

## MEDLARS BIBLIOGRAPHY

PUBLICATIONS OF RELEVANCE TO PAPUA NEW GUINEA AND MELANESIA

### Bibliographic Citation List generated from MEDLARS

- 1 **Aghanwa HS.**  
 Recurrent unipolar mania in a psychiatric hospital setting in the Fiji Islands.  
*Psychopathology* 2001 Nov-Dec;34(6):312-317.  
 This study aimed to determine the rate of unipolar mania and compare its characteristics with those of other bipolar affective disorders in a psychiatric hospital in the Fiji Islands. Fifty-one patients with unipolar mania seen between January 1999 and October 2000 had their diagnosis confirmed using the Schedules for Clinical Assessment in Neuropsychiatry and the International Classification of Diseases, 10th edition. Their demographic and clinical characteristics were compared with those of 31 manic-depressive patients seen during the period under review. Unipolar mania constituted 47.2% of the bipolar affective disorders in this sample. The frequency of episodes, duration of affective illness, mean age at onset, gender distribution, marital status, employment status and race were not significantly different for the unipolar manic and manic-depressive groups ( $p>0.05$ ). Family history of major psychiatric morbidity was 9.8% for the unipolar manic patients and 22.6% for the manic-depressive group ( $p>0.05$ ). Recurrent unipolar mania may be considered a useful category based on its high rate, although its demographic and clinical characteristics do not clearly distinguish it from manic-depression.
  
- 2 **Baird JK, Lacy MD, Basri H, Barcus MJ, Maguire JD, Bangs MJ, Gramzinski R, Sismadi P, Krisin, Ling J, Wiady I, Kusumaningsih M, Jones TR, Fryauff DJ, Hoffman SL, United States Naval Medical Research Unit 2 Clinical Trials Team.**  
 Randomized, parallel placebo-controlled trial of primaquine for malaria prophylaxis in Papua, Indonesia.  
*Clin Infect Dis* 2001 Dec 15;33(12):1990-1997.  
 Malaria causes illness or death in unprotected travellers. Primaquine prevents malaria by attacking liver-stage parasites, a property distinguishing it from most chemoprophylactics and obviating 4-week postexposure dosing. A daily adult regimen of 30 mg primaquine prevented malaria caused by *Plasmodium falciparum* and *P. vivax* for 20 weeks in 95 of 97 glucose-6-phosphate dehydrogenase (G6PD)-normal Javanese transmigrants in Papua, Indonesia. In comparison, 37 of 149 subjects taking placebo in a parallel trial became parasitemic. The protective efficacy of primaquine against malaria was 93% (95% confidence interval [CI] 71%-98%); against *P. falciparum* it was 88% (95% CI 48%-97%), and >92% for *P. vivax* (95% CI >37%-99%). Primaquine was as well tolerated as placebo. Mild methemoglobinemia (mean of 3.4%) returned to normal within 2 weeks. Blood chemistry and hematological parameters revealed no evidence of toxicity. Good safety, tolerance, and efficacy, along with key advantages in dosing requirements, make primaquine an excellent drug for preventing malaria in nonpregnant, G6PD-normal travellers.
  
- 3 **Bangs MJ, Rusmiarto S, Gionar YR, Chan AS, Dave K, Ryan JR.**  
 Evaluation of a dipstick malaria sporozoite panel assay for detection of naturally infected mosquitoes.  
*J Med Entomol* 2002 Mar;39(2):324-330.  
 The determination of the presence or absence of malaria sporozoites in wild-caught *Anopheles* mosquitoes remains an integral component to the understanding of the transmission dynamics in endemic areas. To improve that capability, there has been on-going development of a new device using dipstick immunochromatographic technology for simplifying the testing procedure and reducing the time required to obtain results. As part of a larger multi-center effort, we evaluated the sensitivity and specificity of a prototype malaria sporozoite antigen panel assay (Medical Analysis Systems, Camarillo, CA) against three human *Plasmodium* species/polymorphs. The wicking (dipstick) assay was compared against a standard parasite antigen capture enzyme-linked immunosorbent assay (ELISA) for the detection of human circumsporozoite protein (CSP) in wild-caught mosquitoes. Over 6,800 *Anopheles* mosquitoes, representing 20 species collected from malaria endemic areas of Indonesia were tested either individually or in pools of up to 10 mosquitoes each. From 1,442 pooled test strip assays and ELISA formats, nine mosquito pools were found reactive for *P. falciparum*, *P. vivax* 210, or *P. vivax* 247 CSP. There was complete concordance between test strip results and ELISA results. Sensitivity was 100% and given some minor problems with false positives or negatives, specificity ( $n=488$ ) was 97%. Most strips judged as false positive produced very weak signals compared with negative control blank strips and paired ELISA-negative samples. The dipstick test proved technically simpler to perform and interpret than the ELISA and results were obtained within 15 min of exposure to mosquito suspension. This qualitative assay appears an attractive alternative to the CSP ELISA for detection of sporozoites in fresh or dried mosquitoes.
  
- 4 **Beebe NW, Cooper RD.**  
 Distribution and evolution of the *Anopheles punctulatus* group (Diptera: Culicidae) in Australia and Papua New Guinea.  
*Int J Parasitol* 2002 May;32(5):563-574.
  
- 5 **Beebe NW, van den Hurk AH, Chapman HF, Frances SP, Williams CR, Cooper RD.**  
 Development and evaluation of a species diagnostic

polymerase chain reaction-restriction fragment-length polymorphism procedure for cryptic members of the *Culex sitiens* (Diptera: Culicidae) subgroup in Australia and the southwest Pacific.

*J Med Entomol* 2002 Mar;39(2):362-369.

Members of the *Culex sitiens* subgroup are important vectors of arboviruses, including Japanese encephalitis virus, Murray Valley encephalitis virus and Ross River virus. Of the eight described species, *Cx. annulirostris* Skuse, *Cx. sitiens* Wiedemann, and *Cx. palpalis* Taylor appear to be the most abundant and widespread throughout northern Australia and Papua New Guinea (PNG). Recent investigations using allozymes have shown this subgroup to contain cryptic species that possess overlapping adult morphology. We report the development of a polymerase chain reaction-restriction fragment-length polymorphism (PCR-RFLP) procedure that reliably separates these three species. This procedure utilizes the sequence variation in the ribosomal DNA ITS1 and demonstrates species-specific PCR-RFLP profiles from both colony and field collected material. Assessment of the consistency of this procedure was undertaken on mosquitoes sampled from a wide geographic area including Australia, PNG, and the Solomon Islands. Overlapping adult morphology was observed for *Cx. annulirostris* and *Cx. palpalis* in both northern Queensland and PNG and for all three species at one site in northwest Queensland.

6 **Bockarie MJ, Tavul L, Kastens W, Michael E, Kazura JW.**

Impact of untreated bednets on prevalence of *Wuchereria bancrofti* transmitted by *Anopheles farauti* in Papua New Guinea.

*Med Vet Entomol* 2002 Mar;16(1):116-119.

Despite the growing evidence that insecticide-treated mosquito nets reduce malaria morbidity and mortality in a variety of epidemiological conditions, their value against lymphatic filariasis infection and disease is yet to be established. The impact of untreated bednets on the prevalence of *Wuchereria bancrofti* (Cobbold) (Nematoda: Filarioidea) infection and disease was investigated on Bagabag island in Papua New Guinea, where both malaria and filariasis are transmitted by the same vector mosquitoes of the *Anopheles punctulatus* Dönitz group (Diptera: Culicidae). Community-wide surveys were conducted recording demographic characteristics including bednet usage. Physical examinations for hydrocele and lymphoedema were performed and blood samples assessed for filarial and malaria parasites. Mosquitoes were sampled using the all-night landing catch method and individually dissected to determine *W. bancrofti* infection and infective rates. Bednet usage among residents was 61% and the mean age of users (25.6 years) was similar to non-users (22.5 years). *Anopheles farauti* Laveran was the only species found to contain filarial larvae: 2.7% infected (all stages), 0.5% infective (L3). The overall *W. bancrofti* microfilaraemia and antigenaemia rates were 28.5% and 53.1%, respectively. Bednet users had lower prevalence of *W. bancrofti* microfilaraemia, antigenaemia and hydrocele rates than non-users. In comparison, untreated bednets had no effect on the prevalence and intensity of *Plasmodium falciparum*

and *P. vivax* infections. The impact of bednet usage on rates of microfilaraemia and antigenaemia remained significant even when confounding factors such as age, location and sex were taken into account, suggesting that untreated bednets protect against *W. bancrofti* infection.

7 **Bourée P, Lancon A, Anquetil R, Menager C.**

Dengue in New Caledonia. Study of 68 pediatric cases. [Fr]

*Arch Pediatr* 2001 Dec;8(12):1311-1317.

New Caledonia is a French territory of the Pacific Ocean, where frequent dengue outbreaks occur. In 1995 and 1996, 3042 cases (including 18.3% children) were diagnosed in the Pasteur Institute of Noumea. PATIENTS AND METHODS: This work was a clinical and biological study of 68 in-patients of different ethnic groups of children. Among these young patients, 14 cases of dengue hemorrhagic fever occurred. RESULTS: The children were admitted to hospital after an average of 2.7 days of complaint, and stay averaged 6.7 days. The most important symptoms were fever at 39 degrees C (100%) during 2.2 days, sweating (100%), malaise (57%) and headache (50%). Forty children had at least one hemorrhagic symptom. Leucopenia was noticed for 42 children, on an average of 4.2 days. Thrombocytopenia (mean 114,746 platelets/mm<sup>3</sup>) occurred for 5.3 days in 34 children (six cases with less than 10,000 platelets/mm<sup>3</sup>). A bacterial infection arose in 23.5% of children. CONCLUSION: Dengue is an important problem of public health, which occurs in all parts of the population, including young children. Fighting against dengue fever by rapid destruction of larvae and adult mosquitoes led to the decrease of the outbreak.

8 **Casals-Pascual C, Allen S, Allen A, Kai O, Lowe B, Pain A, Roberts DJ.**

Short report: codon 125 polymorphism of CD31 and susceptibility to malaria.

*Am J Trop Med Hyg* 2001 Dec;65(6):736-737.

Platelet-endothelial cell adhesion molecule 1 (PECAM-1/CD31) has been identified as an endothelial cell receptor of *Plasmodium falciparum*-infected erythrocytes. The significance of adhesion of infected erythrocytes to this receptor in malaria infection has not been determined. We have therefore studied the association of the functional mutation CTG→GTG (Leu→Val) in codon 125 of the *Cd31* gene with severe disease in 2 case-control studies of malaria in Madang Hospital, Papua New Guinea, and in Kilifi District Hospital, Kenya. We analyzed data from 442 cases and controls from Papua New Guinea and data from 396 cases and controls from Kenya. The codon 125 polymorphism was not associated with severe malaria in either study. We conclude that the presence of CTG→GTG (Leu→Val) substitution in codon 125 in CD31 is not associated with protection from severe malaria, and we suggest that selective forces other than malaria may maintain this high-frequency polymorphism.

9 **Chang LC, Otero-Quintero S, Hooper JN, Bewley CA.**

Batzelline D and isobatzelline E from the Indopacific sponge *Zyzya fuliginosa*.

*J Nat Prod* 2002 May;65(5):776-778.

Two new pyrroloquinoline alkaloids, isobatzelline E (1) and batzelline D (2), together with the known compounds batzelline C (3), isobatzelline C (4), and makaluvamine D (5), were isolated from an Indopacific collection of the marine sponge *Zyzya fuliginosa*; the known compounds makaluvamines A (9), H (10), J (7), K (8), and P (6) were obtained from *Z. fuliginosa* collected in Papua New Guinea. The structures were elucidated by interpretation of 1D (1)H and (13)C NMR spectra and 2D HSQC and HSQC-LR spectra. Compounds 1-10 were isolated because the crude extracts of both *Zyzya* species inhibited HIV-1 envelope-mediated cell fusion. However, the inhibition profile observed for the pure compounds 1-10 mirrors that reported for the inhibition of topoisomerase II by other pyrroloquinolines, leaving open the possibility that the activity results from interactions with DNA-modifying enzymes.

- 10 **Ciasullo L, Casapullo A, Cutignano A, Bifulco G, Debitis C, Hooper J, Gomez-Paloma L, Riccio R.** Renieramide, a cyclic tripeptide from the Vanuatu sponge *Reniera* n. sp.

*J Nat Prod* 2002 Mar;65(3):407-410.

The polar extract of the Vanuatu sponge *Reniera* n. sp., which showed immunomodulating activity in preliminary tests, was found to contain a cyclic tripeptide, which we named renieramide (1). This metabolite is identical to a synthetic derivative mentioned in a patent concerning the preparation of cyclic peptides of the OF4949 family of anticancer agents. We describe here the first isolation of this metabolite from natural sources and its complete characterization by spectroscopic and chemical approaches. Renieramide (1) possesses a 17-membered cyclic side-chain-linked biphenyl ether skeleton, typical of the class that includes the natural products OF4949 I-IV, K13, and eurypamides. A tridimensional model of 1, obtained by NMR restrained molecular mechanics and dynamics, is also presented.

- 11 **Cooper RD, Waterson DG, Frances SP, Beebe NW, Sweeney AW.**

Speciation and distribution of the members of the *Anopheles punctulatus* (Diptera: Culicidae) group in Papua New Guinea.

*J Med Entomol* 2002 Jan;39(1):16-27.

Mosquito collections were made throughout the mainland of Papua New Guinea to identify the members of the *Anopheles punctulatus* group present and to determine their distribution. Identification was made using morphology, DNA hybridization, and polymerase chain reaction (PCR)-RFLP analysis. Nine members of the group were identified: *An. farauti* s.s. Laveran, *An. farauti* 2, *An. koliensis* Owen, and *An. punctulatus* Dönitz, were common and widespread; *An. farauti* 4 was restricted to the north of the central ranges where it was common; *An. farauti* 6 was found only in the highlands above 1,000 m; and *An. farauti* 3, *An. sp. near punctulatus* and *An. clowi* Rozeboom & Knight were uncommon and had restricted distributions. Identification of *An. koliensis* and *An. punctulatus* using proboscis morphology was found to be unreliable wherever *An. farauti* 4 occurred. The

distribution and dispersal of the members of the *An. punctulatus* group is discussed in regard to climate, larval habitats, distance from the coast, elevation, and proximity to human habitation.

- 12 **Davila N, Shea BT, Omoto K, Mercado M, Misawa S, Baumann G.**

Growth hormone binding protein, insulin-like growth factor-I and short stature in two pygmy populations from the Philippines.

*J Pediatr Endocrinol Metab* 2002 Mar;15(3):269-276.

The molecular basis and biochemical mediators of genetic growth propensity and adult height achievement in the general population are largely unknown. Pygmies represent one extreme of the height spectrum that may provide important clues regarding this issue. Previous studies in pygmies from Africa and Papua New Guinea have shown decreased serum levels of growth hormone binding protein (GHBP), the circulating ectodomain of the growth hormone receptor (GHR). By inference, a similar limitation in tissue GHR expression has been assumed to be responsible for the partial growth hormone (GH) resistance observed in African pygmies. It is not clear how generalizable this concept is to other populations. To address this question, we studied two pygmy populations from the Philippines (Aeta and Mamanwa people) that are unrelated to the African pygmies. Serum GHBP and IGF-I levels were significantly decreased in both pygmy populations, compared to normal-statured Philippino controls. The results, together with previous observations in African and New Guinean pygmies, indicate that short stature is associated with low serum GHBP levels in pygmy populations of diverse origins and in different parts of the world. This strengthens the tentative postulate that the GHBP/GHR system plays an important role in the genetic and perhaps nutritional determination of adult stature in humans. Molecular genetic studies of the GHR gene in various pygmy populations may shed further light on the mystery of pygmy short stature.

- 13 **Donaldson IJ, Shefta J, Lawson CA, Bushnell JR, Morgan AW, Isaacs JD, Carpenter D, Shaw MA, Rooth I, Quinell RJ, Zumla AM, Ollier WR, Chintu CZ, Muyinda GP, Hill AS, Boylston AW.**

Unique TCR beta-subunit variable gene haplotypes in Africans.

*Immunogenetics* 2002 Feb;53(10-11):884-893.

This study investigated polymorphisms of genes in two regions of the T-cell antigen receptor beta-subunit (TCRB) locus, including BV9S2P, and BV6S7 in a 5' linkage group, and BV8S3, BV24S1, BV25S1, BV18S1, BV2S1, BV15S1 and BV3S1 in a 3' linkage group. These loci have been genotyped in individuals from five regions in Africa, including The Gambia, Nigeria, Cameroon, Tanzania, and Zambia, and in individuals from northern Britain, northern India, and Papua New Guinea (PNG). In the 3' linkage group, 11 unique haplotypes were identified in the combined African populations; two equally frequent haplotypes represent the majority of African chromosomes. One haplotype was found in all four regions studied. This is the most frequent haplotype in the northern British, northern Indian and PNG populations. Although present, it is infrequent in the African populations. A

North-South gradient in the frequency of a common African haplotype was observed. The distribution did not represent that of a known disease. Evidence suggests that malaria is not responsible for selection of these haplotypes. Overall, this study highlights large differences in the genetic constitution of the TCRB locus between Africans and other populations.

**14 Duke T, Blaschke AJ, Sialis S, Bonkowsky JL.**

Hypoxaemia in acute respiratory and non-respiratory illnesses in neonates and children in a developing country.

*Arch Dis Child* 2002 Feb;86(2):108-112.

**AIMS:** To determine, in sick neonates and children requiring admission to a hospital in the highlands of Papua New Guinea: (1) the incidence and severity of hypoxaemia; (2) the proportion with hypoxaemia who do not fulfil criteria for acute lower respiratory infection (ALRI); and (3) the power of clinical signs to predict hypoxaemia, according to age and disease category. **METHODS:** Age dependent normal values for transcutaneous oxygen saturation (SpO<sub>2</sub>) were established in 218 well neonates and children in Goroka. A total of 491 sick neonates and children were then studied on presentation to the paediatric department at Goroka Hospital. **RESULTS:** A total of 257 sick neonates and children (52%) were hypoxaemic. Hypoxaemia was present in 179/245 (73%) with clinical criteria for ALRI; 79/246 (32%) with non-ALRI illnesses (including meningitis, septicaemia, severe malnutrition, low birth weight, birth asphyxia, and congenital syphilis) were also hypoxaemic. For children aged 1 month to 5 years with ALRI, the clinical signs best predicting hypoxaemia were cyanosis, respiratory rate >60, poor feeding, or reduced spontaneous activity; in those without ALRI the best predictors were cyanosis, respiratory rate >60 per minute, and inability to feed, but the positive predictive value was much lower than for children with ALRI. For neonates cyanosis was predictive of hypoxaemia, but tachypnoea or inability to feed were not. **CONCLUSIONS:** Hypoxaemia is an under recognised complication of non-ALRI illnesses in children and in sick neonates in developing countries. Use of algorithms with high sensitivity for the recognition of hypoxaemia, and protocols for administration of oxygen to neonates, and to children with non-ALRI illnesses, might substantially reduce case fatality.

**15 Duke T, Michael A, Mgone J, Frank D, Wal T, Sehuko R.**

Etiology of child mortality in Goroka, Papua New Guinea: a prospective two-year study.

*Bull World Health Organ* 2002;80(1):16-25.

**OBJECTIVE:** To collect accurate data on disease- and microbial-specific causes and avoidable factors in child deaths in a developing country. **METHODS:** A systematic prospective audit of deaths of children seen at Goroka Hospital in the highlands of Papua New Guinea was carried out. Over a 24-month period, we studied 353 consecutive deaths of children: 126 neonates, 186 children aged 1-59 months, and 41 children aged 5-12 years. **FINDINGS:** The most frequent age-specific clinical diagnoses were as follows: for neonates - very low birth weight,

septicaemia, birth asphyxia and congenital syphilis; for children aged 1-59 months - pneumonia, septicaemia, marasmus and meningitis; and for children aged 5-12 years - malignancies and septicaemia. At least one microbial cause of death was identified for 179 (50.7%) children and two or more were identified for 37 (10.5%). Nine microbial pathogens accounted for 41% of all childhood deaths and 76% of all deaths that had any infective component. Potentially avoidable factors were identified for 177 (50%) of deaths. The most frequently occurring factors were as follows: no antenatal care in high-risk pregnancies (8.8% of all deaths), very delayed presentation (7.9%), vaccine-preventable diseases (7.9%), informal adoption or child abandonment leading to severe malnutrition (5.7%), and lack of screening for maternal syphilis (5.4%). Sepsis due to enteric Gram-negative bacilli occurred in 87 (24.6%). The strongest associations with death from Gram-negative sepsis were adoption/abandonment leading to severe malnutrition, village births, and prolonged hospital stay. **CONCLUSIONS:** Reductions in child mortality will depend on addressing the commonest causes of death, which include disease states, microbial pathogens, adverse social circumstances and health service failures. Systematic mortality audits in selected regions where child mortality is high may be useful for setting priorities, estimating the potential benefit of specific and non-specific interventions, and providing continuous feedback on the quality of care provided and the outcome of health reforms.

**16 Duke T, Poka H, Dale F, Michael A, Mgone J, Wal T.**

Chloramphenicol versus benzylpenicillin and gentamicin for the treatment of severe pneumonia in children in Papua New Guinea: a randomised trial.

*Lancet* 2002 Feb 9;359(9305):474-480.

**BACKGROUND:** Pneumonia is the most frequent cause of child mortality in less-developed countries. We aimed to establish whether the combination of benzylpenicillin and gentamicin or chloramphenicol would be better as first-line treatment in children with severe pneumonia in Papua New Guinea. **METHODS:** We did an open randomised trial in which we enrolled children aged 1 month to 5 years of age who fulfilled the WHO criteria for very severe pneumonia and who presented to hospitals in two provinces. Children were randomly assigned to receive chloramphenicol (25 mg/kg 6 hourly) or benzylpenicillin (50 mg/kg 6 hourly) plus gentamicin (7.5 mg/kg daily) by intramuscular injection. The primary outcome measure was a good or an adverse outcome. **FINDINGS:** 1116 children were enrolled; 559 children were treated with chloramphenicol and 557 with benzylpenicillin and gentamicin. At presentation the median haemoglobin oxygen saturation was 71% (IQR 57-77) for those allocated chloramphenicol and 69% (55-77) for those allocated penicillin and gentamicin. 147 (26%) children treated with chloramphenicol and 123 (22%) treated with penicillin and gentamicin had adverse outcomes (p=0.11). 36 children treated with chloramphenicol and 29 treated with penicillin and gentamicin died. More children treated with chloramphenicol than

penicillin and gentamicin represented with severe pneumonia within 1 month of hospital discharge ( $p=0.03$ ). INTERPRETATION: For children with severe pneumonia in less-developed countries the probability of a good outcome is similar if treated with chloramphenicol or with the combination of benzylpenicillin and gentamicin.

17 **Foley B, Donegan E, Silitonga N, Wignall FS, Busch MP, Delwart EL.**

Importation of multiple HIV type 1 strains into West Papua, Indonesia (Irian Jaya).

*AIDS Res Hum Retroviruses* 2001 Nov 20;17(17):1655-1659.

HIV-1 from 16 sexually transmitted disease clinic patients in Timika, West Papua, Indonesia was amplified by RT-PCR and subtyped by a combination of envelope and gag region heteroduplex mobility analysis (HMA) and direct PCR DNA sequencing. HMA showed the presence of 14 subtype E (CRF01\_AE) and 2 subtype B HIV-1. Phylogenetic analysis of a 540-bp V3-V4 region of gp120 showed that 9 of 10 CRF01\_AE variants clustered tightly with a median distance of 1.3% (range, 0.5 to 2.2%) whereas 1 CRF01\_AE variant diverged significantly from the others (median distance, 10.7%; range, 10.1 to 11.8%). One subtype B virus envelope was typical of United States/European strains whereas the other appeared to be related to Thai subtype B' variants. These results reflect the independent introduction of multiple HIV-1 strains into West Papua, with the rapid spread in the majority of infected patients tested of a single strain of HIV-1E (CRF01\_AE).

18 **Fowler EV, Peters JM, Gatton ML, Chen N, Cheng Q.**

Genetic diversity of the DBLalpha region in *Plasmodium falciparum* var genes among Asia-Pacific isolates.

*Mol Biochem Parasitol* 2002 Mar;120(1):117-126.

In *Plasmodium falciparum* a highly polymorphic multi-copy gene family, var, encodes the variant surface antigen *P. falciparum* erythrocyte membrane protein 1 (PfEMP1), which has an important role in cytoadherence and immune evasion. Using previously described universal PCR primers for the first Duffy binding-like domain (DBLalpha) of var we analysed the DBLalpha repertoires of Dd2 (originally from Thailand) and eight isolates from the Solomon Islands (n=4), Philippines (n=2), Papua New Guinea (n=1) and Africa (n=1). We found 15-32 unique DBLalpha sequence types among these isolates and estimated detectable DBLalpha repertoire sizes ranging from 33-38 to 52-57 copies per genome. Our data suggest that var gene repertoires generally consist of 40-50 copies per genome. Eighteen DBLalpha sequences appeared in more than one Asia-Pacific isolate with the number of sequences shared between any two isolates ranging from 0 to 6 (mean=2.0  $\pm$  1.6). At the amino acid level DBLalpha sequence similarity within isolates ranged from 45.2  $\pm$  7.1 to 50.2  $\pm$  6.9%, and was not significantly different from the DBLalpha amino acid sequence similarity among isolates ( $p>0.1$ ). Comparisons with published sequences also revealed little overlap among DBLalpha sequences from different regions. High DBLalpha sequence diversity

and minimal overlap among these isolates suggest that the global var gene repertoire is immense, and may potentially be selected for by the host's protective immune response to the var gene products, PfEMP1.

19 **Genton B, Betuela I, Felger I, Al-Yaman F, Anders RF, Saul A, Rare L, Baisor M, Lorry K, Brown GV, Pye D, Irving DO, Smith TA, Beck HP, Alpers MP.**

A recombinant blood-stage malaria vaccine reduces *Plasmodium falciparum* density and exerts selective pressure on parasite populations in a phase 1-2b trial in Papua New Guinea.

*J Infect Dis* 2002 Mar 15;185(6):820-827.

The malaria vaccine Combination B comprises recombinant *Plasmodium falciparum* ring-infected erythrocyte surface antigen and 2 merozoite surface proteins (MSP1 and MSP2) formulated in oil-based adjuvant. A phase 1-2b double-blind, randomized, placebo-controlled trial in 120 children (5-9 years old) in Papua New Guinea demonstrated a 62% (95% confidence limits: 13%, 84%) reduction in parasite density in children not pretreated with sulfadoxine-pyrimethamine. Vaccinees had a lower prevalence of parasites carrying the MSP2-3D7 allelic form (corresponding to that in the vaccine) and a higher incidence of morbid episodes associated with FC27-type parasites. These results demonstrate functional activity of Combination B against *P. falciparum* in individuals with previous malaria exposure. The specific effects on parasites with particular *mSP2* genotypes suggest that the MSP2 component, at least in part, accounted for the activity. The vaccine-induced selection pressure exerted on the parasites and its consequences for morbidity strongly argue for developing vaccines comprising conserved antigens and/or multiple components covering all important allelic types.

20 **Gupta PC, Warnakulasuriya S.**

Global epidemiology of areca nut usage.

*Addict Biol* 2002 Jan;7(1):77-83.

A substantial proportion of the world's population is engaged in chewing areca nut and the habit is endemic throughout the Indian subcontinent, large parts of south Asia and Melanesia. A large variety of ingredients, including tobacco, may be used along with areca nut constituting a betel quid. The composition and method of chewing can vary widely from country to country and these population variations are described in this review. Some populations are known to use areca nut without tobacco providing good opportunities to further research the carcinogenicity of areca nut. Some interesting trends on chewing patterns have emerged from recent data, suggesting a decline in the habit in some countries such as Thailand while the prevalence of areca nut use is rising in India and Taiwan.

21 **Hall MJ, Edge W, Testa JM, Adams ZJ, Ready PD.**

Old World screwworm fly, *Chrysomya bezziana*, occurs as two geographical races.

*Med Vet Entomol* 2001 Dec;15(4):393-402.

A morphological and molecular analysis was undertaken with the objective of identifying markers for geographical populations of Old World screwworm

flies, *Chrysomya bezziana* Villeneuve (Diptera: Calliphoridae). The morphological analysis involved 192 adult flies from 14 countries, and the molecular analysis involved 45 larvae or adults from 14 populations in 11 countries. Principal components and cluster analysis of 10 morphological characters indicated that flies from Papua New Guinea (PNG) were a distinct group and most similar to flies from nearby Asian islands (Java, Sabah). There was poor resolution of other geographical regions, but some support for clustering of flies from Africa or India. Cladistic analysis of mitochondrial DNA sequences gave strong support for recognizing two races of Old World screwworm, one from sub-Saharan Africa and the other from the Gulf region and Asia. This latter race could be further divided into two lineages, i.e. one from mainland Asia (from Iraq to the Malay Peninsula) and the other from two islands of PNG.

22 **Hurles ME, Nicholson J, Bosch E, Renfrew C, Sykes BC, Jobling MA.**

Y chromosomal evidence for the origins of Oceanic-speaking peoples.

*Genetics* 2002 Jan;160(1):289-303.

A number of alternative hypotheses seek to explain the origins of the three groups of Pacific populations – Melanesians, Micronesians, and Polynesians – who speak languages belonging to the Oceanic subfamily of Austronesian languages. To test these various hypotheses at the genetic level, we assayed diversity within the nonrecombining portion of the Y chromosome, which contains within it a relatively simple record of the human past and represents the most informative haplotypic system in the human genome. High-resolution haplotypes combining binary, microsatellite, and minisatellite markers were generated for 390 Y chromosomes from 17 Austronesian-speaking populations in southeast Asia and the Pacific. Nineteen paternal lineages were defined and a Bayesian analysis of coalescent simulations was performed upon the microsatellite diversity within lineages to provide a temporal aspect to their geographical distribution. The ages and distributions of these lineages provide little support for the dominant archeo-linguistic model of the origins of Oceanic populations that suggests that these peoples represent the Eastern fringe of an agriculturally driven expansion initiated in southeast China and Taiwan. Rather, most Micronesian and Polynesian Y chromosomes appear to originate from different source populations within Melanesia and Eastern Indonesia. The Polynesian outlier, Kapingamarangi, is demonstrated to be an admixed Micronesian/Polynesian population. Furthermore, it is demonstrated that a geographical rather than linguistic classification of Oceanic populations best accounts for their extant Y chromosomal diversity.

23 **Lavu EK, Oswyn G, Vince JD.**

Sickle-cell/ $\beta^+$ -thalassaemia in a Papua New Guinean: the first reported case of the sickle gene in Papua New Guinea.

*Med J Aust* 2002 Jan 21;176(2):70-71.

We document the first case of the sickle-cell gene – Hb-S gene importation leading to Hb-S/ $\beta^+$ -thalassaemia double heterozygosity – in the apparently

previously Hb-S gene-free setting of Papua New Guinea.

24 **Lehmann D, Pomat WS, Combs B, Dyke T, Alpers MP.**

Maternal immunization with pneumococcal polysaccharide vaccine in the highlands of Papua New Guinea.

*Vaccine* 2002 Mar 15;20(13):1837-1845.

In Tari, Southern Highlands Province (SHP), Papua New Guinea (PNG), pneumococcal polysaccharide (Pnc PS) vaccine was offered to women at 28-38 weeks gestation. Blood samples were collected for measurement of pneumococcal antibody titres prior to immunization, from mother and cord at delivery and from their children at ages 1-3 and 4-6 months; samples were also collected in a subset of children before and 1 month after Pnc PS vaccine was given at age 8-9 months. Serum was collected from unimmunized women and their children at delivery and from children of unimmunized women at the same ages in infancy. There were no differences in neonatal or post-neonatal mortality rates or congenital abnormalities in the children of 235 immunized and 202 unimmunized women. There was a significant increase in antibody titres to pneumococcal serotypes 5, 14 and 23F in immunized women but not for serotype 7F. Geometric mean titres (GMTs) of antibodies for serotypes 5 and 23F were significantly higher in children of immunized women than in the unimmunized group up to age 2 months and for serotype 14 significantly higher to age 4 months. Maternal immunization did not significantly affect the children's capacity to make antibody responses to immunization with Pnc PS vaccine in infancy. The findings of this study and those in several other developing countries provide support for the concept of Pnc PS maternal immunization and justify the planning of large-scale efficacy trials.

25 **Menard D.**

Toxoplasmosis, rubella, syphilis, hepatitis B and HIV infection in women being followed for pregnancy in a population on the east coast of New Caledonia. [Fr] *Bull Soc Pathol Exot* 2001 Dec;94(5):403-405.

In view of the sparse available data concerning the main infectious illnesses screened for during pregnancy (toxoplasmosis, rubella, syphilis, hepatitis B virus and HIV) in the Northern Province and generally throughout New Caledonia, we decided to undertake a retrospective study based on the files of pregnant women having consulted between September 1996 and September 1999 in the East Coast provincial hospital (New Caledonia). First, we wished to estimate the prevalence of toxoplasmosis, rubella, syphilis, hepatitis B virus and HIV. Second, we wished to specify the main characteristics of these pregnant women, to trace the evolution of seroprevalence over the study time period and consider the influence of various factors such as age, place of residence and professional occupation. The biological study of these pregnancies was hindered by the fact that approximately half of women consult only from the second trimester of their pregnancy. This result underlines the importance of emphasising efforts aiming to bring women to consult earlier and of

improving the regularity and also the interpretation of serological tests (especially for toxoplasmosis serology). Within this population, we found the following percentages of seroprevalence: for toxoplasmosis between 83.6% and 89.6% (zone of hyperendemia), for rubella between 91.6% and 95.8%, for syphilis between 7% and 12.4%, for hepatitis B virus between 61.8% and 76% and for HIV 0%. The hepatitis B surface antigen (HbsAg) carrier rate was estimated between 1.7% and 4.9%. Following and informing pregnant women of the risk of toxoplasmosis appears to be of key importance as well as screening HbsAg carriers in order to limit viral transmission to the fetus.

26 **Mgone CS, Passey ME, Anang J, Peter W, Lupiwa T, Russell DM, Babona D, Alpers MP.**

Human immunodeficiency virus and other sexually transmitted infections among female sex workers in two major cities in Papua New Guinea. *Sex Transm Dis* 2002 May;29(5):265-270.

**BACKGROUND:** Treatable sexually transmitted infections are very common in developing countries and quite often are inadequately treated or remain untreated despite the fact that they enhance the transmission of human immunodeficiency virus (HIV). **GOAL:** To estimate the prevalence of HIV, syphilis, chlamydial infection, gonorrhoea, and trichomoniasis among female sex workers in Port Moresby and Lae, Papua New Guinea, and to collect data on associated behaviors. **STUDY DESIGN:** Self-identified female sex workers recruited through our peer-mediated sexually transmitted disease (STD)/HIV risk-reduction community outreach program were invited to participate in the study. Participants underwent pretest counseling, were interviewed, and were asked to self-collect vaginal swab specimens for the detection of STDs and to provide 10 mL of blood for HIV and syphilis testing. **RESULTS:** A total of 407 female sex workers, 207 in Port Moresby and 200 in Lae, were enrolled in the study. The overall prevalence rates of HIV, syphilis, genital chlamydial infection, gonorrhoea, and trichomoniasis among these women were estimated to be 10%, 32%, 31%, 36%, and 33%, respectively. The sex workers in Port Moresby had a significantly higher HIV infection rate (17%) than those in Lae (3%) and a significantly lower trichomoniasis rate (21%) than those in Lae (44%). Mixed infections were common, occurring in 45% of the cases. Despite a high rate of symptoms, the rate of treatment-seeking was low. Condom use among the sex workers was very inconsistent; 85% reported that they did not use condoms at all times when having sex with their clients. Common reasons cited were dislike by clients, unavailability, alcohol use, and familiarity with a client. **CONCLUSIONS:** STDs are very common among female sex workers in Port Moresby and Lae and very often present as multiple infections. Despite STD/HIV awareness campaigns, unsafe sex – particularly irregular use of condoms – continues among sex workers and their clients. Barriers to safer sexual behavior need to be addressed, as do improvements in provision of STD services.

27 **Mola GD, Amoa AB, Edilyong J.**

Factors associated with success or failure in trials of vacuum extraction.

*Aust NZ J Obstet Gynaecol* 2002 Feb;42(1):35-39.

Failure rates for vacuum extraction of between one in 16 and one in 600 have been reported. Most studies report that unexpected failure carries a greater risk to both mother and fetus. The aim of this study was to determine factors that were likely to predict success or failure in trials of vacuum extraction. At the Port Moresby General Hospital, 59 trials of vacuum extraction were performed between 1 December 1997 and 30 November 1999. These cases were analysed according to whether vacuum extraction was achieved with more than or less than three pulls, or an alternative method of delivery was required to effect delivery. Factors that were predictive of failure were: (i) Highlands origin of the mother; (ii) longer duration of the second stage of labour; (iii) severe moulding of the fetal head; (iv) cup detachments and deflexing cup applications; and (v) operator persisting with the procedure after three pulls. The cervix being less than fully dilated when the trial was commenced was not associated with a higher risk of failure, nor was it associated with a significantly higher risk of cervical trauma. Perinatal death and serious fetal scalp trauma were associated with deflexing cup applications, making more than three pulls and failed vacuum extractions.

28 **Müller I, Betuela I, Hide R.**

Regional patterns of birthweights in Papua New Guinea in relation to diet, environment and socio-economic factors.

*Ann Hum Biol* 2002 Jan-Feb;29(1):74-88.

Regional differences in mean birthweight in rural Papua New Guinea (PNG) and the importance of differences in family diet and maternal education and socio-economic status on such patterns were explored using birthweight data collected by the 1982/83 PNG National Nutrition Survey. A total of 6137 birthweight measurements from 85 PNG districts were available, representing 22% of all children included in the survey. The nature of possible selection biases are assessed and their implications discussed. Hierarchical Bayesian spatial models based on conditional autoregressive (CAR) priors were used to model spatial patterns in birthweights and their relation to different sets of covariates. Birthweights were found to exhibit striking geographical differences. Children from the central PNG highlands and from affluent lowland areas had the highest birthweights, while they were lowest in the (largely lowland) Sepik, Western, Madang and Milne Bay Provinces and in remote highland fringe areas. Maternal education, socio-economic status and diet were all important predictors, but only differences in family diet were correlated with the observed spatial patterns. The results of the present study highlight the importance of nutrition and socio-economic status in explaining differences in birthweights in PNG. Besides improving maternal health, interventions for improving birthweights in PNG should therefore aim at strengthening the economic base of rural populations and promote the cultivation and consumption of high quality foods.

29 **Owen IL, Pozio E, Tamburrini A, Danaya RT, Bruschi F, Gomez Morales MA.**

Focus of human trichinellosis in Papua New Guinea. *Am J Trop Med Hyg* 2001 Nov;65(5):553-557.

Human trichinellosis and teniasis (*Taenia solium*) are meat-borne helminthic infections with a wide distribution throughout the world. However, there is little information on the prevalence of these infections in Papua New Guinea. In 1999, serum samples were collected from 97 people in 6 villages in the remote Bensbach area of Papua New Guinea. Enzyme-linked immunosorbent assay and Western blot analyses were used to detect anti-*Trichinella* immunoglobulin (Ig) G and anti-cysticercus IgG in this population. The prevalence of *Trichinella* antibodies among inhabitants of the Bensbach area was 28.9% (28 of 97; 67.8% in men), suggesting a high consumption of poorly cooked meat. The higher prevalence of infection for *Trichinella* in men compared with women may be explained by the inclination of men to eat undercooked pork while hunting. All serum samples were negative for cysticercus antibodies. This is to our knowledge the first serosurvey showing anti-*Trichinella* antibodies in a human population living in Papua New Guinea (Australian region).

30 **Pasvol G.**

Ovalocytosis in Papua New Guinea. *Trends Parasitol* 2002 Apr;18(4):150.

31 **Patel SS, Mehlotra RK, Kastens W, Mgone CS, Kazura JW, Zimmerman PA.**

The association of the glycoporin C exon 3 deletion with ovalocytosis and malaria susceptibility in the Wosera, Papua New Guinea. *Blood* 2001 Dec 1;98(12):3489-3491.

Erythrocyte polymorphisms, including ovalocytosis, have been associated with protection against malaria. This study in the Wosera, a malaria holoendemic region of Papua New Guinea, examined the genetic basis of ovalocytosis and its influence on susceptibility to malaria infection. Whereas previous studies showed significant associations between Southeast Asian ovalocytosis (caused by a 27-base pair deletion in the anion exchanger 1 protein gene) and protection from cerebral malaria, this mutation was observed in only 1 of 1019 individuals in the Wosera. Polymerase chain reaction strategies were developed to genotype individuals for the glycoporin C exon 3 deletion associated with Melanesian Gerbich negativity (GPC $\Delta$ x3). This polymorphism was commonly observed in the study population (GPC $\Delta$ x3 frequency=0.465, n=742). Although GPC $\Delta$ x3 was significantly associated with increased ovalocytosis, it was not associated with differences in either *Plasmodium falciparum* or *P. vivax* infection measured over the 7-month study period. Future case-control studies will determine if GPC $\Delta$ x3 reduces susceptibility to malaria morbidity.

32 **Pedersen NS, Smith E.**

Prion diseases: epidemiology in man. *APMIS* 2002 Jan;110(1):14-22.

Prion disease in man was first described as Creutzfeldt-Jacob disease (CJD) in the 1920s. CJD may have three different origins: sporadic, familial, due to mutations in the prion gene, or infectious, due to iatrogenic exposure to infectious brain material. As

an example of the latter, kuru, in Papua New Guinea, was a variant of CJD transmitted by cannibalism. Between 1957 and 1982 more than 2500 died of kuru. Sporadic CJD is the most common form of CJD and occurs with an incidence of around one per million in most parts of the world. Familial CJD accounts for approximately 10% of all European cases of CJD, and is associated with inherited mutations of the prion protein gene, caused by one of the 24 single amino acid substitutions or insertions of octapeptide repeats. CJD caused by infections involves either iatrogenic cases of CJD, resulting from exposure to infectious brain, pituitary or ocular tissue, or from ingestion of infected food items. As of today, a few hundred iatrogenic cases of CJD have been diagnosed worldwide, the majority due to transmission by cadaveric pituitary HCG. So far, 111 cases of vCJD have been diagnosed caused by BSE-contaminated food. The size of the epidemic is still unclear and worst-case scenarios indicate that we may expect many thousands of cases in the future.

33 **Poser CM.**

Notes on the history of the prion diseases. Part I. *Clin Neurol Neurosurg* 2002 Jan;104(1):1-9.

The astute observation by William Hadlow, an American veterinary neuropathologist of the similarity between the histopathology of kuru, an obscure disease of the primitive tribe in New Guinea, and scrapie of sheep, was the first clue to the etiology of the transmissible spongiform encephalopathies (TSE). The knowledge that scrapie was transmissible but only after an unusually long incubation period, that the causative agent was highly resistant to heat and formalin, and that it seemed to be able to replicate in the absence of nucleic acid, eventually led to the discovery of the prion by Stanley Prusiner and the still controversial protein-only hypothesis of etiology of the TSE.

34 **Radford D.**

Traumatic false aneurysm in the popliteal artery of a child. *Med J Aust* 2001 Dec 3-17;175(11-12):658.

35 **Randazzo A, Bifulco G, Giannini C, Bucci M, Debitus C, Cirino G, Gomez-Paloma L.**

Haliptins A and B: two novel potent anti-inflammatory cyclic depsipeptides from the Vanuatu marine sponge *Haliclona* species. *J Am Chem Soc* 2001 Nov 7;123(44):10870-10876.

Two new metabolites, named haliptins A and B, have been isolated from the marine sponge *Haliclona* sp. Their structures were determined by extensive use of one- and two-dimensional NMR experiments, mass spectrometry, and UV and IR spectroscopy. Haliptin A is a novel 17-membered cyclic depsipeptide, consisting of five residues including two alanines (with L stereochemistry) and three new residues that appear to be previously undescribed from natural sources: 1,2-oxazetidine-4-methyl-4-carboxylic acid, 3-hydroxy-2,2,4-trimethyl-7-methoxydecanoic acid (HTMMD), and N-methyl- $\Delta$ -hydroxyisoleucine. The HTMMD residue is substituted with 3-hydroxy-2,2,4-trimethyl-7-hydroxydecanoic acid in haliptin B. Haliptin A was found to possess very potent

anti-inflammatory activity in vivo, causing about 60% inhibition of edema in mice at the dose of 300 µ/kg (i.p.).

36 **Reid SA.**

*Trypanosoma evansi* control and containment in Australasia.

*Trends Parasitol* 2002 May;18(5):219-224.

Animal trypanosomiasis caused by *Trypanosoma evansi* is endemic throughout Southeast Asia, where it is an important constraint on the productivity of smallholder livestock. In the past decade, *T. evansi* has emerged as a serious threat to the viability of smallholder livestock industries in the Philippines and causes severe disease outbreaks with high mortality. *Trypanosoma evansi* also poses a threat to livestock and native fauna in Australia and Papua New Guinea (PNG), where it is absent, but the risk of it spreading from Indonesia is high. Surveillance for *T. evansi* in PNG and Australia, and its control in the Philippines is restricted by the poor sensitivity and inadequate validation of existing diagnostic tests and lack of information on the determinants of infection.

37 **Sakihama N, Kaneko A, Hattori T, Tanabe K.**

Limited recombination events in merozoite surface protein-1 alleles of *Plasmodium falciparum* on islands.

*Gene* 2001 Nov 14;279(1):41-48.

Intragenic recombination is a principal mechanism for the generation of allelic variation in the merozoite surface protein-1 gene (*Msp-1*) of the human malaria parasite *Plasmodium falciparum*. In the present study, linkage disequilibrium between the 5'- and 3'-polymorphic sites was analyzed to determine the frequency of recombination events in *Msp-1* in parasite populations on four islands in Vanuatu, the southwestern Pacific, where malaria transmission is moderate and comparable to other mesoendemic areas. Of 141 isolates, whose 5'-haplotypes (*Msp-1* blocks 2-6) were determined by PCR-based typing, 138 were successfully sequenced for the 3'-polymorphism (block 17). A total of four distinct 5'-haplotypes and three distinct 3'-sequence types were identified with apparently different frequency distribution among islands. The number of 5'-haplotypes in each island was one to four, far smaller than in other previously studied geographic areas (ten to 21). Associations between the 5'- and 3'-polymorphisms (here termed *Msp-1* gene types) were subjected to the R(2) linkage disequilibrium test. The test revealed complete or very strong linkage disequilibrium in all four islands. Mixed infection was unusually rare (2.1%) and the mean number of *Msp-1* alleles per person was nearly 1.0. The heterozygosity of the *Msp-1* gene type calculated for each island ( $h=0.41-0.65$ ) was significantly lower than that in other areas of comparable endemicity ( $h=0.81-0.89$ ) ( $p<0.01$ ). These results indicate that recombination events in *Msp-1* would be extremely limited in Vanuatu, and stress that the frequency of recombination in *Msp-1* is determined by not only the intensity of malaria transmission but the frequency of mixed clone infections, the mean number of clones per person and a repertoire of clones in a local area.

38 **Smith T, Genton B, Betuela I, Rare L, Alpers MP.**

Mosquito nets for the elderly?

*Trans R Soc Trop Med Hyg* 2002 Jan-Feb;96(1):373-378.

Nine-year follow-up (ending 1999) of survival of 3738 individuals in a malaria-endemic area of Papua New Guinea found that the use of mosquito nets was associated with a large reduction in mortality in people aged  $\geq 40$  years as well as in children aged  $< 5$  years. There may be substantial benefits of malaria transmission reduction for older people, that have been overlooked in public health programmes and burden of disease calculations.

39 **Storz JF, Ramakrishnan U, Alberts SC.**

Determinants of effective population size for loci with different modes of inheritance.

*J Hered* 2001 Nov-Dec;92(6):497-502.

Here we report an assessment of the determinants of effective population size ( $N(e)$ ) in species with overlapping generations. Specifically, we used a stochastic demographic model to investigate the influence of different life-history variables on  $N(e)/N$  (where  $N$  = population census number) and the influence of sex differences in life-history variables on  $N(e)$  for loci with different modes of inheritance. We applied an individual-based modeling approach to two datasets: one from a natural population of savannah baboons (*Papio cynocephalus*) in the Amboseli basin of southern Kenya and one from a human tribal population (the Gainj of Papua New Guinea). Simulation-based estimates of  $N(e)/N$  averaged 0.329 for the Amboseli baboon population (SD = 0.116, 95% CI = 0.172 - 0.537) and 0.786 for the Gainj (SD = 0.184, 95% CI = 0.498 - 1.115). Although variance in male fitness had a substantial impact on  $N(e)/N$  in each of the two primate populations, ratios of  $N(e)$  values for autosomal and sex-linked loci exhibited no significant departures from Poisson-expected values. In each case, similarities in sex-specific  $N(e)$  values were attributable to the unexpectedly high variance in female fitness. Variance in male fitness resulted primarily from age-dependent variance in reproductive success, whereas variance in female fitness resulted primarily from stochastic variance in survival during the reproductive phase.

40 **Tefuarani N, Hawker R, Vince J, Sleight A, Williams G.**

Congenital heart disease in Papua New Guinean children.

*Ann Trop Paediatr* 2001 Dec;21(4):285-292.

The aim of the study was to analyse critically the programme for surgical management of children in Papua New Guinea (PNG) with congenital heart disease. A hospital record-based analysis was undertaken to document the pattern, management and short-term outcome of surgery in PNG children referred with a diagnosis of congenital heart disease to the Royal Alexandra Hospital for Children in Sydney, Australia. On admission, physical examination, chest radiogram, electrocardiogram, cross-sectional echocardiogram and, in most cases, cardiac catheterization were performed. Of the 170 children referred over the 17-year period, 1978-1994, 165 were confirmed to have congenital heart disease and were included in the study. Their ages ranged from 2 months to 16 years (median 5.5) and the male to

female ratio was 1:1. One-sixth had delayed milestones and one-fifth long-term wasting. A large number were tachypnoeic, in heart failure or had pulmonary hypertension on admission. Ventricular septal defect, 34%, tetralogy of Fallot, 23%, and patent ductus arteriosus, 16.4%, were the predominant defects. Lesions such as aortic stenosis, coarctation of the aorta and transposition of the great arteries are under-represented. Altogether, 133 children (81%) had surgery; 75% were open- and 25% closed-heart operations. The complications were unremarkable and the mortality rate (6%) acceptable for the era. The programme was therefore very successful for a small proportion of children born in PNG with congenital heart disease.

41 **Tefuarani N, Hawker R, Vince J, Sleigh A, Williams GM.**

Surgical programme at Royal Alexandra Hospital, Sydney, for Papua New Guinea children with congenital heart disease, 1978-1994.

*J Paediatr Child Health* 2002 Apr;38(2):178-182.

**OBJECTIVE:** To report the history of the Royal Alexandra Hospital for Children (RAHC) Papua New Guinea (PNG) cardiac surgical programme and describe the selection, preoperative clinical features and postoperative outcome of children with congenital heart disease managed by the programme. **METHODS:** Details for each of the PNG cardiac patients admitted to RAHC following selection by visiting cardiologists between 1978 and 1994 were entered into a database, and analysed and interpreted. **RESULTS:** A congenital heart defect was confirmed in 165 of the 170 children selected. The male to female ratio was 1:1 and the mean age on admission to RAHC was 5.5 years. Almost all of the children for whom data were available (98%) had a weight for age and 41% had a height for age less than the 3rd centile. One-sixth had delayed milestones. A large number were tachypnoeic, in heart failure, or had pulmonary hypertension on admission. Ventricular septal defect and tetralogy of Fallot were the commonest defects, and lesions such as aortic stenosis, coarctation of the aorta and transposition of the great arteries were absent or rare. Thirty-one (19%) of the children selected initially did not receive surgery because of pulmonary hypertension, or because the lesions did not fall within the programme guidelines for operation. One hundred and twenty-nine children had corrective and four had palliative procedures. Half of the operated children had postoperative complications. Eight children died, all following open-heart procedures, giving a case fatality rate of 6%. Preoperative tachypnoea, hepatomegaly, cardiac failure and pulmonary hypertension were strongly associated with poor outcome. **CONCLUSIONS:** The programme was an arduous exercise for all organizations concerned, but achieved comparatively good short-term outcomes. The experience gained should assist in planning for similar programmes.

42 **Ting JY, Brown AF.**

Ciguatera poisoning: a global issue with common management problems.

*Eur J Emerg Med* 2001 Dec;8(4):295-300.

Ciguatera poisoning, a toxinological syndrome

comprising an enigmatic mixture of gastrointestinal, neurocutaneous and constitutional symptoms, is a common food-borne illness related to contaminated fish consumption. As many as 50000 cases worldwide are reported annually, and the condition is endemic in tropical and subtropical regions of the Pacific Basin, Indian Ocean and Caribbean. Isolated outbreaks occur sporadically but with increasing frequency in temperate areas such as Europe and North America. Increase in travel between temperate countries and endemic areas and importation of susceptible fish has led to its encroachment into regions of the world where ciguatera has previously been rarely encountered. In the developed world, ciguatera poses a public health threat due to delayed or missed diagnosis. Ciguatera is frequently encountered in Australia. Sporadic cases are often misdiagnosed or not medically attended to, leading to persistent or recurrent debilitating symptoms lasting months to years. Without treatment, distinctive neurologic symptoms persist, occasionally being mistaken for multiple sclerosis. Constitutional symptoms may be misdiagnosed as chronic fatigue syndrome. A common source outbreak is easier to recognize and therefore notify to public health organizations. We present a case series of four adult tourists who developed ciguatera poisoning after consuming contaminated fish in Vanuatu. All responded well to intravenous mannitol. This is in contrast to a fifth patient who developed symptoms suggestive of ciguatera in the same week as the index cases but actually had staphylococcal endocarditis with bacteraemia. In addition to a lack of response to mannitol, clinical and laboratory indices of sepsis were present in this patient. Apart from ciguatera, acute gastroenteritis followed by neurological symptoms may be due to paralytic or neurotoxic shellfish poisoning, scombroid and pufferfish toxicity, botulism, enterovirus 71, toxidromes and bacteraemia. Clinical aspects of ciguatera toxicity, its pathophysiology, diagnostic difficulties and epidemiology are discussed.

43 **Tommaseo-Ponzetta M, Attimonelli M, De Robertis M, Tanzariello F, Saccone C.**

Mitochondrial DNA variability of West New Guinea populations.

*Am J Phys Anthropol* 2002 Jan;117(1):49-67.

This paper reports human mitochondrial DNA variability in West New Guinea (the least known, western side of the island of New Guinea), not yet described from a molecular perspective. The study was carried out on 202 subjects from 12 ethnic groups, belonging to six different Papuan language families, representative of both mountain and coastal plain areas. Mitochondrial DNA hypervariable region 1 (HVS 1) and the presence of the 9-bp deletion (intergenic region COII-tRNA(Lys)) were investigated. HVS 1 sequencing identified 73 polymorphic sites defining 89 haplotypes; the 9-bp deletion, which is considered a marker of Austronesian migration in the Pacific, was found to be absent in the whole West New Guinea study sample. Statistical analysis applied to the resulting haplotypes reveals high heterogeneity and an intersecting distribution of genetic variability in these populations, despite their

cultural and geographic diversity. The results of subsequent phylogenetic approaches subdivide mtDNA diversity in West New Guinea into three main clusters (groups I-III), defined by sets of polymorphisms which are also shared by some individuals from Papua New Guinea. Comparisons with worldwide HVS 1 sequences stored in the MitBASE database show the absence of these patterns outside Oceania and a few Indonesian subjects, who also lack the 9-bp deletion. This finding, which is consistent with the effects of genetic drift and prolonged isolation of West New Guinea populations, lead us to regard these patterns as New Guinea population markers, which may harbor the genetic memory of the earliest human migrations to the island.

44 **Umezaki M, Yamauchi T, Ohtsuka R.**

Time allocation to subsistence activities among the Huli in rural and urban Papua New Guinea. *J Biosoc Sci* 2002 Jan;34(1):133-137.

Time spent on subsistence activities was compared between rural sedentes and urban migrants of the Huli population in Papua New Guinea. Person-day observation data were collected for rural sedentes (441) in the Tari basin and for urban migrants in Port Moresby (175). The time spent on subsistence activities by males was longer in the urban area than in rural areas, while that by females was similar in both areas. Conspicuous gender inequality with respect to labour hours in rural areas seems to diminish when people move to urban areas, reflecting the different subsistence regime between rural and urban environments.

45 **Watts KJ, Thompson CH, Cossart YE, Rose BR.**

Sequence variation and physical state of human papillomavirus type 16 cervical cancer isolates from Australia and New Caledonia. *Int J Cancer* 2002 Feb 20;97(6):868-874.

Sequence diversity over 2600 nucleotides of the upstream regulatory region (URR) and the E6 and E2/E4 genes of 34 human papillomavirus (HPV)16 cervical cancer isolates from Australia and New Caledonia was investigated. One 81 base duplication, 41 single base substitutions and 1 single base insertion were identified in the URRs. Some of these changes are reported here for the first time. Several of the 19 changes impacting transcription factor binding sites had the potential to alter promoter activity. Twenty-eight (82%) of the variants belonged to the European lineage, 4 (12%) were Asian and 2 (6%) were Asian-American. Eighteen of 27 (67%) isolates where the E6 gene was examined contained amino acid substitutions. Of 13 isolates sequenced with intact E2 genes, 12 (92%) contained amino acid substitutions in the E2 protein and 3 (23%) amino acid substitutions in the overlapping E4 protein. Some of the changes in E6 and E2 may alter immunological epitopes or protein function. The physical state of HPV DNA was assessed by Southern hybridization and PCR for an intact E2 gene. Overall, 11 of 25 isolates contained only integrated HPV DNA, 10 only episomal HPV DNA and 4 both integrated and episomal DNA. No particular patterns of variation in the URR, E6 or E2/E4 genes predicted physical state. This investigation represents one of the most

comprehensive studies of its kind and fills an important gap in global sequence data.

46 **Williams DE, Craig KS, Patrick B, McHardy LM, van Soest R, Roberge M, Andersen RJ.**

Motuporamines, anti-invasion and anti-angiogenic alkaloids from the marine sponge *Xestospongia exigua* (Kirkpatrick): isolation, structure elucidation, analogue synthesis, and conformational analysis. *J Org Chem* 2002 Jan 11;67(1):245-258.

Extracts of the sponge *Xestospongia exigua* collected in Papua New Guinea were positive in a new assay for anti-invasion activity. Bioassay-guided fractionation led to the identification of the three known motuporamines A (1), B (2), and C (3) along with the new motuporamines D (4), E (5), and F (6) and a mixture of G, H, and I (15). Motuporamines A (1), B (2), and C (3) and the mixture of G, H, and I (15) were responsible for the anti-invasion activity of the crude extract. Motuporamine C (3) has also been found to be anti-angiogenic. A series of analogues of the motuporamines have been synthesized and evaluated for anti-invasive activity. These SAR results revealed that a saturated 15-membered cyclic amine fused to the natural motuporamine diamine side chain (13) represented the optimal structure for anti-invasive activity in this family. Single-crystal X-ray diffraction analysis of one of the analogues 20 showed that in the solid state its 16-membered macrocyclic amine fragment adopted the [4444] quadrangular conformation predicted by calculations to be the lowest energy conformation for the corresponding cycloalkane, cyclohexadecane. These data along with literature X-ray data and conformational analysis for derivatives of azacyclotridecane have been used as precedents for predicting the lowest energy ring conformations of other motuporamines. The SAR data from the natural and synthetic motuporamines have been combined with the conformational analyses to provide an outline of the functionality and shape required for activity in this family of alkaloids and to design a new analogue 49 that showed good anti-invasion activity.

47 **Wongsrichanalai C, Pickard AL, Wernsdorfer WH, Meshnick SR.**

Epidemiology of drug-resistant malaria. *Lancet Infect Dis* 2002 Apr;2(4):209-218.

Since the first reports of chloroquine-resistant falciparum malaria in southeast Asia and South America almost half a century ago, drug-resistant malaria has posed a major problem in malaria control. By the late 1980s, resistance to sulfadoxine-pyrimethamine and to mefloquine was also prevalent on the Thai-Cambodian and Thai-Myanmar (Thai-Burmese) borders, rendering them established multidrug-resistant (MDR) areas. Chloroquine resistance spread across Africa during the 1980s, and severe resistance is especially found in east Africa. As a result, more than ten African countries have switched their first-line drug to sulfadoxine-pyrimethamine. Of great concern is the fact that the efficacy of this drug in Africa is progressively deteriorating, especially in foci in east Africa, which are classified as emerging MDR areas. Urgent efforts are needed to lengthen the lifespan of sulfadoxine-pyrimethamine and to identify

effective, affordable, alternative antimalarial regimens. Molecular markers for antimalarial resistance have been identified, including *pfcr* polymorphisms associated with chloroquine resistance and *dhfr* and *dhps* polymorphisms associated with sulfadoxine-pyrimethamine resistance. Polymorphisms in *pfmdr1* may also be associated with resistance to chloroquine, mefloquine, quinine, and artemisinin. Use of such genetic information for the early detection of

resistance foci and future monitoring of drug-resistant malaria is a potentially useful epidemiological tool, in conjunction with the conventional in-vivo and in-vitro drug-sensitivity assessments. This review describes the various features of drug resistance in *Plasmodium falciparum*, including its determinants, current status in diverse geographical areas, molecular markers, and their implications.

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