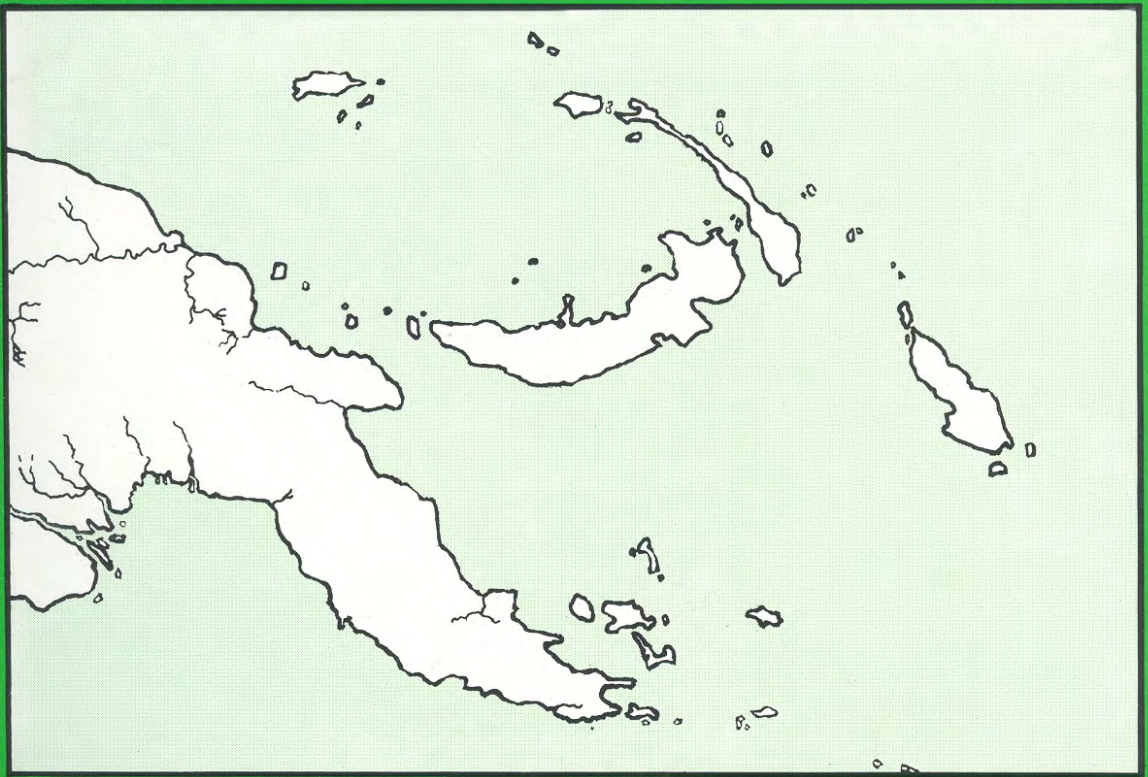


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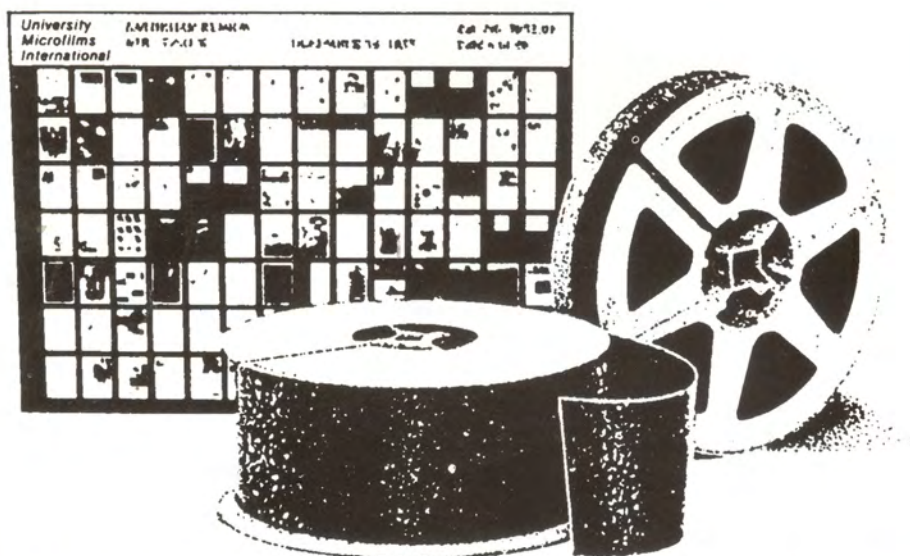
# PAPUA NEW GUINEA MEDICAL JOURNAL



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## EDITORIAL

**Treatment of uncomplicated malaria in Papua New Guinea: what should be done?**

In a recently published document, 'Guidelines for the Treatment of Malaria', the World Health Organization (WHO) (1) recommends that assessment of antimalarial treatment policy should be based on: i) efficacy assessments in which the parasitological cure rate is defined over  $\geq 28$  days of follow-up with polymerase chain reaction (PCR) genotyping to distinguish recrudescence from new infections, ii) initiation of change of the antimalarial treatment when the cure rate with current therapy falls to  $< 90\%$ , and iii) introduction of new antimalarial therapy with an average cure rate of  $\geq 95\%$  in clinical trials. In the same document, the WHO recommends artemisinin-based combination therapy (ACT) for uncomplicated falciparum malaria, specifically artemether-lumefantrine, artesunate-amodiaquine, artesunate-mefloquine or artesunate-sulfadoxine-pyrimethamine. The choice between these ACTs should be based on the local level of parasite resistance to the partner drug. If ACTs are unavailable, non-artemisinin-based combinations such as amodiaquine-sulfadoxine-pyrimethamine may be used as an interim measure provided that the component therapies retain efficacy.

These recommendations were published in the aftermath of strong criticism of the WHO that appeared in the *Lancet*, including the statement that "WHO should publish malaria treatment guidelines that countries can depend on as authoritative norms" (2). They seem simple and evidence-based, and capable of being put into place in a country such as Papua New Guinea (PNG). But is it all that easy? While the WHO should be applauded for getting to grips with this important subject, there are issues with the recommendations that could have consequences for their implementation. In this article, each of the key WHO recommendations will be assessed critically.

The three WHO recommendations relating to antimalarial treatment policy guidelines assume that valid data will be collected at regular intervals for existing therapies and that efficacy assessments will also be done

to determine the value of alternative regimens in advance of need. This assumes that funding, facilities and staff will be in place to carry out what are usually quite technically and logistically demanding studies. Aspects of study design including selection of study sites, sample sizes, and appropriate inclusion and exclusion criteria need to be considered carefully. For example, a 28-day treatment failure rate of 86% for existing treatment might be associated with an upper 95% confidence limit that is  $> 90\%$  (and thus not significantly different from a failure rate the WHO considers acceptable) if the sample size is  $< 225$  patients. In remote areas, the attrition rate is usually relatively high, which can increase the sample size required and prolong the duration of the study. In areas in which pharmaceuticals including antimalarial drugs are relatively freely available in the community, prior treatment can itself bias the results or, if pre-treated patients are rigorously excluded, impair efficient recruitment.

The recently published results of a study from Karimui (Simbu Province), South Wosera (East Sepik Province) and the North Coast (Madang Province) are illustrative (3). Despite variation between the three study areas, the overall 28-day PCR-confirmed cure rate for chloroquine plus sulfadoxine-pyrimethamine in 128 children with a mean age close to 6 years was 83% with a 95% confidence interval of 75-89%. For a larger group of 521 younger children (mean age approximately 4 years) treated with amodiaquine-sulfadoxine-pyrimethamine, there was an 81% (78-84%) cure rate. In both cases, the upper limit of the confidence interval was below 90%, consistent with WHO recommendations that alternative treatment should be introduced for both age groups.

Prospective testing of candidate replacement regimens should follow the same principles. A cure rate of 95% needs at least 160 subjects so that the lower 95% confidence limit is  $\geq 90\%$  and thus significantly better than the failure rate the WHO considers unacceptable. In addition,

the use of the word 'average' in respect of the  $\geq 95\%$  recommended cure rate in the WHO guidelines (1) implies that there should be more than one study performed (or perhaps one study with multiple sites or arms) before a decision on replacement therapy is made. This may mean 'borrowing' data from another country or region in which the parasite sensitivity and patient immunity may be quite different. In the case of PNG, the results of a large-scale comparison between chloroquine-sulfadoxine-pyrimethamine and three ACTs (artesunate-sulfadoxine-pyrimethamine, artemether-lumefantrine and dihydroartemisinin-piperaquine) will soon be available. This study, conducted by the PNG Institute of Medical Research and the University of Western Australia School of Medicine and Pharmacology, was co-sponsored by the WHO and the National Health and Medical Research Council of Australia. The data should be useful in informing treatment policy for uncomplicated malaria in PNG, especially if they are consistent with other studies in the region or in other geographical areas with a similar epidemiology and history of antimalarial drug deployment.

Expert microscopy and laboratory facilities for PCR differentiation of recrudescence from re-infection in efficacy studies are essential for successful efficacy studies, and are well established in PNG. 'Routine' PCR cannot determine whether parasite DNA in a sample is from sexual or asexual forms, and so microscopy for gametocytes becomes important. Despite this, there are still patients who become PCR positive during follow-up without symptoms or asexual/sexual parasite forms on blood smear, even after ACT (4). Are these true treatment failures or the harbinger of clinically significant resistance? Unfortunately, the presence of parasite mutations that are known to be associated with resistance such as those involving *pfprt*, *dhfr* and *dhps* may not accurately predict clinical response (4) and they require the availability of relatively sophisticated laboratory techniques. In addition, in vitro parasite culture of local strains to generate concentrations that inhibit parasite growth by pre-specified amounts (typically 50% or 90%) do not correlate well with the in vivo response either.

In these cases, and even when the recrudescence is relatively clear-cut, could factors related to drug quality, treatment

adherence and pharmacokinetic variability be implicated rather than parasite resistance? Efficacy studies should use drug formulations manufactured under good manufacturing practice (GMP) specifications and stored under optimal conditions to ensure stability during the trial, but this does not always happen. Even when treatment is directly observed and vomiting has not occurred, there are occasions, especially in children, when unmeasurable drug concentrations in subsequent blood samples suggest that the patient has managed to expel the dose without this being detected – this may be particularly so if a drug has an unpleasant taste or is administered rectally to a young child unable to tolerate oral therapy (5).

Between-subject variability in drug disposition is also a factor. In the case of artemether-lumefantrine, this is marked in part due to the need for the lipid-soluble lumefantrine component to be taken with fat (usually a biscuit or milk) so that bioavailability is enhanced. In one recent study (6), day 7 plasma lumefantrine concentrations were close to undetectable in some patients despite directly supervised treatment. Unfortunately, measurement of plasma drug concentrations is not part of WHO efficacy assessment despite being a useful way of identifying important non-parasite causes of treatment failure.

While there are a number of issues with efficacy studies of both contemporary and candidate replacement regimens that are an important part of the WHO's antimalarial treatment policy, usual care throws up its own problems. The effectiveness of unsupervised treatment is what determines treatment failure in the community outside the confines of a clinical trial. Complex regimens with frequent side-effects, such as the 7 days of quinine and tetracycline that was used in countries such as Thailand as recently as the 1990s, are associated with poor adherence. Even 3 days of artemether-lumefantrine, which is relatively well tolerated, gives significantly lower plasma lumefantrine concentrations when given in an unsupervised than in a supervised treatment setting, with the risk of increased recrudescence or reinfection (6). Apparent treatment failures may even reflect the local appearance of counterfeit or poor quality antimalarial drugs (7).

Ideally, efficacy studies in the WHO mould



can be done reliably and efficiently, and on a regular basis, so that trends in treatment failure rate can be detected early, and replacement regimens assessed and implemented in a timely fashion. However, there may also be the opportunity to use routine surveillance mechanisms to identify evidence of developing parasite resistance. In countries with even simple malaria notification schemes, epidemiological markers such as the percentage of patients presenting again with malaria requiring treatment within 28 days could provide a signal that parasite resistance is on the increase.

Given that the WHO recommendation is for ACT to be first-line therapy for uncomplicated malaria, which one should be used? The WHO considers artemether-lumefantrine to be the only ACT that can be used both in areas of multidrug resistance (South-East Asia) and in Africa (1). It is also an ACT that is co-formulated (thus simplifying administration compared to separate drug dosing) and satisfies the WHO requirement that the artemisinin derivative component must be given for at least three days for optimum effect (1). However, it is relatively expensive unless heavily subsidized or donated, has to be given in 6 doses, preferably with fat-containing food, and the lumefantrine component has a shorter half-life than other partner drugs such as mefloquine and piperazine (8). This latter characteristic means that there is a greater risk of re-infection in the aftermath of treatment (9).

Other co-formulated ACTs such as dihydroartemisinin-piperazine and artemisinin-naphthoquine are not yet on the WHO-recommended list, perhaps because they may not be GMP-manufactured, are given over less than 3 days and still require evidence of efficacy, but they may prove to be as effective as artemether-lumefantrine. Although there is a view that using an artemisinin drug with a partner drug with failing efficacy is not to be recommended (10), artesunate-amodiaquine and artesunate-sulfadoxine-pyrimethamine remain on the WHO list and they have the advantage that artesunate, primarily because of its water solubility, is the artemisinin derivative with the most favourable pharmacological profile (11). In addition, despite the WHO stance on ACT, non-artemisinin-based combination therapies

may still have a role where they are shown to be at least as effective as ACT in well-designed studies (12).

What do the WHO guidelines mean for PNG? There should soon be evidence from properly designed and conducted efficacy studies that ACT should replace chloroquine-sulfadoxine-pyrimethamine and, perhaps, an indication of which of the three candidate ACTs should be used. The epidemiological context of these studies (3,13) differs greatly from those of previous studies in South-East Asia and even Indonesian Papua (9), and resembles the hyperendemic transmission seen in Africa, where relatively few adequately powered trials of ACT have been conducted to date. Ideally the choice between ACTs will be made on the basis of cost-effectiveness and considerations such as adherence in a real-world vs clinical trial setting. For oral therapy, non-GMP-standard treatment might be considered (as it is in a number of other tropical countries) provided that tablet content is within acceptable bounds, especially as the supply of GMP-manufactured artemether-lumefantrine has been problematic in the recent past (14). However, when treatment is supplied by the Global Fund or other sponsor, GMP-manufactured product is usually mandatory.

Above all, there needs to be a plan for regular efficacy assessments so that, as implied by the WHO recommendations (1), failing conventional therapy can be identified early and an assessment of candidate replacement regimen(s) can be implemented. This will need government sponsorship and support, involvement of key local agencies such as the PNG Institute of Medical Research and their international partners, and assistance from external agencies such as WHO. The alternative is to risk the consequences of increasing antimalarial treatment failures, which has been interpreted by some authorities as equivalent to 'medical malpractice' (2).

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## Knowledge and attitudes about infant feeding among nulliparous and parous women in Port Moresby: a comparative study

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### SUMMARY

Knowledge of the advantages of breastfeeding, the disadvantages of bottle feeding and the Papua New Guinean legislation to protect breastfeeding was determined in a comparative study of nulliparous and parous women attending the Antenatal Clinic of Port Moresby General Hospital. A high proportion (40%) of both groups had had experience of bottle feeding. Whilst the large majority (94%) of the women indicated that breastfeeding was the best way to feed babies, knowledge of the reasons for its superiority over bottle feeding and of the dangers of bottle feeding was poor in both groups. Knowledge of the legislation to protect breastfeeding was also poor and was the only area in which there was a significant difference between the groups, nulliparous women having poorer knowledge ( $p = 0.015$ ). The level of education did not appear to be associated with knowledge about feeding. There is an urgent need to review the legislation, to find ways of enforcing it, and to improve the education of young people on issues of infant feeding.

### Introduction

Exclusive breastfeeding for the first 6 months of life is recommended as the best feeding option for the vast majority of the world's children, and exclusive breastfeeding for the first 4-6 months of life is the foundation of the Papua New Guinea (PNG) Infant Feeding Policy (1,2). The association of bottle feeding with high infant mortality and morbidity from infection and malnutrition in resource-poor countries has been well documented (3,4). Papua New Guinea was the first country to legislate to protect breastfeeding, with the Baby Foods (Control) Act in 1977 (5) (subsequently amended to include control of sales of baby feeding cups in 1984 (6)), some 4 years before the International Code of Marketing of Breast-milk Substitutes was introduced in 1981 (7). The introduction of the legislation appeared to have an immediate impact on the

prevalence of bottle feeding in Port Moresby with rates falling from 33% in 1976 (with 2 out of 3 artificially fed infants being malnourished) to 11% three years later (8,9). Unfortunately the impact was short-lived, and bottle feeding has flourished in the city and in other parts of Papua New Guinea (10). A large infant feeding survey in 1995 showed that 20% of 1822 mothers in different parts of the country had used bottle feeding (11). It has become clear that although there is a law to protect breastfeeding and control bottle feeding, it is not being implemented (12), and several attempts by the Paediatric Society of Papua New Guinea to amend the law to make its implementation more practical and effective have been unsuccessful.

Having a law to control the sale of bottles is, however, only one aspect of the matter. It would seem reasonable to assume that mothers wish the best for their babies and

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children. Of equal – if not greater – importance to legislation, therefore, is mothers' knowledge about best infant feeding practices and the dangers associated with bottle feeding. Relatively little is known about this, and the present study was designed to determine the extent of knowledge on this issue among pregnant women.

The aims of the study were:

1. To assess and compare knowledge of the benefits of breastfeeding and the disadvantages of bottle feeding in and between nulliparous (those who have not borne any children but who may have been pregnant previously) and parous (those who have borne at least one child) pregnant women.
2. To assess and compare knowledge about the legislation relating to the control of bottle feeding in and between nulliparous and parous women.

### Methods

The comparative study was carried out between May and August 2004 at the Antenatal Clinic of the Port Moresby General Hospital (PMGH), which enrolls around 4000 of the 10,000 women who deliver in the hospital each year (13). Patients were selected for the study at their first antenatal visit, and before any health education instruction by the antenatal staff. For every nulliparous woman two parous but otherwise unmatched women who had previously delivered a live baby were invited to participate. No woman declined to be interviewed, and all women gave informed consent. There were no specific inclusion

criteria. Women who were currently or previously employed, trained or training as health workers, those who had previously attended another antenatal clinic during the current pregnancy and those unable to communicate in Tok Pisin or English and who had no interpreter were excluded.

All women were interviewed by the first author in a quiet and confidential setting. Interviews usually lasted about 10 minutes and an interpreter was used for only two women. Data were collected on a pretested questionnaire and entered and analyzed using SPSS v10 software.

### Results

#### Study participants

50 nulliparous women with a median age of 22 years and 100 parous women with a median age of 26 years were interviewed (Table 1). 3 of the nulliparous women were unmarried. There were no statistical differences between the groups in education or employment status. A higher, but not significantly different, proportion of the parous women had received some formal education on infant feeding. Of these, 81% of the total study group indicated that they had received formal education on infant feeding from school.

#### Past and proposed feeding practices

70 of the parous women had exclusively breastfed their previous children, 2 had totally bottle fed, and 26 had used both breast and bottle feeding. Cup and spoon feeding and adoption accounted for the remaining 2. Of the women who had ever breastfed, 14% had

**TABLE 1**

CHARACTERISTICS OF NULLIPAROUS AND PAROUS WOMEN

	<b>Nulliparous (N = 50)</b>	<b>Parous (N = 100)</b>
Age (years): median (interquartile range)	22 (20-24)	26 (23-31)
No education	4	10
Grade 1-5 education only	7	15
Unemployed	35	77
Formal education on infant feeding	15	39



experienced difficulties, mainly due to insufficient milk.

Details of previous feeding practices and proposed feeding for the current pregnancy are shown in Table 2. There were no differences between the proportions of nulliparous and parous women having previously bottle fed. For the nulliparous women, their experience had in nearly all cases been gained by babysitting. Mothers returning to work was the main reason for bottle feeding. When asked specifically if there were medical reasons for bottle feeding, none of the mothers gave a positive response.

There were no differences in the feeding plans for the current pregnancy, although

some mothers had not given a great deal of thought to the matter. The mean age at which parous women reported weaning their children was 3.6 months. Parous women planned to wean the current child earlier than the nulliparous women.

### Advantages of breastfeeding

94% of the total study population responded that breastmilk was the best way to feed the baby, whilst 3% responded that bottle feeding was best and 3% responded that both bottle and breast, or other methods, were best.

The knowledge about the main advantages of breastfeeding for the child, mother and family is shown in Table 3.

**TABLE 2**

PREVIOUS AND PROPOSED FEEDING PRACTICES

	<b>Nulliparous (N = 50)</b>	<b>Parous (N = 100)</b>
<b>Previously used bottle</b>		
Own child	0	32
Babysitting	20	6
Other	2	2
<b>Total</b>	<b>22</b>	<b>40</b>
<b>Reasons for bottle feeding</b>		
Working mother	13	20
Mother pregnant	1	5
Breastfeeding problems	1	6
Others	7	9
<b>Plans for present pregnancy</b>		
Exclusive breastfeeding	36	85
Mainly breastfeeding	10	9
Total bottle feeding	2	2
Mainly bottle feeding	1	2
Adopt	1	2

Although there were no significant differences between the nulliparous and parous women's knowledge in each of the three categories, the proportions of 'Don't know' responses was consistently higher in the nulliparous group. 75% of the total study population responded that they would be unlikely to become pregnant again whilst breastfeeding, whilst 23% either did not know about the contraceptive effect of breastfeeding, or thought they were more likely to become pregnant again if they had sex whilst they were still breastfeeding.

### Problems associated with bottle feeding

A similar proportion of both groups (32 nulliparous and 71 parous) were aware of problems associated with bottle feeding. 42 (70%) of 60 women who had previously bottle fed had been advised of the advantages of breastfeeding and of how to care for the bottle and properly mix the milk. 30 (36%) of the 84 parous women who indicated that bottle feeding was not good for the baby had bottle fed.

**TABLE 3**

KNOWLEDGE OF THE ADVANTAGES OF BREASTFEEDING

	<b>Nulliparous (N = 50)</b>	<b>Parous (N = 100)</b>
<b>For child</b>		
Best nutrition	15	32
Healthier/grows better	16	46
Don't know	14	13
Others	5	9
<b>For mother</b>		
Less postpartum problems	0	8
Eats better	14	22
More time available	1	14
Don't know	32	47
Others	3	9
<b>For family</b>		
Saves money/resources	9	26
Healthier family	5	4
Supportive family	2	9
Don't know	33	56
Others	1	5

## Knowledge of legislation

Significantly fewer of the nulliparous than the parous women (4 vs 25, Fisher's exact test,  $p = 0.015$ ) were aware of the legislation about bottle feeding, and only 19% overall, although 69% of the total study population knew that it was not possible to get a feeding bottle from the pharmacy without a prescription.

## Relationship between education status and knowledge of best feeding practices

Within the total study sample of 149 women for whom information was available, 1 of 13 with no formal education, 5 of 54 with education up to grade 6 (primary school) and 2 of 82 with education up to grade 12 indicated bottle feeding, both bottle and breast feeding, or other forms of feeding as being best for the baby ( $\chi^2$  test,  $p = 0.2$ )

## Discussion

The study has highlighted some worrying facts. In this opportunity-based but otherwise unselected sample, the experience of bottle feeding was widespread – 40% of parous women and a similar proportion of nulliparous women had previously bottle fed either their own or another person's children. This indicates that, in spite of the efforts to protect and encourage breastfeeding and limit bottle feeding, the latter practice is well established in the community and accepted as an alternative to breastfeeding and that bottles are easily accessible. Factors influencing the widespread community acceptance of bottle feeding may include the increasing numbers of working mothers, the acceptance of the working mother as an important income earner for the family, and increased awareness of bottle feeding as a feeding option from exposure to magazines, television and other media sources. Bottles are readily and legally accessible from registered pharmacies on prescription, and prescriptions are easily obtained from medical personnel in the public and especially the private sector. Bottles can also be obtained without prescription. In the PNG Infant Feeding Survey of 1995 just over half of the bottle-feeding mothers had obtained the bottle from a pharmacy or store without prescription and others had been given the bottle by a relative or friend (12).

In this study relatively fewer women educated beyond primary school than those with no or primary education responded that feeding other than breastfeeding was best for babies – but the numbers were small and the differences were not considered significant. Whilst the large majority of the women responded that breastfeeding was the best way to feed the child, 40% of the parous women had previously bottle fed. This might suggest that knowledge of the reasons for the superiority of breast over bottle feeding was poor. Knowledge of the advantages for the mother and family appeared to be particularly poor in both groups of women and knowledge of problems associated with bottle feeding was also poor in both groups.

30 (36%) of the 84 parous women who indicated that bottle feeding was not good for babies had bottle fed. 20 of the 40 parous women, and 13 of the 22 nulliparous women who had previously bottle fed indicated the mother's return to employment as the reason. There is little doubt that the return to work influences the working mother's decision to introduce bottle feeding even though she may be aware that it is not the best way of feeding. In a study of urban clinic nursing staff carried out 4 years after the PNG Baby Feed Supply Control Act was passed, those who returned to work within the first 6 months postpartum were more likely than those who returned later to have used bottle feeding (14). The same study, however, suggested that where facilities for breastfeeding at work were provided or where the workplace was near enough for the babysitter to bring the child for breastfeeding the large majority of the nurses exclusively breastfed. The current situation is that although PNG subscribes to the International Labour Organization recommendations for working mothers, which includes the provision of breastfeeding breaks, these recommendations are rarely implemented in either the public or private sector.

None of the women asked to participate in the study declined, and we think the women were a representative sample of those attending the PMGH Antenatal Clinic. Whether or not they are representative of all antenatal mothers in Port Moresby is perhaps open to question. It is possible that the ready availability of doctors at the PMGH Antenatal Clinic may have introduced some bias. Although many of the more educated and

affluent women choose to attend the private system it is still possible that PMGH may attract more highly educated women than the urban clinics, where those less well educated may feel more comfortable. The fact that 82 (55%) of the women had had secondary education above Grade 6, with 70 (47%) reaching Grade 10 suggests that this might be so. Nevertheless there was a broad and similar spectrum of educational attainment in both nulliparous and parous women.

There is clearly an urgent need to improve the knowledge of the population about the advantages of breastfeeding and the disadvantages of bottle feeding. Even though more than half of the women surveyed had been educated to Grade 8 or higher, their knowledge of the advantages of breastfeeding, the disadvantages of bottle feeding and the existence of the breastfeeding protection legislation was poor. This is disappointing since infant feeding is supposedly taught to Grade 8 girls in Home Economics, and currently to both girls and boys in Grade 8 Design and Technology classes in the education reform curriculum (15).

The HIV (human immunodeficiency virus) epidemic has added a further dimension to the importance of knowledge about infant feeding. For most HIV-infected women in PNG exclusive breastfeeding for the first 6 months of the infant's life offers the lowest risk of transmission whilst non-exclusive, mixed feeding is likely to be associated with significantly increased transmission (16). Mixed feeding in the first 6 months of life is common in PNG (11) and in the present study 22 of the 150 mothers interviewed planned to use some degree of mixed feeding. Clear and consistent messages need to be provided about the benefits of exclusive breastfeeding and the risks of bottle and mixed feeding for the infants of all women, irrespective of their HIV status.

The World Health Organization (WHO) has recently stated (16) that, "Governments and other stakeholders should revitalize breastfeeding protection, promotion and support in the general population. They should also actively support HIV-infected mothers who choose to exclusively breastfeed and take measures to make replacement feeding safer for HIV-infected women who chose that option." The promotion and support of breastfeeding in

the general population and the support of breastfeeding for individual women, HIV-infected or not, are tasks which should not be left to government agencies alone. Organizations such as Susu Mamas have experience and expertise in this area and they should receive financial and logistical support from and appropriate recognition by the government.

Studies in Malaysia, Africa and other resource-poor countries including Papua New Guinea have shown that legislation or the introduction of guidelines on feeding can positively affect feeding practices (17-20). For these gains to be maintained, however, constant reminding of the population concerned, together with means of enforcing the regulations are required. Knowledge of the legislation in PNG is poor. In the present study, although 69% of the women reported that a prescription was necessary to get a bottle from a pharmacy, only 19% knew about the legislation protecting breastfeeding. Sadly, and for a number of reasons, enforcement of the PNG legislation is lacking.

## Conclusions

Whilst there appears to be general recognition that breastfeeding is the best way to feed babies, knowledge of its advantages and of the disadvantages of bottle feeding is poor. Knowledge of the legislation to protect breastfeeding is also poor. Experience of bottle feeding is widespread in the community and appears to be as common among young female babysitters as it is among the parous population.

## Recommendations

- Attention needs to be focused on revitalizing and sustaining the education of young people about the importance of breastfeeding for themselves, their children and their families. Such education should begin in primary school and be reinforced at subsequent levels of the education system.
- More active, innovative and repeated education on infant feeding at antenatal clinics is required.
- The Papua New Guinean legislation to protect breastfeeding and control bottle and baby cup feeding urgently needs updating.



- Effective ways of enforcing the law to protect breastfeeding need to be devised.
- Effective ways of supporting breastfeeding in the workplace are needed.
- More support for organizations such as Susu Mamas that promote and support breastfeeding in the community is needed.

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## A review of the current state of malaria among pregnant women in Papua New Guinea

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### SUMMARY

Besides young children, pregnant women are at high risk of malaria in highly endemic countries. This paper reviews evidence from studies conducted in Papua New Guinea (PNG) in the last 20 years on the burden and prevention of malaria in pregnancy and highlights gaps in our knowledge of malaria in pregnancy in PNG. Overall, primigravidae were found to be at higher risk than multigravidae, with up to 40% of primigravidae but only 10-25% of multigravidae infected with *Plasmodium falciparum* at delivery. Such infections were found to be associated with a 128-145 g decrease in birthweight. Mean birthweights reported between 1980 and 2003 range from 2.58 to 2.72 kg in primigravidae and 2.84 to 3.09 kg in multigravidae, with 21% to 48% and 9% to 19% of babies born to primigravidae and multigravidae, respectively, of low birthweight (<2500 g). The negative impact of malaria in pregnancy is compounded by relatively low rates of antenatal coverage. The current PNG national treatment policy which prescribes a treatment course of first-line antimalarial treatment (currently chloroquine and sulphadoxine-pyrimethamine) at first antenatal clinic contact, followed by weekly chloroquine prophylaxis and iron and folate supplementation, may no longer be effective given the high levels of resistance to chloroquine in PNG and poor compliance. In order to reduce the burden of malaria in pregnancy in PNG, alternative methods of control such as insecticide-treated nets and intermittent preventive treatment in pregnancy (IPTp), as well as improved modes of delivery of maternal health interventions, are urgently needed.

### Introduction

Malaria in Papua New Guinea (PNG) is the leading cause of outpatient attendances nationally, the third commonest cause of hospital admission and the second commonest cause of death, and causes the greatest burden of lost disability-adjusted life-years (DALYs) at 4894/100,000 per year. Accordingly, malaria is a top priority of the national health response. As in highly endemic areas elsewhere in the world, in PNG both prevalence of malaria infection and incidence of morbidity are highest in young children (1,2) and pregnant women (3). Maternal deaths (to which malaria in pregnancy contributes significantly) are the

fifth leading cause of lost DALYs. With a maternal mortality ratio of 370/100,000 childbirth is still among the highest mortality risks for women of childbearing age in PNG.

### Malaria in pregnancy and maternal health

Precise estimates of the burden of malaria in pregnancy are not available, but regional patterns of birthweight indicate that alongside maternal nutrition and socioeconomic factors malaria is a major causative factor for the high prevalence of low birthweight (LBW) in lowland and coastal parts of PNG (4). In Madang and Maprik, where most in-depth studies on malaria in pregnancy have been

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done, mean birthweights reported between 1980 and 2003 range from 2.58 to 2.72 kg in primigravidae (PG) and 2.84 to 3.09 kg in multigravidae (MG), with 21% to 48% and 9% to 19% of babies born to PG and MG, respectively, of low birthweight (<2500 g) (3,5-9). Comparative studies between malaria-endemic coastal PNG and the malaria-free highlands suggest that malaria in pregnancy is responsible for up to 11% of anaemia and 40% of low birthweight in coastal areas (6).

In the only published study looking at the history of infections during pregnancy, Brabin et al. (3) found that the prevalence of malaria infections at first antenatal clinic (ANC) visit in primigravidae peaked at 9-16 weeks of gestation (55%). No similar trend was observed for multigravidae. Despite receiving chloroquine prophylaxis at all ANC visits, the average prevalence of infections at any ANC visit was 34% in PG, 30% in secundigravidae (SG) and 19% in MG. Several published studies looked at

prevalence of malaria infection at delivery. Infection rates were significantly higher in primigravidae, reaching over 40% both in peripheral and placental blood in some studies (Table 1).

Placental pathology was not investigated in early studies, but a recent study in Madang found that 42% of women delivering at Alexishafen Health Centre showed evidence of active, chronic or past chronic malaria infection on placental histology (10).

In a pooled sample that contained roughly equal numbers of PG, SG and MG, Allen et al. (9) found that peripheral and placental infection at delivery were associated with a 128 g and 145 g decrease in birthweight respectively. Other PNG studies lacked sufficiently large sample sizes to find significant differences in birthweight in relation to malaria infection status.

Anaemia is a very common feature in pregnant women in many parts of lowland

TABLE 1

PREVALENCE OF MALARIAL INFECTIONS AT DELIVERY

	Positive for malaria infection				Reference
	PG	SG	SG and MG	MG	
<b>Peripheral</b>					
Madang, 1986-1987	44%		26%		(5)
Madang, 1994-1996	25%	20%		13%	(9)
Madang, 2002-2003	26%	11%		11%	(10)
<b>Placental</b>					
Maprik, 1986-1988	41%	23%		8%	(7)
Madang, 1994-1996	34%	26%		14%	(9)
Madang, 2002-2003	24%	13%		13%	(10)
<b>Placental histology</b>					
Madang, 2002-2003	63%	50%		33%	(10)

PG = primigravidae  
SG = secundigravidae  
MG = multigravidae

PNG. In 1986-1988, 89% of women delivering at the major referral hospital in Madang had a haemoglobin level (Hb) of <11 g/dl and 19% of PG and 17% of MG had severe anaemia, ie, Hb <7 g/dl (6). Haemoglobin values measured at first booking at a rural health centre in Madang were significantly lower in both PG (8.6 g/dl) and MG (8.7 g/dl) than in non-pregnancy controls (10.4 and 10.2 g/dl respectively), despite similar levels of iron deficiency, with a tendency for haemoglobin levels to decrease with increasing length of gestation and to be lower in PG with concurrent malaria infection ( $-0.7$  g/dl,  $p = 0.15$ ) (5). How far these drops are directly related to malaria or simply due to physiological dilution in pregnancy, most of which will have occurred in PNG women prior to booking, is unclear. However, the fact that malaria control interventions such as intermittent preventive treatment in pregnancy (IPTp) result in significantly increased haemoglobin levels (11), underlines the importance of malaria as a cause of anaemia in pregnancy. Up to 40% of women showed signs of iron deficiency. With chloroquine (CQ) prophylaxis and treatment for severe anaemia, Hb in these women recovered to 9.6 g/dl in PG and 9.3 g/dl in MG at delivery with no significant difference between women positive and negative for malaria. Perhaps related to increasing coverage of iron/folate supplementation following their introduction into the national treatment guidelines in 1985, haemoglobin values during pregnancy and at delivery have been higher in recent studies (9), and the proportion of women severely anaemic (Hb <7 g/dl) at delivery decreased to 13% in 2002-2003 (10).

Anaemia (Hb <8 g/dl) was significantly associated with a decrease in birthweight in PG ( $-281$  g) but not in MG ( $-84$  g) (5). However, in-depth studies showed that anaemia is mainly linked to an increased risk of preterm delivery rather than a decrease in birthweight in term infants (9).

Although non-falciparum malaria is common in PNG, little is known about its effect on pregnant mothers and their babies. In a study in the mid-1980s the prevalence of *P. vivax* was lower in pregnant mothers attending ANC (3) (and under CQ prophylaxis) than in the postnatal period, but this is likely to be more a reflection of the high effectiveness of CQ prophylaxis against non-falciparum malaria than of reduced risk

in pregnancy. However, further in-depth studies are needed to assess the contribution of non-falciparum malaria to malarial disease in pregnancy in PNG.

There have been only a few studies on congenital malaria, but the limited data indicate that transplacental transfer of *P. falciparum* parasites is common. In a small study in Madang umbilical cord infection was found in 7 of 15 children (47%) born to women with parasitaemia at time of delivery (12); 4 of these children also had detectable peripheral parasitaemia. Little is known about transplacental transfer of other malaria species, although at least one case of a symptomatic *P. vivax* infection acquired in utero has been described (13).

Very little is known about the problem of malaria in non-immune women living in areas of low endemicity such as the highlands. The overall burden of malaria in pregnancy is likely to be low as indicated by the substantially higher haemoglobin levels and lower rates of LBW in highland areas (6). However, due to low immune status acquired infections are more likely to be severe and mortality rates in pregnant mothers with severe malaria can be as high as 50% (14).

The detrimental effects of malaria in pregnancy are compounded by low rates of antenatal coverage and supervised deliveries. Nationally, only 33% of women receive any antenatal care during their pregnancy and 44% of deliveries are supervised; however, there are large regional variations. Antenatal coverage can drop below 50% and the proportion of supervised deliveries falls to as low as 10-15% in some rural districts of the country (15).

Two factors contribute to this low antenatal coverage and low rate of supervised deliveries: limited access to health care and strong customary beliefs surrounding childbirth. While the number of women delivering at provincial hospitals has greatly increased over the past two decades, rates of supervised deliveries in rural areas have been decreasing due to a range of factors. In many rural parts of PNG, women will have to walk for several hours through often difficult terrain to reach the nearest health centre. With a decline in mobile ANC clinic coverage, access to both ANC and delivery services is therefore severely limited. Unless a delivery plan for supervised birth is worked



out with the woman and her husband during the ANC period, many women will not be able to reach the health centre once labour has started, regardless of complications. Staffing levels and morale are other important obstacles to good clinical care. Women often state that they do not deliver at the health centres because they do not want to be attended to by male nurses, or because they are not sure if the health centre will be open or they will be able to find a nurse if they arrive after hours.

In addition, childbirth is still the focus of many customary beliefs and restrictions in some PNG cultures. Childbirth, like menstruation, is often believed to have a 'polluting' influence, in particular on men, and assistance to women in labour is often limited. In some places women in labour will go to the bush and deliver their babies completely unattended. There may also be strong beliefs associated with the disposal of placentas that inhibit women from delivering at a health facility.

### **Policy, prevention and treatment**

Both malaria and safe motherhood have been identified as priority areas in the 2001-2010 PNG National Health Plan (15). The plan calls for a reduction of maternal mortality to 260/100,000 and LBW to <10%, while at the same time aiming to increase ANC coverage to 90% and the proportion of supervised deliveries to 70%. The goals for maternal mortality and LBW will not be reached without effective control of the detrimental effects of malaria in pregnancy.

Given the problems with access to adequate health care and the reluctance of mothers to deliver at health centres, preventive interventions have to be the main approach to improving the health of pregnant mothers and their babies.

The current PNG national treatment policy prescribes a treatment course of first-line antimalarial treatment (currently chloroquine and sulphadoxine-pyrimethamine (SP)) at first ANC contact followed by weekly chloroquine prophylaxis and iron and folate supplementation. However, the usefulness of chloroquine prophylaxis is questionable, given the high levels of resistance to chloroquine (16) in PNG and well-known problems of compliance. Even in the mid-1980s and 1990s chloroquine prophylaxis

had little effect on malaria infection rates at delivery (5,9,17) although it was associated with increased haemoglobin levels (5,9) and decreased risk of preterm delivery (9). Thus, in the absence of information regarding alternative approaches, the policy is continuing today.

The use of insecticide-treated bed nets (ITNs) during pregnancy is also advised as part of the national guidelines, but to date no special bed net distribution for pregnant mothers is in place. In many areas ITNs can be bought from health centres but supplies are unreliable and prices often a deterrent. This situation is expected to change in the near future, as PNG has secured a grant from the Global Fund for AIDS, Tuberculosis and Malaria that will allow the provision of long-lasting ITNs to all people living in malarious areas in PNG. Monitoring the impact of this program on adverse pregnancy outcomes will be an important part of assessing its effectiveness.

Current treatment guidelines for malaria in pregnancy indicate the use of CQ and SP for uncomplicated disease, oral quinine with SP for treatment failure, and parenteral quinine for severe malaria in pregnancy. The clinical efficacy of CQ plus SP against *P. falciparum* is still high (93%) (18); however, the high levels of parasitological failure (up to 15%) indicate that these drugs will reach the end of their life span sooner rather than later. Although not yet part of the official treatment guidelines for pregnancy malaria, artesunate and IM artemether are second-line treatments for malaria in non-pregnant people, and are regularly used to treat women in their third trimester admitted to hospital with a presumptive diagnosis of malaria.

### **Future research needs**

The high levels of morbidity and mortality indicate that the current policies for prevention and treatment of malaria in pregnancy are inadequate and new or improved approaches are needed. Research into new options for the prevention of malaria in pregnancy such as intermittent preventive treatment (IPTp), the better integration of ITNs and/or new and improved forms of prophylaxis is of high priority. In the medium term, new drugs for the treatment of malaria in pregnancy will be needed.

The above interventions will, however, only be successful if they can fit into local circumstances, customs and beliefs. Operational research studies into modes of delivery of maternal health interventions, in particular on ways of increasing coverage of ANC and supervised deliveries, as well as a better understanding of women's perceptions of their own health, are thus needed if the high levels of maternal mortality, severe maternal anaemia and low birthweight are to be reduced.

The special epidemiology of malaria, and the genetic and cultural diversity, as well as imminent changes to malaria control policies, make PNG an ideal location to conduct in-depth studies into different aspects of malaria in pregnancy. Of particular interest are the aetiology and pathology of non-falciparum malaria in pregnancy or the effect of PNG-specific host genetic protective traits such as Southeast Asian ovalocytosis, alpha-thalassaemia or Gerbich blood group negativity on the risk and effects of malaria in pregnancy.

Building on earlier work the PNG Institute of Medical Research is committed to tackling the challenges posed by the high levels of malaria and maternal mortality in the country and thereby contributing to a better and healthier future for all PNG women.

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## **A case-control study of VDRL-positive antenatal clinic attenders at the Port Moresby General Hospital Antenatal Clinic and Labour Ward to determine outcomes, sociodemographic features and associated risk factors**

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### **SUMMARY**

Between June 2001 and December 2002, 152 antenatal patients at Port Moresby General Hospital who were Venereal Disease Research Laboratory (VDRL) serology positive and 150 unselected antenatal patients who tested negative were studied to determine the gestational age at which the tests were performed, the time it took for results to become available, the proportion of patients who received treatment, the sociodemographic characteristics associated with VDRL positivity and the effect of VDRL positivity on maternal and perinatal outcomes. The prevalence rate of VDRL positive among antenatal clinic attenders in Port Moresby at that time was 4.4%. Of the 152 VDRL-positive patients in this study 97% were also *Treponema pallidum* haemagglutination (TPHA) positive. Significantly more of the positive patients were of highlands origin, lived in settlements, had previous marriages, had lower parities, delivered preterm babies, had stillbirths, had growth-restricted babies and had babies with lower Apgar scores at both 1 and 5 minutes. The mean birthweight was significantly lower among the positive patients. Significantly more of the positive patients were married to spouses with occupations which were regarded as 'risky' for sexually transmitted infections. There was no difference between the two groups with respect to patient's education, marital status, husband's education, gestational age at delivery and the number of days the baby spent in the Special Care Unit. The study concluded that the current antenatal screening does not provide adequate coverage for our patients. If the current availability of clinic-based strip tests provided by a non-government organization can be continued by the Ministry of Health we should be able to overcome this problem.

### **Introduction**

The importance of maternal syphilis as a cause of abortion, perinatal death and congenital syphilis is well known. The detection of syphilis in antenatal populations and its proper management has been one of the major success stories of antenatal care. In most antenatal clinics, in both developed and developing countries, serological

screening for syphilis is a routine. This public health measure is particularly rewarding as three patients – the mother, her sexual partner and her unborn child – may be protected from the ravages of this disease. In the USA from the 1940s to the late 1980s, the number of infant deaths from congenital syphilis fell by 99%; and rates of clinically apparent congenital syphilis were reduced almost 100-fold (1). In the National Capital

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District (NCD) of Papua New Guinea (PNG), where some 12,000 women attend public antenatal clinics each year, about 4-5% are Venereal Disease Research Laboratory (VDRL) positive. Prevalence rates among asymptomatic pregnant women have been found to be 1% in The Gambia (2), 12.5% in Zambia (3) and 17.5% in Ethiopia (4); in the highlands provinces of Papua New Guinea the prevalence rate ranges from 10% to 20% (5). For the devastating effects of syphilis to be obviated, it is important to find out the current situation of routine testing and the management of patients who test positive. It is also important to determine the sociodemographic characteristics of those who test positive so that, where necessary, awareness and educational programs can usefully and effectively be put in place for primary prevention.

### Aims of the study

To determine:

- The prevalence of syphilis in the Port Moresby General Hospital (PMGH) Antenatal Clinic population and the gestational age (GA) at diagnosis
- Risk factors associated with VDRL positivity
- The perinatal outcomes in those who are syphilis serology positive.

Measurable objectives:

- The proportion of subjects who are VDRL reactive
- The proportion of the reactive VDRLs who are *Treponema pallidum* haemagglutination (TPHA) positive
- The gestational age at which the syphilis serology diagnosis was made
- The time interval between sending the specimen and linking the result/report with the patient
- How many of the positive patients complete treatment before delivery
- The proportion of partners treated
- The stillbirth and neonatal death rates

- To determine if the positive patients have any sociodemographic characteristics which may be used to identify them.

### Patients and methods

#### Study design and study population

This was a case-control study conducted between June 2001 and December 2002. The study population consisted of all pregnant patients attending the Antenatal Clinic of the PMGH and patients delivering at the Labour Ward of the PMGH, and their babies. The cases were VDRL-positive mothers attending the Antenatal Clinic or delivering at the PMGH Labour Ward.

Controls were as follows:

- The next VDRL-negative mother after a VDRL-positive case who booked in the same trimester as the case at the PMGH Antenatal Clinic, or
- The next VDRL-negative mother delivering at the Labour Ward of the PMGH who booked at the same gestational age as the case.

#### Data sources

1. Antenatal Clinic VDRL register.
2. Central Public Health Laboratory VDRL register.
3. Labour Ward birth registers.
4. Patients' hospital records.
5. A structured interviewer-administered questionnaire.

#### Definition of terms

*Husbands' occupation 'risky'* – this was defined as a husband who worked with the police, army or prison service, was a taxi or public motor vehicle (PMV) driver or was a freelance business man or politician. Previous studies (6) have shown that these occupations have been associated with increased sexually transmitted infection (STI) risk.

*Intrauterine growth restriction (IUGR)* – the diagnosis of IUGR was based mostly on



clinical grounds by paediatricians after birth. Only a few cases were diagnosed antenatally. In order to accurately detect IUGR one must have a reliable menstrual date or an early ultrasound scan. Many of our antenatal patients do not keep accurate records of their last menses and we are not able to do routine early pregnancy ultrasound scans to assess or confirm gestation. Moreover the majority of our antenatal patients book after 20 weeks gestation.

*Prematurity* – as with IUGR, the prenatal diagnosis of this relies largely on an accurate menstrual date or an early ultrasound scan date. Most of our cases were diagnosed by paediatricians by neonatal assessment using the Dubowitz system.

## Results

Between June 2001 and December 2002 there were 15,232 deliveries at the PMGH Labour Ward. A total of 356 (178 cases and 178 controls) antenatal attenders were recruited for study. Unfortunately 26 (15%) of the cases were unaccounted for by the completion of the study. Most of the cases lost to follow-up did not attend the PMGH for delivery. The corresponding controls were automatically excluded from the study. Records were available for 152 cases and 150 controls.

The mean gestational age at booking for the cases in the study was 24 weeks; this was similar in both groups.

Sociodemographic characteristics are shown in Table 1. Significantly more of the cases were of highland region origin (36% vs 25%,  $p = 0.040$ ) and significantly more of them lived in settlements (46% vs 27%,  $p = 0.003$ ). There was no difference between the two groups as far as age, village residence, patient education, occupation and marital status were concerned. Husband's education and employment status were also not significantly different between cases and controls. However, significantly more of the cases had husbands who had 'risky' occupations as defined above (31% vs 14%,  $p = 0.0004$ ).

Marital status and number of years married were not different between cases and controls; however, significantly more of the cases had previous marriages (30% vs 6%,

OR 6.59 (2.94 -15.18),  $p < 0.00000$ ).

Pregnancy characteristics are shown in Table 2. The proportion with a previous bad perinatal outcome was not different in the two groups. The mean parity of the cases was significantly lower than in the control group, (1.4 vs 2.8,  $p = 0.0109$ ); the cases had blood collected at a significantly later GA than the controls (25 weeks vs 23 weeks,  $p = 0.0195$ ). The mean interval between test and linkage of the result with the patient was 3 weeks.

In the period under study, the VDRL positivity rate amongst all the antenatal bookings in the National Capital District was 4.4% and, of these, 86% were also TPHA positive (5). Among the cases in this study, 97% were also TPHA positive; and 92% were treated (Table 2). The mean gestational age at which the patients were treated was 27.6 weeks. Only 5% were treated before 19 weeks gestation, 84% were treated between 19 and 35 weeks gestation and 3% were treated after 35 weeks. 74% of partners of the cases were also treated.

Labour and perinatal outcomes are shown in Table 3. There were 12 stillbirths among the cases and none among the controls ( $p = 0.00045$ ). There were significantly more preterm deliveries among the cases (OR 2.9 (1.1-7.9),  $p = 0.015$ ). Significantly more babies with IUGR were found among the cases (OR 5.3 (2.3-12.4),  $p < 0.00000$ ). The mean birthweight was significantly lower among the cases (2835 g vs 3069 g,  $p = 0.043$ ) and the mean Apgar scores at both 1 and 5 minutes were significantly lower among the cases ( $p = 0.0365$  and  $p = 0.0027$  respectively). However, the mean GA at delivery and the mean number of days the baby spent in the Special Care Unit were not significantly different for cases and controls.

84% of the babies of the cases were given treatment with benzathine penicillin shortly after birth.

## Discussion

Serological testing for syphilis in pregnancy has been done routinely in Britain for over 45 years, in Norway and France by law since 1948 and 1932 respectively, as a routine in Hong Kong for 50 years, and in PNG for the last 4 decades.

This study and others in recent times have

**TABLE 1**

## SOCIODEMOGRAPHIC CHARACTERISTICS

<b>Variables</b>	<b>Cases (%) N = 152</b>	<b>Controls (%) N = 150</b>	<b>OR (95% CI)</b>	<b>M-H p</b>
<b>Categorical variables</b>				
<b>Region of origin</b>				
Highlands	54	37		
Islands	9	6		
Momase	11	14		
Southern	78	93		
Highlands versus Southern Region	54/152 (35.5)	37/150 (24.7)	1.74 (1.01-3.01)	0.034
Highlands versus the rest	54/152 (35.5)	37/150 (24.7)	1.62 (0.99-2.86)	0.0401
<b>Age &lt;20</b>	19/152 (12.5)	11/150 (7.3)	0.55 (0.23-1.29)	0.1340
<b>Residence: urban residence as the reference point</b>				
Village	22/152 (14.5)	35/150 (23.3)	1.27 (0.65-2.52)	0.4550
Settlement	70/152 (46.1)	40/150 (26.7)	2.19 (1.26-3.79)	0.003
<b>Patient's education</b>				
Duration 0-6 years	87/152 (57.2)	74/150 (49.3)		
Duration >6 years	65/152 (42.8)	76/150 (50.7)	1.37 (0.85-2.22)	0.1693
<b>Patient's occupation</b>				
Unemployed	111/152 (73.0)	114/150 (76)		
Skilled	19/152 (12.5)	25/150 (16.7)		
Semiskilled	12/152 (7.9)	6/150 (4)		
Unskilled	10/152 (6.6)	5/150 (3.3)		
<b>Marital status</b>				
Married	143	144		
Separated	2	0		
Widow	1	5		
Single	6	1		
<b>Married versus single status</b>				
Single	6/152 (3.9)	1/150 (0.7)	6.0 (0.71-134.8)	0.061
Unmarried	9/152 (5.9)	6/150 (4)	1.5 (0.48-4.92)	0.44

**Number of years married to present partner**

1-5 years	43/152 (28.3)	55/150 (36.7)		
>5 years	109/152 (71.7)	95/150 (63.3)	0.68 (0.41-1.14)	0.07
<b>Previous marriages</b>	45/152 (29.6)	9/150 (6)	6.59 (2.94-15.18)	<0.00000

**Husband's education**

Duration 0-6 years	41/152 (27.0)	47/149 (31.5)		
Duration >6 years	111/152 (73.0)	102/149 (68.5)	1.25 (0.73-2.13)	0.38

**Husband's employment status**

Villager	9	17
Employed	102	99
Unemployed	41	33
Total	152	149

**'Risky' husband's occupation**

Yes	47/152 (30.9)	21/150 (14)	2.75 (1.49-5.10)	0.0004
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<b>Continuous variables</b>	<b>Cases Mean (SD)</b>	<b>Controls Mean (SD)</b>	<b>K-W H p value</b>
Age (years)	24.5 (5.13)	25.5 (4.76)	0.011
Patient's school years completed	6.5 (3.42)	7.3 (3.55)	0.046
Years with present partner	4.5 (4.32)	5.3 (4.10)	0.018
Husband's years at school	8.7 (3.56)	9.3 (5.85)	0.628

OR = odds ratio

95% CI = 95% confidence interval of odds ratio

M-P p = Mantel-Haenszel Chi squared p value

SD = standard deviation

K-W H p = Kruskal-Wallis test p value

shown that syphilis is still one of the major causes of perinatal morbidity and mortality. It is well known that infection with syphilis leads to late spontaneous abortion, preterm delivery, intrauterine growth restriction, stillbirth and early neonatal death (3,7). A study done at the Goroka Base Hospital in 2000, where the babies were diagnosed with syphilis on clinical and serological findings, showed that congenital syphilis accounted for 5.5% of neonatal admissions and 22% of all neonatal deaths (8).

In this study we identified some major risk factors associated with this infection in our antenatal mothers. One of them was highlands ethnicity. Past studies have shown

higher rates of STIs in the highlands than in the rest of the country. For example, Garner et al. in 1972 showed a very high incidence (28.9%) of syphilis in adults in residences along the Highlands Highway (9) whilst a more recent study showed the incidence of syphilis in antenatal clinic attenders at the Goroka Base Hospital to be 7.1% (8). This rate was higher than the 4.4% found in the antenatal clinics of Port Moresby in 2002 (5).

Women in urban settlements were significantly more likely to be seropositive than their village and urban metropolitan counterparts. This is not surprising. In the United States and some developing countries syphilis is associated with poverty, drug

TABLE 2

## PREGNANCY CHARACTERISTICS

Categorical variables	Cases (%) N = 152	Controls (%) N = 150	OR (95% CI)	M-H p
Previous perinatal deaths	13/152 (8.6)	7/149 (4.7)	1.90 (0.68-5.44)	0.180
TPHA positive	147/152 (96.7)			
Treated	140/152 (92.1)			
Mean GA at which VDRL-positive patients were treated (weeks)	27.6 (SD 6.3)			
GA at treatment <19 weeks	8/152 (5.3)			
GA at treatment 19-35 weeks	127/152 (83.6)			
GA at treatment >35 weeks	5/152 (3.3)			
Continuous variables	Cases Mean (SD)	Controls Mean (SD)	K-W H p	
Parity	1.37 (1.227)	2.75 (1.327)	0.0109	
GA at booking (weeks)	23.7 (6.62)	23.2 (6.07)	0.4392	
GA at blood collection (weeks)	24.9 (6.18)	23.2 (5.97)	0.0195	
Interval between test and result (weeks)	3.07 (1.508)	2.91 (0.885)	0.849	

OR = odds ratio

95% CI = 95% confidence interval of odds ratio

M-H p = Mantel-Haenszel Chi squared p value

TPHA = *Treponema pallidum* haemagglutination

GA = gestational age

VDRL = Venereal Disease Research Laboratory

SD = standard deviation

K-W H p = Kruskal-Wallis test p value

abuse and social instability (7,10,11), all of which are not uncommon in the Port Moresby urban squatter settlements.

STIs including syphilis are said to be associated with the single marital status and adolescence (10). While our study failed to demonstrate this, patients with these sociodemographic characteristics are more likely to be exposed to multiple sexual partners and perhaps a larger sample may show this trend. We did not demonstrate any significant difference in age, education, marital status or socioeconomic status. This is in agreement with a study in Zambia (3). An interesting finding was that women whose husbands had 'risky' occupations were more

likely to have positive VDRL serology. Husbands with these occupations have the opportunity for sexual encounters with multiple sexual partners. Members of the disciplined forces (police and the defence force) for example, who usually go on night patrols or travel to other provinces or places on duty, where they are taken away from the family setting for long periods of time, are more likely to have the opportunity to engage in other sexual relationships. Politicians and business men often go on domestic and international trips and spend time in hotels and places where they can seek extramarital female companions. As Cunningham et al. put it, "among the fighting armies... and prostitutes syphilis continues rampant" (11).

TABLE 3

## LABOUR AND PERINATAL OUTCOMES

Variables	Cases* N = 152	Controls N = 150	OR (95% CI)	M-H p
<b>Categorical variables</b>				
Fresh stillbirths	1/152	0/150	Undefined	0.32
Macerated stillbirths	11/152	0/150	Undefined	0.0020
Total stillbirths	12/152	0/150	Undefined	0.00045
Preterm delivery	19/152	7/150	2.9 (1.1-7.9)	0.015
IUGR (N = 150)	38/150	9/150	5.3 (2.3-12.4)	<0.00000
<b>Continuous variables</b>				
	Cases Mean (SD)	Controls Mean (SD)	K-W H p	
Gestational age at delivery (weeks)	38.3 (2.9)	38.5 (2.3)	0.7052	
Birthweight (g)	2835.3 (729)	3069.3 (494)	0.043	
Apgar score at 1 minute	8.16 (2.6)	9.07 (0.9)	0.0365	
Apgar score at 5 minutes	9.19 (2.3)	9.85 (0.4)	0.0027	
Number of days admitted to Special Care Unit	0.21 (1.35)	0.07 (0.6)	0.245	

\*128 out of 152 (84.2%) of the babies of the cases were given treatment

OR = odds ratio

95% CI = 95% confidence interval of odds ratio

M-H p = Mantel-Haenszel Chi squared p value

IUGR = intrauterine growth restriction

SD = standard deviation

K-W H p = Kruskal-Wallis test p value

This view is given credence from interviews with sex workers in our city, which showed that high profile clients, including politicians, were regular visitors (12). Drivers (and sailors likewise) all over the world have been known to have a 'partner' at every port of call. A study done in 1972 clearly showed high prevalence rates of syphilis along the Highlands Highway, and several speakers in the main scientific meeting at the 2003 Symposium on HIV/AIDS in Mt Hagen spoke of a 'thriving sex industry' along the Highlands Highway. These simply reflect the activities and impact of drivers along the Highlands Highway (9).

We expected women with previous history of stillbirths to show a higher rate of seroreactivity. Often in our practice, the first

suggestion of syphilis may be a past history of stillbirth. The impact of syphilis on perinatal outcome has been well demonstrated in studies elsewhere, where significantly more seroreactive than seronegative women are likely to have had a previous abortion or stillbirth (3,13,14). At the PMGH syphilis contributed to 10% of stillbirths (15). Women with syphilis abort more than 60% of their pregnancies (13).

It is not surprising therefore that our seroreactive patients showed significantly higher rates of preterm deliveries, low birthweights, IUGR and perinatal mortality. These are well known sequelae of maternal syphilis infection, documented by numerous studies all over the world. Even as early as 1923, syphilis was found to be the aetiological



agent in about 40% of premature stillborn babies and 80% of macerated babies (16). In Goroka the average birthweight in the infected group of infants was 2.4 kg, whilst the average birthweight in the infants of our cases was 2.8 kg; both are significantly lower than the birthweights of babies born of seronegative mothers (8).

The mean gestational age at which most of our antenatal mothers first attended the clinic was 24 weeks and the mean GA at blood collection was 25 weeks (Table 2). Since the mean interval between blood collection and the receiving of results and therefore commencing treatment is about 3 weeks, the mean GA of our cases commencing syphilis treatment would be about 28 weeks. Most of them were treated between 19 and 35 weeks gestation; only 5% were treated at <19 weeks gestation and 3% after 35 weeks. It was previously widely accepted that syphilis is a major factor in fetal loss in the latter half of pregnancy and appreciable damage to the fetus results only later in the pregnancy when an adequate immune response has developed in the fetus (13). The current belief is that fetal infection does occur as early as 9-10 weeks (14). With this in view, many of the babies would have had significant damage caused to them by the time treatment was instituted at the mean gestation of 28 weeks. In any case even when treatment is given early, and a full course of the correct treatment is given to the mother, there have been some treatment failures, as were reported from Fiji (10). These are babies who go on to develop congenital syphilis despite the mother completing treatment. It is therefore reassuring to note that the standard treatment for common illnesses of children in Papua New Guinea recommends treatment of all 'normal-looking' babies from VDRL-positive mothers with a single dose of benzathine penicillin.

Of the 152 babies born of the seroreactive mothers, 128 (84%) of them were treated; 8% of them were perinatal deaths and the other 8% did not receive any form of treatment. The main reason for failure to treat was that they left hospital before there was time to locate the serology result and treat them. Many patients leave our hospital before the discharge procedure is complete, especially patients from poor socioeconomic backgrounds. They often do this to avoid paying hospital fees. Some patients may

have left hospital before staff had the opportunity to discuss the serious nature of their condition with them. When patients are aware of the seriousness of their condition, they are often willing to wait for necessary treatment. Unfortunately it may also be the case that the hospital staff find themselves too busy to educate or provide awareness for our patients, or we lack the understanding and therefore fail to see the seriousness of the problem; or worse still, we just do not care.

As far as the mothers themselves were concerned, 140 of the 152 cases (92%) were treated for syphilis according to our protocol. 8% of the cases and 26% of the husbands of the cases did not receive or complete the treatment. The reasons are the same as for failure to treat the babies.

At the antenatal clinics of the National Capital District the rate of seroreactive mothers was 4.4%. However, 1265 women (12%) either had no records of the VDRL test or were not screened during the antenatal period (5). Furthermore, of those screened, 20% did not have their VDRL test result by the time they came to labour. The proportion of unscreened mothers at other centres is worse, as shown by the Goroka study where the proportion of antenatal mothers not screened was as high as 70% (8). Even our once-only testing is not foolproof. Studies have shown seroreactivity in women at delivery who were initially seronegative. In addition the presence of early active syphilis in the latter half of pregnancy indicates recently acquired infection (3).

Though our rates are lower it is not surprising that the pattern of the complications associated with syphilis seen in our population (high rates of stillbirth, preterm delivery and low birthweight in the seroreactive women) is similar to that found in Africa (3) and in the pre-antibiotic era (14). Most of the seroreactive women in our study (87%) were treated after 18 weeks gestation, when significant fetal damage may have occurred. This fact is reflected in the high rate of stillbirths, 8% (12/152), despite 92% treatment coverage, in the serologically positive women, compared to a low stillbirth rate of 1.7% overall at the PMGH maternity unit (5).

The treatment of syphilis itself is simple. The main problem in PNG is getting the

women screened early and treated so as to avoid the destructive effects of the disease. Even when patients book early in pregnancy, the time it takes to receive the result and the necessary treatment is too long.

Further analysis of our data showed the following:

- 36 women (24%) were either not treated or did not complete treatment before delivery.
- Of the 38 babies with IUGR 30 (79%) received treatment after 20 weeks gestation.
- Of the perinatal deaths, 58% of them either did not receive any treatment or had not completed treatment by delivery; all the perinatal death cases who were treated received treatment after 20 weeks gestation.

Despite good treatment coverage of our seropositive attenders, there are still unsatisfactory outcomes because many women are treated too late. Penicillin is still the drug of choice for all stages of the disease, both in the pregnant and the non-pregnant. It has been the treatment of choice since 1944 when it was first used in pregnancy (10); and it is still the treatment of choice today because of its efficiency and lack of toxicity to both the mother and her baby. The benefits outweigh the small associated risks. We rarely encounter women who are allergic to penicillin. It must also be kept in mind that 90% of patients who say they are 'allergic' to penicillin do not have the true IgE-mediated anaphylactic reaction and therefore can still be treated with penicillin (17). We have not encountered patients with Jarisch-Herxheimer reaction.

Since the introduction of penicillin (in the 1940s), syphilis has declined in incidence in developed countries. We do not have data to demonstrate trends of syphilis since its discovery in PNG in 1960. On the other hand the incidence may well be getting worse like many other maternal and child health indicators. The rate of positive syphilis serology in the antenatal clinics of the NCD in PNG has shown a slow rise from 3.0% in 1996 to 4.4% in 2002.

The recent rise in the incidence of syphilis has been noted to be coexistent with HIV

(human immunodeficiency virus) infection in parts of Africa and the United States (11). Both infections are transmitted via the same route and the genital lesions associated with syphilis facilitate the transmission of HIV. Therefore, our increasing rates of syphilis and HIV infection should give us cause for concern, as HIV alters the clinical pattern of syphilis, with more cases presenting with the secondary disease, slower resolution of chancres and other cutaneous manifestations, and a higher incidence and earlier onset of neurosyphilis (10,18).

## Conclusions

The current antenatal screening and treatment of cases is not adequate. New ways should be looked at to get women booked early at the antenatal clinics, preferably before 16 weeks when syphilis infection can start damaging the fetus. Screening for syphilis should be a priority at the booking visit at all antenatal clinics throughout Papua New Guinea so that treatment can start as early as possible. The screening test should ideally be simple and fast, so as to allow the whole screening and treatment process to be completed in a single antenatal visit. A recent study by Angue et al. (19) clearly showed that the Abbot Determine® test is simple and fast, has acceptable sensitivity and specificity rates, requires less equipment and expertise to perform, and, overall, costs less. Their recommendation that the Determine test be made available in areas of the country where VDRL is unavailable, or where logistics do not allow for the test results to be available early enough to make a difference, is a valid one.

Babies born of mothers who do not have antenatal care are at risk of congenital syphilis, and therefore these mothers should have an urgent screening test done at the labour or postnatal wards so that they and their babies can be treated if positive.

Our standard management protocol allows antenatal attenders only one chance to be tested. This policy is inadequate. Some women will become infected during pregnancy and others may seroconvert after the initial test. There is a need to increase public health awareness to promote early antenatal booking and routine syphilis testing of all pregnant women in PNG. In addition a proposal to study syphilis infection during

pregnancy by repeat testing may reveal interesting findings.

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## Variations of the middle thyroid vein in Papua New Guinean Melanesians

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### SUMMARY

**The middle thyroid vein has been noted to be frequently absent during thyroidectomies in Papua New Guinea (PNG). To verify this and other known inconsistencies in the neck a total of 103 bodies were dissected at the Port Moresby General Hospital in 2002. The middle thyroid vein was absent in 59% of the cases. It would be to the advantage of surgeons in PNG to be aware of this.**

### Introduction

The thyroid veins drain the thyroid lobes, the oesophagus and the trachea. The middle thyroid vein (MTV) is described as short and wide and drains into the internal jugular vein (IJV) (1). In rare instances it drains into the brachiocephalic vein (2). It exhibits a small internal diameter (average of 2.0 mm) (3). The vein is at risk during thyroidectomy and tearing from the IJV can lead to a difficult haemorrhage. The middle thyroid vein is found to be frequently absent in Papua New Guineans. This study was undertaken to establish the prevalence of the middle thyroid vein in Papua New Guinean Melanesians.

### Patients and methods

This study was carried out at the Port Moresby General Hospital (PMGH) mortuary from February to August 2002. A consecutive series of 32 females and 71 males were dissected. The autopsies were performed for routine reasons by the resident pathologist, such as mandatory coroner's cases and others. Consent was obtained from the relatives. One newborn baby was

excluded. No additional incision was made apart from the usual symphysis menti to symphysis pubis extensile cut for post-mortem studies. For the purpose of the study, our part of the dissection was confined to the neck. Bilateral flaps were raised subplatysmally and the strap muscles were retracted in the plane of the sternothyroid muscle to expose the carotid sheath. The sternothyroid plane was carefully retracted and the lateral aspect of the thyroid gland and the internal jugular vein inspected. The loose areolar tissue was cleared in search of the middle thyroid vein. Apart from the MTV other possible variations were also considered.

### Results

The results in Table 1 show that the MTV was absent in 59% (61/103) of the cases. In males it was absent in 56% and in females in 66%. The Chi-squared value with Yates correction equals 0.45 at 1 degree of freedom and the two-tailed p value equals 0.5023. Thus there was no significant difference between the sexes with respect to MTV absence. There were no unusual variations

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**TABLE 1**

OCCURRENCE OF THE MIDDLE THYROID VEIN IN PAPUA NEW GUINEAN  
MELANESIANS BY SEX

Sex	Middle thyroid vein		
	Absent	Present	Total
Male	40	31	71
Female	21	11	32
<b>Total</b>	61	42	103

found in this series of cases.

### Discussion

In the 103 Melanesians we studied the middle thyroid vein was absent in 59%. There was no significant difference between males and females though the vein was slightly more often absent in females in this series. Surgeons practising in PNG usually note that the MTV is absent and this study provides the answer for its absence. Although this finding does not absolve the surgeon from carefully looking for the vein during thyroidectomy, it does help to put the surgeon at ease when the vein is not found. Our study illustrates that clinically important information can be gleaned by careful clinical observation and laboratory studies that do not require expensive equipment. This study is small;

any significant variations in anatomy by sex and ethnic origin that may exist will need a much larger study to demonstrate.

### ACKNOWLEDGEMENTS

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## **A focused ethnography about treatment-seeking behaviour and traditional medicine in the Nasioi area of Bougainville**

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### **SUMMARY**

**A focused ethnographic study examining knowledge, behaviour and attitudes related to treatment-seeking behaviour and traditional medicine was conducted in the Nasioi area of Bougainville. The study was conducted in two separate locations within the Nasioi area. Some similarities as well as some differences in knowledge and behaviour were exhibited in the two study locations which could be further investigated. People from both areas had a similar perception of common and serious illnesses. People from both areas also attributed illness to both biological factors and supernatural forces. Home management was the most common initial response to illness and the local village clinic or urban health centre were most frequently used as the first treatment resort. The most important factors in determining treatment-seeking responses to illness in both locations were cost and proximity to home or convenience. The study found that there may be considerable potential for an integrated health system in the Nasioi area and provided suggestions as to how this could be progressed. The study also provided information that could be useful in a wider context in informing the implementation of the national policy on traditional medicine in Papua New Guinea.**

### **Introduction**

A focused ethnographic study looking at knowledge, behaviour and attitudes related to traditional medicine was conducted in the Nasioi area which lies around the coastal town of Arawa in Central Bougainville. The purpose of the study was to provide information that could be used to develop a provisional explanatory model of treatment-seeking behaviour and design a structured questionnaire which would be administered to a larger cross-section of the Nasioi population. It was anticipated that information from both the broader population sample and the more in-depth information from those interviewed for the initial focused ethnography would be used to formulate policy recommendations specific to the Nasioi area as well as to inform the implementation of the recently drafted National Policy on Traditional Medicine for Papua New Guinea (1).

The North Nasioi Council of Elders (COE) is the local government authority presiding over an area of approximately 240 square kilometres and comprising 8 smaller Village Council of Chiefs (VCC) areas. These are Bava Pirung, Kerei East, Kerei West, Doue, Tasipo, Konampai, Dangua and Apiatei.

The North Nasioi area includes Panguna, which was the site of one of the world's largest open-cut mines, operational in the 1970s and 1980s and associated with the unrest that forced the closure of the copper mine and led to the 10-year civil conflict known as the Bougainville Crisis. A blockade imposed by the government of Papua New Guinea (PNG) during the crisis prevented supplies from reaching many parts of the island and caused services to collapse. Much infrastructure was destroyed during the fighting. Consequently people were forced to rely on their own local resources including traditional medicine (2). This relatively recent

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resurgence or focus on traditional medicine is predictive of its continued widespread use and makes the Nasioi area of particular interest for a study on traditional medicine.

### Population size and characteristics

The National Census data indicate that a total of 5854 persons reside in the North Nasioi area (3). This includes 3078 males and 2776 females occupying 1316 houses. A breakdown by age and sex is not available for the North Nasioi area on its own. However, the next largest government area is the Arawa Local Level Government (LLG) area for which the age and sex population breakdown is shown in Figure 1. The structure of the North Nasioi area is expected to be similar to that of the Arawa LLG population.

Nasioi society is matrilineal. A Nasioi person inherits land, if they are female, and clan membership from their mother. The clan is an important organizational unit in Nasioi society. The other fundamental social unit is the family, which in Nasioi society includes the extended family. People typically live in small communities or villages based on clan and extended family relationships. A village may comprise 3 or 4 clan groups. A village

chief is elected who sits on the VCC, which governs each local area.

The vast majority of Nasioi people are Catholic. Other religious groups with some following are Seventh Day Adventist and United Church. A few other religious groups have very small followings.

70% of people aged 10 years and over in the Arawa LLG are literate in one language (3). The most common languages spoken are Nasioi, Melanesian Pidgin and English.

The last National Census found that 11,864 people in the Arawa LLG (or 53% of those aged 10 years or more) were economically active. The main employment category was agriculture. People were involved in various types of agriculture for both income generation and personal consumption. Cocoa was the main cash crop. Selling produce provided an income for some families and a few people ran their own business (3). The number of people engaged in various types of income-generating activity is shown in Figure 2.

Arawa is the main urban centre in the Nasioi area. Some telecommunications, retail outlets and health and education

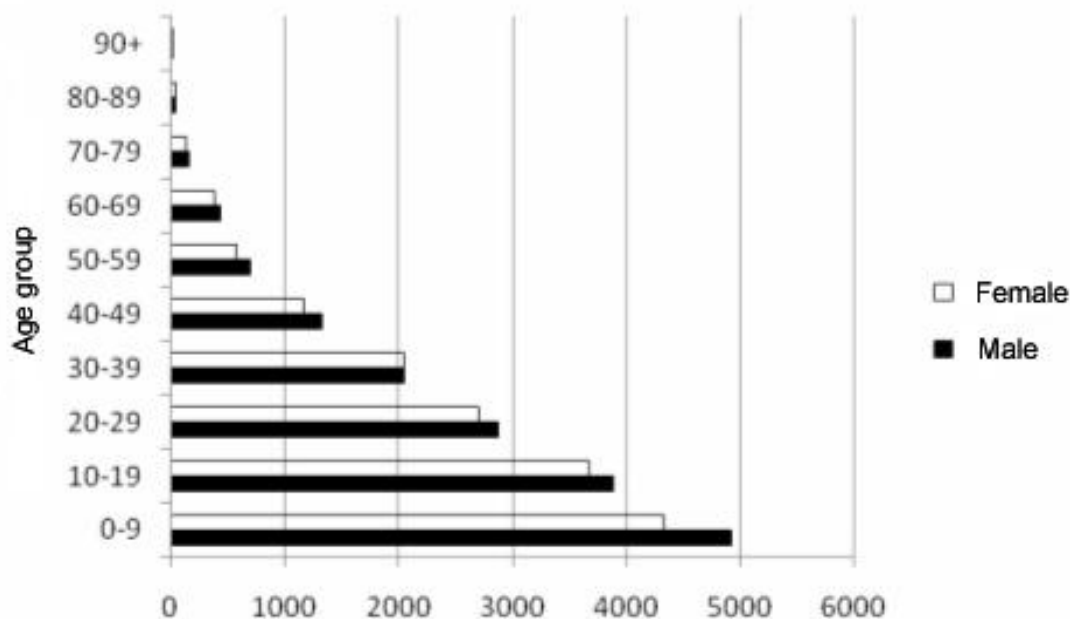


Figure 1. Population by age and sex, Arawa Local Level Government area, 2000. Source: National Statistical Office (3).

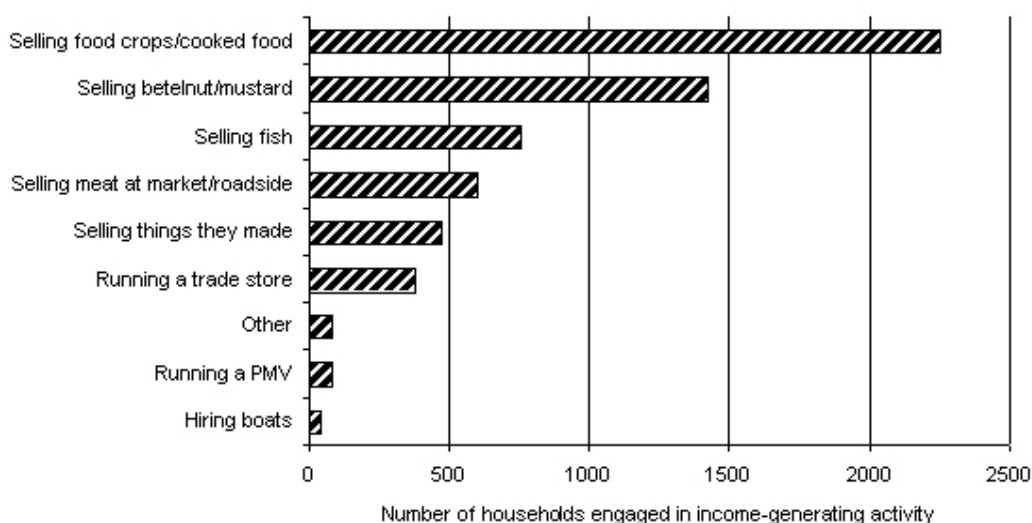


Figure 2. Income-generating activities, Arawa Local Level Government area, 2000. Data were obtained from 5863 households in private dwellings headed by a PNG citizen. Source: National Statistical Office (3).

services are available in Arawa including a secondary school for students in year 9 and above. The closest banking and postal facilities are located in Buka at a distance of 200 kilometres or 4 hours and K50 by public bus.

### Health services

Arawa Town Health Centre is the main health facility in the North Nasioi area and is supported by 6 aid posts and 2 smaller clinics. For most people, aid posts are located at a distance of between 1 and 3 hours' walk from home. Arawa Town Health Centre is a 40-bed facility comprising postnatal ward, intensive care ward, paediatric ward, medical ward and general ward. Other services available at Arawa Town Health Centre include outpatients clinic, maternal and child health and antenatal clinic, dental clinic, pathology laboratory, delivery room, theatre, X-ray machine (but no technician), dispensary and an ambulance. Other providers of western health care are 1 general practitioner and 2 health extension officers who all run private practices in Arawa.

A plethora of traditional healers provide health care services to the Nasioi population. Traditional healers reside in virtually every Nasioi village although their level of traditional medical knowledge varies. Some practitioners can treat a range of conditions and are referred to as generalists. Other

'specialists' are well known for being able to treat 1 or 2 conditions. Some can treat a range of conditions but have 1 or 2 specialties. The different types of traditional practitioner include herbalists, bonesetters and spiritualists. There are also practitioners who deal with sorcery and illness thought to be caused by evil spirits.

### Methods

Before commencing the study approval for it to be conducted was obtained from the Medical Research Advisory Committee of PNG and Curtin University's Human Research Ethics Committee. Participation was voluntary and all respondents were required to give written or, if not literate, oral consent before interviews were conducted.

As recommended in rapid assessment procedures (4), data were collected using several different methods of assessment and investigation to obtain information from a variety of sources, allowing for data verification through triangulation. A focused ethnographic approach (5), incorporating in-depth and semi-structured interviews, was adopted. Data were collected from key informants, people who had recently experienced an illness episode, community members and practitioners.

For specificity, the research focused on 2 illness categories: febrile illnesses and skin conditions. Febrile illnesses and skin

conditions were selected because they accounted for more presentations to outpatients in Bougainville than any other conditions between 1997 and 1999. While other measures of morbidity and mortality are available, it was appropriate to base the selection of conditions for this study on presentation to outpatients as this is the measure most likely to be comparable with presentation to traditional healers.

Two teams of 3 research assistants were engaged to conduct interviews with assistance from the North Nasioi COE. All research assistants had grown up and lived in the area where they were to conduct interviews. They were fluent in Nasioi, had a minimum Grade 10 level of education and were adults of some standing in their local communities. Each team included a male and a female. Prior to commencing data collection, a 3-day training workshop was conducted.

The VCCs of Tasipo and Bava Pirung were purposively selected as the study sites. Two contrasting areas were selected that would together reflect the diversity that exists within the Nasioi area. Tasipo is in the mountains at a distance of about 7 kilometres from the town of Arawa. Since there is no public transport in this area getting to Arawa requires more than an hour's walk. Bava Pirung lies along the coastline approximately 15 kilometres east of Arawa. Access to Arawa may involve walking for people from some inland villages but there are many villages beside the sealed road that runs along the coastline. A semi-regular public bus service operates along this route and the one-way fare to Arawa is K2.

Selection of respondents within each location was also purposive to conform to the criteria stipulated for the various respondent categories (6). The research assistants had an intimate knowledge of their respective locations and so were ideally placed to identify suitable key informants and other respondents. Before starting to conduct interviews, each group of research assistants and the principal investigator discussed and collectively agreed upon potential key informants, community respondents and health care practitioners whom they would invite to participate in the study.

Guided by the principal investigator both

groups of research assistants agreed on 8 key informants, including males and females and comprising traditional healers from different villages and providers of western health care in the two locations. All key informants had considerable health knowledge and were experienced in treating or managing illness. Key informants helped to identify people who could provide an illness narrative, that is, people who had experienced a recent illness episode. The research assistants identified other community respondents. Some health care practitioners were known to research assistants and others were identified during key informant interviews. A sample of health care practitioners was chosen for interview in each location as the total number identified included more than it was possible to interview. The samples included the better-known traditional healers as well as some lesser-known practitioners. All health workers and nurses providing western health care in each location were included in the sample of health care practitioners.

Almost without exception, the people initially identified as potential key informants and community members were interviewed. Among people who were invited to participate in the study only 2 declined, claiming that they were too busy. Through the COE and local chiefs some information about the study had reached residents in each area before the actual data collection commenced. A few people expressed concerns about the nature of the research but once they were reassured that no information would be sought about the actual plant or other preparations used in traditional medicine people were receptive and happy to contribute to the research. The fact that all the research assistants were indigenous to the areas where they conducted interviews and familiar to respondents probably contributed to the excellent response rate.

A series of explicit and detailed question guides and recording sheets were designed for use with various groups of respondents during the qualitative data collection. The various instruments were designed specifically for this study but were adapted from instruments used in other focused ethnographies (6,7). Pre-testing of the instruments in the study area was not possible due to administrative, logistical and time limitations. Procedures were adjusted during the course of data collection as

deemed necessary; for example, community members were asked to list signs and symptoms of illnesses that had been identified by key informants because using cards proved too cumbersome. Overall the integrity of the original instruments was maintained. All data collection instruments were in English with a common understanding and interpretation across interviewers attained during the training workshop. The number and type of interviews completed in each location are shown in Table 1.

The choice of practitioner instrument followed a forced-choice methodology (7) and was designed to yield information about the respondents' preferences for different health care providers. In this methodology hypothetical scenarios were posed whereby respondents were asked, if they suffered from a febrile illness and only two types of service providers were available, which one they would approach for treatment. This question was repeated for every possible combination of provider types available in the local community (15 pairs of providers). Respondents were then asked if their choices would be different if they suffered from a skin

condition, to which the response was invariably negative. Thus the exercise was not repeated separately for skin conditions. Each provider type was given a score based on the number of votes received as a percentage of the total votes for the pair of service providers. Providers were then ranked according to overall popularity using the results obtained in this manner for febrile illnesses.

The majority of the data were qualitative and analyzed using the qualitative data analysis software package 'MAXQDA' (registered trademark of VERBI Software). MAXQDA was used to facilitate the analysis of the following interview types: Explanatory Model, Illness Narratives, Health Care Practitioner and Illness Descriptions (characteristics and relationships between illnesses) provided by community members. Some of the data collected in Tasipo and Bava Pirung were of a quantitative nature. The statistical package SPSS (registered trademark of SPSS Inc.) Version 10.0 was used to facilitate the analysis of Signs and Symptoms of Common Illnesses, Severity Rating of Common Illnesses and Choice of Practitioners.

**TABLE 1**

NUMBER OF COMPLETED INTERVIEWS BY LOCATION

Type of interview	Tasipo		Bava Pirung	
	Febrile	Skin	Febrile	Skin
Explanatory model for illness	7	6	9	8
Illness narrative	19	13	23	27
Matching signs and symptoms to illness names	10	10	9	9
Severity rating	10	10	9	9
Health care resources in community	3		9	
Choice of practitioner	28		34	
Inventory of household medicines	10		8	
Household composition and characteristics of residence	10		10	
Interview guide for health care service providers	13		10	



## Results

### Information and knowledge systems

Key informants in Tasipo and Bava Pirung had very similar ideas about which febrile illnesses are the most common and serious. Most of the illnesses included in the short list of 10 common and serious febrile illnesses (11 in Bava Pirung) were identified in both areas. These illnesses included cough (*kou*), deep and persistent cough (*eenu*), respiratory conditions (*domang o*), diarrhoea (*kubiri*), urinary tract infection (*pintuu*), enlarged spleen (*maana*), fever (*malaria*), malaria-like fever (*pari*) and headache (*bore bana*). The relationships between and descriptions of each of these illnesses provided by people from both locations were also very similar suggesting that people from different parts of the Nasioi area share a common understanding of everyday and more serious febrile illnesses.

Many of the common and serious febrile illnesses appeared to be roughly equivalent to particular illnesses known in western medicine. However, it cannot be assumed that any condition described by respondents corresponds precisely to any western medical condition. Western medical terms beside bracketed Nasioi disease names denote the closest equivalent condition and should not be interpreted as an exact translation of the local term. For example, it became apparent during the course of the study that a diagnosis of *malaria* under the Nasioi taxonomy of illness is not the same as the western medical diagnosis of malaria. For Nasioi speakers '*malaria*' is a syndrome of signs and symptoms, characterized especially by fever, which can be caused by

one of several different agents.

Although many respondents attributed febrile illnesses to biological factors such as poor hygiene and poor nutrition it was evident that people in both study locations believe that febrile illnesses are caused by a mixture of scientific and non-biological agents such as breach of geographic or dietary taboos, exposure to the blood of a relative, or spiritual or divine intervention. Taxonomies of illness showing how most respondents tended to group febrile illnesses are depicted in Figures 3 and 4 for each respective location.

As for febrile illnesses there was a high level of concurrence between people in Tasipo and Bava Pirung regarding the most common and/or serious skin conditions. Key informants in both locations identified leprosy (*oramu* and *erepu*), sores from head lice (*kitei*), rashes (*kasikasi*), ringworm (*aaroa*), whitespot (*kokosi*), boils (*moona*) and cellulitis (*sisisi*) as being among the most common types of skin conditions affecting local communities. Descriptions of each of these conditions were also very similar among respondents from both Tasipo and Bava Pirung although respondents in Bava Pirung introduced 'fungal infections' as a separate category, which included 3 skin conditions that were classified as 'sores or skin irritations' in Tasipo. Thus, the core of common knowledge and understanding of illnesses among respondents from Tasipo and Bava Pirung extends to skin conditions. As was the case for febrile illnesses, respondents believed that the causal pathway for skin conditions could be both biological and supernatural. Parasites, mites, worms, germs or bacteria and poor personal hygiene were identified by many respondents

FEBRILE ILLNESSES		
RESPIRATORY SYSTEM	DIGESTIVE TRACT	MALARIA-RELATED
<i>Kou</i> <i>Eenu</i> <i>Domang O</i>	<i>Kubiri</i> <i>Ereng Piri</i>  <i>Pintuu</i> <i>Maana</i>	<i>Malaria</i> <i>Pari</i> <i>Bore Bana</i>  <i>Pintuu</i>

Figure 3. Taxonomy of febrile illnesses, Tasipo.

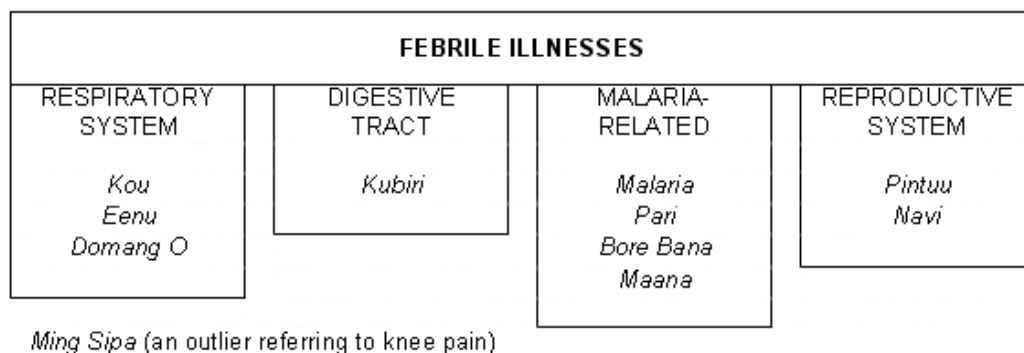


Figure 4. Taxonomy of febrile illnesses, Bava Pirung.

as causes of skin conditions. Allergies, irritant grasses, flies, pigs or other animals also featured in explanations for skin conditions. Traditional beliefs about the cause of skin conditions included ignoring dietary taboos, spitting on relatives, sorcery and coming into contact with the blood of a dead person. Sorcery (*nenura*), blood contact and ignoring dietary taboos are thought to cause a number of different conditions. Respondents grouped skin conditions according to similarities in signs and symptoms. Taxonomies of skin conditions for Tasipo and Bava Pirung are shown in Figures 5 and 6 respectively.

### Treatment-seeking response to illness

The general treatment-seeking response to illness was the same for respondents from Tasipo and Bava Pirung. The initial response to illness for at least three-quarters of respondents who provided an illness narrative (75% in Tasipo and 84% in Bava Pirung) was to try and manage the condition at home. The percentage of respondents who first used home management was even higher (96%) among Bava Pirung residents who had recently suffered from a skin condition. Either traditional or western medicine or a combination of the two is used in home management. In Tasipo, half of those who tried to manage their febrile illness or skin condition at home used some type of traditional medicine. Bava Pirung respondents who tried to manage febrile illnesses at home were more likely to use western medicine purchased from a store or left over from a previous illness episode than a traditional remedy. When people in Bava

Pirung treated skin conditions at home they more commonly used traditional remedies. The most common form of home management for skin conditions was to bathe in solutions made from different types of leaves. *Popo*, guava, *bantu* and lime leaves were commonly used. Sometimes juice extracted from leaves would be mixed with lime and rubbed onto the affected area of skin.

Most of those who provided an illness narrative reported using treatment services outside the home at some stage during the illness episode. 84% of Tasipo and 60% of Bava Pirung respondents sought assistance from a health care provider. The first health care service used outside the home was most often the local village clinic, followed by Arawa Health Centre for people in both locations. The number of respondents who approached various categories of service provider in each location is shown in Table 2. The 2 health care services most likely to be used by respondents as the first treatment resort are both providers of western medical services. Worsening of the condition, development of more serious symptoms or failure of home treatment to resolve the condition is what usually prompts respondents to seek treatment from someone outside their immediate family.

Respondents were generally satisfied with the service provided by the first service provider they approached outside the home. However, 15 respondents in Tasipo and 8 in Bava Pirung found it necessary to seek treatment from a second service provider. At the second treatment resort there was a more

SKIN CONDITIONS			
LEPROUS CONDITIONS		SORES OR SKIN IRRITATIONS	SKIN INFLAMMATIONS
<i>Erepu</i> <i>Oramu</i>		<i>Kitei</i> <i>Kasikasi</i> <i>Atuatu</i> <i>Kaakepesi</i> <i>Aaroa</i> <i>Kokosi</i>	<i>Moona</i> <i>Sisisi</i>

Figure 5. Taxonomy of skin conditions, Tasipo.

SKIN CONDITIONS			
FUNGAL INFECTIONS	SORES OR SKIN IRRITATIONS	VIRAL INFECTIONS	LEPROUS CONDITIONS
<i>Kokosi</i> <i>Aaroa</i> <i>Kasikasi</i>	<i>Tudaa</i> <i>Penta Pankaing</i> <i>Moona</i> <i>Sisisi</i> <i>Kitei</i>	<i>Sikeni Bokisi</i> <i>Poneng Poneng</i>	<i>Oramu</i> <i>Erepu</i> <i>Ereng Koing</i>

Figure 6. Taxonomy of skin conditions, Bava Pirung.

even spread across the available service providers although traditional healers were the most popular treatment option of second resort in both study locations. People approached a second service provider because they were not fully satisfied or had not fully recovered with the treatment received at the health care service provider of first resort.

In Bava Pirung there appeared to be a preference for western health care services among people in the study population for treating febrile illnesses and when they seek treatment outside the home, but it was also common for people to use their own traditional treatment at the same time as western medicine. Sequential use of traditional and western medicine was more common in Tasipo. Thus, medical pluralism, that is, the use of two or more health systems

either in concert or sequentially, is widely practised. People were very satisfied with and had great confidence in the efficacy of pluralistic use of medicine.

### Explanatory model for treatment-seeking responses

Several factors that are important in treatment-seeking decisions were identified. Respondents' understanding of illness pathways includes both biological causative factors and traditional beliefs. Relationships with family and neighbours are believed to have an impact on health as does leading a spiritual life. Much illness is attributed to sorcery. These beliefs about the aetiology of disease mean that traditional medicine is an important part of the local health paradigm. At the same time people perceive that biological factors contribute to many

TABLE 2

## HEALTH CARE SERVICE OF FIRST RESORT

Service provider	Number of responses (%)	
	Tasipo	Bava Pirung
Village clinic	10 (37)	15 (50)
Arawa Health Centre	6 (22)	8 (27)
Private GP	6 (22)	0 (0)
Traditional healer	3 (11)	6 (20)
Private HEO	2 (7)	1 (3)
<b>Total</b>	<b>27 (100)</b>	<b>30 (100)</b>

GP = general practitioner

HEO = health extension officer

illnesses. With this understanding of disease it is logical that people would resort to both western and traditional health services for treatment.

In practice, respondents do not necessarily seek treatment from their preferred provider. Service provider preferences in each location, obtained using the forced choice of practitioner instrument, are shown in Table 3. Respondents in both Tasipo and Bava Pirung indicated that their practitioner choices would be the same for febrile illnesses and skin conditions and so only one column of data is presented for each location. Comparison of these data with those in Table 2, actual treatment option of first resort, shows some anomalies. Where people say they prefer to go does not necessarily correspond with where they actually go in the first instance. However, since the data in Table 3 include multiple preferences, strict comparison between the two tables is not possible.

Differences between preferences and actual behaviour suggest that at the time of illness events sometimes conspire to prevent the sick person from getting treatment from their preferred provider. Barriers to getting treatment from the preferred provider reported by respondents included cost, distance, non-attendance of staff at village

clinics and non-availability of traditional healer. In Tasipo, the most common reason given for not using the preferred practitioner in the illness episode being narrated was cost, nearly always in relation to the cost of services provided by the private general practitioner (GP). Despite the cost, the private GP was the treatment option of first resort for 22% of Tasipo respondents. In Bava Pirung cost and distance were the factors that most often prevented respondents from seeking treatment from their preferred provider.

The most important factors in treatment-seeking responses to illness for respondents in both Tasipo and Bava Pirung were cost and proximity to home or convenience. Another slightly less important consideration was confidence in the effectiveness of the treatment. The data presented in Tables 4 and 5 relate to the perceived efficacy of various service providers. In Tasipo, 3 providers of western medical services are seen as providing very effective treatment. In particular, treatment provided by the private general practitioner is thought to be highly effective. The treatment provided by traditional practitioners is well regarded because it has an immediate effect rather than because it is better treatment. It would appear that there is little confidence in treatment provided by village clinics. In view

**TABLE 3**

SERVICE PROVIDER PREFERENCES, TASIPO AND BAVA PIRUNG

Service provider	Percentage of choices for service provider	
	Tasipo	Bava Pirung
Family member	93	60
Traditional healer	81	29
Village clinic	75	65
Arawa Health Centre	33	71
Private GP	23	44
Private HEO	11	31

Number of respondents was 28 in Tasipo and 34 in Bava Pirung

GP = general practitioner

HEO = health extension officer

**TABLE 4**

PERCEIVED EFFICACY OF SERVICE PROVIDERS, TASIPO\*

	GP in private clinic	HEO in private clinic	Arawa Health Centre	Village clinic	Traditional healer**
<b>Advantages</b>					
Immediate relief/effect	11	3	-	-	33
Superior treatment	20	14	13	1	7
<b>Disadvantages</b>					
Ineffective treatment	-	3	2	10	-
Treatment is painful	-	-	-	-	10
Treatment slow to take effect	-	-	1	-	-
Uses too many drugs	1	-	-	-	-

Total number of respondents = 28

GP = general practitioner

HEO = health extension officer

\*Numbers denote number of responses

\*\*'Traditional healer' column includes responses for up to 4 traditional healers per respondent



of the popularity of village clinics among Tasipo respondents perhaps convenience outweighs perceived efficacy in treatment-seeking decisions. Efficacy of treatment may also be of less importance to the Bava Pirung study population than cost and proximity in treatment-seeking decisions. The data shown in Table 5 suggest that the private GP and Arawa Health Centre are both thought to provide a high standard of treatment. It would appear that there is less confidence in treatment provided by the village clinic and yet this was most often the health care service of first resort (Table 2). In view of the usage patterns of the village clinic and the private GP by Bava Pirung respondents, perhaps convenience and cost outweigh efficacy in treatment-seeking decisions. The services that are most used in both locations, village clinics and Arawa Health Centre, both provide western health care services, are cheap and are fairly easy to get to.

### Potential for integrated health care

A sample of western and traditional health care practitioners in both areas were asked what they thought about the development of an integrated health care system, that is, one

that incorporates and recognizes both traditional and western medicine. Practitioners reported that some degree of collaboration is already occurring. There is more intra- than inter-medical stream collaboration and there is only limited support for more collaboration between traditional and western practitioners. Reservations about collaboration were expressed because some practitioners prefer to provide treatment just to their own family members. Often traditional practitioners are reluctant to share information about their medicine. Despite the common view that current levels of collaboration are adequate, western and traditional practitioners alike wholeheartedly supported the formal recognition of traditional medicine as part of the government's health care system.

In both Tasipo and Bava Pirung, health care practitioners identified a range of specific benefits that would accrue from an integrated health care system. Many practitioners could see that services would be more accessible, affordable, broader and more effective. Some practitioners in Tasipo also believed that recognition of traditional medicine could have benefits at the

**TABLE 5**

PERCEIVED EFFICACY OF SERVICE PROVIDERS, BAVA PIRUNG\*

	GP in private practice	HEO in private practice	Arawa Health Centre	Village clinic	Traditional healer**
<b>Advantages</b>					
Immediate relief/effect	9	5	8	4	10
Superior treatment	15	5	15	8	9
<b>Disadvantages</b>					
Ineffective treatment	-	-	1	-	2
Treatment is painful	-	-	1	-	-
Treatment slow to take effect	-	-	1	-	1

Total number of respondents = 34

GP = general practitioner

HEO = health extension officer

\*Numbers denote number of responses

\*\*'Traditional healer' column includes responses for up to 2 traditional healers per respondent

psychological and spiritual levels. In Bava Pirung a number of practitioners believed that recognition of traditional medicine would result in financial benefits for service providers. Two Bava Pirung practitioners thought that if traditional medicine was formally recognized as part of the government's health care system it would become better organized, which would be advantageous in terms of processing supplies of traditional medicine and preserving traditional medical knowledge.

Although support for recognition and integration of traditional medicine was universal and many real benefits were volunteered, practitioners were cognizant of some obstacles that would need to be overcome if an integrated system is to be achieved. In Tasipo these related to the tendency to blame and seek retribution when a patient fails to recover, the imprecision and lack of scientific verification surrounding traditional medicine and the anticipated reluctance of some practitioners to reveal information about their treatments. In Bava Pirung lack of understanding and trust, disparity in education levels of different types of practitioners, and the sheer number of traditional practitioners were identified as potential barriers to integration.

Respondents could envisage an integrated health care system where traditional and western health care services are co-located. Most practitioners thought that separate rooms would be required for practitioners to be able to work in comfort. Several respondents also suggested establishing a traditional medicine section within Arawa Health Centre. In Tasipo it was suggested that traditional practitioners were ideally placed to assume a primary health care role at the village level.

Practitioners in both areas were able to suggest strategies to progress integration. These included: developing a better understanding of the services that each stream of medicine can provide; creating a registry of practitioners and conditions that each can treat; verifying the curative properties of particular traditional treatments and establishing doses and side-effects through scientific testing; registering and issuing licenses to traditional practitioners. It was suggested that meetings between leaders of each stream of medicine be held to work out how integration could proceed.

## Discussion

Respondents in the two locations shared a core of knowledge and had similar perceptions about febrile illnesses and skin conditions. The usual illness response pathway was also common to both locations. At least three-quarters of respondents tried to manage their illness at home before seeking treatment from someone outside the family. Village clinics and Arawa Health Centre were most often the treatment option of first resort once assistance was sought from outside the family. Low cost and easy access were the two most important factors in treatment choices. Efficacy of treatment was also a consideration. Some discrepancies between treatment preferences, treatment-seeking behaviour and the most important determinants of treatment choices were evident.

There is an anomaly between the low use of traditional healers and the importance of cost and proximity in treatment-seeking decisions. Many traditional healers provide services in the villages where respondents live and do not charge high fees. However, traditional healers were the treatment option of first resort for a minority of respondents in both Tasipo and Bava Pirung. Rank ordering of preferences for the available service providers or treatment options suggested traditional healers are the preferred provider in Tasipo but the least preferred in Bava Pirung (Table 3). Further investigation may be warranted to determine why traditional practitioners are not popular or very frequently utilized in Bava Pirung and why they are popular but infrequently used in Tasipo despite their services being low in cost and readily accessible to villagers.

Differences between the type of treatment provided by the preferred provider and the treatment option of first resort in Tasipo suggest that, in actual fact, many respondents do not have a strong preference for either traditional or western medicine. Practical circumstances surrounding an episode of illness may be the factors that determine what type of treatment is sought because people consider both traditional and western medicine to be effective (Tables 4 and 5). Although respondents perceive the scientific rigour and precision that surround western medicine as desirable, traditional medicine is more affordable and readily available to the majority of the population who

live in rural areas.

There appears to be considerable support among health care practitioners in both Tasipo and Bava Pirung for the concept of a health care system where traditional and western medicine are integrated. Respondents thought an integrated health system would mean better services for the community and preservation of important cultural knowledge on traditional medicine. It was also perceived that traditional healers would benefit financially under an integrated system.

In order for an integrated health care system to be established, open, trusting and equal relationships would need to be developed between traditional practitioners and providers of western health care services. Mutual understanding and respect should be the basis of these relationships and would pave the way for integration. Providing basic training courses in each stream of medicine could help to build this type of understanding and respect.

Home management is a common initial response to illness the world over and the Nasioi area is no exception. Some gains in health status in the Nasioi area might be achieved by ensuring that basic first aid knowledge, either traditional or western, and the ability to recognize signs and symptoms of common ailments and serious illness become more widespread. Health care practitioners said that people often wait too long and allow their condition to deteriorate before seeking treatment. Encouraging early presentation to a health care service provider may also help to improve health status. Traditional healers may be able to play a role in making home management more effective, providing health promotion and disease prevention information and encouraging early presentation through referral to an appropriate health care provider.

### Conclusion

The focused ethnography that has been reported in this paper produced considerable data on knowledge of illness, treatment-seeking behaviour and attitudes toward an integrated health system in two VCCs within the North Nasioi area. Although some homogeneity was evident between the two study sites, some differences were also noted. There was a common core of

knowledge about febrile illnesses and skin conditions in the two VCC areas although the way people classified or grouped illnesses differed somewhat. The belief that illness may be caused by both biological factors and spiritual or supernatural forces was common in both areas. Home management was the most common initial response to illness in both areas. Whereas in Tasipo respondents most often used some form of traditional medicine to treat illness at home, in Bava Pirung western medicine was more likely to be used for febrile illnesses. The majority of respondents in both areas sought the assistance of a health care practitioner during the course of an illness and in both areas the first treatment resort was most often the village clinic followed by Arawa Town Health Centre. Traditional healers were the most frequently used second treatment resort for people from both areas. Cost and convenience appeared to be the two most important factors in determining treatment choices. Perceived efficacy of the treatment appeared to be slightly less important. The extent to which the two study locations reflect the broader Nasioi population, reasons for the apparent anomalies regarding hypothetical preferences and actual behaviour that were detected in this focused ethnography and further refinement of the provisional explanatory model are all issues that could be elucidated through further research.

The research has also provided information that could be used by health authorities who wish to pursue an integrated form of health care. Although the sample of practitioners interviewed expressed limited support for more collaboration than is currently occurring, there was unanimous support for formal recognition of traditional medicine. Practitioners believed an integrated health service would offer better access, affordability and effectiveness than the current formal health system as well as a holistic alternative. Practitioners' ideas about how integration could be progressed contributed to the development of recommendations that could be useful to authorities in the Nasioi area should they choose to recognize and incorporate traditional medicine into the formal health system (J.E. Macfarlane and M.P. Alpers, Health care preferences among the Nasioi people of Bougainville: steps toward incorporating traditional medicine into the health care system, unpublished

manuscript).

The information could also be used to inform the implementation of the recently drafted National Policy on Traditional Medicine for PNG (1). The National Policy needs to be locally relevant and a better understanding of the knowledge, behaviour and attitudes of people at the community level is important in this context. Of course, the Nasioi are just one amongst PNG's multitude of cultural groups and implementation of the Policy in other areas would require information about the relevant cultural groups. The research method used in this study could be incorporated into studies designed to collect the required information in other parts of PNG where conditions are conducive to the development of an integrated form of health care.

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# Primary repair of colonic injuries at the Kundiawa and Madang General Hospitals, Papua New Guinea

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## SUMMARY

In this study, we evaluated the safety of primary repair of colon injury in a low-volume tropical hospital setting. Between 1998 and 2005, 18 consecutive patients who underwent emergency operation for civilian traumatic colon injury were studied. The main outcome measures were the mortality and morbidity rates and the total length of the hospital stay. The mean hospital stay for one-stage repair was 12 days versus 29 days for the two-stage procedure, which was a significant difference ( $p = 0.009$ ). There was no death reported from this study. There was no significant difference in postoperative septic complications between the one-stage and two-stage procedures. One-stage repair of colonic injury is a safe and cost-effective option for selected patients in the tropical hospital setting.

## Introduction

Over the last two decades there has been a shift in the management of colon injuries toward one-stage repair. Before that, most colonic injuries were managed by a two-stage procedure including colostomy because of the fear of anastomotic and wound breakdowns.

However, at present in specialized centres the results of one-stage repair are so superior that the two-stage procedure has become obsolete in the management of these injuries (1-7). Although there are a few reports from high-volume tropical hospitals (1,5) where colonic injuries were safely managed with one-stage repair, there is a paucity of data (2,8) on one-stage primary repair in a low-volume tropical hospital.

The primary purpose of this study was to evaluate the safety of primary repair of colon injury in a low-volume tropical hospital setting. Additionally, we aimed to determine whether one-stage primary repair in selected patients is safe in the presence of early diffuse peritonitis.

## Patients and methods

Between January 1998 and April 2005 in Kundiawa General Hospital and Modilon General Hospital an open case series study was conducted on 18 consecutive patients who underwent operation for colonic injury.

The criteria for inclusion were full-thickness colonic injury and informed consent obtained from the participant. All patients qualified for laparotomy had penetrating abdominal injury and were diagnosed with local or diffuse peritonitis. There was no exclusion from the study except lack of consent. The study was approved by the local ethics committee.

To classify patients in terms of general physical fitness we employed the American Society of Anesthesiologists classification (ASA). The patients in a good general condition (ASA grade 1 and 2) were allocated to one-stage repair whereas those critically ill (ASA grade 4 and 5) were managed by the two-stage procedure. The selection for one-stage repair or colostomy for the patients in the third ASA grade was at the

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surgeon's discretion. The longer the time from the injury to the operation and the more severe the associated injury, the more likely the patient was to be selected for the two-stage procedure.

The severity of peritonitis was classified according to the modified Hughes' classification (9, as quoted in 10): grade II, localized peritonitis or paracolic abscess; and grade III, diffuse faecal or purulent peritonitis.

We compared the one-stage versus the two-stage group with regard to the main outcome measures: morbidity rate and the total length of the hospital stay. Additionally, we compared the main outcome measures between the subgroups with local peritonitis and diffuse peritonitis.

All data, including mechanism of injury, time from the injury to the operation, ASA grade, intraoperative findings, severity of peritonitis, early postoperative septic complications, mortality rate and overall hospital stay, were recorded prospectively. Overall hospital stay was expressed in days in hospital after operation including the hospitalization period of patients readmitted for second-stage repair or because of complications related to colon injury.

The patients were resuscitated and optimized for surgery according to Advanced Trauma Life Support guidelines with crystalloids and blood transfusion if necessary. Antibiotic prophylaxis was

administered to all patients at the time of induction of general anaesthesia and continued for at least 48 hours. Postoperative management included monitoring of the patient's vital signs, continuation of intravenous fluid until the patient resumed oral diet, early postoperative oral feeding (12 hours after operation) and early mobilization.

Comparison between means was performed using the 2-sided t test for independent samples, while comparison of frequencies was performed by  $\chi^2$  using Yates' correction. We considered a difference with  $p < 0.05$  to be significant.

## Results

A total of 18 patients (13 men and 5 women) with penetrating colon injury were assessed. The median age was 25 years (range 6-50). The distribution of the injured segment of colon was as follows: 7 in the transverse colon, 5 in the descending colon, 5 in the sigmoid colon, and 1 in the caecum.

Regarding associated injuries, 6 patients had small bowel injury, 3 mesentery injury, 2 spleen injury, 2 vagina injury and 1 each of the following injuries: retroperitoneal haematoma, diaphragm, stomach, liver, lung, pancreas and urinary bladder.

The relationship between the surgical procedure and ASA grade is presented in Table 1. The average duration of time between the injury and operation for the

**TABLE 1**

AMERICAN SOCIETY OF ANESTHESIOLOGISTS (ASA) GRADE AND SURGICAL PROCEDURE FOR PENETRATING COLON INJURY

Type of operation	ASA grade				
	I	II	III	IV	V
Primary repair	2	3	6	0	0
Right hemicolectomy	0	0	1	0	0
Colostomy and repair	0	0	2	2	0
Hartmann's procedure	0	0	1	0	1
<b>Total</b>	<b>2</b>	<b>3</b>	<b>10</b>	<b>2</b>	<b>1</b>

whole group was 17.4 hours; for the one-stage repair it was 12.9 hours while for the two-stage procedure it was 81.6 hours.

The mean overall hospital stay for the one-stage procedure was significantly shorter than for the two-stage procedure: 11.9 ( $\pm 5.64$ ) versus 28.8 ( $\pm 18.63$ ) days ( $p = 0.009$ ).

The difference between the one-stage and the two-stage procedure with respect to early postoperative septic complications was not significant (Table 2). There was no death reported in the series and there was one relaparotomy due to intraperitoneal abscess following colostomy.

Our findings also showed a tendency for increased mean overall hospital stay and postoperative complication rate in the diffuse versus the localized peritonitis subgroup but the difference was not considered significant.

### Discussion

At present, 60% to 84% of patients with colonic injuries are treated by primary repair (1-3).

Our main finding is that there was no significant difference in the rate of early postoperative septic complication between the one-stage and two-stage procedures for perforating colon injuries. These results are in agreement with others who reported that the one-stage compared to the two-stage procedure has not increased postoperative septic complications and mortality (3-6). Furthermore, several prospective randomized trials found either lower (4) or similar (3-6,11) rates of septic complications

after primary repair as compared to colostomy. Curran and Borzotta's review of 2964 cases of primary repair of colonic injury (7) revealed that the leak rate after simple suture of perforation is very low (1.4%). In addition, the advantage of one-stage repair is not only reduction in morbidity but also decrease in the cost associated with colostomy (11,12).

Another question is whether one-stage repair can be carried out safely in the presence of peritonitis. Our findings suggest that diffuse peritonitis is not a significant risk factor despite a tendency for an increased rate of postoperative septic complications and longer hospital stay. The classical approach in the presence of diffuse peritonitis is a two-stage procedure. Recently, many reports recommend primary anastomosis as a safe management in the presence of diffuse purulent peritonitis (3,11,13).

In our study the mean overall hospital stay was significantly longer for the two-stage than for the one-stage procedure. Similarly, Berne et al. (12) have shown that the two-stage colostomy group had increased overall hospital stay compared to patients in the one-stage primary repair group.

Although in this series the choice for the two-stage procedure was guided by the severity of the patient's general condition and the presence of such risk factors as the time from the injury to the operation longer than 12 hours, associated injury, severe anaemia or presence of septic shock, there is a lot of discussion whether primary repair

**TABLE 2**

EARLY POSTOPERATIVE INFECTIOUS COMPLICATIONS AFTER ONE-STAGE AND TWO-STAGE PROCEDURES FOR PENETRATING COLON INJURY

<b>One-stage procedure (12 patients)</b>	<b>Two-stage procedure (6 patients)</b>
Wound infection (2 patients)	Wound infection (3 patients)
Intraperitoneal abscess (1 patient)	Intraperitoneal abscess (1 patient)
Acute epididymitis (1 patient)	Pneumonia (1 patient)
<b>Total: 4 (33%)</b>	<b>Total: 5 (83%)</b>

can be safely performed in the presence of these risk factors. A prospective multicentre study (3) has shown that severe faecal contamination, transfusion of more than 4 units of blood within the first 24 hours and single-agent antibiotic prophylaxis are independent risk factors for abdominal complications. Though mortality and rate of septic complications are generally higher in patients with a greater number of associated organ injuries, it was demonstrated in randomized trials (4,10) that there was no difference in the postoperative complication rate between the one-stage and the two-stage groups. Furthermore, some have recommended colostomy for patients with colon injuries presenting in shock or with associated multiple injuries (14). More recently, Kamwendo et al. (4) in a randomized trial have demonstrated that primary repair of civilian penetrating colonic injury is safe irrespective of the presence of high-risk factors such as shock, massive blood transfusion, delay in presentation, intraabdominal faecal soiling and associated injuries.

It is acknowledged that the sample size of our study is small, and the results need to be validated in a larger multicentre study with possible random allocation to the treatment groups.

In summary, our findings suggest that in a low-volume tropical hospital setting, one-stage repair of colonic injury is a safe and cost-effective option. However, having in mind the current trend towards one-stage repair of colonic injury, and on the other hand insufficient evidence from powered randomized trials on the association between the risk factors and results in both treatment groups, we suggest caution and opt rather for two-stage repair in critically ill patients with late diffuse peritonitis.

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## Barriers to the delivery of the hepatitis B birth dose: a study of five Papua New Guinean hospitals in 2007

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### SUMMARY

Hepatitis B is highly endemic in Papua New Guinea (PNG). Vaccination at birth is a key mother-to-child transmission prevention strategy. Despite recommendations for newborns to be vaccinated within 24 hours of delivery, a 2005 survey showed 23% coverage among children born in health facilities. Our study examined hepatitis B birth-dose coverage and knowledge, practices and barriers to vaccine delivery in five major PNG hospitals. Data on births and vaccines administered were sourced from the National Department of Health (NDoH) and directly from the five hospitals. A maternity unit audit and staff survey were undertaken. Across the five hospitals, the hospital-level data of hepatitis B birth-dose coverage was 79% (range: 40-96%) compared to 19% from national data (range: 0-106%). Despite hospitals having adequate vaccine supply, access to appropriately stored vaccine in maternity units was compromised with only one unit having a vaccine-specific temperature-monitored refrigerator. In interviews of 25 staff, incorrect reasons given for delaying vaccination were prematurity (60%), low birthweight (48%) and difficult birth (36%). This study found encouraging birth-dose coverage rates in five major hospitals but 20% of babies still missed receiving the recommended vaccine. The NDoH Immunization Unit will use the results of this study to inform strategies to improve hepatitis B birth-dose coverage in hospitals.

### Introduction

Hepatitis B virus (HBV) is an important cause of morbidity and mortality worldwide. The World Health Organization estimates that two billion people have serological evidence of past or present HBV infection, with 360 million chronically infected (1). An estimated 15-25% of people with chronic HBV infections will die prematurely from cirrhosis or hepatocellular carcinoma (2,3). These two conditions account for

approximately 500,000 to 750,000 deaths worldwide annually (1). The development of chronic HBV infection is inversely related to age: it occurs in approximately 90% of persons infected perinatally, in 30% infected in early childhood and in 6% infected after five years of age (4-7). There is a highly effective vaccine for HBV infection (1) and the provision of infant hepatitis B immunization is a proven public health strategy in preventing HBV transmission at population level (8,9).

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In highly endemic countries (defined as >8% of the population having chronic HBV carriage (10)) HBV is most commonly spread from mother to child at birth (perinatal transmission) or from person to person in early childhood (10). Infants born to mothers with hepatitis B surface antigen have a 5% to 20% risk of perinatal transmission which increases to 70% to 90% if the mother is hepatitis B e antigen positive (11). There are multiple hepatitis B infant vaccination schedules recommended throughout the world, ranging from two to four doses. In highly endemic countries the World Health Organization recommends that the initial hepatitis B vaccine dose be given within 24 hours of birth (12). This initial dose acts as a post-exposure prophylaxis following possible exposure to HBV during the birthing process. Birth-dose administration will prevent perinatal transmission in 80% to 95% of cases; however, the efficacy declines with increasing intervals between birth and administration of the vaccine (12).

HBV seroprevalance studies have shown that the disease is highly endemic in Papua New Guinea (PNG) with carrier rates of 12% to 37% (13-15). The PNG national immunization guidelines recommend that hepatitis B vaccine be administered at birth and at one and three months of age (16) but despite this the 2005 PNG vaccination cluster coverage survey showed that the coverage rate for hepatitis B vaccine at birth was low. Only 16% of all children surveyed were reported to have received the hepatitis B birth dose within 24 hours of birth, irrespective of place of delivery, and of the children born in health facilities the coverage was only slightly higher (23%) (17). These data suggest that within PNG there are many missed opportunities for a hepatitis B birth dose within health facilities.

We report the findings of a study examining HBV coverage, the attitudes and practices of staff, and the barriers to delivery of a hepatitis B birth dose in five major PNG hospitals.

### Methods

The study was undertaken during October and November 2007 in PNG.

#### Site selection

PNG has 20 provinces which can be

grouped into four geographical regions: Highlands, Southern, Islands and Momase. The selection of the five hospitals included in the study was based on representation of the four PNG regions and the national capital hospital, the provision of specialist obstetric services and high numbers of reported births. Hospitals selected were Port Moresby General (National Capital District), Goroka (Highlands Region), Madang (Momase Region), Nonga (Islands Region) and Alotau (Southern Region).

There were three main sources of information: (i) a comparison of nationally reported and hospital-level immunization data; (ii) a maternity unit audit and observation of vaccination practices; and (iii) staff interviews on knowledge and attitudes, practices and barriers.

#### Comparison of nationally reported and hospital-level immunization data

Hepatitis B immunization coverage rates were calculated with data obtained from two sources: National Department of Health (NDoH) and directly from the five hospitals.

##### *National level*

The NDoH collates data provided by all provincial health offices (PHOs) including the number of hospital births and vaccines administered at the facility. The timing of the administration of the birth-dose vaccine in relation to time of delivery is not captured through this system. The number of births and hepatitis B birth-dose vaccinations provided during 2006 at each of the selected hospitals was obtained from this database.

##### *Hospital level*

The five hospitals in this study maintain a paper-based birth register of all births that take place in that facility. This register records standard treatments provided to the baby at birth, including administration of vaccines, although the recording of this information is not routine for all maternity units. A separate immunization recording book is also maintained by the maternity units to document all vaccines administered to babies in the labour ward. The number of births and the number of hepatitis B birth doses administered over a minimum two-month period were obtained from the five hospitals using the birth register and the



immunization recording books. The two most recent complete months of data were collected with the months varying between hospitals according to the timing of the visit. If time permitted further months of hospital data were collected.

For both national and hospital-level data the proportion of newborns receiving a hepatitis B birth dose (coverage rate) in each facility was calculated by dividing the number of documented vaccines administered by the number of births reported for the same time period.

### **Maternity unit audit**

An audit was undertaken of the maternity unit at each hospital using a pre-tested standardized structured data collection tool covering the following main areas: vaccine and cold chain management, documentation, policies/guidelines and clinical practices. The most senior nursing staff member on duty at the time of the audit provided the information and observations of clinical practice were also documented during this process.

### **Staff interviews**

Confidential interviews with individual staff were conducted using a pre-tested standardized semi-structured interview tool. All willing maternity unit health care workers who were involved with vaccination and were on duty at the time of the visit were eligible to participate. The questionnaire collected sociodemographic details and contained a series of statements relating to HBV knowledge that required a true or false response from the interviewee. If the interviewee appeared to have difficulty understanding the question it was explained in different terms or translated into Tok Pisin. The questionnaire also contained open-ended questions related to common vaccination practices and barriers/enabling factors to delivery of hepatitis B vaccination.

Interview findings were entered into an Access database designed for this survey. The sociodemographic characteristics of the interviewed staff were analysed descriptively. Responses to the 14 knowledge statements were tallied and individuals grouped as either having  $\geq 10$  or  $\leq 9$  correct answers. A univariate analysis using STATA v9 with a cut off of  $p < 0.05$  was undertaken to identify predictors of staff knowledge.

## **Results**

### **Comparison of nationally reported and hospital-level immunization data**

The 2006 NDoH data for the five selected hospitals recorded that 17,395 children were born and 3265 received a hepatitis B birth-dose vaccination, giving an overall coverage rate of 19%. This rate varied widely across hospitals; three facilities reported coverage rates of less than 3% while the other two hospitals had coverage rates greater than 95%.

Based on data sourced directly from the five hospitals, the overall proportion of children receiving a hepatitis B birth dose was 79% with less variation by hospital. Four of the five selected hospitals showed coverage levels of greater than 80% for the birth dose in the months examined (Table 1, Figure 1).

### **Maternity unit audit**

#### *Vaccine and cold-chain management*

The vaccine management systems and cold-chain practices varied considerably across hospitals. Three hospitals maintained their vaccine stock in temperature-monitored, vaccine-only, ice-lined refrigerators. One refrigerator was located in the labour ward and the remaining two were located in other wards and could be accessed by labour ward staff twice a day at designated times. The remaining two hospitals used standard refrigerators without temperature monitors to maintain a one-week supply of vaccine in the labour ward. Both of these refrigerators were used for storage of other medications and/or staff lunches.

Four maternity units used vaccine carriers to store a small quantity of vaccines required for each shift. This practice is recommended as a means to minimize the opening and closing of vaccine refrigerators. The vaccine carriers in one unit were an older style with ill-fitting ice packs. The remaining maternity unit used vaccines directly from the refrigerator.

#### *Documentation, policies and guidelines*

All maternity units had good documentation of information in their birth

**TABLE 1**

NATIONAL HEALTH INFORMATION SYSTEM (NHIS) AND HOSPITAL-LEVEL HEPATITIS B BIRTH-DOSE COVERAGE RATES

Hospital	National Health Information System Jan-Dec 2006			Hospital-level records 2-4 month period 2007*			Difference between NHIS and hospital data
	Births	Birth doses	Coverage	Births	Birth doses	Coverage	
	N	N	%	N	N	%	
Hospital 1	2730	0	0	995	859	86	86
Hospital 2	10625	213	2	1711	1453	85	83
Hospital 3	1034	3	0.3	815	325	40	40
Hospital 4	1477	1560	106	457	430	94	12
Hospital 5	1529	1489	97	406	390	96	1
<b>Total</b>	<b>17395</b>	<b>3265</b>	<b>19</b>	<b>4384</b>	<b>3457</b>	<b>79</b>	<b>60</b>

\*Hospital 1 (Jul-Sep), Hospital 2 (Aug-Sep), Hospital 3 (Jul-Oct), Hospital 4 (Jul-Oct), Hospital 5 (Aug-Oct)

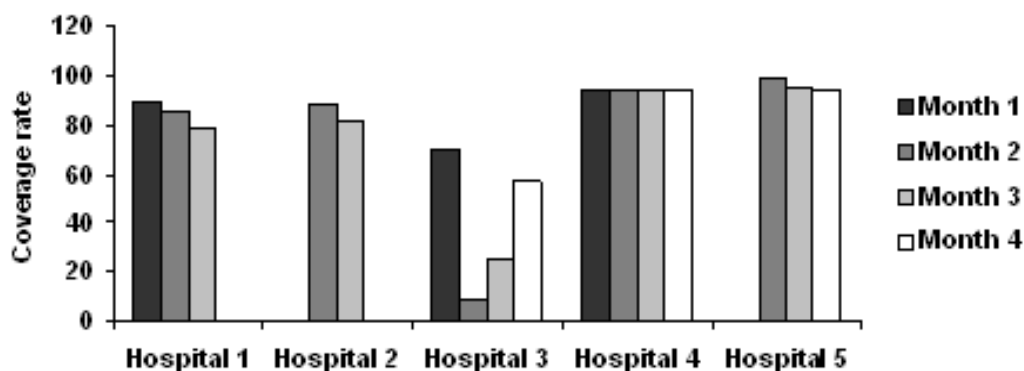


Figure 1. Hospital-level hepatitis B birth-dose coverage rates, 2007.

registers and vaccination record books, evidenced by complete (no obvious missing entries) and legible information. The maternity unit birth register was completed by the person who delivered the baby and the vaccination record book was completed by the person administering the vaccine. Neither register records the timing of the hepatitis B birth-dose administration in relation to birth. It was usual practice for mothers and babies to be transferred out of

the labour ward within two hours; therefore, it would be reasonable to assume that vaccines administered in the labour ward were given within 24 hours of birth.

The senior staff from four of the five maternity units reported the total number of births and vaccinations to the hospital records unit. The hospital records unit is responsible for forwarding these data to the PHO, who in turn report to the NDoH. The remaining

maternity unit reported vaccination data directly to the PHO and only provided data on the vaccinations provided in the post-natal ward and not those administered in the labour ward.

The staff at the maternity units said that all mothers received a record of immunization for their baby before discharge. Baby health books were provided free of charge at one hospital and cost one to three kina at the other hospitals. During the hospital visit it was recorded that only one maternity unit had a copy of the PNG immunization guidelines (16) and that it was kept in a locked office occupied by the sister in charge of the unit.

### *Clinical practices*

Hepatitis B vaccine was routinely provided in labour wards in all five hospitals; newborns transferred to the Special Care Nursery, however, had vaccination delayed until their condition was stable, unlike other routine interventions such as administration of vitamin K and eye ointment, which were provided irrespective of the newborn's condition. A range of incorrect practices were observed, including: changing needles after drawing up the vaccine (all units), large-bore needles being left inserted in the vial for drawing up purposes (two units) and hard plastic bottles being used instead of sharps disposal boxes (one unit). All units had multiple injecting equipment options and reported inconsistent supply of auto-disable syringes.

### **Staff interviews**

Interviews were conducted with 25 staff representing 28% of all staff on the maternity unit rosters at the five selected hospitals. The proportion of those interviewed varied from 23% to 33% across individual maternity units. The majority of staff interviewed were midwives (64%), were aged 36 years and above (72%) and had worked in maternity units for more than ten years (52%) (Table 2).

### *Immunization*

Of the 25 staff interviewed, nearly three-quarters (68%) were aware that HBV can be spread from mother to child at birth and 80% agreed that it was important to give hepatitis B vaccine within 24 hours of delivery (see Table 3). Further informal questioning

revealed that none of the interviewed staff were aware of the rationale for providing the birth dose within 24 hours of delivery.

### *Vaccine contraindications*

The only contraindication to administration of hepatitis B vaccine in newborns is a fever of  $>38.5^{\circ}\text{C}$ ; however, 52% of staff did not correctly identify this as a contraindication. On the other hand, a number of other conditions were incorrectly reported as reasons for delaying vaccination: prematurity (60%), low birthweight (48%) and a difficult birth such as forceps or vacuum delivery (36%). The majority of staff (56%) were unsure or unable to identify inflammation at the injection site and fever as potential side-effects of hepatitis B vaccination.

### *Vaccination practices and cold-chain maintenance*

The majority (88%) of staff correctly stated that hepatitis B vaccine is not administered subcutaneously but 52% of staff were unsure whether opened multidose vaccine vials could be reused or not. Discussions revealed a generally poor understanding of cold-chain management amongst staff. The majority of staff were unaware of the recommended practice of monitoring refrigerator temperatures and of the vaccine vial monitors used to monitor the heat exposure of individual vials.

### *HBV transmission*

Over 80% of staff correctly answered that people with hepatitis B can look and feel well but still spread the infection and that infection as a child can lead to chronic infection and liver disease. Although over 84% of staff knew that hepatitis B can be spread from person to person via infected body fluids, 52% incorrectly reported that it could be spread via contaminated food and water.

Univariate analysis showed no statistically significant association between sociodemographic characteristics (hospital, cadre, year of graduation, years working in maternity units, age group) and HBV knowledge.

### *Barriers to the delivery of a timely hepatitis B birth-dose vaccination*

Discussions with staff revealed that a lack

**TABLE 2**

SOCIODEMOGRAPHIC CHARACTERISTICS OF MATERNITY UNIT STAFF INTERVIEWED

Characteristics		Number interviewed	
		N	%
Cadre	Midwife	16	64
	Registered nurse	4	16
	Community health worker	5	20
Year of graduation	Before 1990	10	40
	1991-1995	1	4
	1996-2001	6	24
	2002-2007	8	32
Age (years)	<25	0	0
	25-30	4	16
	31-35	3	12
	36-40	8	32
	>40	10	40
Years working in maternity units	0-2	7	28
	3-5	3	12
	6-10	2	8
	>10	13	52

of hepatitis B vaccine stock in the labour ward was the main and often the only reason staff did not routinely offer vaccination to newborns. Daily collection of vaccine from another part of the hospital at designated times was also reported to be a barrier to maintaining adequate stock at the labour ward level. Staff confirmed that a poor understanding of contraindications to vaccination resulted in babies who were transferred to the Special Care Nursery having their hepatitis B vaccination delayed unnecessarily.

#### **Enabling factors in the delivery of a timely hepatitis B birth-dose vaccination**

Informal discussions with staff revealed that a designated vaccine refrigerator in the labour ward to maintain vaccine stock levels and having hepatitis B vaccination as part of routine care of the newborn were good strategies to ensure that newborns received a timely hepatitis B birth-dose vaccination.

Attendance at the 2007 Family Health

**TABLE 3**

HEPATITIS B KNOWLEDGE OF 25 MATERNITY UNIT STAFF IN FIVE PNG HOSPITALS, 2007

True or False knowledge statements	Incorrect or unsure answers	
	N	%
People with HBV infection can look and feel well but can still spread hepatitis B	3	12
Infection with hepatitis B as a child can lead to chronic infection and liver disease	4	16
Babies with a temperature of greater than 38.5°C should not be given the hepatitis B vaccination	13	52
Hepatitis B vaccine is administered subcutaneously	3	12
It is important that babies are given the hepatitis B birth dose within 24 hours of birth	5	20
Hepatitis B vaccine should never be frozen	10	40
Potential side-effects of hepatitis B vaccine include pain and/or inflammation at the injection site and fever	14	56
Vaccination should be delayed if the baby is born prematurely	15	60
Hepatitis B can be spread from person to person through contact with infected body fluids (blood, wound discharge, saliva etc)	4	16
Babies who have had a difficult birth (vacuum extraction, caesarian section etc) should have hepatitis B vaccination delayed	9	36
Hepatitis B can be spread via contaminated food and water	13	52
Low birthweight babies should have hepatitis B vaccination delayed	12	48
Hepatitis B can be spread from mother to child at birth	8	32
Opened multidose vials of hepatitis B vaccine can be returned to the refrigerator and used for subsequent doses	13	52

HBV = hepatitis B virus

Services coordinators' meeting by senior maternity and paediatric nursing staff from one hospital had resulted in the appointment of a designated immunization nurse and increased awareness within the labour ward of hepatitis B vaccination. Since this intervention, recorded hepatitis B birth-dose administration had risen from less than 40% to over 80% coverage. Service improvement planning undertaken at another hospital had resulted in a recent change in practice with hepatitis B vaccination now being administered in the labour ward rather than

at discharge from the post-natal ward, ensuring that it is given within 24 hours of birth.

Univariate analysis revealed no statistically significant sociodemographic predictors of knowledge or any difference between the knowledge of staff from the five hospitals.

### Discussion

The findings of the most recent (2005)



national vaccination coverage survey that only 23% of children born in health facilities received a hepatitis B birth dose was concerning. Similarly the combined coverage across the five hospitals at the national level through the National Health Information System (NHIS) was only 19%. The results of our review were far more encouraging with more than 80% of babies born in four of the five selected hospitals receiving a hepatitis B birth-dose vaccination before discharge. In the fifth, the proportion was 40%; however, during one of the months when data were collected structural work being conducted in the maternity unit resulted in increased logistical challenges accessing vaccine. Based on our review, the data available at the primary source, ie, maternity units, appears to be accurate and the wide discrepancy between the sources suggests there are limitations in reporting systems where information at the national level has passed through both hospital and PHO reporting processes.

While an 80% coverage rate in four of the five hospitals is encouraging, the missed vaccination opportunities for the other 20% or more of children born in these health facilities must be addressed. Two key barriers to hepatitis B birth-dose vaccination emerged during this study: i) lack of access to hepatitis B vaccine in the maternity units; and ii) limited staff knowledge and awareness.

Access to appropriately stored vaccine by maternity unit staff was compromised in various ways despite all five hospitals having adequate supply of hepatitis B vaccine. Two maternity units did not have their own refrigerators and were reliant on twice-daily collection of vaccine from other parts of the hospital. Of the three maternity units with refrigerators, only one had appropriate temperature-monitoring systems in place.

Limited staff knowledge and awareness resulted in vaccination being delayed for newborns transferred to the Special Care Nursery. The optimal timing for administration of the hepatitis B birth dose is within 24 hours of delivery and delays may reduce the effectiveness of the vaccine in preventing mother-to-child transmission of hepatitis B (12). It was concerning that most staff incorrectly believed that prematurity, low birthweight and a difficult birth were reasons to delay vaccination. Furthermore, although

many staff were aware that the hepatitis B birth dose should be given within 24 hours of delivery, none had a clear understanding of the rationale.

This study has some limitations: firstly, it was restricted to five major government-run hospitals and the results cannot be generalized to all hospitals in PNG. It is not unreasonable to expect that the main themes identified will be similar to those in other major hospitals; however, the situation in rural hospitals and health centres may be different as they are more likely to have issues with vaccine supply given the increased distance from the central supply stores. Secondly, only about a quarter of all staff on maternity unit rosters were included in the staff surveys; nevertheless, participation was high for the shift. It is unlikely that findings would vary considerably between shifts as all hospitals have rosters requiring staff to rotate through all shifts.

This study has found higher than anticipated hepatitis B birth-dose coverage levels in five major PNG hospitals and identified barriers to provision of the birth dose in maternity units. The large difference identified between coverage levels recorded at hospital level and that reported nationally suggests that there could be value in a more comprehensive audit and investigation of reporting practices. Accurate reporting, including time of vaccination in relation to birth, would greatly assist decision-making and planning at health facility, provincial and national level. The two key barriers to increasing vaccination coverage could be rectified by i) locating vaccine-specific refrigerators in maternity units and ii) training sessions or other strategies to raise awareness and improve knowledge about vaccine practices and the importance of the hepatitis B birth dose, among both clinical staff and management. Further studies in smaller and rural facilities would be useful to identify their specific issues and develop targeted strategies ensuring that all babies born in health facilities receive a timely hepatitis B birth dose.

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## The prevalence of HIV infection in women attending antenatal clinics in Fiji

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### SUMMARY

**HIV (human immunodeficiency virus) is an increasing concern in the South Pacific. We estimate, based on reported figures, that the prevalence of HIV infection in women attending antenatal clinics in Fiji in 2003 was 0.04%. The number of children born to HIV-positive mothers is small, though perinatal transmission appears to be high. Fiji's preliminary strategies for prevention of perinatal transmission have been significant, but require ongoing support and implementation.**

### Introduction

There is a significant push to implement HIV (human immunodeficiency virus) and AIDS (acquired immune deficiency syndrome) prevention programs in Pacific Island countries, including Fiji, to prevent a full-scale epidemic as is occurring in nearby Papua New Guinea (1, as cited in 2). Fiji's first official case of HIV infection was diagnosed in 1989. As of September 2003, 129 cases of HIV infection have been serologically confirmed (3). More than half of these cases have been diagnosed in the last three years, marking an increase in detection and possibly transmission.

In 1995 antenatal testing began at Fiji's only tertiary hospital, the Colonial War Memorial Hospital (CWMH). During a routine antenatal visit pregnant women were provided pre-HIV test counselling and subsequently offered an HIV-antibody test.

Approximately one-third of all deliveries in Fiji occur at CWMH (4). Other hospitals commenced antenatal HIV testing in later years. In 1999, Fiji adopted a prevention of mother-to-child transmission (pMTCT) protocol at CWMH based on the 'Thai short-long' regimen (5).

The Fiji protocol recommends maternal zidovudine (AZT) 300 mg twice daily from 34 weeks gestation to delivery by elective caesarian at 38 weeks, and 6 weeks of AZT 2 mg/kg four times daily for the infant. No AZT is administered during caesarian section as there is currently no access to intravenous AZT. Artificial feeding of infants is recommended for infants born to HIV-positive mothers.

The goals of this retrospective study were to estimate the prevalence of HIV infection in pregnant women, and to document cases of perinatal transmission and the outcome in

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affected infants.

### Methods

We retrospectively studied clinic records of all 23 hospitals providing antenatal care in Fiji. These hospitals had various HIV testing implementation dates ranging from 1995 to 2003. HIV-positive cases were compiled from the Ministry of Health, the Department of Statistics and laboratory records. All hospitals providing antenatal care were visited or contacted by telephone to verify that no cases had been missed. Only births that occurred when HIV testing was available at each specific hospital were included in estimates of prevalence.

The national HIV testing protocol states that children born to HIV-positive mothers are to be tested in the first week of life, with additional testing performed at follow-up visits and at 18 months of age. Initial testing for both pregnant women and infants was done by Serodia HIV-1/2 (Fujirebio Inc, Tokyo, Japan) antibody detection tests. Positive or indeterminate tests were retested on-site and at CWMH (the national laboratory). Confirmatory HIV testing by Western blot was performed at the Australian National Reference Laboratory (NRL).

The study was approved by the Fiji National Research Ethics Review Committee.

### Results

52,783 pregnant women were tested for HIV in Fiji from 1995 to 2003. The yearly maternal prevalence of HIV infection ranged from 0 to 0.05% (Table 1). In 2003, approximately 64% (10,837) of pregnant women received antenatal testing and 4 were found to be HIV positive (0.037%). Of the 12 HIV-positive women whose ethnicity was known, 11 (92%) were indigenous Fijian women.

13 HIV-positive women have given birth since the implementation of the pMTCT protocol. Of these, 5 women received antenatal AZT and delivered by elective caesarian, 3 women received antenatal AZT but delivered vaginally, and 5 women did not receive antenatal AZT and delivered vaginally. Of the 8 women receiving antenatal AZT, all initiated treatment between 35 and 37 weeks gestation. Of the 5 women not receiving any interventions, 4 women were diagnosed postpartum (3 of these women were determined to be HIV positive after their children developed symptoms of

**TABLE 1**

ANNUAL PREVALENCE OF HIV INFECTION IN WOMEN WITH ANTENATAL CLINIC BOOKINGS BEFORE DELIVERY

Year	Number HIV positive	Number tested	Prevalence (%)
1995	0	3681	0.000
1996	2	3829	0.052
1997	0	3984	0.000
1998	0	5172	0.000
1999	2	5431	0.037
2000	1	5705	0.018
2001	1	6147	0.016
2002	4	7997	0.050
2003	4	10837	0.037

HIV infection including failure to thrive and severe malnutrition) and 1 woman was previously known to be HIV positive but did not seek antenatal care before delivery. Of the 11 women with follow-up information, 4 died, 2 were sick with possible AIDS-related conditions and the other 5 were healthy. Causes of death included oesophageal candidiasis, cytomegalovirus infection and other AIDS-related conditions.

Medical records were identified for 12 children from 12 HIV-positive women. 10 of these deliveries occurred after 1999. Of those 10, all 8 children for whom their mother's status was known before delivery received AZT. The first HIV test occurred at birth for 5 children, at 1 month of age for 1 child, and by 4 months of age for the other 2 children. The last available test results for these 8 children were: 2 were positive (1 by NRL, 1 by Serodia), 3 were negative (2 by NRL, 1 by Serodia), and 3 were indeterminate (all NRL). Overall, 4 of these children are known to be dead (1 positive by NRL, 1 negative by NRL, 2 indeterminate) and 2 are known to be alive; the remaining 6 have not had recent follow-ups and their status is unknown. Co-morbidities in all of the children included scabies, malnutrition, failure to thrive, persistent pneumonia and anaemia, but the proximate cause of death was not able to be determined.

### Discussion

Our study documents a relatively low prevalence of HIV infection among pregnant women and infants. Although there has been an increase in HIV-positive mothers in Fiji, it is difficult to determine if this increase is a trend. There has been a rapid uptake of HIV testing in antenatal clinics in Fiji, progressing from the testing of 3681 women in 1995 to 10,837 women in 2003, although testing is still not universal. Given that approximately 89% of women in Fiji receive antenatal care and 97% of births occur in a hospital, antenatal testing provides a systematic method of providing HIV testing to a population in which prevention of disease transmission is possible (3).

Given the small number of cases and high loss to follow-up, our study is not able to assess the effectiveness of the current PMTCT policy, including elective caesarean sections (CS), in Fiji; however, transmission appears to be high. Performing CS in HIV-

positive women of unknown immune status has been shown to increase morbidity and mortality, particularly in women from developing country settings (6,7). In Fiji, women have access to sound perinatal services; therefore judgment on whether to perform a caesarian section or not will depend on the clinical status of the pregnant woman, as determined by the treating physician, in the absence of being able to determine immune status.

Interviews conducted during the course of the study revealed multiple challenges to further interruption of vertical transmission of HIV. Structural challenges include: lack of infrastructure for monitoring adherence; stigma and discrimination within the health care system; insufficient medical, social and mental health support programs; and limited counselling and confidentiality. Cultural traditions also need to be addressed. For example, one Fijian custom encourages the father's parents to determine the age at which the child should be weaned from breastfeeding. This is one of the barriers to the uptake of artificial feeding, along with the stigma and suspicion associated with women who do not breastfeed their infants.

The current World Health Organization guidelines recommend exclusive formula feeding, if it is "acceptable, feasible, affordable, sustainable and safe"; otherwise exclusive breastfeeding is recommended (8). These guidelines stem from the large reduction in diarrhoeal and respiratory disease in breastfed infants in developing countries (9). The breastmilk immune factors of HIV-infected women are similar to those of HIV-uninfected women; this argues for exclusive breastfeeding for the first 4-6 months of life followed by early and sudden weaning, which provides the best protection from early infant death for babies of HIV-positive mothers in developing countries or settings where mixed methods of feeding are used (10-13). In the context of Fiji, a low-middle-income country, with relatively low infant mortality indicating a sound health care system and reasonable access to environmental hygiene practices, it is not clear if exclusive breastfeeding with rapid weaning should be the universal recommendation for all. However, given the social stigma associated with not breastfeeding, the same recommendation as for higher-mortality countries may well be the preferred option.



Counselling (pre- and post-test) is not only necessary, but it is also an opportunity for HIV education of the general population rather than just the positive women. The counselling should be continued throughout the pregnancy and include infant feeding, family planning, nutrition, overall care, and support. Additionally, national testing guidelines, alteration and implementation of the pMTCT protocol, increased laboratory capacity for early diagnosis and improved monitoring of HIV-positive women and children are required and are currently being addressed by national policy.

This study has several limitations, including small numbers, lack of a country-wide antenatal clinic HIV screening program, high loss to follow-up, lack of definitive diagnosis of children in Fiji, and inability to assess adherence to the antiretroviral therapy and artificial feeding protocols. Our data are limited, but they document the annual prevalence of HIV infection in women visiting antenatal clinics and give insight into the climate and challenges surrounding HIV in Fiji.

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Malaria in pregnancy in the Solomon Islands: barriers to prevention and control.

*Am J Trop Med Hyg* 2008 Mar;78(3):449-454.

A study of malaria in pregnancy (MIP) was undertaken in Marovo Lagoon, Solomon Islands, to evaluate pregnancy-specific control strategies for malaria. Peripheral parasitemia was present in 18% (19/106) of women: 15 *Plasmodium falciparum* and 4 *P. vivax*. Primigravidae were twice as likely to be parasitemic as multigravidae (31% versus 14%; relative risk: 2.24; 95% confidence interval: 1.01-4.96;  $p = 0.05$ ). Although ante-natal clinic attendance was high, women booked late (mean, 19.7 weeks) and attended irregularly. Free insecticide-treated nets (ITN) were not distributed despite government policy. Primigravidae were less likely to have an ITN in their homes than multigravidae (relative risk: 2.13; 95% confidence interval: 1.03-4.40). Coverage with chloroquine prophylaxis was low. This study revealed barriers to control of MIP at both the health service and client level. To develop an evidence-based malaria control policy in pregnancy for this region, further study of the epidemiology of malaria and its effects, including social and behavioral aspects, is needed.

- 2 **Bulletin of the World Health Organization.**

Primary health care: Fiji's broken dream.

*Bull World Health Organ* 2008 Mar;86(3):166-167.

- 3 **Chanteau S, Roux JF.**

Bancroftian lymphatic filariasis: toward its elimination from the Pacific? [Fr]

*Bull Soc Pathol Exot* 2008 Jun;101(3):254-260.

The region of the Pacific is historically affected by lymphatic filariasis (LF). Following the World Health Assembly resolution in 1997, the Global Program to Eliminate Lymphatic Filariasis (GPELF) was launched. In the Pacific, the World Health Organization (WHO) has implemented from 1999 the Pacific Program to Eliminate Lymphatic Filariasis (PacELF) bringing together the 22 countries and territories in a common effort to eliminate the disease. The strategy is based on mass drug administration (MDA); an annual single dose during 5 years of a diethylcarbamazine/albendazole combination is distributed to all the populations at risk. Among the 22 countries and territories of the Pacific, 16 are endemic and 6 are non-endemic. The classification is based according to the filarial antigen prevalence being above or below 1%. MDA is indicated when the rate of the filarial antigen prevalence is  $>1\%$ . The objective of PacELF is to reduce this rate down to  $<1\%$ , the threshold under which transmission is supposed to be stopped. From 1999 to 2007, 14 of the 16 endemic countries organized MDA. Eleven of them completed the cycle of 5 treatments and even beyond. But these MDA reached only 19% of the at-risk population, mainly because of logistic difficulties in Papua New Guinea,

the most populated country in the Pacific. The investigations carried out in sentinel sites showed a public health impact, by the fall in the number of microfilaria carriers, often down to a rate  $<1\%$ . However, the rate of circulating antigen prevalence often remained above the required threshold of 1%. Prevalence surveys carried out in 2007, in different endemic countries, revealed the necessity to intensify efforts and to refine the strategy for the elimination of LF from the Pacific. A lot of progress was made, but a few problems were identified. Reevaluations are urgently required and are in progress. They deal with maintenance of the MDA coverage rates in the face of a certain lassitude in the populations and among health staff, the methods to evaluate the effectiveness of MDA, the reliability of the diagnostic tools to decide when to stop MDA and to certify the absence of transmission, the relevance of universal biological criteria for the whole Pacific area, and the need for active surveillance for several years after stopping MDA, particularly in the countries affected by the very efficient vector *Aedes polynesiensis*. Seven years after its launching, despite undeniable success, the PacELF program has not achieved its very ambitious goal of stopping transmission. Three years before its term, strong efforts have to be made and additional strategies implemented. However, it is reasonable to expect the prolongation of the program in order to achieve the final objective. Beyond that, in some countries, it will still be necessary to ensure a sustained global drug pressure and an active surveillance program to prevent the re-emergence of the disease.

- 4 **Chao YC, Huang CS, Lee CN, Chang SY, King CC, Kao CL.**

Higher infection of dengue virus serotype 2 in human monocytes of patients with G6PD deficiency.

*PLoS ONE* 2008 Feb 13;3(2):e1557.

The prevalence of glucose-6-phosphate dehydrogenase (G6PD) deficiency is high in Asia. An ex vivo study was conducted to elucidate the association of G6PD deficiency and dengue virus (DENV) infection when many Asian countries are hyper-endemic. Human monocytes from peripheral mononuclear cells collected from 12 G6PD-deficient patients and 24 age-matched controls were infected with one of two DENV serotype 2 (DENV-2) strains – the New Guinea C strain (from a case of dengue fever) or the 16681 strain (from a case of dengue hemorrhagic fever) with a multiplicity of infection of 0.1. The infectivity of DENV-2 in human monocytes was analyzed by flow cytometry. Experimental results indicated that the monocytes of G6PD-deficient patients exhibited a greater level of infection with DENV-2 New Guinea C strain than did those from healthy controls [mean  $\pm$  SD:  $33.6\% \pm 3.5$  vs  $20.3\% \pm 6.2$ ,  $p < 0.01$ ]. Similar observations were made of infection with the DENV-2 16681 strain [ $40.9\% \pm 3.9$  vs  $27.4\% \pm 7.1$ ,  $p < 0.01$ ]. To our knowledge, this study demonstrates for the first time higher infection of human monocytes in G6PD

patients with the dengue virus, which may be important in increasing epidemiological transmission and perhaps with the potential to develop more severe cases pathologically.

**5 Chaves LF, Kaneko A, Taleo G, Pascual M, Wilson ML.**

Malaria transmission pattern resilience to climatic variability is mediated by insecticide-treated nets. *Malar J* 2008 Jun 2;7:100.

**BACKGROUND:** Malaria is an important public-health problem in the archipelago of Vanuatu and climate has been hypothesized as an important influence on transmission risk. Beginning in 1988, a major intervention using insecticide-treated bed nets (ITNs) was implemented in the country in an attempt to reduce *Plasmodium* transmission. To date, no study has addressed the impact of ITN intervention in Vanuatu, how it may have modified the burden of disease, and whether there were any changes in malaria incidence that might be related to climatic drivers. **METHODS AND FINDINGS:** Monthly time series (January 1983 through December 1999) of confirmed *Plasmodium falciparum* and *Plasmodium vivax* infections in the archipelago were analysed. During this 17-year period, malaria dynamics underwent a major regime shift around May 1991, following the introduction of bed nets as a control strategy in the country. By February of 1994 disease incidence from both parasites was reduced by at least 50%, when at most 20% of the population at risk was covered by ITNs. Seasonal cycles, as expected, were strongly correlated with temperature patterns, while inter-annual cycles were associated with changes in precipitation. Following the bed net intervention, the influence of environmental drivers of malaria dynamics was reduced by 30-80% for climatic forces, and 33-54% for other factors. A time lag of about five months was observed for the qualitative change ("regime shift") between the two parasites, the change occurring first for *P. falciparum*. The latter might be explained by interspecific interactions between the two parasites within the human hosts and their distinct biology, since *P. vivax* can relapse after a primary infection. **CONCLUSION:** The Vanuatu ITN programme represents an excellent example of implementing an infectious disease control programme. The distribution was undertaken to cover a large, local proportion (approximately 80%) of people in villages where malaria was present. The successful coverage was possible because of the strategy for distribution of ITNs by prioritizing the free distribution to groups with restricted means for their acquisition, making the access to this resource equitable across the population. These results emphasize the need to implement infectious disease control programmes focusing on the most vulnerable populations.

**6 Chung S, Watters D.**

Academic surgery in Papua New Guinea. *ANZ J Surg* 2008 May;78(5):347-349.

**7 Fotinatos N, Warmington A, Walker T, Pilbeam M.**

*Trichomonas vaginalis* in Vanuatu. *Aust J Rural Health* 2008 Feb;16(1):23-27.

**OBJECTIVE:** To assess the prevalence of *Trichomonas vaginalis* in two island populations of Vanuatu using the Pap smear as the screening technique. **STUDY DESIGN:** Women were

randomly selected from specific sites on the islands of Efate (urban setting) and Ambae (rural setting). Pap smears were collected, screened and reported. **SETTING:** The first collection site was the Women's Health/Antenatal Care Clinic at Vila Central Hospital in Port Vila, the capital city located on the island of Efate, and the second collection site was a rural village on a sparsely populated inhabited northern island, Ambae. **PARTICIPANTS:** A total of 905 Ni-Vanuatu women participants: Efate (n = 562) 62%, and Ambae (n = 343) 38%. The mean age was 35.8 years: Efate 32.6 years, and Ambae 40.8 years. **MAIN OUTCOME MEASURE:** The presence or absence of *T. vaginalis* in these Pap smears was documented during the study's cervical screening process. **RESULTS:** The overall prevalence of *T. vaginalis* within the study participants was 25.3%. Almost half of the infected sample group were in the age group of 30-39 years (43.8%). The prevalence of *T. vaginalis* in Efate was 14.7%, compared with 43.4% in Ambae. **CONCLUSION:** The prevalence of *T. vaginalis* in Vanuatu women is significantly higher than in developed countries. Women in rural settings are less likely to have access to sexually transmitted disease prevention and treatment programs, thus contributing to high infection rates compared with women in urban settings. Cultural and educational differences in the rural setting might also contribute to higher sexually transmitted disease rates among these women.

**8 Fowkes FJ, Allen SJ, Allen A, Alpers MP, Weatherall DJ, Day KP.**

Increased microerythrocyte count in homozygous alpha(+)-thalassaemia contributes to protection against severe malarial anaemia. *PLoS Med* 2008 Mar 18;5(3):e56.

**BACKGROUND:** The heritable haemoglobinopathy alpha(+)-thalassaemia is caused by the reduced synthesis of alpha-globin chains that form part of normal adult haemoglobin (Hb). Individuals homozygous for alpha(+)-thalassaemia have microcytosis and an increased erythrocyte count. Alpha(+)-thalassaemia homozygosity confers considerable protection against severe malaria, including severe malarial anaemia (SMA) (Hb concentration <50 g/l), but does not influence parasite count. We tested the hypothesis that the erythrocyte indices associated with alpha(+)-thalassaemia homozygosity provide a haematological benefit during acute malaria. **METHODS AND FINDINGS:** Data from children living on the north coast of Papua New Guinea who had participated in a case-control study of the protection afforded by alpha(+)-thalassaemia against severe malaria were reanalysed to assess the genotype-specific reduction in erythrocyte count and Hb levels associated with acute malarial disease. We observed a reduction in median erythrocyte count of approximately  $1.5 \times 10^{12}/l$  in all children with acute falciparum malaria relative to values in community children ( $p < 0.001$ ). We developed a simple mathematical model of the linear relationship between Hb concentration and erythrocyte count. This model predicted that children homozygous for alpha(+)-thalassaemia lose less Hb than children of normal genotype for a reduction in erythrocyte count of  $>1.1 \times 10^{12}/l$  as a result of the reduced mean cell Hb in homozygous alpha(+)-thalassaemia. In addition, children homozygous for alpha(+)-thalassaemia require a 10% greater reduction in erythrocyte count than children of normal genotype

( $p = 0.02$ ) for Hb concentration to fall to 50 g/l, the cutoff for SMA. We estimated that the haematological profile in children homozygous for alpha(+)-thalassaemia reduces the risk of SMA during acute malaria compared to children of normal genotype (relative risk 0.52; 95% confidence interval [CI] 0.24-1.12,  $p = 0.09$ ). CONCLUSIONS: The increased erythrocyte count and microcytosis in children homozygous for alpha(+)-thalassaemia may contribute substantially to their protection against SMA. A lower concentration of Hb per erythrocyte and a larger population of erythrocytes may be a biologically advantageous strategy against the significant reduction in erythrocyte count that occurs during acute infection with the malaria parasite *Plasmodium falciparum*. This haematological profile may reduce the risk of anaemia by other *Plasmodium* species, as well as other causes of anaemia. Other host polymorphisms that induce an increased erythrocyte count and microcytosis may confer a similar advantage.

- 9 **Fowkes FJ, Michon P, Pilling L, Ripley RM, Tavul L, Imrie HJ, Woods CM, Mgone CS, Luty AJ, Day KP.**

Host erythrocyte polymorphisms and exposure to *Plasmodium falciparum* in Papua New Guinea. *Malar J* 2008 Jan 3;7:1.

BACKGROUND: The protection afforded by human erythrocyte polymorphisms against the malaria parasite, *Plasmodium falciparum*, has been proposed to be due to reduced ability of the parasite to invade or develop in erythrocytes. If this were the case, variable levels of parasitaemia and rates of seroconversion to infected-erythrocyte variant surface antigens (VSA) should be seen in different host genotypes. METHODS: To test this hypothesis, *P. falciparum* parasitaemia and anti-VSA antibody levels were measured in a cohort of 555 asymptomatic children from an area of intense malaria transmission in Papua New Guinea. Linear mixed models were used to investigate the effect of alpha+ thalassaemia, complement receptor-1 and South-east Asian ovalocytosis, as well as glucose-6-phosphate dehydrogenase deficiency and ABO blood group on parasitaemia and age-specific seroconversion to VSA. RESULTS: No host polymorphism showed a significant association with both parasite prevalence/density and age-specific seroconversion to VSA. CONCLUSION: Host erythrocyte polymorphisms commonly found in Papua New Guinea do not effect exposure to blood stage *P. falciparum* infection. This contrasts with data for sickle cell trait and highlights that the above-mentioned polymorphisms may confer protection against malaria via distinct mechanisms.

- 10 **Friedlaender JS, Friedlaender FR, Reed FA, Kidd KK, Kidd JR, Chambers GK, Lea RA, Loo JH, Koki G, Hodgson JA, Merriwether DA, Weber JL.** The genetic structure of Pacific Islanders. *PLoS Genet* 2008 Jan;4(1):e19.

Human genetic diversity in the Pacific has not been adequately sampled, particularly in Melanesia. As a result, population relationships there have been open to debate. A genome scan of autosomal markers (687 microsatellites and 203 insertions/deletions) on 952 individuals from 41 Pacific populations now provides the basis for understanding the remarkable nature of Melanesian variation, and for a more accurate comparison of these Pacific populations with previously studied groups from other

regions. It also shows how textured human population variation can be in particular circumstances. Genetic diversity within individual Pacific populations is shown to be very low, while differentiation among Melanesian groups is high. Melanesian differentiation varies not only between islands, but also by island size and topographical complexity. The greatest distinctions are among the isolated groups in large island interiors, which are also the most internally homogeneous. The pattern loosely tracks language distinctions. Papuan-speaking groups are the most differentiated, and Austronesian or Oceanic-speaking groups, which tend to live along the coastlines, are more intermixed. A small 'Austronesian' genetic signature (always <20%) was detected in less than half the Melanesian groups that speak Austronesian languages, and is entirely lacking in Papuan-speaking groups. Although the Polynesians are also distinctive, they tend to cluster with Micronesians, Taiwan Aborigines, and East Asians, and not Melanesians. These findings contribute to a resolution to the debates over Polynesian origins and their past interactions with Melanesians. With regard to genetics, the earlier studies had heavily relied on the evidence from single locus mitochondrial DNA or Y chromosome variation. Neither of these provided an unequivocal signal of phylogenetic relations or population intermixture proportions in the Pacific. Our analysis indicates the ancestors of Polynesians moved through Melanesia relatively rapidly and only intermixed to a very modest degree with the indigenous populations there.

- 11 **Genton B, D'Acremont V, Rare L, Baea K, Reeder JC, Alpers MP, Müller I.**

*Plasmodium vivax* and mixed infections are associated with severe malaria in children: a prospective cohort study from Papua New Guinea. *PLoS Med* 2008 Jun 17;5(6):e127.

BACKGROUND: Severe malaria (SM) is classically associated with *Plasmodium falciparum* infection. Little information is available on the contribution of *P. vivax* to severe disease. There are some epidemiological indications that *P. vivax* or mixed infections protect against complications and deaths. A large morbidity surveillance conducted in an area where the four species coexist allowed us to estimate rates of SM among patients infected with one or several species. METHODS AND FINDINGS: This was a prospective cohort study conducted within the framework of the Malaria Vaccine Epidemiology and Evaluation Project. All presumptive malaria cases presenting at two rural health facilities over an 8-y period were investigated with history taking, clinical examination, and laboratory assessment. Case definition of SM was based on the World Health Organization (WHO) criteria adapted for the setting (i.e., clinical diagnosis of malaria associated with asexual blood stage parasitaemia and recent history of fits, or coma, or respiratory distress, or anaemia [haemoglobin <5 g/dl]). Out of 17,201 presumptive malaria cases, 9,537 (55%) had a confirmed *Plasmodium* parasitaemia. Among those, 6.2% (95% confidence interval [CI] 5.7%-6.8%) fulfilled the case definition of SM, most of them in children <5 years. In this age group, the proportion of SM was 11.7% (10.4%-13.2%) for *P. falciparum*, 8.8% (7.1%-10.7%) for *P. vivax*, and 17.3% (11.7%-24.2%) for mixed *P. falciparum* and *P. vivax* infections. *P. vivax* SM presented more often with respiratory distress than did *P. falciparum* (60% versus 41%,  $p = 0.002$ ),



but less often with anaemia (19% versus 41%,  $p = 0.0001$ ). **CONCLUSION:** *P. vivax* monoinfections as well as mixed *Plasmodium* infections are associated with SM. There is no indication that mixed infections protected against SM. Interventions targeted toward *P. falciparum* only might be insufficient to eliminate the overall malaria burden, and especially severe disease, in areas where *P. falciparum* and *P. vivax* coexist.

**12 Gilpin CM, Simpson G, Vincent S, O'Brien TP, Knight TA, Globan M, Coulter C, Konstantinos A.**

Evidence of primary transmission of multidrug-resistant tuberculosis in the Western Province of Papua New Guinea.

*Med J Aust* 2008 Feb 4;188(3):148-152.

**OBJECTIVE:** To review patient outcomes and the molecular epidemiology of multidrug-resistant tuberculosis (MDR-TB) strains isolated from patients living in the Western Province of Papua New Guinea (PNG) seeking treatment in Australia. **DESIGN, SETTING AND PARTICIPANTS:** Review of all cases of MDR-TB among people living in the open border region between the Western Province of PNG and the Torres Strait Islands of Australia who presented to health clinics in the region between 2000 and 2006. All cases of suspected TB were bacteriologically confirmed at the time of presentation by the Mycobacterium Reference Laboratory in Brisbane. **MAIN OUTCOME MEASURES:** Drug resistance patterns; drug use and duration; molecular typing of TB strains; patient outcomes. **RESULTS:** Between 2000 and 2006, 60 patients from the Western Province of PNG were diagnosed with TB, of which 15 had MDR-TB. Mortality was high, although no patient who was able to maintain access to supervised therapy died. All 15 MDR-TB isolates were Beijing-family strains showing the same unique mycobacterial interspersed repetitive unit (MIRU) profile, with the exception of a single strain that differed by a single repeat at one locus. Restriction fragment length polymorphism (RFLP) typing on 10 of these strains further differentiated them into two distinct clusters. **CONCLUSION:** Transmission of MDR-TB is occurring in the Western Province of PNG. Additional resources are urgently needed to interrupt the ongoing transmission of MDR-TB from the Western Province of PNG to the Torres Strait Islands. Good supervision and management of patient treatment, which includes ensuring a regular supply of second-line anti-TB drugs, are essential elements of TB control.

**13 Gutiérrez M, Suyama TL, Engene N, Wingerd JS, Matainaho T, Gerwick WH.**

Apratoxin D, a potent cytotoxic cyclodepsipeptide from Papua New Guinea collections of the marine cyanobacteria *Lyngbya majuscula* and *Lyngbya sordida*.

*J Nat Prod* 2008 Jun;71(6):1099-1103. Epub 2008 Apr 30.

Cancer cell toxicity-guided fractionation of extracts of the Papua New Guinea marine cyanobacteria *Lyngbya majuscula* and *Lyngbya sordida* led to the isolation of apratoxin D (1). Compound 1 contains the same macrocycle as apratoxins A and C but possesses the novel 3,7-dihydroxy-2,5,8,10,10-pentamethylundecanoic acid as the polyketide moiety. The planar structures and stereostructures of compound 1 were determined

by extensive 1D and 2D NMR and MS data analyses and by comparison with the spectroscopic data of apratoxins A and C. Apratoxin D (1) showed potent in vitro cytotoxicity against H-460 human lung cancer cells with an IC<sub>50</sub> value of 2.6 nM.

**14 Habgood PJ, Franklin NR.**

The revolution that didn't arrive: a review of Pleistocene Sahul.

*J Hum Evol* 2008 Aug;55(2):187-222. Epub 2008 May 15.

There is a 'package' of cultural innovations that are claimed to reflect modern human behaviour. The introduction of the 'package' has been associated with the Middle-to-Upper Palaeolithic transition and the appearance in Europe of modern humans. It has been proposed that modern humans spread from Africa with the 'package' and colonised not only Europe but also southern Asia and Australia (McBrearty and Brooks, 2000; Mellars, 2006a). In order to evaluate this proposal, we explore the late Pleistocene archaeological record of Sahul, the combined landmass of Australia and Papua New Guinea, for indications of these cultural innovations at the earliest sites. It was found that following initial occupation of the continent by anatomically and behaviourally modern humans, the components were gradually assembled over a 30,000-year period. We discount the idea that the 'package' was lost en route to Sahul and assess the possibility that the 'package' was not integrated within the material culture of the initial colonising groups because they may not have been part of a rapid colonisation process from Africa. As the cultural innovations appear at different times and locations within Sahul, the proposed 'package' of archaeologically visible traits cannot be used to establish modern human behaviour. Whilst the potential causal role of increasing population densities/pressure in the appearance of the 'package' of modern human behaviour in the archaeological record is acknowledged, it is not seen as the sole explanation because the individual components of the 'package' appear at sites that are widely separated in space and time.

**15 Hasan AU, Suguri S, Fujimoto C, Itaki RL, Harada M, Kawabata M, Bugoro H, Albino B, Tsukahara T, Hombhanje F, Masta A.**

Phylogeography and dispersion pattern of *Anopheles farauti* sensu stricto mosquitoes in Melanesia.

*Mol Phylogenet Evol* 2008 Feb;46(2):792-800.

**16 Hawkins VN, Auliff A, Prajapati SK, Rungsihirunrat K, Hapuarachchi HC, Maestre A, O'Neil MT, Cheng Q, Joshi H, Na-Bangchang K, Sibley CH.**

Multiple origins of resistance-conferring mutations in *Plasmodium vivax* dihydrofolate reductase.

*Malar J* 2008 Apr 28;7:72.

**BACKGROUND:** In order to maximize the useful therapeutic life of antimalarial drugs, it is crucial to understand the mechanisms by which parasites resistant to antimalarial drugs are selected and spread in natural populations. Recent work has demonstrated that pyrimethamine-resistance conferring mutations in *Plasmodium falciparum* dihydrofolate reductase (dhfr) have arisen rarely de novo, but spread widely in Asia and Africa. The origin and spread of mutations in *Plasmodium vivax* dhfr were assessed by constructing haplotypes based on sequencing dhfr and its flanking regions.



**METHODS:** The *P. vivax dhfr* coding region, 792 bp upstream and 683 bp downstream were amplified and sequenced from 137 contemporary patient isolates from Colombia, India, Indonesia, Papua New Guinea, Sri Lanka, Thailand, and Vanuatu. A repeat motif located 2.6 kb upstream of *dhfr* was also sequenced from 75 of 137 patient isolates, and mutational relationships among the haplotypes were visualized using the programme Network. **RESULTS:** Synonymous and non-synonymous single nucleotide polymorphisms (SNPs) within the *dhfr* coding region were identified, as was the well-documented in-frame insertion/deletion (indel). SNPs were also identified upstream and downstream of *dhfr*, with an indel and a highly polymorphic repeat region identified upstream of *dhfr*. The regions flanking *dhfr* were highly variable. The double mutant (58R/117N) *dhfr* allele has evolved from several origins, because the 58R is encoded by at least 3 different codons. The triple (58R/61M/117T) and quadruple (57L/61M/117T/173F, 57L/58R/61M/117T and 57L/58R/61M/117T) mutant alleles had at least three independent origins in Thailand, Indonesia, and Papua New Guinea/Vanuatu. **CONCLUSION:** It was found that the *P. vivax dhfr* coding region and its flanking intergenic regions are highly polymorphic and that mutations in *P. vivax dhfr* that confer antifolate resistance have arisen several times in the Asian region. This contrasts sharply with the selective sweep of rare antifolate resistant alleles observed in the *P. falciparum* populations in Asia and Africa. The finding of multiple origins of resistance-conferring mutations has important implications for drug policy.

- 17 **Holden C.**  
Evolutionary genetics. Polynesians took the express train through Melanesia to the Pacific.  
*Science* 2008 Jan 18;319(5861):270.

- 18 **Ichiyama T, Matsushige T, Siba P, Suarkia D, Takasu T, Miki K, Furukawa S.**  
Cerebrospinal fluid levels of matrix metalloproteinase-9 and tissue inhibitor of metalloproteinase-1 in subacute sclerosing panencephalitis.  
*J Infect* 2008 May;56(5):376-380. Epub 2008 Apr 18.

**OBJECTIVES:** To investigate the brain inflammation and damage in subacute sclerosing panencephalitis (SSPE), the cerebrospinal fluid (CSF) concentrations of matrix metalloproteinase-9 (MMP-9) and tissue inhibitor of metalloproteinase-1 (TIMP-1) were determined in SSPE patients. **METHODS:** CSF MMP-9 and TIMP-1 levels were measured in 23 patients with SSPE in Papua New Guinea by ELISA. **RESULTS:** CSF MMP-9 levels and MMP-9/TIMP-1 ratios of SSPE patients were significantly higher than controls ( $p < 0.001$  and  $p = 0.005$ , respectively). There were no significant differences in CSF TIMP-1 levels between SSPE patients and controls. **CONCLUSIONS:** Previous studies suggested that CSF MMP-9 levels reflect inflammatory damage to the brain. Our findings suggest that the MMP-9 level in CSF is an indicator of inflammatory damage to the brain in SSPE.

- 19 **Karl S, David M, Moore L, Grimberg BT, Michon P, Mueller I, Zborowski M, Zimmerman PA.**  
Enhanced detection of gametocytes by magnetic deposition microscopy predicts higher potential for *Plasmodium falciparum* transmission.

*Malar J* 2008 Apr 25;7:66.

**BACKGROUND:** Aggregated haemozoin crystals within malaria-infected erythrocytes confer susceptibility of parasitized cells to a magnetic field. Here the utility of this method for diagnosis of human malaria is evaluated in a malaria-endemic region of Papua New Guinea (PNG). **METHODS AND FINDINGS:** Individuals with *Plasmodium falciparum* malaria symptoms ( $n = 55$ ) provided samples for conventional blood smear (CBS) and magnetic deposition microscopy (MDM) diagnosis. Standard Giemsa staining and light microscopy was performed to evaluate all preparations. *Plasmodium falciparum* parasitaemia observed on MDM slides was consistently higher than parasitaemia observed by CBS for ring (CBS = 2.6 vs. MDM = 3.4%; t-test  $p$ -value = 0.13), trophozoite (CBS = 0.5 vs. MDM = 1.6%; t-test  $p$ -value = 0.01), schizont (CBS = 0.003 vs. MDM = 0.1%; t-test  $p$ -value = 0.08) and gametocyte (CBS = 0.001 vs. MDM = 0.4%; t-test  $p$ -value = 0.0002) parasitaemias. Gametocyte prevalence determined by CBS compared to MDM increased from 7.3% to 45%, respectively. **CONCLUSION:** MDM increased detection sensitivity of *P. falciparum*-infected, haemozoin-containing erythrocytes from infected humans while maintaining detection of ring-stage parasites. Gametocyte prevalence five-fold higher than observed by CBS suggests higher malaria transmission potential in PNG endemic sites compared to previous estimates.

- 20 **Kayser M, Choi Y, van Oven M, Mona S, Brauer S, Trent RJ, Suarkia D, Schiefenhövel W, Stoneking M.**

The impact of the Austronesian expansion: evidence from mtDNA and Y chromosome diversity in the Admiralty Islands of Melanesia.  
*Mol Biol Evol* 2008 Jul;25(7):1362-1374. Epub 2008 Apr 3.

The genetic ancestry of Polynesians can be traced to both Asia and Melanesia, which presumably reflects admixture occurring between incoming Austronesians and resident non-Austronesians in Melanesia before the subsequent occupation of the greater Pacific; however, the genetic impact of the Austronesian expansion to Melanesia remains largely unknown. We therefore studied the diversity of nonrecombining Y chromosomal (NRY) and mitochondrial (mt) DNA in the Admiralty Islands, located north of mainland Papua New Guinea, and updated our previous data from Asia, Melanesia, and Polynesia with new NRY markers. The Admiralties are occupied today solely by Austronesian-speaking groups, but their human settlement history goes back 20,000 years prior to the arrival of Austronesians about 3,400 years ago. On the Admiralties, we found substantial mtDNA and NRY variation of both Austronesian and non-Austronesian origins, with higher frequencies of Asian mtDNA and Melanesian NRY haplogroups, similar to previous findings in Polynesia and perhaps as a consequence of Austronesian matrilocality. Thus, the Austronesian language replacement on the Admiralties (and elsewhere in Island Melanesia and coastal New Guinea) was accompanied by an incomplete genetic replacement that is more associated with mtDNA than with NRY diversity. These results provide further support for the 'Slow Boat' model of Polynesian origins, according to which Polynesian ancestors originated from East Asia but genetically mixed with Melanesians before colonizing the Pacific. We also observed that non-Austronesian

groups of coastal New Guinea and Island Melanesia had significantly higher frequencies of Asian mtDNA haplogroups than of Asian NRY haplogroups, suggesting sex-biased admixture perhaps as a consequence of non-Austronesian patrilocality. We additionally found that the predominant NRY haplogroup of Asian origin in the Admiralties (O-M110) likely originated in Taiwan, thus providing the first direct Y chromosome evidence for a Taiwanese origin of the Austronesian expansion. Furthermore, we identified a NRY haplogroup (K-P79, also found on the Admiralties) in Polynesians that most likely arose in the Bismarck Archipelago, providing the first direct link between northern Island Melanesia and Polynesia. These results significantly advance our understanding of the impact of the Austronesian expansion and human history in the Pacific region.

- 21 **Kayser M, Lao O, Saar K, Brauer S, Wang X, Nürnberg P, Trent RJ, Stoneking M.** Genome-wide analysis indicates more Asian than Melanesian ancestry of Polynesians. *Am J Hum Genet* 2008 Jan;82(1):194-198.

Analyses of mitochondrial DNA (mtDNA) and nonrecombining Y chromosome (NRY) variation in the same populations are sometimes concordant but sometimes discordant. Perhaps the most dramatic example known of the latter concerns Polynesians, in which about 94% of Polynesian mtDNAs are of East Asian origin, while about 66% of Polynesian Y chromosomes are of Melanesian origin. Here we analyze on a genome-wide scale, to our knowledge for the first time, the origins of the autosomal gene pool of Polynesians by screening 377 autosomal short tandem repeat (STR) loci in 47 Pacific Islanders and compare the results with those obtained from 44 Chinese and 24 individuals from Papua New Guinea. Our data indicate that on average about 79% of the Polynesian autosomal gene pool is of East Asian origin and 21% is of Melanesian origin. The genetic data thus suggest a dual origin of Polynesians with a high East Asian but also considerable Melanesian component, reflecting sex-biased admixture in Polynesian history in agreement with the Slow Boat model. More generally, these results also demonstrate that conclusions based solely on uniparental markers, which are frequently used in population history studies, may not accurately reflect the history of the autosomal gene pool of a population.

- 22 **Kimura R, Ohashi J, Matsumura Y, Nakazawa M, Inaoka T, Ohtsuka R, Osawa M, Tokunaga K.** Gene flow and natural selection in oceanic human populations inferred from genome-wide SNP typing. *Mol Biol Evol* 2008 Aug;25(8):1750-1761. Epub 2008 Jun 3.

It is suggested that the major prehistoric human colonizations of Oceania occurred twice, namely, about 50,000 and 4,000 years ago. The first settlers are considered as ancestors of indigenous people in New Guinea and Australia. The second settlers are Austronesian-speaking people who dispersed by voyaging in the Pacific Ocean. In this study, we performed genome-wide single-nucleotide polymorphism (SNP) typing on an indigenous Melanesian (Papuan) population, Gidra, and a Polynesian population, Tongans, by using the Affymetrix 500K assay. The SNP data were analyzed together with the data of the HapMap samples provided by Affymetrix. In agreement with previous studies, our phylogenetic analysis indicated that

indigenous Melanesians are genetically closer to Asians than to Africans and European Americans. Population structure analyses revealed that the Tongan population is genetically originated from Asians at 70% and indigenous Melanesians at 30%, which thus supports the so-called Slow Train model. We also applied the SNP data to genome-wide scans for positive selection by examining haplotypic variation and identified many candidates of locally selected genes. Providing a clue to understand human adaptation to environments, our approach based on evolutionary genetics must contribute to revealing unknown gene functions as well as functional differences between alleles. Conversely, this approach can also shed some light onto the invisible phenotypic differences between populations.

- 23 **King CL, Michon P, Shakri AR, Marcotty A, Stanisic D, Zimmerman PA, Cole-Tobian JL, Mueller I, Chitnis CE.**

Naturally acquired Duffy-binding protein-specific binding inhibitory antibodies confer protection from blood-stage *Plasmodium vivax* infection. *Proc Natl Acad Sci USA* 2008 Jun 17;105(24):8363-8368. Epub 2008 Jun 3.

Individuals residing in malaria-endemic regions acquire protective immunity after repeated infection with malaria parasites; however, mechanisms of protective immunity and their immune correlates are poorly understood. Blood-stage infection with *Plasmodium vivax* depends completely on interaction of *P. vivax* Duffy-binding protein (PvDBP) with the Duffy antigen on host erythrocytes. Here, we performed a prospective cohort treatment/reinfection study of children (5-14 years) residing in a *P. vivax*-endemic region of Papua New Guinea (PNG) in which children were cleared of blood-stage infection and then examined biweekly for reinfection for 25 weeks. To test the hypothesis that naturally acquired binding inhibitory antibodies (BIABs) targeting PvDBP region II (PvDBPII) provide protection against *P. vivax* infection, we used a quantitative receptor-binding assay to distinguish between antibodies that merely recognize PvDBP and those that inhibit binding to Duffy. The presence of high-level BIABs (>90% inhibition of PvDBPII-Duffy binding,  $n = 18$ ) before treatment was associated with delayed time to *P. vivax* reinfection diagnosed by light microscopy ( $p = 0.02$ ), 55% reduced risk of *P. vivax* reinfection (hazard ratio = 0.45,  $p = 0.04$ ), and 48% reduction in geometric mean *P. vivax* parasitemia ( $p < 0.001$ ) when compared with children with low-level BIABs ( $n = 148$ ). Further, we found that stable, high-level BIABs displayed strain-transcending inhibition by reducing reinfection with similar efficiency of PNG *P. vivax* strains characterized by six diverse PvDBPII haplotypes. These observations demonstrate a functional correlate of protective immunity in vivo and provide support for developing a vaccine against *P. vivax* malaria based on PvDBPII.

- 24 **Kuruppu S, Smith AI, Isbister GK, Hodgson WC.** Neurotoxins from Australo-Papuan elapids: a biochemical and pharmacological perspective. *Crit Rev Toxicol* 2008;38(1):73-86.

Most of the medically important snakes in Papua New Guinea and Australia belong to the family Elapidae and are referred to as 'Australo-Papuan' elapids. Neurotoxicity is often a life-threatening symptom of envenoming by these snakes; therefore,

much attention has been paid to the isolation and detailed pharmacological and biochemical characterization of the presynaptic (beta) and postsynaptic (alpha) neurotoxins from these elapid venoms. These studies have highlighted the potential for these toxins to be used as highly potent and selective probes for biomedical research and, perhaps, the potential for their use as lead compounds for the development of pharmaceutical agents. Historically, the potency of neurotoxins/crude venoms has been determined using murine LD50 (lethal dose) assays. However, a different rank order of potency often results when crude venoms/toxins are ranked based on their *in vitro* pharmacological parameters (e.g., t90 values). The lack of neurotoxicity following envenoming by brown snakes, despite the presence of a potent neurotoxin in their venom, has puzzled clinical toxicologists for years. This paradox also appears to include envenoming by the Stephen's banded snake. Lastly, the *in vitro* studies examining the effectiveness of antivenoms as well as the potential for alternative compounds to reverse/prevent neurotoxicity are discussed. This review presents for the first time a detailed comparative analysis of the pharmacology and biochemistry of neurotoxins isolated from the Australo-Papuan elapids, placing emphasis on the time taken for onset of action, receptor binding parameters, reversibility, and the methods for determining potency.

- 25 **Law I, Ilett KF, Hackett LP, Page-Sharp M, Baiwog F, Gomorrai S, Mueller I, Karunajeewa HA, Davis TM.**

Transfer of chloroquine and desethylchloroquine across the placenta and into milk in Melanesian mothers.

*Br J Clin Pharmacol* 2008 May;65(5):674-679. Epub 2008 Feb 15.

**WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT:** The literature on placental and milk transfer of chloroquine and its major bioactive metabolite desethylchloroquine is sparse and incomplete. **WHAT THIS STUDY ADDS:** We have provided data on the transplacental transfer of chloroquine and desethylchloroquine in Melanesian women (n = 19), measured transfer of these drugs into breast milk (n = 16) and estimated absolute and relative infant doses for the breastfed infant. The data for desethylchloroquine are novel. In all three areas we have significantly increased both quantity and quality of the available database. **AIMS:** To investigate the transfer of chloroquine and its major bioactive metabolite desethylchloroquine across the placenta and into breastmilk. **METHODS:** In Papua New Guinea, chloroquine (CQ; 25 mg base/kg) is recommended for prophylaxis of malaria during pregnancy, and at the Alexishafen Health Centre women are routinely prescribed CQ at the time of delivery. Fetal-cord and maternal serum samples were collected at delivery (n = 19) and milk samples were collected from day 3 to day 17-21 after delivery (n = 16). CQ and its primary active metabolite desethylchloroquine (DECQ) were quantified by high-performance liquid chromatography. For both CQ and DECQ cord/maternal ratios (C/M) were calculated to characterize placental transfer, and infant exposure via milk was estimated by standard methods. **RESULTS:** The median (interquartile range) C/M was 1.1 (0.9, 1.6) for CQ and 1.2 (0.5, 1.8) for DECQ. The average concentration in milk over the time of sampling was 167 microg/l (27, 340)

for CQ and 54 microg/l (22, 106) for DECQ. Estimated absolute and relative infant doses were 34 microg/kg/day (7, 50) and 15 microg/kg/day (4, 26), and 2.3% (0.5, 3.6) and 1.0% (0.4, 2.0) for CQ and DECQ (as CQ equivalents), respectively. **CONCLUSION:** Infant exposure to CQ and DECQ during pregnancy will be similar to that in the maternal circulation, and dependent on maternal dose and frequency. The median CQ + DECQ relative infant dose of 3.2% (as CQ equivalents) was low, confirming that use of CQ during lactation is compatible with breastfeeding.

- 26 **Lusida MI, Nugrahaputra VE, Soetjipto, Handajani R, Nagano-Fujii M, Sasayama M, Utsumi T, Hotta H.**

Novel subgenotypes of hepatitis B virus genotypes C and D in Papua, Indonesia.

*J Clin Microbiol* 2008 Jul;46(7):2160-2166. Epub 2008 May 7.

Eight genotypes (A to H) and nine subtypes (adw2, adw4, ayw1, ayw2, ayw3, ayw4, adrq+, adr- and ayr) of hepatitis B virus (HBV) have been identified worldwide. They appear to be associated with geographical distribution, virological characteristics, and possibly clinical outcomes. We performed sequence analysis of part of the S gene and the entire precore/core gene of HBV isolates obtained from HBsAg-positive blood donors in Papua Province, Indonesia. Phylogenetic analysis of the S gene sequences revealed that 23 (85.2%) of the 27 HBV isolates tested belonged to genotype C (HBV/C) and 2 (7.4%) each to HBV/B and HBV/D. Interestingly, 19 (82.6%) of the 23 isolates of HBV/C clustered in a branch that was distinct from the previously reported subgenotypes C1 to C5 (HBV/C1 to HBV/C5). Similarly, two isolates of HBV/D clustered in a branch distinct from the reported subgenotypes HBV/D1 to HBV/D5. Phylogenetic analysis of the entire precore/core gene confirmed the consistent presence of the distinct branches in HBV/C and HBV/D. We therefore propose novel subgenotypes designated HBV/C6 and HBV/D6. The majority of HBV/C6 isolates in Papua had alanine at positions 159 and 177 (A159/A177) in the HBsAg. A159/A177 is different from the determinants for adrq+ (A159/V177), found throughout Asia, and adr- (V159/A177), found in New Caledonia and Polynesia, possibly representing a unique antigenic group (provisionally referred to as adr- indeterminate). In conclusion, we have identified two novel HBV subgenotypes, HBV/C6 and HBV/D6, the first of which is the most prevalent subgenotype of HBV in Papua, Indonesia.

- 27 **Marfurt J, Müller I, Sie A, Oa O, Reeder JC, Smith TA, Beck HP, Genton B.**

The usefulness of twenty-four molecular markers in predicting treatment outcome with combination therapy of amodiaquine plus sulphadoxine-pyrimethamine against falciparum malaria in Papua New Guinea.

*Malar J* 2008 Apr 19;7:61.

**BACKGROUND:** In Papua New Guinea (PNG), combination therapy with amodiaquine (AQ) or chloroquine (CQ) plus sulphadoxine-pyrimethamine (SP) was introduced as first-line treatment against uncomplicated malaria in 2000. **METHODS:** We assessed *in vivo* treatment failure rates with AQ+SP in two different areas in PNG and twenty-four molecular drug resistance markers of *Plasmodium falciparum* were characterized in pre-treatment

- samples. The aim of the study was to investigate the association between infecting genotype and treatment response in order to identify useful predictors of treatment failure with AQ+SP. RESULTS: In 2004, Day-28 treatment failure rates for AQ+SP were 29% in the Karimui and 19% in the South Wosera area, respectively. The strongest independent predictors for treatment failure with AQ+SP were *pfmdr1* N86Y (OR = 7.87,  $p < 0.01$ ) and *pfdhps* A437G (OR = 3.44,  $p < 0.01$ ). Mutations found in CQ/AQ related markers *pfcr* K76T, A220S, N326D, and I356L did not help to increase the predictive value, the most likely reason being that these mutations reached almost fixed levels. Though mutations in SP related markers *pfdhfr* S108N and C59R were not associated with treatment failure, they increased the predictive value of *pfdhps* A437G. The difference in treatment failure rate in the two sites was reflected in the corresponding genetic profile of the parasite populations, with significant differences seen in the allele frequencies of mutant *pfmdr1* N86Y, *pfmdr1* Y184F, *pfcr* A220S, and *pfdhps* A437G. CONCLUSION: The study provides evidence for high levels of resistance to the combination regimen of AQ+SP in PNG and indicates which of the many molecular markers analysed are useful for the monitoring of parasite resistance to combinations with AQ+SP.
- 28 **Matai S, Peel D, Wandt F, Jonathan M, Subhi R, Duke T.**  
Implementing an oxygen programme in hospitals in Papua New Guinea.  
*Ann Trop Paediatr* 2008 Mar;28(1):71-78.  
In Papua New Guinea (PNG), the most common cause of death among children under 5 years of age is pneumonia. Children with severe pneumonia need antibiotics and oxygen but oxygen shortages are common owing to the cost and complex logistics of transporting it in cylinders. Detection of hypoxaemia using clinical signs can be difficult, especially in highly pigmented children in whom cyanosis is difficult to recognise. Pulse oximetry is the most reliable, non-invasive way of detecting hypoxaemia. However, most hospitals in PNG do not have pulse oximetry. We proposed that the installation of a reliable, sufficient and cheap supply of oxygen in hospitals coupled with the use of pulse oximetry would make a significant difference to child survival rates in PNG. Oxygen concentrators, which extract oxygen from ambient air, were installed in the children's wards of five hospitals during 2005. Pulse oximeters were also introduced to enable better detection of hypoxaemia. This paper describes the technical aspects of this programme: the equipment used and the rationale behind choosing it, the installation, commissioning and testing processes. The ongoing training of clinical and engineering staff as well as two follow-up evaluations are described.
- 29 **Mathieu A, Cauli A, Fiorillo MT, Sorrentino R.**  
HLA-B27 and ankylosing spondylitis geographic distribution as the result of a genetic selection induced by malaria endemic? A review supporting the hypothesis.  
*Autoimmun Rev* 2008 May;7(5):398-403. Epub 2008 Apr 9.  
The geographic distribution of HLA-B27 shows a latitude-related gradient inverse to that of malaria endemic. An apparent exception occurs in New Guinea, a region where malaria is present, but where HLA-B27 frequency shows, however, an orographic gradient antithetic to that of malaria incidence. We therefore suggest that *Plasmodium falciparum* may have exerted a negative selection on this gene. This might be due to a higher susceptibility to severe forms of malaria, associated with HLA-B27 or other close gene(s). In addition, we suggest here that the same selective pressure that has contributed to reduce the HLA-B27 frequency in some regions has favoured the fixing of newly generated B27 subtypes included in more advantageous HLA haplotypes. In some cases, as for B\*2709 in Sardinia and B\*2706 in Southeast Asia, these haplotypes may harbour factors that protect from ankylosing spondylitis, an autoimmune disease strongly associated with HLA-B27, thus offering a novel, powerful tool to dissect disease pathogenesis, and to identify additional genetic factors of susceptibility.
- 30 **McBride WJ, Hannah RC, Le Cornec GM, Bletchly C.**  
Cutaneous chancroid in a visitor from Vanuatu.  
*Australas J Dermatol* 2008 May;49(2):98-99.  
A 23-year-old woman from Vanuatu presented to an Australian hospital with a 3-week history of a non-healing ulcer on the lower leg. A swab was submitted for a multiplex polymerase chain reaction designed to investigate genital ulcerative conditions. *Haemophilus ducreyi* was detected and the gene product was subsequently sequenced, confirming the diagnosis of cutaneous chancroid. The lesion responded to intramuscular benzathine penicillin. This report adds further evidence that cutaneous chancroid should be considered in the evaluation of skin ulcers in the south Pacific.
- 31 **Olsson DJ, Grant WD, Glick JM.**  
Conjunctivitis outbreak among divers.  
*Undersea Hyperb Med* 2008 May-Jun;35(3):169-174.  
In March 2006, an outbreak of conjunctivitis that occurred over a six day period among twenty-nine individuals who partook in recreational scuba diving trips on two boats off Vitu Levu Island, Fiji. We investigated the likelihood that a communal container used to store diving masks facilitated the spread of conjunctivitis among individuals. The diagnosis of conjunctivitis was based on clinical assessment by a physician. Transmission of conjunctivitis from person to person was documented with eventual identification of the index case, the dive master, a Fijian resident. Topical antibiotics were dispensed accordingly and detergent and bleach were used as mask cleaning agents in an effort to control the outbreak. Follow-up surveys were mailed to all twenty-nine participants. Ultimately, fourteen cases of conjunctivitis were documented (46.7%). Eleven cases were verified during the six days in Fiji, two upon arrival back in the US, and one case of familial transmission in the US. All but two cases resolved within one week. Unknown to these divers was a coincidental, generalized outbreak of acute haemorrhagic conjunctivitis among the Fijian residents. The communal container used to store diving masks was the likely vector for the spread of infectious conjunctivitis, the first such documented outbreak involving communal diving equipment.
- 32 **Pauli J, Gundelach R, Vanelli-Rees A, Rees G, Campbell C, Dubey S, Perry C.**  
Juvenile nasopharyngeal angiofibroma: an immunohistochemical characterisation of the stromal cell.



*Pathology* 2008 Jun;40(4):396-400.

**AIMS:** Juvenile nasopharyngeal angiofibroma (JNA) is a rare tumour occurring almost exclusively in young adult males. Although histologically benign, it can be locally aggressive with a significant recurrence rate. The finding of activating beta-catenin gene mutations in the stromal cells indicates these are the neoplastic cells and supports the association of JNA and familial adenomatous polyposis (FAP). Previous immunohistochemical studies have demonstrated a null or focal myoepithelial immunophenotype in the stromal cells. Recently, expression of several growth factors and oncoproteins including CD117 (c-kit) in the stromal cells has been demonstrated. Our objective is to evaluate the immunohistochemical phenotype of the stromal cell of JNA, particularly within the proliferative zone of the tumour, by application of antibodies against MNF116, CAM5.2, S-100, CD31, CD34, CD99, CD68, vimentin, EMA, SMA, desmin, calponin, Bcl-2 and (CD117) c-kit in a series of 54 cases. **METHODS:** A routine immunohistochemical protocol was applied to representative paraffin sections of 54 JNAs collected from the Port Moresby General Hospital, Papua New Guinea, and Princess Alexandra and Royal Brisbane Hospitals, Queensland, Australia. Immunoreaction of each antigen was assessed in the stromal cells and the vessels. **RESULTS:** The majority of stromal cells in more than half of the cases demonstrated no staining with any of the 14 antibodies other than vimentin. Of 54 cases, 22 contained a microvascular component (usually peripherally located and indicating the active growth front of the tumour) in which the stromal cells demonstrated a hybrid immunophenotype with both smooth muscle and endothelial differentiation; c-kit was negative in all cases. **CONCLUSIONS:** The majority of stromal cells have an undifferentiated immunophenotype with no evidence of epithelial, myoid, endothelial or other lineage specific differentiation. In the microvascular component the stromal cells appear able to show smooth muscle or endothelial differentiation. No c-kit expression was identified.

**33 Pihet M, Bourgeois H, Mazière JY, Berlioz-Arthaud A, Bouchara JP, Chabasse D.**

Isolation of *Trichophyton concentricum* from chronic cutaneous lesions in patients from the Solomon Islands.

*Trans R Soc Trop Med Hyg* 2008 Apr;102(4):389-393. Epub 2008 Mar 4.

Tinea imbricata, also known as 'tokelau', is an uncommon superficial mycosis caused by the anthropophilic dermatophyte *Trichophyton concentricum*. Cutaneous lesions appear characteristically as scaly and concentric rings that may cover all parts of the body. Often acquired in childhood, tinea imbricata is a chronic disease and lichenification is extremely common due to pruritus. The dermatophytosis mainly occurs in the South Pacific, but also in some regions of Southeast Asia and Central or South America. Tinea imbricata usually affects people living in primitive and isolated conditions. Mycological analysis is required for the diagnosis. The epidemiological and mycological study reported here took place in the Solomon Islands from June to September 2006. Skin scrapings were collected from 29 Melanesian patients (aged 8 months to 58 years) with chronic cutaneous lesions and were analysed mycologically in the Laboratory of Parasitology and Mycology of

Angers University Hospital (France). Ten patients showed very evocative lesions with a positive direct examination, but *T. concentricum* was only isolated from three patients. Identification of the strains was confirmed by sequencing of the internal transcribed spacer (ITS) regions. With the increase in international travel, one cannot disregard that this very rare species may be isolated by mycologists in temperate areas from patients coming from endemic foci.

**34 Poespoprodjo JR, Fobia W, Kenangalem E, Lampah DA, Warikar N, Seal A, McGready R, Sugiarto P, Tjitra E, Anstey NM, Price RN.**

Adverse pregnancy outcomes in an area where multidrug-resistant *Plasmodium vivax* and *Plasmodium falciparum* infections are endemic.

*Clin Infect Dis* 2008 May 1;46(9):1374-1381.

**BACKGROUND:** *Plasmodium falciparum* infection exerts a considerable burden on pregnant women, but less is known about the adverse consequences of *Plasmodium vivax* infection. **METHODS:** In Papua, Indonesia, where multiple drug resistance to both species has emerged, we conducted a cross-sectional hospital-based study to quantify the risks and consequences of maternal malaria. **RESULTS:** From April 2004 through December 2006, 3046 pregnant women were enrolled in the study. The prevalence of parasitemia at delivery was 16.8% (432 of 2570 women had infections), with 152 (35.2%) of these 432 infections being associated with fever. The majority of infections were attributable to *P. falciparum* (250 [57.9%]); 146 (33.8%) of the infections were attributable to *P. vivax*, and 36 (8.3%) were coinfections with both species. At delivery, *P. falciparum* infection was associated with severe anemia (hemoglobin concentration, <7 g/dL; odds ratio [OR], 2.8; 95% confidence interval [95% CI], 2.0-4.0) and a 192 g (95% CI, 119-265) reduction in mean birth weight ( $p < 0.001$ ). *P. vivax* infection was associated with an increased risk of moderate anemia (hemoglobin concentration, 7-11 g/dL; OR, 1.8; 95% CI, 1.2-2.9;  $p = 0.01$ ) and a 108 g (95% CI, 17.5-199) reduction in mean birth weight ( $p < 0.019$ ). Parasitemia was associated with preterm delivery (OR, 1.5; 95% CI, 1.1-2.0;  $p = 0.02$ ) and stillbirth (OR, 2.3; 95% CI, 1.3-4.1;  $p = 0.007$ ) but was not associated with these outcomes after controlling for the presence of fever and severe anemia, suggesting that malaria increases the risk of preterm delivery and stillbirth through fever and contribution to severe anemia rather than through parasitemia per se. **CONCLUSIONS:** These observations highlight the need for novel, safe, and effective treatment and prevention strategies against both multidrug-resistant *P. falciparum* and multidrug-resistant *P. vivax* infections in pregnant women in areas of mixed endemicity.

**35 Ricaut FX, Thomas T, Arganini C, Staughton J, Leavesley M, Bellatti M, Foley R, Mirazon Lahr M.**

Mitochondrial DNA variation in Karkar islanders.

*Ann Hum Genet* 2008 May;72(Pt 3):349-367. Epub 2008 Feb 28.

We analyzed 375 base pairs (bp) of the first hypervariable region (HVS-I) of the mitochondrial DNA (mtDNA) control region and intergenic COII/tRNA<sup>Lys</sup> 9-bp deletion from 47 Karkar islanders (north coast of Papua New Guinea) belonging to the Waskia Papuan language group. To address



questions concerning the origin and evolution of this population we compared the Karkar mtDNA haplotypes and haplogroups to those of neighbouring East Asians and Oceanic populations. The results of the phylogeographic analysis show grouping in three different clusters of the Karkar islander mtDNA lineages: one group of lineages derives from the first Pleistocene settlers of New Guinea-Island Melanesia, a second set derives from more recent arrivals of Austronesian speaking populations, and the third contains lineages specific to the Karkar islanders, but still rooted to Austronesian and New Guinea-Island Melanesia populations. Our results (i) suggest the absence of a strong association between language and mtDNA variation and (ii) reveal that the mtDNA haplogroups F1a1, M7b1 and E1a, which probably originated in Island Southeast Asia and may be considered signatures of Austronesian population movements, are preserved in the Karkar islanders but absent in other New Guinea-Island Melanesian populations. These findings indicate that the Karkar Papuan speakers retained a certain degree of their own genetic uniqueness and a high genetic diversity. We present a hypothesis based on archaeological, linguistic and environmental datasets to argue for a succession of (partial) depopulation and repopulation and expansion events, under conditions of structured interaction, which may explain the variability expressed in the Karkar mtDNA.

- 36 **Rogerson SJ, Carter R.**  
Severe vivax malaria: newly recognised or rediscovered.  
*PLoS Med* 2008 Jun 17;5(6):e136.  
Comment on: *PLoS Med* 2008 Jun 17;5(6):e127 (Genton et al.) and *PLoS Med* 2008 Jun 17;5(6):e128 (Tjitra et al.).
- 37 **Rothwell SP, Rosengren DJ.**  
Severe exercise-associated hyponatremia on the Kokoda Trail, Papua New Guinea.  
*Wilderness Environ Med* 2008 Spring;19(1):42-44.  
Exercise-associated hyponatremia is the most common medical complication of ultradistance exercise and is usually caused by excessive hypotonic fluid intake. We report a case of severe hyponatremia in a healthy male trekking the Kokoda Trail in the remote Southern Highlands of Papua New Guinea. A 43-year-old male collapsed and had a generalized seizure in the afternoon of the third day of a guided trek. He was evacuated the following morning and was found to have a serum sodium level of 107 mmol/L on arrival to hospital. The case highlights that a high index of suspicion is required to identify patients with exercise-associated hyponatremia. Early diagnosis and appropriate management is critical to avoid the potentially fatal consequences of severe hyponatremia. The diagnosis and treatment of exercise-associated hyponatremia is particularly challenging in the remote Papua New Guinea jungle. Education of trek leaders, medics, and trekkers in appropriate preventative measures and the rapid treatment of exercise-associated hyponatremia is essential to avoid recurrences of this life-threatening condition.
- 38 **Russell B, Chalfein F, Prasetyorini B, Kenangalem E, Piera K, Suwanarusk R, Brockman A, Prayoga P, Sugiarto P, Cheng Q, Tjitra E, Anstey NM, Price RN.**  
Determinants of in vitro drug susceptibility testing of

*Plasmodium vivax*.

*Antimicrob Agents Chemother* 2008 Mar;52(3):1040-1045. Epub 2008 Jan 7.

In Papua, Indonesia, the antimalarial susceptibility of *Plasmodium vivax* (n = 216) and *P. falciparum* (n = 277) was assessed using a modified schizont maturation assay for chloroquine, amodiaquine, artesunate, lumefantrine, mefloquine, and piperazine. The most effective antimalarial against *P. vivax* and *P. falciparum* was artesunate, with geometric mean 50% inhibitory concentrations (IC50s) (95% confidence intervals [CI]) of 1.31 nM (1.07 to 1.59) and 0.64 nM (0.53 to 0.79), respectively. In contrast, the geometric mean chloroquine IC50 for *P. vivax* was 295 nM (227 to 384) compared to only 47.4 nM (42.2 to 53.3) for *P. falciparum*. Two factors were found to significantly influence the in vitro drug response of *P. vivax*: the initial stage of the parasite and the duration of the assay. Isolates of *P. vivax* initially at the trophozoite stage had significantly higher chloroquine IC50s (478 nM [95% CI, 316 to 722]) than those initially at the ring stage (84.7 nM [95% CI, 45.7 to 157]; p < 0.001). Synchronous isolates of *P. vivax* and *P. falciparum* which reached the target of 40% schizonts in the control wells within 30 h had significantly higher geometric mean chloroquine IC50s (435 nM [95% CI, 169 to 1118] and 55.9 nM [95% CI, 48 to 64.9], respectively) than isolates that took more than 30 h (39.9 nM [14.6 to 110.4] and 36.9 nM [31.2 to 43.7]; p < 0.005). The results demonstrate the marked stage-specific activity of chloroquine with *P. vivax* and suggest that susceptibility to chloroquine may be associated with variable growth rates. These findings have important implications for the phenotypic and downstream genetic characterization of *P. vivax*.

- 39 **Schoepflin S, Marfurt J, Goroti M, Baisor M, Mueller I, Felger I.**

Heterogeneous distribution of *Plasmodium falciparum* drug resistance haplotypes in subsets of the host population.

*Malar J* 2008 May 6;7:78.

**BACKGROUND:** The emergence of drug resistance is a major problem in malaria control. For mathematical modelling of the transmission and spread of drug resistance the determinant parameters need to be identified and measured. The underlying hypothesis is that mutations associated with drug resistance incur fitness costs to the parasite in absence of drug pressure. The distribution of drug resistance haplotypes in different subsets of the host population was investigated. In particular newly acquired haplotypes after radical cure were characterized and compared to haplotypes from persistent infections. **METHODS:** Mutations associated with antimalarial drug resistance were analysed in parasites from children, adults, and new infections occurring after treatment. Twenty-five known single nucleotide polymorphisms from four *Plasmodium falciparum* genes associated with drug resistance were genotyped by DNA chip technology. **RESULTS:** Haplotypes were found to differ between subsets of the host population. A seven-fold mutated haplotype was significantly reduced in adults compared to children and new infections, whereas parasites harbouring fewer mutations were more frequent in adults. **CONCLUSION:** The reduced frequency of highly mutated parasites in chronic infections in adults is likely a result of fitness costs of drug resistance that increases with number of

mutations and is responsible for reduced survival of mutant parasites.

40 **Singh PI, Carapetis JR, Buadromo EM, Samberkar PN, Steer AC.**

The high burden of rheumatic heart disease found on autopsy in Fiji.

*Cardiol Young* 2008 Feb;18(1):62-69. Epub 2007 Dec 20.

Rheumatic heart disease causes more than 200,000 deaths worldwide annually, with the vast majority of these deaths occurring in developing countries, yet there are few autopsy studies of rheumatic heart disease in these countries. We performed a retrospective review of 6218 autopsies performed during the period from 1990 through 2006, searching for cases of rheumatic heart disease based upon the macroscopic pathologic examination of the heart. We found 147 cases (2.4%) of rheumatic heart disease. There was an apparent increase in the number of cases in the past 5 years. There were 95 deaths that were directly attributable to rheumatic heart disease, with congestive cardiac failure being the most common cause of death in 75 cases. The mean age at death due to rheumatic heart disease was 38 years. There were more cases of rheumatic heart disease in Indigenous Fijians than Indo-Fijians, with an adjusted relative risk of 1.26 (95% confidence intervals from 0.87 to 1.86). Our findings reflect the high burden and early age of death due to rheumatic heart disease in Fiji and the Pacific region generally, and underline the need for early detection and adequate secondary penicillin prophylaxis in this region.

41 **Smith BJ, Phongsavan P, Bampton D, Peacocke G, Gilmete M, Havea D, Chey T, Bauman AE.**

Intentional injury reported by young people in the Federated States of Micronesia, Kingdom of Tonga and Vanuatu.

*BMC Public Health* 2008 Apr 30;8:145.

**BACKGROUND:** Intentional injury presents a threat to the physical and psychological well being of young people, especially in developing countries, which carry the greatest part of the global injury burden. While the importance of this problem is recognized, there are limited population data in low and middle income countries that can guide public health action. The present study investigates the prevalence and distribution of intentional injury among young people in three Pacific Island societies, and examines behavioural and psychosocial factors related to risk of intentional injury. **METHODS:** Population surveys were conducted with students aged 11-17 years in Pohnpei State in the Federated States of Micronesia (n = 1495), the Kingdom of Tonga (n = 2808) and Vanuatu (n = 4474). Surveys measured self-reported injury and intentional injury, sources of intentional injury, and the range of behavioural, psychological, educational and social variables that may be related to injury risk. **RESULTS:** Among boys and girls aged 14-17 years the respective period prevalence of intentional injury was 62% and 56% in Pohnpei, 58% and 41% in Tonga, and 33% and 24% in Vanuatu. The prevalence of intentional injury declined with age in Tonga and Vanuatu, but there was little evidence of an age-trend in Pohnpei. Across the three societies, the major sources of intentional injury among boys were 'other persons' followed by boyfriends/girlfriends and fathers. Mothers, boyfriends/girlfriends and other persons were primary sources

of injury among girls. An intentional injury was reported more often by those who had been bullied (OR 1.40-1.66, p < 0.05), by regular smokers in Tonga and Vanuatu (OR 1.52-2.21, p < 0.05), and illicit drug users in Pohnpei and Vanuatu (OR 1.87-1.92, p < 0.05). **CONCLUSION:** Intentional injury was reported extensively in these three populations. Interventions directed towards the school environment and which take into account the role of bullying and drug use need to be considered.

42 **Steer AC, Jenney AJ, Oppedisano F, Batzloff MR, Hartas J, Passmore J, Russell FM, Kado JH, Carapetis JR.**

High burden of invasive beta-haemolytic streptococcal infections in Fiji.

*Epidemiol Infect* 2008 May;136(5):621-627. Epub 2007 Jul 16.

We undertook a 5-year retrospective study of group A streptococcal (GAS) bacteraemia in Fiji, supplemented by a 9-month detailed retrospective study of beta-haemolytic streptococcal (BHS) infections. The all-age incidence of GAS bacteraemia over 5 years was 11.6/100,000. Indigenous Fijians were 4.7 times more likely to present with invasive BHS disease than people of other ethnicities, and 6.4 times more likely than Indo-Fijians. The case-fatality rate for invasive BHS infections was 28%. On 23 isolates emm-typing was performed: 17 different emm-types were found, and the emm-type profile was different from that found in industrialized nations. These data support the contentions that elevated rates of invasive BHS and GAS infections are widespread in developing countries, and that the profile of invasive organisms in these settings reflects a wide diversity of emm-types and a paucity of types typically found in industrialized countries.

43 **Tisch DJ, Bockarie MJ, Dimber Z, Kiniboro B, Tarongka N, Hazlett FE, Kastens W, Alpers MP, Kazura JW.**

Mass drug administration trial to eliminate lymphatic filariasis in Papua New Guinea: changes in microfilaremia, filarial antigen, and Bm14 antibody after cessation.

*Am J Trop Med Hyg* 2008 Feb;78(2):289-293.

Laboratory tools to monitor infection burden are important to evaluate progress and determine endpoints in programs to eliminate lymphatic filariasis. We evaluated changes in *Wuchereria bancrofti* microfilaria, filarial antigen and Bm14 antibody in individuals who participated in a five-year mass drug administration trial in Papua New Guinea. Comparing values before treatment and one year after four annual treatments, the proportion of microfilaria positive individuals declined to the greatest degree, with less marked change in antibody and antigen rates. Considering children as sentinel groups who reflect recent transmission intensity, children surveyed before the trial were more frequently microfilaria and antibody positive than those examined one year after the trial stopped. In contrast, antigen positive rates were similar in the two groups. All infection indicators continued to decline five years after cessation of mass drug administration; Bm14 antibody persisted in the greatest proportion of individuals. These data suggest that Bm14 antibody may be a sensitive test to monitor continuing transmission during and after mass drug administration aimed at eliminating transmission of lymphatic filariasis.

- 44 **Tjitra E, Anstey NM, Sugiarto P, Warikar N, Kenangalem E, Karyana M, Lampah DA, Price RN.**

Multidrug-resistant *Plasmodium vivax* associated with severe and fatal malaria: a prospective study in Papua, Indonesia.

*PLoS Med* 2008 Jun 17;5(6):e128.

**BACKGROUND:** Multidrug-resistant *Plasmodium vivax* (Pv) is widespread in eastern Indonesia, and emerging elsewhere in Asia-Pacific and South America, but is generally regarded as a benign disease. The aim of the study was to review the spectrum of disease associated with malaria due to Pv and *P. falciparum* (Pf) in patients presenting to a hospital in Timika, southern Papua, Indonesia. **METHODS AND FINDINGS:** Data were prospectively collected from all patients attending the outpatient and inpatient departments of the only hospital in the region using systematic data forms and hospital computerised records. Between January 2004 and December 2007, clinical malaria was present in 16% (60,226/373,450) of hospital outpatients and 32% (12,171/37,800) of inpatients. Among patients admitted with slide-confirmed malaria, 64% of patients had Pf, 24% Pv, and 10.5% mixed infections. The proportion of malarial admissions attributable to Pv rose to 47% (415/887) in children under 1 year of age. Severe disease was present in 2634 (22%) inpatients with malaria, with the risk greater among Pv (23% [675/2937]) infections compared to Pf (20% [1570/7817]; odds ratio [OR] = 1.19 [95% confidence interval (CI) 1.08-1.32],  $p = 0.001$ ), and greatest in patients with mixed infections (31% [389/1273]); overall  $p < 0.0001$ . Severe anaemia (haemoglobin  $< 5$  g/dl) was the major complication associated with Pv, accounting for 87% (589/675) of severe disease compared to 73% (1144/1570) of severe manifestations with Pf ( $p < 0.001$ ). Pure Pv infection was also present in 78 patients with respiratory distress and 42 patients with coma. In total 242 (2.0%) patients with malaria died during admission: 2.2% (167/7722) with Pf, 1.6% (46/2916) with Pv, and 2.3% (29/1260) with mixed infections ( $p = 0.126$ ). **CONCLUSIONS:** In this region with established high-grade chloroquine resistance to both Pv and Pf, Pv is associated with severe and fatal malaria particularly in young children. The epidemiology of *P. vivax* needs to be re-examined elsewhere where chloroquine resistance is increasing.

- 45 **Vilar MG, Kaneko A, Hombhanje FW, Tsukahara T, Hwaihwanje I, Lum JK.**

Reconstructing the origin of the Lapita Cultural Complex: mtDNA analyses of East Sepik Province, PNG.

*J Hum Genet* 2008;53(8):698-708. Epub 2008 May 23.

The colonization of Oceania occurred in two waves. By 32,000 BP, humans had reached New Guinea and settled all intervisible islands east to the Solomon Islands. Around 3,500 BP, a distinct intrusive group from Southeast Asia reached coastal New Guinea, integrated their components with indigenous resources, and gave rise to the Lapita Cultural Complex. Within 2,500 years, Lapita and its descendant cultures colonized the Pacific. To uncover the origin of the Lapita Cultural Complex, we analyzed the hypervariable region I of the mitochondrial deoxyribonucleic acid (mtDNA) in 219 individuals from eight East Sepik Province villages: two villages in each of four environmental zones.

Same-zone villages spoke different languages: one Austronesian and three Papuan (Arapesh, Abelam, and Boiken). Our analysis examined whether language or geography better predicted gene flow. In general, language better predicted genetic affinities. Boiken villages across all four zones showed no significant genetic difference ( $F_{ST}$   $p$  value  $> 0.05$ ). In contrast, the Austronesian village was significantly different to most other villages ( $p < 0.05$ ). Only the mountains and coast showed zonal gene flow ( $p > 0.05$ ). We interpret the data to reflect limited gene flow inland by Austronesians overshadowed by a regional displacement by inland Boiken speakers migrating seaward. These results are consistent with oral histories and ethnographic accounts.

- 46 **Wadsworth JD, Joiner S, Linehan JM, Desbruslais M, Fox K, Cooper S, Cronier S, Asante EA, Mead S, Brandner S, Hill AF, Collinge J.**

Kuru prions and sporadic Creutzfeldt-Jakob disease prions have equivalent transmission properties in transgenic and wild-type mice.

*Proc Natl Acad Sci USA* 2008 Mar 11;105(10):3885-3890. Epub 2008 Mar 3.

Kuru provides our principal experience of an epidemic human prion disease and primarily affected the Fore linguistic group of the Eastern Highlands of Papua New Guinea. Kuru was transmitted by the practice of consuming dead relatives as a mark of respect and mourning (transumption). To date, detailed information of the prion strain type propagated in kuru has been lacking. Here, we directly compare the transmission properties of kuru prions with sporadic, iatrogenic, and variant Creutzfeldt-Jakob disease (CJD) prions in *Prnp*-null transgenic mice expressing human prion protein and in wild-type mice. Molecular and neuropathological data from these transmissions show that kuru prions are distinct from variant CJD and have transmission properties equivalent to those of classical (sporadic) CJD prions. These findings are consistent with the hypothesis that kuru originated from chance consumption of an individual with sporadic CJD.

- 47 **Wall JD, Cox MP, Mendez FL, Woerner A, Severson T, Hammer MF.**

A novel DNA sequence database for analyzing human demographic history.

*Genome Res* 2008 Aug;18(8):1354-1361. Epub 2008 May 20.

While there are now extensive databases of human genomic sequences from both private and public efforts to catalog human nucleotide variation, there are very few large-scale surveys designed for the purpose of analyzing human population history. Demographic inference from patterns of SNP variation in current large public databases is complicated by ascertainment biases associated with SNP discovery and the ways that populations and regions of the genome are sampled. Here, we present results from a resequencing survey of 40 independent intergenic regions on the autosomes and X chromosome comprising approximately 210 kb from each of 90 humans from six geographically diverse populations (i.e., a total of approximately 18.9 Mb). Unlike other public DNA sequence databases, we include multiple indigenous populations that serve as important reservoirs of human genetic diversity, such as the San of Namibia, the Biaka of the Central African Republic, and Melanesians from Papua New

Guinea. In fact, only 20% of the SNPs that we find are contained in the HapMap database. We identify several key differences in patterns of variability in our database compared with other large public databases, including higher levels of nucleotide diversity within populations, greater levels of differentiation between populations, and significant differences in the frequency spectrum. Because variants at loci included in this database are less likely to be subject to ascertainment biases or linked to sites under selection, these data will be more useful for accurately reconstructing past changes in size and structure of human populations.

**48 Warrell DA.**

Unscrupulous marketing of snake bite antivenoms in Africa and Papua New Guinea: choosing the right product – 'what's in a name?'.

*Trans R Soc Trop Med Hyg* 2008 May;102(5):397-399. Epub 2008 Mar 21.

Snake bite envenoming, mainly caused by the saw-scaled or carpet viper (*Echis ocellatus*), is a neglected disease of West Africa. Specific antivenoms can save life and limb but, for various reasons, supply of these essential drugs to Africa has dwindled to less than 2% of estimated requirements. Other problems include maldistribution, inadequate conservation and inappropriate clinical use of antivenoms. In the face of this crisis, several promising new antivenoms have been developed. However, some dangerously inappropriate products of Indian origin are being marketed by unscrupulous manufacturers or distributors in Africa and Papua New Guinea, with disastrous results. A major source of confusion is labelling antivenom with ambiguous snake names that fail to distinguish the Asian species whose venoms are used in their production from the local snakes whose venoms are antigenically dissimilar.

**49 Williams C, Szetu JL, Ramke J, Palagyi A, du Toit R, Brian G.**

Evaluation of the first 5 years of a national eye health programme in Vanuatu.

*Clin Experiment Ophthalmol* 2008 Mar;36(2):162-167.

**PURPOSE:** To evaluate against its objectives the achievements of the first 5 years of a national eye health programme in Vanuatu. **METHODS:** Programme clinical activity data were collated from surgical logs, clinic and outreach reports, and patient register books. Cataract surgical outcomes were retrieved from monitoring software. Programme annual reports provided information about management, infrastructure improvements, equipment supplied, repaired or replaced, the supply and use of consumables, and human resource development and deployment. Costs were determined from project budgets and acquittals. **RESULTS:** The programme promoted eye health, including through the integration of eye care into existing health services; established adequate facilities, at referral hospitals, provincial hospitals and rural health clinics, with equipment and manpower to provide eye care appropriate to the location; established a primary eye care programme;

strengthened cataract services, although its effect on any cataract backlog is unknown; developed a diabetic eye disease diagnosis and treatment service, but its reach and effectiveness are unknown; provided accessible comprehensive eye care, but its effect on the prevalence of vision impairment is unknown; and established medical records and data collection systems, but these need more attention. **DISCUSSION:** This programme achieved much. However, the evaluation highlighted the limitations of inadequate project design and that, without addressing further human resource development and the Ministry of Health's wavering financial commitment, there are potential risks to ongoing services. That revenue generating capacity was not incorporated into this programme may prove to be a flaw that will limit ongoing access to eye care, especially in rural areas.

**50 Zhang X, Perugini MA, Yao S, Adda CG, Murphy VJ, Low A, Anders RF, Norton RS.**

Solution conformation, backbone dynamics and lipid interactions of the intrinsically unstructured malaria surface protein MSP2.

*J Mol Biol* 2008 May 23;379(1):105-121. Epub 2008 Mar 28.

Merozoite surface protein 2 (MSP2), one of the most abundant proteins on the surface of the merozoite stage of *Plasmodium falciparum*, is a potential component of a malaria vaccine, having shown some efficacy in a clinical trial in Papua New Guinea. MSP2 is a GPI-anchored protein consisting of conserved N- and C-terminal domains and a variable central region. Previous studies have shown that it is an intrinsically unstructured protein with a high propensity for fibril formation, in which the conserved N-terminal domain has a key role. Secondary structure predictions suggest that MSP2 contains long stretches of random coil with very little alpha-helix or beta-strand. Circular dichroism spectroscopy confirms this prediction under physiological conditions (pH 7.4) and in more acidic solutions (pH 6.2 and 3.4). Pulsed field gradient NMR diffusion measurements showed that MSP2 under physiological conditions has a large effective hydrodynamic radius consistent with an intrinsic pre-molten globule state, as defined by Uversky. This was supported by sedimentation velocity studies in the analytical ultracentrifuge. NMR resonance assignments have been obtained for FC27 MSP2, allowing the residual secondary structure and backbone dynamics to be defined. There is some motional restriction in the conserved C-terminal region in the vicinity of an intramolecular disulfide bond. Two other regions show motional restrictions, both of which display helical structure propensities. One of these helical regions is within the conserved N-terminal domain, which adopts essentially the same conformation in full-length MSP2 as in corresponding peptide fragments. We see no evidence of long-range interactions in the full-length protein. MSP2 associates with lipid micelles, but predominantly through the N-terminal region rather than the C terminus, which is GPI-anchored to the membrane in the parasite.



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