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PUBLICATIONS OF RELEVANCE TO PAPUA NEW GUINEA AND MELANESIA

Bibliographic Citation List generated from MEDLARS

- 1 **Amoa AB, Klufio CA, Kariwiga G, Heywood S.**
Antenatal haemoglobin profile at the Port Moresby General Hospital.
PNG Med J 1998 Sep-Dec;41(3-4):119-125.
From 1 November 1995 to 10 April 1996, 1001 consecutive mothers who had attended the Port Moresby General Hospital (PMGH) antenatal clinic and were delivered in the Maternity Unit of the PMGH were surveyed for their antenatal haemoglobin (Hb) levels. One or more Hb results had been noted in the antenatal records of 997 subjects. The mean of the first Hb level for this sample was 10.6 ± 1.72 g/dl. The first Hb level was below 10.0 g/dl in 33% of the 997 subjects. The dates were reliable in 777 subjects. The mean first Hb for this group was the same as for the total sample. A subgroup of 449 subjects with reliable dates and first Hb measurement at ≤ 26 weeks gestation had a first Hb mean of 10.9 ± 1.78 g/dl. Among those with reliable dates, 569 had two or more Hb measurements, the last being at ≥ 34 weeks. In this subgroup, the mean of the last Hb was 11.1 ± 1.60 g/dl. The first Hb was measured at ≤ 26 weeks in 352 subjects in this subgroup. The means for the first and last Hb levels for this subset were 10.9 ± 1.78 and 11.1 ± 1.57 g/dl, respectively; the paired t test did not show any difference between the first and last Hb levels. For subjects in the total sample who had two or more Hb measurements, the mean for the lowest Hb level was 10.0 ± 1.54 ; 45% had levels below 10.0 g/dl at some time during the pregnancy.
- 2 **Amoa AB, Klufio CA, Moro M, Kariwiga G, Mola G.**
A case-control study of stillbirths at the Port Moresby General Hospital.
PNG Med J 1998 Sep-Dec;41(3-4):126-136.
From September 1995 to May 1997, 315 consecutive stillbirths and 315 randomly selected controls were studied at the Port Moresby General Hospital to determine the causes of the deaths, to describe the sociodemographic and reproductive characteristics of the mothers, and to see if there were any avoidable factors in the stillbirths and where the responsibility for them lay. 249 (79%) of the stillbirths were antepartum and 14% were intrapartum; the timing of death could not be determined in the remaining 21 (7%). 36% of the stillbirths were unexplained. The common identified causes were: syphilis (VDRL and TPHA positive) 10%, intrauterine growth restriction/placental insufficiency 9%, antepartum haemorrhage 9%, malaria 6%, major congenital abnormalities 6%, cord accidents 6%, pregnancy-induced hypertension 5% and acute intrapartum asphyxia 4%. Multiple logistic regression analysis showed a significant association between stillbirth and the following variables: husband's occupation unskilled, age over 35 years, poor antenatal attendance, a past history of stillbirth, syphilis and malaria. An avoidable factor was established in 41% of the cases; in 60% the responsibility for the avoidable factor lay with the patient and her relatives.
- 3 **Beebe NW, Cooper RD, Foley DH, Ellis JT.**
Populations of the south-west Pacific malaria vector *Anopheles farauti* s.s. revealed by ribosomal DNA transcribed spacer polymorphisms.
Heredity 2000 Feb;84(Pt 2):244-253.
Malaria in the south-west Pacific is transmitted by members of the *Anopheles punctulatus* group which comprises 12 cryptic species with overlapping morphology. The most widely distributed species of the group is *Anopheles farauti* s.s. (*An. farauti* 1) found throughout northern Australia, Papua New Guinea, eastern Indonesia, the Solomon Islands and Vanuatu. A study of the population structure of this species using PCR-RFLP analysis on the ribosomal DNA internal transcribed spacer 1 reveals five genotypes which had distinct geographical distributions. Where these distributions overlap, genotype hybrids can be identified. Heteroduplex analysis of the ITS2 region reveals combinations of nonhomogenized ITS2 sequences and subsequently seven identifiable genotypes, reflecting the ITS1 distribution. Sequence analysis of these ITS2 polymorphisms reveals a minimum of 13 ITS2 sequence types present in heterogeneous combinations in individual mosquitoes. It appears that there are different levels of evolution occurring within the ITS1 and ITS2 regions. These data suggest that *An. farauti* s.s. may contain multiple loci for the rDNA gene family or that the homogenization of these regions is relatively slow and can be used in genetic studies of population distribution and structure.
- 4 **Broom AK, Wallace MJ, Mackenzie JS, Smith DW, Hall RA.**
Immunisation with gamma globulin to Murray Valley encephalitis virus and with an inactivated Japanese encephalitis virus vaccine as prophylaxis against Australian encephalitis: evaluation in a mouse model.
J Med Virol 2000 Jun;61(2):259-265.
In northwestern Australia, the flavivirus Murray Valley encephalitis (MVE) poses a significant health risk to infants in some Aboriginal communities, particularly during each wet season. While there are too few cases to warrant the development of a vaccine against MVE, a safe, effective prophylaxis for these children is still urgently required. The use of passive transfer of

- human gamma globulin to MVE or immunisation with a vaccine to the closely related Japanese encephalitis (JE) virus were investigated as potential strategies. When 40 µg of IgG was purified from MVE-immune human sera and transferred to 3-week-old mice, the animals were protected from lethal IP inoculation with MVE virus while still producing a detectable immune response to the virus. Similarly, sera from adult mice infected sublethally with MVE or JE virus provided significant protection against MVE infection. However, sera from mice sublethally infected with the related Kunjin or immunised with the inactivated JE vaccine (Biken) provided no protection against MVE challenge. In fact, mice immunised passively with the latter appeared to succumb to MVE challenge more rapidly than mice that received serum from unimmunised animals, suggesting that antibody to the vaccine had accelerated the progression of disease. These preliminary trials in mice indicate that passive immunisation with human gamma globulin has the greatest potential as a strategy for MVE prophylaxis, whilst the apparent enhancement of MVE by antibodies to the JE vaccine requires further investigation, with particular reference to current vaccination programs in areas of Australia and Papua New Guinea, where both JE and MVE occur.
- 5 **Bruce MC, Donnelly CA, Alpers MP, Galinski MR, Barnwell JW, Walliker D, Day KP.** Cross-species interactions between malaria parasites in humans. *Science* 2000 Feb 4;287(5454):845-848.
- 6 **Clavano Harding AB, Ambler GR, Cowell CT, Garnett SP, Al Toumah B, Coakley JC, Ho KK, Baxter RC.** Initial characterization of the GH-IGF axis and nutritional status of the Ati Negritos of the Philippines. *Clin Endocrinol (Oxf)* 1999 Dec;51(6):741-747.
BACKGROUND AND OBJECTIVE: The Ati Negritos are a Pygmy-like aboriginal population from the Philippines with physical characteristics of short stature, dark skin and woolly, kinked hair. Their final height, components of their GH-IGF axis and various nutritional markers are described. **SUBJECTS, DESIGN AND MEASUREMENTS:** Auxological data and sera for the components of the GH-IGF axis and nutritional parameters were collected from 9 adult Ati Negritos in their native environment and 10 Filipinos in Sydney. **RESULTS:** The height SDS (- 3.66 ± 1.1 vs. - 1.01 ± 1.2), weight SDS (- 2.30 ± 1.6 vs. 0.10 ± 0.7), and BMI SDS (- 1.4 ± 1.8 vs. - 0.2 ± 0.5) between the two groups were significantly different (P < 0.01). The mean height of the 6 male Ati Negritos was 149 ± 7 and 144 ± 3 cm for the females, which are comparable with the African Pygmies and the Mountain Ok people of Papua New Guinea. The Ati Negritos showed lower growth hormone binding protein (GHBP), insulin-like growth factor I (IGF-I), insulin-like growth factor binding protein 3 (IGFBP-3), acid labile subunit (ALS), zinc, albumin, ferritin, iron and iron saturation and much higher insulin-like growth factor binding protein 2 (IGFBP-2) and plasma transferrin concentrations. No differences were noted in random growth hormone (GH), plasma insulin-like growth factor II (IGF-II), nor in their plasma concentrations of prealbumin, thyroid stimulating hormone (TSH) and free thyroxine (T4). **CONCLUSION:** Perturbations of both the GH-IGF-I axis and nutritional markers exist in the Ati Negritos. These findings may be determinants of their stature; however, the aetiology of these changes remains to be fully elucidated.
- 7 **Crouch Chivers PR.** The public health imperative in Papua New Guinea. *PNG Med J* 1998 Sep-Dec;41(3-4):97-101.
- 8 **Dean M.** Launching a lymphatic filariasis campaign in the Pacific Islands. *Lancet* 2000 Jul 8;356(9224):143.
- 9 **Dugoujon JM, Guitard E, Senegas MT, Roth MP, Sanchez A, Barny S, Simon D, Papoz L.** Genetic markers of immunoglobulins and diabetes mellitus in the multiracial population of New Caledonia. The CALDIA Study Group. *Diabetes Res Clin Pract* 2000 Mar;47(3):209-215.
 GM and KM immunoglobulin allotypes, which are the markers, respectively, of the constant parts of the heavy and the light chains of the IgG1, IgG2 and IgG3 subclasses, have been analysed in diabetic mellitus patients and controls living in New Caledonia. We tested 40 Europeans, 256 Melanesians and 44 Polynesians, as well as their 340 matched controls, in order to search for a genetic susceptibility at those polymorphic loci. All the subjects were tested for G1M (1, 2, 3, 17), G2M (23), G3M (5, 6, 10, 11, 13, 14, 15, 16, 21, 24, 28) and KM (1) by the classical hemagglutination method. The frequencies of GM haplotypes and KM alleles have been estimated by a maximum likelihood method. The results are in favour of no influence of the GM and KM loci. The prevalence of diabetes mellitus varies in the populations of New Caledonia: Polynesians are at much higher risk than Melanesians or Europeans. The GM haplotype distribution differs among ethnic groups; so they provide a useful marker to measure genetic admixture. The higher prevalence of diabetes observed among New Caledonians of European origin compared to the prevalence in Europe may be explained by genetic admixture with neighbouring Pacific populations, notably Polynesians (Asian haplotypes are present at a frequency of 9.4%). So, the genetic admixture should be measured in any genetic epidemiological study.
- 10 **Durden LA, Beaucournu JC.** The flea genus *Sigmactenus* (Siphonaptera: Leptopsyllidae): a new species from Timor and new material from New Guinea and the Philippines. *J Parasitol* 2000 Jun;86(3):432-437.

Both sexes of *Sigmactenus timorensis* n. sp. are described from *Rattus tanezumi* and *Rattus exulans* collected in West Timor, Indonesia. The true host presumably is a native murine rat such as the extant, endemic *Rattus timorensis* or 1 of several extinct, endemic Timorese rats. Analyses of new collections of *Sigmactenus cavifrons* and *Sigmactenus toxopeusi* from New Guinea demonstrate that these fleas show considerable morphological variation. We propose that they represent a single species with the name *S. toxopeusi* having priority. New collections of *Sigmactenus werneri* from the Philippines expand the known hosts and geographical distribution of this flea.

11 **Foley DH, Bryan JH.**

Shared salinity tolerance invalidates a test for the malaria vector *Anopheles farauti* s.s. on Guadalcanal, Solomon Islands.

Med Vet Entomol 2000 Mar;14(1):102-104.

Among the Punctulatus Group of *Anopheles* mosquitoes (Diptera: Culicidae), first-instar larvae of the medically unimportant freshwater *Anopheles farauti* species No. 7 survives a seawater tolerance test (SST) that was previously thought to be diagnostic for the saltwater-tolerant malaria vector species, *An. farauti* Laveran s.s. Salt tolerance in these two closely related isomorphic species appears to be a shared derived character within the Farauti Complex. Failure to differentiate *An. farauti* s.s. from *An. farauti* No. 7 will overestimate potential malaria vector numbers and waste limited larval control resources. Use of the SST should therefore be discontinued on Guadalcanal and other techniques such as allozyme electrophoresis used instead.

12 **Garner P, Baea M.**

Where is the mother in maternal and child health? *Lancet* 2000 Feb 5;355(9202):498.

13 **Hombhanje FW.**

Halofantrine versus quinine-Fansidar combination in the treatment of post-chloroquine falciparum parasitaemia.

PNG Med J 1998 Sep-Dec;41(3-4):112-115.

The standard first-line treatment for malaria in adults in Papua New Guinea is chloroquine; for severe and treatment-failure malaria standard therapy is a combination of quinine and Fansidar (sulphadoxine-pyrimethamine). These standard treatments are currently under revision. The present study evaluated the effect of halofantrine in treatment-failure falciparum malaria in adults in Port Moresby compared to standard therapy. In the halofantrine group all parasites were cleared by day 5 after starting therapy, in the quinine-Fansidar group by day 7. There was no evidence of recurrence of parasitaemia during the 21-day follow-up in either group. Nausea was associated with halofantrine use in 68% of patients. In the quinine-Fansidar group 79% had muffled deafness, 32% tinnitus and 26% dizziness; 32% of patients withdrew from treatment on day 2 because of

intolerance to quinine. Halofantrine in this study population provided an efficacy against treatment-failure falciparum malaria similar to that of quinine-Fansidar, with a more favourable profile of adverse effects.

14 **Hombhanje FW.**

In vitro susceptibility of *Plasmodium falciparum* to four antimalarial drugs in the Central Province of Papua New Guinea.

PNG Med J 1998 Jun;41(2):51-58.

The susceptibility of *Plasmodium falciparum* to chloroquine, quinine, mefloquine and halofantrine was investigated in the Central Province of Papua New Guinea between March 1995 and September 1996, when chloroquine resistance was widely present in the country. The standard World Health Organization in vitro microtest methodology was used in the study. Of the 30 isolates tested for chloroquine susceptibility all were resistant to chloroquine with median IC50 of 1.15 µmol/l (range 0.54 to 4.24), indicating a high prevalence and degree of resistance. Three isolates each for quinine (3/31) and halofantrine (3/28) showed resistance at concentrations of 51.2 µmol/l and 10 nM respectively, while all 31 isolates tested for mefloquine were fully susceptible. The comparative analysis of median IC50 values between isolates resistant and susceptible to chloroquine showed chloroquine-resistant isolates to be less susceptible to quinine and halofantrine while fully susceptible to mefloquine. It seems that the evolution of chloroquine resistance together with increased use of quinine treatment of *P. falciparum* malaria may increase the risk of emergence of quinine resistance and possibly of halofantrine resistance as well. The development of mefloquine resistance, however, is independent of chloroquine resistance.

15 **Hombhanje FW.**

Plasmodium ovale species in Papua New Guinea – lest we forget.

PNG Med J 1998 Sep-Dec;41(3-4):116-118.

The microscopical diagnosis of *Plasmodium ovale* infection is reviewed and its similarity to *Plasmodium vivax* emphasized. Its presence in Papua New Guinea has been recognized for many years, from a time not long after Stephens first described the species in 1922, but it is rarely reported. There is no doubt of its presence in Papua New Guinea, together with *P. falciparum*, *P. vivax* and *P. malariae*, but its exact prevalence and distribution has not been determined.

16 **Jobs DV, Friedlaender JS, Mgone CS, Koki G, Alpers MP, Ryschkewitsch CF, Stoner GL.**

A novel JC virus variant found in the Highlands of Papua New Guinea has a 21-base pair deletion in the agnoprotein gene.

J Hum Virol 1999 Nov-Dec;2(6):350-358.

OBJECTIVES: This paper describes a unique JC virus (JCV) variant recovered from the Highlands of Papua New Guinea that contains an inframe 21-bp deletion in the agnoprotein gene. We characterize the mutation and suggest possible

- roles for the deletion in JCV evolution. **STUDY DESIGN/METHODS:** JCV DNA was extracted from urine and polymerase chain reaction (PCR) amplified using whole genome primers. PCR products were cloned, and multiple clones were sequenced. The JCV agnogene was PCR amplified to verify the presence of the agnogene deletion. **RESULTS:** This mutation creates a 21-bp deletion near the 3' end, which alters the predicted secondary structure of the messenger RNA and changes local codon usage at the 3' end of the agnogene. Protein secondary structure predictions suggest the deleted portion of the agnoprotein may be a flexible surface feature. **CONCLUSIONS:** We describe the first stable coding region deletion in JCV that presumably signifies a single evolutionary event that led to the split from other Highlands viral groups and occurred well after the human expansions that led to the peopling of the Southwest Pacific.
- 17 **Lehmann D, Kakazo M, Yarsley S, Javati A, Taime J, Saleu G, Namuigi P, Alpers MP, Mendelman PM, Staub T.** Safety and immunogenicity of *Haemophilus influenzae* type b conjugate vaccine (PedvaxHIB) in Papua New Guinean children. *PNG Med J* 1998 Sep-Dec;41(3-4):102-111.
- BACKGROUND:** In view of high mortality and morbidity from *Haemophilus influenzae* type b (Hib) in young Papua New Guinean children, the incorporation of a Hib conjugate vaccine into a nationwide immunization program would be of major public health benefit. The choice of the Hib conjugate vaccine will be based on the evaluation of several Hib conjugate vaccines, after consideration of such factors as the ease of incorporation into the current vaccination schedule, cost, kinetics of antibody responses and safety. **METHODS:** This study evaluated the safety and immunogenicity of Hib polysaccharide-*Neisseria meningitidis* outer membrane protein complex conjugate vaccine (PRP-OMPC) in Papua New Guinea. 95 children were recruited at Goroka Base Hospital, Eastern Highlands Province, and enrolled in the study. PRP-OMPC was administered at ages 2, 4 and 12 to 15 months. Blood was collected before each dose, one month after the second and booster doses, and at ages 18 and 24 months. Antibody to PRP (anti-PRP) was measured by radioimmunoassay. **RESULTS:** PRP-OMPC was generally well tolerated. At successive sampling times from the prevaccination bleed through the 1-month post-booster bleed, geometric mean titres were 0.18, 1.45, 2.54, 1.03 and 8.05 micrograms/ml, respectively (n = 60). The proportions of subjects with anti-PRP titres > or = 1.0 microgram/ml were 26%, 62%, 73%, 47% and 93%, respectively (n = 60). Persistence of anti-PRP was ascertained in 41 subjects. The GMTs at 18 and 24 months were 3.42 and 2.0 micrograms/ml, respectively. **CONCLUSIONS:** PRP-OMPC was found to be immunogenic after the first dose and to elicit a robust booster response. Antibody titres persisted until age 24 months, at which time 100% of subjects had anti-PRP > or = 0.15 microgram/ml. These results are consistent with previous studies in US Native American infants and in Gambian infants.
- 18 **Levy MH, Dakulala P, Koiri JB, Stewart G, Krause V.** Tuberculosis control in Papua New Guinea. *PNG Med J* 1998 Jun;41(2):72-76.
- 19 **Lucas RE.** A survey to gather sexually transmitted disease epidemiological and management data in the Solomon Islands. *Trop Doct* 2000 Apr;30(2):97-99.
- A survey of 15 clinics and hospitals in the Solomon Islands (a South Pacific nation with a 45% rate of penicillin-resistant gonorrhoea) was undertaken to audit the quality of sexually transmitted diseases data collection, adherence to public health fundamentals and knowledge of the national gonorrhoea management guidelines. With the exception of one town clinic, data collection was limited, syphilis serological testing was low (28%) and correct knowledge of the national gonorrhoea treatment guidelines was also limited to 4/8 clinics (50%). Contact tracing was definitely undertaken in 2/8 (25%) of clinics. A high male/female notification ratio (3.6:1) for gonorrhoea was detected. Solomon Island clinics may be typical of other South Pacific Island communities in their inadequate attention to public health fundamentals. Every effort should be made to identify these shortcomings and provide feedback to clinic health workers to improve this service, particularly in the context of the more recent arrival of the HIV epidemic in the region.
- 20 **Lucas RE, Faoagali JL.** The serological status of Solomon Island blood donors. *Southeast Asian J Trop Med Public Health* 1999 Sep;30(3):542-545.
- The serological status of Solomon Island blood donors in 1995 and in particular the seroprevalence of antibodies to Hepatitis B and C and prevalence of risk factors for these chronic infections was studied. A questionnaire of risk factors for Hepatitis B and C was undertaken. All blood donors had been previously screened for HIV antibody without any positive cases recorded. 598 donors had serum collected of which 36 samples (6.0%) were third generation HCV EIA antibody positive and 3 samples were RIBA positive but none were PCR positive. 25.1% of samples were positive for HBsAg and anti-HBc antibody was found in 84.4%. Elevated ALT levels (>35 U/l) were found in 6.5% of samples but there was no statistically significant association with HCV or HBsAg status. 15.4% were TPHA positive and 5.4% had RPR titers more than or equal to 1. Anti-HTLV-1 antibody was positive in 12.3% randomly selected samples. All 10 positive samples were then found to be antibody indeterminate with Western blot assay. Of the 585 samples with completed questionnaires, analysis of the relationship between anti-HCV status with tattoo

status and ear piercing also failed to reach statistical significance. Consistent with other studies from tropical malaria-prone countries, a positive anti-HCV antibody test even by the third generation EIA is probably a false positive test in most cases. In addition, high prevalence rates of HBV, yaws or syphilis infection were demonstrated.

- 21 **Maitland K, Kyes S, Williams TN, Newbold CI.** Genetic restriction of *Plasmodium falciparum* in an area of stable transmission: an example of island evolution?

Parasitology 2000 Apr;120(4):335-343.

To date, a high degree of polymorphism has been demonstrated at both the MSP1 and MSP2 loci in parasites from areas of stable malaria transmission. As a consequence, in such areas it is rare to find parasites of the same 2-locus genotype in more than 1 subject. We have studied MSP1 and MSP2 diversity in parasites collected from subjects with both symptomatic (n = 86) and asymptomatic (34) malaria living on the island of Santo, Vanuatu, an area of stable malaria transmission. Polymorphism at the MSP1 and MSP2 loci was considerably less than previously reported: only 5 MSP1 and 5 MSP2 alleles were detected and these showed no size variation within alleles. Santo is unique amongst the areas studied so far in that it is a small island at the limit of the malaria belt in the South Pacific. Thus, the evolution of the parasite population may have been affected by the small size and isolation of this island population. Moreover, limited parasite diversity may explain the unusually mild nature of *Plasmodium falciparum* disease on Santo. Islands have fascinated biologists for centuries and fuelled the advancement of evolutionary theory, since they are natural laboratories for the study of evolution. The simplicity of the Vanuatu *P. falciparum* population may facilitate the use and interpretation of sequence level analyses to address the mechanisms by which genetic diversity is generated and maintained in natural populations.

- 22 **McMaster P, Haina T, Vince JD.** Kangaroo care in Port Moresby, Papua New Guinea.

Trop Doct 2000 Jul;30(3):136-138.

Kangaroo care is a simple and highly practical method of care of the low birthweight newborn which has been shown in some studies to significantly improve survival. We describe the introduction of 'kangaroo care' to the special care nursery at Port Moresby General Hospital, discuss the problems encountered and attempt to assess its impact in a 1-year retrospective study, during which it was associated with a reduction in hypothermia and an increased rate of weight gain.

- 23 **Mehlotra RK, Lorry K, Kastens W, Miller SM, Alpers MP, Bockarie M, Kazura JW, Zimmerman PA.**

Random distribution of mixed species malaria infections in Papua New Guinea.

Am J Trop Med Hyg 2000 Feb;62(2):225-231.

Plasmodium falciparum (Pf), *P. vivax* (Pv), *P.*

malariae (Pm), and *P. ovale* (Po) infections are endemic in coastal areas of Papua New Guinea. Here 2,162 individuals living near Dreikikir, East Sepik Province, have been analyzed for complexity of malaria infection by blood smear and polymerase chain reaction (PCR) diagnoses. According to blood smear, the overall prevalence of *Plasmodium* infection was 0.320. Most individuals (0.283) were infected with a single species only. The prevalence of mixed species infections was low (0.037). Further analysis of a 173-sample subset by nested PCR of small subunit ribosomal DNA resulted in an overall 3.0-fold increase in prevalence of infection, with a 17.5-fold increase in the frequency of mixed species infections. Among mixed species infections detected by PCR, the frequency of double species was 0.364, and that of triple species was 0.237. Nine individuals (0.052) were infected with all 4 species. To determine if infection status (uninfected, single, and multiple infections) deviates from an independent random distribution (null hypothesis), observed versus expected frequencies of all combinations of *Plasmodium* species infections, or assemblages (Pf-, Pv-, Pm-, Po-, to Pf+, Pv+, Pm+, Po+), were compared using a multiple-kind lottery model. All 4 species were randomly distributed whether diagnosed by blood smear or PCR in the overall population and when divided into age group categories. These findings suggest that mixed species malaria infections are common, and that *Plasmodium* species appear to establish infection independent of one another.

- 24 **Michelangeli VP, Pawape G, Sinha A, Ongugu K, Linge D, SenGupta SK, Tait B, Colman PG.**

Clinical features and pathogenesis of thyrotoxicosis in adult Melanesians in Papua New Guinea.

Clin Endocrinol (Oxf) 2000 Mar;52(3):261-266.

OBJECTIVE: To investigate the cause of an apparent increase in the incidence of thyrotoxicosis in the Melanesian population of the coastal areas around Port Moresby, Papua New Guinea. **DESIGN:** Consecutive patients attending the thyroid clinic at Port Moresby General Hospital were included in the study which collected clinical and immunogenetic data. **PATIENTS:** One hundred and ninety-four patients with thyrotoxicosis were studied. The mean age was 31 years. The clinical features were typical for thyrotoxicosis apart from increased pigmentation, which occurred in the majority of patients and which reversed with treatment with antithyroid drugs and resolution of the thyrotoxicosis. **MEASUREMENTS:** Antibodies to thyroid peroxidase, thyroglobulin and the thyrotropin receptor were present in 99%, 52% and 69% of patients, respectively, confirming that all cases were caused by autoimmune thyroid disease. Fine needle aspirations in 42 of 43 patients were consistent with Graves' disease. **CONCLUSIONS:** The cause of this apparent sudden increase in Graves' disease in the coastal region around Port Moresby, an apparently iodine-replete area, remains unexplained.

- 25 **Murthy DP, Ray U, Morewaya J, SenGupta SK.**
A study of the correlation of prostatic pathology and serum prostate-specific antigen (PSA) levels: a perspective from Papua New Guinea.
PNG Med J 1998 Jun;41(2):59-64.

A review of serum prostate-specific antigen (PSA) values from January 1994 to May 1997 and their correlation with the histopathology of prostate specimens was carried out in the Department of Pathology, Port Moresby General Hospital. The study has shown that this biochemical investigation has not been properly used for the maximum benefit of the patient population. Remedial measures are suggested to improve the sensitivity and specificity of PSA in a setting with limited resources.

- 26 **Ohashi J, Yoshida M, Ohtsuka R, Nakazawa M, Juji T, Tokunaga K.**
Analysis of HLA-DRB1 polymorphism in the Gidra of Papua New Guinea.
Hum Biol 2000 Apr;72(2):337-347.

The genetic structure of the Gidra-speaking population inhabiting 13 villages in Papua New Guinea was investigated, based on the analysis of HLA-DRB1 polymorphism. Nei's fixation indices (F(IS), F(IT), and F(ST)) showed that the Gidra villages were genetically differentiated. The genetic distances significantly correlated with the geographic distances among the 13 villages. Thus, it is likely that a low intervillage migration rate has been maintained since the Gidra community was established. Correspondence analysis revealed that the Gidra, who belong to non-Austronesian-speaking groups, are genetically located at the intermediate point between the Aboriginal Australian groups and the Austronesian-speaking groups. Moreover, the HLA-DRB1*0802 allele, which has been observed in only two Polynesian groups (Austronesian-speaking groups) of Oceanian populations, was also found in the Gidra. These results suggest that the admixture of Austronesian and indigenous non-Austronesian groups beyond the linguistic boundary occurred partly in Papua New Guinea before Austronesian groups spread to the Pacific.

- 27 **Pearn J.**
Pediatric diseases and operational deployments.
Mil Med 2000 Apr;165(4):283-286.

Many nations now export military health as a proactive arm of the nation's contribution to the maintenance of international peace in trouble regions of the world; and all nations are called upon from time to time in emergency and disaster situations to help out in their regions of interest. Children and young teenagers constitute some 50% of war-stricken populations. This paper explores this increasingly important role of military medicine from the point of view of a practicing pediatrician and career doctor-soldier. Many international operational deployments undertaken in the last 5 years have required the insertion of pediatric clinical and preventive health resources. Deployments to Rwanda, the countries of the former Yugoslavia, Somalia, Bougainville (in

Papua New Guinea), Irian Jaya (in Indonesia), and the Aitape tsunami disaster response (the Sepik region of Papua New Guinea) have all necessitated major pediatric interventions. In some operational deployments, in excess of one-third of patient and clinical contacts have involved the care of children, including clinical treatments ranging from life-saving resuscitation to the care of children with both tropical and subtropical illnesses. They have also involved mass immunization campaigns (e.g., in Rwanda) to prevent measles and meningococcal septicemia. In developing countries, at any time approximately 1 in 4 teenage and adult women is pregnant; and of these, 1 in 15 is suffering a miscarriage during any 2-week period. The implications of this audit are that service members must be multi-skilled not only in the traditional aspects of military medicine and nursing but also in (a) the developmental aspects of childhood; (b) the prevention of infectious childhood diseases by immunization and other means; (c) the recognition and management of diseases of childhood; and (d) the management of the normal neonate and infant, especially those orphaned in refugee, disaster and other emergency situations. Doctor-soldiers hold special credentials to be advocates for the protection of children caught up in armed conflict and its aftermath. In this context, advocacy to ban anti-personnel land mines is topical, because unfortunately the more than 2,000 deaths and injuries each month involve children and their families, often injured long after the cessation of hostilities. Pediatric issues are now the business of all who serve in the health disciplines in the broader profession of arms.

- 28 **Poidinger M, Hall RA, Lindsay MD, Broom AK, Mackenzie JS.**
The molecular epidemiology of Kokobera virus.
Virus Res 2000 Jun;68(1):7-13.

We describe herein the molecular epidemiology and phylogeny of Kokobera (KOK) virus, a flavivirus found in Australia and Papua New Guinea. We sequenced a region encompassing the 200 nucleotides of the 3' terminus of the NS5 gene, and the first 300 nucleotides of the 3' untranslated region (UTR). The study included 25 isolates of the virus, including an isolate from PNG, and several recent isolates from the south-west of Western Australia (WA), where the virus had not previously been detected. We found that the KOK isolates clustered according to geographic location and time of isolation into three distinct topotypes: one covering Queensland and New South Wales; another represented by the single isolate from PNG; and a third covering the Northern Territory and WA. This latter group was further subdivided into northern and south-west isolates. This molecular epidemiology is significantly different from other Australian flaviviruses, such as Murray Valley encephalitis (MVE) and Kunjin (KUN) viruses, which exist as single genetic types across the entire Australian continent. However, it is similar to the molecular epidemiology of the alphavirus Ross River (RR) virus. This may be explained by the fact that MVE and KUN viruses

are known to have birds as their main vertebrate hosts, whereas RR virus utilises macropods, which have also been implicated as the vertebrate host for KOK virus. In addition, the south-west isolates exhibited a degree of sequence heterogeneity, including one isolate that has a nine nucleotide deletion in the 3'UTR. This suggests that KOK virus has been in the south-west of WA for some time, and was not recently introduced.

29 **Rosales FJ, Topping JD, Smith JE, Shankar AH, Ross AC.**

Relation of serum retinol to acute phase proteins and malarial morbidity in Papua New Guinea children.

Am J Clin Nutr 2000 Jun;71(6):1582-1588.

BACKGROUND: Acute phase proteins (APPs) are associated with malaria-induced hypoproteinemia (serum retinol <0.70 µmol/L); however, the degree of the association is not well documented. **OBJECTIVE:** The association between malaria-induced hypoproteinemia and APPs was assessed. **DESIGN:** In a cross-sectional study, 90 children with serum retinol concentrations from <0.35 to >1.05 micromol/L were selected from children in a clinical trial of vitamin A supplementation. Serum was collected before treatment allocation. Retinol binding protein (RBP) concentrations were determined by radioimmunoassays, and transthyretin, alpha(1)-acid glycoprotein (AGP), alpha(1)-antichymotrypsin, C-reactive protein (CRP), haptoglobin, and albumin concentrations by radial immunodiffusion assays. **RESULTS:** Children in the subsample had high rates of splenomegaly and *Plasmodium*-positive blood-smear slides ($P < 0.01$); AGP (Pearson's $r = -0.40$, $P < 0.001$) and CRP ($r = -0.21$, $P = 0.04$) were inversely correlated with retinol. The negative APPs RBP, transthyretin, and albumin were positively and significantly associated with retinol. All APPs, except alpha(1)-antichymotrypsin, were significantly correlated with splenomegaly. Of the positive APPs, AGP correlated with CRP ($r = 0.37$, $P < 0.001$), indicating chronic inflammation. In a stepwise regression analysis, 73% of retinol's variability was explained by RBP and transthyretin. The model predicted that a 1-SD increase in RBP or transthyretin increases retinol by approximately 0.38 or 0.47 micromol/L, respectively, whereas an equivalent increase in AGP decreases retinol by 0.12 micromol/L. **CONCLUSIONS:** The RBP-transthyretin transport complex of retinol is not altered by inflammation. Positive APPs are useful markers of type and severity of inflammation; however, except for AGP, it is unlikely that they can correct for malaria-induced hypoproteinemia.

30 **Sachs M.**

[Observations on traditional healers ('medicine men') of Indonesian aborigines.] [Ger] *Zentralbl Chir* 2000;125(5):471-476.

The observations were done during expeditions to tribes of Indonesian aborigines on the islands of New Guinea/Irian Jaya (Korowai tribe) and Borneo/Kalimantan (Benuaq tribe). Neither the

Korowai people, who are still living under stone age-like circumstances in up to 30 m high tree-houses, nor the Benuaq people of Borneo, being already influenced by missionaries, treat injuries or wounds by traditional healers. All 'internal' disorders, not being caused by injuries, are diagnosed and treated in certain ceremonies, during which the healer tries to get in contact with the spirits triggering the disease. The idea is to know the reason for the disorder being caused by demons, though the patient can be treated by bringing offerings or sacrifices. This way of treating is due to the image of a magic-demoniac relationship between the patient and his disease.

31 **Scrimgeour EM.**

Suspected Ross River virus encephalitis in Papua New Guinea [letter].

Aust NZ J Med 1999 Aug;29(4):559.

32 **Spicer PE, Clapham G.**

Multiple liver abscesses: an unusual case which demonstrates the importance of ultrasonography in the detection of liver pathology.

PNG Med J 1998 Jun;41(2):77-82.

A 48-year-old caucasian male was admitted to hospital with right-sided chest pain, pyrexia and cough. He had no history of dysentery. He was treated with erythromycin and cotrimoxazole for right lower lobe pneumonia but failed to respond. Tender hepatomegaly developed and ultrasound scan demonstrated multiple abscesses in the liver. *Entamoeba histolytica* was identified in his faeces. He was treated with intravenous metronidazole, chloramphenicol and gentamicin and then oral tinidazole, after which improvement was rapid. He was later transferred to Australia. Subsequent abdominal CAT scan and aspiration of abscesses confirmed the diagnosis of multiple amoebic liver abscesses with secondary bacterial infection. Final treatment was with oral ciprofloxacin and metronidazole for four weeks. Ultrasonography is a noninvasive technique which is invaluable in the diagnosis of abdominal and especially liver pathology. This technique should be available in larger centres in tropical countries. Anyone living in or visiting the tropics should be aware of possible exotic diseases presenting in unusual ways.

33 **Spicer PE, Lucena G.**

X-ray survey for pulmonary tuberculosis and chest diseases in the Ok Tedi region of Western Province, Papua New Guinea.

PNG Med J 1998 Sep-Dec;41(3-4):137-140.

X-ray photofluorography is a relatively expensive way to detect pulmonary tuberculosis (PTB). Those patients with suggestive positive chest X-ray still require Mantoux skin testing, blood tests and a positive sputum smear for the acid-fast bacillus *Mycobacterium tuberculosis* to make a definitive diagnosis of PTB. Photofluorography does detect most pulmonary pathological conditions, including lesions suggestive of PTB, and possible cardiac abnormalities. It is more cost-effective for large

- numbers in urban areas where there is poverty and overcrowding; and it is useful in early detection of cases of PTB. It is impractical to use in the isolated mountainous areas in the highlands region of Papua New Guinea and in Western Province, and where there is no road system. It cannot detect other forms of TB. In children and infants it is difficult to obtain good quality films and to interpret them. The scoring chart devised by Biddulph and Edwards is an excellent alternative where a diagnosis is not obvious in a chronically ill child. Active case detection by health workers in the field offers an excellent chance of finding TB cases. Although the cost of staining and looking at sputum smears and performing Mantoux tests can also be time consuming, these methods are relatively less expensive and more accurate. A simple method of processing sputum before Ziehl-Neelsen staining using ordinary household bleach vastly improves the detection rate of acid-fast bacilli. The new technology of demonstrating positive TB antigens in the blood of patients with active disease is still being assessed.
- 34 **Stinear T, Davies JK, Jenkin GA, Portaels F, Ross BC, Oppedisano F, Purcell M, Hayman JA, Johnson PD.**
A simple PCR method for rapid genotype analysis of *Mycobacterium ulcerans*.
J Clin Microbiol 2000 Apr;38(4):1482-1487.
Two high-copy-number insertion sequences, IS2404 and IS2606, were recently identified in *Mycobacterium ulcerans* and were shown by Southern hybridization to possess restriction fragment length polymorphism between strains from different geographic origins. We have designed a simple genotyping method that captures these differences by PCR amplification of the region between adjacent copies of IS2404 and IS2606. We have called this system 2426 PCR. The method is rapid, reproducible, sensitive, and specific for *M. ulcerans*, and it has confirmed previous studies suggesting a clonal population structure of *M. ulcerans* within a geographic region. *M. ulcerans* isolates from Australia, Papua New Guinea, Malaysia, Surinam, Mexico, Japan, China, and several countries in Africa were easily differentiated based on an array of 4 to 14 PCR products ranging in size from 200 to 900 bp. Numerical analysis of the banding patterns suggested a close evolutionary link between *M. ulcerans* isolates from Africa and southeast Asia. The application of 2426 PCR to total DNA, extracted directly from *M. ulcerans*-infected tissue specimens without culture, demonstrated the sensitivity and specificity of this method and confirmed for the first time that both animal and human isolates from areas of endemicity in southeast Australia have the same genotype.
- 35 **Takao S, Ishida T, Bhatia KK, Saha N, Soemantri A, Kayame OW.**
Seroprevalence of human T-lymphotropic virus type 1 in Papua New Guinea and Irian Jaya measured using different western blot criteria.
J Clin Virol 2000 Apr;16(2):129-133.
- 36 **Tan LT, Okino T, Gerwick WH.**
Hermitamides A and B, toxic malyngamide-type natural products from the marine cyanobacterium *Lyngbya majuscula*.
J Nat Prod 2000 Jul;63(7):952-955.
A Papua New Guinea collection of the marine cyanobacterium *Lyngbya majuscula* yielded two new and toxic natural products, hermitamides A (1) and B (2). The hermitamides were isolated using a brine shrimp (*Artemia salina*) toxicity assay. Planar chemical structures of 1 and 2 were established through 1D and 2D NMR, as well as FABMS data. Semisyntheses of hermitamides A (1) and B (2) were achieved by coupling the acid chloride derivative of 7(S)-methoxytetradec-4(E)-enoic acid (4), obtained from the same cyanobacterium collection, and the respective free amines, phenethylamine and tryptamine. Hermitamides A (1) and B (2) exhibited LD(50) values of 5 microM and 18 microM in the brine shrimp bioassay, and IC(50) values of 2.2 µM and 5.5 µM to Neuro-2a neuroblastoma cells in tissue culture, respectively. Hermitamide A was mildly ichthyotoxic to goldfish, with an LD(50) value of 19 microM, while hermitamide B was inactive at 25 microM.
- 37 **Ulijaszek SJ.**
Hypertension among adults of the Purari delta of the Gulf Province, Papua New Guinea.
PNG Med J 1998 Jun;41(2):65-71.
This study, carried out in 1995, found evidence of high blood pressure in a rural population in the Gulf Province of Papua New Guinea. Although the prevalence of obesity as assessed by the body mass index has increased since 1980, blood pressure was not associated with height or weight. Rather, it was associated with fat patterning: increased truncal fatness was associated with greater systolic blood pressure in both males and females. Of the modernization variables examined, the only one associated with blood pressure was type of income, and this for systolic blood pressure among females only. Body mass index was also associated with type of income, this being greatest among the small number of adults with some form of paid employment. Blood pressure showed no association with age, thus conforming to the hypertension pattern seen at early stages of modernization.
- 38 **Valley L.**
Reaching Rabaraba.
Nurs Times 1999 Oct 27-Nov 2;95(43):32-33.
- 39 **Vince JD, Baki M, Chakravarti P.**
Meckel-Gruber syndrome: report of an affected Papua New Guinean family.
PNG Med J 1998 Jun;41(2):83-84.
We present the first case report of a Papua New Guinean family affected by Meckel-Gruber syndrome. Of six children, five of whom died, three definitely and two possibly were affected.
- 40 **Watters DA, Theile DE.**
Progress of surgical training in Papua New Guinea to the end of the 20th century.
Aust NZ J Surg 2000 Apr;70(4):302-307.

BACKGROUND: Health care in Papua New Guinea (PNG) throughout the 20th century has been characterized by a significant shortage of medical practitioners and surgical expertise. A number of initiatives within the country and from outside have sought to address these deficiencies of numbers and quality. The present paper seeks to review the development of surgery and surgical training in PNG. **METHODS:** Review of the surgical literature, reports and records in the Division of Surgery at the University of Papua New Guinea (UPNG), and personal observations are used to look critically at the content and productivity of the various training initiatives. **RESULTS:** For the first half of the century, PNG relied on national medical assistants who were trained, supervised and directed by expatriate doctors. Medical training of PNG doctors began in 1951 and by 1999 more than 600 doctors had graduated. Expatriate specialist surgeons arrived in 1950 and were the only surgeons until the postgraduate Master of Medicine (surgical) programme produced its first graduates in 1978. This programme has now produced 37 surgeons who are reasonably well distributed throughout the country. Higher surgical diplomas were introduced in 1994 for more specialized training of some of the general surgeons. These training developments have been supported by AusAid as well as by Australian surgeons. **CONCLUSIONS:** Surgical expertise has progressively improved throughout the 20th century with the most major advances being achieved in the last decade. Training programmes have provided an expanding core of expertise of considerable quality, but the numbers of doctors and surgeons remain well below requirements.

41 **Wright SD, Yong CG, Dawson JW, Whittaker DJ, Gardner RC.**

Riding the Ice Age El Niño? Pacific biogeography and evolution of *Metrosideros* subg. *Metrosideros* (Myrtaceae) inferred from nuclear ribosomal DNA. *Proc Natl Acad Sci USA* 2000 Apr 11;97(8):4118-4123.

Metrosideros subg. *Metrosideros* (Myrtaceae) comprises approximately 26 species distributed widely across the Pacific basin. They occur on the ancient Gondwanan landmasses of New Zealand and New Caledonia, as well as on the volcanic islands of the remote Pacific, from Melanesia to tropical Polynesia and the Bonin Island. Phylogenetic analysis based on nuclear ribosomal DNA spacer sequences from all named species showed *Metrosideros umbellata* of New Zealand as basal in the subgenus, with the remaining species falling into three monophyletic clades. One includes the seven New Caledonian species together with three daughters in western Oceania that probably dispersed during the mid/late Tertiary. A second contains six taxa located in east Melanesia and Samoa that may also have arisen from a mid/late Tertiary dispersal, in this instance from New Zealand. The third includes three New Zealand endemics along with all of the taxa in remote Polynesia and accounts for much of the total range of the subgenus. These dispersed taxa in

Polynesia either are identical to the New Zealand species *Metrosideros excelsa* or differ by a single nucleotide change. We suggest that they are all derived from a Pleistocene dispersal out of New Zealand. A relatively recent dispersal is surprising, given that this wind-dispersed genus has occupied New Zealand for much of the Tertiary and that some of the islands in remote Polynesia date to at least the Miocene. We attribute this dramatic range expansion to climate change – specifically changes in wind flow patterns – in the southern hemisphere during worldwide glaciation.

42 **Yip SP, Putt W, Hopkinson DA, Whitehouse DB.**

Identification and characterisation of polymorphisms in human phosphoglucomutase (PGM1).

Ann Hum Genet 1999 Mar;63(2):129-140.

This study is part of our effort to map recombination hotspots in two regions (site A, 18 kb; site B, 40 kb) of the human phosphoglucomutase PGM1 gene. Twenty-two PCR amplified fragments comprising six groups, covering about 5.2 kb, were screened for single nucleotide polymorphisms (SNPs) using non-isotopic single stranded conformation polymorphism (SSCP) analysis. Fourteen fragments were variable and seven of these showed common polymorphism. Our strategy for screening for polymorphic sites in the PGM1 gene was based on the results of allelic association analysis between each new marker and the sites of the classical isozyme polymorphism (2/1 in exon 4 and \pm in exon 8). Samples from four populations (Caucasian, Chinese, Vietnamese and New Guinean) were typed for each of the seven polymorphic markers. Between two and four common alleles were found in each case, together with a few rare alleles. Co-dominant inheritance patterns were demonstrated by family studies. The molecular basis of each new marker was determined by direct sequencing of the PCR products: most were SNPs except two that were small insertions/deletions. Direct sequence analysis of a 2.1 kb segment in sixteen individuals revealed no additional nucleotide variation indicating a very high level of efficiency of the SSCP screening method used in this study. The overall nucleotide diversity (θ) for PGM1 was estimated as 0.9×10^{-3} based on 33 segregating sites in a sequence of 5187 nt and a sample size of 614 individuals.

43 **Zampella A, D'Auria MV, Debitus C, Menou JL.**

New isomalabaricane derivatives from a new species of *Jaspis* sponge collected at the Vanuatu islands.

J Nat Prod 2000 Jul;63(7):943-946.

Six new cytotoxic isomalabaricane-type triterpenoids and nortriterpenoids with a 3 alpha-acetoxy group were isolated, along with the known globostellatic acids B (1) and C (2), from the marine sponge *Jaspis* sp. collected at a Vanuatu island. The structures were determined by 2D NMR data and by comparison with spectral data of known related compounds.