

## SPECIAL ARTICLE

### **Past and present research activities of the Papua New Guinea Institute of Medical Research**

MICHAEL P. ALPERS<sup>1</sup>

**Papua New Guinea Institute of Medical Research<sup>2</sup>, Goroka, Madang, Tari, Wewak and  
Maprik, Lae and Port Moresby**

#### **What is the Papua New Guinea Institute of Medical Research and what does it do?**

The Papua New Guinea Institute of Medical Research (PNGIMR or, within PNG itself, simply the IMR) was established in 1968 as a Statutory Body of the Government of Papua New Guinea, responsible to the Minister for Health. It began as the Institute of Human Biology. After a hiatus at the time of Independence, the activities of the Institute, consistent with the change to its present name, have been directed towards the primary goal of conducting research into the health problems of the people of Papua New Guinea. Major research programs have been established in respiratory diseases, malaria, malnutrition, enteric diseases, sexually transmitted diseases and women's health, thus addressing the biggest health problems of Papua New Guinea. The principal funding of the Institute as the national medical research institute comes from the national Government. Its affairs are governed by a Council of 14 members with wide representation. Though independent of the Department of Health the Institute effectively acts as the research arm of the Department. In 1999 this relationship has become even closer: following deletion of the Government's budgetary support to all its statutory institutions in 1999, the Institute's recurrent or core funding for this year is being provided by the Health Department. The strong support given by both the Minister for Health and the Secretary for Health has enabled the Institute to survive the current economic crisis.

The Institute conducts its work from laboratory and office complexes in Goroka (Eastern Highlands Province), Madang (Madang Province) and Maprik (East Sepik Province), with smaller branches in Tari (Southern Highlands Province), Port Moresby, Lae and Wewak. Various field stations support ongoing research in rural areas. The head administration, main library and largest laboratories of the Institute are in the headquarters in Goroka. The malaria research program is conducted from the Institute base at Yagaum near Madang and in the Wosera area of Maprik District from bases in Maprik and Kunjingini. The Maprik branch also serves the filariasis research program in Dreikikir. The pneumonia research program has so far been conducted in Goroka and Tari, though studies in coastal areas are planned. The enteric diseases research program is based in Goroka though the principal work on pigbel in the past was carried out in Simbu Province. The sexual health research program has been conducted in a number of provinces and in the urban centres of Port Moresby and Lae. The program on women's health has taken place in Madang, Maprik, Tari, Goroka and, more recently, Port Moresby and Lae. The nutrition research program has been based in both Goroka and Madang and has been carried out also in Tari, Karimui (Simbu Province) and the Wosera, in addition to the National Nutrition Survey. Apart from the Survey itself, which was nation-wide, research studies, from bases in the IMR's strategically placed branches, have been conducted in virtually every province of Papua New Guinea. A particular emphasis has been

---

<sup>1</sup> Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, EHP 441, Papua New Guinea

<sup>2</sup> This account of the Institute's research activities was approved by the Institute Council in March 1999; its publication has created the opportunity to add selected references drawn from the Institute's Publication List.

placed on the health problems of people living in the remote and marginalized fringe highlands.

The activities of the Institute cover a wide span: its laboratory and computer facilities make use of the latest technology, yet most of its research programs are firmly rooted in the community, with community-based staff and active involvement from the participating communities.

Budgetary cuts in the last five years have required reduction in the scope of activities in all programs. This initially fell most heavily on the nutrition research program and on the Tari branch of the IMR, but the progressive loss of staff and reduction in activities have now affected all our research programs.

In 1993 the twenty-fifth anniversary of the Institute was celebrated with a Silver Jubilee International Colloquium held in Madang. The collegial network of research, training and goodwill which links current staff, collaborating colleagues and previous members of staff, now working in institutes throughout the world, was made clearly evident during the scientific sessions and social events of the Colloquium. The Institute Council has recently supported the establishment of a Butressing Coalition of scientific colleagues and institutions which will strengthen the central structure of the Institute and assist it to carry on its essential national health research.

### **The Institute's programs and units**

All the Institute's research is applied research: it is problem driven rather than curiosity driven. The problems are specific diseases or the health problems in a particular area or among a particular group. The Institute is organized principally around its problem-based research programs - pneumonia, malaria, enteric diseases, nutrition, sexual health, women's health, filariasis, and other diseases. Cutting across these are units based on scientific disciplines: the Asaro Surveillance Unit for epidemiology, the Tari Research Unit for demography and epidemiology, the Wosera Studies Unit for epidemiology and community development studies, the laboratory-based bacteriology, parasitology, virology and

immunology units, the entomology unit, the molecular genetics unit, the medical anthropology unit, the computing and statistics unit, the information and communication unit and the research implementation unit. A third structural dimension is provided by the sections of administration, finances, transport, library and laboratory management which support all programs and units.

The ultimate aim of all the Institute's research programs is to provide effective interventions which will lead to improvements in people's health and in the control and prevention of disease. The basis for achieving this aim is greater understanding of the relevant disease processes and the constraints to change. In part this understanding comes from knowledge of the external causative agents of disease and in part from examining the host factors involved, in particular behavioural, genetic, immunological and nutritional (1). Some of this work on host factors derives from the problem-based programs but, in addition, separate units of the Institute are devoted to the particular disciplines of medical anthropology and human genetics.

With respect to anthropology, all field staff working in Institute programs are expected to adopt an anthropological approach to their work; this means establishing a strong rapport with participating communities that is based on an understanding of their motivation and social organization; it means adopting an open attitude to their beliefs and customs; and it means asking open-ended questions about health-related behaviour. However, particular studies require more detailed information about social and behavioural factors and for this the expertise of the Institute's **Medical Anthropology Unit** is required. Detailed community studies of nutrition, growth, fertility, endocrine status, genetics, disease patterns and social organization have been undertaken by the unit, particularly in the fringe areas between the highlands and the lowlands, in Bundi, Gainj, Karimui, the Anga groups and the Hagahai. The unit has carried out nutritional studies in the Madang and Wosera areas and in other parts of Papua New Guinea in collaboration with members of various government departments. It has contributed to the Institute's studies on

malaria, in particular on the local production and use of bednets. It has examined the disease-recognition and treatment-seeking behaviour of mothers. It took part in a survey of poverty in Papua New Guinea. Studies on behavioural constraints to family planning and to the prevention of sexually transmitted diseases and AIDS, and the evaluation of methods of sexual health education have been undertaken, in both rural and urban areas. In the face of a potentially explosive epidemic of AIDS, studies on sexual and reproductive behaviours in a range of cultural groups throughout PNG were carried out by the unit; the findings of these studies were published as a monograph in the Institute's monograph series (2). Evaluation of peer education as a means of preventing HIV transmission and AIDS is now being undertaken in groups at high risk, such as youth, truckers, sailors and dockers, security guards, police and commercial sex workers.

The **Molecular Genetics Unit** originally concentrated on the human major histocompatibility complex (HLA) and genetic associations with a number of diseases, such as malaria, arthritis and asthma. The unit has now expanded into a fully equipped laboratory of molecular genetics. Its new emphasis is on molecular techniques for the diagnosis and characterization of a wide range of infections. These techniques are currently in use to study malaria, chlamydial infections in mothers and their newborn children, human papillomavirus infection, measles and typhoid. The unit has also contributed to many other studies of the Institute and has carried out its own extensive survey of human genetics in different parts of Papua New Guinea. Powerful new genetic techniques have created the field of bioarchaeology, which enables ancestral relationships between human groups to be determined; collaborative studies in this field are being conducted with colleagues in Australia and the United States.

The **Computing and Statistics Unit** maintains the function and proper use of the many microcomputers held by individual sections and staff members of the Institute and the network that allows communication between the various units and branches. The unit is responsible for regular back-up of

computers and archiving of data. The statisticians assist all staff members and other colleagues in the planning, conduct and analysis of research projects. The staff of the unit also conduct their own research into the appropriate statistical handling of the various kinds of data generated by the Institute's scientific projects and contribute their own scientific input to particular studies where more innovative analysis is required.

The **Entomology Unit** is based in Madang with its own laboratories, offices, field equipment store and insectary. Its major activities have been directed to the mosquito vectors of malaria, filariasis and arbovirus infections. The abundance and distribution of vector species have been studied in the field. Infected and infective mosquitoes have been analyzed in the laboratory. Behavioural and genetic studies have been conducted in the field and laboratory. The unit provides a national resource for entomological reference, for studying the effect of insecticides and for the monitoring of vector control programs.

The **Information and Communication Unit** includes staff in the library, maintaining the collection of books and journals and the capacity to search the world literature through Medlars and other data bases; the publications section concerned with Institute publications such as reports, papers and the Monograph Series and maintaining the Institute's Publication List (over 1650 references); the bibliographical and journal section responsible for the Bibliography of Medicine and Human Biology of Papua New Guinea and for editing the *Papua New Guinea Medical Journal*, the peer-reviewed quarterly journal of the Medical Society of Papua New Guinea and a highly respected international journal in tropical medicine; and the audio-visual section, equipped with dark-room and other facilities for research documentation, for providing illustrative material for lectures and publications and for conducting research using modern audio-visual technology.

### **Respiratory diseases**

Pneumonia and other acute respiratory infections are first on the list of major health problems in Papua New Guinea. They are

studied in the **Pneumonia Research Program**. In adults the causative organism of pneumonia is principally the pneumococcus (*Streptococcus pneumoniae*); in children both pneumococcus and haemophilus are equally involved. These are both capsulated bacteria whose virulence is dependent on a polysaccharide capsule, of which there are many serotypic variants. Respiratory carriage of these organisms is established very early in life (3). The aetiological findings in pneumonia and meningitis were determined in a series of studies conducted in collaboration with the Goroka Base Hospital (4-6). Pathogenic viruses are frequently isolated from the respiratory tract of sick children and may have a critical role in initiating severe acute lower respiratory tract infection (7). Therefore the bacteriology and virology of acute respiratory infections were investigated in a defined population in the Asaro Valley near Goroka. In children many of the isolates of pneumococcus are relatively resistant to penicillin, a phenomenon which was first described in PNG many years ago (8) but which was not well accepted by first-world scientists until recently, when isolates resistant to many antibiotics have emerged throughout the world. This gives added justification for the well-established monitoring of antibiotic resistance in respiratory bacteria carried out in Goroka (9); this study has recently been expanded to include isolates from Port Moresby and other centres.

Clinical studies of acute respiratory infections and meningitis (10), examining the optimal case management appropriate for aid posts, health centres and hospitals, and investigations of the most relevant clinical signs and the capacity of health staff to elicit them, have been undertaken over many years in close collaboration with doctors and nurses working in the Goroka Base Hospital. These studies have influenced the standard management of acute respiratory infection (ARI) in PNG and, through the World Health Organization (WHO), elsewhere in the tropical world.

A multivalent pneumococcal polysaccharide vaccine is available against 23 serotypes of pneumococcus. Previous studies in Tari had shown that pneumococcal vaccine reduced the

mortality from pneumonia in adults. One of the first aims of the pneumonia research program was therefore to test the pneumococcal vaccine in children and mothers, in an attempt to reduce the serious morbidity and mortality from pneumonia in young children. The trial in children was carried out in Tari and the Asaro Valley. The trial demonstrated the efficacy of the vaccine in preventing death from pneumonia in children under 5 years of age, with a 59% reduction in mortality. In children aged less than 2 years the efficacy was 50% and there was a 25% reduction in all deaths in this age group (11). Analysis of the effect on morbidity has shown a reduction in severe (but not mild) disease by the vaccine, clearly demonstrated during epidemic periods of acute respiratory infection (12). The immune responses to pneumococcal polysaccharides in young children were shown to increase with age and to be serotype dependent; there was no general threshold at 18 months or any other age and with the most immunogenic serotypes responses were detected as early as 6 months of age (13,14).

The major needs now are to evaluate the vaccine in other communities within Papua New Guinea, especially in coastal areas, with epidemiological characteristics which would predict a similar impact of the vaccine, and to work towards securing the vaccine at a unit cost which we can afford. For this to be achieved it will be necessary for the study to be replicated in other tropical countries. The campaign to promote these results in international meetings and through the World Health Organization has been a long one and still continues (15,16).

Evaluation of the effectiveness of the vaccine when distributed through the health services and further immunogenicity studies have been conducted in Tari. Conjugate pneumococcal vaccines (in which each serotypic polysaccharide is conjugated to a protein carrier), which are more immunogenic in infants, are being developed overseas and should eventually become available; but they will be made for only a limited number of serotypes and will be very expensive. Nevertheless, it is hoped to undertake studies on these vaccines in the future. Since pneumonia is such a serious and common

disease, worldwide, even a vaccine of modest efficacy can have a profound effect in terms of the number of lives saved; furthermore, the cost of an effective vaccine should be subsidized by the international programs and agencies which promote the immunization of the world's children.

An alternative approach to protecting young infants from pneumonia is to immunize mothers with the 23-valent pneumococcal vaccine in the third trimester of pregnancy. A study to evaluate this approach has been carried out in Tari; preliminary analysis of the serological immune status of the children of vaccinated mothers compared to controls supports the idea of maternal immunization and justifies a trial of its efficacy. The laboratory assays of the breastmilk samples from the study have recently been started.

*Haemophilus influenzae* is the other major cause of pneumonia in children; the aetiological studies in Goroka have shown that many invasive strains are non-serotypable (non-capsulated) (4). Nevertheless, an effective vaccine against type b organisms alone would protect against the most serious forms of *Haemophilus* infection, especially meningitis, and conjugate vaccines against *Haemophilus influenzae* type b (Hib) are available. Immunogenicity studies of two types of Hib vaccine carried out in Goroka have shown that the vaccines are immunogenic and safe in Papua New Guinean children (17). The campaign to promote the use of Hib vaccine in PNG and obtain it through WHO at an affordable price continues.

Longitudinal studies have been conducted in village communities on the respiratory carriage of pathogenic bacteria and viruses and on the factors which enhance the severity of acute respiratory infection (18,19). The organisms are known to be widespread, and one of the major questions is why certain individuals develop severe or fatal pneumonia. Studies on host factors, immunological, nutritional and genetic, have been undertaken in the study populations. Poor nutritional status and low levels of pneumococcal antibody have been shown to increase the risk of children getting moderate or severe pneumonia; and malnourished children have an increased

chance of dying of the disease (20). The immune status of young children and the generally low level of cell-mediated immune responses in the population have been investigated. Transmission studies are planned which will investigate the ecology of the organisms in the village environment in more detail. Studies on **chronic lung disease** in adults have shown that patients have very heavy carriage loads of pathogenic bacteria and this provides an obvious source of infection for young children living in the same household. An oral haemophilus vaccine has given encouraging results in reducing morbidity and bacterial carriage when tested in these adult patients; and preliminary evidence suggests that its use might also reduce household transmission of respiratory bacteria. Many patients with chronic lung disease have a hyperreactive component as well as obstruction and infection, and their symptoms are helped to some extent by the bronchodilating treatment given for asthma.

A study of neonatal infections (which have a different aetiology from those in older infants) has been conducted in the Goroka Base Hospital, with funding from the World Health Organization, as part of a coordinated global study. Preliminary results indicate the importance of pneumococcus, other streptococci, staphylococcus, respiratory syncytial virus and chlamydia (21) (for both conjunctivitis and pneumonia) as causes of infection in young infants.

The pneumonia research program exemplifies the general approach taken by the Institute to the study of a major disease. An epidemiological study in a well-defined community is supported by laboratory studies of the aetiology and pathogenesis of the disease; both the causative organisms (together with vectors and intermediate hosts, if any) and the human host factors are considered, with an investigation of the place of these organisms and factors in the local ecosystem; and a novel intervention is evaluated as soon as possible in the course of the study. At the same time the health care sought, both traditional and western, is documented, and the effectiveness of such care in handling the disease problem under study is evaluated. Such a research program is multifaceted and requires careful

integration; it also needs a relatively large staff, hard work, good funding - and time. We believe that all these are required in studying the major diseases of the tropical world if we are ever to achieve the desired practical outcomes. Moreover, if the results of such research are to be applied generally within Papua New Guinea - as is the intention - then the conditions under which particular causes operate or an intervention program proves successful must be known in detail, so that, if necessary, the new methods can be modified in appropriate ways when they are applied in different areas.

Another respiratory disease which the Institute is studying is **asthma**. Asthma was a new disease to the highlands of Papua New Guinea in 1970 when the first case in the Okapa area was diagnosed. It has since become highly prevalent in adults in some, but by no means all, parts of the rural highlands. It is being investigated to determine its nature and cause in the hope that this knowledge will lead to methods of preventing the disease, which is severe and often fatal (22-24). Reduction in exposure to house dust mite through spraying of blankets has been shown to reduce episodes of asthma and improve lung function. This may also be achieved through the regular airing and washing of blankets, though paradoxically it is hard to maintain compliance with such a simple intervention. Studies on the best method of treatment of asthma in village communities have also been undertaken; unfortunately, it has proved difficult for the health services to provide a sufficient supply of metered aerosol treatment to those living in the more remote places where the disease is prevalent. A new finding of considerable interest has been the fall in incidence of the disease in the study area in the last few years, for which there is no ready explanation. In contrast to the increasing asthma associated with expanding urbanization in PNG, which characteristically begins in childhood, the rural asthma of the highlands has been confined to adults.

**Measles** is a common respiratory infection in children and evaluation of a heat-stable measles vaccine was conducted by the Institute before measles vaccination was introduced into routine childhood immunizations in Papua

New Guinea. Maternally derived immunity to measles has been shown in PNG to have declined significantly by the age of 4 months, when many infants become both susceptible to severe and fatal measles and capable of making a good response to vaccination (25). As a result of these studies it has now become national policy to vaccinate against measles from the age of 6 months. After a disturbingly high incidence of subacute sclerosing panencephalitis (SSPE), the delayed, 'slow virus' form of measles, was found in a number of provincial hospitals, its epidemiology was investigated in Goroka (26). The disease can only be prevented by early immunization with a potent measles vaccine. The responsibility for the surveillance of SSPE has now been handed over to the Central Public Health Laboratory. Further molecular studies of SSPE, which in PNG has now unfortunately reached the highest reported incidence in the world, are continuing in collaboration with colleagues in Japan.

Another respiratory virus of importance is **influenza**. The Institute is the National Reference Centre for Influenza, but lack of resources and the failure of other centres to send in samples have made its function dormant; however, it could readily be stirred to action if a new epidemic arose.

The Institute is not carrying out research on **tuberculosis**, for which methods of control and treatment regimens have been well established. However, because of its public health importance as a cause of mortality, and its association with AIDS, new approaches to the prevention and treatment of tuberculosis developed elsewhere are being kept under close scrutiny.

## **Malaria**

An approach similar to that for pneumonia is being undertaken in the **Malaria Research Program**, directed against the second major disease problem of the country. The ultimate aim of the program is to reduce the burden of severe disease and death from malaria. From its inception the program has adopted as its principal objective the achievement of an effective vaccine against malaria, which seems to be a feasible though still distant goal. The

program has ensured that the vaccines evaluated are appropriate for use in an endemic area, and specifically in Papua New Guinea. Epidemiological studies have been given prominence from the beginning of the program since knowledge gained of the epidemiology of malaria will be essential for the evaluation of any future vaccine (27,28). These studies have clearly indicated a high degree of variability in microepidemiological patterns of infection over relatively small areas and short periods of time (29). Studies of the molecular epidemiology and immunoepidemiology of malaria have also been a central feature of the research program (30,31). These studies have examined the spatio-temporal variability in immune responses to a range of malarial antigens, and the evidence for protection by immunity to defined antigens under consideration for inclusion in future malarial vaccines (32-35). Most work has been done on blood-stage antigens, but the liver-stage antigen LSA1 has also been studied. The principal emphasis has been on *Plasmodium falciparum*, because it causes fatal disease, but all four plasmodial species of human malaria occur and their interactions have been investigated (36). There have been a number of studies on *Plasmodium vivax*, in particular of its genetic variation and interaction with human host factors.

Longitudinal studies on the morbidity caused by malaria have been undertaken in rural communities in preparation for vaccine trials (37,38). Recent work has emphasized that variable morbidity may be associated with molecular strain variation in *Plasmodium falciparum* and infection with multiple strains. The biological and immunological mechanisms involved in the interaction between species and strains have been investigated over many years, with contributions from many members of staff and collaborating colleagues. Studies on plasmodial genetics, of gradually increasing complexity, and studies of reproductive strategies in *Plasmodium* have been carried out, notably in the Madang area.

Since malaria is transmitted by anopheline mosquitoes, detailed entomological investigations in the ecosystem of the study area form an essential part of the research program (39-41). More specific studies of the

vectors include work on the biology and behaviour of the members of the *Anopheles punctulatus* complex (42), with an emphasis on the importance of sibling species, in the highlands as well as on the coast and lowlands. Sympatric and allopatric species, many of them morphologically indistinguishable, are now defined by genetic techniques. Detailed spatial studies using global positioning system (GPS) technology have been carried out. Transmission-blocking immunity and the infectivity of human populations to mosquitoes have been studied, and sporozoite rates and densities for the different species of *Plasmodium* in the mosquitoes have been determined (43).

In the absence of a vaccine, a drug intervention was evaluated using the standard antimalarial drugs (chloroquine and amodiaquine) distributed by village health aides in a community-based program. This study indicated the value of village aides where health services are not readily available but, as with other levels of health care, supervision of the health worker is essential if a high level of performance is to be sustained. The now well-known intervention of using permethrin-treated bednets to reduce the transmission of malaria has been investigated by the Institute since 1983; this appears to be an effective method of controlling malaria and one which can be widely used (44). This method is now officially recommended for malaria control throughout Papua New Guinea. Further studies on insecticide-treated bednets are continuing. A project to evaluate the capacity of a group of Amele village women to make, treat and sell bednets was undertaken. Another project has been designed to evaluate different insecticides and monitor their efficacy. As part of the program, the value of simpler antivector methods such as untreated bednets (45) and woodsmoke (46) has not been neglected.

Genetic and epidemiological studies have shown that ovalocytosis, a red cell polymorphism which reaches a prevalence of 35% in the Madang area, protects against malaria (47-49). Of particular significance is the finding that ovalocytosis completely prevents cerebral malaria, the most fatal form of the disease (50). Ovalocytosis is now being studied by molecular techniques which define a

27-base-pair deletion in the gene for band 3, an important red-cell membrane protein. This polymorphism has been selected for at significant cost to the host, to the extent that homozygosity for the genetic deletion is lethal. We have also discovered that in the Madang area there is a remarkably high prevalence of  $\alpha$ -thalassaemia and a number of variants of glucose-6-phosphate dehydrogenase, two other genetic polymorphisms which protect against malaria. Because of the very high prevalence of  $\alpha$ -thalassaemia it is possible to compare the response to malaria of homozygotes for an  $\alpha$ -globin gene deletion with that of heterozygotes, and such a study has been carried out in collaboration with colleagues from Oxford. The study has confirmed the protective effect of  $\alpha$ -thalassaemia against severe malaria and also, more surprisingly, against other severe infections (51). In the Wosera area (where ovalocytosis does not occur) individuals who are negative for the Gerbich blood group are being investigated for protection against malaria. More detailed studies of the relationship between HLA and malaria have been initiated. Long-standing projects have advanced our knowledge of hyperreactive malarious splenomegaly (tropical splenomegaly syndrome) in Papua New Guinea (52,53) and of amyloidosis, one of the complications of recurrent malaria.

Studies on malaria in pregnant women, who are at special risk from the disease, even in a holoendemic area, and in newborn babies have been carried out, with the aims of understanding how the changes in pregnancy tip the balance in favour of the parasite and of determining the best methods for preventing malaria in pregnant women. The incidence of malarial infections in young infants in the Madang area has been shown to be unusually high. However, despite high infection rates in pregnant women and infants severe malarial morbidity in these groups is uncommon. Particular studies have examined the immune responses of pregnant women to malaria (54), the importance of placental infections, the effect on birthweight, the transfer of maternal immunity (55), and the evidence for immune responses stimulated in utero.

Clinical and immunological studies of cerebral malaria have been carried out in

collaboration with colleagues in the Madang Hospital. Drug resistance in malaria has been studied *in vitro* and *in vivo* in both the Madang and Maprik areas (56-58). The results of these studies have led to recommendations for changes in the standard treatment of malaria in PNG.

In 1988 funding was provided by the United States Agency for International Development for a project to establish a field site in Papua New Guinea for malaria vaccine epidemiology and evaluation (59). This increased our staff in the malaria research program and provided a new research station in Maprik in East Sepik Province, a refurbished entomology laboratory in Yagaum and new equipment for malaria work. The communities taking part in the study live in the Wosera area of Maprik District. This area has since become our major field site for research on malaria. Baseline demographic, epidemiological, parasitological, immunological, entomological and genetic studies were carried out in the area, and have been regularly updated and expanded. When in 1994 USAID suddenly withdrew their funding for the project it was kept going by funds from AusAID, which is now providing long-term support for the malaria vaccine trials field site. This enables the evaluation of malaria vaccine candidates to be undertaken in populations fully defined for the necessary outcome variables relevant to malaria. The AusAID project also provides for community development and training components.

Our early work on malaria depended on the growth in culture of malarial parasites and a number of lines were successfully established in the Institute laboratories at Yagaum (60). Further investigations of these parasites were carried out in Australia. In particular, this collaborative work was directed towards the production of defined molecular vaccines against the blood stages of malaria. Though this has been the thrust of our collaborative malaria research program from the beginning, it took 20 years from conception to the start of the first vaccine trial. It is gratifying to report that a combination vaccine of three blood-stage malaria antigens (MSP1, MSP2 and RESA) has now been tested in adult males and children aged 5-10 years from the Wosera and shown to be safe and immunogenic.

Further stages in the evaluation of this vaccine and the first trials of an AMA1 vaccine, the second malaria vaccine in the collaborative program, are planned and will start soon.

### **Nutrition**

Despite much work in the past on the problems of suboptimal nutrition and frank malnutrition in the diverse parts of Papua New Guinea, it had not been possible to draw conclusions about the most critical deficiencies in the various diets of the people nor about the levels of nutrition, as measured by standard anthropometry, which constitute 'malnutrition', that is, represent some threat to the well-being and life of the individual. Nutritional status is a continuous variable and nutrient intake and expenditure interact in a complex way with genetic and adaptive mechanisms to produce both acute and chronic effects, which have a varying influence on the quality of life and the full achievement of individual human potential. The chronic effects are hard to assess though undoubtedly important. The most important acute effect of malnutrition is its interaction with infection to produce a vicious cycle which carries a high risk of serious morbidity and death. It is not known exactly how this vicious cycle operates. However, it is possible to obtain a functional definition of malnutrition, signalling the need for urgent intervention, by relating levels of nutritional status as measured by standard anthropometry to the subsequent outcomes of morbidity and mortality (61). This study was an important initial part of the **Nutrition Research Program** of the Institute and was carried out in Tari.

Malnutrition as assessed by the currently used standards has been shown to be a potent risk factor for the severity of pneumonia in children in Goroka (20). Those members of the community most affected by the vicious cycle between infection and malnutrition are young children from the time of weaning. Detailed studies of infant nutrition and weaning practices have been carried out. Studies on lactation, breastmilk, the introduction of solid food, growth (62) and the relationship between motor and psychological development and nutritional status (63,64) have been undertaken, as well as studies on

maternal nutrition during pregnancy and lactation. Birthweight has been examined in a number of contexts and shown to have potent effects on the subsequent life of the child (65). Food intake has been evaluated in urban and rural households.

Nitrogen metabolism was studied in the highlands near Lufa and on the coast at Yagaum using a stable heavy isotope of nitrogen. Composition of Papua New Guinean foods is not known with any degree of certainty; a limited number of food analyses were undertaken in the Institute's nutrition laboratory in Madang while that laboratory was operational. Micronutrients have also been studied, including iron (discussed under anaemia), iodine (discussed under endemic cretinism), zinc (deficiency of which occurs in some areas and leads to increased susceptibility to infection) and vitamin A (which is present in the diet in PNG but may be deficient in children suffering from severe infection).

Collaborative studies were undertaken on agricultural aspects of food and the use to which land and other agricultural resources in the community were being put, the economic basis of subsistence agriculture and food crops, the effect of the introduction of cash crops, attitudes to food and nutritional information, the effectiveness of health services in providing nutrition education, the importance of social and behavioural factors in food preferences and nutrition, particularly in children and mothers, and the effect of westernization and change on the nutritional health of Papua New Guineans (66). A study on the nutritional effects of a development project was completed in Karimui. Many of these findings have yet to be implemented.

The National Nutrition Survey was successfully carried out under the technical direction of the Institute (67). The first analysis by district indicated clearly that there were a few areas of the country which were significantly disadvantaged nutritionally compared to the rest. The next task was to study the causes of this relatively poor level of nutrition, with the aim of being able to make practical suggestions for improving it. We had hoped, in collaboration with other sectors, to determine the deficiencies, devise ways of

correcting them, evaluate interventions and monitor change. Unfortunately, because of the increasing financial constraints faced by the Institute and other government agencies, none of these important follow-up activities to the National Nutrition Survey were carried out.

Because of the Institute's lack of funds, virtually all activities in the nutrition research program have been deferred. However, outside project funding has enabled two important new projects to go ahead. A collaborative intervention study on vitamin A, zinc and malaria has been carried out in the Wosera area of Maprik District: it was found that both vitamin A and zinc successfully reduced morbidity from malaria. A research implementation project based on nutrition and hygiene in rural households is being conducted in Tari, and has become a model for sustainable self-help development projects in the country.

### Enteric diseases

The **Enteric Diseases Research Program** (which includes work on diarrhoeal disease, typhoid, pigbel and intestinal parasitic infections) is, again, principally a community-based program, with input from a wide range of scientific disciplines.

Since **diarrhoeal disease** is often epidemic it was necessary to adopt a more flexible approach in the program to ensure that outbreaks and epidemics of diarrhoeal disease could be quickly investigated. The primary studies have determined the aetiology of diarrhoea in patients admitted to Goroka Base Hospital and it was planned subsequently to investigate these organisms in carriage studies in epidemiologically defined rural communities of the Asaro Valley from which the Goroka Hospital draws its patients. However, delays in analysis have led to delays in the initiation of this phase of the project. The role of pigs as a reservoir and amplification site for enteric infection has been examined. Enteric bacteria, viruses and parasites have all been investigated in the laboratory. The program has achieved new findings on rotavirus, *Campylobacter* and *Cryptosporidium*. Pathogenic strains of *Escherichia coli* and enteric adenoviruses have been studied. The water in which sweet potato

has been cooked was found to be acceptable as an oral rehydration fluid in preliminary studies, but further evaluation has not yet been undertaken. Attitudes to diarrhoea and to the acceptance of particular interventions have been examined. Behaviour patterns that may be relevant to the transmission of different organisms have been studied in detail using a case-control methodology (68), though the difficulties of changing hygiene behaviour are clearly recognized (69). Because of recent financial constraints further work on diarrhoeal disease has been deferred.

The bacteriology unit has studied **peptic ulceration**, which is very common in parts of the highlands, and the association between both gastritis and gastric ulcer and *Helicobacter pylori* infection has been confirmed in PNG patients.

**Intestinal parasitic infections** are widely prevalent and lead to considerable morbidity. The distribution of hookworm, *Ascaris* and other parasitic infections, their treatment (leading to a change in standard management) and their interaction with nutritional factors were studied. Separately funded, collaborative studies on hookworm infection, and the relevant human immune responses, are currently being carried out in a coastal population. *Blastocystis hominis* was found to be a very common parasite in the highlands though its role in producing disease has not been proven. A parasite of particular interest is *Strongyloides fuelleborni kellyi*, which causes the **swollen belly syndrome** (70,71), a disease apparently peculiar to Papua New Guinea. The parasite has been shown to be widely distributed, though not found in all areas. Work has been completed on the biology and taxonomy of this organism. Its mode of transmission has still to be worked out. The tapeworm *Taenia solium*, from which originates the disease **cysticercosis**, is not found in Papua New Guinea, but has been introduced to Irian Jaya. There is consequently concern over the possibility of its crossing the border, and the infection has been sought in refugee communities. More systematic and regular surveillance is urgently required.

**Pigbel**, or enteritis necroticans, is a necrotizing disease of the small bowel caused

by the beta-toxin of *Clostridium perfringens* type C and promoted by a generally low-protein diet and by heat-stable trypsin inhibitors present in sweet potato, the main staple of the highlands (72). It was the commonest cause of death in highlands children over the age of one year. The Institute helped develop a vaccine against pigbel and then evaluated it in the field. The vaccine was shown to be successful in preventing pigbel and is now part of the routine immunization program in the highlands provinces. Since the introduction of the vaccine there has been a dramatic drop in the incidence of pigbel (73), and this has continued to the extent that doctors now working in the highlands hospitals have become less familiar with the disease. Unfortunately, the country ran out of pigbel vaccine after the original supplier ceased production. Though a new source has been found there have been long delays in obtaining supplies of the vaccine. The Institute has agreed to carry out studies to check its safety and immunogenicity and these should begin in 1999.

**Typhoid** became an increasing problem some years ago, particularly in the highlands. The Institute evaluated a slide agglutination test for the diagnosis of typhoid that could be used in health centres, but its diagnostic discrimination was lost with the marked increase in the endemicity of typhoid. Reevaluation has established a new appropriate cut-off titre, but the test now requires hospital-level laboratory facilities to carry it out. An epidemiological study of typhoid, with a defined demographic base in the Asaro Valley, has determined the very high incidence of typhoid, identified carriers, who were mainly convalescent patients, and established the sources of infection in the community (74). It is planned to use this epidemiologically characterized population for the future evaluation of new typhoid vaccines. Though budgetary constraints have forced a reduction in the scope of the enteric diseases research program, every effort has been made to maintain activities on typhoid. Studies are being undertaken on new diagnostic tests for typhoid, on molecular typing of *Salmonella typhi* and on the relationship between strains of *Salmonella typhi* and clinical severity. A study is planned on the use of fluoroquinolone

antibiotics in typhoid: by improving compliance with treatment and by reducing the convalescent excretion of *S. typhi*, these drugs, though expensive, may prove to be more cost-effective than chloramphenicol in the management of typhoid.

### Sexual health

Sexually transmitted diseases (STDs) have been studied for many years, including work on donovanosis, which is very common in Papua New Guinea, and on the treponematoses - syphilis and its relationship to endemic yaws, which is not sexually transmitted. Studies within the **Sexual Health Research Program** on *Neisseria gonorrhoeae*, the causative organism of gonorrhoea, first demonstrated that penicillin-resistant strains are present in Papua New Guinea. We also showed the high prevalence of infection with *Chlamydia trachomatis* (21). These studies led to changes in the standard treatment of sexually transmitted diseases as recommended by the Health Department. Surveys of genital ulcer disease and the most prevalent causative organisms of sexually transmitted disease, including viruses, have been undertaken (75). Community studies in the Asaro Valley have demonstrated that over half of randomly selected, apparently healthy women from rural villages were suffering from one or more STD (76).

Infection with the human immunodeficiency virus (HIV) and the disease AIDS (acquired immune deficiency syndrome) are increasing exponentially in Papua New Guinea and the rapid spread is related to the high transmission rates for sexually transmitted diseases. The Institute made an early committed response to the incipient AIDS epidemic. Studies on sexual and reproductive health (2,77), on the range of sexual behaviours which might place people at risk, on sexual and reproductive knowledge and attitudes, on sexual health education, with particular emphasis on AIDS and the use of peer educators, and on the acceptability and distribution of condoms have been carried out. In this field close liaison with other agencies and departments working on STD and AIDS has been maintained. The Institute made a strong effort to promote the establishment of a National AIDS Council, to

support and coordinate the urgent multisectoral national program which was needed to prevent the spread of AIDS, and it is pleasing to report that the Council was established - albeit belatedly - in 1998. The main recent thrust of the Institute's work in the sexual health program has been on targeted peer education, among groups at greatest risk of HIV transmission - youth (78), transport workers, police and security staff and commercial sex workers (the Transex Project). This project has been conducted in Port Moresby, Lae and Goroka and along the Highlands Highway. Monitoring of antibiotic susceptibilities in the gonococcal isolates from different sources continues. A study of HIV positivity in urban sex workers was recently conducted: 16% of those tested in Port Moresby were positive.

### **The improvement of women's health**

Studies on the particular problems and needs of women which are directed towards improving women's health have been undertaken in many places over a number of years. The early work culminated in a monograph on the health of women in Papua New Guinea (79). This has been followed up with a range of clinical, microbiological and educational research activities. Obstetrical complications are now recognized as a major health problem in Papua New Guinea (80). Maternal mortality was studied in Tari and the perinatal health of women and their infants investigated in the Wosera (81). Health education workshops for women, with an emphasis on reproductive health, have been conducted in Madang. Studies on postpartum sepsis, pelvic inflammatory disease and genital tract infection, which link with studies of sexually transmitted diseases and neonatal infection, are being carried out in the Goroka area. Community development studies are being undertaken in the Wosera, with a particular emphasis on the perceived needs of women.

### **Filariasis**

Lymphatic filariasis is widespread throughout coastal Papua New Guinea, but only in certain areas is there a high prevalence of clinical disease. One such area is around Dreikikir in East Sepik Province, where the

Institute's principal filariasis research project is being carried out, in collaboration with colleagues from Case Western Reserve University. Epidemiological, parasitological, immunological, clinical and vector studies (82-84) are in progress as well as a long-term, community-based treatment program against the disease which compares the efficacy of diethylcarbamazine (DEC) alone and in combination with ivermectin (85). The results from the study so far indicate striking effects on infection and transmission which give encouragement to the campaign for the elimination of lymphatic filariasis. A national working group has been established and communities at risk have been encouraged to carry out their own program of supervised mass drug administration. In Papua New Guinea the anopheline mosquito is the vector for both filariasis and malaria (86). Interventions against the vector have been assessed and are also likely to be of value. More recently, a study of the effect on filariasis of community-based treatment with albendazole has been started on Bagabag, off the coast of Madang.

### **Other disease studies**

There is a wide range of studies conducted by the Institute on other diseases, which individually have a more restricted focus. **Kuru** is a remarkable disease with many unusual features and although the incidence of the disease has declined considerably in recent years it is still a major health concern of people of the Fore area of the Okapa District in the Eastern Highlands Province (87,88). Kuru has an average duration of about a year and is always fatal. There have been only about 2 or 3 new cases a year in recent years (compared to 200 in the 1950s); the age of the youngest living patient has gone up each year and is now well over 40 years, and the age of all cases has been consistent with transmission by endocannibalism (transumption of relatives at mortuary feasts) before 1960. It is predicted that the disease will eventually die out, but the rate of decline is now slow and we do not know the limit of the incubation period, which in current cases is already 40 years.

**Arbovirus infections** have always been important in PNG, and they have been given

recent prominence as emerging infections. In addition to the widely endemic virus of Murray Valley encephalitis (MVE), Japanese encephalitis virus (JE) has been found in Western Province and along the south coast to Milne Bay; it is also spreading eastwards from Vanimo and Wewak on the north coast. Because of its association with pigs as an amplifying host, JE is likely to be much more dangerous to the people of PNG than MVE has been. Dengue is common and, disturbingly, a few cases of dengue haemorrhagic fever have recently been reported. The Institute's virology and entomology units combine to study these infections, in collaboration with colleagues from Queensland.

The Institute is the national centre responsible for the eradication of **poliomyelitis** and for providing the evidence in support of the certification of its eradication, and will continue this activity until these objectives have been successfully achieved.

A number of studies on **cancer** have been carried out. Burkitt lymphoma is a relatively common tumour in coastal children and Papua New Guinea has the only focus of the disease outside Africa. The immune responses to the causative Epstein-Barr virus and the relationship of the viral infection to malaria in both pregnancy and neonatal life have been investigated. New variants of the virus have been found in Papua New Guinea. Studies on another virus which causes lymphoma, human T-lymphotropic virus type I (HTLV-I), have also been undertaken in collaboration with colleagues overseas. The exact nature of the virus and its clinical importance in Papua New Guinea are still being determined but the isolation of the local variant of HTLV-I has advanced these studies considerably. This variant has also been found in Solomon Islanders and Aboriginal Australians and is significantly different from the cosmopolitan strain found globally. Hepatoma is a common cancer of adults in Papua New Guinea, especially in the highlands, and it is also caused by a virus, the hepatitis B virus. Since newborn transmission is believed to be critical for the development of adult hepatoma, vaccination with a hepatitis vaccine should begin at birth. Naturally acquired immunity to hepatitis B virus and the likely ways the virus

is transmitted have been studied in Tari (89). Cancer of the mouth and of the cervix are the two leading cancers in PNG and among the factors involved in their causation are different strains of human papillomavirus (HPV). The prevalence of HPV infection and the genetic typing of the viruses are being investigated in a joint study with the Department of Pathology, University of Papua New Guinea.

Research was conducted on **tinea imbricata**, or grille, a disfiguring fungal skin infection, with emphasis on the role of host factors in determining susceptibility to the disease (90). Bacterial **skin infections** are a major cause of morbidity in all communities in Papua New Guinea and studies of their aetiology have been carried out (91); particular attention was given, in collaborative projects, to **tropical ulcer** and **yaws**, which are still significant public health problems in certain areas. Collaborative studies were also carried out on **leprosy** in the Karimui area.

Studies on **arthritis** have established the importance of reactive arthritis as a common disease and its genetic association with HLA-B27 (92). Further work is required to determine the infections which initiate the process of reactive arthritis.

**Anaemia** is a widespread condition in Papua New Guinea; it causes significant morbidity in itself and may predispose to serious infection and death. It may be caused by nutritional deficiency, in particular of iron, or infection, in particular malaria and hookworm. The effect of an intervention giving intramuscular iron on the incidence of serious infection in young children was investigated in Madang; it was shown that correction of iron deficiency in infants predisposed to malaria infection, with increased morbidity from respiratory disease. This result was followed up with a double-blind study carried out in schoolchildren given oral iron supplementation; in this case there was no associated increase in malaria.

In its early days the Institute undertook a major program on goitre and endemic cretinism, for which iodized oil was used and promoted (93,94). More recent studies on **endemic cretinism** have found a few remote

areas with little goitre but new cases of cretinism (95). Further studies on iodine status would be of interest but the findings have emphasized the need for the required iodine levels in salt to be enforced by the Department of Health. This should be sufficient to prevent the incidence of iodine deficiency disorders in nearly all parts of PNG.

### Diseases of modernization

More general studies on populations and their disease problems in Papua New Guinea are being conducted, all on a long-term basis. With urbanization, westernization and other changes in the social conditions and way of life of the people, long-term **changes in disease patterns** are already evident. To some extent all Papua New Guineans are affected, but for the urban elite western diseases have become a serious problem. Papua New Guinea faces a protracted epidemiological transition, with traditional infectious diseases, new infections (such as HIV/AIDS) and degenerative diseases of modernization all prevalent at the same time. The IMR had been monitoring the prevalence of diseases such as diabetes, cardiovascular disease (96) and some forms of cancer, and their known risk factors, in a few selected population groups, in order to detect warning signals of increasing prevalence. However, financial constraints have temporarily stopped this project. At the same time attempts to modify individual behaviour and lifestyle to avoid these new diseases, for example, in the reduction of **cigarette smoking**, are being made through established health and other agencies. The campaign against cigarette smoking has been one of the IMR's long-standing activities; the proceedings of a national workshop on smoking which we organized were published as an Institute monograph (97). Studies on **diabetes** have indicated that diabetes and glucose intolerance are becoming alarmingly prevalent in urban and some coastal communities, and already in rural highland areas there is early evidence of changes in tolerance to glucose (98). The Institute took part in an international collaborative study on **hypertension** and salt intake, which showed clearly that there was a relationship between them; reduction in salt intake would therefore be a sensible preventive public health measure in PNG.

### Environmental health

A study on a community-based intervention was undertaken in the South Fore area of the Okapa District, investigating the effect of the establishment of **village water supplies**. Despite their generally acknowledged importance, water supplies provided to villages in Papua New Guinea have in many cases been inappropriate, and maintenance has not been adequately considered. Furthermore, the key issue is often not so much the introduction of a more convenient water supply but the use of such water in more frequent washing of people, clothing and bedding. Social and behavioural aspects have been seriously neglected. Recommendations on rural water supplies arising from a workshop organized by the Institute (99) formed the basis of a national policy on rural water supplies. However, little progress has been made in the provision of appropriate water supplies and sanitation to rural communities and the related health education which is necessary.

A project on the effects of **deforestation** on health, using malaria, arbovirus infections and sexually transmitted diseases as sentinel diseases and changes in mammals, birds, moths and mosquitoes as indices of environmental disturbance, was undertaken in the Hawain area of East Sepik Province. In another area, developing sustainable uses for forest products has been part of a study among the Hagahai people promoting their health and development.

### Population studies

Studies on the **demography** of the Tari Basin were conducted for many years and are being continued through extensive data analysis, though the collection of new demographic data has now ceased. The database in Tari begins in 1970 and provides a valuable resource for a number of potential studies. Other population studies have been undertaken in the Asaro Valley, Madang, Wosera, Karimui, Bundi, the Anga linguistic groups and the Hagahai people of the Western Schrader mountains. Studies have been undertaken on **fertility** among the Gainj, in Hawain and as part of the major demographic studies in Tari. Papua New Guinea is passing

through a protracted demographic transition, with a mixture of traditional and modern influences acting together, and with different parts of its society at different stages in the transition (100). This makes drawing general conclusions about population trends in Papua New Guinea difficult. The Institute took part in a recently concluded national Population and Family Planning Project.

### Health monitoring and surveillance

Large economic development projects may have short-term as well as long-term effects on health in the communities involved. The Institute has been able to contribute to the evaluation of some of these projects, even though it was not itself responsible for the health monitoring. An early attempt was made to establish a health surveillance unit for the North Fly area, to monitor the effects on the health of the local people and those involved in the mining over the life of the Ok Tedi mining project, but the unit was not funded. However, collaborative studies on nutrition and malaria, in particular, were carried out in the North Fly area. Working with the provincial and district health authorities, the Institute conducted baseline health studies of the population affected by the Lihir gold mining development. Similar activities took place in the Gogol Valley, in relation to the woodchipping industry, and in the Purari River system, at the time when the Wabo dam was under consideration, where the particular emphasis was on arbovirus infection. The impact of an agricultural development project on nutrition and health was studied in detail in research carried out in Karimui. The IMR is represented on the committee which monitors the environmental and health impacts of the Porgera gold mine, and staff from both Goroka and Tari have taken part in field assessments along the Strickland River.

### The delivery of health care

The Institute is not primarily responsible for research on health services and delivery of health care (**health systems research**). However, these aspects form a component of the integrated studies of major diseases, and new methods of providing health care and disease prevention, particularly at the

community level, have been evaluated. The Institute has contributed to studies on health services undertaken by the Health Department, and we believe that the agency responsible for health care delivery should itself be the prime mover in such studies, to ensure that the findings will be implemented. One such study was completed on maternal and child health services in the Eastern Highlands Province. The Institute took part in a study on the cost of rural health services conducted by the Department of Health. District health management and the performance of community health workers have been studied. The role of communities in making their own decisions for improved health and participating in the process of carrying out these decisions is of fundamental importance to long-term, sustainable community development. Ways to study and promote these communal activities have been investigated by the Women's Health Unit.

Further developments in national disease control programs may lead to the formation of a collaborative **Operational Research Unit** supported by the Institute and the Health Department, and this would enable many proposed studies on health monitoring and surveillance and health systems research to go ahead. These studies would also be promoted if the Institute's plans for expanding its research implementation activities are successful.

Some preliminary studies on **traditional medicine** have been carried out, but the Institute does not have the substantial resources necessary for the rigorous screening and evaluation of traditional herbal medicines. Such a facility is included in the Institute's current Development Plan.

### Training

The statutory function of the Institute is to carry out medical research and this must remain its first priority. In the course of undertaking research and as part of the function of each contract staff member there are many opportunities for providing training for members of staff and also for students assigned to the Institute for limited periods of instructional training. Since the Institute

provides expertise and experience in specific aspects of the disciplines of epidemiology, bacteriology, parasitology, virology, immunology, entomology, genetics and molecular biology that are not available elsewhere in Papua New Guinea, the training opportunities within the Institute are significant, and with additional funding could be more fully exploited. A closer working relationship with the universities, the Commission for Higher Education and the relevant ministry or ministries for higher education, science and technology would help to realize these opportunities.

Each professional member of the Institute staff has a career development plan which is implemented by the Training Officer. This creates opportunities for staff to be seconded for academic and technical training overseas or within Papua New Guinea, as appropriate, and thus enable them to earn higher qualifications and enlarge their sphere of professional contacts.

### Collaboration

It is clear that many of the Institute's research programs, and all of its major ones, are collaborative and integrated in nature. This means that the assistance of colleagues in a number of scientific disciplines and with local knowledge in different areas will continue to be necessary, whatever the range of disciplines included among its own staff. The Institute welcomes collaboration, both national and international. Those who are interested are encouraged to seek help from IMR staff where this may be of value to their work; or to offer their own expertise in helping to expand the coverage and competence of the Institute's research programs.

### ACKNOWLEDGEMENTS

I acknowledge the work over many years of many hundreds of Institute staff, whose dedication, perseverance and skill have enabled the research activities of the IMR, so baldly described here, to be successfully achieved. This includes colleagues from a range of disciplines who are now scattered throughout the world and a small but expanding cadre of Papua New Guinean scientists. A large

number of technical, administrative and support staff have maintained high levels of performance and intense loyalty to PNGIMR. Without locally recruited field staff and the full participation of the communities from which they are drawn we could have made no progress in our epidemiological and intervention studies. I am deeply grateful to them all.

### REFERENCES

- 1 **Attenborough RD, Alpers MP, eds.** Human Biology in Papua New Guinea: The Small Cosmos. Research Monographs on Human Population Biology No 10. Oxford: Clarendon Press, 1992:427p.
- 2 **National Sex and Reproduction Research Team, Jenkins C.** National Study of Sexual and Reproductive Knowledge and Behaviour in Papua New Guinea. Papua New Guinea Institute of Medical Research Monograph No 10. Goroka: Papua New Guinea Institute of Medical Research, 1994:147p.
- 3 **Gratten M, Gratten H, Poli A, Carrad E, Raymer M, Koki G.** Colonisation of *Haemophilus influenzae* and *Streptococcus pneumoniae* in the upper respiratory tract of neonates in Papua New Guinea: primary acquisition, duration of carriage, and relationship to carriage in mothers. *Biol Neonate* 1986;50:114-120.
- 4 **Shann F, Gratten M, Germer S, Linnemann V, Hazlett D, Payne R.** Aetiology of pneumonia in children in Goroka Hospital, Papua New Guinea. *Lancet* 1984;2:537-541.
- 5 **Barker J, Gratten M, Riley I, Lehmann D, Montgomery J, Kajoi M, Gratten H, Smith D, Marshall TFdeC, Alpers MP.** Pneumonia in children in the Eastern Highlands of Papua New Guinea: a bacteriologic study of patients selected by standard clinical criteria. *J Infect Dis* 1989;159:348-352.
- 6 **Gratten M, Montgomery J.** The bacteriology of acute pneumonia and meningitis in children in Papua New Guinea: assumptions, facts and technical strategies. *PNG Med J* 1991;34:185-198.
- 7 **Phillips PA, Lehmann D, Spooner V, Barker J, Tulloch S, Sungu M, Canil KA, Pratt RD, Lupiwa T, Alpers MP.** Viruses associated with acute lower respiratory tract infections in children from the Eastern Highlands of Papua New Guinea (1983-1985). *Southeast Asian J Trop Med Public Health* 1990;21:373-382.
- 8 **Gratten M, Naraqi S, Hansman D.** High prevalence of penicillin-insensitive pneumococci in Port Moresby, Papua New Guinea. *Lancet* 1980;2:192-195.
- 9 **Montgomery J, West B, Michael A, Kadivaion B.** Bacterial resistance in the Eastern Highlands Province. *PNG Med J* 1987;30:11-19.
- 10 **Lehmann D, Yeka W, Rongap T, Javati A, Saleu G, Clegg A, Michael A, Lupiwa T, Omena M, Alpers MP.** Aetiology and clinical signs of bacterial meningitis in children admitted to Goroka

- Base Hospital, Papua New Guinea, 1989-1992. *Ann Trop Paediatr* 1999;19:21-32.
- 11 **Riley ID, Lehmann D, Alpers MP, Marshall TFdeC, Gratten H, Smith D.** Pneumococcal vaccine prevents death from acute lower-respiratory-tract infections in Papua New Guinean children. *Lancet* 1986;2:877-881.
- 12 **Lehmann D, Marshall TFdeC, Riley ID, Alpers MP.** Effect of pneumococcal vaccine on morbidity from acute lower respiratory tract infections in Papua New Guinean children. *Ann Trop Paediatr* 1991;11:247-257.
- 13 **Pomat WS, Smith TA, Sanders RC, Witt CS, Montgomery J, Lehmann D, Alpers MP.** Levels of antipneumococcal antibodies in young children in Papua New Guinea. *Epidemiol Infect* 1993;111:109-120.
- 14 **Pomat WS, Lehmann D, Sanders RC, Lewis DJ, Wilson J, Rogers S, Dyke T, Alpers MP.** Immunoglobulin G antibody responses to polyvalent pneumococcal vaccine in children in the highlands of Papua New Guinea. *Infect Immun* 1994;62:1848-1853.
- 15 **Riley ID, Lehmann D, Alpers MP.** Pneumococcal vaccine trials in Papua New Guinea – relationships between epidemiology of pneumococcal infection and efficacy of vaccine. *Rev Infect Dis* 1991;13(Suppl 6):S535-S541.
- 16 **Lehmann D.** Pneumococcal vaccine trials in children in the highlands of Papua New Guinea. In: Gardiner W, Foley W, eds. Proceedings of the Third Annual Australian Tropical Health and Nutrition Conference, Brisbane, 4-6 Nov 1991. Brisbane: Tropical Health Program, University of Queensland, 1992:63-79.
- 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;41:102-111.
- 18 **Montgomery JM, Lehmann D, Smith T, Michael A, Joseph B, Lupiwa T, Coakley C, Spooner V, Best B, Riley ID, Alpers MP.** Bacterial colonization of the upper respiratory tract and its association with acute lower respiratory tract infections in highland children of Papua New Guinea. *Rev Infect Dis* 1990;12(Suppl 8):S1006-S1016.
- 19 **Smith T, Lehmann D, Montgomery J, Gratten M, Riley ID, Alpers MP.** Acquisition and invasiveness of different serotypes of *Streptococcus pneumoniae* in young children. *Epidemiol Infect* 1993;111:27-40.
- 20 **Lehmann D, Howard P, Heywood P.** Nutrition and morbidity: acute lower respiratory tract infections, diarrhoea and malaria. *PNG Med J* 1988;31:109-116.
- 21 **Suarkia D, Lupiwa T.** Health implications for Papua New Guinea of chlamydial infections. *PNG Med J* 1995;38:73-78.
- 22 **Woolcock AJ, Dowse GK, Temple K, Stanley H, Alpers MP, Turner KJ.** The prevalence of asthma in the South Fore people of Papua New Guinea. A method for field studies of bronchial reactivity. *Eur J Respir Dis* 1983;64:571-581.
- 23 **Dowse GK, Turner KJ, Stewart GA, Alpers MP, Woolcock AJ.** The association between *Dermatophagoides* mites and the increasing prevalence of asthma in village communities within the Papua New Guinea highlands. *J Allergy Clin Immunol* 1985;75:75-83.
- 24 **Turner KJ, Dowse GK, Stewart GA, Alpers MP.** Studies on bronchial hyperreactivity, allergic responsiveness and asthma in rural and urban children of the highlands of Papua New Guinea. *J Allergy Clin Immunol* 1986;77:558-565.
- 25 **Rogers S, Sanders RC, Alpers MP.** Immunogenicity of standard dose Edmonston-Zagreb measles vaccine in highland Papua New Guinean children from four months of age. *J Trop Med Hyg* 1991;94:88-91.
- 26 **Lucas KM, Sanders RC, Rongap A, Rongap T, Pinai S, Alpers MP.** Subacute sclerosing panencephalitis (SSPE) in Papua New Guinea: a high incidence in young children. *Epidemiol Infect* 1992;108:547-554.
- 27 **Cattani JA, Tulloch JL, Vrbova H, Jolley D, Gibson FD, Moir JS, Heywood PF, Alpers MP, Stevenson A, Clancy R.** The epidemiology of malaria in a population surrounding Madang, Papua New Guinea. *Am J Trop Med Hyg* 1986;35:3-15.
- 28 **Genton B, Al-Yaman F, Beck HP, Hii J, Mellor S, Narara A, Gibson N, Smith T, Alpers MP.** The epidemiology of malaria in the Wosera area, East Sepik Province, Papua New Guinea, in preparation for vaccine trials. I. Malariometric indices and immunity. *Ann Trop Med Parasitol* 1995;89:359-376.
- 29 **Cattani JA, Moir JS, Gibson FD, Ginny M, Paino J, Davidson W, Alpers MP.** Small-area variations in the epidemiology of malaria in Madang Province. *PNG Med J* 1986;29:11-17.
- 30 **Forsyth KP, Anders RF, Kemp DJ, Alpers MP.** New approaches to the serotypic analysis of the epidemiology of *Plasmodium falciparum*. *Philos Trans R Soc Lond [Biol]* 1988;321:485-493.
- 31 **Cox MJ, Kum DE, Tavul L, Narara A, Raiko A, Baisor M, Alpers MP, Medley GF, Day KP.** Dynamics of malaria parasitaemia associated with febrile illness in children from a rural area of Madang, Papua New Guinea. *Trans R Soc Trop Med Hyg* 1994;88:191-197.
- 32 **Beck HP, Felger I, Genton B, Alexander N, Al-Yaman F, Anders RF, Alpers M.** Humoral and cell-mediated immunity to the *Plasmodium falciparum* ring-infected erythrocyte surface antigen in an adult population exposed to highly endemic malaria. *Infect Immun* 1995;63:596-600.
- 33 **Al-Yaman F, Genton B, Anders R, Taraika J, Ginny M, Mellor S, Alpers MP.** Assessment of the role of the humoral response to *Plasmodium falciparum* MSP2 compared to RESA and SPf66 in protecting Papua New Guinean children from clinical malaria. *Parasite Immunol* 1995;17:493-501.
- 34 **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;54:443-448.
- 35 **Al-Yaman F, Genton B, Taraika J, Anders R, Alpers MP.** Association between cellular response (IL-4) to RESA/Pf155 and protection from clinical malaria among Papua New Guinean children living in a malaria-endemic area. *Parasite Immunol* 1997;19:249-254.
- 36 **Burkot TR, Graves PM, Wirtz RA, Brabin BJ, Battistutta D, Cattani JA, Maizels RM, Alpers MP.** Differential antibody responses to *Plasmodium falciparum* and *P. vivax* circumsporozoite proteins in a human population. *J Clin Microbiol* 1989;27:1346-1351.
- 37 **Smith T, Genton B, Baea K, Gibson N, Taime J, Narara A, Al-Yaman F, Beck HP, Hii J, Alpers M.** Relationships between *Plasmodium falciparum* infection and morbidity in a highly endemic area. *Parasitology* 1994;109:539-549.
- 38 **Genton B, Al-Yaman F, Beck HP, Hii J, Mellor S, Rare L, Ginny M, Smith T, Alpers MP.** The epidemiology of malaria in the Wosera area, East Sepik Province, Papua New Guinea, in preparation for vaccine trials. II. Mortality and morbidity. *Ann Trop Med Parasitol* 1995;89:377-390.
- 39 **Charlwood JD, Birley MH, Dagoro H, Paru R, Holmes PR.** Assessing survival rates of *Anopheles farauti* (Diptera: Culicidae) from Papua New Guinea. *J Anim Ecol* 1985;54:1003-1016.
- 40 **Graves PM, Burkot TR, Saul AJ, Hayes RJ, Carter R.** Estimation of anopheline survival rate, vectorial capacity and mosquito infection probability from malaria vector infection rates in villages near Madang, Papua New Guinea. *J Appl Ecol* 1990;27:134-147.
- 41 **Hii JLK, Smith T, Mai A, Mellor S, Lewis D, Alexander N, Alpers MP.** Spatial and temporal variation in abundance of *Anopheles* (Diptera: Culicidae) in a malaria endemic area in Papua New Guinea. *J Med Entomol* 1997;34:193-205.
- 42 **Charlwood JD, Graves PM, Alpers MP.** The ecology of the *Anopheles punctulatus* group of mosquitoes from Papua New Guinea: a review of recent work. *PNG Med J* 1986;29:19-26.
- 43 **Burkot TR, Graves PM, Cattani JA, Wirtz RA, Gibson FD.** The efficiency of sporozoite transmission in the human malarial, *Plasmodium falciparum* and *P. vivax*. *Bull World Health Organ* 1987;65:375-380.
- 44 **Graves PM, Brabin BJ, Charlwood JD, Burkot TR, Cattani JA, Ginny M, Paino J, Gibson FD, Alpers MP.** Reduction in incidence and prevalence of *Plasmodium falciparum* in under-5-year-old children by permethrin impregnation of mosquito nets. *Bull World Health Organ* 1987;65:869-878.
- 45 **Genton B, Hii J, Al-Yaman F, Paru R, Beck HP, Ginny M, Dagoro H, Lewis D, Alpers MP.** The use of untreated bednets and malaria infection, morbidity and immunity. *Ann Trop Med Parasitol* 1994;88:263-270.
- 46 **Paru R, Hii J, Lewis D, Alpers MP.** Relative repellency of woodsmoke and topical applications of plant products against mosquitoes. *PNG Med J* 1995;38:215-221.
- 47 **Serjeantson S, Bryson K, Amato D, Babona D.** Malaria and hereditary ovalocytosis. *Hum Genet* 1977;37:161-167.
- 48 **Cattani JA, Gibson FD, Alpers MP, Crane GG.** Hereditary ovalocytosis and reduced susceptibility to malaria in Papua New Guinea. *Trans R Soc Trop Med Hyg* 1987;81:705-709.
- 49 **Mgone CS, Koki G, Panu MM, Kono J, Bhatia KK, Genton B, Alexander NDE, Alpers MP.** Occurrence of the erythrocyte band 3 (AE1) gene deletion in relation to malaria endemicity in Papua New Guinea. *Trans R Soc Trop Med Hyg* 1996;90:228-231.
- 50 **Genton B, Al-Yaman F, Mgone CS, Alexander N, Panu MM, Alpers MP, Mokela D.** Ovalocytosis and cerebral malaria. *Nature* 1995;378:564-565.
- 51 **Allen SJ, O'Donnell A, Alexander NDE, Alpers MP, Peto TEA, Clegg JG, Weatherall DJ.**  $\alpha^+$ -thalassemia protects children against disease caused by other infections as well as malaria. *Proc Natl Acad Sci USA* 1997;94:14736-14741.
- 52 **Crane GG, Prior DS.** Malaria and the tropical splenomegaly syndrome in New Guinea. *Trans R Soc Trop Med Hyg* 1971;65:315-324.
- 53 **Bhatia KK, Crane GG.** HLA heterozygosity and hyperreactive malarious splenomegaly in the Upper Watut Valley of Papua New Guinea. *PNG Med J* 1989;32:277-286.
- 54 **Brabin BJ, Brabin LR, Sapau J, Alpers MP.** A longitudinal study of splenomegaly in pregnancy in a malaria endemic area in Papua New Guinea. *Trans R Soc Trop Med Hyg* 1988;82:677-682.
- 55 **Sehgal VM, Siddiqui WA, Alpers MP.** A seroepidemiological study to evaluate the role of passive maternal immunity to malaria in infants. *Trans R Soc Trop Med Hyg* 1989;83(Suppl):105-106.
- 56 **Knowles G, Davidson WL, Jolley D, Alpers MP.** The relationship between the in vitro response of *Plasmodium falciparum* to chloroquine, quinine and mefloquine. *Trans R Soc Trop Med Hyg* 1984;78:146-150.
- 57 **Sapak P, Garner P, Baea M, Narara A, Heywood P, Alpers M.** Ineffectiveness of amodiaquine against *Plasmodium falciparum* malaria in symptomatic young children living in an endemic malarious area of Papua New Guinea. *J Trop Pediatr* 1991;37:185-190.
- 58 **Al-Yaman F, Genton B, Mokela D, Narara A, Raiko A, Alpers MP.** Resistance of *Plasmodium falciparum* malaria to amodiaquine, chloroquine and quinine in the Madang Province of Papua New Guinea, 1990-1993. *PNG Med J* 1996;39:16-22.
- 59 **Alpers MP, Al-Yaman F, Beck HP, Bhatia KK, Hii J, Lewis DJ, Paru R, Smith TA.** The Malaria Vaccine Epidemiology and Evaluation Project of Papua New Guinea: rationale and baseline studies. *PNG Med J* 1992;35:285-297.
- 60 **Knowles G, Davidson WL, McBride JS, Jolley D.** Antigenic diversity found in isolates of *Plasmodium falciparum* from Papua New Guinea by using monoclonal antibodies. *Am J Trop Med Hyg* 1984;33:204-211.
- 61 **Heywood P, Heywood A.** The functional significance of protein-energy malnutrition. *PNG Med J* 1988;31:103-108.
- 62 **Smith T, Earland J, Bhatia K, Heywood P, Singleton N.** Linear growth of children in Papua

- New Guinea in relation to dietary, environmental and genetic factors. *Ecol Food Nutr* 1993;31:1-25.
- 63 **Heywood AH, Marshall T, Heywood PF.** Motor development and nutritional status of young children in Madang, Papua New Guinea. *PNG Med J* 1991;34:109-116.
- 64 **Groos AD.** Delayed motor development in relation to nutritional status among children under two years of age in two districts of Simbu Province. *PNG Med J* 1991;34:238-245.
- 65 **Lehmann D, Heywood P.** Effect of birthweight on pneumonia-specific and total mortality among infants in the highlands of Papua New Guinea. *PNG Med J* 1996;39:274-283.
- 66 **Harvey PW, Heywood PF.** Twenty-five years of dietary change in Simbu Province, Papua New Guinea. *Ecol Food Nutr* 1983;13:27-35.
- 67 **Heywood P, Singleton N, Ross J.** Nutritional status of young children - the 1982/83 National Nutrition Survey. *PNG Med J* 1988;31:91-101.
- 68 **Jenkins C, Howard P.** The use of ethnography and structured observations in the study of risk factors for the transmission of diarrhea in highland Papua New Guinea. *Med Anthropol* 1992;15:1-16.
- 69 **Jenkins C.** Changing hygiene behaviour in Papua New Guinea. *PNG Med J* 1995;38:320-324.
- 70 **Barnish G, Ashford RW.** *Strongyloides cf fuelleborni* in Papua New Guinea: epidemiology in an isolated community, and results of an intervention study. *Ann Trop Med Parasitol* 1989;83:499-506.
- 71 **Smith T, Bhatia K, Barnish G, Ashford RW.** Host genetic factors do not account for variation in parasite loads in *Strongyloides fuelleborni kellyi*. *Ann Trop Med Parasitol* 1991;85:533-537.
- 72 **Davis MW, ed.** Pigbel: Necrotising Enteritis in Papua New Guinea. Proceedings of a Workshop on Pigbel, Goroka, 2-5 Sep 1980. Papua New Guinea Institute of Medical Research Monograph No 6. Goroka: Papua New Guinea Institute of Medical Research, 1984:118p.
- 73 **Lawrence GW, Lehmann D, Anian G, Coakley CA, Saleu G, Barker MJ, Davis MW.** Impact of active immunisation against enteritis necroticans in Papua New Guinea. *Lancet* 1990;336:1165-1167.
- 74 **Passey M.** The new problem of typhoid fever in Papua New Guinea: how do we deal with it? *PNG Med J* 1995;38:300-304.
- 75 **Hudson BJ, van der Meijden WI, Lupiwa T, Howard P, Tabua T, Tapsall JW, Phillips EA, Lennox VA, Backhouse JL, Pyakalyia T.** A survey of sexually transmitted diseases in five STD clinics in Papua New Guinea. *PNG Med J* 1994;37:152-160.
- 76 **Passey M, Mgone CS, Lupiwa S, Suve N, Tiwara S, Clegg A, Alpers MP.** Community based study of sexually transmitted diseases in rural women in the highlands of Papua New Guinea: prevalence and risk factors. *Sex Transm Infect* 1998;74:120-127.
- 77 **Jenkins C, ed.** Liklik buk bilong pasim sik AIDS. Goroka: Papua New Guinea Institute of Medical Research, 1995:30p.
- 78 **Jenkins C, Alpers M.** Urbanization, youth and sexuality: insights for an AIDS campaign for youth in Papua New Guinea. *PNG Med J* 1996;39:248-251.
- 79 **Gillett JE.** The Health of Women in Papua New Guinea. Papua New Guinea Institute of Medical Research Monograph No 9. Goroka: Papua New Guinea Institute of Medical Research, 1990:180p.
- 80 **Garner P, Lai D, Baea M.** Childbirth in rural areas: maternal deaths, village deliveries and obstetric service use. *PNG Med J* 1994;37:166-172.
- 81 **Garner P, Lai D, Baea M, Edwards K, Heywood P.** Avoiding neonatal death: an intervention study of umbilical cord care. *J Trop Pediatr* 1994;40:24-28.
- 82 **Kazura JW, Spark R, Forsyth K, Brown G, Heywood P, Peters P, Alpers M.** Parasitologic and clinical features of bancroftian filariasis in a community in East Sepik Province, Papua New Guinea. *Am J Trop Med Hyg* 1984;33:1119-1123.
- 83 **Day KP, Spark R, Garner P, Raiko A, Wenger JD, Weiss N, Mitchell GF, Alpers MP, Kazura JW.** Serological evaluation of the macrofilaricidal effects of diethylcarbamazine treatment in bancroftian filariasis. *Am J Trop Med Hyg* 1991;44:528-535.
- 84 **Kazura JW, Bockarie M, Alexander N, Perry R, Bockarie F, Dagoro H, Dimber Z, Hyun P, Alpers MP.** Transmission intensity and its relationship to infection and disease due to *Wuchereria bancrofti* in Papua New Guinea. *J Infect Dis* 1997;176:242-246.
- 85 **Bockarie MJ, Alexander NDE, Hyun P, Dimber Z, Bockarie F, Ibam E, Alpers MP, Kazura JW.** Randomised community-based trial of annual single-dose diethylcarbamazine with or without ivermectin against *Wuchereria bancrofti* infection in human beings and mosquitoes. *Lancet* 1998;351:162-168.
- 86 **Burkot TR, Molineaux L, Graves PM, Paru R, Battistutta D, Dagoro H, Barnes A, Wirtz RA, Garner P.** The prevalence of naturally acquired multiple infections of *Wuchereria bancrofti* and human malaria in anophelines. *Parasitology* 1990;100:369-375.
- 87 **Hornabrook RW, ed.** Essays on Kuru. Papua New Guinea Institute of Human Biology (now Papua New Guinea Institute of Medical Research) Monograph No 3. Faringdon: EW Classey, 1976:150p.
- 88 **Alpers MP.** Kuru. In: Attenborough RD, Alpers MP, eds. Human Biology in Papua New Guinea: The Small Cosmos. Oxford: Clarendon Press, 1992:313-334.
- 89 **Sanders RC, Lewis D, Dyke T, Alpers MP.** Markers of hepatitis B infection in Tari District, Southern Highlands Province, Papua New Guinea. *PNG Med J* 1992;35:197-201.
- 90 **Serjeantson S, Lawrence G.** Autosomal recessive inheritance of susceptibility to tinea imbricata. *Lancet* 1977;1:13-15.
- 91 **Montgomery J.** The aerobic bacteriology of infected skin lesions in children of the Eastern Highlands Province. *PNG Med J* 1985;28:93-103.
- 92 **Richens JE, Prasad MI, Bhatia K, Tung M.** Arthritis and HLA-B27 in Papua New Guinea. *BMJ* 1986;293:1209.
- 93 **Hetzel BS, Pharoah POD, eds.** Endemic Cretinism. Proceedings of a Symposium on

- Endemic Cretinism, Goroka, 27-29 Jan 1971. Institute of Human Biology Monograph No 2. Goroka: Institute of Human Biology (now Papua New Guinea Institute of Medical Research), 1971:133p.
- 94 **Hornabrook RW.** Endemic cretinism. In: Hornabrook RW, ed. Topics on Tropical Neurology. Contemporary Neurology Series No 12. Philadelphia: FA Davis, 1975:91-108,294.
- 95 **Heywood PF, Buttfield IH, Buttfield BL, Anian G.** Endemic cretinism and endemic goitre in two areas of Madang Province, Papua New Guinea. *PNG Med J* 1986;29:149-152.
- 96 **King H, Collins V, King LF, Finch C, Alpers MP.** Blood pressure, hypertension and other cardiovascular risk factors in six communities in Papua New Guinea, 1985-1986. *PNG Med J* 1994;37:100-109.
- 97 **Smith DE, Alpers MP, eds.** Cigarette Smoking in Papua New Guinea. Proceedings of an Anti-Smoking Seminar, Port Moresby, 7-8 Apr 1983. Papua New Guinea Institute of Medical Research Monograph No 7. Goroka: Papua New Guinea Institute of Medical Research, 1984:83p.
- 98 **King H, Finch C, Collins A, Koki G, King LF, Heywood P, Zimmet P.** Glucose tolerance in Papua New Guinea: ethnic differences, association with environmental and behavioural factors and the possible emergence of glucose intolerance in a highland community. *Med J Aust* 1989;151:204-210.
- 99 **Smith DE, Alpers MP, eds.** Village Water Supplies in Papua New Guinea. Proceedings of a Workshop on Village Water Supplies, Goroka, 19-20 Jul 1984. Papua New Guinea Institute of Medical Research Monograph No 8. Goroka: Papua New Guinea Institute of Medical Research, 1985:94p.
- 100 **Riley ID, Lehmann D.** The demography of Papua New Guinea: migration, fertility, and mortality patterns. In: Attenborough RD, Alpers MP, eds. Human Biology in Papua New Guinea: The Small Cosmos. Oxford: Clarendon Press, 1992:67-92.