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PUBLICATIONS OF RELEVANCE TO PAPUA NEW GUINEA AND MELANESIA

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- 1 **Al-Yaman F, Genton B, Kramer KJ, Chang SP, Hui GS, Baisor M, Alpers MP.**
Assessment of the role of naturally acquired antibody levels to *Plasmodium falciparum* merozoite surface protein-1 in protecting Papua New Guinean children from malaria morbidity. *Am J Trop Med Hyg* 1996 May;54(5):443-448.
We investigated the prevalence and magnitude of naturally acquired humoral immune responses to the major merozoite surface protein (MSP-1) in a malaria-endemic population in Papua New Guinea. A prospective longitudinal study in 0.5-15-year-old children was conducted for one year to examine the relationship between acquired immune response to MSP-1 and subsequent susceptibility to clinical disease. The prevalence and concentration of antibodies to both N- (195A) and C-terminal (BVp42) regions of MSP-1 as well as to the parasite-derived MSP-1 increased with age, with the highest prevalence and concentration of antibodies being detected for the parasite-derived MSP-1 molecule and the C-terminal region of MSP-1. As malaria morbidity decreases with age, a significant negative correlation was observed between antibody levels to both 195A and BVp42 and the incidence rate of clinical malaria. When age and past exposure were corrected for, only antibody concentrations against BVp42 and to a lesser extent parasite-derived MSP-1 were significantly associated with protection from clinical malaria and severe parasitemia. The reduction in the incidence rate of clinical malaria observed in individuals with high antibody concentration to MSP-1 may be due to antibodies directed against epitopes within the C-terminal region of MSP-1.

- 2 **Beebe NW, Foley DH, Cooper RD, Bryan JH, Saul A.**
DNA probes for the *Anopheles punctulatus* complex. *Am J Trop Med Hyg* 1996 Apr;54(4):395-398.
Genomic DNA probes were made for two recently identified members of the *Anopheles punctulatus* complex: *Anopheles* sp. near *punctulatus* from Papua New Guinea and *Anopheles farauti* No. 7 from the Solomon Islands. The probes are species-specific and with the use of 32P labeling sensitive enough so that a squash blot of only a small segment of the mosquito is required for identification. The 119-basepair (bp) probe for *An.* sp. near *punctulatus* and the 1106-bp probe for *An. farauti* No. 7 have been sequenced in full and the probes have been tested on field collected specimens. These probes now make it possible to distinguish *An.* sp. near *punctulatus* and *An. farauti* No. 7 from the other eight members of the *An. punctulatus* complex. A pan-species probe was also made from the 18S ribosomal DNA that binds to DNA from all members of the complex. These three probes complete the set required for distinguishing all known members of the *An. punctulatus* complex by DNA hybridization.

- 3 **Benkmann HG, Agarwal DP, Vasisht S, Srivastava LM, Goedde HW.**
Distribution of apolipoprotein E genotypes in Asian Indians, Hungarians and Papua New Guineans. *Anthropol Anz* 1996 Mar;54(1):31-34.
We report here the distribution of apo E genotypes and allele frequencies in Asian Indians, Hungarians and Papua New Guineans using DNA-based analysis. Frequency of the apo E4 allele was three times as high in Papua New Guineans as in Caucasians. The rare apo E2 allele was also present in higher frequency in the Papua New Guineans as compared to other populations.

- 4 **Bockarie M, Kazura J, Alexander N, Dagoro H, Bockarie F, Perry R, Alpers M.**
Transmission dynamics of *Wuchereria bancrofti* in East Sepik Province, Papua New Guinea. *Am J Trop Med Hyg* 1996 Jun;54(6):577-581.
Bancroftian filariasis is endemic in many areas of Papua New Guinea. This study describes the entomologic indices of transmission near Dreikikir in East Sepik Province, Papua New Guinea. A total of 1735 culicine mosquitoes, including *Culex* and *Mansonia* species, were dissected, but none were infected with filarial larvae. In contrast, *Anopheles punctulatus* and *An. koliensis* were found to be potential vectors: 7.3% of *Anopheles* were infected and the mean number of first- to third-stage larvae per infected mosquito was 2.7. Transmission indices varied significantly in five villages located within a 50-km radius of each other. Annual biting rates ranged from 4,789 to 48,020 bites/person/year; annual infective biting rates from 15 to 836/person/year; and annual transmission potential from 31 to 2340 third-stage larvae/person/year. Monthly transmission potential and monthly infective biting rate varied significantly in each village, with the highest indices of transmission observed in villages nearest sites where puddles formed in river beds during the dry season. These data indicate that there is small-area variation in the intensity and temporal pattern of filariasis transmission and that culicine mosquitoes are not important vectors of *W. bancrofti* in this area.

- 5 **Burrows JM, Burrows SR, Poulsen LM, Sculley TB, Moss DJ, Khanna R.**
Unusually high frequency of Epstein-Barr virus genetic variants in Papua New Guinea that can escape cytotoxic T-cell recognition: implications for virus evolution.

J Virol 1996 Apr;70(4):2490-2496.

Cytotoxic T lymphocytes (CTLs) which recognize viral antigens in association with human leukocyte antigens (HLAs) play an important role in controlling persistent virus infections. These viruses use several mechanisms to evade the immune response, including mutations that affect either T-cell receptor recognition or binding of viral epitopes to the HLA. It has recently been proposed that the distribution of HLA frequencies and the specific CTL response may influence the long-term evolution of Epstein-Barr virus (EBV) by selecting variants which lack immunodominant CTL epitopes. To test this hypothesis, we have studied EBV isolates from two genetically distinct Papua New Guinea (PNG) populations, residing in coastal and highland regions, for polymorphism within seven viral CTL epitope sequences restricted through several class I HLAs. Surprisingly, all EBV isolates analyzed displayed identical amino acid substitutions within HLA A11-, B35- and B8-restricted CTL epitope sequences which completely abrogated CTL recognition and binding of synthetic peptides to HLA molecules. Furthermore, these substitutions revealed no correlation with the contemporary distribution of HLAs in the different PNG populations, which argues for a minimal influence of immune pressure. The sequence homology between EBV isolates from coastal and highland PNG suggests that the virus may have had a single origin and, more importantly, that these isolates are genetically distinct from those present in a Caucasian population.

6 **Burrows JM, Khanna R, Sculley TB, Alpers MP, Moss DJ, Burrows SR.**

Identification of a naturally occurring recombinant Epstein-Barr virus isolate from New Guinea that encodes both type 1 and type 2 nuclear antigen sequences.

J Virol 1996 Jul;70(7):4829-4833.

In this report we describe an Epstein-Barr virus isolate, derived from the peripheral blood lymphocytes of a healthy adult from Papua New Guinea, that is a recombinant of the two major Epstein-Barr virus types, encoding type 1 Epstein-Barr nuclear antigen 2 (EBNA2) sequences, and type 2 EBNA3, EBNA4 and EBNA6 sequences.

7 **Collins VR, Dowse GK, Cabealawa S, Ram P, Zimmet PZ.**

High mortality from cardiovascular disease and analysis of risk factors in Indian and Melanesian Fijians.

Int J Epidemiol 1996 Feb;25(1):59-69.

BACKGROUND: In recent years, developing populations such as the Pacific island nation of Fiji have seen decreases in infectious diseases and increasing frequency of cardiovascular diseases (CVD), diabetes and cancer. However, cohort studies of mortality in these populations are scarce. Here we report 11-year all-cause and cause-specific mortality rates and risk factors for total, CVD and coronary heart disease (CHD) for indigenous Melanesian and Asian Indian people of Fiji. **METHODS:** Following a baseline risk factor survey in 1980, mortality surveillance continued

until 1991 in a representative cohort of 1325 Melanesians and 1221 Indians from urban and rural areas of Fiji. Date and cause of death were recorded and total, CVD and CHD mortality rates calculated. Baseline predictors of mortality were assessed using Cox regression. **RESULTS:** Total mortality rates in Melanesians were 15.9 and 9.2/1000 person-years, and in Indians were 13.5 and 6.8/1000 person-years, in men and women respectively. Death due to CHD was more common in men than women, and in Indian than Melanesian men, although total CVD deaths were more common in Melanesian men. Deaths due to CHD were more common in the urban than the rural area. After adjusting for other risk factors Indian ethnicity was associated with a significantly reduced risk of total and CVD mortality in men, and total mortality in women. Age and systolic blood pressure were consistently and independently associated with mortality from all causes, as well as CVD and CHD (except in Indian women). In men associations were also identified for total cholesterol with CVD and CHD mortality in Melanesians, and 2-hour plasma glucose with total and CVD mortality in Indians. In women, 2-hour glucose was important for total, CVD and CHD mortality in both ethnic groups as was smoking in Indians. Obesity had inconsistent associations with mortality. **CONCLUSION:** Cardiovascular disease is now responsible for a large proportion of total mortality in both Indian and Melanesian Fijians. The major risk factors identified in Fijians are similar to those observed in developed populations.

8 **Collins VR, Dowse GK, Ram P, Cabealawa S, Zimmet PZ.**

Non-insulin-dependent diabetes and 11-year mortality in Asian Indian and Melanesian Fijians. *Diabet Med* 1996 Feb;13(2):125-132.

This study reports 11-year all-cause and cause-specific mortality rates according to baseline glucose tolerance for a population-based sample of adult Melanesian and Indian Fijians (n = 2638), first surveyed in 1980. Risk factors for all-cause and cardiovascular disease (CVD) mortality in subjects with non-insulin-dependent diabetes (NIDDM) are also described. The baseline survey included 75 g oral glucose tolerance tests, measurements of blood pressure, body mass index and triceps skinfold, assays of plasma cholesterol and triglycerides, electrocardiograms, and details of smoking habits and physical activity. Mortality status was ascertained for 2546 subjects through surveillance of death certificates, medical records and interview of subjects (or relatives). Mortality rates were increased in diabetic men and women of both ethnic groups: relative risks compared to subjects without diabetes at baseline were 1.7 (CI:0.9-3.1) and 2.0 (1.1-3.7) in Melanesian and 4.2 (2.7-6.5), 3.2 (1.9-5.7) in Indian men and women, respectively. A large proportion of mortality among diabetic subjects was attributed to CVD (62%, 66% in Melanesian and 54%, 58% in Indian men and women, respectively). Mortality rates tended to be higher in Melanesians than Indians, except for diabetic men where Indians had higher total and cardiovascular disease rates. In contrast to non-

- diabetic Fijians, diabetic women of both ethnic groups lost their relative protection from coronary heart disease (CHD). Cox regressions for diabetic subjects showed age and fasting plasma glucose to be independent predictors of all-cause mortality in men, and age, body mass index (inversely) and systolic blood pressure in women, but lipid concentrations and cigarette smoking were not related. After accounting for conventional CVD risk factors, diabetes conferred significantly increased risk of total, CVD and CHD mortality. The mortality experience of Melanesian and Indian Fijians with NIDDM is similar to that documented in developed populations, with excess mortality due to cardiovascular causes.
- 9 **Dent AW, Seyfang M, Wallace S.**
Cytology and fine-needle aspiration biopsy: appropriate technology, quick, safe and cheap.
Trop Doct 1996 Jan;26(1):37-39.
- 10 **Gubag R, Omoloso DA, Owens JD.**
Sapal: a traditional fermented taro [*Colocasia esculenta* (L.) Schott] corm and coconut cream mixture from Papua New Guinea.
Int J Food Microbiol 1996 Jan;28(3):361-367.
Sapal is a traditional fermented food made by mixing cooked, grated taro [*Colocasia esculenta* (L.) Schott] corm with coconut cream and allowing it to ferment at ambient temperature. The fermentation was primarily due to heterofermentative lactic acid bacteria, which reached 10(10) cfu/ml. Seven out of 10 isolated bacterial strains were identified as *Leuconostoc mesenteroides* or *Leuc. paramesenteroides*. The initial microbial flora was derived from the coconut cream. Yeasts grew on the surface of the sapal in the later stages of the fermentation. Overnight storage of the grated taro corm resulted in the glucose concentration increasing from 1.1 to about 5 g/l. During the fermentation the glucose concentration decreased to undetectable levels. The pH value fell from an initial value of 6.1 to 4.1 after 24 h.
- 11 **Hodge AM, Dowse GK, Collins VR, Zimmet PZ.**
Mortality in Micronesian Nauruans and Melanesian and Indian Fijians is not associated with obesity.
Am J Epidemiol 1996 Mar 1;143(5):442-455.
The association of obesity with mortality was investigated in population-based samples of Micronesian Nauruans (n = 1400), Melanesian Fijians (n = 1279) and Indian Fijians (n = 1182), over 10 years from 1982 in Nauru, and 11 years from 1980 in Fiji. At the end of follow-up, vital status was known for all Nauruans and all but 3.5% of Fijians. Mortality rates were higher in Nauru than Fiji, and in Melanesians than Indians. The mean body mass index of decedents was similar to or less than (Nauruan men, $p < 0.001$) that of survivors in each sex-ethnic group. Crude mortality rates showed an inverse relation with body mass index in Nauruan men, with inconsistent relations in other sex-ethnic groups. After stratification by diabetes status, there was no relation between mortality and obesity in nondiabetic subjects, but an inverse relation was observed among diabetic subjects in each population. These findings persisted even after the exclusion of subjects who died within the first 2 years of follow-up. After controlling for age, smoking and diabetes status in Cox proportional hazard models, body mass index (as a continuous variable) was not related to mortality in any sex/ethnic group and tended to be negatively associated with mortality risk. Interactions of body mass index with age, smoking and diabetes status were not significant. Mortality risk was significantly increased in older subjects and in diabetic subjects, and cigarette smoking also increased risk in some groups. Stratification of analyses according to cigarette smoking did not alter the nature of the results. The association of mortality and body mass index categorized by quartiles was also investigated. After adjusting for age alone, or age, smoking and diabetes status, the lower quartiles of body mass index were consistently associated with the highest relative risk for mortality. Quadratic terms for body mass index did not improve Cox models in subjects with normal glucose tolerance. Relations with cardiovascular disease mortality were also assessed and results were inconsistent, although positive trends were observed in Nauruan women ($p = 0.02$) and Melanesian men ($p = 0.06$). Overall, there was little evidence to suggest that obesity was a risk factor for total or cardiovascular mortality in these populations. However, obesity is clearly associated with a high risk of diabetes and other morbid conditions and at least on this basis it would seem desirable to prevent obesity in these and other Pacific populations.
- 12 **Humphries J, Akintunde C, Richens J, Cann K, Farrar J, Woodrow D, Tong W, Keat A.**
Search for infective agents in undifferentiated oligoarthritis in Papua New Guinea.
Br J Rheumatol 1996 May;35(5):492-493.
- 13 **Kelly KM.**
IGHG3 G and the pathogenesis of hyperreactive malarious splenomegaly.
Med Hypotheses 1996 Feb;46(2):135-139.
Hyperreactive malarious splenomegaly is an aberrant response to chronic malarial infection, defined by persistent gross splenomegaly and elevated serum IgM and IgG. The populational and familial patterns of this disorder suggest genetically based, immune incompetence. In Papua New Guinea, the disease occurs among populations characterized by high frequencies of IGHG3 G haplotypes. Elsewhere, the distribution and prevalence of hyperreactive malarious splenomegaly is consistent with the distributions of IGHG3 alleles. Drawing upon this relationship, I suggest that expression of the G3M G phenotype is a necessary precondition for hyperreactive malarious splenomegaly, consistent with the pathogenesis of malaria and the functions of the immune system.
- 14 **Kolakovich KA, Ssengoba A, Wojcik K, Tsuboi T, Al-Yaman F, Alpers M, Adams JH.**
Plasmodium vivax: favored gene frequencies of the merozoite surface protein-1 and the multiplicity of

infection in a malaria-endemic region.
Exp Parasitol 1996 Jun;83(1):11-19.

In this study, we present an analysis of the *Plasmodium vivax* MSP-1 polymorphic region 5 and identify a new recombinant gene element. In clinical isolates from Papua New Guinea (PNG), the *P. vivax* MSP-1 gene type was characterized by restriction fragment length polymorphisms and by Southern blot oligonucleotide hybridizations using probes to type-specific sequences. There were three pairs of dimorphic gene elements in the MSP-1 polymorphic region 5; four of the eight potential different combinations of sequence elements for this region have been identified. The center gene segment was the most polymorphic, especially for the glutamine (Q) repeat element with virtually every gene containing a different length of Q repeats, a finding consistent with database sequence information. The frequencies of all of the polymorphic MSP-1 gene elements were approximately equal except for the first segment, which was biased 10:1 for the Type II (Sal-I type) versus Type I (Belem type) gene segment. In fact, only one combination (I/Q/S) of the genetic elements containing the type I gene segment for polymorphic region 5 was identified, a finding consistent with sequences reported to gene data banks. Considering only the multiplicity of MSP-1 gene types, 38% of the patients were identified as having multiple infections; when correlated with the circumsporozoite protein and the Duffy antigen-binding protein gene types, the multiple infection rate increased to 65% of 23 isolates characterized. Increased age was the only clinical parameter that positively correlated with multiclonal infections and there was no other apparent bias or linkage of gene types among the three loci. These data identify multiple clonal populations of *P. vivax* in the PNG population and potentially a high rate of concurrent infections in clinical cases. The extreme polymorphism of the MSP-1 polymorphic region 5 suggests that frequent recombination occurs within this gene. The bias in frequency for one recombinant gene motif indicates that intrinsic host or parasite factors may engender increased frequency of one genetic element over another. Failure to identify this type of discrete clonal marker as well as reliance on a single marker can mask the true multiclonal nature of an infection and lead to underestimation of the multiplicity of infection.

15 **Lehrman S.**
 Anthropologist cleared in patent dispute.
Nature 1996 Apr 4;380(6573):374.

16 **McClatchey W.**
 The ethnopharmacopoeia of Rotuma.
J Ethnopharmacol 1996 Mar 1996;50(3):147-156.
 The traditional Rotuman herbal pharmacopoeia consists of many plants, each of which is used in a specific way for specific disease states. The practitioners of traditional medicine are specialists recognized by the culture as having spiritual power to promote health. These individuals have been interviewed in order to determine which plants are presently in use. The healers interviewed represent

a disappearing tradition which is not being passed on to the next generation. An effort has been made to record all of the plants used by all of the healers which remain in the Rotuman culture (on the island). This information is presented as a table of plant species and their respective indications.

17 **Roberts Thomson JM, Martinson JJ, Norwich JT, Harding RM, Clegg JB, Boettche RB.**
 An ancient common origin of aboriginal Australians and New Guinea highlanders is supported by alpha-globin haplotype analysis.
Am J Hum Genet 1996 May;58(5):1017-1024.

The origins of aboriginal Australians and their relationship with New Guineans and neighboring Southeast Asians remains controversial. We have studied the alpha-globin haplotype composition of an aboriginal tribe from central Australia, to address some of the ambiguities of previous studies. Australians have a haplotype repertoire that is shared with New Guinea highlanders, a fact that strongly supports a common origin of these two populations. Further, Australians and New Guinea highlanders have a different set of alpha haplotypes from Southeast Asians and a lower genetic diversity. This, coupled with the presence of many locally specific central Australian haplotypes, suggests that much of the original diversity was lost in a population bottleneck prior to or during the early colonization of Sahul and that subsequent recovery of diversity has been accompanied by the generation of new haplotypes. These conclusions contrast with some previous genetic studies suggesting links between Australians, coastal New Guineans, and present-day Southeast Asians. Much of this discrepancy appears to be due to more recent Southeast Asian admixture on the north coast of Australia.

18 **Rosenfeld JV, Watters DA, Jacob OJ.**
 Neurosurgery in Papua New Guinea.
Aust NZ J Surg 1996 Feb;66(2):78-84.

BACKGROUND: An audit of neurosurgery in Papua New Guinea (PNG) based on the experience of a visiting neurosurgeon is presented. The objectives of the study were to determine the type and frequency of neurosurgical conditions in PNG, whether major neurosurgery can be performed successfully in PNG, and to develop a strategy for the development of neurosurgical services in PNG. **METHODS:** The audit was carried out over two periods of 2 weeks duration in 1992 and 1993 in Port Moresby and Goroka. Instrumentation and equipment were limited and no additional equipment was used. Myelography and angiography were available in Port Moresby. **RESULTS:** There were 82 patients in total, 55 (67.1%) were consultations, 23 (28%) had elective surgery, 4 (4.8%) had emergency surgery and 16 (19.5%) await surgery. Cases were subdivided into nine major groupings: neurotrauma 18 (7 severe); spine 18; congenital 13; hydrancephaly 4; scalp, skull and orbit 6; vascular 3; peripheral nerve 3; and neurology 5. Seventy-two (87.8%) patients required CT/MRI which were unavailable. Four ventriculograms were performed in lieu of CT/MRI. Fifteen (18.3%) cases could not be treated

in PNG. CONCLUSIONS: Neurosurgical problems in PNG can often be adequately managed with limited resources. Complex procedures were performed with gratifying results and acceptable morbidity. There is sufficient pathology in a country of four million people to justify training a small number of neurosurgeons by the end of the decade. CT scanning will be a necessary adjunct.

- 19 **Rowling D, Hartley D, Owen J, Strachan J.**
Family planning: personal and political perspectives from Choiseul Province, Solomon Islands.
Aust J Public Health 1995 Dec;19(6):616-622.
Rapid population growth has put family planning on personal and political agendas in the Solomon Islands. With the release of a population policy in 1988, national leaders sanctioned the concept of family planning as a key strategy in reducing the rate of population growth. On a personal level, Solomon Islanders share their government's concern about population problems. There is a shortage of arable land, health services are stretched, and there are limited places in school for children. A study in Choiseul Province, a rural area in Solomon Islands, suggests that people want smaller families but have limited means to control their fertility. Meagre resources and infrastructure, compounded by geography, climate, culture and religion, constrain the development of family planning services.
- 20 **Tajima K, Cartier L.**
Epidemiological features of HTLV-I and adult T-cell leukemia.

Intervirology 1995;38(3-4):238-246.

Adult T-cell leukemia (ATL) patients and human T-cell leukemia virus type I (HTLV-I) carriers are clustered in limited groups in the world, especially among Japanese in Asia, Blacks in Central Africa, Melanesians in Papua New Guinea and Andeans in South America. The major transmission routes of HTLV-I under natural conditions are from mother to child through breast milk and from man to woman through semen. The whole life risk of ATL among persistent HTLV-I carriers is estimated at 2-6%. The detailed manifestation mechanism of ATL is not yet clarified; however, it is certain that HTLV-I infection in infancy is the main cause of ATL. Therefore, the prevention measure against mother-to-child transmission of HTLV-I is indispensable from a viewpoint of public health.

- 21 **Westermarck P, Sletten K, Westermarck GT, Raynes J, McAdam KP.**
A protein AA variant derived from a novel serum AA protein, SAA1 delta, in an individual from Papua New Guinea.
Biochem Biophys Res Commun 1996 Jun 14;223(2):320-323.
A major protein AA amyloid protein was purified and characterised from a Papua New Guinean individual. This AA protein differed from all previously characterised SAA variants by the combination of Ala52, Val57, Asn60, Phe68, Phe69 and Gly72. Since the prevalence of AA-amyloidosis is unusually high in Papua New Guinea this AAdelta must originate from a novel SAAdelta which may represent a particularly amyloidogenic variant.

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- 3 **Garner PA, Hill G.** Brainwashing in tuberculosis management. *PNG Med J* 1985;28:291-293.

- 4 **Cochrane RG.** A critical appraisal of the present position of leprosy. In: Lincicome DP, ed. *International Review of Tropical Medicine*. New York: Academic Press, 1961:1-42.

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