipto, Hayashi Y, Hotta H, Lusida MI.**
Another novel subgenotype of hepatitis B virus genotype C from Papuans of highland origin.
J Med Virol 2011 Feb;83(2):225-234.

Hepatitis B virus (HBV) genotypes and subtypes have been identified worldwide. As HBV genotypes/subtypes, the HBV subgenotypes seem to be associated with their geographical distribution and ethnic origin. A previous study showed the novel HBV subgenotype C6, based on the complete genome sequences of isolates in Papua, Indonesia. In the present study, further characterization of HBV in Jayapura (capital of Papua Province), particularly from native people of Papua originating from the highlands (highland Papuans) and those from the lowlands (lowland Papuans) were examined. Of 32 HBV isolates from both highland and lowlands Papuan blood donors with HBsAg positive, part of the S gene and the core gene sequences were analyzed. Analyses of some isolates from highland Papuans were confirmed by the complete genome sequences. Most HBV isolates were classified into genotype C (78.1%), followed by genotype B (18.8%), and genotype D (3.1%). The subtype adr was predominant (71.9%), followed by adw2 (25.1%), and ayw2 (3.1%). As with previous findings, phylogenetic analyses revealed that most HBV isolates from Papuans, C/adr, belonged to subgenotype C6. Interestingly, some C/adr isolates from highland Papuans formed a distinct cluster from all reported subgenotypes of HBV/C, and they differed from HBV/C1-C10 by 4.2-7.2% over the complete genome. SimPlot analysis showed no evidence of recombination with HBV/C1-C10. The isolated life and closed social systems of highland Papuans, even though some have been moving to Jayapura, likely contribute to the formation of this unique cluster of infection with a novel subgenotype of HBV, named C11.

34 **Kelly A, Kupul M, Frankland A, Worth H, Nosi S, Mek A, Kepa B, Walizopa L, Emori R, Pirpir L, Akuani F, Cangah B, Siba P.**
Living serodiscordantly in Papua New Guinea: sexual practices of HIV-positive people on ART by serostatus of regular heterosexual partner.
AIDS Care 2011 Jun;23(6):734-740.

This paper examines condom use in intimate relationships amongst Papua New Guineans on antiretroviral therapy (ART). These findings are from a mixed-method study in six provinces throughout Papua New Guinea (PNG). A total of 374 HIV-positive adult Papua New Guineans, over the age of 16 and on ART for more than two weeks, were recruited using a non-probability, convenience sampling methodology. Participants were recruited through ART prescribing sites, People Living with HIV/AIDS (PLWHA) drop-in clinics and support groups. A small number (36) also participated in in-depth interviews. Of the sample 226 (60.4%) were women and 148 (39.6%) were men. The majority of the sample was aged below 40 years, with a median age of 30 years. Of the sample who were in a regular relationship 64.7% identified themselves as being in a relationship where both they and their partner were HIV-positive (seroconcordant). Smaller proportions reported being in a relationship with an HIV-negative partner (serodiscordant) (21.0%), or in a relationship where they were not aware of their partner's HIV status (14.3%). The majority of participants who reported having a regular partner also reported having disclosed their HIV serostatus to their partner (91.8%). A significantly greater proportion of participants who reported being in relationships where they did not know the status of their partner also reported living in the Southern Region of PNG (52.9%), while the majority of those in seroconcordant relationships lived in the Highlands Region (71.2%). There did not appear to be any differences in sexual practice of using condoms between the three groups. Knowledge of serostatus is important for 'positive prevention'.

35 **Kennedy E, Gray N, Azzopardi P, Creati M.**
Adolescent fertility and family planning in East Asia and the Pacific: a review of DHS reports.
Reprod Health 2011 May 5;8:11.

BACKGROUND: Adolescent pregnancy has significant health and socio-economic consequences for women, their families and communities. Efforts to prevent too-early pregnancy rely on accurate information about adolescents knowledge, behaviours and access to family planning; however, available data are limited in some settings. Demographic and Health Survey (DHS) reports are recognised as providing nationally representative data that are accessible to policymakers and programmers. This paper reviews DHS reports for low and lower

middle income countries in East Asia and the Pacific to determine what information regarding adolescent fertility and family planning is available, and summarises key findings. METHODS: The most recent DHS reports were sought for the 33 low and lower middle income countries in the East Asia and Pacific region as defined by UNICEF and World Bank. Age-disaggregated data for all indicators relevant to fertility and current use, knowledge and access to family planning information and services were sought to identify accessible information. Reported data were analysed using an Excel database to determine outcomes for adolescents and compare with adult women. RESULTS: DHS reports were available for eleven countries: Cambodia, Indonesia, Marshall Islands, Nauru, Papua New Guinea, Philippines, Samoa, Solomon Islands, Timor-Leste, Tuvalu and Vietnam. 27 of 40 relevant DHS indicators reported outcomes for adolescent women aged 15-19 years. There were limited data for unmarried adolescents. A significant proportion of women commence sexual activity and childbearing during adolescence in the context of low contraceptive prevalence and high unmet need for contraception. Adolescent women have lower use of contraception, poorer knowledge of family planning and less access to information and services than adult women. CONCLUSION: DHS reports provide useful and accessible data; however, they are limited by the failure to report data for unmarried adolescents and reportage-disaggregated data for some indicators. Further research is required to better understand the barriers that both married and unmarried adolescents face accessing reproductive health information and services, and their information and service delivery preferences.

36 **Koepfli C, Schoepflin S, Bretscher M, Lin E, Kiniboro B, Zimmerman PA, Siba P, Smith TA, Mueller I, Felger I.**
How much remains undetected? Probability of molecular detection of human Plasmodia in the field.
PLoS One 2011 Apr 28;6(4):e19010.

BACKGROUND: In malaria-endemic areas, most people are simultaneously infected with different parasite clones. Detection of individual clones is hampered when their densities fluctuate around the detection limit and, in case of *P. falciparum*, by sequestration during part of their life cycle. This has important implications for measures of levels of infection or for the outcome of clinical trials. This study aimed at measuring the detectability of individual *P. falciparum* and *P. vivax* parasite clones in consecutive samples of the same patient and at investigating the impact of sampling strategies on basic epidemiological measures such as multiplicity of infection (MOI). METHODS: Samples were obtained in a repeated cross-sectional field survey in 1 to 4.5 year old children from Papua New Guinea, who were followed up in 2-monthly intervals over 16 months. At each follow-up visit, two consecutive blood samples were collected from each child at intervals of 24 hours. Samples were genotyped for the polymorphic markers *msp2* for *P. falciparum* and *msp1F3* and *MS16* for *P.vivax*. Observed prevalence and mean MOI estimated from single samples per host were compared to combined data from sampling twice within 24 h. FINDINGS AND CONCLUSION: Estimated detectability was high in our data set (0.79 [95% CI 0.76-0.82] for *P. falciparum* and, depending on the marker, 0.61 [0.58-0.63] or 0.73 [0.71-0.75] for *P. vivax*). When genotyping data from sequential samples, collected 24 hours apart, were combined, the increase in measured prevalence was moderate, 6 to 9% of all infections were missed on a single day. The effect on observed MOI was more pronounced: 18 to 31% of all individual clones were not detected in a single bleed. Repeated sampling revealed little difference between detectability of *P. falciparum* and *P. vivax*.

37 **Kurth F, Bélard S, Basra A, Ramharter M.**
Pyronaridine: a new 'old' drug on the verge of entering the antimalaril armamentarium.
Expert Rev Anti Infect Ther 2011 Apr;9(4):393-396.

Pyronaridine-artesunate is a promising new artemisinin-based combination therapy for the treatment of uncomplicated falciparum malaria and the first systematically evaluated artemisinin-based combination therapy for vivax malaria. The 3-day regimen proved to be highly efficacious in clinical trials in Africa and Asia and is currently under review by the EMA. Price et al. report data of an in vitro drug-susceptibility study evaluating the activity of pyronaridine against *Plasmodium vivax* and *Plasmodium falciparum* field isolates from Papua, Indonesia. The authors demonstrate high in vitro activity of pyronaridine at low nanomolar concentrations that is only paralleled by the artemisinin class of antimalarials. Besides exciting methodological insights into the new field of in vitro drug-susceptibility testing for *P. vivax*, these data are encouraging evidence for the future implementation of pyronaridine in combination therapy for the fight against malaria.

38 **Lampah DA, Yeo TW, Hardianto SO, Tjitra E, Kenangalem E, Sugiarto P, Price RN, Anstey NM.**
Coma associated with microscopy-diagnosed *Plasmodium vivax*: a prospective study in Papua, Indonesia.
PLoS Negl Trop Dis 2011 Jun;5(6):e1032. Epub 2011 Jun 7.

BACKGROUND: Coma complicates *Plasmodium falciparum* infection but is uncommonly associated with *P. vivax*. Most series of vivax coma have been retrospective and have not utilized molecular methods to exclude mixed infections with *P. falciparum*. METHODS: We prospectively enrolled patients hospitalized in Timika, Indonesia, with a Glasgow Coma Score (GCS) ≤10 and *P. vivax* monoinfection on initial microscopy over a four-year period. Hematological, biochemical, serological, radiological and cerebrospinal fluid (CSF) examinations were performed to identify other causes of coma. Repeat microscopy, antigen detection and polymerase chain reaction (PCR) were performed to exclude infections with other *Plasmodium* species. RESULTS: Of 24 patients fulfilling enrolment criteria, 5 had clear evidence for other non-malarial etiologies. PCR demonstrated 10 mixed infections and 3 *P. falciparum* monoinfections. 6 (25%) patients had vivax monoinfection and no apparent alternative cause, with a median GCS of 9 (range 8-10) and a median coma duration of 42 (range 36-48) hours. CSF leukocyte counts were <10/μl (n=3); 2 of the 3 patients without CSF examination recovered with antimalarial therapy alone. One patient had a tremor on discharge consistent with a post-malarial neurological syndrome. No patient had other organ dysfunction. The only death was associated with pure *P. falciparum* infection by PCR. Vivax monoinfection-associated risk of coma was estimated at 1 in

29,486 clinical vivax infections with no deaths. In comparison, the risk of falciparum-associated coma was estimated at 1 in 1,276 clinical infections with an 18.5% mortality rate. CONCLUSIONS: *P. vivax*-associated coma is rare, occurring 23 times less frequently than that seen with falciparum malaria, and is associated with a high proportion of non-malarial causes and mixed infections using PCR. The pathogenesis of coma associated with vivax malaria, particularly the role of comorbidities, is uncertain and requires further investigation.

39 **Lu F, Lim CS, Nam DH, Kim K, Lin K, Kim TS, Lee HW, Chen JH, Wang Y, Sattabongkot J, Han ET.**
Genetic polymorphism in *pvmdr1* and *pvcrt-o* genes in relation to in vitro drug susceptibility of *Plasmodium vivax* isolates from malaria-endemic countries.
Acta Trop 2011 Feb;117(2):69-75. Epub 2010 Oct 8.

Treatment failure of chloroquine for *Plasmodium vivax* infection has increased in endemic countries. However, the molecular mechanisms for resistance and in vitro susceptibility of *P. vivax* to chloroquine remain elusive. We investigated the prevalence of mutations in the *pvmdr1* and *pvcrt-o* genes, and the copy number of the *pvmdr1* gene in isolates from the Republic of Korea (ROK), Thailand, the Union of Myanmar (Myanmar) and Papua New Guinea (PNG). We also measured in vitro susceptibility of Korean isolates to antimalarial drugs. The *pvmdr1* analysis showed that mutations at amino acid position Y976F of *pvmdr1* were found in isolates from Thailand (17.9%), Myanmar (13.3%) and PNG (100%), but none from the ROK, and mutation at position F1076L was present in isolates from the ROK (100%), Thailand (60.7%) and Myanmar (46.7%). One copy of the *pvmdr1* gene was observed in most isolates and double copy numbers of the gene were observed in two Thai isolates. In the exons of the *pvcrt-o* gene that were sequenced, a K10 insertion was present in isolates from Thailand (56.0%) and Myanmar (46.2%), and the wild type was found in all Korean isolates. The results suggest that gene polymorphisms and copy number variation were observed in isolates of *P. vivax* from Southeast Asian countries. In Korean isolates polymorphism was limited to the F1076L variant, and no isolates with high level of resistance were found by in vitro susceptibility determinations. Moreover, our results provide a baseline for future prospective drug studies in malaria-endemic areas.

40 **Malloy KL, Villa FA, Engene N, Matainaho T, Gerwick L, Gerwick WH.**
Malyngamide 2, an oxidized lipopeptide with nitric oxide inhibiting activity from a Papua New Guinea marine cyanobacterium.
J Nat Prod 2011 Jan 28;74(1):95-98. Epub 2010 Dec 14.

A Papua New Guinea collection of the marine cyanobacterium cf. *Lyngbya sordida* yielded three known compounds as well as a new PKS-NRPS-derived malyngamide with anti-inflammatory and cytotoxic activity. Malyngamide 2 features an extensively oxidized cyclohexanone ring. Resolution of the ring core as a 6,8,9-triol rather than a 7,8,9-triol and relative configuration was based on chemical shift and bond geometry modeling in conjunction with homonuclear and heteronuclear coupling constants, NOE and ROE correlations, and other structural information. Malyngamide 2 exhibited anti-inflammatory activity in LPS-induced RAW macrophage cells (IC50 = 8.0 μM) with only modest cytotoxicity to the mammalian cell line.

41 **Manning L, Laman M, Edoni H, Mueller I, Karunajeewa HA, Smith D, Hwaiwhanje I, Siba PM, Davis TM.**
Subacute sclerosing panencephalitis in Papua New Guinean children: the cost of continuing inadequate measles vaccine coverage.
PLoS Negl Trop Dis 2011 Jan 4;5(1):e932.

INTRODUCTION: Subacute sclerosing panencephalitis (SSPE) is a late, rare and usually fatal complication of measles infection. Although a very high incidence of SSPE in Papua New Guinea (PNG) was first recognized 20 years ago, estimated measles vaccine coverage has remained at ≤70% since and a large measles epidemic occurred in 2002. We report a series of 22 SSPE cases presenting between November 2007 and July 2009 in Madang Province, PNG, including localized clusters with the highest ever reported annual incidence. METHODOLOGY/PRINCIPAL FINDINGS: As part of a prospective observational study of severe childhood illness at Modilon Hospital, the provincial referral center, children presenting with evidence of meningo-encephalitis were assessed in detail including lumbar puncture in most cases. A diagnosis of SSPE was based on clinical features and presence of measles-specific IgG in cerebrospinal fluid and/or plasma. The estimated annual SSPE incidence in Madang Province was 54/million population aged <20 years, but four sub-districts had an incidence >100/million/year. The distribution of year of birth of the 22 children with SSPE closely matched the reported annual measles incidence in PNG, including a peak in 2002. CONCLUSIONS/SIGNIFICANCE: SSPE follows measles infections in very young PNG children. Because PNG children have known low seroconversion rates to the first measles vaccine given at 6 months of age, efforts such as supplementary measles immunisation programs should continue in order to reduce the pool of non-immune people surrounding the youngest and most vulnerable members of PNG communities.

42 **Manning L, Laman M, Stanisic D, Rosanas-Urgell A, Bona C, Teine D, Siba P, Mueller I, Davis TM.**
Plasma *Plasmodium falciparum* histidine-rich protein-2 concentrations do not reflect severity of malaria in Papua New Guinean children.
Clin Infect Dis 2011 Feb 15;52(4):440-446. Epub 2011 Jan 7.

BACKGROUND: In areas of unstable malaria transmission, plasma *Plasmodium falciparum* histidine-rich protein 2 (PfHRP-2) concentrations parallel total parasite biomass and thus infection severity. However, where transmission is more intense, plasma PfHRP-2 might not reliably predict complications and mortality. METHODS: As part of a prospective case-control study of severe pediatric illness in Madang, Papua New Guinea, we recruited 220 children aged 6 months to 10 years with severe falciparum malaria, 48 with uncomplicated malaria and 139 healthy controls. Groups were matched by age, sex and province of parental birth. Plasma PfHRP-2 levels were quantified by validated immunoassay. RESULTS: Detectable plasma PfHRP-2 concentrations were present in 21 healthy controls (15.1%). Although plasma PfHRP-2 levels were higher in the children with clinical malaria ($p<0.001$), there was no difference between those with uncomplicated and severe infections (median,

584 and 456 ng/mL, respectively [interquartile range, 77-1114 and 113-1113 ng/mL, respectively]; p = 0.43). Log parasitemia, hemoglobin, log plasma bilirubin and plasma creatinine levels were independently associated with plasma PfHRP-2 levels in multiple regression analysis (p ≤0.014), but coma, blood lactate level and plasma bicarbonate level were not. The 1 severely ill child who died had a plasma PfHRP-2 concentration of 483 ng/mL, close to the group median. CONCLUSIONS: The clinical and prognostic utility of plasma PfHRP-2 concentrations depends on the epidemiologic circumstances. In areas of intense malaria transmission, plasma PfHRP-2 reflects recent as well as present infections.

43 **Marfurt J, Chalfein F, Prayoga P, Wabiser F, Kenangalem E, Piera KA, Fairlie DP, Tjitra E, Anstey NM, Andrews KT, Price RN.**
Ex vivo activity of histone deacetylase inhibitors against multidrug-resistant clinical isolates of *Plasmodium falciparum* and *P. vivax*.
Antimicrob Agents Chemother 2011 Mar;55(3):961-966. Epub 2010 Dec 6.

Histone acetylation plays an important role in regulating gene transcription and silencing in *Plasmodium falciparum*. Histone deacetylase (HDAC) inhibitors, particularly those of the hydroxamate class, have been shown to have potent in vitro activity against drug-resistant and -sensitive laboratory strains of *P. falciparum*, raising their potential as a new class of antimalarial compounds. In the current study, stage-specific ex vivo susceptibility profiles of representative hydroxamate-based HDAC inhibitors suberoylanilide hydroxamic acid (SAHA), 2-ASA-9 and 2-ASA-14 (2-ASA-9 and 2-ASA-14 are 2-aminosuberic acid-based HDAC inhibitors) were assessed in multidrug-resistant clinical isolates of *P. falciparum* (n = 24) and *P. vivax* (n = 25) from Papua, Indonesia, using a modified schizont maturation assay. Submicromolar concentrations of SAHA, 2-ASA-9 and 2-ASA-14 inhibited the growth of both *P. falciparum* (median 50% inhibitory concentrations [IC_{50}s] of 310, 533 and 266 nM) and *P. vivax* (median IC_{50}s of 170, 503 and 278 nM). Inverse correlation patterns between HDAC inhibitors and chloroquine for *P. falciparum* and mefloquine for *P. vivax* indicate species-specific susceptibility profiles for HDAC inhibitors. These HDAC inhibitors were also found to be potent ex vivo against *P. vivax* schizont maturation, comparable to that in *P. falciparum*, suggesting that HDAC inhibitors may be promising candidates for antimalarial therapy in geographical locations where both species are endemic. Further studies optimizing the selectivity and in vivo efficacy of HDAC inhibitors in *Plasmodium* spp. and defining drug interaction with common antimalarial compounds are warranted to investigate the role of HDAC inhibitors in antimalarial therapy.

44 **McMillan K, Worth H.**
The impact of socio-cultural context on young people's condom use: evidence from two Pacific Island countries.
Cult Health Sex 2011 Mar;13(3):313-326.

Young people are a key group for HIV prevention in the Pacific region where levels of STIs are high and condom use is low. During 2008, 62 in-depth interviews were conducted with people aged between 18 and 25 years in Tonga and Vanuatu. The research was aimed at understanding factors impacting on young people's condom use in two Pacific Island nations. The data show a marked disjuncture between attitudes and practice with regard to condoms. This paper discusses factors underpinning that inconsistency and directs attention to the effect of social and cultural influences on young people's condom use. The authors conclude that individual-level approaches to improving rates of condom use will be inadequate unless they are informed by an understanding of the role of identity, culture and tradition in young people's decisions around condom use. The findings also underline the need for country-specific approaches to condom promotion efforts in the Pacific.

45 **Mediannikov O, Cabre O, Qu F, Socolovschi C, Davoust B, Marié JL, Parola P, Raoult D.**
Rickettsia felis and *Bartonella clarridgeiae* in fleas from New Caledonia.
Vector Borne Zoonotic Dis 2011 Feb;11(2):181-183. Epub 2010 Jun 23.

Dog fleas collected in New Caledonia harbored flea-borne pathogens *Rickettsia felis* and *Bartonella clarridgeiae* in 81% and 5%, respectively.

46 **Mitjà O, Hays R, Ipai A, Gubaila D, Lelngei F, Kiara M, Paru R, Bassat Q.**
Outcome predictors in treatment of yaws.
Emerg Infect Dis 2011 Jun;17(6):1803-1805.

To estimate failure rates after treatment with benzathine penicillin and to identify determinants of failure that affected outcomes for yaws, we conducted a cohort study of 138 patients; treatment failed in 24 (17.4%). Having low initial titers on Venereal Disease Research Laboratory test and living in a village where yaws baseline incidence was high were associated with increased likelihood of treatment failure.

47 **Mitjà O, Hays R, Ipai A, Wau B, Bassat Q.**
Osteoperiostitis in early yaws: case series and literature review.
Clin Infect Dis 2011 Mar;52(6):771-774.

We describe the clinical and radiological manifestations and outcome after treatment of 7 children who received a diagnosis of early yaws osteoperiostitis. Osteoperiostitis occurred some weeks after the primary infection, and the most common finding was hypertrophic periostitis of long bones. All treated patients had excellent responses to benzyl-penicillin therapy.

48 **Mulyanto, Depamede SN, Wahyono A, Jirintai, Nagashima S, Takahashi M, Okamoto H.**
Analysis of the full-length genomes of novel hepatitis B virus subgenotypes C11 and C12 in Papua, Indonesia.
J Med Virol 2011 Jan;83(1):54-64.

Two novel subgenotypes (C6 and D6) of hepatitis B virus (HBV) were identified recently in Papua, a multiethnic area of Indonesia. To characterize further the HBV strains in Papua, serum samples collected from 59 viremic subjects (44 males and 15 females; mean age: 30.0 ± 15.5 years) among indigenous inhabitants in Papua were subjected to phylogenetic analysis of an 1.6-kb partial sequence. 45 samples (76%) had genotype C HBV (HBV/C) [C5 (n = 1), C6 (n = 40) and unclassifiable (n = 4)], while 7 samples (12%) were HBV/D [D1 (n = 1) and D6 (n = 6)] and 6 samples (10%) were HBV/B [B2 (n = 1), B3 (n = 3), B7 (n = 1) and B8 (n = 1)]; the remaining sample possessed B3 and C6. An analysis of the full-length sequence of the four HBV/C

isolates (NMB09122, NMB09124, NMB09075 and MRK89073) that were unclassifiable into any of the 10 known HBV/C subgenotypes (C1-C10) showed no significant evidence of recombination. Over the entire genome, the NMB09122 and NMB09124 isolates shared 99.8% identity and segregated into a cluster with a bootstrap value of 100%, differing from HBV/C1-HBV/C10 by 3.8-6.9% (mean, ≥4.0%), indicating that NMB09122 and NMB09124 can be classified into a novel subgenotype within genotype C (tentatively designated C11). The NMB09075 and MRK89073 isolates were 97.4% identical to each other and differed from known HBV/C isolates, including the C11 strains, by 4.0-7.2% (mean, ≥4.5%) over the entire genome, indicating that NMB09075 and MRK89703 can be classified into another novel HBV/C subgenotype (C12). The distribution of C11 and C12 seemed to be associated with particular language speakers in Papua.

49 **Natuzzi ES, Kushner A, Jagilly R, Pickacha D, Agiomea K, Hou L, Houasia P, Hendricks PL, Ba'erodo D.**
Surgical care in the Solomon Islands: a road map for universal surgical care delivery.
World J Surg 2011 Jun;35(6):1183-1193.

BACKGROUND: Access to surgical care and emergency obstetrical care is limited in low-income countries. The Solomon Islands is one of the poorest countries in the Pacific region. Access to surgical care in Solomon Islands is limited and severely affected by a country made up of islands. Surgical care is centralized to the National Referral Hospital (NRH) on Guadalcanal, leaving a void of care in the provinces where more than 80% of the people live. METHODS: To assess the ability to provide surgical care to the people living on outer islands in the Solomon Islands, the provincial hospitals were evaluated using the World Health Organization's Global Initiative for Emergency and Essential Surgical Care Needs Assessment Tool questionnaire. Data on infrastructure, workforce and equipment available for treating surgical disease was collected at each provincial hospital visited. RESULTS: Surgical services are centralized to the NRH on Guadalcanal in Solomon Islands. Two provincial hospitals provide surgical care when a surgeon is available. Six of the hospitals evaluated provide only very basic surgical procedures. Infrastructure problems exist at every hospital including lack of running water, electricity, adequate diagnostic equipment, and surgical supplies. The number of surgeons and obstetricians employed by the Ministry of Health is currently inadequate for delivering care at the outer island hospitals. CONCLUSIONS: Shortages in the surgical workforce can be resolved in Solomon Islands with focused training of new graduates. Training surgeons locally, in the Pacific region, can minimize the 'brain drain'. Redistribution of surgeons and obstetricians to the provincial hospitals can be accomplished by creating supportive connections between these hospitals, the NRH and international medical institutions.

50 **Ongugo K, Hall J, Attia J.**
Implementing tuberculosis control in Papua New Guinea: a clash of culture and science?
J *Community Health* 2011 Jun;36(3):423-430.

Tuberculosis (TB) remains a major health problem in Papua New Guinea (PNG) and the Directly Observed Treatment Short course (DOTS) strategy has been adopted as a framework for controlling the disease. We review here the local and cultural factors in PNG that act as barriers to implementing each component of the DOTS program. Political will is needed to tackle the underlying conditions that lead to squatter settlements, e.g. poverty and unemployment, and to build infrastructure for access to rural populations. Better case detection may be obtained by addressing the cultural beliefs that delay presentation to health facilities, as well as providing ongoing training for laboratory technicians, introducing better sputum microscopy techniques and regular service of radiology equipment. Direct observation of therapy may need to be done using the traditional clan structure, e.g. clan chiefs and extended family system in rural areas. Effective drug supply is provided by the World Health Organization (WHO) Global Drug Facility (GDF). Monitoring and evaluation will require innovative approaches, perhaps through financial incentives on completion of the program or texting through the mobile text messaging for reminders. There are unique cultural and local issues that need to be addressed when implementing DOTS strategy in PNG.

51 **Pattison DA, Walters TE, Seal E.**
Exercise-associated hyponatraemia on the Kokoda Track.
Med J Aust 2011 Mar 7;194(5):247-248.

52 **Phongsavan P, Smith BJ, Chey T, Gilmete M, Havea D, Bauman AE; Members of the Health Behaviour and Lifestyle of Pacific Youth Survey Collaborating Group and Tonga Core Survey Team.**
Psychosocial profiles of adolescent nonsmokers in the Pacific.
Asia Pac J Public Health 2011 Jan;23(1):57-69.

Studies examining adolescent smoking have focused on at-risk individuals, while overlooking the psychosocial profiles of those adolescents who have managed to remain nonsmokers. Accumulating evidence suggests that positive emotions such as happiness may be associated with the adoption of healthy practices, but limited evidence has emerged from developing countries. This study examined the association between nonsmoking and positive emotions and psychosocial correlates in 3 large population samples of Pacific youths (N = 5659) living in Tonga, Vanuatu and Pohnpei in the Federated States of Micronesia. Across all 3 samples, being confident was significantly associated with nonsmoking and being happy (Tonga, odds ratio [OR] = 1.39, 95% confidence interval [CI] = 1.12-1.73; Vanuatu, OR = 1.29, 95% CI = 1.02-1.63; Pohnpei, OR = 2.34, 95% CI = 1.60-3.34). Some cross-country differences in relationships were found in the associations between societal factors (ie, perceived connections with school, teachers and peers, and perceived community importance and involvement) and nonsmoking and happiness. Findings have implications for developing innovative strategies aimed at preventing smoking uptake and suggest the need for focusing on identifying the determinants of nonsmoking and measuring positive emotions.

53 **Pulford J, Hetzel MW, Bryant M, Siba PM, Mueller I.**
Reported reasons for not using a mosquito net when one is available: a review of the published literature.
Malar J 2011 Apr 11;10:83.

BACKGROUND: A review of the barriers to mosquito net use in malaria-endemic countries has yet to be presented in the published literature despite considerable research interest in this area. This paper partly addresses this gap by reviewing one component of the evidence base, namely, published research pertaining to self-reported reasons for not using a mosquito net among net 'owning' individuals. It was anticipated that the review findings would potentially inform an intervention or range of interventions best suited to promoting greater net use amongst this group. METHOD: Studies were sought via a search of the Medline database. The key inclusion criteria were: that study participants could be identified as owning a mosquito net or having a mosquito net available for use; that these participants on one or more occasions were identified or self-reported as not using the mosquito net; and that reasons for not using the mosquito net were reported. Studies meeting these criteria were included irrespective of mosquito net type. RESULTS: A total of 22 studies met the inclusion criteria. Discomfort, primarily due to heat, and perceived (low) mosquito density were the most widely identified reasons for non-use. Social factors, such as sleeping elsewhere, or not sleeping at all, were also reported across studies as were technical factors related to mosquito net use (i.e. not being able to hang a mosquito net or finding it inconvenient to hang) and the temporary unavailability of a normally available mosquito net (primarily due to someone else using it). However, confidence in the reported findings was substantially undermined by a range of methodological limitations and a dearth of dedicated research investigation. CONCLUSIONS: The findings of this review should be considered highly tentative until such time as greater quantities of dedicated, well-designed and reported studies are available in the published literature. The current evidence-base is not sufficient in scope or quality to reliably inform mosquito net promoting interventions or campaigns targeted at individuals who own, but do not (reliably) use, mosquito nets.

54 **Reeder JC, Wapling J, Mueller I, Siba PM, Barry AE.**
Population genetic analysis of the *Plasmodium falciparum* 6-cys protein Pf38 in Papua New Guinea reveals domain-specific balancing selection.
Malar J 2011 May 14;10:126.

BACKGROUND: The *Plasmodium falciparum* merozoite surface protein Pf38 is targeted by antibodies of malaria immune adults and has been shown to be under balancing (immune) selection in a Gambian parasite population, indicating potential as a malaria vaccine candidate. This study explores the population genetics of *Pf38* in Papua New Guinea, to determine the extent and geographic distribution of diversity and to measure selective pressure along the length of the gene. METHODS: Using samples collected during community-based cross-sectional surveys in the Mugil and Wosera regions, the *Pf38* genes of 59 *P. falciparum* isolates were amplified and sequenced. These sequences, along with previously sequenced Gambian and laboratory isolates, were then subjected to an array of population genetic analyses, examining polymorphisms, haplotype diversity and balancing selection. In addition to whole-gene analysis, the two 6-cys domains were considered separately, to investigate domain-specific polymorphism and selection. RESULTS: Nineteen polymorphic sites were identified in the *Pf38* gene. Of these, 13 were found in the Gambia, 10 in Mugil and 8 in Wosera. Notably, the majority of common polymorphisms were confined to domain I. Although only moderate levels of nucleotide diversity were observed, the haplotype diversity was high in all populations, suggesting extensive recombination. Analyses of the full-length sequence provided only modest evidence for balancing selection. However, there was a strong contrast between domain I, which showed strong evidence for positive balancing selection, and domain II, which was neutral. Analyses of the geographic distribution of *Pf38* haplotypes showed that four haplotypes accounted for the majority of sequences found world-wide, but there were many more haplotypes unique to the African than the PNG populations. CONCLUSION: This study confirmed previous findings that *Pf38* is a polymorphic gene under balancing selection. However, analysing polymorphism and selection across the length of the gene painted a considerably different picture. Domain I is highly polymorphic and the target of significant balancing selection. In contrast, domain II is relatively conserved and does not show evidence of immune selective pressure. The findings have implications for future population genetic studies on vaccine candidates, showing that the biological context must also be considered as a framework for analysis.

55 **Rosewell A, Dagina R, Murhekar M, Ropa B, Posanai E, Dutta S, Barr I, Mola G, Zwi A, MacIntyre CR.**
Concurrent influenza and shigellosis outbreaks, Papua New Guinea, 2009.
Emerg Infect Dis 2011 Apr;17(4):756-758.

56 **Rosewell A, Dagina R, Murhekar M, Ropa B, Posanai E, Dutta SR, Jennison A, Smith H, Mola G, Zwi A, MacIntyre CR.**
Vibrio cholerae O1 in 2 coastal villages, Papua New Guinea.
Emerg Infect Dis 2011 Jan;17(1):154-156.

57 **Russell FM, Carapetis JR, Burton RL, Lin J, Licciardi PV, Balloch A, Tikoduadua L, Waqatakirewa L, Cheung YB, Tang ML, Nahm MH, Mulholland EK.**
Opsonophagocytic activity following a reduced dose 7-valent pneumococcal conjugate vaccine infant primary series and 23-valent pneumococcal polysaccharide vaccine at 12 months of age.
Vaccine 2011 Jan 10;29(3):535-544. Epub 2010 Oct 31.

Opsonophagocytic activity (OPA) was measured following reduced infant doses of 7-valent pneumococcal conjugate vaccine (PCV-7) with or without 23-valent pneumococcal polysaccharide vaccine (PPV-23) at 12 months, and subsequent re-exposure to a small dose of pneumococcal polysaccharide antigens (mPPS) at 17 months. Fijian infants were randomized to receive 0, 1, 2 or 3 PCV-7 doses. Half received PPV-23 at 12 months and all received mPPS at 17 months. OPA was performed on up to 14 serotypes. Three and 2 PCV-7 doses resulted in similar OPA for most PCV-7 serotypes up to 9 months and for half of the serotypes at 12 months. A single dose improved OPA compared with the unvaccinated group. PPV-23 significantly improved OPA for all serotypes tested but, in general,

was associated with diminished responses following re-challenge.

58 **Salman S, Griffin S, Kose K, Pitus N, Winmai J, Moore B, Siba P, Ilett KF, Mueller I, Davis TM.**
Pharmacokinetic properties of conventional and double-dose sulfadoxine-pyrimethamine given as intermittent preventive treatment in infancy.
Antimicrob Agents Chemother 2011 Apr;55(4):1693-1700. Epub 2011 Jan 31.

Intermittent preventive treatment in infancy (IPTi) entails routine administration of antimalarial treatment doses at specified times in at-risk infants. Sulfadoxine-pyrimethamine (SDX/PYR) is a combination that has been used as first-line IPTi. Because of limited pharmacokinetic data and suggestions that higher milligram/kilogram pediatric doses than recommended should be considered, we assessed SDX/PYR disposition, randomized to conventional (25/1.25 mg/kg of body weight) or double (50/2.5 mg/kg) dose, in 70 Papua New Guinean children aged 2 to 13 months. Blood samples were drawn at baseline, 28 days, and three time points randomly selected for each infant at 4 to 8 h or 2, 5, 7, 14 or 21 days. Plasma SDX, PYR and N(4)-acetylsulfadoxine (NSX, the principal metabolite of SDX) were assayed by high-performance liquid chromatography (HPLC). Using population modeling incorporating hepatic maturation and cystatin C-based renal function, two-compartment models provided best fits for PYR and SDX/NSX plasma concentration profiles. The area under the plasma concentration-time curve from 0h to infinity (AUC(0-∞)) was greater with the double dose versus the conventional dose of PYR (4,915 versus 2,844 µg/day/liter) and SDX (2,434 versus 1,460 mg/day/liter). There was a 32% reduction in SDX relative bioavailability with the double dose but no evidence of dose-dependent metabolism. Terminal elimination half-lives (15.6 days for PYR, 9.1 days for SDX) were longer than previously reported. Both doses were well tolerated without changes in hemoglobin or hepatorenal function. Five children in the conventional and three in the double-dose group developed malaria during follow-up. These data support the potential use of double-dose SDX/PYR in infancy, but further studies should examine the influence of hepatorenal maturation in very young infants.

59 **Salwati E, Minigo G, Woodberry T, Piera KA, de Silva HD, Kenangalem E, Tjitra E, Coppel RL, Price RN, Anstey NM, Plebanski M.**
Differential cellular recognition of antigens during acute *Plasmodium falciparum* and *Plasmodium vivax* malaria.
J Infect Dis 2011 Apr 15;203(8):1192-1199.

BACKGROUND: *Plasmodium falciparum* and *Plasmodium vivax* are co-endemic in the Asia-Pacific region. Their capacity to induce and sustain diverse T-cell responses underpins protective immunity. We compared T-cell responses to the largely conserved merozoite surface protein-5 (PfMSP5) during acute and convalescent falciparum and vivax malaria. METHODS: Lymphoproliferation and IFN–γ secretion to PfMSP5 and purified protein derivate were quantified in adults with falciparum (n=34) and vivax (n=12) malaria or asymptomatic residents (n=10) of Papua, Indonesia. Responses were reassessed 7-28 days following treatment. RESULTS: The frequency of IFN-γ responders to PfMSP5 was similar in acute falciparum (63%) or vivax (67%) malaria. However, significantly more IFN-γ-secreting cells were detectable during vivax compared with falciparum infection. Purified protein derivative responses showed a similarly enhanced pattern. While rapidly lost in vivax patients, PfMSP5-specific responses in falciparum malaria remained to day 28. By contrast, frequency and magnitude of lymphoproliferation to PfMSP5 were similar for falciparum and vivax infections. CONCLUSION: Cellular PfMSP5-specific responses are most frequent during either acute falciparum or vivax malaria, indicating functional T-cell responses to conserved antigens. Both effector and central memory T-cell functions are increased. Greater IFN-γ responses in acute *P. vivax* suggest enhancement of pre-existing effector T-cells during acute vivax infection.

60 **Silitonga N, Davies SC, Kaldor J, Wignall S, Okoseray M.**
Prevalence over time and risk factors for sexually transmissible infections among newly arrived female sex workers in Timika, Indonesia.
Sex Health 2011 Mar;8(1):61-64.

BACKGROUND: HIV rates are escalating in Indonesia. At Timika in Papua, the world's largest gold mine employs many single and migrant men, who frequently have sex with female sex workers (FSWs). We investigated trends of sexually transmissible infections (STIs) in FSWs in Timika. METHODS: From 1997 to 2002, FSWs at clinics were recruited for their first STI screening. Sociodemographic and sexual behaviour data were obtained and laboratory tests were performed to diagnose STIs. RESULTS: From 1997 to 2002, 3086 FSWs were recruited. Prevalence of gonorrhea varied from 11% to 19% (p = 0.71). Positive treponemal serology varied from 1.4% to 5.1% (p = 0.50). Trichomoniasis declined from 16% to 11% (p = 0.03). HIV infection increased significantly from 0.0% to 1.4% (p = 0.002). Chlamydia prevalence did not significantly change from 33% in 1997 compared with 41% in 1998 (p = 0.10). Consistent condom use was low, but increased from 8% to 16% (p = 0.001). Any STI was independently associated with younger age, high frequency of sexual activity, and not using contraceptives. CONCLUSIONS: The high rates of STIs, low condom use and increasing prevalence of HIV among these FSWs require enhanced interventions, and consideration of periodic presumptive treatment. A partnership with industry can aid and sustain an intervention program.

61 **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 Apr;15(4):551-552.

Few data are available on tuberculosis (TB) drug resistance patterns in Papua New Guinea (PNG) due to the lack of facilities for mycobacterial culture. Many patients from the Western Province seek care in Queensland health clinics in the Torres Strait. Since 2000, we have treated 161 TB cases from PNG, of whom 40 proved to have multidrug-resistant TB (MDR-TB; two human immunodeficiency virus positive). Drug susceptibility testing (DST) shows high levels of resistance to other drugs in the MDR-TB cases (streptomycin 93%, ethionamide 87%, ethambutol 18%, pyrazinamide 10%). No extensively drug-resistant TB (XDR-TB) has been identified. MDR-TB seems to be highly prevalent in the Western

Province of PNG, and unless treatment is guided by DST, the risk of XDR-TB emerging is high.

62 **Siswantoro H, Russell B, Ratcliff A, Prasetyorini B, Chalfein F, Marfurt J, Kenangalem E, Wuwung M, Piera KA, Ebsworth EP, Anstey NM, Tjitra E, Price RN.**
In vivo and in vitro efficacy of chloroquine against *Plasmodium malariae* and *P. ovale* in Papua, Indonesia.
Antimicrob Agents Chemother 2011 Jan;55(1):197-202. Epub 2010 Oct 11.

Reports of potential drug-resistant strains of *Plasmodium malariae* in western Indonesia raise concerns that chloroquine resistance may be emerging in *P. malariae* and *P. ovale*. In order to assess this, in vivo and in vitro efficacy studies were conducted in patients with monoinfection in Papua, Indonesia. Consecutive patients with uncomplicated malaria due to *P. ovale* or *P. malariae* were enrolled in a prospective clinical trial, provided with supervised chloroquine treatment, and followed for 28 days. Blood from patients with *P. malariae* or *P. ovale* parasitemia greater than 1,000 per microliter underwent in vitro antimalarial drug susceptibility testing using a modified schizont maturation assay. Of the 57 evaluable patients in the clinical study (*P. malariae*, n = 46; *P. ovale*, n = 11), none had recurrence with the same species during follow-up. The mean parasite reduction ratio at 48 h was 86 (95% confidence interval [CI], 57 to 114) for *P. malariae* and 150 (95% CI, 54 to 245) for *P. ovale* (p = 0.18). One patient infected with *P. malariae*, with 93% of parasites at the trophozoite stage, was still parasitemic on day 4. In vitro drug susceptibility assays were carried out successfully for 40 isolates (34 infected with *P. malariae* and 6 with *P. ovale*). The *P. malariae* infections at trophozoite stages had significantly higher chloroquine 50% effective concentrations (EC 50s) (median, 127.9 nM [range, 7.9 to 2,980]) than those initially exposed at the ring stage (median, 14.0 nM [range, 3.5 to 27.0]; p = 0.01). The EC 50 for chloroquine in *P. ovale* was also higher in an isolate initially at the trophozoite stage (23.2 nM) than in the three isolates predominantly at ring stage (7.8 nM). Chloroquine retains adequate efficacy against *P. ovale* and *P. malariae*, but its marked stage specificity of action may account for reports of delayed parasite clearance times.

63 **Teschke R, Sarris J, Lebot V.**
Kava hepatotoxicity solution: a six-point plan for new kava standardization.
Phytomedicine 2011 Jan 15;18(2-3):96-103. Epub 2010 Nov 26.

Kava-induced liver injury has been demonstrated in a few patients worldwide and appears to be caused by inappropriate quality of the kava raw material. When cases of liver disease in connection with the use of kava emerged, this was an unexpected and challenging event considering the long tradition of safe kava use. In order to prevent kava hepatotoxicity in future, a set of quality specifications as standard is essential for the preparation not only of kava drugs and kava dietary supplements in the Western world but also for traditional kava drinks in the South Pacific Islands. For all these purposes a uniform approach is required, using water-based extracts from the peeled rhizomes and roots of a noble cultivar such as Borogu with at least 5 years of age at the time of harvest. Cultivated in Vanuatu for centuries, noble varieties (as defined in the Vanuatu Kava Act of December 2002) are well tolerated traditional cultivars with a good safety record. At present, Vanuatu kava legislation is inadequately enforced to meet quality issues for kava, and further efforts are required in Vanuatu, in addition to similar legislation in other kava-producing South Pacific Islands. Future regulatory and commercial strategies should focus not only on the standardization of kava drugs, kava dietary supplements, and traditional kava extracts, but also on thorough surveillance during the manufacturing process to improve kava quality for safe human use. The efficacy of kava extracts to treat patients with anxiety disorders is well supported, but further clinical trials with aqueous kava extracts are necessary. We thereby propose a six-point kava solution plan: (1) use of a noble kava cultivar such as Borogu, at least 5 years old at time of harvest, (2) use of peeled and dried rhizomes and roots, (3) aqueous extraction, (4) dosage recommendation of ≤250 mg kavalactones per day (for medicinal use), (5) systematic rigorous future research, and (6) a Pan-Pacific quality control system enforced by strict policing. In conclusion, at different levels of responsibility, new mandatory approaches are now required to implement quality specification for international acceptance of kava as a safe and effective anxiolytic herb.

64 **Thedja MD, Muljono DH, Nurainy N, Sukowati CH, Verhoef J, Marzuki S.**
Ethnogeographical structure of hepatitis B virus genotype distribution in Indonesia and discovery of a new subgenotype, B9.
Arch Virol 2011 May;156(5):855-868. Epub 2011 Feb 12.

The distribution of hepatitis B virus (HBV) in the populations of island Southeast Asia is of medical and anthropological interest and is associated with an unusually high genetic diversity. This study examined the association of this HBV genetic diversity with the ethnogeography of the populations of the Indonesian archipelago. Whole genome analysis of 21 HBV isolates from East Nusa Tenggara and Papua revealed two recently reported HBV/B subgenotypes unique to the former, B7 (7 isolates) and B8 (5 isolates), and uncovered a further novel subgenotype designated B9 (4 isolates). Further isolates were collected from 419 individuals with defined ethnic backgrounds representing 40 populations. HBV/B was predominant in Austronesian-language-speaking populations, whereas HBV/C was the major genotype in Papua and Papua-influenced populations of Moluccas; HBV/B3 was the predominant subgenotype in the western half of the archipelago (speakers of the Western Malayo-Polynesian [WMP] branch of Austronesian languages), whereas B7, B8 and B9 were specific to Nusa Tenggara (Central Malayo-Polynesian (CMP)). The result provides the first direct evidence that the distribution of HBV genotypes/subgenotypes in the Indonesian archipelago is related to the ethnic origin of its populations and suggests that the HBV distribution is associated with the ancient migratory events in the peopling of the archipelago.

65 **Thomas JJ, Crosby RD, Wonderlich SA, Striegel-Moore RH, Becker AE.**
A latent profile analysis of the typology of bulimic symptoms in an indigenous Pacific population: evidence of cross-cultural variation in phenomenology.
Psychol Med 2011 Jan;41(1):195-206. Epub 2010 Mar 29.

BACKGROUND: Previous efforts to derive empirically based eating disorder (ED) typologies through latent structure modeling have been limited by the ethnic and cultural homogeneity of their study populations and their reliance on DSM-IV ED signs and symptoms as indicator variables. METHOD: Ethnic Fijian schoolgirls (n=523) responded to a self-report battery assessing ED symptoms, herbal purgative use, co-morbid psychopathology, clinical impairment, cultural orientation, and peer influences. Participants who endorsed self-induced vomiting or herbal purgative use in the past 28 days (n=222) were included in a latent profile analysis (LPA) to identify unique subgroups of bulimic symptomatology. RESULTS: LPA identified a bulimia nervosa (BN)-like class (n=86) characterized by high rates of binge eating and self-induced vomiting, and a herbal purgative class (n=136) characterized primarily by the use of indigenous Fijian herbal purgatives. Both ED classes endorsed greater eating pathology and general psychopathology than non-purging participants, and the herbal purgative class endorsed greater clinical impairment than either the BN-like or non-purging participants. Cultural orientation did not differ between the two ED classes. CONCLUSIONS: Including study populations typically under-represented in mental health research and broadening the scope of relevant signs and symptoms in latent structure models may increase the generalizability of ED nosological schemes to encompass greater cultural diversity.

66 **Trejaut J, Lee CL, Yen JC, Loo JH, Lin M.**
Ancient migration routes of Austronesian-speaking populations in oceanic Southeast Asia and Melanesia might mimic the spread of nasopharyngeal carcinoma.
Chin J Cancer 2011 Feb;30(2):96-105.

Mitochondrial DNA (mtDNA) and non-recombining Y chromosome (NRY) are inherited uni-parentally from mother to daughter or from father to son respectively. Their polymorphism has initially been studied throughout populations of the world to demonstrate the 'Out of Africa' hypothesis. Here, to correlate the distribution of nasopharyngeal carcinoma (NPC) in different populations of insular Asia, we analyze the mtDNA information (lineages) obtained from genotyping of the hypervariable region (HVS I & II) among 1400 individuals from island Southeast Asia (ISEA), Taiwan and Fujian and supplemented with the analysis of relevant coding region polymorphisms. Lineages that best represented a clade (a branch of the genetic tree) in the phylogeny were further analyzed using complete genomic mtDNA sequencing. Finally, these complete mtDNA sequences were used to construct a most parsimonious tree which now constitutes the most up-to-date mtDNA dataset available on ISEA and Taiwan. This analysis has exposed new insights of the evolutionary history of insular Asia and has strong implications in assessing possible correlations with linguistic, archaeology, demography and the NPC distribution in populations within these regions. To obtain a more objective and balanced genetic point of view, slowly evolving biallelic Y single nucleotide polymorphism (Y-SNP) was also analyzed. As in the first step above, the technique was first applied to determine affinities (macroanalysis) between populations of insular Asia. Secondly, sixteen Y short tandem repeats (Y-STR) were used as they allow deeper insight (microanalysis) into the relationship between individuals of a same region. Together, mtDNA and NRY allowed a better definition of the relational, demographic, cultural and genetic components that constitute the make-up of the present day peoples of ISEA. Outstanding findings were obtained on the routes of migration that occurred along with the spread of NPC during the settlement of insular Asia. The results of this analysis will be discussed using a conceptual approach.

67 **Umbers AJ, Boeuf P, Clapham C, Stanisic DI, Baiwog F, Mueller I, Siba P, King CL, Beeson JG, Glazier J, Rogerson SJ.**
Placental malaria-associated inflammation disturbs the insulin-like growth factor axis of fetal growth regulation.
J Infect Dis 2011 Feb 15;203(4):561-569. Epub 2011 Jan 7.

BACKGROUND: The pathogenetic mechanisms of fetal growth restriction associated with placental malaria are largely unknown. We sought to determine whether placental malaria and related inflammation were associated with disturbances in the insulin-like growth factor (IGF) axis, a major regulator of fetal growth. METHOD: We measured IGF-1 and IGF-2 concentrations in plasma from 88 mother-neonate pairs at delivery and IGF-binding proteins 1 and 3 (IGFBP-1 and IGFBP-3, respectively) in cord plasma from a cohort of Papua New Guinean women with and without placental malaria. Messenger RNA levels of IGF-1, IGF-2 and the IGF receptors were measured in matched placental biopsy specimens. RESULTS: Compared with those for uninfected pregnancies, IGF-1 levels were reduced by 28% in plasma samples from women with placental *Plasmodium falciparum* infection and associated inflammation ($p = 0.007$) and by 25% in their neonates ($p = 0.002$). Levels of fetal IGFBP-1 were elevated in placental malaria with and without inflammation ($p = 0.08$ and $p = 0.006$, respectively) compared with uninfected controls. IGF-2 and IGFBP-3 plasma concentrations and placental IGF ligand and receptor messenger RNA transcript levels were similar across groups. CONCLUSION: Placental malaria-associated inflammation disturbs maternal and fetal levels of IGFs, which regulate fetal growth. This may be one mechanism by which placental malaria leads to fetal growth restriction.

68 **Utsumi T, Yano Y, Truong BX, Kawabata M, Hayashi Y.**
Characteristics of occult hepatitis B virus infection in the Solomon Islands.
Int J Mol Med 2011 Jun;27(6):829-834. doi: 10.3892/ijmm.2011.660. Epub 2011 Mar 31.

Hepatitis B virus (HBV) infection is highly endemic in the Solomon Islands. However, little is known about the status of occult HBV infection in the Solomon Islands. This study aimed to investigate the prevalence of occult HBV infection and its clinical and virological features in the community of Solomon Islands. Blood samples were collected from a total of 564 asymptomatic individuals aged over 18 years in the Western Province. The samples used in the present study consisted of 200 samples from 108 males and 92 females (mean age, 37.4 years; range, 18-71 years) that were randomly selected among the hepatitis B surface antigen (HBsAg)-negative samples from all the participants enrolled in this study. HBV-DNA was detected by real-time PCR in 25 (12.5%) of the 200 HBsAg-negative samples. Most of the HBV-DNA-positive individuals were infected with wild-type HBV, and only 3 strains demonstrated specific

amino acid substitutions (P121X, T123N, C138S, P142S and D144E) in the α determinant region. In conclusion, occult HBV infection was documented in 12.5% of individuals that demonstrated serologic evidence of resolved HBV infection in this study. The prevalence of occult infection was also influenced by ethnicity; it was more prevalent in Melanesians than Micronesians. In addition, occult HBV infection demonstrated a weak association with the S-variants.

69 **Vargas M, Segura A, Herrera M, Villalta M, Estrada R, Cerdas M, Paiva O, Matainaho T, Jensen SD, Winkel KD, León G, Gutiérrez JM, Williams DJ.**
Preclinical evaluation of caprylic acid-fractionated IgG antivenom for the treatment of taipan (*Oxyuranus scutellatus*) envenoming in Papua New Guinea.
PLoS Negl Trop Dis 2011 May;5(5):e1144. Epub 2011 May 17.

BACKGROUND: Snake bite is a common medical emergency in Papua New Guinea (PNG). The taipan, *Oxyuranus scutellatus*, inflicts a large number of bites that, in the absence of antivenom therapy, result in high mortality. Parenteral administration of antivenoms manufactured in Australia is the current treatment of choice for these envenomings. However, the price of these products is high and has increased over the last 25 years; consequently the country can no longer afford all the antivenom it needs. This situation prompted an international collaborative project aimed at generating a new, low-cost antivenom against *O. scutellatus* for PNG. METHODOLOGY/PRINCIPAL FINDINGS: A new monospecific equine whole IgG antivenom, obtained by caprylic acid fractionation of plasma, was prepared by immunizing horses with the venom of *O. scutellatus* from PNG. This antivenom was compared with the currently used F(ab')(2) monospecific taipan antivenom manufactured by CSL Limited, Australia. The comparison included physicochemical properties and the preclinical assessment of the neutralisation of lethal neurotoxicity and the myotoxic, coagulant and phospholipase A(2) activities of the venom of *O. scutellatus* from PNG. The F(ab')(2) antivenom had a higher protein concentration than whole IgG antivenom. Both antivenoms effectively neutralised, and had similar potency, against the lethal neurotoxic effect (both by intraperitoneal and intravenous routes of injection), myotoxicity and phospholipase A(2) activity of *O. scutellatus* venom. However, the whole IgG antivenom showed a higher potency than the F(ab')(2) antivenom in the neutralisation of the coagulant activity of *O. scutellatus* venom from PNG. CONCLUSIONS/SIGNIFICANCE: The new whole IgG taipan antivenom described in this study compares favourably with the currently used F(ab') (2) antivenom, both in terms of physicochemical characteristics and neutralising potency. Therefore, it should be considered as a promising low-cost candidate for the treatment of envenomings by *O. scutellatus* in PNG, and is ready to be tested in clinical trials.

70 **Viney K, O'Connor J, Wiegandt A.**
The epidemiology of tuberculosis in Pacific Island countries and territories: 2000-2007.
Asia Pac J Public Health 2011 Jan;23(1):86-99.

This is a descriptive study of routinely collected tuberculosis (TB) surveillance data from 19 Pacific Island countries and territories. The objectives of the study are to describe (a) the epidemiology of TB during the period 2000-2007 (with a focus on 2007), (b) progress against World Health Organization (WHO) targets, and (c) how TB control can be enhanced in the region. In 2007, there were 1544 cases of TB notified in the Pacific (excluding Papua New Guinea). The case notification rate was 52 per 100 000 population. The case detection rate for sputum smear positive cases in 2007 was 66%, slightly below the WHO target of 70%. The treatment success rate for new sputum smear positive cases in 2006 was 89%, above the WHO target of 85%. It is likely that the regional prevalence and mortality targets will be narrowly missed in 2010. There has been good progress in TB control in the Pacific region, but intensified efforts are needed to further reduce the burden of TB.

71 **Wang Y, Jackson KJ, Gäeta B, Pomat W, Siba P, Sewell WA, Collins AM.**
Genomic screening by 454 pyrosequencing identifies a new human IGHV gene and sixteen other new IGHV allelic variants.
Immunogenetics 2011 May;63(5):259-265. Epub 2011 Jan 20.

Complete and accurate knowledge of the genes and allelic variants of the human immunoglobulin gene loci is critical for studies of B cell repertoire development and somatic point mutation, but evidence from studies of VDJ rearrangements suggests that our knowledge of the available immunoglobulin gene repertoire is far from complete. The reported repertoire has changed little over the last 15 years. This is, in part, a consequence of the inefficiencies involved in searching for new members of large, multigenic gene families by cloning and sequencing. The advent of high-throughput sequencing provides a new avenue by which the germline repertoire can be explored. In this report, we describe pyrosequencing studies of the heavy chain IGHV1, IGHV3 and IGHV4 gene subgroups in 10 Papua New Guineans. Thousands of 454 reads aligned with complete identity to 51 previously reported functional IGHV genes and allelic variants. A new gene, IGHV3-NL1*01, was identified, which differs from the nearest previously reported gene by 15 nucleotides. 16 new IGHV alleles were also identified, 15 of which varied from previously reported functional IGHV genes by between one and four nucleotides, while 1 sequence appears to be a functional variant of the pseudogene IGHV3-25. BLAST searches suggest that at least six of these new genes are carried within the relatively well-studied populations of North America, Europe or Asia. This study substantially expands the known immunoglobulin gene repertoire and demonstrates that genetic variation of immunoglobulin genes can now be efficiently explored in different human populations using high-throughput pyrosequencing.

72 **Wang Y, Jackson KJ, Chen Z, Gaëta BA, Siba PM, Pomat W, Walpole E, Rimmer J, Sewell WA, Collins AM.**
IgE sequences in individuals living in an area of endemic parasitism show little mutational evidence of antigen selection.
Scand J Immunol 2011 May;73(5):496-504. doi: 10.1111/j.1365-3083.2011.02525.x.

Patterns of somatic mutation in IgE genes from allergic individuals have been a focus of study for many years, but IgE sequences have never been reported from parasitized individuals. To study the role of antigen selection in the evolution of the anti-parasite response, we therefore generated 118

IgE sequences from donors living in Papua New Guinea (PNG), an area of endemic parasitism. For comparison, we also generated IgG1, IgG2, IgG3 and IgG4 sequences from these donors, as well as IgG1 sequences from Australian donors. IgE sequences had, on average, 23.0 mutations. PNG IgG sequences had average mutation levels that varied from 17.7 (IgG3) to 27.1 (IgG4). Mean mutation levels correlated significantly with the position of their genes in the constant region gene locus (IgG3 < IgG1 < IgG2 < IgG4). Interestingly, given the heavy, life-long antigen burden experienced by PNG villagers, average mutation levels in IgG sequences were little different to that seen in Australian IgG1 sequences (19.2). Patterns of mutation provide clear evidence of antigen selection in many IgG sequences. The percentage of IgG sequences that showed significant accumulations of replacement mutations in the complementarity-determining regions ranged from 22% of IgG3 sequences to 39% of IgG2 sequences. By contrast, only 12% of IgE sequences had such evidence of antigen selection, and this was significantly less than in PNG IgG1, IgG2 and IgG4 subclass sequences ($p<0.01$). The anti-parasite IgE response therefore has the reduced evidence of antigen selection that has previously been reported in studies of IgE sequences from allergic individuals.

73 **Watts KR, Morinaka BI, Amagata T, Robinson SJ, Tenney K, Bray WM, Gassner NC, Lokey RS, Media J, Valeriote FA, Crews P.**
Biostructural features of additional jasplakinolide (jaspamide) analogues.
J Nat Prod 2011 Mar 25;74(3):341-351. Epub 2011 Jan 11.

The cyclodepsipeptide jasplakinolide (1) (aka jaspamide), isolated previously from the marine sponge *Jaspis splendens*, is a unique cytotoxin and molecular probe that operates through stabilization of filamentous actin (F-actin). We have recently disclosed that two analogues of 1, jasplakinolides B (3) and E, were referred to the National Cancer Institute's (NCI) Biological Evaluation Committee, and the objective of this study was to reinvestigate a Fijian collection of *J. splendens* in an effort to find jasplakinolide congeners with similar biological properties. The current efforts have afforded six known jasplakinolide analogues (4-7, 9, 10), two structures requiring revision (8 and 14), and four new congeners of 1 (11-13, 15) including open-chain derivatives and structures with modified β-tyrosine residues. Compounds were evaluated for biological activity in the NCI's 60 cell line screen and in a microfilament disruption assay in both HCT-116 and HeLa cells. These two phenotypic screens provide evidence that each cytotoxic analogue, including jasplakinolide B (3), operates by modification of microfilaments. The new structure jasplakinolide V (13) has also been selected for study by the NCI's Biological Evaluation Committee. In addition, the results of a clonogenic dose-response study on jasplakinolide are presented.

74 **WHO Western Pacific and South East Asian Gonococcal Antimicrobial Surveillance Programmes. Collaborators: Tapsall JW, Limnios EA, Lahra MM, Dorji D, Abu Bakar HM, Guillard B, Sopheak H, Yue Ping Y, Buadromo EM, Kumar P, Singh S, Lo J, Bala M, Deguchi T, Tanaka M, Watanabe Y, Lee K, Chong Y, Noikaseumsy S, Phouthavane T, Sam IC, Tundev O, Lwin KM, Eh PH, Goarant C, Goursaud R, Bathgate T, Brokenshire M, Toliman P, Yoannes M, Latorre L, Velemu E, Carlos C, Lagrada M, Leano S, Telan EO, Goh SS, Koh ST, Ngan C, Tan AL, Mananwatte S, Piyanoot N, Lokpichat S, Sirivongranson P, Fakahau M, Sitanilei H, Hung le V.**
Surveillance of antibiotic resistance in *Neisseria gonorrhoeae* in the WHO Western Pacific and South East Asian Regions, 2009.
Commun Dis Intell 2011 Mar;35(1):2-7.

Long-term surveillance of antimicrobial resistance in *Neisseria gonorrhoeae* has been conducted in the World Health Organization (WHO) Western Pacific Region (WPR) to optimise antibiotic treatment of gonococcal disease since 1992. From 2007, the Gonococcal Antimicrobial Surveillance Programme (GASP) has been enhanced by the inclusion of data from the South East Asian Region (SEAR) and recruitment of additional centres in the WPR. Approximately 8,704 isolates of *N. gonorrhoeae* were examined for their susceptibility to one or more antibiotics used for the treatment of gonorrhoea, incorporating External Quality Assurance controlled methods, from reporting centres in 21 countries and/or jurisdictions. A high proportion of penicillin and/or quinolone resistance was again detected amongst isolates tested in North Asia and the WHO SEAR. In contrast, from the Pacific Island states Fiji reported low penicillin and quinolone resistance, New Caledonia again reported no penicillin resistance and little quinolone resistance, Tonga reported no penicillin resistance and there was a continued absence of quinolone resistance reported in Papua New Guinea in 2009. The proportion of gonococci reported as 'decreased susceptibility' and 'resistant' to the third-generation cephalosporin antibiotic ceftriaxone varied widely but no major changes were evident in cephalosporin minimum inhibitory concentrations (MIC) patterns in 2009. Altered cephalosporin susceptibility has been associated with treatment failures following therapy with oral third-generation cephalosporins. There is a need for revision and clarification of some of the in vitro criteria that are currently used to categorise the clinical importance of gonococci with different ceftriaxone and oral cephalosporin MIC levels. The number of instances of spectinomycin resistance remained low. A high proportion of strains tested continued to exhibit high-level plasmid-mediated resistance to tetracyclines. The continuing emergence and spread of antibiotic-resistant gonococci in and from the WHO WPR and SEAR suggests that surveillance programs such as GASP be maintained and expanded.

75 **Wijesinghe RS, Atkinson JA, Bobogare A, Wini L, Whittaker M**.
Exploring provider and community responses to the new malaria diagnostic and treatment regime in Solomon Islands.
Malar J 2011 Jan 10;10:3.

BACKGROUND: Improvements in availability and accessibility of artemisinin-based combination therapy (ACT) for malaria treatment and the emergence of multi-drug-resistant parasites have prompted many countries to adopt ACT as the first-line drug. In 2009, Solomon Islands (SI) likewise implemented new national treatment guidelines for malaria. The ACT, Coartem® (artemether-lumefantrine) is now the primary pharmacotherapy in SI for *Plasmodium falciparum* malaria, *Plasmodium vivax* malaria or mixed infections. Targeted treatment

is also recommended in the new treatment regime through maintenance of quality microscopy services and the introduction of Rapid Diagnostic Tests (RDTs). Ascertaining the factors that influence community and provider acceptance of and adherence to the new treatment regime will be vital to improving the effectiveness of this intervention and reducing the risk of development of drug resistance. METHODS: In order to understand community and prescriber perceptions and acceptability of the new diagnostic and treatment interventions, 12 focus group discussions (FGDs) and 12 key informant interviews (KII) were carried out in rural and urban villages of Malaita Province, Solomon Islands four months subsequent to roll-out of these interventions. RESULTS: Lack of access to microscopy or distrust in the accuracy of diagnostic tools were reported by some participants as reasons for the ongoing practice of presumptive treatment of malaria. Lack of confidence in RDT accuracy has negatively impacted its acceptability. Coartem® had good acceptability among most participants; however, some rural participants questioned its effectiveness due to lack of side-effects and the larger quantity of tablets required to be taken. Storing of left-over medication for subsequent fever episodes was reported as common. CONCLUSION: To address these issues, further training and supportive supervision of healthcare workers will be essential, as will the engagement of influential community members in health promotion activities to improve acceptability of RDTs and adherence to the new treatment regime. Exploring the extent of these issues beyond the study population must be a priority for malaria programme managers. Practices such as presumptive treatment and the taking of sub-curative doses are of considerable concern for both the health of individuals and the increased risk it poses to the development of parasite resistance to this important first-line treatment against malaria.

76 **Wong RP, Karunajeewa H, Mueller I, Siba P, Zimmerman PA, Davis TM.**
Molecular assessment of *Plasmodium falciparum* resistance to antimalarial drugs in Papua New Guinea using an extended ligase detection reaction fluorescent microsphere assay.
Antimicrob Agents Chemother 2011 Feb;55(2):798-805. Epub 2010 Nov 15.

Surveillance for *Plasmodium falciparum* drug resistance mutations is becoming an established tool for assessing antimalarial treatment effectiveness. We used an extended version of a high-throughput post-PCR multiplexed ligase detection reaction fluorescent microsphere assay (LDR-FMA) to detect single-nucleotide *P. falciparum* drug resistance polymorphisms in 402 isolates from children in Papua New Guinea (PNG) participating in an antimalarial treatment trial. There was a fixation of *P. falciparum crt (pfcrt)* K76T, *pfdhfr* C59R and S108N, and *pfmdr1* mutations (92%, 93%, 95% and 91%, respectively). Multiple mutations were frequent. 88% of isolates possessed a quintuple mutation, SVMNT, NRNI, KAA and YYSND, in codons 72 to 76 for *pfcrt*; 51, 59, 108 and 164 for *pfdhfr*; 540, 581 and 613 for *pfdhps*; and 86, 184, 1034, 1042 and 1246 for *pfmdr1*; and four of these carried the K540E *pfdhps* allele. The *pfmdr1* D1246Y mutation was associated with PCR-corrected day 42 in vivo treatment failure in children allocated piperaquine-dihydroartemisinin ($p = 0.004$). Although the *pfmdr1* NFSDD haplotype was found in only four isolates, it has been associated with artemether-lumefantrine treatment failure in Africa. LDR-FMA allows the large-scale assessment of resistance-associated single-nucleotide polymorphisms (SNPs). Our findings reflect previous heavy 4-aminoquinoline/sulfadoxine-pyrimethamine use in PNG. Since artemether-lumefantrine and piperaquine-dihydroartemisinin will become first- and second-line treatments, respectively, the monitoring of *pfmdr1* SNPs appears to be a high priority.

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