

# Journal Abstracts

EDITOR: ANNETTE SACHS ROBERTSON

## Dengue type 1 epidemic with haemorrhagic manifestations in Fiji, 1989-90

Fagbami A, Mataika J, Shrestha M, Gubler D. *Bulletin of the World Health Organization*, 1995; 73(3):291-297.

Clinical, virological and epidemiological investigations were undertaken of the Dengue Type 1 epidemic in Fiji between July 1989 and July 1990. The official number of reported cases of Dengue Fever was 3686 cases. A review of Dengue Fever cases reported in the medical records of the Ministry of Health and the Wellcome Virus Laboratory from 1971 until 1990 provided information on the background incidence of this disease and incidence of four sporadic outbreaks involving Types 1 and 4. A house to house survey conducted between March and April 1990 involving 81 households indicated that 41% of the interviewees had a history of clinical Dengue fever over the previous six months with a history of hemorrhagic manifestations reported by 8% of the interviewees. An analysis of 202 hospitalized children revealed that 43% had one or more haemorrhagic manifestations and 13% developed shock. Autopsies on six of the fifteen fatal cases demonstrated varying degrees of haemorrhage in the stomach, lungs, spleen, pancreas and brain. A total of 36 strains of Dengue 1 Virus became evident from the virological studies involving tissue culture and mosquito inoculation. There were 55% positive of 269 paired serum samples examined for Dengue IgM antibody and of 123 serum samples examined for H1 antibody, 75 had positive serological responses. Neutralization indices supported the virological results of a single serotype epidemic. While Dengue type 3 virus has not been isolated in Fiji, all four of the virus types are present in the Pacific. Improved surveillance and vector control efforts are needed if further epidemics are to be prevented in the future.

**“ It is vital that strict surveillance throughout the Pacific and early case recognition are practiced by health care workers in order to try to control the next epidemic of DHF when it occurs. ”**

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**Editorial Comment:** This comprehensive overview of the clinical, virological and epidemiological aspects of the Dengue Fever epidemic of 1989-90 provides the reader with the classic epidemic curve of cases and background information on previous epidemics. While it is not highly technical, it should provide interesting reading for any medical doctor. Although the results of the house-to-house survey are not unexpected given the less-than-strict criteria of the case definition of Dengue-like illness, the information does yield support for under reporting of Dengue Fever during the months of the epidemic. The inclusion of “few” and “many” in the tables were obviously out of necessity due to paucity of data. However, such inclusions leave the reader feeling less sure of the exact magnitude of Dengue Haemorrhagic Fever cases in the corresponding years of the outbreaks. It is vital that strict surveillance throughout the Pacific and early case recognition are practiced by health care workers in order to try to control the next epidemic of DHF when it occurs. Mathematical modelling of previous epidemics would be able to predict future epidemics and stochastic simulations would allow policy makers to evaluate the effect of various prevention strategies that may not only be useful to the Pacific situation but may also provide clues for global control of Dengue Fever.

## Modelling prevention strategies for gonorrhoea and chlamydia using stochastic network simulations

Kretzschmar M, van Duynhoven Y, Severijnen A. *American Journal of Epidemiology*, 1996; 144: 306-17.

Using a simulation Markov model, study of the spread of gonorrhoea and chlamydia shed light on the usefulness of various strategies for prevention of these sexually transmitted diseases. Utilizing transmission dynamics such as the fraction of asymptomatic infections, transmission probabilities per sexual contact from male to female and vice versa, incubation times and patient delays, and duration of infectious period for symptomatic and asymptomatic males and females from a survey in the Netherlands and from other existing information, the article discussed a mathematical approach based on stochastic theory, to determine prevalence and distribution of these sexually transmitted diseases. The article also discussed the comparison of various preventive strategies including contact tracing, screening of various subgroups including high activity core groups, and condom use. Chlamydia appeared to spread at a more efficient rate in the low activity population than gonorrhoea and was more difficult to control with the various preventive strategies. Treatment of both conditions was more effective

in reducing prevalence in symptomatically treated persons. With gonorrhea, contact tracing and treating 25% percent of all current partners of symptomatic infected persons was able to bring the disease to extinction in ten years whereas chlamydia required that 50% of the partners be treated in order to reach a level where stochastic extinction was feasible. Screening strategies aimed at high activity core groups in certain age groups were more effective in reducing the prevalence of both conditions than screening strategies in certain age groups of the general population. Condom use was highly effective in reducing prevalence, especially if a high percent of the high activity group as well as a small percent of non-core group utilized them consistently.

**Editorial Comment:** The concept and application of mathematical stochastic models for the study of infectious disease is arousing attention in the fields of public health and epidemiology. Not only does the method provide a means of predicting patterns of disease occurrence, future epidemics, and possible eradication, but the model can incorporate the utilization of preventive strategies to study their effectiveness in reducing disease. Anderson and May have made significant contributions to the field of infectious epidemiology with their incorporation of mathematical models, whose application has extended to infectious diseases such as tuberculosis, malaria, childhood viral infections and sexually transmitted diseases. The ability to modify transmission dynamics parameters make their use for policy makers invaluable. This article is an example of how mathematical models can be used to identify the most effective strategy for preventing infectious disease. Certain limitations to the Markov models used in this study included the lack of consideration of behavioral change with time, delay between treatment of an index patient and his/her partner, and gender differences in condom use. Assumptions in the model may be based on situational specific sociological or behavioral surveys and current epidemiological research to determine the specifics of the transmission parameters such as latency periods. More studies using this method would add to the body of knowledge as well as guide policy makers in the Pacific about how to distribute scarce resources for specific strategies for control of various infectious diseases.

**“ The study indicated that tuberculosis in French Polynesia is due to both reactivation of latent infections and recent transmissions within the community and family. ”**

infections and recent transmissions within the community and family. The authors concluded that two genetic markers should be used to detect and identify strains responsible for transmission and outbreaks.

### **Chromosomal DNA fingerprinting analysis using the insertion sequence IS6110 and the repetitive element DR as strain-specific markers for epidemiological of tuberculosis in French Polynesia.**

Torrea G, Levee G, Grimont P, et al. *Journal of Clinical Microbiology*, 1995; 33(7): 1899-1904.

The use of genetic biomarker analysis to determine specific strains of *Mycobacterium tuberculosis* in French Polynesia enabled distinctions to be made between new infections and reactivation in relapsed patients. Such DNA Fingerprinting using a specific sequence to *Mycobacterium tuberculosis* (IS6110) and a repetitive element (DR) on specimens from 64 patients, enabled the observation of genetic polymorphisms to determine whether strains were related. Typically, French Polynesia is an area of low incidence of tuberculosis with a population which has been geographically stable over the past several decades. Of the strains studied, there were 38 RFL types and 12 groups. Analysis of the geographical distribution of the patterns showed that some types were restricted to cities and towns and some types identified resulted from active transmission between family contacts.

Genetic marker IS 6110 appeared satisfactory for typing strains carrying multiple IS6110 copies. The similarity of the types (DRRFLP) showed that these strains had the same origins evolving into new IS6110 types. The study indicated that tuberculosis in French Polynesia is due to both reactivation of latent

**Editorial Comment:** The use of genetic biomarkers for strain identification in determining transmission pathways of infectious diseases has important implications for expansion of epidemiological knowledge and possible demystification of the “black box”.

Chromosomal DNA fingerprinting has become more popular in recent epidemiological studies and offers considerable promise if the geneticist, microbiologist and the epidemiologist can collaborate in order to design studies with potentially significant contributions to the fields of infectious disease epidemiology and microbiology. This study evaluating polymorphism of *Mycobacterium tuberculosis* strains can assist in determining the pathway of transmission of TB in French Polynesia. While this is a technical microbiological review of the study, some discussion of validity of the methods employed; selection of subjects and possible biases may have

helped epidemiologically minded readers to get a clearer sense of the study. The concepts that emanate from the implementation and documentation of such a study should serve to highlight the importance of multidisciplinary collaboration, particularly in molecular epidemiology, and encourage Pacific health researchers to consider the use of some of these technologies, even DNA fingerprinting to further understand disease causation and transmission in the islands.

### Geographic latitude and the efficacy of Bacillus Calmette-Guerin vaccine

Wilson M, Fineberg II, Colditz G. *Clinical Infectious Diseases*, 1995; 20: 982-91.

Geographic location has been identified in a meta-analysis study as accounting for 41 % of the efficacy of Bacillus Calmette-Guerin (BCG) vaccine. This article discusses the factors that vary with latitude that may explain the effectiveness of BCG vaccine in populations. Some of the factors that vary with geographic location have impact on the host, agent and their interaction, ultimately influencing the incidence of tuberculosis and the apparent effectiveness of the vaccine. While infection with non-tuberculous mycobacteria (NTM) could explain some of the variation with latitude, the exact role of NTM is unclear. Reduction in the number of curable particles in BCG vaccine differs significantly in tropical and temperate countries. While completeness of surveillance and followup studies in BCG may account for some of the variation in efficacy, the storage and handling of the vaccines, the difference in the amount of photosynthesis of Vitamin D in fairer and heavily pigmented skin, and dietary intake differences may also influence the vaccine's impact. Variation in genetic susceptibility to TB, immune response affecting susceptibility and expression of TB, and in the virulence of different strains of *M. tuberculosis* may also be important. Thus the variation with geographic latitude appears to be a result of several factors. Further epidemiologic, genetic and molecular studies are needed to understand the impact of these factors on vaccinated populations.

**Editorial Comment:** This well written review article consolidates information from immunological, epidemiological, and animal studies as well as other scientific data to discuss the explanation of the role of geographic location in the efficacy of BCG vaccination.

Given tuberculosis is such a prevalent and debilitating condition throughout the Pacific, it is important that we understand the reasons for its occurrence in order to combat its impact. While this article provides insight into relevant

factors affecting TB occurrence, it also offers a novel model for understanding the efficacy of BCG vaccines. The policies governing BCG vaccination vary in different parts of the world. For countries like the Pacific Islands, where BCG vaccination is utilized, it is important that we understand the factors that will maximize its effectiveness. Herein lies another area for research in the Pacific, an area with widely differing latitudes.

### Outbreak of gastrointestinal illness associated with consumption of seaweed, Hawaii, 1994

*JAMA*, 1995; 274(22):1753-1754.

An outbreak of gastrointestinal illness was reported after a picnic in Maui, Hawaii in September 1994. The contact case reported a burning sensation to her mouth and throat, fifteen minutes following consumption of the food, which lasted four hours. A classic epidemic investigation into the role of the various foods revealed that the only statistically significant food associated with risk of illness was seaweed. The seaweed had been washed and cooked in boiling water and then refrigerated before consumption. Individuals affected with the illness suffered from diarrhea, nausea, vomiting and a burning sensation of the mouth and throat. Analysis of a leftover sample of the seaweed identified as *Gracilaria coronopifolia*, revealed a non-identifiable toxin. Mice that were fed extracts of the seaweed, developed diarrhea and those on high dosages died within 15 minutes at the highest concentration levels. *Pseudomonas* and *vibrio* grew in the culture media. There was no evidence that the seaweed had been contaminated with pesticides. Physicians were requested to notify any similar cases to the Department of Health.

**Editorial Comment:** This extremely succinct overview of the more detailed investigation report in the MMWR is yet another reminder to Pacific dwellers who consume seaweed on a regular basis to be alert to possible signs of seaweed poisoning. While there was no fatal case in this outbreak, an outbreak in Guam in 1991 killed three of thirteen persons who became ill following consumption of a seaweed known as *Gracilaria tsudai*. Similar cases have recently been reported in Japan and California. Possible explanations for the toxicity include toxicity at the end of the reproductive cycle, over-harvesting causing stress induced elaboration of the toxin and increased pollution encouraging toxin producing bacteria. It is therefore important that in order to maintain a high level of clinical suspicion among doctors about toxic seaweed, doctors be aware that such an illness can occur. It

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is equally important that certain species of seaweed be analyzed to determine possible levels of toxicity within the Pacific. Cases should be reported to Ministries of Health and adequate surveillance of this seaweed-related disease be maintained.

### **A prospective investigation of the long term auditory-neurological sequelae associated with bacterial meningitis: a study from Vanuatu**

Caroll, K.; Caroll, C. *Journal of Tropical Medicine and Hygiene*, 1994; 97(3): 145-150.

Vanuatu has an annual incidence of 134 bacterial meningitis cases per 100,000 persons. The followup of 83 bacterial meningitis cases admitted to Lenakel Hospital in Vanuatu from August 1988 to July 1991 is described. Of 75 survivors, 65 were followed up for a mean duration of 17.5 months. *Neisseria meningitidis* was identified in 53.8% (35), *Streptococcus pneumoniae* in 21.5% (14) and *Haemophilus influenzae* in 6.2% (4). No pathogen was identified in the remaining 12 cases. When grouped according to the severity of the illness, there were no significant differences in mean age, duration of symptoms or sex of the patient. Severity of illness and risk of auditory-neurological sequelae was statistically significant. Those with more severe disease were more likely to suffer from sequelae. One or more auditory-neurological sequelae were found in 31.5% of the survivors at the time of discharge, with suspected hearing impairment being the most common. Of the survivors followed, the most frequent abnormality was hearing impairment in 32.3%. Besides deafness and speech disorders, three of the patients also suffered from other severe neurological sequelae. Significant disabilities likely to impair their ability to lead independent lives occurred in nine patients. *Strep pneumoniae* was associated with the highest incidence of sequelae and *H. Influenza* with the lowest. The article discusses the use of dexamethasone along with antibiotics to treat patients with meningitis in developing countries and the importance of vaccination to prevent bacterial meningitis.

**Editorial comment:** This article of a followup of inpatients for post meningitis sequelae is well written, interesting and informative. The tables and the body of the text are consistent, the statistical analysis correct ANC aptly presented, and the discussion skillfully weaves the situation in Vanuatu within the context of other studies conducted in developing and developed countries. The lack of a statistically significant

difference in mean age and duration of symptoms with severity illness may be a result of an inadequate sample size or simply no difference. As long term disability resulting from bacterial meningitis is potentially preventable, the use of the most cost effective strategy, immunization, should be given serious attention in developing countries. Although Vanuatu's case fatality rate of 15.7% compares less favorably with developed countries (7-10%) and more favorably than many developing countries (as high as 67%), like most Pacific Island countries there is always need for improving care, through early detection, appropriate antibiotics and possibly early dexamethasone use. Furthermore, the implementation of vaccination strategies that will prevent these diseases from occurring, particularly in the vulnerable groups, is an important step towards overcoming infectious diseases with serious long term sequelae. Ensuring such strategies are effectively implemented and evaluated is vital to improving health care in the Pacific.

### **Medical effects of exposure of human beings to fallout radiation from a thermonuclear explosion**

Cronkite E, Bond V, Conard R. *Stem Cells*. 1995; 13(suppl.1) 49-57.

This study documents the short and long term medical effects of exposure to radioactive fallout from the detonation of a nuclear device on Bikini Atoll in 1954 among Marshallese inhabitants of nearby atolls. On Rongelap the average gamma dose in air was 1.9 Gy and in Ailinginae was 1.10 Gy. Hematological indices of exposed Marshallese were compared to age-matched non-exposed Marshallese. Approximately/30 days after exposure, there was a significant decline in average total leukocytes and neutrophil counts. From Day 8 to Day 30, there was a significant reduction in platelets to about 100,000 per mm<sup>3</sup>. Plots of the cumulative percent of the blood counts for neutrophils and platelets as a function of time illustrate that at the time of maximum depression the cumulative counts are significantly shifted to the left of

the control populations. With greater doses of exposure to radiation, the shift to the left is increased. For platelets, this shift to the left is still significant even seven years after exposure. There has been one case of acute myeloblastic leukaemia in a 19 year old who was one year old when he was exposed to 1.9 Gy radiation on Rongelap. Twenty five percent of the Marshallese exposed experienced itching and burning of the eyes with lacrimation, and nausea and vomiting. Loss of hair, scalp ulceration and hyperpigmentation of the skin with early cutaneous lesions, that were

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hyperpigmented macules, papules and raised plaques as well as blisters were also experienced. Bluish brown pigmentation of the nails were observed on Day 23 post exposure. Cretinism became evident in two infants. There were 15 cancers of the thyroid among the 53 thyroid tumors. The adenomatous nodules were observed approximately ten years post exposure. Children who were less than ten years old when they were exposed had the highest incidence of thyroid nodules and cancer.

**Editorial Comment:** This account of the medical effects of radioactive fallout on the Marshallese population describes in some detail the clinical problems that were seen by the examining physicians from the ninth day post exposure in 1954 until 1987. While the survival curves of the exposed and unexposed Marshallese showed no significant difference in this study, the small sample size may preclude any significant difference in the survival trends from being observed. Furthermore, one wonders how unexposed the "unexposed" Rongelap Marshallese group may indeed be and whether this exposed population, which is the most intensively studied population exposed to whole body radiation (examined 6-12 months for 40 years), has received more medical attention, enabling a prolongation of survival. Obviously, a comparison of quality of life would show a significant differential. The presentation of the data from the graph showing the total cumulative dose in air from beginning of fallout at 4 hours post detonation to 51 hours later when they were evacuated from Rongelap, to the graph illustrating cumulative distribution of platelet counts at time of maximum depression and seven years after exposure is effective. Despite the advent of the post-cold war era and especially in the era of smaller country/terrorist nuclear warfare, this article should be read by all physicians as a reminder of devastating effects of nuclear detonations on humans. In the Pacific, most health care workers, politicians and the general public may find that this account may fuel further disdain and opposition to the French nuclear testing in Polynesia.

### A new variant of Creutzfeldt-Jacob disease in the UK

Will R, Ironside J, Zeidler M, et al. *Lancet*, 1996; 347: 921-25.

This article is a report of ten cases of a new variant of Creutzfeldt-Jacob Disease in the UK whose clinical onset was in 1994-1995. The CJD Surveillance Unit was re-established in May, 1990, following an outbreak of Bovine Spongiform Encephalitis (BSE) in cattle, to determine patterns of change in occurrence of CJD in the UK. Cases were referred to the unit through references from neurologists and neuropathologists as well as information collected from autopsy reports

where CJD was a cause of death. Clinical information pertaining to each of the cases was collected from case records and risk factor information from close relatives of the cases. Neuropathological examination was also undertaken. Ten patients of 207 patients identified since 1990 had

distinctly different neuropathological findings. The age of onset was significantly younger, 19.41 yrs; their duration of illness longer, 7.5-22.5 months; and their clinical course dissimilar. Behavioral changes and ataxia were seen early in the course in nine patients while progressive dementia in all patients was accompanied by memory impairment in only two patients. There was an absence of EEG changes typical of CJD. Spongiform change and distinct Kuru-like PrP (Prion Protein) plaques throughout the cerebrum and cerebellum, and to a lesser extent in the basal ganglia, thalamus, and hypothalamus, were detected by neuropathological examination in all ten patients. While none of the patients had a history of possible iatrogenic exposure, blood transfusion or occupational exposure through abattoirs or farming, nine of the ten reported to have eaten beef or beef products in the last ten years. The recognition of a new variant of CJD and the possible links with BSE raises concern that many more cases of CID are likely in the near future.

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**Editorial Comment:** The situation with BSE-CJD has received considerable attention in the media and political arena over the past eight-ten months in the UK and Europe and the subsequent banning of UK beef products has had significant impact on the cattle industry and British economy. It has been an episode where publication of peer-reviewed scientific research, effective communication of risk to the general public, and multidisciplinary collaboration required careful coordination and management. From a scientific perspective, the recognition of a new clinicopathological variant of prion disease raises the important question of whether a new risk factor has emerged, namely exposure to bovine prions, particularly in the UK in the mid 1980s where the practice of feeding scrapie contaminated offal to cattle occurred. Furthermore, the possibility of transmission to humans across the species barrier by bovine prions presents a great challenge to scientists interested in understanding the pathogenesis of this disorder. While this recent epidemic suggests an incubation period of at least 5-10 years only time will tell whether these ten cases are the forerunners of a larger approaching epidemic of this previously unrecognized type of human spongiform encephalopathy. The BSE-CJD episode would be an interesting case-study for medical students and doctors, even in the Pacific, as it emphasizes the importance of multidisciplinary collaboration and the value of national and global epidemiological surveillance for the detection of disease, whether they are new emerging variants, newly recognized species, changing patterns of occurrence of disease or recurrences of well-established disease. □