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England
## Medical Society of Papua New Guinea

### Executive 2005

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<td>Vice-President</td>
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FOREWORD

50th year celebration

This issue of the Papua New Guinea Medical Journal is a special one as it celebrates the 50th year of the Journal's existence. The issue has been put together for the purpose of honouring those who have contributed and worked tirelessly to ensure that this quality Journal continues to be published.

Michael Alpers has meticulously recorded the history of the first 50 years of the Journal (1) and together with the Editors has selected 11 articles from past issues of the Journal. Some of these articles will bring back memories of past research and achievements of Papua New Guinean scientists and doctors and for others, who might be reading them for the first time, they will be examples of why the Journal has been described as a national asset (2).

Over the years there have been problems with the printing of the Journal and the publication schedule has fallen badly behind, but despite this the Journal has continued to be published. Finance has also been a problem and the Medical Society has at times struggled to find the funds to pay for its publication. There has never been a problem with people being willing to contribute papers for publication and the Editors have always encouraged authors and especially new authors to submit their papers.

The editorial staff are now preparing a print-ready copy of the Journal and this will reduce the time it takes to produce an issue of the Journal. There are many issues in the pipeline and it is hoped that we will shortly get back on track.

Peter M. Siba

Editor, Papua New Guinea Medical Journal
Papua New Guinea Institute of Medical Research
PO Box 60
Goroka
EHP 441
Papua New Guinea

REFERENCES

The Papua New Guinea Medical Journal was founded in May 1955. In a Foreword to the first issue the Founding Editor, John T. Gunther, who was Director of Public Health, outlined the purpose of the Journal and its philosophy. It was initially an instrument of the Department of Public Health and, after the first 2 issues, the editorial responsibility for it devolved on Eric J. Wright, who was Assistant Director (Medical Training) in the Department. The Medical Society of Papua New Guinea was established on 28 July 1964 and very quickly, in March 1965, took over responsibility for the Journal, though publication was continued by the Department of Public Health. This final link as an 'instrument of the Department' came to an end in June 1974, when the Government printed its last issue of the Journal. The September 1974 issue came out under the imprint of Kristen Pres and was paid for by the Society. The Journal had achieved independence (a year before the nation), and with it came the beginning of its financial uncertainties.

However, other parts of John Gunther’s purpose and philosophy have persisted to the present day. The Journal was to be “devoted to the disease pattern and other problems peculiar” to Papua New Guinea (PNG) – then called the Territory of Papua and New Guinea. The Journal was intended “to keep all our varied grades of medical personnel abreast of world progress in the prevention and treatment” of the diseases found in PNG, “to promote medical research locally into these diseases” and “to facilitate an exchange of ideas between...geographically isolated” members of the health professions.

The Journal was to be published quarterly. It began that way, with 4 issues in the first year and the publication of Volume 2 No 1 in May 1956. However, after that its publication record became spasmodic: in 1957, 1961, 1962 and 1964 there was only one issue and there was none in 1958 and 1963. Fortunately, once Ian Maddocks took charge as Editor in March 1965 the quarterly publication schedule very quickly became firmly established and persisted, with minor exceptions, until 1999; since then the Journal has been reduced, as a survival measure, to two double issues a year (Table 1).

The first issue included an editorial, original articles, clinical notes, reviews of patrol reports and other sections such as literature reviews and an obituary. The first article was a paper, which has often been quoted, by J. T. Gunther on the epidemiology of malaria in PNG (1).

In the second issue of the Journal one editorial was about the Journal itself and expanded on the point made in the first issue that the Journal should be for all members of the health professions in PNG, at all levels. This intention was carried out for a while but, as the Journal became more scientific and more successful, the interest for nurses, health extension officers and junior doctors diminished. For this reason, a series of Clinical Practice articles was initiated in December 1985 and over the next 20 years 47 such articles were published (Table 2).

The next commentary on the Journal itself was in Ian Maddocks’ editorial (2) in the first issue that was ‘edited and prepared' by the Medical Society of Papua New Guinea. Firstly, he announced the formation of the Society and stated its objectives:

---

1 Curtin University of Technology, Centre for International Health, Shenton Park Campus, GPO Box U1987, Perth, Western Australia 6845, Australia

Formerly Director of the Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, EHP 441, Papua New Guinea
(a) To promote the advance of medical knowledge, and to assist in the dissemination of such knowledge amongst its members;

(b) To promote such ethical rules, conduct and practice as will best maintain the honour of the profession; and

(c) To represent the corporate interest of all medical practitioners in the country [Territory].

In accord with these objectives the Medical Society undertook to prepare and edit the PNG Medical Journal. The Editor expressed the hope of increasing involvement of Papua New Guinean doctors in the research and administrative problems of their country and looked for evidence of this in the pages of the Journal. In this issue Papua New Guineans appear for the first time as authors, and there was a photograph of the first three graduates of the Papuan Medical College, Dr Jeffrey Tuvi, Dr Amelia Homba and Dr Ilomo Batton.

The Society has continued to flourish. In 1965 it held its first symposium in Goroka, on the theme of pigbel. The Medical Symposium has been held every year since then: the Society can boast that it has never missed holding its Annual Symposium, a significant achievement indeed. The themes from the past are listed in the Program and Abstracts of each symposium and are not forgotten. These annual meetings have always been successful and have maintained a very high standard, scientifically, medically and socially.

The Journal has also flourished since the Society took it over. For most of this period there were, as has been noted, four issues a year though recently, because of financial and logistic problems with its printing, the Journal has been reduced to two double issues annually. We hope that the newly acquired desktop publishing capability in the editorial office of the Journal will make future printing both efficient and affordable.

In the first issue edited by D. Graeme Woodfield, when he was still Acting Editor, he reviewed the role of the Journal (3). He planned to extend the scope of the Journal, in the same search for a Papua New Guinean character as had engaged Ian Maddocks – but with a different outcome. His idea was to present medical reviews of both research projects and medical problems related to PNG. In addition, he felt strongly that visiting research workers should be obliged to contribute in some way to the local journal in order to try and bridge the communication gap between research workers and health care practitioners. In a letter published a few issues later John Rooney (4) suggested that the Journal should cater more for the needs of Papua New Guinean doctors by adopting a less formal and forbidding style. How to cater for different needs is a dilemma faced by all editors and articulated by many of them. Sirus Naraqi, when editing his first issue, described the Journal as a national asset (5). He pointed out that the Journal was indexed by Index Medicus and Current Contents and he intended to maintain the high standard of the Journal set by previous editors. He encouraged all health workers and researchers to publish the ‘significant results of their clinical or research work’ in the Journal.

The editor of any journal is critical to its success. In celebrating the success of the Papua New Guinea Medical Journal we must celebrate all of its editors: they are set out in Table 3. Their close colleagues and assistants have also been important: in Table 4 are listed the Assistant Editors, in Table 5 the Business Managers and in Table 6 perhaps the most important of all, the Editorial Assistants, who keep the gears of the Journal in constant motion. Although the Journal comes out as a quarterly event – and when there are printing problems we all wonder whether it will come out at all – the toil of reaching these occasional outputs is daily and unremitting. Manuscripts have to be accessioned and sent for review, reviewers and authors have to be chased up, manuscripts have to be edited into final shape to comply with the House Rules of the Journal, proofs have to be checked and authors’ final – often impossible – changes assessed and, since the Journal is a family affair, accommodated wherever possible. How much work goes on in the back room can only really be appreciated by those who toil there, but with all the display of the
### TABLE 1

**CATALOGUE OF THE PAPUA NEW GUINEA MEDICAL JOURNAL**

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Journal in this celebratory issue we must take a moment to reflect on the work that makes it possible.

Talking about display, we think naturally about the cover of the Journal, the dress which it shows to the world. In all, in its first 50 years, the Journal has had 7 different kinds of cover. A cover change was usually associated with a new editor, clearly hoping to stamp his character on the Journal from the beginning. The current cover, with its annual colour variation in a three-year cycle, has survived 8 changes of editor since it was first introduced by Euan Scrimgeour. It has established itself as a familiar face, having been used now for 76 issues, almost half the total number in the Journal's history (Table 7). Representative covers are illustrated in Figure 1, unfortunately not in colour.

One of the special features of the Papua New Guinea Medical Journal is the practice of having focus issues. The concept was introduced by D. Graeme Woodfield, who edited many focus issues, but Ian Maddocks had produced one on pigbel six years before and, subsequently, another on health in the village, true focus issues before the name was created. The first guest editor for a focus issue was Richard W. Hornabrook, who edited one on neurology, the last issue put out during D. G. Woodfield's term as editor. After that time, with 3 exceptions, all focus issues have had a guest editor. The titles, numbers and editors of the 40 focus issues are set out in Table 8.

Finding papers on particular topics or by particular authors in the Journal in recent issues is easy for those with access to Medlars and PubMed. Furthermore, for those searching their hard copies the Journal staff have since 1982 produced a series of three-year indexes (coinciding with the same colour change on the Journal's cover) that have been published in the Journal itself, in the following December issue (always in a
TABLE 2
CLINICAL PRACTICE ARTICLES IN THE JOURNAL, 1985-2002

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<th>Author</th>
<th>Title</th>
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<td>Biddulph J</td>
<td>Oral rehydration therapy</td>
<td>1985 Dec;28(4):303-309</td>
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<tr>
<td>Everett VJ</td>
<td>Post-partum haemorrhage</td>
<td>1986 Mar;29(1):109-110</td>
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<tr>
<td>Clezy JKA</td>
<td>Current management of the ruptured spleen</td>
<td>1986 Jun;29(2):189-191</td>
</tr>
<tr>
<td>Lindeman GJ, Naraqi S</td>
<td>Tuberculous meningitis in adults: practical comments on the diagnosis</td>
<td>1986 Sep;29(3):269-273</td>
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<tr>
<td>Aitken W</td>
<td>The management of reactions in leprosy</td>
<td>1987 Sep;30(3):239-246</td>
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<tr>
<td>Clezy JKA</td>
<td>Simpler treatment of the fractured ulna</td>
<td>1987 Dec;30(4):315-316</td>
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<tr>
<td>Glare PA, Naraqi S</td>
<td>A bedside approach to patients with peripheral oedema</td>
<td>1988 Sep;31(3):207-210</td>
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<tr>
<td>Mola G</td>
<td>Dysfunctional uterine bleeding: when an 'abortion' is not an abortion</td>
<td>1988 Dec;31(4):295-297</td>
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<tr>
<td>Edwards K</td>
<td>The diagnosis and management of childhood undernutrition</td>
<td>1989 Jun;32(2):143-150</td>
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<tr>
<td>Clezy JKA</td>
<td>Raised intracranial pressure</td>
<td>1989 Dec;32(4):287-290</td>
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<td>Oberoi GS</td>
<td>Anaesthesia and surgery in sepsis</td>
<td>1990 Sep;33(3):253-256</td>
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<td>Sinha SN</td>
<td>Management of thermal burns</td>
<td>1991 Mar;34(1):75-78</td>
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<td>Richens J</td>
<td>The diagnosis and management of common forms of arthritis in adults in Papua New Guinea</td>
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<td>Rongap AB</td>
<td>Clinical management of acute respiratory infections and measles in Papua New Guinea</td>
<td>1991 Sep;34(3):220-224</td>
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<td>Author(s)</td>
<td>Title</td>
<td>Volume and Issue Details</td>
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<td>Vince JD</td>
<td>Convulsions in children</td>
<td>1992 Jun;35(2):144-151</td>
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<td>Watters DAK</td>
<td>The early management of hypovolaemic shock</td>
<td>1993 Sep;36(3):249-255</td>
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<td>Klufox CA, Amoa AB, Rageau O</td>
<td>Abdominal pain in pregnancy</td>
<td>1993 Dec;36(4):342-352</td>
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<td>Seaton A</td>
<td>The role of corticosteroids in the management of infections in Papua New Guinea</td>
<td>1994 Jun;37(2):125-130</td>
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<tr>
<td>Clezy JKA</td>
<td>Inguinal hernia repair under local anaesthesia</td>
<td>1994 Sep;37(3):189-191</td>
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<td>Mola GDL</td>
<td>Symphysiotomy: technique, problems and pitfalls, and how to avoid them</td>
<td>1995 Sep;38(3):231-238</td>
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<td>Watters DAK</td>
<td>When does the patient with diarrhoea need surgery?</td>
<td>1995 Dec;38(4):332-338</td>
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<td>Jackson AS</td>
<td>Emergency care of the trauma patient in remote regions of Papua New Guinea</td>
<td>2002 Sep-Dec;45(3-4):222-232</td>
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### Table 3

**Editors of the Journal in its first 50 years, with their first issue, the number of issues they edited and their affiliation**

<table>
<thead>
<tr>
<th>Editor</th>
<th>Affiliation</th>
<th>First issue</th>
<th>Number of issues edited</th>
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<tr>
<td>John T. Gunther, Founding Editor</td>
<td>Director, Department of Public Health</td>
<td>Vol 1 No 1, May 1955</td>
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<tr>
<td>Eric J. Wright</td>
<td>Assistant Director (Medical Training), Department of Public Health</td>
<td>Vol 1 No 3, Nov 1955 (first named in Vol 4 No 2, Jul 1960)</td>
<td>12</td>
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<tr>
<td>Ian Maddocks</td>
<td>Lecturer in Medicine (later Professor and Dean), Papuan Medical College (later Faculty of Medicine)</td>
<td>Vol 8 No 1, Mar 1965*</td>
<td>25</td>
</tr>
<tr>
<td>D. Graeme Woodfield</td>
<td>Director, Red Cross Blood Transfusion Service</td>
<td>Vol 14 No 3, Sep 1971** (Acting Editor)</td>
<td>17</td>
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<td></td>
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<td>Vol 15 No 1, Mar 1972† (Editor)</td>
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<tr>
<td>Dominick Amato</td>
<td>Haematologist, Port Moresby General Hospital</td>
<td>Vol 19 No 1, Mar 1976</td>
<td>7</td>
</tr>
<tr>
<td>Sirus Naraqi</td>
<td>Senior Lecturer in Medicine (later Professor), University of Papua New Guinea</td>
<td>Vol 20 No 4, Dec 1977†</td>
<td>8</td>
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<tr>
<td>J.K.A. (Ken) Clezy</td>
<td>Professor of Surgery and Dean, Faculty of Medicine, UPNG</td>
<td>Vol 22 No 4, Dec 1979</td>
<td>2</td>
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<tr>
<td>Euan M. Scrimgeour</td>
<td>Senior Lecturer in Medicine, Faculty of Medicine, UPNG</td>
<td>Vol 23 No 2, Jun 1980†</td>
<td>11</td>
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<tr>
<td>John Lourie, Isi Kevau and Mohamed Patel</td>
<td>Professor of Human Biology, Senior Lecturer in Medicine (later Professor) and Lecturer in Medicine, Faculty of Medicine, UPNG</td>
<td>Vol 26 No 1, Mar 1983</td>
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<td>John Lourie</td>
<td>Professor of Human Biology, Faculty of Medicine, UPNG</td>
<td>Vol 26 No 3-4, Sep-Dec 1983</td>
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<td>Michael Alpers</td>
<td>Director, Papua New Guinea Institute of Medical Research</td>
<td>Vol 27 No 2, Jun 1984</td>
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<td>Charles S. Mgone and Peter M. Siba</td>
<td>Deputy Director and Assistant Director, PNGIMR</td>
<td>Vol 43 No 1-2, Mar-Jun 2000</td>
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<td>Charles S. Mgone</td>
<td>Deputy Director, PNGIMR</td>
<td>Vol 44 No 3-4, Sep-Dec 2001</td>
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<td>Charles S. Mgone and Peter M. Siba</td>
<td>Deputy Director and Assistant Director, PNGIMR</td>
<td>Vol 45 No 1-2, Mar-Jun 2002</td>
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</table>
Selecting a First Eleven of the Journal's classic papers

There have been many excellent papers published in the Journal since its inception 50 years ago. The Medical Society of Papua New Guinea has decided to reproduce a Classic Eleven in this celebratory Jubilee issue. Choosing this short list has not been an easy matter. A few simple rules helped to narrow the choice – and by necessity eliminated some well-deserving papers. To be ‘classic’ we decided that a paper must be at least 10 years old – so the field was restricted to papers published before 1996. To be eligible for reproduction a paper should not be too long – this automatically excluded a few great papers (6-9). Also if we are to include papers that are substantial, they should not be too short. Ideally the papers should reflect the theme of the Annual Symposium of the Medical Society being held in Goroka this year: Medical Research – a tool for health care delivery in the new millennium. Some of those selected do not fit the theme but have particular merit and special interest to warrant a place in the Classic Eleven in their own right. The initial screen identified over 40 papers that merited inclusion but the choice had to be made and, in doing so, a balance was maintained between subject matter, geographical location and publication date.

The special diseases of Papua New Guinea are kuru, pigbel and swollen belly syndrome. Of cosmopolitan diseases Papua New Guinea has contributed significantly to the control and understanding of neonatal tetanus, infant malnutrition and diarrhoeal disease, pneumonia, malaria, endemic cretinism, filariasis and leprosy. There have been many fine research investigators who have lived and worked in Papua New Guinea: it would be good if we could acknowledge them all. Furthermore, it would be a shame if some of the good papers written by Papua New Guineans were not included. There are papers too that are striking, unusual and memorable for their style and panache and we would all be reluctant to see our particular favourites left out. In one issue of the Journal we cannot satisfy all these desirables: compromises necessarily have had to be made. If anyone is not happy with the selection, I encourage them to go back and read or re-read all the papers in the Journal since May 1955 – which is an entirely pleasurable undertaking – and make their own selection.

One problem arising from the important contributions made by Papua New Guinea to the world of tropical medicine is that most of the key papers reporting these discoveries have been published in the international literature. In some fields, such as neonatal tetanus, this leaves nothing for the Journal;
in others, such as malaria, there is still great wealth here – in fact, we could easily make a good Classic Eleven out of malaria alone. You are encouraged to tap into the wider literature on medical research in Papua New Guinea in a manuscript, as yet unpublished, that is available electronically through the Papua New Guinea Institute of Medical Research (PNGIMR) (M.P. Alpers, Medical research in Papua New Guinea: a review).

Kuru secures 11 explicit references in the Journal though it is also mentioned or discussed elsewhere. One reference has been cited already (7). The others are listed here (10-19) together with 3 on the geographically related neurological condition of kogaisantamba (20-22). There has not been a focus issue on kuru, though the one on neurology (Table 8) includes 2 papers on kuru (17,18) and 1 on Creutzfeldt-Jakob disease in PNG (23). Alpers (24) and Lindenbaum (25) provide more recent, yet still classical, updates on various aspects of the kuru story. Kuru has now all but disappeared (M.P. Alpers, The epidemiology of kuru in the period 1987 to 1995, submitted manuscript), which is a blessing for us all, but globally it has become more significant than ever with the advent of bovine spongiform encephalopathy and its human form, variant Creutzfeldt-Jakob disease.

There have been many good papers published on pigbel in the Journal, including two focus issues devoted to the subject (Table 8). The early workers had first to discover the disease: by identifying necrotizing enteritis out of all the other conditions subjected to abdominal surgery. They then had to define it, and name it, and establish its cause. This was all done most efficiently by Timothy Murrell, Lajos Roth, John Egerton and Peter Walker between 1961 and 1964 (26-28). These ideas were not accepted by the medical establishment, as can be seen in the first focus issue: this story is recounted by Peter Walker in his obituary of Tim Murrell (29). Tim’s work was extended and justified by Gregor Lawrence, who clarified the pathogenesis of pigbel (30) and conducted a successful trial of a toxoid vaccine against the beta toxin of Clostridium perfringens type C to prevent the disease in highland children (31). The second focus issue on pigbel was edited by Greg Lawrence, Tim Murrell and Peter Walker (Table 8). With good vaccination coverage in the highlands pigbel disappeared. Then the vaccine ran out. By the time new stocks of the vaccine had been secured it looked as if pigbel, to our great relief, had in most places stayed low and had not sprung back (32). Its incidence needs now to be carefully monitored.

Swollen belly syndrome was discovered in Papua New Guinea. Its cause proved to be an unusual intestinal nematode first described elsewhere in PNG 6 years earlier (33). This enabled the disease to be treated so it has now effectively disappeared – before we could fully investigate the life cycle of the organism or the pathogenesis of the disease. The causative organism was named Strongyloides fuelleborni kellyi after its discoverer, Alan Kelly. The disease investigation was conducted by John Vince, Richard Ashford, Michael Gratten and Joe Bana Koiri (34,35). Later, Jennifer Shield (36) and Guy Barnish (37) and their colleagues studied infection with this parasite in various communities in the fringe highlands.

In the September 1977 issue of the Journal (Vol 20 No 3, p 150) is the following news item: “Baby feeding bottle bill passed in Parliament early this year, will be gazetted this month.” The passing of this bill, which made baby feeding bottles available only on prescription, was a triumph for Professor John Biddulph and is another of the medical achievements of PNG. The justification for the legislation came from the work of John Biddulph and his colleagues on weanling diarrhoea (38) and the advantages of breastfeeding (39) in the face of increasing use of artificial feeding in urban areas (40). Six years later John Biddulph reviewed the outcome of the Baby Feed Supplies (Control) Act of 1977; he concluded that it had been a success but warned that maintenance of that success would require constant vigilance (41). John Biddulph’s contributions to child health, in Papua New Guinea and internationally, were so outstanding that, after his death, a memorial issue of the Journal was devoted to his achievements (Table 8).

Research on pneumonia in PNG began with Robert Douglas and Ian Riley (42). The
### TABLE 4

**Assistant Editors of the Journal in its First 50 Years**

<table>
<thead>
<tr>
<th>Editor</th>
<th>Title</th>
<th>Volume Years</th>
<th>Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michael Price</td>
<td>Physician, Port Moresby General Hospital</td>
<td>Vol 14 No 3, Sep 1971 and Vol 14 No 4, Dec 1971</td>
<td>2</td>
</tr>
<tr>
<td>David Smith</td>
<td>Research Fellow, Acute Respiratory Infections, PNGIMR</td>
<td>Vol 27 No 2, June 1984 and Vol 27 No 3-4, Sep-Dec 1984</td>
<td>2</td>
</tr>
<tr>
<td>Kuldeep Bhatia</td>
<td>Human Geneticist, PNGIMR</td>
<td>Vol 28 No 1, Mar 1985 and Vol 28 No 2, Jun 1985; Vol 30 No 1, Mar 1987 to Vol 32 No 3, Sep 1989; Vol 33 No 1, Mar 1990 to Vol 33 No 3, Sep 1990</td>
<td>16</td>
</tr>
<tr>
<td>Carol Jenkins</td>
<td>Medical Anthropologist, PNGIMR</td>
<td>Vol 28 No 3, Sep 1985 to Vol 29 No 4, Dec 1986; Vol 32 No 4, Dec 1989</td>
<td>7</td>
</tr>
<tr>
<td>John Richens</td>
<td>Physician, Goroka Base Hospital</td>
<td>Vol 31 No 3, Sep 1988 to Vol 33 No 3, Sep 1990</td>
<td>9</td>
</tr>
<tr>
<td>Michael Alpers</td>
<td>Professor of International Health, Curtin University (Emeritus Editor)</td>
<td>Vol 43 No 1-2, Mar-Jun 2000 to Vol 47 No 3-4, Sep-Dec 2004</td>
<td>10</td>
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</tbody>
</table>

### TABLE 5

**Business Managers of the Journal in its First 50 Years**

<table>
<thead>
<tr>
<th>Manager</th>
<th>Volume Years</th>
<th>Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stan Wigley</td>
<td>Vol 15 No 1, Mar 1972 to Vol 15 No 4, Dec 1972</td>
<td>4</td>
</tr>
<tr>
<td>David Dowd</td>
<td>Vol 19 No 1, Mar 1976 to Vol 20 No 1, Mar 1977</td>
<td>5</td>
</tr>
<tr>
<td>P. Hayden</td>
<td>Vol 20 No 2, Jun 1977 to Vol 23 No 4, Dec 1980</td>
<td>15</td>
</tr>
<tr>
<td>Susan Baxter</td>
<td>Vol 25 No 3, Sep 1982 to Vol 27 No 3-4, Sep-Dec 1984</td>
<td>8</td>
</tr>
<tr>
<td>Rob Whaites</td>
<td>Vol 28 No 1, Mar 1985 to Vol 30 No 4, Dec 1987</td>
<td>12</td>
</tr>
<tr>
<td>Nivritti G. Patil</td>
<td>Vol 31 No 1, Mar 1988 to Vol 33 No 4, Dec 1990</td>
<td>12</td>
</tr>
<tr>
<td>Leonard Kaupa</td>
<td>Vol 34 No 1, Mar 1991 to Vol 38 No 1, Mar 1995</td>
<td>17</td>
</tr>
</tbody>
</table>
pneumococcus \((\text{Streptococcus pneumoniae})\) was the predominant causative organism. To the surprise (and, characteristically, disbelief) of those working in the first world, isolates of pneumococcus in PNG frequently showed intermediate resistance to penicillin – 12% in David Hansman's series (43). The other surprising result, which has occasioned similar levels of disbelief, is the protection attained against death from pneumonia in young children by immunization with the pneumococcal polysaccharide vaccine (44-46). Aetiological studies have been undertaken over many years, confirming the importance of the pneumococcus and \(\text{Haemophilus influenzae}\) in both pneumonia and meningitis (47-49). The achievement of years of work in PNG and the solution of many technical problems led to Michael Gratten being chosen to write the manual for respiratory bacteriology for the World Health Organization. He and Janet Montgomery comprehensively reviewed all aspects of their work on the bacteriology of pneumonia and meningitis in children in PNG for a focus issue of the Journal (49). Epidemiological studies have been conducted in Tari since 1970 and have formed the basis for many research investigations and interventions, in particular on acute lower respiratory tract infections (ALRI) (50). We should note that ALRI, in the PNG context, is equivalent to pneumonia. In 2002 a focus issue of the Journal was devoted to the wide range of research conducted in Tari (Table 8). How nutritional status interacts with ALRI – and with diarrhoea and malaria – has been studied by Deborah Lehmann and colleagues (51). Children with low birthweight have 4 times the risk of dying from ALRI in the first year of life; children under two years of age who are malnourished are 4 times more likely to be admitted with pneumonia and, if admitted, are 4 times more likely to die (51). Obtaining the evidence for these interactions has been a major achievement.

**TABLE 6**

**EDITORIAL ASSISTANTS OF THE JOURNAL IN ITS FIRST 50 YEARS**

<table>
<thead>
<tr>
<th>Assistant</th>
<th>Vol Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terence Hillier</td>
<td>Vol 20 No 3, Sep 1977 to Vol 21 No 2, Jun 1978 (4 issues)</td>
</tr>
<tr>
<td>Janet Williamson</td>
<td>Vol 21 No 4, Dec 1978; Vol 22 No 2, Jun 1979 to Vol 22 No 4, Dec 1979 (4 issues)</td>
</tr>
<tr>
<td>Jenny Benham</td>
<td>Vol 28 No 1, Mar 1985 to Vol 29 No 4, Dec 1986 (8 issues)</td>
</tr>
<tr>
<td>Julie Briggs</td>
<td>Vol 30 No 1, Mar 1987 to Vol 32 No 2, Jun 1989; Vol 34 No 1, Mar 1991 to Vol 37 No 4, Dec 1994 (26 issues)</td>
</tr>
<tr>
<td>Joanne Bryant</td>
<td>Vol 30 No 1, Mar 1987 and Vol 30 No 2, Jun 1987 (2 issues)</td>
</tr>
<tr>
<td>Pat Pearson</td>
<td>Vol 30 No 1, Mar 1987 and Vol 30 No 2, Jun 1987 (2 issues)</td>
</tr>
<tr>
<td>Elspeth Macgregor</td>
<td>Vol 30 No 3, Sep 1987 and Vol 30 No 4, Dec 1987 (2 issues)</td>
</tr>
<tr>
<td>Kathleen Carey</td>
<td>Vol 31 No 3, Sep 1988 and Vol 31 No 4, Dec 1988 (2 issues)</td>
</tr>
<tr>
<td>Louise Brian</td>
<td>Vol 32 No 2, Jun 1989 to Vol 33 No 4, Dec 1990 (7 issues)</td>
</tr>
<tr>
<td>Karen Knight</td>
<td>Vol 32 No 2, Jun 1989 to Vol 34 No 1, Mar 1991 (8 issues)</td>
</tr>
<tr>
<td>Jacob Wani</td>
<td>Vol 35 No 4, Dec 1992 to Vol 36 No 4, Dec 1993 (5 issues)</td>
</tr>
<tr>
<td>Cynthea Leahy</td>
<td>Vol 37 No 1, Mar 1994 to Vol 47 No 3-4, Sep-Dec 2004 (30 issues)</td>
</tr>
<tr>
<td>Norries Pomat</td>
<td>Vol 38 No 2, Jun 1995 to Vol 44 No 1-2, Mar-Jun 2001 (18 issues)</td>
</tr>
<tr>
<td>Elanna Lowes</td>
<td>Vol 45 No 1-2, Mar-Jun 2002 (1 issue)</td>
</tr>
</tbody>
</table>
TABLE 7

COVERS OF THE JOURNAL IN ITS FIRST 50 YEARS

Volume 1 No 1, May 1955 to Volume 3 No 1, Feb 1959 (7 issues)
Red covers with, on the front cover, the title (Papua and New Guinea Medical Journal), the volume and issue number and date, Department of Public Health, Port Moresby and the Australian coat of arms. Contents inside.

Volume 3 No 2, Aug 1959 to Volume 7 No 1, Dec 1964 (7 issues)
New design with the same information on the front cover; the title is boxed. Colour: 2 issues pale grey, 5 issues buff. Contents inside.

Volume 8 No 1, Mar 1965
New design, buff colour, contents on front cover under the title and the volume and issue number and date. Australian coat of arms omitted. At the bottom of the front cover there is the following statement. "Edited and prepared by the Medical Society of Papua New Guinea. Published by the Department of Public Health, Port Moresby."

Volume 8 No 2, Aug 1965 to Volume 14 No 4, Dec 1971 (26 issues)
New design, pale green colour. Contents on front cover under a partially boxed title and the volume and issue number and date. The editing and publishing statement is on the inside front cover. In Vol 14 No 3, Sep 1971 the name of the journal was changed to Papua New Guinea Medical Journal.

Volume 15 No 1, Mar 1972 to Volume 20 No 3, Sep 1977 (22 issues)
Completely new design. Bird and pole, in traditional design, on the front cover. Colour variable, by issue. On the right-hand side the title, Papua New Guinea Medical Journal, in block letters, the volume and issue number and date and a small map of the island of New Guinea plus the Papua New Guinean islands. Papua New Guinea being in the colour of the cover design. At the top left-hand corner the highlights or Focus of the issue.
Contents on the back cover with a logo of the Papua New Guinea Medical Journal. In Vol 18 No 1, Mar 1975 the map was changed to Papua New Guinea only, in outline, with a snake entwining a spear superimposed.

Volume 20 No 4, Dec 1977 to Volume 24 No 4, Dec 1981 (17 issues)
New traditional art design, with masks running vertically and an ancestral figure, by Mr Lahui Sabona.
The journal title and the volume and issue number and date on the right-hand side and, on the left, above the figure, the same small map with the Papua New Guinean 'caduceus'. Colour variable, by issue. Contents on the back cover with a logo of the Papua New Guinea Medical Journal; from Vol 22, No 1, Mar 1979 the logo no longer on the back cover but retained on the editor's page inside. From Vol 20 No 4, Dec 1977 to Vol 21 No 2, Jun 1978 and from Vol 23 No 1, Mar 1980 to Vol 24 No 4, Dec 1981 (11 issues) the Contents were also printed inside.

Volume 25 No 1, Mar 1982 to Volume 47 No 3-4, Sep-Dec 2004 (76 issues)
Completely new design, with the journal title in large block letters at the top of the front cover, over a map of Papua New Guinea almost half the size of the cover, and the volume and issue number and date at the bottom. Three colours used, varying by volume, annually: blue, red and green, in various shades, exactly the same colour being used for the issues of one volume.
Contents on the back cover, and inside.
The journal name, volume and issue number, the date and, from Vol 25 No 2, Jun 1982, the inclusive pages printed on the spine. From Vol 28 No 2, Jun 1985 the ISSN 0031-1480 was added to the front cover in the top right-hand corner. All volumes from Volume 25 on are indexed and the indexing after 1987 follows the blue-red-green 3-year cycle, appearing in the next blue December issue.
Figure 1. Representative examples of the 7 different types of cover that the Journal has had in its first 50 years. See also Table 7.
Chronic lung disease and asthma have been extensively studied in PNG and some of this work has been reported in the Journal (52-56). The epidemic of asthma in adults in Okapa and neighbouring areas, without affecting children, is a puzzle that has been well defined but not yet completely solved. This is another remarkable and unexpected fact of medical life in Papua New Guinea, though few outside of the Eastern Highlands seem to be aware of it. Unlike kuru, pigbel or swollen belly syndrome, rural adult asthma is still prevalent, still a major worry for people living in this part of the highlands and is crying out for further investigation. The combined topics of chronic lung disease and asthma were reviewed by Ross Anderson and Ann Woolcock in 1992 (57).

There have been 3 focus issues on malaria (Table 8), indicating not only its importance to the health of Papua New Guineans but also the amount of research that has been done on it. Unfortunately, it is still a major problem. However, we are beginning to understand malaria better – and much of that new understanding has come from work carried out in PNG. We have the knowledge and tools to control malaria, even if they are not being fully utilized. One of these new insights was the frequent occurrence of small-area variations in malaria epidemiology and the importance of local ecologies in explaining differences in the burden of malaria. In the second focus issue on malaria Jacqueline Cattani and colleagues reported on their findings in Madang (58) which demonstrated variation in malaria at the village level. The ecology was studied in relation to humans by James Moir and Paul Garner (59) and in relation to mosquito vectors by Derek Charlwood and colleagues (60). This built on years of work by malarialogists in the past, much of it reported in the Journal, especially in the first focus issue on malaria (Table 8). However, the philosophy had changed from eradication to control between the two focus issues. There was “a move away from centrally organized campaigns applying a single method towards more flexible control programs. Such programs should be based on a knowledge of the local epidemiology of malaria with the aim of using a variety of different control methods in an integrated approach” (59). Indeed, others, such as John Gunther (61) and Terence Spencer (62), had been saying this before but were not heeded. Terry Spencer’s opinion was based on detailed ecological studies that he conducted with Margaret Spencer and colleagues in several areas of PNG (63). It is hard to recapture the religious fervour of the arguments about malaria eradication through residual house spraying with DDT but the conflicts and the seeds of doubt even among the faithful can be recognized between the lines of many, otherwise austere, papers on malaria in the Journal.

Wallace Peters, the Malariologist in the Department of Public Health, described the eradication campaign in detail in a paper entitled ‘Malaria control in Papua and New Guinea’ (64). In his earlier, meticulous survey of Western Province (65) Peters raised doubts about whether “total control of transmission is feasible” in areas such as Western Province but he remained optimistic that “success may be achieved in the next few years in this type of situation”. How wrong this proved to be.

One aspect of malaria for which PNG is famous is hyperreactive malarious splenomegaly (HMS) or, as it used to be called, tropical splenomegaly syndrome. Gregory Crane spent much of his life working on this disease. He has 8 substantive papers on HMS in the PNG Medical Journal, including the effect of regular chemoprophylaxis in reducing the prevalence and severity of the disease. Greg Crane’s obituary includes his bibliography, where his achievements on HMS and his contributions to the Journal, among other important work, are recorded (66).

Malaria has been present among the people of Papua New Guinea for long enough for them to have evolved together. There are several polymorphisms that protect against severe malaria that are peculiar to Papua New Guinea or the region. One of the most interesting is ovalocytosis. The first paper specifically about ovalocytosis in Papua New Guineans was published in the Journal by Dominick Amato and Peter Booth (67). The protection afforded by ovalocytosis against severe malaria that was predicted by Amato and Booth proved to be highly significant, and uniquely so: absolute protection against cerebral malaria (68). This extraordinary result should enable us to find clues to the pathogenesis of cerebral malaria, and
investigation of this continues to be vigorously pursued by the Papua New Guinea Institute of Medical Research.

Another important advance in our understanding of malaria has been achieved through the use of the polymerase chain reaction (PCR) to detect parasites. This was pioneered by Ingrid Felger and her colleagues in PNG (69). Through the use of this more sensitive method of detection parasite rates in adults increased from 23%, as detected by microscopy, to 47%. The use of PCR also enables strains of malaria parasites to be described. Adult immunity in an area of high endemicity is maintained by low-level, asymptomatic chronic infection with multiple strains of malaria parasites. We have to be cautious in any control program about disturbing this ecological balance.

Some of the earliest work on the use of impregnated bednets to control malaria was carried out in PNG, there have been many studies on drug resistance and on malaria in pregnancy, recent achievements have included malaria mapping in the highlands ... The list goes on. Unfortunately, we cannot cover them all. However, in discussing aspects of malaria that have been prominently reported in the Journal we cannot omit the drive towards a malaria vaccine led by the Papua New Guinea Institute of Medical Research. The carefully planned project with complex baseline studies (70) resulted in a very encouraging outcome (71), though we still have a long way to go before an appropriate malaria vaccine will be available. We hope that Papua New Guineans will be among the first to benefit from a malaria vaccine when it comes, but this will not just happen because of good work done in the past: it will have to be constantly fought for.

Of the great work done in PNG on maternal immunization to prevent neonatal tetanus there is much in the international literature but nothing in the Journal. This was true also for the innovative and successful studies on filariasis until the focus issue on filariasis in 2000 (Table 8). In that issue is a report on the study in Dreikikir, where there are communities with rates of filariasis among the highest recorded in the world – another distinction for PNG. The results showed that community-wide, annual single-dose treatment with diethylcarbamazine (DEC) and ivermectin could lead to complete interruption of transmission and ultimately elimination of lymphatic filariasis (79), an outcome of great significance, not only for PNG. Now the global elimination of filariasis is within our grasp, and we must seize the opportunity – especially in PNG, where these studies were first carried out.

For leprosy, mercifully a disease now in steep decline in PNG, the focus issue came early, in 1973. Douglas Russell described leprosy in PNG in 1960 (80) and also in 1973 (81), when he made brief reference to studies being carried out in Karimui, in particular to a field trial, which began in 1962, of BCG vaccine as a prophylaxis against leprosy. The successful outcome of the trial was reported later (82). Ken Clezy is a surgeon who worked in Papua New Guinea for many years. He became Professor of Surgery and Dean of the Medical School. He made a great contribution to teaching and training. He was briefly Editor of the Journal in 1979-1980 and contributed 4 Clinical Practice articles to our series. His major interest, however, was in the surgery of
### TABLE 8
**FOCUS ISSUES OF THE JOURNAL IN ITS FIRST 50 YEARS**

<table>
<thead>
<tr>
<th>Focus Title</th>
<th>Focus Issue Number</th>
<th>Guest Editor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pigbel</td>
<td>Vol 9 No 2, Jul 1966</td>
<td>I. Maddocks (editor)</td>
</tr>
<tr>
<td>Health in the Village</td>
<td>Vol 13 No 1, Mar 1970</td>
<td>I. Maddocks (editor)</td>
</tr>
<tr>
<td>The concept of the Focus Issue was introduced by D. Graeme Woodfield</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haematology</td>
<td>Vol 15 No 1, Mar 1972</td>
<td>D.G. Woodfield (editor)</td>
</tr>
<tr>
<td>Liver Disease</td>
<td>Vol 15 No 2, Jun 1972</td>
<td>D.G. Woodfield (editor)</td>
</tr>
<tr>
<td>Respiratory Disease</td>
<td>Vol 16 No 1, Mar 1973</td>
<td>D.G. Woodfield (editor)</td>
</tr>
<tr>
<td>Leprosy</td>
<td>Vol 16 No 2, Jun 1973</td>
<td>D.G. Woodfield (editor)</td>
</tr>
<tr>
<td>Malaria</td>
<td>Vol 16 No 4-Vol 17 No 1, Dec 1973-Mar 1974</td>
<td>D.G. Woodfield (editor)</td>
</tr>
<tr>
<td><em>Mycobacterium ulcerans</em> Disease</td>
<td>Vol 17 No 2, Jun 1974</td>
<td>D.G. Woodfield (editor)</td>
</tr>
<tr>
<td>Cardiovascular Disease</td>
<td>Vol 17 No 3, Sep 1974</td>
<td>D.G. Woodfield (editor)</td>
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<tr>
<td>Obstetrics</td>
<td>Vol 17 No 4, Dec 1974</td>
<td>D.G. Woodfield (editor)</td>
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<tr>
<td>Ophthalmology</td>
<td>Vol 18 No 2, Jun 1975</td>
<td>D.G. Woodfield (editor)</td>
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<tr>
<td>Neurology</td>
<td>Vol 18 No 4, Dec 1975</td>
<td>Richard W. Hornabrook</td>
</tr>
<tr>
<td>Psychiatry</td>
<td>Vol 19 No 1, Mar 1976</td>
<td>Burton G. Burton-Bradley</td>
</tr>
<tr>
<td>Occupational Health</td>
<td>Vol 19 No 2, Jun 1976</td>
<td>Bruce Hocking</td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>Vol 19 No 3, Sep 1976</td>
<td>D. Amato (editor)</td>
</tr>
<tr>
<td>Haematology</td>
<td>Vol 20 No 1, Mar 1977</td>
<td>D. Amato (editor)</td>
</tr>
<tr>
<td>Community Medicine</td>
<td>Vol 20 No 3, Sep 1977</td>
<td>George Wyatt</td>
</tr>
<tr>
<td>Tropical Immunology</td>
<td>Vol 21 No 1, Mar 1978</td>
<td>Michael P. Alpers</td>
</tr>
<tr>
<td>Psychiatry</td>
<td>Vol 21 No 3, Sep 1978</td>
<td>Burton G. Burton-Bradley</td>
</tr>
<tr>
<td>Pigbel</td>
<td>Vol 22 No 1, Mar 1979</td>
<td>Gregor W. Lawrence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Timothy G.C. Murrell, Peter D. Walker</td>
</tr>
<tr>
<td>Delivery of Health Care</td>
<td>Vol 22 No 3, Sep 1979</td>
<td>S. Naraqi (editor)</td>
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<tr>
<td>Tropical Psychosomatics</td>
<td>Vol 23 No 1, Mar 1980</td>
<td>Burton G. Burton-Bradley</td>
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<td>Social Science and Medicine</td>
<td>Vol 28 No 3, Sep 1985</td>
<td>Carol Jenkins</td>
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<td>Malaria</td>
<td>Vol 29 No 1, Mar 1986</td>
<td>Jacqueline Cattani</td>
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<td>Tropical Paediatrics</td>
<td>Vol 30 No 2, Jun 1987</td>
<td>John Biddulph</td>
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<td>Nutrition</td>
<td>Vol 31 No 2, Jun 1988</td>
<td>Peter Heywood</td>
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</table>
leprosy, and his contributions to this field were warmly appreciated throughout PNG and recognized internationally. The achievements of Ken Clezy and Doug Russell are recounted and praised in an excellent history of leprosy management and control in PNG by Hugo Ree (83).

Sexually transmitted diseases (STDs) do not get much coverage in the early pages of the Journal until syphilis spread up the Highlands Highway to affect a newly emerging population without the traditional immunity acquired from yaws (84,85). In 1984 Candy Lombange reported on gonorrhoea and syphilis in the previous 10 years and found a significant increase in both despite the introduction of a National STD Control Program. He analyzed the data by region and in the major urban centres of Port Moresby and Lae. He discussed operational problems and made recommendations for improving the Control Program (86). This paper was a wake-up call for Papua New Guinea, later re-emphasized by a multicentre laboratory-based study conducted in 1989-1990 (87). Unfortunately our progress was slow while the many organisms causing STDs exploded. By the time of the second survey they had been joined by HIV (human immunodeficiency virus), and AIDS (acquired immune deficiency syndrome) added a frightening new dimension to the problem of STDs. In 1994 another wake-up call was published: the PNGIMR Monograph on Sexual and Reproductive Knowledge and Behaviour (88). Unfortunately, its small voice was insufficient to calm the epidemic. Since then many papers have been published on the extraordinarily high rates of sexually transmitted infections (often unrecognized) in our communities and on the increasing prevalence of HIV infection. The Journal’s first focus issue on sexually transmitted infections was on HIV and AIDS in 1996; in 2004 we had a second one, on sexual health (Table 8).

Papers on nutrition and growth have been published in the Journal since the beginning (6). The one focus issue on nutrition contains a paper on the 1982/83 National Nutrition Survey by Peter Heywood and colleagues (89) and the account of nutrition and morbidity (51) discussed previously in relation to ALRI/pneumonia. How virus
infections and protein-energy malnutrition interact had been reviewed 10 years earlier by John Mackenzie (90). Peter Heywood and Alison Heywood, in studying the functional significance of protein-energy malnutrition, showed that growth retardation is a risk factor not only for certain infectious diseases but also is associated with delayed motor development, delayed eruption of teeth and reduced visual attention (91). To obtain such results careful studies must be carried out in the community, with full participation by members of the hamlet, village or settlement. The extensive and comprehensive work done in Tari has already been mentioned. During the last 50 years other communities have been studied demographically and epidemiologically, with many variables measured, and the results published in the Journal: Anguganak (92,93), Kiriwina (94), Baiyer River (95), Bundi (96), Oro Bay (97) and Pari village (98,99), to restrict ourselves to some early examples. Roy Scragg studied four populations continuously for 19 years – Lemankua and Solas on Buka and Tabar and Tigak (near Kavieng) in New Ireland. He showed a decline in mortality rates, overall and for specific diseases, over this period. This meticulously conducted study was reported in the Journal in 1969 (100). Another remarkable study of that time was the epidemiological sample survey of the whole country by Peter Vines; he described his methodology in the Journal in 1965 (101). The results of the survey were published by the Department of Public Health in 1970 (102). In this context we should not forget Peter Sinnett’s monumental work on the Engan people of Tukisenta, which was published as a PNGIMR monograph (103).
Other population studies concentrated on specific variables or diseases. Blood pressure has been widely studied and most emphasis has been on the changes that have occurred with the modernization which now affects every community, to a variable degree, in the country (104). Some studies, in contrast, have provided a link with the traditional past, which is now lost to us forever. Ian Maddocks and Luke Rovin measured blood pressures in communities in Simbu Province, where, as they reported in the Journal in 1965, blood pressure fell with age in both males and females (105). I recorded the same findings in Waisa village in the Okapa District in 1962 (M.P. Alpers, unpublished data). Moreover, as they did, I investigated this further by studying the electrolytes in 24-hour urine samples. The samples were meticulously collected and sent to the United States for analysis. My colleagues refused to believe or publish the results: the urinary volumes were considered too small to be true 24-hour collections and the sodium and potassium levels were bizarre! This of course was exactly what the study was intended to show – and document, in the last opportunity we would ever have in the Okapa District in 1962 (M.P. Alpers, unpublished data). Moreover, as they did, I investigated this further by studying the electrolytes in 24-hour urine samples. The samples were meticulously collected and sent to the United States for analysis. My colleagues refused to believe or publish the results: the urinary volumes were considered too small to be true 24-hour collections and the sodium and potassium levels were bizarre! This of course was exactly what the study was intended to show – and document, in the last opportunity we would ever have of doing so. Traditionally, salt was made from potash and contained potassium, not sodium; the diet was high in potassium, low in sodium; and fluid intakes in the highlands were remarkably low, partly because of the burden of carrying water in bamboo cylinders to hamlets built on high ridges for security. The paper by Maddocks and Rovin is an important link to this not so remote but now traditional past, which is now lost to us forever. Ian Maddocks and Luke Rovin measured blood pressures in communities in Simbu Province, where, as they reported in the Journal in 1965, blood pressure fell with age in both males and females (105). I recorded the same findings in Waisa village in the Okapa District in 1962 (M.P. Alpers, unpublished data). Moreover, as they did, I investigated this further by studying the electrolytes in 24-hour urine samples. The samples were meticulously collected and sent to the United States for analysis. My colleagues refused to believe or publish the results: the urinary volumes were considered too small to be true 24-hour collections and the sodium and potassium levels were bizarre! This of course was exactly what the study was intended to show – and document, in the last opportunity we would ever have of doing so. Traditionally, salt was made from potash and contained potassium, not sodium; the diet was high in potassium, low in sodium; and fluid intakes in the highlands were remarkably low, partly because of the burden of carrying water in bamboo cylinders to hamlets built on high ridges for security. The paper by Maddocks and Rovin is an important link to this not so remote but now totally obliterated past in the highlands of PNG. It is a tribute too to a remarkable Papua New Guinean, who was tragically killed in 1972: Luke Rovin’s obituary appeared in the Journal (106) and in A History of Medicine in Papua New Guinea (107).

Burkitt lymphoma is one of the special diseases of PNG, though the focus of the disease here ranks only number two in the world. Among various studies carried out over many years some promising new work shed light on the relationship of the tumour with Epstein-Barr virus and malaria (108) and these findings need to be explored further. Here is yet another local research problem waiting to be tackled by a keen young scientist. However, it is by going back in time that we reach the most interesting connection between Burkitt lymphoma and PNG: it was first described here, and should not be called by that name at all. Jan Saave reported on ‘lymphadenosis’ in PNG (109) 3 years before Denis Burkitt described ‘a sarcoma involving the jaw in African children’, which eventually became ‘his’ tumour.

Betelnut chewing is another special feature of life in Papua New Guinea. It has an important social function but, unfortunately, does help to explain the high incidence of oral cancer. However, the exact roles of smoking, the lime used, the person’s diet and other factors in the pathogenesis of their cancer have not been worked out. This is important to investigate since it may be possible to establish rules for ‘safe chewing’ if we had better evidence about the critical combination of factors in the pathogenesis. Other aspects of betelnut chewing have been addressed in the Journal: its possible nutrient value (110); its effect of reducing dental caries (111); its possibly beneficial effects in pregnancy (112); its short-term elevation of heart rate without a central effect on visual processing or alertness (113); its aggravation of asthma (114,115); and its association with diabetes (116).

The selection of the First Eleven of the Journal’s classic papers has now been made (Table 10) and it is time to draw this discursive review to a close. The number of topics not covered is large and to include them all would mean extending the review to more than twice its current length. A glance at the list of focus issues in Table 8 will reveal immediately the most important topics not considered; and there are many more. However, there are just a few small, but interesting, items that I would like to draw attention to before I close.
generated by an aloof, paternalistic attitude by some health officials towards the people they are trying to help. This attitude is mainly due to a lack of understanding and rapport with the community.” “In order to be truly successful, the health worker must be able to make the educational mechanisms function as a two-way process in which he learns from the people even as they learn from him.” Paul Freeman, Jane Thomason and Gilbert Bukenya studied the factors that made urban settlement dwellers take their children for immunization (118). They found that “the provision of information to mothers on when to start immunization and how often the child should be immunized were key factors in determining immunization status”. Better knowledge about immunization did not lead to improved practice. They recommended that “maximal use must be made of local community organizations to disseminate the key immunization information”. Carol Jenkins enlarges on the difficulties of changing hygiene behaviour (119); indeed, essentially the same problems have to be faced in trying to achieve any desirable behaviour change. In the context of her paper she argues that “improved hygiene and sanitation could be achieved if sufficient resources were focused on the people who use water and sanitation systems and not simply on the systems themselves”.

TABLE 10
A First Eleven of the Journal’s Classic Papers, Listed in the Order of Citation in this Review


I have a few other favourites scattered among the papers of the Journal. Wilfred Moi describes his cultural background, his growing up in Ambasi in Milne Bay Province and the relevance of this to his career as a psychiatrist (120). This paper should be an inspiration to other Papua New Guineans to realize that their own background and life story will be equally fascinating and relevant to others, and that they should convince themselves to write it up. I cite it also to honour the memory of Wilfred Moi, a gentle man of great achievement, who also died in tragic circumstances. Peter Sharp contributed several excellent, well-written papers to the Journal; three of them are memorable not only for their content but also for their title (121-123). I am pleased to cite them for that reason alone, but also as a way of encouraging everybody to read – or re-read – them.

Finally, though the Journal articles are usually about Papua New Guinea, not all are, and some even come from outside our local region. Takeo Doi was Professor of Psychiatry at the University of Tokyo and he introduced the Japanese concept of *amae* to readers of our Journal (124): it means ‘to depend and presume upon another’s love or bask in another’s indulgence’. As I close this review I hope, as Takeo Doi recommends, that *amae* is something that we all can feel dear to our hearts. This will make my neglect here of so much good work published in our Journal easier to bear.

ACKNOWLEDGEMENTS

I acknowledge the commission from the President, Mathias Sapuri, and the Executive of the Medical Society of Papua New Guinea to prepare this review of the first 50 years of our Journal and I thank them warmly for according me this privilege. I acknowledge the Editors of the Journal, Peter Siba, Nakapi Tefuarani and John Reeder, and our dedicated and skilful Editorial Assistant, Cynthea Leahy, and thank them very much for all the support they have given me. I also thank Jason Kovacs for his indispensable help in establishing the Journal’s newly acquired publishing capability and, especially for this issue, in enabling us to reproduce the classic papers from the past.

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SPONTANEOUS gangrene of the small intestine, without obvious vascular or mechanical cause, is an extremely rare disease. It is rarely associated with the known enteric and dysenteric infections of the bowel. Within the framework of the present pathological services available in the Highland hospitals of New Guinea, the story of the ecology and epidemiology of a widespread gangrenous enteritis was rather slow in unfolding. The condition was first noticed in subjects undergoing laparotomy for an “acute abdomen” in Goroka early in 1961. It was then termed a “necrotizing jejunitis” because initial bacteriological investigations failed to establish a cause (Murrell and Roth, 1963). Beta toxin producing strains of Clostridium perfringens (Cl. welchii) were subsequently recovered from the bowel contents and faeces of subjects with the condition (Egerton and Walker, 1964; Murrell et al. 1966).

This condition, synonymous with “enteritis necroticans”, can be defined as an acute necrotizing inflammatory disease of the small bowel, of patchy distribution and commencing in the duodenum or jejunum. In New Guinea Clostridium welchii (Cl. perfringens) Type C is thought to be one of the aetiological components of its cause. Because the term includes a group of conditions known by a multiplicity of names, the New Guinea syndrome warrants definition by a specific name. ‘Pig-bel’ is suggested as a suitable name for the disease because of its aetiological association with the pig-feasting practices of the New Guinea Highlander.

A similar disease, ‘Darmbrand’, appeared in epidemic form in North-West Germany in the latter and post-war years, and was believed to be due to Clostridium perfringens Type F (Hansen et al., 1949; Oakley, 1949; Marcuse and Konig, 1950). Zeissler and Rassfeld-Sternberg (1949) and Hain (1949) established a foodborne origin for the disease but other workers believed that additional dietary, nutritional and possibly viral factors were associated with the pathogenesis – Pietzonka and Rassfeld-Sternberg, 1950; Hermann, 1948; Siegmund 1948; Kloor and Brummond, 1951). As a result of the recovery of Type C strains from man in New Guinea, the strains of Cl. perfringens Type F, believed to cause ‘Darmbrand’, have been reclassified on toxicological grounds as a Type C variety (Sterne and Warrack, 1964).

Heat resistant Type A strains are the only other recognized Welchii enteric pathogens of man (Hobbs et al., 1953), and cause food poisoning usually via a medium of re-heated meat dishes. These strains produce alpha toxin as the major antigen and are one of the organisms responsible for the ordinary gas gangrene of wounds. Strains from other groups, producing different toxins, cause enterotoxaemic diseases in animals, each type having a limited host range. Thus Type B is associated chiefly with lamb dysentery (Dalling, 1928), Type C with enterotoxaemias of sheep, calves, and piglets (Griner and Bracken, 1953; Field and Gibson, 1955), Type D with pulpy kidney disease of sheep (Bennett, 1932), and Type E is occasionally found as a saprophyte in the intestines of calves (Bosworth, 1943). Overfeeding and dietary change play a significant part in the aetiology of these diseases which may be analogous to Pig-bel of man in New Guinea.

Clinically the disease in New Guinea is characterized by the symptom triad of severe and spasmodic upper abdominal pain, bloody diarrhoea with melaena and nausea with occasional vomiting. In advanced cases there is constipation, abdominal distension and constant generalized pain. The signs may be those of dehydration from a severe enteritis, shock and toxæmia, or those of an acute or sub-acute small bowel obstruction with localized or diffuse abdominal tenderness. The disease progresses, if untreated, to complete segmental gangrene of parts of the small intestine with the development of ileus, both mechanical and paralytic, oligæmic shock and severe toxæmia. Gas bubbles can sometimes be seen in the distal mesenteric venous arches and the mesenterium is oedematous, with swollen ‘spongy’ regional lymph glands. Tissue
emphysema along the mesenteric attachment and in the subserosa is a frequent finding at operation or autopsy.

A small proportion of persons with the disease survive the initial stages without treatment, or with conservative management, but perforation and peritonitis or the development of an acute malabsorption syndrome results in death. The malabsorption is due to chronic small bowel obstruction by adhesive bands, stenosis by cicatrization or the development of short circuits, blind loops and rigid scarred bowel segments denuded of normal mucosa. Follow-up studies indicate that certain features of the malabsorption syndrome develop in a group with residual chronic jejunitis.

This paper describes the cumulative investigations into the condition during the four years, 1961 to 1964, and attempts to review some of the epidemiological and aetiological features.

**MATERIALS AND METHODS.**

Case records were kept of patients with known and suspected enteritis necroticans, during the period January, 1961, to November, 1964. A total of 210 cases are reviewed in this study. The diagnosis was made on clinical grounds alone in 73 instances and on the pathological features at autopsy or operation in 137 patients. They were classified clinically into acute toxic, acute surgical, sub-acute surgical and mild groups. The diagnosis was established on the history of pork consumption, the clinical features, X-ray findings, bowel appearances at operation or autopsy, the isolation of *Cl. perfringens* Type C from a significant proportion of resected intestinal segments, the detection of rising *Cl. perfringens* beta antitoxin levels in the sera of recovered patients, and marked clinical improvement following the intravenous administration of specific Type C antiserum (Murrell *et al.*, 1966).

Bacteriological and radiological investigations have been presented in other papers. Antitoxin levels to the beta toxin of *Cl. perfringens* were estimated in 58 cases, serial samples being taken from 21 persons with the disease. The serum was separated, kept under refrigeration and one drop of 50 per cent. o-cresol-ether added to each ml. of serum as a preservative. These were despatched in batches to the Wellcome Research Laboratories for estimation of *Cl. perfringens* beta antitoxin (Glenny, Bar, Llewellyn-Jones, Dalling and Ross, 1933).

Epidemiological information included a survey of beta antitoxin levels in the normal population in high and low prevalence areas; a bacteriological survey of faeces from the normal human and porcine populations to determine, if any, a ‘carrier rate’ of *Cl. perfringens* strains; a bacteriological search for these organisms in cooked and uncooked pig meat; and general observations in the preparation of food at pig-killing ceremonies in Western and Eastern Highland clans. A disease prevalence rate was established at Goromougo in the Upper Chimbu during 1964 and trends in the prevalence of diarrhoeal disease were obtained from hospital records of the Goroka, Kundiawa, Mount Hagen, Baiyer River, Wabag and Tari hospitals following known pig-killing activities.

Specific *Cl. perfringens* Type C antiserum was given to consecutive patients with pig-bel, and the mortality compared to an unmatched series of patients treated consecutively prior to the arrival of the anti-serum.

**RESULTS.**

**Distribution.**

Age and sex distribution of the 210 cases are listed in *Table 1.*, and illustrated in Figures 1 and 2. The condition was most common in pre-adolescent children. 52.3 per cent. of patients were two to ten years old. Children in the six to ten year group made up the largest segment of cases (29 per cent.). Males were affected more than females in the ratio of 2.2 : 1. This ratio was generally maintained in all age groups except in the 16 to 20 year group when more females were recorded with the disease. The numbers recorded in this group, however, were too small to be significant.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Males %</th>
<th>Females %</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>0.4</td>
<td>2.1</td>
<td>3</td>
<td>1.4</td>
</tr>
<tr>
<td>2-5</td>
<td>16.7</td>
<td>6.2</td>
<td>49</td>
<td>23.3</td>
</tr>
<tr>
<td>6-10</td>
<td>21.9</td>
<td>7.1</td>
<td>61</td>
<td>29.0</td>
</tr>
<tr>
<td>11-15</td>
<td>8.1</td>
<td>2.4</td>
<td>22</td>
<td>10.5</td>
</tr>
<tr>
<td>16-20</td>
<td>4.8</td>
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<td>5.7</td>
<td>3.3</td>
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<tr>
<td>41+</td>
<td>4.8</td>
<td>1.4</td>
<td>13</td>
<td>6.2</td>
</tr>
<tr>
<td>Total</td>
<td>69.0</td>
<td>31.0</td>
<td>210</td>
<td>99.9</td>
</tr>
</tbody>
</table>

**Table 1.—Age and sex distribution of 210 cases of Pig-bel.**
Of the 210 persons reviewed in this series, only one was European. All other persons, with one exception, were inhabitants from areas where they contracted the disease. The exception was a Mount Hagen native working as a plantation labourer on Kar Kar Island, in the Madang District. The European, a 28-year old Polish linesman, contracted his disease at Tari following a meal of native pork.

Incidence of pig-bel in general population.

Assessment of the incidence of the disease was made from census figures taken of five clans at the Government Rest House at Goromaugo (Upper Chimbu) in October of 1964. The total population, including absentees, was 1,448 (Table 2). Following pork feasting in May and August of the same year, seven persons were known to have contracted Pig-bel, and two died.

Mortality.

The overall death rate of cases was 36 per cent. In the severe forms of the disease the case mortality was 49.8 per cent. This was highest in the acute toxic group (84.6 per cent.). The rate was 57.7 per cent. in children under five years of age and 46.2 per cent. in persons over 40 years of age. The lowest death rate occurred in the 11 to 15 year group. The overall rate for females was slightly higher (38.5 per cent.) than that for males (35.2 per cent.). (Figure 3.)

For all ages, enteritis necroticans accounted for 2.1 per cent. of deaths at the Goroka and Kundiawa hospitals and 3.5 per cent. at the Baiyer River hospital during the period 1st April, 1962, to 31st August, 1964. The Kundiawa period reviewed was slightly longer,
The diagnosis was established bacteriologically in three cases, serologically in two and by autopsy in a further two. The incidence in this area was therefore assessed at 48.3 per 10,000. A high prevalence of *Cl. perfringens* beta antitoxin in population groups sampled in the Upper Chimbu supported the impression that Goromaugo represented a high incidence area. Age and sex distribution showed no marked difference from hospital cases.

**Outbreaks and geographical distribution.**

The geographical distribution of cases over the four years 1st January, 1961, to 31st December, 1964, is shown in *Figure 4*. Epidemics occurred in the Upper Asaro during the months...
June to September of 1961; in the Tari Basin just prior to this; most of Baiyer River in the Western Highlands in March to June, 1962, and in Bundi and the Chimbu throughout 1964.

When pig feasting activities commenced in May in the Upper Chimbu, the prevalence of enteritis necroticans rose. There was a further spread following the pig cycles in the Central Chimbu (Dom, Kup and Koronigl Census Divisions). Following the ‘Te’ festival of the Enga people of the Western Highlands late in 1963, only six cases of the disease were reported. Serological sampling earlier in the year confirmed the impression that the Wabag-Wapenamanda area was a low incidence area.

*Clostridium perfringens* Type C was isolated from cases at the Upper Asaro, Chimbu, Baiyer River, Wabag, Wapenamanda and Mendi. Bacteriological examinations from cases elsewhere at Bundi, Kainantu, Henganofi, Tari and Minj were not undertaken.

A specific focus or geographical location of the disease cannot be defined and it seems likely that the affection has always been endemic in New Guinea and that recognition and detection of the cause was not made until 1961-1962. Whether *Clostridium perfringens* Type C has been introduced with the advent of civilization remains open to speculation.

**Evidence of local spread.**

During 1964, seven cases of pig-bel were detected from clans near Goromaugo in the Upper Chimbu (Nos. 91 to 93, 97, 99, 101 and 155). *Clostridium perfringens* Type C was recovered from three of these, significant beta antitoxin was found in two others and the diagnosis established at autopsy in two more.

Following the pig killing at Goromaugo there was a bridal exchange of pork between members of a Pagakaune line and one man, Ambane Umba (Case 96), of a Kurumogl line. Ambane subsequently developed a more protracted form of the disease which was confirmed by a rising beta antitoxin and recovery of *Clostridium perfringens* Type C from his faeces. Sera taken from eight relatives exposed to the same meal and from the man who had prepared the meat all contained significant amounts of beta antitoxin.

A further case (No. 100) occurred in a man at Gena (Upper Chimbu) who had eaten pork originating from a line near Goromaugo. Contacts again had immunological evidence of exposure to beta toxin. A "lead pipe" piece of jejunum, denuded of normal mucosa, was removed at laparotomy on the 24th day. The patient also had a rise and fall in beta antitoxin.

There was further evidence of local spread in August when pork exchanges between clans at Mai and Goromaugo resulted in two further acute cases (Nos. 150 and 155). The disease was firmly diagnosed three times in members of one family (Nos 89, 90, 92, 93, 132 and 134). A dietary history of persons consuming the same pork meal was recorded on 42 occasions and in only 17 instances (38 per cent.) were mild symptoms of food poisoning recorded in persons at risk.

**Hospital admissions.**

At the Kundiawa hospital for a 12-month period 1st December, 1963, to 30th November, 1964, admission for diarrhoea conditions under categories 045-049, 571 and 785.6 of the W.H.O. International Disease classification, were reviewed. There were also 71 (1.4 per cent.) admissions for mild and severe forms of pig-bel. The two sets of figures are shown together in Figure 5. Peaks in admissions for the disease corresponded to the maximal rates for the diarrhoeal disease admissions except in December, 1963. These periods were preceded by periods...
known to occur from October to December of 1962 in the Western Highlands. Gastroenteritis was prevalent prior to the pig-killing near Baiyer River in April, 1962.

Most cases were seen during the months of June and August, 1961, in the Upper Asaro, in April and May of 1962 (Baiyer River), the Upper Chimbu in May and June, 1964, and the Central Chimbu later that same year.

Pig-feasting investigations.

1. Description of a pig-kill. Preparations months in advance take place when long houses are built to accommodate residents and visitors round central courtyard clearings. Tables are also built in readiness to receive the pork slabs for distribution. In the Eastern Highlands two to four weeks before a large pig-kill, a smaller celebration takes place, the smaller pigs being sacrificed on such an occasion.

All large pig-killing ceremonies take place at the time of a full moon. Whenever possible they are held during favourable weather which is usually during the dry season. Dancing and singing festivities are held before the killing commences. In the Chimbu the pork preparation and distribution takes place over a period of three or four days, whereas only a little over a day is needed in the Huri and Enga areas. The description which follows is basically applicable to all groups except for the important difference just mentioned. Pig-kills were witnessed at Korfena (July, 1961), Tambul and Wapena-manda (September, 1963) and the Upper Chimbu (May, 1964).

Operative records analysed for almost a four-year period (1st February, 1961, to 30th November, 1964) at the Goroka hospital emphasised the importance of enteritis necroticans as a surgical disease in the Highlands (Figure 6).

Laparotomy was undertaken on 301 occasions during this period. Sixty-nine patients (22.8 per cent.) had acute and complicated forms of Pig-bel and this was the largest group requiring surgical exploration of the abdomen. For acute and sub-acute surgical conditions excluding trauma, the frequency rose to 31.2 per cent. As a surgical disease, therefore, Pig-bel was the most common cause of an “acute abdomen”. It is possible also that some of the causes of strangulation by post-inflammatory bands, listed in the second group of Figure 6, were also sequelae of the disease.

Seasonal distribution.

In Figure 7 admission to hospitals in the Highlands and Madang from enteritis necroticans are grouped at three-monthly intervals. Peaks occurred mostly in the ‘dry’ season between the months of April and September, and coincided with the larger pig-killing ceremonies held at this time of the year because of the prevailing climate and good harvest.

The relationship of Pig-bel and epidemics due to other diseases was not investigated in detail. A widespread influenza epidemic preceded the commencement of pig-killing in the Upper Chimbu in 1964 and a measles epidemic was...
The tethered pigs are clubbed to death by a near relative of the owner, four to five sharp blows to the head with a two to three inch diameter stick usually being sufficient to kill the animal (Plate I). There is no bleeding of the carcase although some blood from the head wounds spills out over the ground. Cassowaries, chickens and dogs are sometimes killed along with the pigs but are cooked separately. The Chimbu people place the dead pigs in radiating lines from a central spirit or ‘Bolim’ house, rather like the spokes of a cartwheel, each spoke representing pigs to be distributed from one man’s house. The clan leaders then welcome visitors and incantate upon the significance of the occasion. After about two hours, the butchering starts. This was well under way by 10 a.m. in the Enga situation. The haste of Enga in preparing and cooking the pork is probably due to the longer distances over which exchanges must take place and the greater number of pigs slaughtered.

The hair is singed over an open fire and the carcases then lifted onto leaf mats of banana, breadfruit and tree fern leaves. An intricate dissection in the dorsal position is commenced with double lateral incisions in the anterior axillary line. The outermost continues down behind the anus and the inner two meet anterior to it. Here spillage may occur and the butcher’s hands can become contaminated directly by pig faeces (Plates II and III). The abdominal skin flaps are dissected up towards the head and the thoracic cage opened laterally by axe cuts. A careful butcher then removes the diaphragm, peritoneal sac and contents intact. However, sometimes the peritoneal cavity is penetrated by the less adept and very occasionally bowel may be perforated at this stage. This evisceration is preferably performed with bamboo knives, which being new, are more hygienic than unwashed steel knives. Women take no part in this process and sit aside watching the proceedings, stray dogs, piglets, fowls and children wander at will about the dissectors, all contributing to a cumulative spoiling of the fresh meat. The boys also help mop up pooled blood with a parsley type of plant Oenanthe jarvanica squeezing it into a bowl under the head. Thoracic viscera, tongue and oesophagus are then removed and the solid organs separated. Not infrequently, butchers had infected and dressed sores on their hands from which meat became contaminated.

The women take the bowels in their ‘bilums’ (string carrying-bags slung over the head) to
to the nearest stream for washing. The Chimbu and Gahuku (Asaro) women evert the small intestine by intussuscepting a stick into the bowel lumen, then siphon and blow water through the large bowel, and anal skin and anus acting as a funnel. Enga fashion is a little less crude as the whole bowel is slit open and cleaned more thoroughly. The bowels are plaited and wrapped in leaves ready for cooking. Stomach is packed with chopped fat, greens and herbs and cooked in the form of a haggis. It is eaten after ‘maturing’ for two or three weeks. While the bowel washing is in progress, the men continue the final filleting of the carcass: Skull, rib cage and backbone being removed in one section. Here, contamination by feet was most apparent as assistants were required to pull the head and spine forward and ventrally.

Children eat raw morsels such as ear tips and snouts. Parents wrap entrails and sex organs about their wrists to promote future fertility. Bladders on inflation are sometimes used as balloons or footballs. The extraneous blood is used as a garnish but the bulk is mixed with chopped fat and leaves, rolled in a banana leaf and cooked over an open fire as a blood sausage. Most of the viscera is consumed soon after cooking. Organs such as liver, spleen and kidney are regarded as having special magic-religious significance. Cooked bowel is eaten mainly by the women and children.

After the butchering is completed, which is in about two to four hours, the night is given to more singing and dancing. Earth pits are dug, long and shallow for the half sides of meat and deep and wide for the offal and prime cuts. The ovens are lined with banana leaves, tree fern fronds (Cyathea contaminans) and leaves of a variety of breadfruit (Ficus dammaropni); the meat, corn-cobs, taro, sweet potato and chopped greens are mixed with the pre-heated stones. Men handling them use long wooden tongs with great dexterity (Plate IV). Layer by layer the oven fills up until the large leaves roof over a final insulating layer formed by the pig’s quarters and flanks. Water is poured in and the oven is again sealed by another layer of leaves and sometimes mounded up with dirt, so that the food is cooked under steam pressure in its own moisture. The juices of all the contents are thus retained in the cooking process. The Chimbu women also cook bowels and other morsels in wooden barrels or ‘stone ovens’.

Plate II.—Technique of dissection.
2. **Temperature observations.**Temperatures failed to rise above 110 degrees Cent. in the centre of the ovens, this temperature being reached one-half hour after completion of the oven. Cooking time was between 1 ½ to 2 hours. The centre of a hind quarter immediately after removal from an oven after two hours' cooking had a mean temperature of 78 degrees Cent. for five pieces sampled. The stones after cooking were a little hotter than warm and could be handled with bare hands.

The results indicated that large chunks of meat were not thoroughly cooked and the lower mean temperatures at Tambul were due to the shallow ovens which also contained relatively fewer hot stones. Following cooking, the meat rapidly cools, further handling occurs, and the same sources of contamination are present—feet, flies, dogs and so on. It is after cooking that contamination is most significant and the arguments and discussions concerning the distribution may continue for a whole day. In transit to its destination, a half side of pork may change hands two to five times and reach consumption point one to four days later. A day or more may then elapse before the pork is further cut up and a second distribution held. The meat is re-heated in a smaller earth oven so that any prior bacterial spoiling becomes a potent culture with a high infective dose. It may be assumed that the cooking temperatures will be the same. The redistribution and piece-meal consumption of this meat increases further the possibilities of food poisoning occurring and it is probably this meat which causes the prolonged upper abdominal pain of which so many people complain after pork eating (Nilles, 1950).

From the foregoing, it may be concluded that the likelihood of disease spread is much greater in the large pig ceremonies than in the much smaller marriage and death distributions, where there is a limit to the number of pigs killed and a smaller number of recipients. Bridal payments do take place within the framework...
of the larger ceremonies and stacks of pork quarters and halves were seen at Goglme for this purpose.

**Sources of Infection.**

1. **Pigs and pork.** *Cl. perfringens* was recovered from the intestinal contents of 53 and 322 pigs chosen at random from pigs killed at Korfena, Tambul and Goglme. All strains isolated proved to be Type A and no Type C strains of this organism were recovered. From 92 samples of cooked and uncooked pork, collected mostly from the medial aspect of the hind-quarters where contamination was considered to be most likely, 15 isolations of *Cl. perfringens* Type A were obtained. Again no Type C strains were recovered. These samples included 18 cooked bowel specimens. On only five occasions, remnants of a pig (hair, bone and fat) suspected as a source of origin for a case of enteritis necroticans, and *Cl. perfringens* Type A was obtained each time but no Type C strains. The failure to enlarge the samples from this latter group was due primarily to the late arrival of cases to hospital and the difficulty in obtaining meal remnants. All traces of meat had gone by the time attempts to get such samples were made. The general reluctance of the people to blame pork as a cause also added to this difficulty.

2. **Human population.** A one in ten systematic sample of faeces of a normal human population failed to yield any *Cl. perfringens* Type C strains. This survey was carried out independently of any pig feasting activity, although in the Upper Chimbu sampling at Goglme, Goromaugo and Kurumogl was undertaken one month following the pig killing there. The results were as follows:—

<table>
<thead>
<tr>
<th></th>
<th>Faeces examined</th>
<th>Isolation of <em>Cl. perfringens</em> Type A</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chuaue</td>
<td>100</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Upper Chimu</td>
<td>100</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>Wabag</td>
<td>68</td>
<td>12</td>
<td>18</td>
</tr>
<tr>
<td>Tari</td>
<td>100</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Lake Kopigao</td>
<td>100</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>468</strong></td>
<td><strong>117</strong></td>
<td><strong>25</strong></td>
</tr>
</tbody>
</table>

**Serological Studies.**

In a normal population sample of 216 persons, 154 (71.3 per cent.) had 0.5 units or more of *Cl. perfringens* beta antitoxin whereas only 4 in a control group of 42 Europeans had such detectable levels. In this normal population there were significantly different levels between individuals from high and low prevalence areas, and between this group and patients with Pig-bel and their contacts (Murrell et al., 1966). Males had a slightly greater immune status than females but the difference was not significant. These investigations together with a rise in beta antitoxin levels in the clinical disease lent further support to the role *Cl. perfringens* plays in the aetiology of Pig-bel. Specific *Cl. perfringens* Type C antisera also significantly reduced case mortality.

**DISCUSSION.**

The aetiology suggests that enteritis necroticans or Pig-bel can be included in with the well-documented group of enterotoxaemic diseases in animals. The mystery remains however as to whether *Cl. perfringens* Type C produces disease by exogenous ingestion or endogenous proliferation secondary to other local factors in the upper intestinal tract. In animals exogenous contaminated food types seem to occur in young animals whereas stimulation of resident gut population by dietary changes produces the endogenous situation in older animals.

The German outbreaks of Darmbrand had well defined seasonal distributions over the years 1947-1948, reaching pandemic levels during the mid and late summer months of those years (Kloos and Brummond, 1951). The disease was more prevalent in cities than in the rural areas. A noteworthy difference in Pig-bel from its German counterpart was the age distribution. In Darmbrand people in the fourth to sixth decades were most affected.

The occurrence of the disease in childhood in New Guinea is readily explained by the dietary practice associated with pork feasting. With the larger pig cycles occurring at three to ten yearly intervals, it is possible that the younger age groups have an initial exposure to massive pork meals. Infants without teeth are not offered solid foods, and toddlers, who are breast fed up to the age of two and one half to three years are given only token amounts of pork. Only three patients in the series reviewed were under two years. The belief that pork imparts strength into the individual is practically demonstrated by encouraging children, especially males, to consume as much as possible. Particular organs, such as the genitalia, liver and kidneys, are also reserved for children.
to eat. Burchett (1964) reported to the author that in the Baiyer River outbreaks in 1962 children actively refused further meals offered to them by their parents because of their fear of becoming ill.

The reluctance of older people to seek medical care, the general regard that illness in the older generation is due to ‘old age’ and the lower life expectancy, account for the fewer case reports in people over 40 years of age. The life expectancy of the Highlander is probably lower than that estimated in life tables by Scragg (1954) for New Ireland natives of New Guinea.

The sex distribution in New Guinea corresponded with that in Germany (2.2 males: 1 female). This distribution may be influenced by the greater frequency with which males seek medical care as indicated by a higher bed occupancy rate both in Papua (Campbell and Arthur, 1964), and the Territory as a whole (Department of Public Health, 1964).

More females contracted the disease than males in the 16 to 20 year age group. At marriage feasts the bride and prospective brides are encouraged to consume unusually large amounts of pork to encourage fertility. This possibly explains the distribution of the disease in this group.

The evidence that large-scale pig-killing activities influence the prevalence and spread of enteritis necroticans in the Highlands is circumstantial. It would appear from the trends in admission figures that this cultural practice influences the prevalence of diarrhoeal disease in the localities of the hospitals reviewed. The possibility that coincident gastro-enteric infections due to a virus or other causes occurred has still to be excluded. In the presence of such a coincidence, the spread of these pathogens would be greatly assisted by consuming contaminated pork segments involved in exchanges. The relative increase in hospital admissions for diarrhoea at Kundiawa following this activity in two separate areas during two different times of the same year suggest an aetiological relationship.

A more accurate index of the morbidity and mortality following pig-feasting could be obtained by measuring the diarrhoeal attack rate in a population sample. Difficulties apparent in this approach were found to be a reluctance of the people to implicate pork as a cause of diarrhoea, and the problem of accounting for people before, during and after the feasting due to the transient migrations which naturally occurred at these times. A lot more anthropological work will be necessary in order to trace the origins and destinies of pork transactions in order to reveal the true epidemiological story.

A significantly high level of Cl. perfringens beta antitoxin was found in contact persons at risk. Perhaps some toxin neutralizing substance in the bowel limits the distribution of the disease in persons at risk. This has been postulated in the case of food poisoning due to Cl. perfringens Type A (Goudie and Duncan, 1956).

It is postulated that the pathogenesis commences with the action of powerful toxins in the upper intestine and this genesis is then stimulated by additional factors, intrinsic and extrinsic, favouring an overwhelming toxæmia of the host. The role that other faecal and oral flora play in this toxæmia requires further investigation. Differential bacteriological analysis of organisms of the bowel flora such as B. coli, Paracolon sp., Bacteroides sp., Strep. faecalis and Proteus mirabilis normally present in bowel obstructed areas needs to be worked out in the New Guinea disease.

The large pork meal, which may or may not contain preformed toxin and a high helminthic infestation, possibly predisposes to motility changes, spasm on one side and stony on the other. This favours further bacterial growth and toxin production setting in motion a chain of events which eventually leads to total bowel necrosis.

The beta toxin of the New Guinea strains when injected subcutaneously into guinea pigs gave a bluish gelatinous necrotic lesion. This was the basis of the toxin-antitoxin neutralization method of determining antitoxin levels (Glenny et al., 1931). Zeissler maintained that the variable pathogenicity in his Type F strains was probably due to slight differences in toxin production by the organism and host susceptibility. He believed that individual variations in this isolate pathogenicity explained the wide range of clinical types of Darmbrand. Most German writers on the subject concluded that Cl. perfringens Type F was probably the initiating infective agent introduced in the diet. The infection failed to establish itself unless other dietary indiscretions occurred (Pietzonka and Rassfeld-Stemberg, 1950). This situation existed in the post-war occupation of Germany, and is analogous to the dietary changes invoked by pork feasting in New Guinea.
McLennan (1962) In his excellent monograph on the histotoxic clostridial infections of man states “ Clostridia are at most facultative pathogens, able to gain a footing and produce those effects which we speak of as disease, only when the tissues of the primary lesion have been altered to the most important pre-requisite for clostridial infection (as distinct from clostridial contamination), that there must be present an area of lower oxidation-reduction potential.”

Because a direct food-borne epidemiological sequence was not demonstrated bacteriologically, further research directed to answer such questions as to why some patients failed to develop ileus, whether other exciting stimuli were operative before or after the pig meal, and why all participants of a contaminated meal were not equally affected seems indicated.

SUMMARY.

The cause of epidemic intestinal gangrene known as Pig-bel or enteritis necroticans is due to invasion by Cl. welchii, in particular, to Type C strains which produce beta toxin. This toxin is lethal, necrotizing and probably induces arteriolar thrombosis and necrosis. The sequence of events leading to the establishment of this infection may involve a number of mechanisms, because a simple food poisoning epidemiology was not firmly established. The radical dietary changes invoked by pork feasting, subsequent pork engorgement and pre-existing immunity probably influence the pathogenesis. This aspect of the disease seems analogous to the enterotoxemias of animals caused by Types B, C and D organisms of the Cl. welchii (Cl. perfringens) group.

ACKNOWLEDGMENTS.

I am indebted to the Director and to members of the Papua and New Guinea Research Advisory Council for their guidance and help. Drs. R. Roderigue, L. Roth, C. Conner, C. Mathews, L. Malcolm and F. Smith graciously provided clinical data.

I owe deep gratitude to Mr. J. Egerton and Dr. P. Walker who isolated and typed the strains of Cl. perfringens and to Mrs. J. Samels of the Wellcome Laboratories also provided the specific Type C antiserum.

REFERENCES.


THE PATHOGENESIS OF PIG-BEL IN PAPUA NEW GUINEA

Gregor Lawrence FRACP*

Introduction:

In Western countries necrotising enteritis is a relatively unusual disease, except in the premature infant and apart from a dramatic temporally limited epidemic involving people in Northern Germany, and Denmark at the end of World War II. The recognition of a similar disease endemic in Papua New Guinea, was a very important finding both in regard to the pathogenesis of the disease and for health workers involved in treatment and prevention.

Pig-bel usually follows a high protein meal, there is a latent period of some hours to some days before the victim develops abdominal pain, vomiting and diarrhoea which often contains blood. Diarrhoea is usually short lived and followed in moderate and severe cases by constipation as intestinal obstruction due to the damaged gut develops. The clinical features of pig-bel are described in other papers in this issue.

The incidence of pig-bel is very variable. Using hospital admission data the incidence in areas served by the hospital changes greatly from year to year. In about 7500 children aged 1 to 15 in Sina Sina followed in the vaccine trial, there has been an annual incidence of 3.3/1,000/year over a two year period. Sina Sina is considered to be a high incidence area; in some other areas the incidence has been higher. Mortality in these patients was 12%, lower than most hospital figures, however two of the six children involved died before reaching hospital.

The organism causing pig-bel has been shown to be Clostridium welchii Type C (CWC). There are number of veterinary diseases with similar pathology, patchy necrosis of the upper small gut, also caused by CWC. Clostridium welchii Types produce a number of different toxins. In the case of CWC β toxin is the most important, it is lethal when given to animals intravenously and causes local necrosis if injected into the tissues.

In the animal and human diseases the typical necrotic lesions are the result of absorbed toxins, principally β, on the gut wall. β toxin is a protein that is extremely sensitive to proteolysis. The basic chain of events in pig-bel is consumption of high protein food which leads to rapid growth of CWC, either contaminating the meat meal, or already present in the gut lumen, with production of β toxin that damages the intestinal wall.

This paper will consider the factors involved in allowing this damage to take place.

The Organism

Clostridium welchii is an anaerobic, gram positive, spore forming rod that is divided into types on the basis of the pattern of exotoxins formed during growth. CWC produces mainly α and β toxin, it causes enterotoxaemias with similar gut necrosis in many other animals as well as in man. The types of Cl. welchii cannot be distinguished by morphology or on colonial appearance. Type A organisms are much more common than any of the other types. Cl. welchii is commonly a faecal organism, it multiplies and sporulates in the intestine of man and other animals. Identification of types can be done in mixed cultures by using fluorescent antibodies produced against the bacterial cells themselves. The types have different surface antigens and

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this method allows the easy demonstration of CWC in the presence of a great numerical excess of Type A cells.

CWC has been shown to be ubiquitous in the Highland environment, present in the stools of over half the people and their pigs and easily demonstrated in village soil samples.\(^\text{12}\)

Another aspect of the biology of CWC that is important in relation to pig-bel is its sporulation. CWC readily forms spores that are relatively heat stable, withstanding heating for some minutes to over 95°C. In the case of the German disease CWC was initially named Type F because of its extreme heat resistance surviving boiling at 100°C for four to six hours.\(^\text{13}\) The New Guinea strains are not as heat stable as this but stand the temperatures reached in parts of the ground oven cooking used in the Highlands. The lower temperature of boiling water here (95°C) also assists its survival. CWC has been found in the soil of mumu ovens in which pig meat involved in a case of pig-bel was cooked.

Spores of CWC exhibit the phenomenon called heat shocking. When a piece of contaminated food is cooked the vegetative organisms are killed. As the food cools the spores, not killed by the temperature reached, all begin to grow at once. After a short time they begin to make spores again. This ability of Cl. welchii to form relatively heat resistant spores, the phenomenon of heat shocking and the very rapid growth of Cl. welchii make it a frequent contaminant of food and a common cause of food poisoning.\(^\text{14}\) Repeated heating and cooling of meat, as is often practiced in the village, is particularly dangerous as a multiplier effect occurs which can lead to extremely high levels of Cl. welchii on the food. So Highland meat may often be heavily populated with vegetative and spore forms of CWC some of which will survive passing through the stomach and begin growing rapidly in the small intestine.

Cl. welchii Type A food poisoning is characteristically caused by strains of Cl. welchii that produce an enterotoxin at the time of sporulation.\(^\text{15}\) CWC strains have been shown to produce this enterotoxin too.\(^\text{16}\) The diarrhoea and vomiting seen at the beginning of pig-bel may be in some cases related to enterotoxin. The enterotoxin probably has no importance in the production of the characteristic pathology seen in pig-bel.

The Toxins

CWC produces the major toxins \(\alpha\) and \(\beta\), other toxins may be produced too. \(\alpha\) toxin is a lethal necrotising toxin that is a lecithinase, and it is produced by all strains of Cl. welchii. Although enteritis in fowls can be caused by Type A strains and Type A strains may contribute to the disease after gut damage by \(\beta\) toxin, \(\alpha\) toxin is probably not of major importance in the aetiology of pig-bel.

\(\beta\) toxin is essential for the production of the veterinary enterotoxaemias\(^\text{17}\) and probably for pig-bel in man. It is a protein exotoxin made by CWC during active growth. It is lethal, necrotising and extremely rapidly destroyed by proteases.\(^\text{18}\) The susceptibility of \(\beta\) toxin to proteolysis is central to the present theory on the pathogenesis of pig-bel.

Purified \(\beta\) toxin has some interesting properties. When injected intraderrally in to the skin of depilated guinea pigs a necrotic patch develops. The appearance of these patches is very reminiscent of the necrotic patches seen in the gut in pig-bel - a yellowish centre surrounded by a haemorrhagic ring at its periphery.

Given intravenously in mice, \(\beta\) toxin is lethal. In doses of 1 \(\mu\)g death occurs in forty minutes to two hours or so. If antibody is given intravenously the animal can be protected, but only if the delay between giving toxin and antibody is short, ten minutes or less. This suggests that \(\beta\) toxin has its effect very quickly, or that it is bound in the body and then
becomes inaccessible to antibody.

Many patients who develop pig-bel show a rise in \( \beta \) anti-toxin after the illness. The presence of detectable \( \beta \) antitoxin in the blood is thought to indicate previous pig-bel, in many cases of mild severity. But in Rooney and Shepherd’s series of patients who had a laparotomy for pig-bel\(^{19}\) and in whom antibody levels were measured, seven out of seventeen did not develop raised \( \beta \) antitoxin levels. This may be due to the small amount of \( \beta \) toxin involved in causing tissue damage and to its rapid destruction in the tissues by lysosomal and other proteases released with tissue death. \( \beta \) toxin has been said to reduce the motility of intestinal villi,\(^{20}\) perhaps initially leading to local stasis in the small gut and allowing more favourable conditions for toxin, being rapidly formed by organisms overgrowing in the bowel contents, to cause more damage to the mucosa and for attachment of organism to the villi. The motility changes described\(^{20}\) were non-specific and were accompanied by severe haemorrhagic effects in the mucosa. This work has not separated any effects of \( \beta \) toxin on motility from its general necrotising properties.

In animal experiments the pathological lesions of necrotising enteritis can be caused by giving a toxic filtrate of CWC containing toxins but no organisms.\(^{17}\) In these experiments in the neonatal pig and in the guinea pig the conditions are not those found in the natural disease here. With guinea pigs the toxic filtrate has to be directly injected into the small bowel at laparotomy. The lesions could not be produced by intragastric dosing, presumably because of destruction of the toxin in the stomach and upper intestine by proteases. But the demonstration that \( \beta \) toxin, without organisms, can cause full thickness necrosis of the intestine, is important when considering the pathogenesis of pig-bel.

In recent experiments in Goroka, a toxic filtrate containing high levels of penicillin and lincomycin produced small bowel pathology, showing that the toxin’s effect was direct and the changes were not due to secondary overgrowth of pathogenic organisms already present in the lumen.

### The Role of Low Protease Levels and Trypsin Inhibitors

When considering the pathogenesis of pig-bel the epidemiology is important. Papua New Guineans get pig-bel; Europeans resident in Papua New Guinea, with one exception, do not. Judging from the history of Darmbrand, as the disease in Germany was called, and from sporadic cases in the literature, Europeans are not intrinsically immune. We have demonstrated CWC in the stools of Europeans here, so, presumably their food is sometimes contaminated with the organism. Why did people in Europe suffer with this disease over a few years only, while it continues in Papua New Guinea endemically? One of the striking things about the German population at the time was a high incidence of malnutrition; in the area where Darmbrand was very common about 70%\(^{21}\) of the population was clinically malnourished. Eating of unusually rich food was also thought to be a factor.

Low protein diet and protein malnutrition lead to decreased levels of proteases in the pancreatic secretions. The malnutrition in Germany may have led to very low levels of trypsin activity, so that \( \beta \) toxin in the gut lumen was not destroyed. In the Papua New Guinea Highlands the normal diet is very low in protein.\(^{22}\) Although clinical malnutrition is not common, subnutrition is; children are small for age and will grow faster if their diet is supplemented.\(^{23}\)

Experimental work with guinea pigs showed that pig-bel-like lesions could be produced if animals were given growing cultures of CWC intragastrically with raw soy-bean flour, which contains inhibitors
of trypsin, but not if the soy-bean flour was first autoclaved destroying the inhibitor. Protein deficient guinea pigs had growing cultures of CWC introduced into the stomach with no effect. But, if the culture was mixed with raw sweet-potato flour first, lesions very similar to those in pig-bel were produced and the animals died. If the sweet-potato flour was autoclaved first no lesions were produced.24

Sweet potato also contains inhibitors of trypsin which are stable at the temperatures reached in normal cooking in the Highlands. The protection of β toxin from proteolysis afforded by the combination of low levels of trypsin and the presence of trypsin inhibitors in the staple diet probably explains the persistence of pig-bel in Papua New Guinea25. Eating sporadic meals of meat provides a good medium for rapid growth of the organism as well as introducing substrate excess to compete for any trypsin present. Another contributing factor may be the presence of trypsin inhibitors in the secretions of Ascaris lumbricoides, which is commonly present in patients with pig-bel. In the chick, infestation with a similar parasite has been shown to delay absorption of dietary protein somewhat suggesting that protein digestion was delayed, possibly due to the presence of inhibitors.

Sugiura et al.26 have described heat stable inhibitors of trypsin in sweet potato. The inhibitor inhibits trypsin only, but not chymotrypsin, the other major protease in pancreatic juice. In monkeys it has been shown that protein deficiency leads to a much more marked decrease in chymotrypsin levels than in those of trypsin.27 In fact, chymotrypsin secretion ceased in the animals studied while trypsin was still being secreted at lowered levels. So, in Highlanders the sweet potato inhibitor might effectively inhibit a large proportion of their pancreatic proteolytic activity. Animals on a high protein diet can compensate for the presence of dietary inhibitors by over-secretion of proteases.28 But in New Guinea, because of dietary inadequacy and reduced stimulation due to low levels of protein in the gut lumen, this is probably not possible.

Using the gelatin film test I have shown low levels of protease activity in the stools of PNG children in Goroka Hospital, who had been on a normal village diet before admission compared with people on a European diet.

The explanation for the non-appearance of pig-bel in Europeans in Goroka may be that their customary good or over-nutrition leads to an abundance of proteases in the upper small intestine, easily able to destroy any β toxin being made there. The disappearance of Darmbrand in Germany would then be attributable to improving nutrition and the return of high levels of trypsic activity.

The case of pig-bel that occurred here in a European, was said to have been in a heavy drinker, who had not eaten meat for some time prior to taking part in a village pig-feast. His nutrition may have been poor and it is possible that his pancreatic secretory capacity was low as a result of chronic pancreatic disease. Other sporadic cases of necrotising enteritis in the Western world have occurred in people malnourished because of illness or gut disease.29 The condition is well recognised following gastric surgery where there is fasting and often physical by-pass of the upper duodenum with reduced stimulus to pancreatic secretion and poor mixing of enzymes and gut contents.

Guinea pig experiments have shown the importance of multiplication of organisms in the upper gut. Animals did not get pig-bel when dosed in tragastrically with a growing 4 hour culture containing high levels of toxin and a protease inhibitor aprotinin (Trasylol, Bayer), but in which the potential for further growth was limited due to a lack of carbohydrate substrate. If the same procedure was followed, but the dose mixture contained autoclaved sweet potato and meat, lesions occurred. The presence of substrate for growth...
and inhibitor to protect β toxin was necessary. CWC culture with autoclaved sweet potato (inhibitors destroyed) alone did not produce lesions after intragastric dosing.

**Studies from Veterinary Diseases**

Bullen and Scarisbrick31 showed that feeding of enormous numbers of pathogenic organisms to sheep did not reproduce Type D enterotoxaemia except when the animal was overfed at the same time. It appears that those ingested organisms that survive passage through the stomach multiply for a limited period in the upper small bowel. In the presence of a sudden change of diet conditions are such that more extensive proliferation and toxin formation with subsequent damage can occur. There are two basic models for CWC enterotoxaemia in the veterinary diseases: one where the organism is already present in the gut, the other where it is introduced on contaminated food. In the sheep the CWC or Type B is a rumen commensal until a change in conditions leads to sudden overgrowth with increased toxin formation and the initiation of disease. In the neonatal pig the organism is eaten with milk because of faecal contamination of the sow’s teats. These organisms can grow rapidly in the piglet’s intestine where gastric and pancreatic secretion is very low. In addition, pigs obtain their maternal antibodies in colostrum rather than transplacentally as in man. The colostral antibodies are protected from tryptic destruction by the presence of colostral trypsin inhibitors. Griner32 suggested that this inhibition with subsequent protection of β toxin was the basic cause of necrotising enteritis in piglets.

In pig-bel in man it seems likely that in many cases the CWC is a contaminant on the protein food that precedes the onset of illness. However, we have seen cases where the food was most unlikely to have been heavily contaminated, such as tinned meat or fish. In these cases and probably in others the CWC may have been a resident or transient in the upper small intestine which then overgrew with a change in environment. One patient seen had eaten pig a week before becoming ill. The pig had been kept in the roof of his father’s house for some weeks and was putrid. He showed no ill effects from eating the pig, but a week later ate a very large meal of marita soup made from the pandanus palm, which is very high in fat and presumably rich in protein. The next day he became ill with pig-bel.

Malnutrition has been shown to increase the number of organisms present in the usually lightly contaminated upper small intestine.35 Enteric parasites may harbour organisms in their intestinal tract, increasing the contamination in the host gut lumen.

**Experiments Relating to Attachment of Clostridia to Villi**

With many enteric pathogens such as entero-pathogenic strains of E. coli, attachment of the organism to the villous surface has been considered essential in the production of disease.34 In the case of these organisms there is an area on the organism that specifically binds to a part of the villous surface. Proximity obviously enhances any effect secreted material will have on the villi. Arbuckle35 has emphasised the importance of attachment in CWC enteritis in piglets. Examination of sections of gut in pig-bel and experimentally produced pig-bel in guinea-pigs shows the villi covered with gram positive rods. However, Arbuckle has not shown that attachment precedes damage to the villus tip by toxin, and it seems likely that toxin damage precedes attachment by the organisms. In a series of experiments in Type A enteritis of chicks, Al-Sheikly36 showed that damage to the villus tip occurred within 15 minutes of instillation of a bacteria free toxin filtrate; the subsequent changes and mucosal shedding examined by electron microscopy look very similar to the early changes Arbuckle described. After toxin damage organisms can attach to the sur-
face and if proliferating there, the effects of the toxin being made will be maximal.

Shutz working in Germany on Darmbrand was able to produce lesions in experimental animals when given growing cultures if a damaging material, was given at the same time. This suggests that mucosal damage, from toxin, parasites or physical causes, is necessary to begin pig-bel.

Further work using washed organisms would be of great interest. To see if attachment can occur without prior toxin damage, and to see if more pathogenic organisms are characterised by the ability to attach to the mucosa.

**Immunity**

The arguments regarding attachment have some significance in relation to immunity against CWC enterotoxaemia. IgG antibodies, produced after the injection of toxoids provide protection against the veterinary diseases and in experimentally produced pig-bel. IgG antibodies pass up the villus and leak out into the lumen playing a part in gastrointestinal immunity. Small amounts of IgG present might prevent initial damage by protecting the villus in the vulnerable short period of rapid organism growth and high levels of toxin production following the initiating meal. If the initial damage necessarily precedes attachment followed by further multiplication and toxin damage, then small amounts of circulating IgG might be protective. We have not seen second episodes of pig-bel in Goroka apart from one recent case where Mr. F. Smith operated on a patient with old resolving pig-bel who had a couple of fresh looking necrotic areas near the obstructive lesion caused by the first attack.

That most pig-bel occurs in children suggests a disease in which immunity is acquired. The serological findings of Murrell support this, with the oldest age groups having a larger proportion with circulating β antitoxin. In Germany the age distribution was different. Good nutrition and high trypsin levels protected the population until the war when privation with malnutrition removed their enzymatic protection. Cases of Darmbrand occurred in all ages.

Obviously a large factor in the natural antibody protection against pig-bel must be IgA immunity, both anti-toxin and antibody activity directed against surface determinants on the organism. In veterinary practice immunisation with toxoid and bacterins - material that raises antibodies to the bacterial surface as well has been shown to give improved protection. IgA antibody to gut pathogens has been shown to prevent specific attachment. Naturally induced immunity is probably directed against the toxin and the organism.

**Pathology**

The pathology of pig-bel is striking. Patchy necrotic areas are seen in the intestine with a strikingly banded appearance- “Tiger-bel” (Smith). The banded appearance suggests a vascular basis for the lesion, but that the lesions are the result of absorbed toxin seems more likely. The typical antimesenteric necrotic patches are full thickness necrosis of the gut wall. Smaller spotty lesions which are also full thickness necrotic areas are seen; these spots are tiny, only 2-3 mm in diameter, yet the necrosis extends right through the gut wall.

It does not seem possible that vascular blockage could cause these lesions. It seems more likely that they are the result of tissue necrosis along the route of toxin absorption, perhaps from an area of damaged mucosa or an area of local damage and organism attachment. Much of the descriptive pathology has referred to the patchy areas of necrosis in pig-bel as in-farction. But Roth noted in the beginning that the mesenteric arteries were pulsatile right up to the gut. In areas of
patchy necrosis thrombosis of vessels is seen in the area of separation between necrotic and living tissue, blocked vessels are found in the zone between complete necrosis and less heavily damaged tissues. In general changes are more marked in veins, the draining vessels where Cooke considers endothelial proliferation to be a hallmark of pig-bel. Although these changes could cause the demonstrated necrosis it seems more likely that they are changes occurring after toxin damage. In guinea pig experimental lesions full thickness necrosis very similar to the human disease can be demonstrated in animals killed 24 hours after exposure to growing cultures and trypsin inhibitors. The vascular changes are not seen, suggesting that, at least in the guinea pig, the necrotic areas are not the result of infarction following vascular obstruction.

The other aspect of the pathology that has not received enough attention is the gross thickening and oedema of the gut wall in areas where full thickness damage has not occurred. This thickening is at least partially a result of lymphatic obstruction. In pig-bel the mesenteric glands draining the damaged area are invariably greatly enlarged and often haemorrhagic. Dilated tortuous lymphatics can be seen running over the serosal surface of the gut, cystic fluid filled spaces are sometimes seen in the gut wall and in most cases when a specimen is transsected clear fluid oozes from the cut surface. The lymphatic obstruction, which also contributes to the nutritional problems that develop in pig-bel, is probably related to the effects of absorbed toxin along the course of the lymphatics.

The patchy segmental distribution of the lesions is very striking. On examination of operative specimens, small ridges of surviving tissue can be found, often surrounded by areas in which the mucosa is totally necrotic. It is difficult to ascribe this distribution to vascular changes followed by infarction. If the initial lesion seen in pig-bel is necrosis caused by absorbed toxin, then the patchy distribution must be caused by non uniform uptake of toxin. Local damage to mucosa by parasites might play some part. Recent work on the processing of antigens in the gut suggests another possibility. Peyer’s patches are lymphoid tissue aggregates that take up gut antigens through a specialised mucosa after which lymphoid cells are stimulated to produce IgA antibodies. These cells divide and travel up the thoracic duct and then home on the gut wall where they populate the lamina propria and produce surface antibodies. It has been shown in small bowel biopsies in man that similar small lymphoid bodies occur in the upper jejunum. It is possible that lymphoid tissue rapidly takes up the very necrotising β toxin which then damages the tissue and surrounding areas allowing CWC to attach to the mucosa, leading to further toxin absorption and setting in train the chain of events leading to pig-bel, and perhaps explaining the patchy distribution.

Time course of Pig-bel lesions

The temporal occurrence of the lesions in pig-bel has been discussed previously. The changes in pig-bel occur in a relatively short period of time after the offending high protein meal. The pathological chain of events occurs in a short time with overgrowth in the upper small gut, toxin damage, stasis, and attachment to damaged mucosa. The luminal contents containing growing organisms, inflammatory exudate and tissue breakdown products could not be expected to contain high levels of β toxin capable of initiating disease further down for long periods of time when the time course of β toxin levels in culture is considered. In vitro cultures of CWC result in maximal levels of β toxin about 3½ to 4 hours after inoculation. The subsequent decline in β toxin has been attributed, apart from exhaustion of carbohydrate for growth, to production of proteolytic enzymes in the culture by the organism itself.
β antitoxin given intravenously before, at the same time as, or two hours after intragastric dosing with growing culture and soybean flour protects the guinea pig from induced pig-bel. Two of five guinea pigs given β antitoxin seven hours after dosing developed typical intestinal lesions of experimental pig-bel, even though the clinical disease in this situation does not become apparent for at least 24 hours after dosing.

In most human cases the lesions are localised and the subsequent history of the case is the result of efforts to repair this damage. In some cases, where the small bowel is affected in its entire length, the situation may be more analogous to gas gangrene with tissue invasion and multiplication of the clostridia. This is not common. After the initial damage other organisms in the gut may become involved in invading the necrotic areas. Type A organisms from the faecal flora may play a part. The strain of CWC used in producing experimental pig-bel, although it produces gross gut lesions, is not very pathogenic when a culture is injected into the thighs of mice. Progressive clostridial myonecrosis does not result, just local gangrene of the leg without progressive disease. Variation in toxin production and pathogenicity is well known in Clostridia. Some of the differences in clinical cases must undoubtedly be due to differences in the organism strains.

Dietary aspects

As discussed earlier, Darmbrand occurred in Germany in a very malnourished population recovering from the hardships of war. The onset of the disease was often related to eating unusually rich food before the onset of symptoms. Meat and high carbohydrate meals were often implicated. After about three years Darmbrand suddenly became much less common and then virtually disappeared. The explanation for this probably lay in improved nutrition with more proteolytic activity in the gut. In Papua New Guinea pig-bel remains, and has, according to local people, been present for a long time. The brother of a present Sina Sina leader probably died of it about fifty years ago. The reasons for its persistence lie in part in the dietary practices in the Highlands.

The diet is very low in protein. Growth in Highland children is retarded, at least partly because of inadequate protein in the diet, although energy is low as well. Sweet potato (Ipomoea batatas) is the staple. It provides a very high proportion of the calories eaten. Sweet potato is eaten every day. It is tasty, bulky, high yielding and relatively easy to grow. The trouble with sweet potato is that it forms such a large proportion of the diet. People have a steady intake of trypsin inhibitor with a very low protein diet. The normal response to consumed inhibitors is pancreatic hypertrophy and compensatory over secretion, which may be difficult with a low protein diet.

Another factor possibly increasing the effects of inhibitors is suggested by the recent discovery of the recirculation of trypsin and chymotrypsin. It has been shown in the rabbit that trypsin and chymotrypsin are absorbed whole in the upper small intestine and quite rapidly secreted again. If this pertains to man and is of reasonable magnitude, then the results of eating inhibitors coupled with a very low protein diet may be even more marked. If the stored pancreatic enzymes available for secretion at the beginning of a meal normally are recycled a number of times during that meal then binding by an inhibitor early would prevent this and the subject would depend on enzymes being made de novo when the capacity was reduced because of a very low protein diet. In growing children the effects would be increased.

All this is of importance because of the sporadic way in which meat is eaten in the Highlands. Pigs are large and they are not killed and eaten very often. Even in Tari Smith has found that eating pig meat is for most of the population about a once a week occasion. Infrequent meat-
containing meals would contribute less nutritionally, than the same total amount if eaten more frequently over a period. They would also introduce substrate excess to the already inadequate proteolytic capacity. Most cases of pig-bel are the result of eating pig from small local celebrations such as bridal exchanges rather than the large widely spaced pig-feasts.

If sweet potato formed a smaller proportion of the diet, other crops contributing more, I think pig-bel would be much less common.

It is obvious that changes in cropping and eating habits are long-term matters. The other possible dietary change, that of killing and eating of the pigs more frequently may actually be dangerous. Smith has reported that pig is eaten at least once per week in a lot of Tari households. I think this may be more often than is usual in Sina Sina. Yet, in Tari, the mortality from pig-bel is much higher than in Sina Sina. More frequent eating of meat, if not enough to result in improved protein nutrition, and coupled with persistence of the sweet potato staple and of CWC in the environment, may lead to more frequent pig-bel.

Advice on changing dietary habits to eliminate pig-bel should be given with caution.

Conclusion

Pig-bel persists in the Papua New Guinea Highlands because of a peculiar group of circumstances. CWC is commonly present in the environment. Undernutrition, the consumption of inhibitors in the dietary staple and intestinal parasites all tend to limit the levels of proteolytic activity in the upper small gut when CWC, either contaminating food, or already present in the intestine, multiplies in the changed environment caused by a high protein meal. β toxin produced by the organism damages the surface of the gut. Motility is impaired and attachment of organisms leads to further toxin damage and the necrotic lesions typical of pig-bel.

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STRONGYLOIDES SPECIES INFESTATION IN YOUNG INFANTS OF PAPUA NEW GUINEA: ASSOCIATION WITH GENERALIZED OEDEMA

John D. Vince, Richard W. Ashford, Michael J. Gratten and Joseph Bana-Koiri

SUMMARY.

Clinical and laboratory details of thirteen infants with “Swollen Belly Sickness” who had abdominal distension, respiratory distress, generalised oedema, and variable disturbance of gastrointestinal function were analysed. The intimate connection between the syndrome and infection with Strongyloides species closely resembling Strongyloides fulleborni - is discussed, and a standard treatment using thiabendazole, plasma transfusion and antibiotics, is proposed.

The Kamea people, known also as the Kukukuku clan, inhabit difficult mountainous terrain some fifty miles north of Kerema, in the Gulf Province. The inaccessibility of their territory, combined with their reputation as fierce warriors, resulted in their relative insulation from the influence of exploration until the early 1960s, when Roman Catholic mission stations were established in Kaintiba and Kanabea. The opening of Menyamya, Kaintiba, and Kanabea airstrips had led to rapidly-increasing Mission and Government influence in the area. Since the introduction of health services, health workers have consistently reported the presence of an apparently previously unknown sickness affecting young babies, which failed to respond to treatment, and which was almost invariably fatal. The sickness, for which the name “Swollen Belly” was used, consisted of respiratory distress, abdominal distension, and generalised oedema. It was both common, and well-recognised by the Kamea people, who regarded the appearance of the swollen abdomen as the end of all hope of the infant’s survival. Early attempts to find the cause of the sickness were inconclusive. The causes of death in two infants on whom post-mor...
back was noted. The abdomen was grossly distended but not tympanitic, there was no splenomegaly, but the liver edge was palpable 3 cm. below the costal margin. Shifting dullness was present, and bowel sounds were high-pitched but not obstructive. Respiratory rate was raised and there was mild intercostal indrawing. Only a few fine crepitations were heard at the bases. Pulse rate was normal. The anterior fontanelle was normotensive, but the infant had a staring expression reported by the Kanabea staff to be typical of such infants. Haemoglobin was 10.5 gm/100 ml and eosinophil count was 24%. Blood culture was negative and the cerebrospinal fluid was crystal clear, with no cells or organisms on microscopy. The serum was noted to be extremely turbid. Total serum protein was subsequently shown to be 3.5 mg/100ml, with albumen of 0.2 mg/100 ml. Abdominal paracentesis produced opalescent fluid. Examination of the greenish stool revealed masses of ova, (404,000 eggs/ml) many in chain-like formation, diagnosed as those of a *Strongyloides* species.

Treatment with thiabendazole (approximately 25 mg/kg/twice daily for 3 days) was commenced, and antibiotics withheld. There seemed to be some improvement in the child’s condition initially but the abdominal distension and oedema persisted, and because of subsequent slight deterioration in condition antibiotic therapy was commenced four days after admission. On the sixth day, although the respiratory signs had improved, the baby looked very unwell, the abdominal distension had increased slightly, and there was no improvement in the oedema. There was no hepatomegaly, and there were no other signs of cardiac failure. 150 ml of plasma was given. At this stage the baby appeared to be in a terminal condition and, in accordance with the parents’ wishes, treatment was discon- tinued and he was allowed home, presumably to die at home. Eleven days later the child was brought back to the clinic: there was no abdominal distension and no oedema and, though he appeared a little weak, he was otherwise well.

**Methods.**

All thirteen patients studied were said by the Kanabea Mission staff to be typical of the Swollen Belly Sickness. Six of these patients were seen personally (JV) - four at Port Moresby General Hospital and two at Kanabea Mission. The Hospital records of five patients referred to Kerema Hospital were studied, as were the record and post mortem report of one patient referred to Port Moresby Hospital in 1975, and the post mortem report of one baby who died in Kanabea, whose body was subsequently transferred to Port Moresby. An analysis was made of the presenting symptoms and signs, duration of illness, laboratory data, outcome and, where applicable, post mortem findings of these babies. Separate analyses were made of those babies who were, and who were not, treated with thiabendazole. Histological sections from three post mortem examinations were reviewed by Dr. G. Aitken, Pathologist, Port Moresby General Hospital.

**Results.**

**1. Patients and Outcome.**

There were six male babies and seven females. Of the nine for whom weights were available, one was below the 60th percentile, three below and five above the 80th percentile of standard weight for age. The median age of presentation was approximately eight weeks, with a range of two weeks to approximately six months. The total duration of illness for nine of the cases with available data varied from six days to seven weeks. Six out of seven cases who presented prior to the introduction of specific treatment with thiabendazole died. All those who presented after the introduction of thiabendazole treatment survived, although there was no record of one case having received this drug.

**2. Symptoms and Signs**
Details are shown in Table I and II.

**TABLE I:**

<table>
<thead>
<tr>
<th>SYMPTOMATOLOGY OF SWOLLEN BELLY SICKNESS</th>
<th>PRESENT IN</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISTENDED ABDOMEN</td>
<td>13/13*</td>
</tr>
<tr>
<td>RESPIRATORY DISTRESS</td>
<td>12/12</td>
</tr>
<tr>
<td>VOMITING</td>
<td>5/10</td>
</tr>
<tr>
<td>CONSTIPATION</td>
<td>2/4</td>
</tr>
<tr>
<td>DIARRHOEA</td>
<td>6/6</td>
</tr>
</tbody>
</table>

* Number Data Available

**TABLE II:**

<table>
<thead>
<tr>
<th>SIGNS PRESENT IN SWOLLEN BELLY SICKNESS</th>
<th>PRESENT IN</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISTENDED ABDOMEN</td>
<td>13/13**</td>
</tr>
<tr>
<td>TACHYNOPEA</td>
<td>12/13</td>
</tr>
<tr>
<td>OTHER RESPIRATORY SIGNS</td>
<td>12†/13</td>
</tr>
<tr>
<td>PERIPHERAL OEDEMA</td>
<td>8/11</td>
</tr>
<tr>
<td>SHIFTING DULNESS*</td>
<td>4/8</td>
</tr>
<tr>
<td>HEPATOMEGALY</td>
<td>3/11</td>
</tr>
<tr>
<td>SPLENOMEGALY</td>
<td>1/9</td>
</tr>
<tr>
<td>FEVER ON ADMISSION</td>
<td>4/10</td>
</tr>
</tbody>
</table>

* Ascites confirmed in 7

† Thirteenth patient, aged 6 months, subsequently died.

** Number Data Available
3. Laboratory Investigations.

(a) Haematological. Details are shown in Table III.

(b) Stool. Five babies were reported as having ova of *Strongyloides* species in the stool, and five were reported to have hookworm ova (in one case the report was of hookworm or *Strongyloides*). Results of specimens were not available from the two babies who died in 1974 and 1975.

(c) Serum Proteins. Three patients in whom oedema and ascites were prominent had total serum proteins of 3.2, 3.5, and 2.7 gm/100 ml with albumins of 0.8, 0.2 and 0.2 gm/100 ml, while a fourth patient in whom oedema was not a feature had values of 5.4 and 1.4 gm/100 ml.

(d) Cerebrospinal Fluid. Results were available from five patients. In three there were no leucocytes. In two the fluid was bloodstained, but there appeared to be a relative lymphocytosis the results being:-

<table>
<thead>
<tr>
<th>Polymorphs</th>
<th>Lymphocytes</th>
<th>Red cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>22</td>
<td>&quot;numerous&quot;</td>
</tr>
<tr>
<td>7</td>
<td>18</td>
<td>69</td>
</tr>
</tbody>
</table>

Cultures of these fluids showed no growth.

(e) X-Ray Findings. Signs of consolidation were present in five of the six patients with Chest X-ray reports available. In three patients abdominal X-rays were reported as normal but in one of these there was progression to non specific changes of slightly distended bowel loops with some small fluid levels, and one showed distension of the large bowel.

4. Patients not treated with thiabendazole.

Seven patients presented prior to the discovery of *Strongyloides* described in case 1 and did not receive thiabendazole therapy. There was no record of one patient, who presented after the discovery, having received treatment. Of those eight patients, six died, five between the ages of two and three months. The sixth, who was also exceptional by virtue of lack of respiratory signs, died at the approximate age of seven months. All eight had a distended abdomen, and seven had signs of respiratory distress. Peripheral oedema was a feature of all six who died, but was absent in at least one of the survivors. Ascites was known to be present in five patients, of whom four, who also had pleural effusions, died. Pericardial effusion was found in two fatal cases. Hookworm was reported in the stool of three, and *Strongyloides* in two. Reports for two of the fatal cases were not available, and the stool of one of the survivors (who had ascites) was initially reported as negative for ova. All eight patients received treatment with antibiotics, and two received blood.

5. Patients treated with thiabendazole.

### Table III

<table>
<thead>
<tr>
<th>TABLE III</th>
<th>LABORATORY RESULTS HAEMATOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEDIAN</td>
</tr>
<tr>
<td>HAEMOGLOBIN (gm per 100 mls)</td>
<td>9.4</td>
</tr>
<tr>
<td>WHITE CELL COUNT (per cu mm)</td>
<td>10,700</td>
</tr>
<tr>
<td>EOSINOPHILS (% of WHITE CELL COUNT)</td>
<td>16</td>
</tr>
<tr>
<td>EOSINOPHILS (per cu mm)</td>
<td>1405</td>
</tr>
</tbody>
</table>
Of the five patients who received thiabendazole, none died. All had a distended abdomen, although in one case this was described as minimal at the time of admission, and all had respiratory distress. Gross peripheral oedema and ascites were present in two cases - both seen personally. All were reported to have either hookworm or *Strongyloides* in the stool. All patients received antibiotics. The two patients with oedema received plasma, and one also received blood.

6. Post mortem findings.

Post mortem reports on three babies gave the cause of death as pneumonia in two cases and peritonitis in one. Small and large bowels appeared macroscopically normal, although in one case the mucosa appeared pale. A review of the histological sections from all three post mortems failed to reveal evidence of systemic strongyloidosis. Unfortunately, sections of small and large bowel were available from only one, and in this case no evidence of mucosal involvement was seen.

Discussion.

From the present analysis, it is possible to describe a typical patient with fully-developed “Swollen Belly Sickness” as an infant of either sex, aged around two months, presenting with symptoms of abdominal distension - which apparently may, at least in the early stages, be intermittent - and respiratory distress, and probably with mild diarrhoea and occasional vomiting. Examination will confirm the presence of abdominal distension, with evidence of both gaseous distension and shifting dullness, and there will be obvious signs of respiratory distress. The child may or may not be febrile, and peripheral oedema is present. The haemoglobin level is probably in the low normal range, and there is probably an eosinophilia. Chest X-ray may show minor pneumonic changes. Microscopic examination of the rather loose greenish stool will reveal the presence of a very large number of ova which superficially resemble those of hookworm, but which, on closer examination (see below), are found to be those of *Strongyloides*. Treatment with antibiotics may produce initial improvement, and the oedema may be temporarily relieved following blood or plasma transfusion: but in the majority, in the absence of anti *Strongyloides* treatment the course is that of deterioration to death.

It seems that abdominal distension is the initial sign, and that the appearance of peripheral oedema is - in the absence of adequate treatment - a pre-terminal event. Other features reported but not adequately documented are the presence of a staring expression, and a rather high-pitched cry.

The features thus described are individually of an unspecific nature, with diverse aetiologies: viewed together, however and occurring at this age, they form a specific and highly unusual clinical syndrome. Of particular interest and of almost certain aetiological significance is the finding of nematode ova in the stool of ten of the eleven patients examined. The distinction between the ova of hookworm and *Strongyloides* is, to the untrained eye, not easy, and it seems likely that the ova seen in the stools of all ten patients were in fact those of *Strongyloides*. This seems all the more likely in view of the finding - fully described in a Separate communication (Ashford, R.W., *et al*¹) - of a very high prevalence of *Strongyloides* infection in infants from the area inhabited by the Kamea people.

The reported absence of ova in one affected case who survived in spite of the presence of ascites and the absence of thiabendazole treatment, is puzzling, though it is pertinent to point out that the presence of *Strongyloides* ova in old samples may be surprisingly easy to overlook.

The *Strongyloides* species has been characterised previously (Vince *et al*²).
It is distinguished from *Strongyloides stercoralis* by the absence of the larval form in fresh stool, and by certain morphological differences which render it very similar to *Strongyloides fulleborni* and to the species found in the Kiunga district and described by Kelly (1), *et al*. It is suggested that infection with this *Strongyloides* species is intimately associated with the Swollen Belly Sickness.

The pathological relationship between the “Kanabea *Strongyloides*” infection and the clinical features, however, remains at present speculative. One indication probably lies in the presence of oedema, an important, and previously almost always pre-terminal, feature. Examination of the available data excludes anaemia and heart failure as its prime cause. The very low total serum protein and serum albumin values found in three babies indicate that the oedema is hypoproteinaemic in origin. Deficient protein intake in this age group in this situation is highly unlikely. Renal protein loss is unlikely, renal histology being normal in three cases, and proteinuria being absent in one grossly oedematous baby.

Malabsorption has however been associated with *Strongyloides stercoralis* infections with in some cases, alterations of small bowel histology (Yoeli *et al.* 4, Bartholemew *et al.* 5, and O’Brien 6) and oedema with hypoproteinaemia was a feature in some of the cases described by Huchton and Horn 7.

We have, at present, no specific histological evidence of bowel involvement in our patients, but it is difficult to escape the conclusion that intestinal function is significantly affected by the extremely heavy infection found in our patients; and although a malabsorptive state is possible, it is equally likely that a protein-losing state results. Such a state has been shown to occur in pigs infected with a *Strongyloides* species (Giese *et al.* 8), and Laudanna *et al.* 9 have similarly demonstrated enteric loss of Cr. 51 albumen in one patient infected with *Strongyloides stercoralis*.

The precise aetiology of the respiratory signs and symptoms remains speculative. Such features, in conjunction with the very heavy intestinal infection with the Kanabea *Strongyloides* is suggestive of autoinfection, but we have no evidence that this process occurred in our patients. Whilst abdominal distension may in itself cause respiratory distress in infants the clinical and radiological signs indicated definite respiratory pathology.

Larvae of *Strongyloides stercoralis* have been found in the meninges in association with bacterial meningitis (Owor *et al.* 10) and it is tempting but purely speculative to ascribe the cerebrospinal fluid changes found in two of our patients to larval migration.

As far as we are aware, there are no reports of *Strongyloides* infections occurring in patients as young as ours. The appearance of extremely heavy intestinal infection with signs and symptoms compatible with larval migration in babies as young as two and three weeks of age suggests to us a method of transmission other than that of skin penetration commonly found in nematode infections. Transmammary passage of nematode larvae from adult milk to suckling young in other mammals has been amply documented (Stone W. and Smith F.W.11) and, in the case of *Strongyloides ransomi* infection in pigs, results in a fatal disease of piglets characterised by many of the features we have described (Moncol D.J. and Batte E.G.12). Brown and Girardeau13 recently reported finding larvae of *Strongyloides fulleborni* in one of 113 samples of milk from twenty-five mothers followed from birth, suggesting at least the possibility of human trans-mammary infection with this nematode. Other possibilities - such as transplacental passage - exist, and these, together with the more conventional mode are discussed elsewhere (Ashford *et al*). Obviously the determination of the mode of transmission is crucial to the institution of
preventive measures.

Of the six patients who died, there was post mortem evidence of bacterial infection in three. These findings, and the transient improvement of several patients following treatment with antibiotics indicate a definite but probably secondary role for infecting organisms in the natural history of the illness. It is pertinent that most of the babies who have died from the swollen belly syndrome have done so at the age of two to three months, a time when humoral antibody defences are low. If there is indeed a protein-losing state as we have postulated, the host defences may be further reduced by loss of both immunoglobulins and lymphocytes from the bowel.

In view of the high prevalence of the Kanabea Strongyloides infection found in infants from the Kamea area to which allusion has already been made (Ashford et al.), there remains another problem, namely, the discovery of the factors determining which babies will, and which will not, develop the Swollen Belly Sickness. All our patients were apparently in good health prior to the illness, and the possibility of underlying debilitative states is unlikely. It was not possible to obtain an adequate family history in many cases, and although one patient had one, one four, and one three affected siblings all of whom had died, this cannot be taken as evidence of a familial predisposition. The possibility that “Swollen Belly” babies are for some reason more heavily infected than their compatriots is discussed elsewhere. At present, the problem remains unsolved.

In conclusion, we believe that the “Swollen Belly Sickness”, a hitherto undescribed clinical entity, is intimately associated with infection with a species of Strongyloides closely resembling Strongyloides fulleborni. As a result of our experience, we recommend that the standard treatment of the patients should consist of

1. Thiabendazole 25 mgs./kg./dose twice daily for three days.
2. Plasma, whole blood, or stabilised plasma protein solution, by intravenous infusion at 40 mls./kg., with frusemide 0.1 mls./kg. imi.
3. Broad spectrum antibiotics.
   a) Crystalline Penicillin 50,000units/kg six hourly IVI or imi.
   b) Chloramphenicol 25 mgs/kg six hourly IVI or orally.

ACKNOWLEDGEMENTS.

This work has its origin in the concern of Sister Gwen Daw and members of the staff of Kanabea Mission for the Kamea people, and in their persistence that the Swollen Belly Sickness was a definite entity. We gratefully acknowledge the help and encouragement given to us by Sister Gwen and the Mission staff under the leadership of Father Cyril Blake. Several of the Medical Officers based in Kerema have greatly assisted us, and in particular we thank Dr. Bill Miles, Dr. Andy Hall and Dr. Ron Anderson. Many of our colleagues have contributed by virtue of encouragement, discussion, and direction, and we specially thank Professor Biddulph, Department of Child Health, and Professor Wyatt, Department of Community Medicine, Medical Faculty, University of Papua New Guinea. We are indebted to Dr. Graeme Aitken, Pathologist at Port Moresby General Hospital, for his review of the post mortem histology, and to the Pathology Department and Dr. Andrew Buck, Medical Faculty of the University of Papua New Guinea for the Protein Estimations. We are grateful to the Papua New Guinea Public Health Department and the University Medical Faculty for allowing us to undertake this work. Finally we thank Mrs. Raka O. Natera for her secretarial help.

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STRONGYLOIDES INFECTION IN A MID—MOUNTAIN PAPUA NEW GUINEA COMMUNITY

Results of an Epidemiological Survey

R.W. Ashford,* J.D. Vince,** M.J. Gratten** and J. Bana–Koiri**

SUMMARY

Following our finding that an acute, fatal disease of infants is associated with massive Strongyloides infection, studies are reported here on the status of the infection in the community concerned. The parasite was found to be abundant in children from 3 weeks to 5 years, but apparently rare in adults. Correlations were sought, but not found, between egg output and serum protein levels, albumin–globulin ratio and eosinophil counts. Very heavy infections were seen without apparent disease. Despite the examination of milk and placentae, the mode of transmission to infants remains unknown.

Strongyloides spp. has been found to be associated with generalized oedema in young infants in Papua New Guinea.

Epidemiological surveys of many types have been conducted over a large proportion of Papua New Guinea. However, there are many geographically isolated communities and the results of a survey in one place may not be applicable quite close by. The most significant recent stool surveys are those of Kelly, in which more than 4000 stools were examined from 19 localities throughout the country. Egg-producing Strongyloides were only found at 3 localities, close to sea level, in Western Province. The nearest of these is 500 km from Kanabea, which is in a quite different climatic zone, at 1350 m above sea level. Both free living and parasitic female worms were collected, and these were described by Kelly, Little and Voge who showed them to be similar, though not identical to S. Fulleborni. No studies were carried out on pathogenicity, and infants were not included in Kelly’s survey. Dr. R. L. Muller (pers. comm.) has found similar eggs in stool samples from Irian Jaya.

In Africa, S. fulleborni is thought usually to be a monkey based zoonosis, though it also occurs as an anthropoanosis. Brown and Girardeau showed it to be highly prevalent in infants in Zaire, but also to infect adults freely. They discovered a small number of larvae in breast milk, strongly suggesting this as a means of transmission to infants. Pathogenicity has only been described by Pampiglione and Ricciardi who infected a volunteer, who suffered a variety of non specific, though rather uncomfortable symptoms.

The survey described here was designed to investigate the prevalence of Strongyloides in the Kamea people, and to look for other information bearing on the transmission of the parasite and its pathogenicity.

MATERIALS AND METHODS

Kanabea Mission was visited between November 28 and December 5, 1977, and patrols were carried out to Paina and Manimango, 8 and 4 hours walk distant.

Most of the people attending the clinics at these centres were known to the mission staff, and detailed histories were available. Thus, infants and children below 5 years could be aged accurately, and for women, details were recorded of their reproductive
history and the survival of their offspring.

In response to the reluctance of many people to donate faeces, no attempt was made to select donors. As many specimens as possible were collected from people of all ages. Faeces were collected in containers which had been distributed the previous day; a thick and thin blood film was taken from each faeces donor. Many faeces samples were examined fresh, in order to identify people with heavy infections for treatment, and for culture of the worm. All samples were also preserved in 10% formalin. Helminth eggs were counted in saturated NaCl, in a 0.5 ml counting chamber, but this was unsatisfactory for Strongyloides eggs, as they were attached together in strings, and were also too heavy to float. Counts were therefore repeated after thorough emulsification of the sample in 10% NaOH; then either a 0.5 ml sample, diluted 20 or 100 times was counted on the floor of the chamber, or a 0.1 ml sample diluted 10 times was counted under a 22mm² coverslip. The highest count for any species in any sample was recorded.

Faeces cultures were set up on damp-filter paper, and also on charcoal and sterile soil. Cultured worms were fixed with hot 10% formalin. Parasitic female worms were expelled in the stool of treated patients, and were subsequently collected by searching with a dissecting microscope, and transferred to 70% ethanol.

Milk samples were collected by nursing mothers following careful swabbing of the breast, and were preserved by adding formalin to approximately 10%.

Serum was collected from heavily infected infants, and from various other people. So many infants were infected with Strongyloides that matched controls were unobtainable. Sera were screened for total protein (biuret method) and for globulin and albumin levels by electrophoresis.

Haemoglobin was estimated in those people from whom serum was collected (Spencer method).

Placentae were collected by the mission nurses from some of the few births occurring at the clinic. They were preserved in 10% formal saline and forwarded to Port Moresby for examination of H. & E. stained sections.

RESULTS

Relevant Aspects of the Area and People

Kanabea is at 1350 m; the surrounding area is steeply hilly, from 1000 m to 2500 m, and is completely forested except near the few settlements and tracks. The few rock outcrops are mostly Miocene limestone. The annual rainfall is around 4500 mm and is not distinctly seasonal. Cloud and mist are often continuous for weeks. No temperature records are available.

The most conspicuous feature of the people is their small stature. Their superficial good health is apparently belied by their extremely poor rating in nutritional surveys. No detailed nutritional observations were made, but the formal diet consisted entirely of vegetables: bananas Musa spp, taro Colocasia esculenta, sweet potato Ipomoea batatas, pumpkin Cucurbita spp, and a wide variety of “bush cabbage”, mostly young leaves of Cucurbitaceae and Chenopodiaceae in small quantities. High protein foods are very rarely eaten, though pigs and dogs are present in small numbers, as well as a few semi-feral cats. Wild animals are hunted avidly, and are very sparse. Small birds, rats and frogs, often eaten raw, provide most of the animal protein.

Recent innovations include the introduction of cows, beans, a good walking track joining villages 4 days’ walk apart, cotton clothes and law and order. These changes have met with limited acceptance, and only materially affect people in the immediate vicinity of the main centres. Improved access has allowed a greater number of people to leave in search of
work, and a growing awareness of the rest of the world is enhanced by the increasing number of strangers who visit and come to work in the area.

While no demographic studies were made, some indication is given by the fact that the oldest women seen were still bearing children, and by the following data taken from the clinic records: 108 youngest children, selected at random from Kanabea and 4 other villages had a total of 337 siblings, of whom 140 were dead. Mothers with 4 or 5 dead babies were commonplace. Pneumonia, malaria and swollen belly syndrome were thought to be responsible for a large proportion of this infant mortality.

**Helminth survey**

One hundred and forty nine stool samples were examined. Thirty eight of these were from adults, and many of the rest from infants. Three samples were anomalous in consistency, and were discarded as being probably incorrectly aged. In 3 cases there was insufficient material for the second, accurate count of *Strongyloides* eggs. The results of the egg counts, and prevalence rates are shown in tables 1 and 2.

Hookworm infection was abundant, and was almost universal in people age above 12 months. The egg counts were, however, rarely very high; the highest count was 12,000 eggs/ml, and only 3 were above 5,000. The high counts were all in children aged below 5 years. No attempt was made to identify the hookworm eggs specifically, though they varied considerably, and in 2 cases resembled *Trichostrongylus*.

*Ascaris* infection was almost as prevalent as that of hookworm, but heavy loads were again infrequent. The prevalence in young children was less than that of hookworm, the prevalence of 80% being reached around 5 years.

*Trichuris* infection was surprisingly rare, and only very light infections were seen. The youngest infected child was aged 2-3 years.

*Enterobius* eggs were unusually abundant in stools. Twenty six infections were seen, and many of these were quite heavy.

*Strongyloides* eggs were passed in enormous numbers (up to 10⁶/ml) by nearly all infants. In the faeces of infants aged less than 12 months, these were usually held together in membranous tubes containing as many as 50 eggs in a single or double strand, and often making up a

<table>
<thead>
<tr>
<th>Helminth</th>
<th>Age</th>
<th>Prevalences (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1w</td>
<td>3w-8w</td>
</tr>
<tr>
<td>Hookworm</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ascaris</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Strongyloides</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Trichuris</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Enterobius</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>No. Examined</td>
<td>1</td>
<td>7</td>
</tr>
</tbody>
</table>

Table 1. Kanabea, December 1977: Stool Survey: Age Graded Helminth Infection Prevalences (%)
### Table 2. Kanabea, December 1977: Stool survey: Summary of Egg Loads of Main Helminth Infections.

<table>
<thead>
<tr>
<th>Age</th>
<th>No. Examined</th>
<th>No. Counted</th>
<th>Mean egg load/ml</th>
<th>No. Counted</th>
<th>Mean egg load/ml</th>
<th>No. Counted</th>
<th>Mean egg load/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1w</td>
<td>1</td>
<td>0</td>
<td>-</td>
<td>0</td>
<td>-</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>3w−8w</td>
<td>7</td>
<td>0</td>
<td>-</td>
<td>0</td>
<td>-</td>
<td>7</td>
<td>94,000</td>
</tr>
<tr>
<td>2m−6m</td>
<td>23</td>
<td>1</td>
<td>400</td>
<td>0</td>
<td>-</td>
<td>20</td>
<td>83,000</td>
</tr>
<tr>
<td>6m−12m</td>
<td>13</td>
<td>3</td>
<td>3100</td>
<td>0</td>
<td>-</td>
<td>10</td>
<td>52,000</td>
</tr>
<tr>
<td>1y−5y</td>
<td>46</td>
<td>40</td>
<td>1700</td>
<td>26</td>
<td>11000</td>
<td>32</td>
<td>1000</td>
</tr>
<tr>
<td>5y−15y</td>
<td>16</td>
<td>15</td>
<td>1800</td>
<td>11</td>
<td>4100</td>
<td>40</td>
<td>3600</td>
</tr>
<tr>
<td>Adult</td>
<td>38</td>
<td>38</td>
<td>1500</td>
<td>32</td>
<td>2900</td>
<td>5</td>
<td>650</td>
</tr>
</tbody>
</table>
large proportion of the faecal matter (Fig. 1). Faeces of 2 babies seen with “Swollen Belly Sickness” had 404,000 and 200,000 eggs/ml. While these were not the heaviest infections seen, they were the heaviest in their age group. Infected children in all age groups up to 10 months had a mean load above 20,000 eggs/ml. The overall mean for children below 2 years, including those uninfected, was 45,400 eggs/ml. In older children both the prevalence and load decreased dramatically and, with a single exception, in those older than 5 years, only light infections were seen. Only 5 adults passed eggs, and these had very light loads.

**Malaria**

One hundred and twenty nine films were examined. Six showed malaria parasites, and of these, 5 were from 33 films from Minimango, the lowest of the 3 villages studied, at 1000 m above sea level. As the blood film collections conformed neither with active nor passive case detection procedures, no conventional epidemiological conclusions can be drawn except that both *P. falciparum* and *P. vivax* are present in the area. There was no correlation detectable between malaria and *Strongyloides* infection or the other parameters measured.

**Eosinophils**

Counts were made on 116 blood films. As these were not related to total white cell counts their interpretation is difficult. Eosinophils varied between < 1% of white cells and 60%. Although 2 adults had counts above 20%, most of the high counts were in children. As shown in table 3, there is no clear age correlation with eosinophilia, though the youngest children, <2 months of age had high counts: mean = 21.5%. Within the age grades there was no correlation between *Strongyloides* egg counts and eosinophilia, though the picture may be blurred by the paucity
of light infections in infants, and the abundance of other helminths in adults.

Sera

Serum protein estimates were obtained for 35 individuals, including seven adults and 23 children aged less than two years. Three of the infants were suffering from swollen belly syndrome and had levels of 3.5, 5.4 and 2.7 gm/100ml. One other infant, with a moderate Strongyloides infection, had a very low level, 3.7 gm/100ml; this child also had a heavy Plasmodium falciparum infection.

Among the remaining 31 “healthy” subjects, the protein values ranged from 6.2 to 9.1gm/100ml. There was no significant difference between the values for subjects with Strongyloides (x = 7.8gm/100ml, n = 20) and those without (x = 7.74gm/100ml, n = 9). Nor was there any indication of correlation between the serum protein levels and the faecal egg output (r = 0.24, t = 1.05, d.f. = 18:p > 0.1).

Albumin globulin ratios were measured for 22 sera. The ratios varied greatly from 0.57 — 2.59, but as with the total serum protein there was no correlation with Strongyloides egg output.

Table 3. Kanabea, December 1977: Age Graded Eosinophil Counts

<table>
<thead>
<tr>
<th>Age</th>
<th>No. Examined</th>
<th>Eosinophil counts % mean</th>
<th>range</th>
</tr>
</thead>
<tbody>
<tr>
<td>3w—8w</td>
<td>6</td>
<td>21</td>
<td>7–58</td>
</tr>
<tr>
<td>2m—6m</td>
<td>21</td>
<td>12.3</td>
<td>1–60</td>
</tr>
<tr>
<td>6m–12m</td>
<td>12</td>
<td>10.6</td>
<td>3–23</td>
</tr>
<tr>
<td>1y—5y</td>
<td>32</td>
<td>13.3</td>
<td>3–30</td>
</tr>
<tr>
<td>5y—15y</td>
<td>13</td>
<td>9.3</td>
<td>3–16</td>
</tr>
<tr>
<td>Adult</td>
<td>28</td>
<td>12.1</td>
<td>1–24</td>
</tr>
</tbody>
</table>

Milk

The sediment from 400ml of milk from 40 mothers was examined. Although various contaminating organisms, an ant and a mite were found, no helminths were seen. Very few samples were available from mothers of new babies, and no colostrum has been examined.

Placentae

Sections of 4 placentae have been examined, but no worms have been found.

Treatment and Reinfection

Longitudinal studies in these circumstances are very difficult, and must largely rely on opportunism. The results to date, shown in table 4 indicate that treatment with thiabendazole drastically reduces, and in most cases eliminates Strongyloides egg output within 48h. Long term studies have been started to see if treated babies become reinfected. The small number of such cases studied to date do not give a reliable indication either way.

The Parasite

The Strongyloides parasite involved will be fully described when specimens are available from a wider geographical area. Those seen so far indicate that the parasitic females are indistinguishable from S. fulleborni, but that the ‘free living adults differ slightly from those of this species as well as from the free living females described by Kelly et al. For the present they cannot be identified, and should be referred to as “Kanabea Strongyloides”.

DISCUSSION

The most significant findings to date are that infection with Kanabea Strongyloides is universal in infants in the area studied, commonly in massive, apparently asymptomatic infections, and that patent infection in adults is rare and light. Efforts to indicate the transmission mechanism are inconclusive so far.

The high prevalence of the infection
raises the question of why only a small proportion of infants become acutely ill, and indeed, whether the worms are responsible for the Swollen Belly Sickness. It is reasonable to postulate that such heavy infections must be in some way inherited from the mother, despite negative findings in milk and placentae, and notwithstanding in rarity of eggs in adult faeces. The pattern of hookworm infection is so different that soil—borne percutaneous infection is most unlikely to be the only route of Strongyloides transmission.

The lack of correlation between serum protein levels or albumin globulin ratios and Strongyloides egg output in “healthy” subjects may indicate that the syndrome is precipitated when some threshold is crossed, or that indeed, the syndrome is unrelated to intestinal infection. The strongest evidence for Strongyloides being responsible for the disease, remains the the response of the syndrome to thiabendazole treatment. Although the sick infants did not have the heaviest egg loads, they did have the heaviest for their age. Possibly it is a heavy infection combined with the early age which promotes pathogenesis. There is also the question of migrating larvae and autoinfection. Lung aspirates were not attempted, and infant sputum was not available. Small quantities of peritoneal fluid did not contain worms, and no worms were found in 10ml of blood from the mother of a swollen baby.

Clearly further studies are indicated, and will be carried out, on the geographical distribution of the infection, its transmission and pathogenesis, and on the taxonomy of the parasite.

ACKNOWLEDGEMENTS

We would like to acknowledge the unstinting, and continuing cooperation

Table 4. Karabea Strongyloides: Egg Output Post Treatment*

<table>
<thead>
<tr>
<th>Patient</th>
<th>24h</th>
<th>48h</th>
<th>2d</th>
<th>2w</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre—treatment eggs/ml</td>
<td>&lt;24h</td>
<td>&lt;48h</td>
<td>&lt;2d</td>
<td>&lt;2w</td>
</tr>
<tr>
<td>8</td>
<td>91 000</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>122 400</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>58 400</td>
<td>53</td>
<td>3.6</td>
<td>0</td>
</tr>
<tr>
<td>21</td>
<td>36 500</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>200 000</td>
<td>0.55</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>28</td>
<td>113 100</td>
<td>6.2</td>
<td>0(18d)</td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>32 600</td>
<td>6.4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>56</td>
<td>127 200</td>
<td>0.17</td>
<td>9(10w)</td>
<td></td>
</tr>
<tr>
<td>91</td>
<td>689 000</td>
<td>0.74</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>92</td>
<td>404 000</td>
<td>18.9</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>102</td>
<td>224 800</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Expressed as % of pre—treatment value.
of the Kanabea Mission staff, both medical and non medical. In particular, Sister Gwen Daw and Rosemary Byrne were responsible for the success of our visit. Dr. Andrew Buck kindly repeated the serum protein estimates by a micro-biuret technique. The Research Committee of University of Papua New Guinea and the Department of Public Health provided funds.

REFERENCES


(2) KELLY, A. Alimentary Parasites of Man in Papua New Guinea, Papua New Guinea Institute of Medical Research, 56pp. (mimeo), undated.


GASTROENTERITIS is a disease of major importance for young children in Papua and New Guinea. It was the second commonest cause of admission to Administration hospitals in Papua and New Guinea of children aged 1 to 11 months for the year ended 31.3.1967, and comprised 24 per cent of the hospital admissions in this age group. Children hospitalised with gastroenteritis in this age group had a mortality rate of 3.4 per cent. It was the second commonest cause of death for children in the 1 to 11 month age group who were admitted to hospital, and accounted for 17 per cent of the hospital deaths in this age group.

Gastroenteritis was the commonest cause of admission to Administration hospitals in Papua and New Guinea of children aged 1 to 4 years for the year ended 31.3.1967, and comprised 17 per cent of the hospital admissions in this age group. The mortality rate in the 1 to 4 year age group of children hospitalised with gastroenteritis was 2.3 per cent. It was the second commonest cause of death for children in the 1 to 4 year age group who were admitted to hospital, and accounted for 17 per cent of the hospital deaths in this age group. (Hospital Disease Statistics 1964-1967.)

Unfortunately the age groups arbitrarily selected for statistical purposes—under one month, 1 to 11 months and 1 to 4 years—mask the relative importance of gastroenteritis in the age group 6 months to 18 months, during which age period gastroenteritis is probably the commonest cause of admission to hospital; and probably accounts for at least one third of the hospital admissions in this age group.

There have been several previous descriptions of gastroenteritis in young children in Papua and New Guinea.

Ryan (1962) described the clinical features of 506 children admitted with gastroenteritis to the Port Moresby General Hospital over a 13-month period (May 1960 to June 1961). There were 22 deaths in his series, giving a mortality rate of 4.5 per cent. Definite malnutrition was stated to be present in one-fifth of the cases. It was noted that gastroenteritis was a more severe disease in the malnourished and that malnutrition was often precipitated by recurrent gastroenteritis.

Lawson and Curtis (1967) described 280 children admitted with gastroenteritis to the Port Moresby General Hospital over a seven-month period (March to October 1964). There were eight deaths in this series, giving a mortality rate of 2.8 per cent. A presumed causative organism was only isolated in 15 per cent of cases; Shigella flexneri type 2 was the most common organism isolated. Approximately 70 per cent of the Shigellae isolated were resistant to sulphonamides. Severe malnutrition was said to be present in one-seventh of the cases, while many others were said to have probable growth retardation due to malnutrition.

Biddulph (1966) described an epidemic of gastroenteritis seen at the Port Moresby General Hospital that involved hospitalisation of 305 children during a two-month period (June to July 1965). There were two deaths in this series, giving a mortality rate of under one per cent. Stool cultures were mainly negative bacteriologically, and virus studies carried out by the Queensland Institute of Medical Research were also unrewarding.

All three of the above studies discussed the low level of isolation of etiological agents despite intensive bacteriological investigation. The association of malnutrition with many of the cases of gastroenteritis was commented on. This theme was developed by Ryan and Murrell (1964) who stated that the vast majority of their cases of marasmus presented as cases of gastroenteritis. Lawson and Biddulph both stressed the importance of a standardised treatment schedule using 2.5 per cent Dextrose in half strength Darrow’s solution as the intravenous rehydration fluid of choice to keep the mortality rate to a minimum.

The purpose of the present paper is to discuss the concept of the epidemiological entity, weanling diarrhoea. Weanling diarrhoea is the gastroenteritis that occurs with the transition of babies from a completely breast fed existence to that of a mixed diet. Gordon (1969) says ‘Acute diarrhoeal disease in developing countries seemingly owes its importance, in clinical effect and as a cause of death, to the particular form of the disease called weanling diarrhoea, a clear synergism of nutrition and infection.’ It is a syndrome associated with a particular age group and determined epidemiologically by the nutritional and environmental stresses attendant on dietary change (Gordon 1963 et al.).
During the 12 months May 1969 to April 1970, 654 children were admitted to the Port Moresby General Hospital with gastroenteritis. There were five deaths, giving a mortality rate of under one per cent. One hundred consecutive cases of gastroenteritis seen during February-March 1970 were assessed for nutritional status. After satisfactory rehydration the child’s weight was plotted on the WHO Western Pacific Regional Office (WPRO) weight chart. These weight charts have been especially prepared for assessing the nutrition of children in developing countries of the Western Pacific Region (WHO, 1969). It was found that 48 per cent of the children had weights that fell below the malnutrition line (Figures 1 and 2).

**Figure 1.**—Weight for age (male)
Analysis of these 100 cases showed some notable differences between those adequately nourished and those malnourished.

**Age and Sex**

Hospital disease statistics and previous surveys of children with gastroenteritis at Port Moresby General Hospital have shown that more males than females are admitted with the disease. Yet more females than males are affected in the malnourished group who have gastroenteritis. This is a reflection of the greater prevalence of malnutrition among girls than among boys. Fifty-eight per cent of the cases of gastroenteritis occurred in the 12-month age group, 6 to 17 months (Figure 3). As previously mentioned

![Graph: Weight for age (female)](image-url)
this concentration of cases in the age group 6 to 17 months is hidden when the usual statistical age groupings are used.

**Duration of Rehydration**

All the children in this series required intravenous rehydration. An approximate assessment of the length of time and recurrence of the diarrhoea is given by the number of days each case required intravenous rehydration (Figure 4). The one adequately nourished child who required intravenous rehydration for four days was intolerant to lactose and had watery diarrhoea whenever he ingested milk containing lactose.

The majority of the adequately nourished group required intravenous rehydration for only one day, while the majority of the malnourished group required intravenous rehydration for longer than one day.

![Figure 3.- Age and sex distribution of 100 consecutive cases admitted with gastroenteritis, Port Moresby General Hospital, February-March, 1970](image)

![Figure 4.- Numbers requiring intravenous rehydration according to nutritional status and duration of rehydration](image)
Lactose Intolerance

Only one of the adequately nourished group, approximately 2 per cent, was intolerant to lactose. Among the malnourished group 12, i.e., 25 per cent were intolerant to lactose.

Associated Conditions

Other illnesses were more frequently present among the malnourished group (Table 1).

Duration of Hospitalisation

The number of days spent in hospital was different for the two groups (Figure 5). The one adequately nourished child who remained in hospital for more than a week was the child who was intolerant to lactose. Over one-third of the malnourished children absconded from hospital, so that many of them stayed in hospital a shorter time than considered necessary.

Type of Malnutrition

The type of malnutrition seen in the malnourished group is shown in Table 2.

Table 1.—Associated conditions seen in adequately nourished (A) and malnourished (M) groups presenting with gastroenteritis

<table>
<thead>
<tr>
<th>Associated Condition</th>
<th>A</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower Respiratory Infection</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Otitis media, Tonsillitis</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Measles</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Septicaemia</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Anaemia</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Lactose intolerance</td>
<td>1</td>
<td>12</td>
</tr>
</tbody>
</table>

DISCUSSION

These differences in gastroenteritis according to the nutritional state of the child support Hardy’s statement (1959) that in general there are two major types of gastroenteritis in developing countries. One type is the acute episode in the previously normal, well-nourished child, in which complete recovery usually occurs after a few days. The second type of gastroenteritis is seen in children with malnutrition. The diarrhoea is not confined to a single episode, but persists or recurs, often leading to a progressive downward course.

Historical Perspective

At the beginning of this century weaning diarrhoea was prevalent in countries that today comprise the technologically advanced nations (Gordon et al. 1963-Table 3). The death rate from diarrhoea in infancy in New York in 1961 was over 100 times lower than it was in 1900. Similarly the death rate from diarrhoea in children aged 1 to 4 years in 1961 was more than 150 times lower than it was in 1900. Many factors such as improved nutrition, better environmental sanitation, a favourable economy and more rational therapy have contributed to this dramatic fall in the death rates from diarrhoea among young children in today’s technologically advanced countries. It can be seen from this table on age specific death rates that the figures for New York in 1900 were just as bad, and probably worse, than the present day figures for developing countries.

Table 3.—Age specific death rates from diarrhoea per 100,000 (Gordon et al. 1963)

<table>
<thead>
<tr>
<th>Place and Year</th>
<th>Age Specific Death Rates from Diarrhoea per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 to 11 months</td>
</tr>
<tr>
<td>New York, 1900</td>
<td>5603</td>
</tr>
<tr>
<td>New York, 1961</td>
<td>45</td>
</tr>
<tr>
<td>Punjab, India, 1959</td>
<td>3446</td>
</tr>
</tbody>
</table>

Age of Maximum Prevalence

Gastroenteritis mainly occurs in the age period 6 to 18 months, the time during which the child is introduced to food other than breast milk. Weaning begins within the same general
period that gastroenteritis appears—6 to 18 months—although the exact timing of the two events differs from one community to another.

Gordon et al. (1963) showed in his longitudinal study of young children in 11 Punjab villages that the age group with the highest diarrhoea death rate was the age group 6 to 17 months (Table 4).

<table>
<thead>
<tr>
<th>Age in months</th>
<th>Age Specific Death Rate from Diarrhoea per 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td></td>
</tr>
<tr>
<td>6-11</td>
<td></td>
</tr>
<tr>
<td>12-17</td>
<td></td>
</tr>
<tr>
<td>18-23</td>
<td></td>
</tr>
</tbody>
</table>

Table 4.—Death rates from diarrhoea per 1,000, Punjab, India, by six-month age periods (Gordon et al. 1963)

Value of Breast Feeding

The mortality from gastroenteritis among young children of developing countries would be much higher than it is, if it were not for the practically universal practice of breast feeding. In Gordon’s longitudinal study in the Punjab, 20 infants were artificially fed from birth and only one survived past the age of one year. An infant mortality rate among the artificially fed of 950 per 1000, compared to an infant mortality rate of 120 per 1000 for those who were breast fed.

The increasing trend of urbanized mothers to exchange the breast for a bottle means that gastroenteritis and malnutrition will continue to rise in the urban areas as more babies are fed dilute mixtures of concentrated bacterial content in feeding bottles.

Risks to the Weanling

The first introduction to food other than breast milk brings two risks. However careful the mother is, the family diet lacks the sanitary quality of breast milk. Usually, however, environmental sanitation is such that many infectious agents are introduced to the child through contamination of the food. The second risk is the usual practice in developing countries for the child to be fed foods of poorer dietary quality than breast milk; often he is restricted by custom to bulky low protein foods.

This transition to adult food is of no consequence among well nourished groups who understand and practice sound principles of infant nutrition. In communities where dietary education is lacking and suitable protein food is not fed to young children the results are serious. The malnourished child reacts more severely to gastroenteritis than does the well nourished child. The converse also occurs, an episode of diarrhoea often precipitates kwashiorkor. Both infection and malnutrition interact with each other, and the interaction is synergistic (Scrimshaw et al. 1968).

Growth of the Weanling

Breast fed babies in developing countries grow as well as babies born into the privileged societies of U.S.A., Europe or Australia during the first months or so of life. Thereafter breast milk by itself is no longer sufficient for continued adequate growth, and marked retardation of growth occurs.

A recent survey of children under the age of five years living in an urban squatter settlement in Port Moresby demonstrated this very clearly (Biddulph 1970). In the under-six month age group approximately half the babies weighed more than the Boston median. The three malnourished babies in this age group were all artificially fed. After the age of six months, retardation of growth occurred; progressively fewer babies weighed more than the Boston median, and progressively more babies became malnourished, until in the two-year age group no child weighed more than the Boston median, and over half the children had weights below the WPRO malnutrition line (Figure 6).

Synergism between Infection and Malnutrition

The introduction of contaminated foods in the weaning period explains the increased incidence of gastroenteritis during this period, but does not explain the high mortality. This is only explainable in terms of the synergistic interaction between malnutrition and infection. As malnutrition develops because of the poor diet in the weaning period gastroenteritis becomes more likely to lead to death. At the same time, gastroenteritis worsens the child’s nutritional state by reducing appetite, increasing metabolic loss of nitrogen and frequently by ill-advised therapeutic restrictions on diet. The stage is thus set for the vicious cycle of diarrhoea-malnutrition.

It is frequently impossible to say which came first, the diarrhoea or the malnutrition. Each has a deleterious effect on the other, and may be caused by or, in turn, cause the other. Because these two conditions are inextricably wedded during the weaning period it is both foolish and misleading for statisticians to assign one cause only as the primary diagnosis for hospital admission or death. Malnutrition is frequently ignored in national statistics because of this absurd statistical convention. Respiratory infections or gastroenteritis are more obvious and dramatic
than malnutrition, so that these diagnoses appear at the top of the list for hospital admissions and deaths, while malnutrition is frequently overlooked. Yet if the child had not been malnourished it is unlikely that his attack of pneumonia or gastroenteritis would have ended fatally.

The situation has been well put by Jelliffe (1970), 'Death is due to an accumulation of disease rather than to any single entity. The immature, anaemic baby, living in overcrowded unhygienic surroundings, becomes relatively malnourished in the second semester of life. His anaemia and nutrition deteriorate still further as a result of persistent malaria, leaving an attack of bronchopneumonia or gastroenteritis to add the last straw to his pathological burden'.

**SUMMARY**

Gastroenteritis can occur at any age, but is most frequent and severe in developing countries during the weaning period, which in most communities is between 6 to 18 months. There are several reasons for this association of gastroenteritis with the weaning period.

First, the introduction of foods other than breast milk exposes the child to potential pathogens. The low standard of environmental sanitation in developing countries ensures that the young child receives a large dose of these potential pathogens.

Second, the weaning period coincides with the period of growth retardation brought about in developing countries by the dietary inadequacy of what young children are fed, mainly due to ignorance and prejudice. This state of nutritional deficiency leaves the child more susceptible to infection.

Third, gastroenteritis produced by contact with contaminated foods itself results in further deterioration of nutritional status. It is the synergistic interaction between infection and poor nutrition during the weaning period that forms the epidemiological entity termed weaning diarrhoea. It is weaning diarrhoea which makes gastroenteritis so important an illness of young children in Papua and New Guinea as in other developing countries.

Control of the condition requires attention to be paid to both nutrition and infection, recognizing that each interacts with the other with profound effects on weanlings.

**REFERENCES**


The bacteriology of acute pneumonia and meningitis in children in Papua New Guinea: assumptions, facts and technical strategies

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Queensland Institute of Medical Research, Brisbane, Australia and Papua New Guinea Institute of Medical Research, Goroka

SUMMARY

Acute respiratory infections in children aged less than 5 years in the Eastern Highlands of Papua New Guinea were investigated bacteriologically for 10 years from November 1978. *Haemophilus influenzae* and *Streptococcus pneumoniae* were responsible for 73% of all bacteria cultured from lung aspirate (83 samples), 85.5% from blood (1024 samples) and 92% from cerebrospinal fluid (155 samples). Nonencapsulated *H. influenzae* was carried by up to 90% of children and was the predominant haemophilus type cultured from lung tissue. Mixed infections of the lung with two types of *H. influenzae* (8 cases) and both *H. influenzae* and *S. pneumoniae* (18 cases), commonly together with other organisms of questionable pathogenicity, reflected the proximity of this organ to the upper respiratory tract. Serotype b accounted for 62% and 82% of *H. influenzae* isolated from bacteraemic pneumonia and meningitis cases, respectively. Polymicrobial bacteraemic pneumonia occurred in 16 children. Both *H. influenzae* and *S. pneumoniae* establish dense, unregulated long-term colonization in the nasopharynx during the neonatal period. Each inhibit autochthonous microflora by mechanisms that are currently unclear. Infections with two or more types occur in 30% (*S. pneumoniae*) and 60% (*H. influenzae*) of carriage-positive children. 70-75% of *H. influenzae* and *S. pneumoniae* isolates from blood concomitantly colonize the upper respiratory tract. Intense exposure of Papua New Guinean children to penicillin at all levels of health care since the 1940s has resulted in widespread relative resistance among pneumococci to this antibiotic. Resistant strains are now found in 32 serotypes, and in children penicillin resistance is present in 75% of all carriage strains and 52% and 22% of blood and cerebrospinal fluid isolates, respectively. Penicillin-susceptible and resistant pneumococcal serotypes commonly coexist in multiply populated carriage sites. Resistance to betalactam antibiotics is rare among *H. influenzae* strains and resistance has not been detected in either *H. influenzae* or *S. pneumoniae* to chloramphenicol, erythromycin, tetracycline or cotrimoxazole. It should not be assumed that the technology of respiratory bacteriology as it is practised in developed countries can be transferred to the third world for utilization in paediatric aetiology and carriage studies. Respiratory bacteriology strategies as they evolved in Goroka were subject to diverse influences. The type distribution of the major causative agents defied fashionable beliefs, generated the need for more precise epidemiological differentiation and, by virtue of their carriage density, cultural properties and response to commonly used antibiotics, required the introduction or development of compatible diagnostic procedures.

Introduction

The Pneumonia Research Program of the Papua New Guinea Institute of Medical Research (PNGIMR) was initiated in 1977; with the full establishment of an Acute Respiratory Infection (ARI) Unit in 1979 a platform was provided from which a comprehensive investigation into the aetiology, epidemiology and prevention of acute respiratory disease in young Papua New Guinean children could be conducted. In

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particular, the support offered by both field and hospital-based activities created a unique opportunity to develop technical strategies for the isolation and characterization of respiratory bacteria from the upper respiratory tract (URT) and normally sterile sites such as lung tissue, blood and cerebrospinal fluid (CSF). This paper summarizes the bacteriological findings of these studies and the establishment of laboratory methods that were compatible with research objectives.

**Invasive Disease**

Studies undertaken in the decade from November 1978 have shown conclusively that *Haemophilus influenzae* (Hi) and *Streptococcus pneumoniae* (Sp) are the major causative agents of acute bacterial pneumonia and meningitis in children aged 5 years or less in Papua New Guinea (PNG).

**Meningitis**

155 children with purulent culture-positive meningitis were studied between March 1980 and September 1984 (1). 92% were infected with Hi (49%) or Sp (43%). Other agents encountered included *Neisseria meningitidis* (8 isolations), *Streptococcus pyogenes* (2 isolations) and *Streptococcus agalactiae* and *Klebsiella pneumoniae* (1 each).

If culture facilities are not immediately available, survival of Hi and Sp strains in purulent CSF is satisfactory if samples are held at 5-10°C. Viability limits for 9 strains of Hi were 2-11 days (mean 5.5) and 2-24 days (mean 10.3) for 8 Sp strains (2).

**Pneumonia**

1105 children with pneumonia were studied in several projects (Table 1). 1025 had either lung aspirate or blood or both cultured. Of 83 children who had lung culture, Hi (including one unspeciated strain) and/or Sp were recovered from 39 (47%) and *Staphylococcus aureus* from 1. Isolations of questionable significance and unaccompanied by primary pathogens were made from a further 8 children and included viridans streptococci, *Staphylococcus epidermidis* and diphtheroid species. *Branhamella catarrhalis* was isolated in conjunction with either Hi, Sp or both on 9 occasions (3). In all, 88 organisms were recovered from lung cultures and 73% were either Hi (40 isolates) or Sp (24 isolates). The need to mix lung aspirate with Hanks buffered saline (for virus isolation) before cultures were set up may have compromised the recovery of small numbers of bacteria. However, primary culture plates were inoculated generously at the bedside with diluted aspirate and incubated without delay in a 5% CO₂ atmosphere.

Consistently good isolation rates from blood cultures were gained in all studies involving both community-based children with mild pneumonia (7% significant isolation rate) (4) and those hospitalized with moderate or severe illness (18.0-25.0%) (5) as defined by standard criteria (6). Isolation rates of 33% were seen when children with severe disease were selected on the basis of a chest X-ray that showed an opacity accessible to lung aspiration (3). Of 1024 children investigated by blood culture, 184 (18.0%) grew 200 significant organisms. 85.5% (171 strains) were either Hi (47.0%) or Sp (38.5%). Others included *Salmonella choleraesuis* (9 strains), other enterobacteria (7 strains), *Streptococcus pyogenes* (7 strains), *S. aureus* (5 strains) and *N. meningitidis* (1 strain).

The selection of a blood culture broth that would support the growth of exacting respiratory pathogens such as *H. influenzae* was essential. Many formulations have been advocated and several were used with mixed success in the early Goroka studies. After some experimentation, tryptose phosphate broth (Difco) was supplemented domestically with gelatin (1%, Difco), agar (0.1%, Difco Noble) and sodium polyanetholsulphonate (0.025%, Roche). This inexpensive medium has been evaluated successfully on separate occasions in parallel with supplemented peptone broth-II (BBL) in 1983 (Gratten and Montgomery, unpublished data) and Trans-Isolate medium (7) in 1987 (Montgomery, unpublished data) and has been used exclusively at the PNGIMR since July 1983.

Antecedent antibiotic usage should be determined in children from whom blood is cultured. It has been found in PNG that more children who received antibiotics within 48
hours before blood culture fail to grow an organism than children who had not received an antibiotic or whose last dose was 48 hours to 7 days before (3). Mothers may either deny earlier therapy or be unaware that an antibiotic has been administered. A simple qualitative test utilizing the Oxford staphylococcus (NCTC 6571) and 6.0mm Schleicher and Schuell discs impregnated with either serum or urine from the child will identify antimicrobial residues (8). The diameter of the zone of inhibition is recorded.

Bacteraemic strains of *S. choleraesuis* were isolated with consistent frequency, which highlights the vigilance required for the recognition of uncommon pathogens (9). While nonhuman isolates of most salmonella serotypes have a variety of animal hosts, *S. choleraesuis* strains are isolated almost exclusively from pigs. The organism is highly invasive, is commonly associated with bacteraemia and has a predilection for extra-intestinal foci such as lung tissue. Its presence in PNG children reflects the domestic environment in the PNG highlands and the close association between people and pigs.

In order to isolate Hi on a solid medium, chocolate agar is required. Oxoid blood agar base No 2 supplemented with 5% horse blood and heated with care produces a highly supportive substrate. Chocolate agar should be stored at refrigeration temperature (4-6°C) for 24-48 hours before use. Failure to use chocolate agar has severely compromised several earlier lung aspiration studies (10).

### Multiple Invasion

Of 48 children with positive lung cultures 22 had mixed infections, 18 of which were due to Hi and Sp (Table 2). *B. catarrhalis* was associated with these organisms in 9 cases. Two populations of Hi were cultured from 8 children and in 7 were also accompanied by Sp. Multiple isolations of Hi invariably consisted of encapsulated and nonencapsulated organisms with the former contributing to 5 of 7 episodes of bacteraemia recorded in these

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### TABLE 1

**HOSPITAL AND COMMUNITY-BASED PNEUMONIA AETIOLOGY STUDIES PERFORMED AT THE PNGIMR, 1978-1987**

<table>
<thead>
<tr>
<th>Study</th>
<th>Duration</th>
<th>Number of children studied</th>
<th>Severity of infection</th>
<th>Material cultured</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Hospital</td>
<td>Oct 81-Oct 84</td>
<td>484</td>
<td>Moderate Severe</td>
<td>– 483, 83</td>
</tr>
<tr>
<td>3. Hospital</td>
<td>Sep 85-Mar 87</td>
<td>186</td>
<td>Moderate Severe</td>
<td>– 186, 85</td>
</tr>
<tr>
<td>5. Family Health Clinic</td>
<td>Oct 85-Jun 86</td>
<td>103</td>
<td>Mild</td>
<td>– 103, 8</td>
</tr>
<tr>
<td>6. Hospital</td>
<td>Apr 87-Nov 87</td>
<td>63</td>
<td>Moderate Severe</td>
<td>– 63, 63</td>
</tr>
</tbody>
</table>

PNGIMR  Papua New Guinea Institute of Medical Research  
LA  lung aspirate  
URT  upper respiratory tract
8 children. Mixed infection of the lung by Hi and Sp was also responsible for the 4 cases of polymicrobial bacteraemia seen in this study. Multiple invasion which occurred in 9% of all episodes of bacteraemic pneumonia seen throughout the decade was caused by Hi and Sp in 14 of 16 cases and was associated with a 31% case fatality rate. All children were less than 12 months of age.

Mixed isolations of respiratory bacteria from lung cultures have been reported by others (11-14) but multiple infections due to more than one type of Hi have not been recognized. The differentiation of encapsulated and nonencapsulated colonies of Hi in primary cultures requires experience. An eye lens (3-4 x magnification) or dissecting microscope is desirable. Pneumonia associated with multiple invasion of lung tissue with haemophili was not suspected before the start of ARI research in Goroka and early cases therefore may not have been recognized. Uncommon isolates or those with unusual properties should be forwarded to an appropriate reference laboratory for confirmation. This ensures that such information, when published or presented, is accepted as valid.

Experience in Goroka has shown that blind subcultures of blood culture broths within 24 hours of receipt and their incubation in a CO2-rich atmosphere will optimize detection of paediatric bacteraemia. In supplemented tryptose phosphate broth, Hi characteristically produces no visible sign of growth. This property has been noted elsewhere (15). Direct Gram stains are of little value for the detection of small gram-negative organisms in blood culture broths.

Austrian and Collins (16) clarified the importance of carbon dioxide for the isolation of pneumococci on solid media and also showed that the phenomenon was type related and, in their study, confined largely to serotypes 1, 3, 16, 28 and 33. In Goroka all type 5 pneumococci from all sites were obligate capnophiles. Carbon dioxide dependency was observed less frequently for types 7, 19 and 46 (Table 3).

**Upper Respiratory Tract Carriage**

The culture of URT secretions defines a transmission reservoir. If properly performed, such studies will monitor the acquisition and duration of carriage of target bacteria in a susceptible population and determine frequency and type distribution, antibiotic sensitivity patterns and the emergence of resistant mutants in the community.

Because carriage studies may involve village communities some distance from laboratory facilities, a reliable specimen transport system that will ensure the survival of respiratory bacteria such as Hi and Sp for up to 48 hours is essential. In PNG a commercially acquired transport system (Transtube, Medical Wire and Equipment Co. Australasia Pty Ltd) employing Amies’ charcoal medium (17) was used. Recent work by one of us (JM) has reconfirmed that nose swabs are preferable to throat swabs for determining URT colonization rates of Hi and Sp (Table 4). The anterior nares of each nostril was sampled and the swab placed in transport medium. An insulated container was used to protect clinical material from adverse environmental temperatures in transit.

Community carriage studies (18,19) have shown that Hi and Sp together colonize the URT of more than 95% of PNG children aged less than 5 years. Colonization by each organism is dense and persistent and is associated with a copious often purulent nasal discharge. One-third of children carry encapsulated Hi and 70-90% have non-serotypable strains. 6-8% harbour type b organisms. All serotypes except type c are evenly distributed. The commonest pneumococcal serotypes are 6, 19 and 23 and account for 44-64% of carriage isolates. Among carriage-positive children 30% and 50-60% harbour more than one type of Sp and Hi, respectively (19,20). Both Hi and Sp are acquired within the neonatal period by 60% of infants and all children are colonized by each within the first 3 months of life (21).

Several important technical manoeuvres govern the successful outcome of carriage projects. The selective culture of each target organism gives a true estimate of the carriage rate by excluding autochthonous microflora, provides a semiquantitative evaluation of carriage density and ensures the isolation of discrete colonies of Hi and Sp in primary
TABLE 2

MIXED INFECTIONS OF RESPIRATORY BACTERIA IN LUNG ASPIRATE, BLOOD AND CEREBROSPINAL FLUID

<table>
<thead>
<tr>
<th></th>
<th>Lung Number (%)</th>
<th>Blood Number (%)</th>
<th>Cerebrospinal fluid Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of samples/children</td>
<td>83</td>
<td>1024</td>
<td>155</td>
</tr>
<tr>
<td>Number culture-positive</td>
<td>48</td>
<td>180</td>
<td>155</td>
</tr>
<tr>
<td>Number with mixed infection</td>
<td>22 (46)</td>
<td>16 (8.9)</td>
<td>1 (0.6)</td>
</tr>
</tbody>
</table>

a 18 of 22 grew H. influenzae (Hi) + S. pneumoniae (Sp); 8 of 22 grew two types of Hi, 7 of which also grew Sp; 9 strains of Branhamella catarrhalis were isolated with Hi only (2 occasions) or Hi + Sp (7 occasions); 2 of 22 grew viridans streptococci + S. epidermidis, one of which also grew Hi
b 14 of 16 grew Hi + Sp; 1 grew Hi + Salmonella choleraesuis and 1 Hi + S. aureus
c Hi + Sp

TABLE 3

CARBON DIOXIDE REQUIREMENT FOR THE ISOLATION OF S. PNEUMONIAE SEROTYPES ON SOLID MEDIA

<table>
<thead>
<tr>
<th>Site of isolation</th>
<th>Absolute</th>
<th>Dependence on carbon dioxide</th>
<th>Not required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>*5[3], 19</td>
<td>7, 46</td>
<td>9,10,14[4], 16, 19[2], 23[2], 33, 34, 36</td>
</tr>
<tr>
<td>CSF</td>
<td>5[6], 7</td>
<td>–</td>
<td>1, 2, 6, 10, 17, 7[2], 45[2], 46[3]</td>
</tr>
</tbody>
</table>

Numbers inside brackets indicate the number of strains per serotype
*Two further strains of serotype 5 isolated from nasal secretions were also obligate capnophiles

TABLE 4

COMPARISON OF THROAT (OROPHARYNX) AND NOSE (LEFT AND RIGHT ANTERIOR NARES) SWABS FROM 54 CHILDREN FOR THE ISOLATION OF H. INFLUENZAE AND S. PNEUMONIAE

<table>
<thead>
<tr>
<th></th>
<th>Throat Number (%)</th>
<th>Nose Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>H. influenzae</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total strains</td>
<td>53 (98.1)</td>
<td>53 (98.1)</td>
</tr>
<tr>
<td>Encapsulated strains</td>
<td>16 (29.6)</td>
<td>16 (29.6)</td>
</tr>
<tr>
<td>Serotype b strains</td>
<td>2 (3.7)</td>
<td>3 (5.6)</td>
</tr>
<tr>
<td>Multiple populations</td>
<td>34 (63.0)</td>
<td>27 (50.0)</td>
</tr>
<tr>
<td><strong>S. pneumoniae</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Encapsulated strains</td>
<td>33 (61.1)</td>
<td>54 (100)</td>
</tr>
<tr>
<td>Multiple populations</td>
<td>11 (20.4)</td>
<td>20 (37.0)</td>
</tr>
<tr>
<td>Viridans streptococci</td>
<td>34 (63.0)</td>
<td>0</td>
</tr>
</tbody>
</table>
cultures. Blood agar with gentamicin sulphate, 5 µg/ml final concentration (22) and chocolate agar with bacitracin, 300 µg/ml (23) characteristically yielded pure or near pure cultures of Sp and Hi, respectively, from URT secretions. This enables the examination of colony profiles in order to determine the presence of multiple types and facilitates single colony subcultures for tests of differentiation. However, different types of both Hi and Sp commonly produce colonies which are indistinguishable. Thus from early 1982, when multiple carriage populations were initially sought and the relationship between carriage and invasion was becoming apparent, a minimum of four colonies each of Hi and Sp were subcultured for typing.

**Interbacterial Antagonism in the Upper Respiratory Tract**

Observations suggesting that interbacterial antagonism occurred in the URT were made by one of us (MG) in the course of a carriage study in infants. Here, nasal cultures occasionally displayed areas of marked regional inhibition effected by Sp at the expense of autochthonous microflora. In vitro experiments confirmed the ability of both Sp and Hi either to inhibit or prevent the growth of other carriage bacteria including *B. catarrhalis*, *Corynebacterium hofmannii* and *Corynebacterium xerosis*. Staphylococci were less susceptible. No antagonism could be demonstrated between strains of Hi and Sp. Kinetic studies using associative cultures (24) indicated that the inhibition was bactericidal. This ability of Hi and Sp to antagonize other nasopharyngeal inhabitants may explain, at least in part, their frequency and persistence of carriage in the URT.

Studies of bacterial interference in the oropharynx have suggested that interbacterial antagonism is one mechanism by which organisms such as viridans streptococci and certain staphylococci maintain the balance of pharyngeal microflora and prevent overgrowth or colonization by potential invaders such as enterobacteria, *S. aureus*, *N. meningitidis* and *S. pyogenes* (24,25). No organism capable of regulating the uncontrolled colonization by Hi and Sp appears to exist among the aerobic nasal microflora in young PNG children.

**Type Distribution, Frequency and Differentiation of *H. influenzae* and *S. pneumoniae***

Serotyping provides a means of epidemiologically differentiating encapsulated bacteria and, in circumstances where vaccination is envisaged, enables a formulation of vaccine compatible with invasive serotypes to be constructed. Encapsulated strains of Hi and Sp cultured at the ARI Unit in Goroka were serotyped with antisera produced by Wellcome Reagents, Beckenham, England, and Statens Seruminstitut, Copenhagen, Denmark, respectively.

No attempt had been made to serotype Hi isolates from aetiology studies involving lung aspiration before that of Shann and others in Goroka (3). In the lung aspirate study (3) the frequency of nonserotypable Hi which were commonly accompanied by non-b serotypes created a technical dilemma which was not resolved until the accuracy of the typing antisera had been established. Valuable lessons were learnt. The ability to confidently distinguish mucoid (encapsulated) and smooth (nonencapsulated) variants of Hi in primary culture was essential. During the learning phase, negative staining of capsules using India ink was helpful. The property of iridescence by which capsular material is identified was exploited using brain heart infusion agar supplemented with Fildes extract (Oxoid).

When Hi serotyping is undertaken, a complete set of monovalent antisera should be available to ensure that types other than b are detected (26). Slide agglutination results should be interpreted within 30 seconds of mixing the reactants in order to avoid misclassification of nonserotypable (nonencapsulated) strains because of nonspecific aggregation. An alternative typing procedure such as counterimmuno-electrophoresis or coagglutination is desirable in order to clarify equivocal slide agglutination results. Occasional strains of Hi may be nontypable on initial isolation because of glycocalyx formation (27). Glycocalyces are lost on serial subculture and antibody binding sites are re-exposed. Multiple subcultures, however, may encourage the loss of capsular material and hence type-specificity.
Lung aspirate bacteriology disclosed the important aetiological role of nonencapsulated Hi in paediatric pneumonia. Biochemical typing (Minitek System, BBL) was introduced to differentiate nonserotypable strains and to clarify their association with upper airway colonization. Biotyping further demonstrated that nonserotypable Hi were unrelated to encapsulated Hi when both were cultured together from lung tissue. A study of 505 Hi isolated from the URT of children and adults revealed close relationships between biotypes and serotypes. Of the serotyped strains, 97% belonged to biotypes I, II and IV. A comparison of serotypes a to f with biotypes I, II and IV exposed a significant association of all serotypes except c with one or two biotypes, viz., serotype f strains were biotype I, 98% of type b strains belonged to biotypes I or II, biotype IV contained 89% of serotype d isolates, serotype e organisms were distributed exclusively in biotypes I and IV and 58% of serotype a strains were found in biotype II. No encapsulated biotype V, VI or VII organisms were isolated (28). The single biotype VII strain reported in this study had only recently been described (29).

Accurate biotyping results are dependent on the preparation and use of a dense inoculum and the layering of seeded substrate discs with sterile mineral oil to ensure that rapidly developing reactions such as urease and indole are not lost during the overnight incubation which is necessary to detect ornithine decarboxylase activity. The inoculum is produced by harvesting surface growth from a chocolate agar plate and mixing with 0.6ml of peptone water broth.

The distribution and frequency of Hi types isolated from the URT, lung, blood and CSF are summarized in Table 5. 80% of 35 lung isolates were types other than b. 54% were nonencapsulated. Significantly more type b haemophili were isolated from blood (62% of 92 strains) and CSF (82% of 73 strains).

'Paediatric' pneumococcal serotypes 6,14,19 and 23 were responsible for 49% of 88 isolates from lung tissue and blood (Table 6) but only 18% of 67 CSF isolates (Table 7) while 'adult' types 1-5,7-9,12,45 and 46 contributed 28% and 66%, respectively. The classification of commonly invasive pneumococcal serotypes as ‘paediatric’ or ‘adult’ is based on findings in developed countries. Studies in Goroka have shown that ‘adult’ types are more invasive than ‘paediatric’ types (30) and the predominance of the former in children with acute meningitis supports this finding.

The proximity of the lung to the densely colonized URT exposes lung tissue to opportunistic infection by organisms of modest pathogenicity. Viral infections, impaired nutrition and defective immune function heighten the susceptibility of young children to acute respiratory disease. Infection of more remote foci such as the blood and meninges is restricted to more highly invasive organisms such as type b haemophili and ‘adult’ pneumococcal types, and polymicrobial invasion becomes less frequent (Table 2).

Relationship between Invasion and Carriage of \textit{H. influenzae} and \textit{S. pneumoniae}

The relationship between invasive strains of \textit{Hi} and \textit{Sp} and URT colonization is close. 70-75% of bacteraemic \textit{Hi} and \textit{Sp} cultured during 1981-1987 were concomitantly carried in the nasopharynx (Tables 8 and 9). While all children at the time of blood culture had nose swabs cultured, URT bacteriology during much of the period was completed only for children shown to be bacteraemic. Data for the specificity of the association between carriage and invasion of \textit{Hi} and \textit{Sp} are therefore not considered in this paper. Pneumococcal serotypes have been grouped into 3 classes on the basis of several studies in PNG (3-5) as follows: less commonly carried, highly invasive types (Class I), ‘paediatric’ types which frequently invade from a heavily colonized carriage site (Class II), and less invasive types with a variable carriage frequency (Class III). Fewer bacteraemic Class I pneumococci were recovered from nasal cultures, as one would expect by definition of this class (Table 8). Among Hi the weaker association between invasion and carriage for nonserotypable strains may imply direct person-to-person transmission or that a more detailed colony assessment of primary carriage cultures is warranted.

The association of invasion with nasopharyngeal colonization may depend on
### TABLE 5

**HAEMOPHILUS INFLUENZAE** TYPES ISOLATED FROM THE NOSE OF 165 HEALTHY CHILDREN AND FROM INVADED SITES OF CHILDREN WITH ACUTE PNEUMONIA (LUNG AND BLOOD) AND MENINGITIS (CEREBROSPINAL FLUID)

<table>
<thead>
<tr>
<th>Types</th>
<th>n</th>
<th>Nose (%)</th>
<th>Lung (%)</th>
<th>OR</th>
<th>n</th>
<th>Blood (%)</th>
<th>OR</th>
<th>n</th>
<th>CSF (%)</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>16</td>
<td>(7.6)</td>
<td>1 (2.9)</td>
<td>0.35</td>
<td>6</td>
<td>(6.5)</td>
<td>0.84</td>
<td>9</td>
<td>(12.3)</td>
<td>1.7</td>
</tr>
<tr>
<td>b</td>
<td>10</td>
<td>(4.8)</td>
<td>7 (20.0)</td>
<td>4.98</td>
<td>57</td>
<td>(62.0)</td>
<td>32.4</td>
<td>60</td>
<td>(82.2)</td>
<td>91.8</td>
</tr>
<tr>
<td>c</td>
<td>1</td>
<td>(0.5)</td>
<td>3 (8.6)</td>
<td>19.5</td>
<td>1</td>
<td>(1.1)</td>
<td>2.28</td>
<td>-</td>
<td>(—)</td>
<td>-</td>
</tr>
<tr>
<td>d</td>
<td>8</td>
<td>(3.8)</td>
<td>3 (8.6)</td>
<td>2.34</td>
<td>5</td>
<td>(5.4)</td>
<td>1.44</td>
<td>-</td>
<td>(—)</td>
<td>-</td>
</tr>
<tr>
<td>e</td>
<td>13</td>
<td>(6.2)</td>
<td>1 (2.9)</td>
<td>0.44</td>
<td>-</td>
<td>(—)</td>
<td>—</td>
<td>-</td>
<td>(—)</td>
<td>-</td>
</tr>
<tr>
<td>f</td>
<td>9</td>
<td>(4.3)</td>
<td>1 (2.9)</td>
<td>0.65</td>
<td>2</td>
<td>(2.2)</td>
<td>0.49</td>
<td>1</td>
<td>(1.4)</td>
<td>0.31</td>
</tr>
<tr>
<td>nst</td>
<td>152</td>
<td>(72.7)</td>
<td>19 (54.3)</td>
<td>0.44</td>
<td>21</td>
<td>(22.8)</td>
<td>0.11</td>
<td>3</td>
<td>(4.1)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Total 209 35* 92 73

**OR** odds ratio when compared to carriage in nose

**nst** nonserotypable

**Note:** Serotyping of further isolates from lung aspirate (5 strains) and blood (1 strain) was not attempted

* The total of 35 given here is the correct final total of serotyped *Hi* isolates in the lung aspirate series and not the total of 31 given in Table 3 of Shann et al. (3)
the persistence of the bacteriologist. In Goroka the failure to confirm the carriage of a bacteraemic isolate of Hi or Sp when four colonies of each were initially examined necessitated the reappraisal of the primary URT cultures. Typing of an additional 5-10 colonies not uncommonly detected the bacteraemic strain.

The presence of selective agents such as gentamicin sulphate and bacitracin in primary isolation media may increase the cell division times of some Hi and Sp types. In this event, the detection of more slowly multiplying organisms currently considered to be infrequently carried may further strengthen the relationship between carriage and invasion.

### TABLE 6

**MINIMAL INHIBITORY CONCENTRATIONS (MIC) OF BENZYLPCINILLIN AND SEROTYPE DISTRIBUTION OF 73 S. PNEUMONIAE STRAINS ISOLATED FROM LUNG ASPIRATE AND BLOOD, 1978-1987**

<table>
<thead>
<tr>
<th>MIC (µg/ml)</th>
<th>Serotype distribution</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0.05</td>
<td>1, 2, 5[4], 6, 7[7], 9[2], 10, 16[3], 19[2], 22, 23[3], 25[2], 28, 31, 35, 45, 46[3]</td>
<td>35</td>
</tr>
<tr>
<td>0.1</td>
<td>10, 33, 34</td>
<td>3</td>
</tr>
<tr>
<td>0.2</td>
<td>7, 9[2], 15, 16[2], 17, 19[5]</td>
<td>12</td>
</tr>
<tr>
<td>0.5</td>
<td>6[5], 13, 14[5], 15, 19[3], 23[3]</td>
<td>18</td>
</tr>
<tr>
<td>1.0</td>
<td>6, 14[3]</td>
<td>4</td>
</tr>
<tr>
<td>2.0</td>
<td>14</td>
<td>1</td>
</tr>
</tbody>
</table>

Numbers inside brackets indicate the number of strains per serotype

**Note 1:** An additional 15 strains – serotypes 4, 6[4], 12, 14[3], 19[2], 23[2], 29, 45 – isolated from lung aspirate and blood in 1978-1987 were not tested for MIC

**Note 2:** Of the total of 88 strains 43 (49%) were ‘paediatric’ serotypes 6, 14, 19 and 23, and 25 (28%) ‘adult’ serotypes 1-5, 7-9, 12, 45 and 46

### TABLE 7

**BENZYLPCINILLIN SUSCEPTIBILITY (MIC) AND SEROTYPE DISTRIBUTION OF 67 STRAINS OF S. PNEUMONIAE ISOLATED FROM THE CSF OF CHILDREN WITH ACUTE MENINGITIS, 1980-1984**

<table>
<thead>
<tr>
<th>MIC (µg/ml)</th>
<th>Serotype distribution</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0.05</td>
<td>1, 2[6], 5[11], 6[2], 7[9], 8[3], 10, 12[4], 18, 23[2], 27[2], 45[4], 46[6]</td>
<td>52</td>
</tr>
<tr>
<td>0.1</td>
<td>10, 24, 33, 35</td>
<td>4</td>
</tr>
<tr>
<td>0.2</td>
<td>6[4], 24, 35</td>
<td>6</td>
</tr>
<tr>
<td>0.5</td>
<td>14, 22, 23</td>
<td>3</td>
</tr>
<tr>
<td>1.0</td>
<td>14, 23</td>
<td>2</td>
</tr>
</tbody>
</table>

Numbers inside brackets indicate the number of strains per serotype

**Note:** Of the 67 strains 12 (18%) were ‘paediatric’ serotypes 6, 14, 19 and 23, and 44 (66%) were ‘adult’ serotypes 1-5, 7-9, 12, 45 and 46
Antibiotic Susceptibility of *H. influenzae* and *S. pneumoniae*

Penicillin became available in PNG after World War II and was widely distributed when the aid post system of primary health care was established. Penicillin was one of several medical agents provided to aid post orderlies and was used mostly indiscriminately at village level. At about the same time a campaign, based on penicillin usage, was initiated throughout PNG to eradicate yaws. From the late 1940s penicillin in different forms at various levels of health care was used intensively. It has been calculated that in the 10 years from 1961 the amount of penicillin used by the PNG Health Department was equivalent to 10 670 000 5-day courses (31). In such circumstances the development of penicillin resistance (PR) among pneumococci in PNG was not surprising. Neither oily procaine penicillin, the first penicillin formulation to be used in PNG, nor its replacement, aqueous procaine penicillin, produce high blood levels. Even with massive penicillin therapy, the effective range of

<table>
<thead>
<tr>
<th>Class</th>
<th>Isolated from URT</th>
<th>Not isolated from URT</th>
<th>Total</th>
<th>Sensitivity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>5, 7[5], 9[3], 14[8], 46[2]</td>
<td>1, 2, 5, 7[3], 9, 10[2], 14, 45, 46</td>
<td>31</td>
<td>61.3</td>
</tr>
<tr>
<td>III</td>
<td>13, 15, 16[3], 25, 28, 31, 33, 34, 35</td>
<td>-</td>
<td>11</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>15</td>
<td>61</td>
<td>75.4</td>
</tr>
</tbody>
</table>

Numbers inside brackets indicate the number of strains per serotype

<table>
<thead>
<tr>
<th>Type</th>
<th>Isolated from URT</th>
<th>Not isolated from URT</th>
<th>Total</th>
<th>Sensitivity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>52</td>
<td>21</td>
<td>73</td>
<td>71.2</td>
</tr>
</tbody>
</table>

Numbers inside brackets indicate the number of strains per type
nst nonserotypable
I-V biotypes

<table>
<thead>
<tr>
<th>TABLE 8</th>
</tr>
</thead>
</table>

**RELATIONSHIP OF BACTERAEMIC ISOLATES OF *S. PNEUMONIAE* TO UPPER RESPIRATORY TRACT (URT) CARRIAGE, 1981-1987**

<table>
<thead>
<tr>
<th>Class</th>
<th>Isolated from URT</th>
<th>Not isolated from URT</th>
<th>Total</th>
<th>Sensitivity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>5, 7[5], 9[3], 14[8], 46[2]</td>
<td>1, 2, 5, 7[3], 9, 10[2], 14, 45, 46</td>
<td>31</td>
<td>61.3</td>
</tr>
<tr>
<td>III</td>
<td>13, 15, 16[3], 25, 28, 31, 33, 34, 35</td>
<td>-</td>
<td>11</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>15</td>
<td>61</td>
<td>75.4</td>
</tr>
</tbody>
</table>

Numbers inside brackets indicate the number of strains per serotype

---

**TABLE 9**

**RELATIONSHIP OF BACTERAEMIC ISOLATES OF *H. INFLUENZA* TO UPPER RESPIRATORY TRACT (URT) CARRIAGE, 1981-1987**

<table>
<thead>
<tr>
<th>Type</th>
<th>Isolated from URT</th>
<th>Not isolated from URT</th>
<th>Total</th>
<th>Sensitivity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>52</td>
<td>21</td>
<td>73</td>
<td>71.2</td>
</tr>
</tbody>
</table>

Numbers inside brackets indicate the number of strains per type
nst nonserotypable
I-V biotypes
**TABLE 10**

**RECOGNITION OF PENICILLIN-RESISTANT SEROTYPES OF S. PNEUMONIAE IN PAPUA NEW GUINEA, 1969-1986**

<table>
<thead>
<tr>
<th>Serotype</th>
<th>Year of isolation</th>
<th>Place</th>
<th>Site</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>4, 19</td>
<td>1969</td>
<td>Anguganak, WSP</td>
<td>Throat</td>
<td>32</td>
</tr>
<tr>
<td>14, 23</td>
<td>1969</td>
<td>Port Moresby</td>
<td>URT</td>
<td>33</td>
</tr>
<tr>
<td>16</td>
<td>1969</td>
<td>Tari, SHP</td>
<td>URT</td>
<td>33</td>
</tr>
<tr>
<td>6</td>
<td>1970</td>
<td>Lufa, EHP; Madang, MP</td>
<td>URT</td>
<td>33</td>
</tr>
<tr>
<td>11, 15, 34, 35</td>
<td>1970</td>
<td>Madang, MP</td>
<td>URT</td>
<td>33</td>
</tr>
<tr>
<td>24</td>
<td>1971</td>
<td>Madang, MP</td>
<td>Unknown</td>
<td>34</td>
</tr>
<tr>
<td>2</td>
<td>1973</td>
<td>Tari, SHP</td>
<td>Unknown</td>
<td>34</td>
</tr>
<tr>
<td>12, 13</td>
<td>1978</td>
<td>Port Moresby</td>
<td>Blood</td>
<td>35</td>
</tr>
<tr>
<td>18</td>
<td>1978</td>
<td>Port Moresby</td>
<td>CSF</td>
<td>35</td>
</tr>
<tr>
<td>10</td>
<td>1980</td>
<td>Goroka, EHP</td>
<td>CSF</td>
<td>18</td>
</tr>
<tr>
<td>17</td>
<td>1980</td>
<td>Goroka, EHP</td>
<td>Lung aspirate</td>
<td>3,18</td>
</tr>
<tr>
<td>20</td>
<td>1980</td>
<td>Madang, MP</td>
<td>Nose</td>
<td>18</td>
</tr>
<tr>
<td>21, 22, 38</td>
<td>1980</td>
<td>Goroka, EHP</td>
<td>Nose</td>
<td>18</td>
</tr>
<tr>
<td>9</td>
<td>1981</td>
<td>Port Moresby</td>
<td>CSF</td>
<td>18</td>
</tr>
<tr>
<td>28, 36</td>
<td>1981</td>
<td>Goroka, EHP</td>
<td>Nose</td>
<td>18</td>
</tr>
<tr>
<td>7, 25, 29, 33</td>
<td>1982</td>
<td>Goroka, EHP</td>
<td>Nose</td>
<td>18</td>
</tr>
<tr>
<td>46, 48</td>
<td>1984</td>
<td>Goroka, EHP</td>
<td>Nose</td>
<td>*</td>
</tr>
<tr>
<td>5</td>
<td>1985</td>
<td>Goroka, EHP</td>
<td>Blood</td>
<td>†</td>
</tr>
<tr>
<td>8</td>
<td>1986</td>
<td>Goroka, EHP</td>
<td>Unknown</td>
<td>†</td>
</tr>
</tbody>
</table>

* Gratten and Montgomery, unpublished data
† Montgomery, unpublished data

WSP, West Sepik Province
SHP, Southern Highlands Province
MP, Madang Province
EHP, Eastern Highlands Province
penicillin activity attained in the URT may only reach 0.06-0.3 µg/ml (25). In the upper airways pneumococci have therefore been exposed to sublethal concentrations of penicillin perfusing across densely colonized surfaces and resistant mutants have emerged. In PNG, pneumococcal resistance is confined to minimum inhibitory concentration (MIC) levels in the range 0.1-1.0 µg/ml of penicillin and is regarded as ‘intermediate’ or ‘relative’. Since the first observation in 1969 the acquisition of penicillin resistance among pneumococcal serotypes in PNG has increased steadily. Between 1969 and 1978 resistance in 15 capsular types was recorded (32-35) and resistant strains within a further 17 serotypes were isolated during 1980-1986 (Gratten and Montgomery, unpublished data) (Table 10). By 1987 nearly 75% of paediatric carriage pneumococci showed PR (19). Among 956 carriage pneumococci isolated from children in 1980-1982 (18) PR was detected in 63%. 79.5% of the most frequently carried types (serotypes 6,19,23) were resistant to penicillin while only 27% of all those strains which individually contributed less than 2% of isolates were resistant. High resistance rates were also present in several infrequently carried types. However, as PNG children commonly harbour coexisting populations of both penicillin-resistant and penicillin-susceptible types, it has been postulated that in such circumstances genetic transfer of PR could occur (20). Although pneumococci in PNG continue to remain only relatively resistant to penicillin, a significant increase is apparent within this area when the MIC values of common carriage types isolated in 1980-1982 are compared with those cultured in 1985-1987 (Table 11).

Of 73 invasive pneumococci cultured from lung and blood during 1978-1987 38 (52%) were relatively resistant to penicillin (Table 6). However, less frequently carried but highly invasive ‘adult’ types were responsible for the lower resistance –15/67 (22%) – seen in CSF isolates (Table 7).

Resistance to betalactam antibiotics among Hi is rare in PNG (36,37) and there is no evidence of any significant increase. Chloramphenicol resistance has not been observed in either Hi or Sp. None of 655 pneumococcal strains tested during 1985-1987 were resistant to erythromycin, tetracycline or cotrimoxazole (19). Standardized disk diffusion procedures such as those of Kirby-Bauer (38) and Stokes (39) provide a practical, accurate and less expensive means of screening antibiotic responses of normally susceptible bacteria. Quantitative technology is required for commonly resistant organisms in order to monitor further increases in resistance in community and hospital strains.

**ACKNOWLEDGEMENTS**

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REFERENCES


Nutrition and Morbidity: Acute Lower Respiratory Tract Infections, Diarrhoea and Malaria

DEBORAH LEHMANN1, PETER HOWARD1 AND PETER HEYWOOD2

Papua New Guinea Institute of Medical Research, Goroka and Madang

SUMMARY

The three most important infectious diseases of young children in Papua New Guinea are acute lower respiratory tract infections, diarrhoea and malaria, each of which has been shown to have a negative effect on growth. Low nutritional status is associated with increased risk and severity of acute lower respiratory tract infections and with increased severity of diarrhoea. There is no evidence to indicate that malnutrition is associated with increased risk of malaria. Adequate control and prompt treatment of infectious diseases will improve nutritional status. At the same time, improvement in nutritional status will reduce morbidity and mortality due to infectious disease, particularly acute lower respiratory tract infections and diarrhoea.

INTRODUCTION

The proximate causes of growth retardation are generally agreed to include low birthweight, deficient nutrient intake and repeated episodes of infectious disease, the importance of each factor varying with the specific situation.

The most important infectious diseases of young children in Papua New Guinea (PNG) are acute lower respiratory tract infections, diarrhoea and malaria. The interaction between these infections and nutrition, particularly protein-energy malnutrition, is reviewed in this paper with particular emphasis on studies carried out in PNG.

NUTRITION AND ACUTE LOWER RESPIRATORY INFECTIONS

Acute lower respiratory tract infections (ALRI) are the commonest cause of admission and death among children in PNG. In the highlands, 47% of admissions under the age of 5 years are for pneumonia while in the lowlands pneumonia accounts for approximately one-quarter of admissions in the same age group (1). Data from Tari, Southern Highlands Province (SHP) show that on average there are 2.5 episodes of ALRI per child under one year of age and 1.6 episodes per child aged 12-23 months (2). Children under one year of age suffer more severe disease than older children: 20% of ALRI episodes in infants are classified as moderate-severe disease (the children have chest indrawing in addition to cough and breathlessness with or without fever), and one-tenth of those with chest indrawing have signs of more severe disease (difficulty in feeding and/or cyanosis and/or heart failure). In children aged 1-4 years, 10% of ALRI illnesses are classified as moderate-severe cases.

Data from Tari on children with known birthweight show that children weighing less than 2.5kg at birth have four times the risk of dying of ALRI in the first year of life compared to children who are born heavier (D. Lehmann and P. Heywood, unpublished data). Furthermore, among children who were weighed between 4 and 59 months of age and then followed in Tari (SHP) and Asaro, Eastern Highlands Province (EHP) it was found that those who were less than 70% weight-for-age (compared to the Harvard median) had eight times the risk of dying of ALRI of heavier children (D. Lehmann, unpublished data).
Effect of ALRI on Nutrition

Mata has shown growth faltering (weight loss and height arrest) when children suffer from measles, whooping cough or ALRI, which may continue for weeks or months (3). Children who are malnourished before developing measles are likely to have more marked growth faltering and are more likely to suffer prolonged respiratory or gastrointestinal symptoms (4).

Under the stress of illness, children go into negative nitrogen balance. Tomkins et al. (5) report that during infection there is an increase in protein breakdown which is greater than the rise in synthesis of protein. If malnutrition is present at the onset of infection, these responses to infection are reduced.

The high incidence of ALRI in young children in PNG contributes to the deterioration in nutritional status over the first two years of life. Children who suffer from ALRI become anorexic and have difficulty feeding because of breathlessness, and therefore their food intake falls.

Effect of Nutrition on ALRI

Malnourished children have depressed immune responses which make them more vulnerable to infection. Delayed cutaneous hypersensitivity (DCH) to various antigens (an expression of cell-mediated immunity) is impaired in malnourished children; the response correlates directly with the nutritional status and improves with nutrition therapy. Serum antibody responses may be normal or decreased, while salivary IgA, which protects against invasion by microorganisms at mucosal surfaces, has been shown to be low in malnourished children. Bactericidal activity of polymorphonuclear leukocytes is reduced in malnourished children and can be corrected with improved nutrition. Malnutrition also results in a reduction of complement components, in particular C3 (6). In highland children in PNG, antibody titres to respiratory pathogens may be lower in young children suffering from ALRI. Moreover, highland children have higher levels of immunoglobulin and depressed cell-mediated immunity compared to expatriate children of the same age (C. Witt, personal communication), suggesting, firstly, that highland children experience more infections than expatriate children and, secondly, that their immune function may be depressed.

James (7) has reported that malnourished children have similar numbers of attacks of respiratory disease as well-nourished children but that malnourished children are sick for longer and are three times more likely to develop bronchitis and nineteen times more likely to develop pneumonia. Mata (4) noted that children who grow well are likely to suffer fewer days of respiratory symptoms than those who do not grow well. By contrast, in an intervention study in India, episodes of lower respiratory infection were of shorter duration where medical services were provided, while nutrition supplementation in addition to medical services did not have a summation effect (8). However, the investigators comment that it was financially beneficial to have the two programs together and that this would provide all the benefits of a medical care program and a nutrition care program.

Data from Goroka Base Hospital, EHP show that children under two years of age who are malnourished are four times more likely to be admitted with pneumonia and, if admitted, are four times more likely to die of the disease (9). Figure 1 shows the mean percent weight for age (compared to the Harvard median) by age, in healthy children from the Asaro Valley near Goroka, in children admitted to hospital with moderate or severe disease who survived and in children who died of severe disease. The relationship between malnutrition and risk of developing ALRI and severity of ALRI is maintained irrespective of the duration of illness before admission.

Data concerning the role of iron in infection are conflicting. Weinberg (10) has reported that microorganisms require iron for growth and that during microbial infections hosts attempt to withhold iron from invading organisms. He also reports that in conditions which result in hyperferraemia or hypotransferrinaemia there is an increased risk of infection. Papua New Guinean highland children under 2 years of age are iron deficient by western standards as determined by free erythrocyte protoporphyrin (FEP) (C. Witt,
personal communication). However, in a prospective study of children from the Asaro Valley, children who were iron deficient, as measured by levels of FEP and mean corpuscular haemoglobin concentration (MCHC), were at no greater risk of developing ALRI than children who were not iron deficient (C. Witt, personal communication).

Interventions

The following measures aimed at controlling ALRI morbidity will assist in preventing malnutrition:

1. Prompt appropriate antibiotic therapy for a minimum of five days will reduce the number of days of illness and the associated anorexia and difficulty in feeding. Parents must be taught that children with cough and breathlessness require a course of penicillin at an aid post and that inpatient care is required for those children who in addition have difficulty feeding.

2. Aid post orderlies must treat children suffering from cough and breathlessness
with the correct dose of penicillin. They must be able to recognize chest indrawing and difficulty in feeding and refer these children for inpatient care.

3. Immunization against measles and whooping cough as near the recommended age as possible will prevent children from developing these diseases and their chronic sequelae.

4. Pneumococcal vaccine has been shown to reduce mortality due to ALRI as the sole cause of death by 50% in young children in the highlands (11). Preliminary analysis of morbidity data from Tari shows that there is a reduction in the number of episodes of moderate and severe ALRI in the first year after being immunized with pneumococcal vaccine (T. Marshall, personal communication). There is no difference in efficacy of pneumococcal vaccine in preventing ALRI deaths among malnourished and well-nourished children (D. Lehmann, unpublished data). If pneumococcal vaccine were delivered through routine health services in the highlands in the future we would almost certainly see a reduction in morbidity and mortality from ALRI in children.

Measures taken to prevent malnutrition discussed elsewhere in this issue will reduce the risk of developing ALRI and also the risk of dying of the disease.

**NUTRITION AND DIARRHOEA**

The evidence for the strong association between diarrhea and malnutrition in many parts of the developing world is compelling. The peak age-specific prevalence rates for both diarrhoeal diseases and malnutrition coincide in infants and children under five years of age. Both are significant problems where predisposing conditions coexist, namely inadequate and polluted water supplies, poor environmental sanitation, low levels of personal and domestic hygiene, poverty, overcrowding and low education levels. In addition, historical evidence from developed countries suggests that the correction of these adverse conditions preceeded, or at least coincided with, a fall in the incidence of diarrhoea and a general improvement of the nutritional status of children.

During the last thirty years the interactions between infections, particularly diarrhoeal diseases, and nutrition have been extensively studied and keenly debated. The pioneering work of Scrimshaw and coworkers in Central America led to the hypothesis that a bidirectional causal relationship exists between diarrhoea and nutritional status. Malnutrition predisposes a child to diarrhoea and, conversely, diarrhoea causes growth retardation and precipitates severe malnutrition (12).

This synergistic relationship (diarrhoea causing acute weight loss, arrest in linear growth and malnutrition) has been demonstrated in detailed prospective studies in Guatemala (4, 13), The Gambia (14,15), Uganda (15) and Bangladesh (16). The evidence for the converse, that malnutrition predisposes to diarrhoea, is not so conclusive and is controversial. Tomkins in Nigeria (17) and Trowbridge in El Salvador (18) found that impaired nutritional status was associated with an increased prevalence of diarrhoea. One study in Guatemala (19) showed an increased incidence of diarrhoea in lighter children (lower weight for age) 1-4 years old. Two studies did not establish a relationship between three parameters of nutritional status (low weight, stunting and wasting) and incidence (7, 20), whereas Tomkins (17) showed wasting, but not low weight or stunting, to be a predictor of incidence. The only study to disentangle the component factors of prevalence (incidence and duration of episodes) is that of Black et al. (21). They found that Bangladeshi children less than 2 years old with low weight for height had episodes of longer duration but similar incidence rates when compared to better-nourished children.

In practice, where severe malnutrition and diarrhoea coexist at high levels of endemicity few could argue that there is not a close relationship between them, whatever its precise nature. Because of their multiple and often shared determinants preventive and therapeutic interventions will be directed at reducing the burden of both problems. In areas where severe malnutrition (low weight for age) and diarrhoea are present at low to moderate endemic levels,
such as PNG, it is probably difficult to define the precise nature of the interaction because of the logistic problems in studying the large sample sizes required to demonstrate the small differences between risk groups.

There are two studies which have addressed the question of the diarrhoea-malnutrition interaction in PNG. Biddulph and Pangkatana (22) showed that malnourished children (less than 75% weight for age) with severe gastro-enteritis required longer periods of rehydration than well-nourished children, suggesting increased severity in the former group. In children between the ages of one and four years in Enga Province, Binns (23) found significantly higher incidence rates of diarrhoea in lighter children (less than 80% weight for age) than in their heavier peers. In addition, following episodes of diarrhoea 83% of children failed to gain weight or lost weight during the month after a diarrhoea episode. The measure of incidence in this study was based on a one-month recall by mothers, which is recognized as unreliable by most experienced field workers, and the methodological description does not allow assessment of the validity of the study for other areas of the country.

In the light of present knowledge it is not possible to draw firm conclusions about the nature of the interaction between diarrhoea and malnutrition in PNG children. However, if, as the available data suggest, the incidence of diarrhoea is low compared to many developing countries (estimated at about one episode per child per year in children less than five years old), it is perhaps worth considering why this should be so. A number of factors related to transmission and severity may combine to produce the low force of infection.

1. It appears that most cultural groups have a natural appreciation of the polluting effects of human faecal material. This is reflected in an awareness not to defaecate near water supplies and the no-touch or indirect methods used for anal cleansing. However, it is not known whether an infant’s faeces or diarrhoea stools are regarded as being more or less polluting. In spite of low levels of personal hygiene, this suggests that the level of contamination of the environment by faecal enteropathogens is low.

2. PNG is a relatively underpopulated country and with the exception of urban and a few rural areas population densities are low and many communities relatively isolated. This probably acts to reduce the amount of inter-household and inter-community transmission. However, this situation is changing as road communications lead to increased local population concentrations.

3. Prolonged breastfeeding is almost universal in PNG societies. This practice has been protected by the Baby Feed Supplies (Control) Act of 1977, which has probably stemmed an increase in the use of bottle feeding, especially in urban areas, although unfortunately there is no hard evidence to demonstrate this.

4. In many parts of the country the nutritional status in the first five years of life is reasonably good.

5. In most rural societies, except after a large mumu (feast), when unconsumed food may be kept for some days, it appears that food is not stored overnight or for long periods during the day. Thus transmission via contaminated food may be uncommon, though this needs verification.

6. In the highlands at least, traditionally little water is drunk. Compared to some lowland areas water is plentiful and reasonably accessible although utilization for all purposes is reportedly low. From what evidence is available, it is not grossly polluted.

Whatever may be the community incidence of diarrhoea and malnutrition in PNG, they are still major public health problems as measured by the burden on curative health services. Preventive and curative interventions to reduce this burden have been given high priority in the government’s current five-year health plan (1986-90) (24). The cornerstone of the diarrhoeal disease control (CDD) program is based on correct case management – the assessment of dehydration status, appropriate oral rehydration therapy (ORT) and improved nutritional management. Current efforts focus on improved management at village level including home-based recognition, the use of home-made fluids, the maintenance of energy intake during episodes and increased feeding
during the recovery phase to ensure catch-up growth.

Preventive CDD interventions which have been given a high priority are:
1. measles immunization to reduce the morbidity and mortality from measles-associated diarrhoea;
2. the provision and increased use of safe and adequate water supplies in rural areas;
3. improved facilities for the safe disposal of faeces (pit latrines);
4. improved personal hygiene; and
5. improved weaning practices (more energy introduced at a younger age) and food hygiene.

It is recognized that the vital component to successful implementation of these interventions is the mobilization of resources at the village level. Emphasis is to be directed at the integrated primary health care approach by motivation and education of individuals and communities through schools, village-level health services (aid posts, MCH clinics and health inspectors) and the use of the mass media.

Recent publications edited by Gracey (25) and Chen and Scrimshaw (26) provide excellent reviews of the relationship between diarrhoea and malnutrition.

**NUTRITION AND MALARIA**

**Effect of Malaria on Growth**

Malaria may affect growth both ante- and post-natally.

Birthweight is an important determinant of postnatal growth (27) and the effect of malaria during pregnancy on birthweight has been investigated in a number of studies. The most convincing of these is that of McGregor et al. in The Gambia (28). The effect of placental malaria infection on birthweight was investigated in more than 6000 births. Pregnant women were more likely to have parasites in the plental than in the peripheral blood, malarious placentae were more likely in primiparous than multiparous women, and dense placental infections were also more frequent in primiparae. Mean singleton birthweight was depressed by 170g in the presence of malaria but the difference was only significant for primiparae.

The effect of malaria on postnatal growth has been investigated in two different types of studies. In the first type, examples of which are the studies in The Gambia of Marsden (29) and Rowland et al. (14), the effect of individual episodes of illness on weight gain during the period in which the illness occurred was estimated. Both studies indicated that an episode of malaria had a negative effect on weight gain in the period immediately following the episode.

Whilst an episode of malaria may have a short-term effect on growth, through depressed food intake and negative energy and nitrogen balance, the net effect of malaria on growth will depend on the extent to which the capacity for catch-up growth is subsequently realized.

The second type of study has addressed this question by estimating the net effect of malaria on growth over a much longer period of time.

The most rigorous study is that of McGregor et al. (30). Two groups of 20 newborns were enrolled in a 3-year prospective study. One group was given weekly chloroquine and the other a placebo. Unprotected children initially gained weight more slowly but subsequently gained ground and by 36 months were just as heavy as the protected group. However, the mean height of the protected children at three years of age was more than 3cm greater than that of the unprotected group.

Thus, the evidence from the one well-designed study of the longer-term effects of malaria on growth is for a negative effect on height but not weight. However, short-term studies of the effect of individual episodes indicate the reverse — a negative effect of malaria on weight but not on height. Part of this conflict can be explained by the greater short-term variability in weight than in height.

Nevertheless, although malaria may be an important factor affecting growth the fact that
both the shortest and the tallest children in PNG are found in districts in which malaria is highly endemic (Maprik and Morehead districts, respectively) indicates that other factors are also very important.

All of the studies quoted above have been in areas where malaria is highly endemic. In areas where malaria is episodic rather than endemic, such as the highlands of PNG, and immunity to malaria is less, an individual episode may be more severe and have greater effects. Thus, in Enga Province, Sharp and Harvey (31) found splenomegaly, used as an index of recent experience of malaria, to be associated with stunting in young children.

**Effects of Nutrition on Malaria**

The few studies which have addressed this question - see Heywood and Harvey (32) - have serious design and analysis flaws and it is not possible at the moment to draw firm conclusions.

**Iron**

Malarial parasitaemia usually results in some degree of anaemia in which red cell morphology is consistent with iron deficiency. Successful intervention studies have resulted in increased haemoglobin levels. At the same time there is a rise in serum iron and serum ferritin. Thus, understanding of the haematological picture in malaria is complicated since, although red cell morphology is consistent with iron deficiency, other measures indicate adequate iron status (32).

The effect of iron status on malaria is controversial. Recent studies in PNG indicate that the effect in children may depend on their immune status. In infants Oppenheirner et al. (33) showed that those subjects injected with iron supplement at 2 months of age showed significantly greater malarial parasitaemia and palpable spleens at 6 and 12 months of age than children who received a placebo. In contrast, Harvey (34) working with school-children showed no effect of an oral iron supplement, and improved iron status, on malaria.

**DISCUSSION**

Each of the important infectious diseases of children has been shown to have a negative effect on growth, at least in the short term. However, if catch-up growth after each episode is complete it is possible for there to be a negative short-term effect and no effect in the long term. One of the most important factors determining the net long-term effect is the extent to which catch-up growth occurs.

Under favourable conditions the rate of growth following a period of illness can be very high. However, most evidence indicates that although only modest increases in food intake are needed to support catch-up growth during the convalescent period, they seldom occur (35). The cultural context in which a disease occurs is likely to be an important variable influencing catch-up growth (32). The cultural context will influence not only the actual foods produced and considered food, but also who receives food and when, as well as the availability of food during an illness episode.

The synergism between nutrition and infection means that there are considerable health gains to be made by a combined attack on both malnutrition and infection. However, because the control measures for infection will often be very different from those used for malnutrition the synergism between the control programs will often not be apparent. It is important that health staff appreciate the relationship between malnutrition and infection so that control programs, including prompt and effective treatment of episodes of infectious disease, may be coordinated and the maximum improvement in the health of young children obtained.

**REFERENCES**


Small-Area Variations in the Epidemiology of Malaria in Madang Province

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SUMMARY

Small-area variations in the epidemiology of malaria can have important consequences in the evaluation of malaria control or intervention programs. Epidemiological features of malaria were studied in six villages in Madang Province through six-monthly surveys over a two-year period and three-monthly surveys for a single year. Data on parasite prevalence, infection density, splenic enlargement and morbidity were analyzed to determine the existence of variation within a previously defined study area. While average parasite rates did not differ greatly among villages, rates in the 1-4 years age group in the dry season were significantly higher (60.2%) in the villages north of Madang town compared with those located to the south (37.7%) (α = 0.05). There were also differences in the parasite species ratio (i.e., 21.7% of infections in one village were Plasmodium vivax compared with 12.6% in another), in spleen rates and in degree of splenic enlargement. Utilization data from village aides were used to estimate fever attacks over a 12-month period, but interpretation of these rates was complicated by the alternative sources of treatment available to the village populations.

INTRODUCTION

The principal reason for studying the epidemiology of malaria today is to facilitate the design and evaluation of interventions directed towards reducing the prevalence of malaria infection and occurrence of disease. Studies in the past have sometimes accepted results of one cross-sectional malarialmetrical survey as defining the endemicity of malaria in a given geographical area. The possible over- or under-estimation of baseline prevalence based on a single survey may not be critical in evaluating interventions designed to have a major impact on parasite prevalence and transmission in a highly endemic area. Evaluation of interventions with more modest objectives such as a 20 to 50% reduction in parasite rates in infants and young children, however, would require greater precision in baseline estimates and careful characterization of any variation within the study area. For the most part efforts to control malaria are now realistically focussed on exploring this limited type of intervention.

The Malaria Research Program of the Papua New Guinea Institute of Medical Research (PNGIMR) has been investigating the epidemiology of malaria in a coastal area of Madang Province since 1981. The objectives of the project include: measurement of malarialmetrical, serological and other health indices in the study population; examination of the relationship between these indices and the impact of environmental and socioeconomic factors; and provision of baseline data on a defined population for the possible field test of an antimalarial vaccine.

The purpose of this paper is to present results from the study of small-area variations in the epidemiology of malaria in six villages from the Madang study area. The parameters investigated longitudinally in these villages include parasite rates, spleen rates, degrees of

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Figure 1. Villages included in the study of small-area variations in the epidemiology of malaria together with the location of Aid Posts and Health Centres.
splenic enlargement, parasite densities and morbidity. Results of selected entomological investigations are reported by Charlwood et al. (1) in this issue.

METHODS

The study area of the PNGIMR Malaria Research Program is contained within a 22km radius of Madang town and includes a population of approximately 16,500. The area and the general epidemiology of malaria within it is described elsewhere (2). Six villages were selected for inclusion in the study. Two are located on the north coast and two on the south coast, at sea level. One is situated inland in the north at 350m and one inland in the south at 150m (Figure 1). The villages are characterized by hyperendemic malaria; however, based upon results of previous epidemiological studies we had evidence for differing levels of hyperendemicity in the area. The present study was designed and the six villages chosen to explore the differences in greater detail.

Malariometrical surveys were conducted at approximately three-monthly intervals from July of 1983. Four surveys were conducted in each of the six villages. Species-specific parasite rates, densities and spleen grades were recorded for all individuals in each survey. The survey methodology, laboratory techniques and quality control procedures are described elsewhere (2).

Morbidity surveys were conducted concurrently with the parasitological surveys to ascertain episodes of fever over a preceding two-week period for each individual. The methodology and results of these surveys are reported by Moir et al. (3). A voluntary village aide was trained from each village to dispense chloroquine and amodiaquine to individuals presenting with fever and to record for each episode the individual’s name, house number, date and treatment given.

A questionnaire was used to collect data on socioeconomic status. Each head of household was interviewed in all villages. In addition to providing information on selected socioeconomic indicators, data from the questionnaire permitted enumeration of the domestic animal populations of each village. Surveys of bed-net utilization by household were conducted, and data on genetic polymorphisms were collected. These data will be reported separately.

RESULTS

Average participation among village inhabitants over the four surveys was as follows: 84.3% in the 1-4 year age group; 85.6% in 5-15 year olds; and 68.6% among adults older than 15 years. Five of the six villages had an overall compliance rate of greater than 78% for all ages (all surveys combined). The remaining village had an overall participation rate of 53.7%; however, compliance in the 5-15 year age group over all surveys was 71.3% and in the 1-4 years group 60%. As these are the age groups of greatest interest, participation was considered adequate to retain this village in the age-group-specific analyses.

Average parasite rates did not differ greatly among the villages; however, more short-term variation was observed in the inland villages and those on the north coast than in those on the south coast. There were consistent differences in the range of variation in parasite rates in 1-9 year olds between villages north of Madang, whether inland or on the coast, and those south of Madang town. Rates in this age group varied in the north from 40.7% (lowest rate among the three villages) to 88% (highest rate). Villages in the south ranged from a low of 21.7% to a high of 72%. Figure 2 shows the parasite rates for all species in 1-4 year olds over time in two groups of villages. Combining the rates from all surveys carried out in the dry season gives an average rate of 60.2% for the three villages north of Madang; the corresponding average rate for villages south of Madang was 37.7%. This difference was statistically significant ($\alpha = 0.05$). Respective rates for the wet season were 60.2 and 48.9%, which were not statistically different. However, the difference between rates in the dry and wet seasons for the villages in the south was statistically significant, suggesting a greater increase in transmission in the wet season in the south. Differences in the 1-9 years age group, while smaller, were also observed.

The predominant species of parasite in the study area is Plasmodium falciparum (2).
Figure 2. Parasite rates over time in the 1-4 years age group. Rates from the three villages south of Madang town are at the top and from those north are at the bottom.
was consistent in the six villages included in the study. In the village with the highest proportion of *Plasmodium vivax* infections (Maraga), 48 of 221 (21.7%) infections were of this species. In the village with the lowest proportion (Butelgut) 26 of 206 (12.6%) infections were positive for *P. vivax*. The difference was significant ($\alpha=0.05$). *Plasmodium malariae* and *Plasmodium ovale* are found in the study area, but at a prevalence too low for meaningful analysis at the village level. With few exceptions parasite densities for *P. falciparum* (asexual forms) were highest in the wet season for all age groups. Densities reached the highest level in 1-4 year olds with averages in two villages during the wet season higher than 3400 parasites/mm$^3$ blood. Adults in all villages had the lowest densities. Average parasite densities were lower than 600 parasites/mm$^3$, with one exception in which a slightly greater average density was observed in one village at the end of the wet season.

Spleen rates in children 2-9 years have consistently been above 75% in Butelgut, Mebat and Budip since 1981. In the village of Sah they were significantly lower but showed a steep rise during the wet season of 1984, which suggests intense transmission at that time. Maraga appeared to show a more gradual rise in spleen rates, again with the steepest rise in the wet season of 1984. Only one data point was available for Dogia before the three-monthly surveys; however, based on analysis of other parameters it is considered likely to demonstrate a pattern similar to that observed in Maraga. Spleen rates in adults were high (> 60%) in Butelgut, Mebat, Budip and Dogia, while in Sah the average rate in adults was 52.5%. Participation in Maraga was too low among adults to be able to report a valid rate. The variation in the proportion of enlarged spleens grade 2 (Hackett) or greater was significant between the wet and dry seasons in all age groups in Butelgut and in 2-9 year olds in Maraga. Table 1 shows the proportion of enlarged spleens grade 2 or greater by season for two age groups. The average enlarged spleen (AES) (4) in the 1-4 years age group varied over the four surveys from a low of 1.7 (Maraga and Dogia) to 3.1 (Mebat). The AES in this age group was consistently higher in the villages of Butelgut, Mebat and Budip than in Maraga, Dogia and Sah, with the exception of Sah in the wet season of 1984. In both groups of villages and

### Table 1

| Village | 2-9 years | | | | 2-9 years | | | | | | 2-9 years | | | |
|---------|-----------|-------------|-------------|-------------|-----------|-------------|-------------|-------------|-------------|-----------|-------------|-------------|-------------|
|         | Wet season | Dry season  | Wet season  | Dry season  | Wet season | Dry season  | Wet season  | Dry season  | Wet season  | Dry season | Wet season  | Dry season  | Wet season  |
|         | No. exam. % enlarged | No. exam. % enlarged | No. exam. % enlarged | No. exam. % enlarged | No. exam. % enlarged | No. exam. % enlarged | No. exam. % enlarged | No. exam. % enlarged | No. exam. % enlarged | No. exam. % enlarged | No. exam. % enlarged | No. exam. % enlarged | No. exam. % enlarged |
| Budip   | 81 95.1  | 36 80.6  | 48 54.2  | 34 52.9  |           |           |           |           |           |           |           |           |           |
| Mebat   | 92 87.0  | 96 79.2  | 56 60.7  | 97 44.3  |           |           |           |           |           |           |           |           |           |
| Butelgut| 86 80.2* | 92 60.9* | 78 53.9* | 120 33.3*|           |           |           |           |           |           |           |           |           |
| Dogia   | 34 79.4  | 51 72.6  | 46 37.0  | 52 38.5  |           |           |           |           |           |           |           |           |           |
| Maraga  | 86 79.1* | 79 57.0* | 60 35.0  | 101 23.8 |           |           |           |           |           |           |           |           |           |
| Sah     | 104 61.5 | 137 54.7 | 92 30.4  | 146 17.8 |           |           |           |           |           |           |           |           |           |

* Significant ($\alpha=0.05$) wet season v. dry season
all age groups the observed AES was higher in the wet season.

Utilization data from voluntary village aides were used to estimate fever attacks over a 12-month period. Table 2 shows the number of fever cases by age group standardized by the population in each age group for each village. Butelgut shows the highest utilization of the village aide, but the interpretation of these data is not entirely straightforward.

**DISCUSSION**

This study suggests significant variation among villages in a relatively small geographical area that is not readily apparent in the standard malariometrical indices from one or even two cross-sectional surveys. The hypothesis that differing levels of endemicity exist in the study area was supported by comparisons of parasite rates in 1-4 year olds and of proportions of enlarged spleens grade 2 or greater in the 2-9 years age group for both seasons. These differences would appear to be influenced both by entomological factors, such as vector density, sporozoite rates and average bites by sporozoite-infected mosquitoes per night (T. Burkot, P.M. Graves and I.D. Charlwood, unpublished data), and the use of antimalarial drugs and bed nets in villages. The number of pigs and dogs available to serve as alternative hosts would also appear to account for some variation in parasite rates as indicated in preliminary multivariate analyses (Cattani, unpublished data). We believe that the relative degrees of infection observed in the study area are important in terms of future evaluation of malaria control measures, including possibly an antimalarial vaccine. The efficacy of intervention has been measured in the past by differences in estimated parasite or spleen rates. If intervention and control areas are selected geographically without regard to moderate but consistent differences in malariometric indices the effects of an intervention could be significantly under- or over-stated.

Morbidity as measured by attacks of fever presenting to the village aide was significantly higher in Butelgut but comparable among the other villages. This finding was also reported by Kass (5) in the same study area. Interpretation of morbidity data from village aide utilization is complicated by the alternative sources of care available to inhabitants in these villages. In addition to the permanent sources of health care identified in Figure 1, maternal and child health mobile clinics visit most villages on a monthly basis and there is a large outpatient clinic at the hospital in Madang. Antimalarial drugs are also dispensed in schools and are

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**TABLE 2**

FEVER CASES SEEN BY VILLAGE AIDE JANUARY-DECEMBER, 1984, BY AGE GROUP STANDARDIZED BY THE VILLAGE POPULATION IN EACH AGE GROUP

<table>
<thead>
<tr>
<th>Village</th>
<th>&lt; 1</th>
<th>1-4</th>
<th>5-9</th>
<th>10-14</th>
<th>15-19</th>
<th>20-29</th>
<th>30+</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butelgut</td>
<td>14.5</td>
<td>7.7</td>
<td>5.1</td>
<td>1.9</td>
<td>1.8</td>
<td>1.8</td>
<td>1.1</td>
<td>2.8</td>
</tr>
<tr>
<td>Mebat</td>
<td>3.3</td>
<td>2.0</td>
<td>0.2</td>
<td>0.2</td>
<td>0.5</td>
<td>0.9</td>
<td>1.6</td>
<td>1.0</td>
</tr>
<tr>
<td>Budip</td>
<td>1.8</td>
<td>3.5</td>
<td>0.7</td>
<td>0.5</td>
<td>1.1</td>
<td>0.3</td>
<td>0.9</td>
<td>1.2</td>
</tr>
<tr>
<td>Maraga</td>
<td>1.6</td>
<td>3.4</td>
<td>0.7</td>
<td>1.2</td>
<td>1.3</td>
<td>0.5</td>
<td>0.3</td>
<td>1.2</td>
</tr>
<tr>
<td>Dogia</td>
<td>3.3</td>
<td>2.0</td>
<td>1.9</td>
<td>0.9</td>
<td>0.2</td>
<td>0.7</td>
<td>0.3</td>
<td>1.0</td>
</tr>
<tr>
<td>Sah</td>
<td>3.0</td>
<td>3.9</td>
<td>1.4</td>
<td>1.0</td>
<td>0.9</td>
<td>1.2</td>
<td>1.3</td>
<td>1.5</td>
</tr>
</tbody>
</table>
available commercially in Madang town. The number and diversity of sources of antimalarials precluded attempts to follow up all fever episodes in the study villages. Moir et al. (3) reported the following figures from a follow-up of 106 fever cases from villages with high utilization of village aides: 50% received chloroquine or amodiaquine from the village aide; 19.6% sought antimalarials from another source; 4.9% received treatment not related to malaria; and 25.5% received no treatment. Four cases were excluded because the fever had developed within 24 hours of the time of the survey. These figures may be used as a guide for interpreting village data, but hypotheses regarding differences in fever attack rates between villages could not be tested from these data. The difficulties of obtaining good data on malaria morbidity on a village basis should be recognized in attempts to design and evaluate interventions.

REFERENCES

Hereditary Ovalocytosis in Melanesians

D. AMATO AND P.B. BOOTH

A distinctive type of hereditary ovalocytosis has been found in Papua New Guinea and a few areas of Southeast Asia. Its main features include a high incidence among tropical lowland dwellers, autosomal recessive inheritance, specific depression of a number of red cell antigens, a characteristic morphology in blood films, and an effect on the erythrocyte sedimentation rate.

Speculation has occurred as to whether the high incidence of ovalocytosis in malarious areas may be related to a selective advantage possessed by ovalocytics with regard to severe malaria. Preliminary data tend to support this hypothesis, but the evidence is not conclusive and much further work is needed.

PRELIMINARY NOTE ON NOMENCLATURE

The terms ‘ovalocytosis’ and ‘elliptocytosis’ have long been used interchangeably for the sporadic type of hereditary elliptocytosis which is inherited in an autosomal dominant manner and which has been known for over 70 years. Since the condition which is the subject of this review, although also hereditary, differs in several important ways from the sporadic type, we shall not use the terms interchangeably. Rather, ‘ovalocytosis’ will refer to the high-frequency type discussed in detail below, and ‘elliptocytosis’ will denote the sporadic type.

INTRODUCTION

A distinctive type of hereditary ovalocytosis is common among Papua New Guineans of coastal and insular origin. In this article, we review the salient features of this condition: its incidence, geographic distribution, inheritance, appearance in blood films, clinical significance, serological findings, and the question of whether the abnormality confers a selective advantage; in addition, the chief differences between this type of ovalocytosis and the sporadic type of hereditary elliptocytosis will be summarized.

INCIDENCE

The first mention of a high frequency of ovalocytosis in this part of the world was made almost 40 years ago in a Dutch language journal by Bonne and Sandground (1939); the phenomenon was mentioned incidentally in an article on echinostomiasis in Celebes. To our knowledge, the first systematic study of high-frequency ovalocytosis was reported by Lie-Injo in 1965; this article mentions a frequency of 12.3% among 440 healthy and hospitalized aboriginal Malayans.

Other studies have revealed high incidences of ovalocytosis among several populations: 6.6 to 20.9% in several groups of Malayan aborigines (Lie-Injo, Fix, Bolton and Gilman, 1972); 12.7% among the land Dayaks and 9.0% among the sea Dayaks of Sarawak (Ganesan, Lie-Injo and Ong, 1975); and 1.7% among the Batak and 7.2% among the Minangkabau in North Sumatra (Sembiring, Siregar and Kosasih, 1975).

Although the condition has been known for some years in Papua New Guinea (P.N.G.), its first mention in the literature did not occur until 1975 (Isbister, Amato and Woodfield, 1975). In that same year, a study of 1,020 blood films of in-patients and out-patients at the Port Moresby General Hospital (P.M.G.H.) found ovalocytosis in 11.2%; analysis of smaller numbers of films from Pari and Hsiu villages in the Central Province showed frequencies of 22.4% and 16.8%, respectively (Amato, 1975).

Its incidence among 334 Waskia Kar Kar Islanders (Madang Province) was 13.8% (Booth, Serjeantson, Woodfield and Amato, 1977); and that among 583 residents of Kikori, Malalaua and Kerema in the Gulf
Province was 12.9% (Amato, 1976). It is also seen frequently at Wewak Hospital in the East Sepik Province, and at the Angau Memorial Hospital in the Morobe Province (Spark, R., and Crane, G.G., personal communications).

Thus its incidence among coastal populations in P.N.G. appears to be between 5 and 20 per cent, i.e., of a similar order to the frequencies reported from the Malaysian and Indonesian populations mentioned above. This is several hundred times more frequent than the sporadic type of elliptocytosis, the incidence of which is about 0.02 - 0.05 per cent (Cooper and Jandl, 1972).

**GEOGRAPHIC DISTRIBUTION**

In the P.M.G.H. study (Amato, 1975), of 97 patients with ovalocytosis whose home province was ascertained, 96 came from 10 coastal or island provinces. The one highlander was from the Tari Sub-province of the Southern Highlands Province. Serological studies (see below) provide further evidence for a coastal distribution of the trait, with the exception of parts of the Southern Highlands (Booth, 1972; Booth and Homabrook, 1972b). Moreover, there is evidence, from other genetic markers, of coastal affinities of some Southern Highlands populations, especially those from the Lake Kutubu area (Booth and Homabrook, 1972a).

At present, ovalocytosis and/or antigenic depression has not been found in any person from the other highland provinces (Booth, 1972; Booth and Homabrook, 1972b; Bashir, H., personal communication; Amato, D., unpublished observations).

There is little doubt, then, that the type of ovalocytosis under discussion is found only among groups originally of coastal or island (i.e., lowland) origin.

**INHERITANCE**

It has long been known that the sporadic type of elliptocytosis is inherited as an autosomal dominant (Cooper and Jandl, 1972).

In contrast, data from Kar Kar Island (Booth et al., 1977) are consistent with an autosomal recessive inheritance for the high frequency type of ovalocytosis seen in P.N.G.

It has been stated (Lie-Injo, L.E., personal communication) or implied (Baer, Lie-Injo, Welch and Lewis, 1976) that the ovalocytosis found in Malaysia and Indonesia is autosomal dominant; however, the type of rigorous statistical study of families necessary to distinguish a dominant from a high-frequency recessive character has not yet been reported from those populations.

It is clear from family studies in P.N.G. (Booth et al., 1977) that individuals heterozygous for ovalocytosis usually display normal red cell morphology. There is evidence (Serjeantson, S., personal communication) that occasionally the red cells of an obligate heterozygote assume the oval shape after storage for a few days in EDTA.

**MORPHOLOGY**

The high-frequency type of ovalocytosis is readily recognized on a well prepared thin blood film. Under low power (100 x), examination of the thicker area of the film reveals that the red cells are ‘piled together’; i.e., they do not form rouleaux as seen in the thick areas of non-ovalocytic films.

At higher power (400 x), in the thin part of the film the great majority of cells are seen to be oval in shape, some of them only mildly so (Figure 1). A few oval macrocytes are usually present, as are a small number of elongated cells with blunt or squared-off ends (‘bacillary’ forms). Stomatocytes (red cells with a slit-shaped central pallor) and knizocytes (cells with a double pallor separated by a well haemoglobinized narrow area) are commonly seen; their numbers range from few to many.

The autosomal dominant type of elliptocytosis is occasionally seen in P.N.G. (Pryor and Pitney, 1967; Crane, G.G., personal communication; Amato, D., unpublished observations). In the families studied with this type, the morphology has been different from the high-frequency type: the red cells of the former have a greater length-to-width ratio, i.e., they are more cigar-shaped. In addition, rouleaux can be seen in the thick part of the film; and stomatocytes, knizocytes and oval macrocytes do not form part of the picture.
Occasionally, a film is seen with a smaller proportion of oval cells (i.e., < 50%), and these may show some of the characteristics of the high-frequency type mentioned above. Whilst it is possible that the gene for ovalocytosis may show variable penetrance, it is our opinion that such films should not be classified as ovalocytic, especially since there are many other conditions which can be associated with small numbers of oval or elliptical cells.

The presence of a few oval macrocytes raised the question of megaloblastosis. However, among 26 patients with ovalocytosis who underwent marrow aspiration in a 2½ year period, only 4 had definite megaloblastic changes. This proportion did not differ significantly from that seen in non-ovalocytics (chi-square = 0.07, p < 0.75) (Amato, D., unpublished observations).

The megaloblastic ovalocytics did not show greater numbers of macrocytes in the peripheral film than those ovalocytics without megaloblastosis. However, other changes were seen in the former which can be associated with megaloblastosis: hypersegmented neutrophils in all 4, Howell-Jolly bodies in 3, basophilic stippling in 1, leucopenia in 1 and thrombocytopenia in 1.

**CLINICAL SIGNIFICANCE**

It has long been known that sporadic hereditary elliptocytosis may be associated with haemolysis. While the majority of cases show no evidence of haemolysis, a minority (10-15%) have a compensated haemolytic state; i.e., there is a mild degree of haemolysis, but this does not exceed the erythropoietic capacity of the marrow and thus there is no anaemia. In an even smaller minority, there is overt haemolytic anaemia which is usually improved or corrected by splenectomy (Cooper and Jandl, 1972).

In contrast, high-frequency ovalocytosis does not appear to be associated with haemolysis. In the survey of P.M.G.H. patients (Amato, 1975), the frequency distribution of haemoglobin concentrations was essentially similar when comparing ovalocytic and non-ovalocytic patients of either sex; the modal range of haemoglobin was the same (9.1 - 11.0 g/dl) in all four groups.

Thus, while patients with ovalocytosis may certainly be anaemic, they are anaemic for the same reasons that other Papua New Guineans may be anaemic, e.g., iron deficiency, infection, folate deficiency, malaria, beta-thalassaemia minor, tropical splenomegaly syndrome, etc. Even when there is evidence of haemolysis, causes other than ovalocytosis can be found.
We have yet to see a patient with the high-frequency type of ovalocytosis who is haemolyzing on the basis of the red cell membrane defect. A similar situation appears to obtain for the high-frequency ovalocytosis seen in Malaysia and Indonesia (Lie-Injo et al., 1972).

The main significance of this type of ovalocytosis for the clinician would appear to be its effect on the erythrocyte sedimentation rate (ESR). The ESR depends on a number of factors, one of the most important being the degree to which the red cells form rouleaux in the sedimentation tube (Dacie and Lewis, 1975). This property is in turn enhanced by several factors, such as high levels of serum globulins, especially fibrinogen (an acute phase reactant) and gamma-globulins, and an increased ratio of plasma to red cells (anaemia).

Yet patients with the high-frequency type of ovalocytosis usually do not develop an increased ESR in association with many conditions where such an increase would be expected. Thus we have seen 3 ovalocytic patients with acute rheumatic fever, 2 with multiple myeloma, and numerous others with acute infections and/or anaemia, in whom the ESR was within normal limits. This phenomenon is most likely due to the inability of these ovalocytes to form rouleaux.

Thus, if a patient has a normal ESR in a situation where one would have expected an elevated rate, the blood film should be checked. If it is typically ovalocytic, then the ESR is of no value in diagnosing or following the patient’s illness.

**SEROLOGICAL CORRELATIONS**

In 1966, Booth, Jenkins and Marsh reported that a cold-acting auto-antibody commonly encountered in Papua New Guinean sera, recognized a ‘new’ blood group antigen, related to Li and designated I$. It was soon apparent that selective depression of I$ occurred in some 15% of coastal Melanesians (Booth, 1972), and this was shown by family studies to be inherited as an autosomal recessive characteristic (Booth and Hornabrook, 1972b).

Unfortunately, during the early work, other antibodies selected to show that the I$ weakness was not artefactual (anti-H, -N, -P$_1$ and -I$^P$) were not among those directed at antigens subsequently shown to be of the depressed series, and so the more widespread nature of the antigenic depression remained unrecognized until in 1974 investigations in Christchurch, New Zealand, of warm type autoimmune haemolytic anaemia antibodies of anti-LW specificity, demonstrated that LW was depressed on L$ weak cells. Further investigations have shown that the depressed series of antigens include I$, I$, LW, D, C, e, S, s, U, Kp$, Jk$, Jk$, Xg$, Wr$, Sc$, En$, and D$i$, which are simultaneously affected when present. Reactivity of H, A, A$_1$, B, I$P$, i, P$_1$, M, N, Lu$^a$, k, Fy$^a$, Co$^a$, Vel, Ge$^a$ and Jr appeared to be within the normal range (Booth, 1975).

It was eventually realized that the work on ovalocytosis, and that on antigenic depression, represented complementary investigations of the same hereditary condition. A series of 235 bloods previously screened for antigenic weakness was examined, blind, for ovalocytosis, and the statistical test for association of antigenic status and red cell morphology gave chi-square > 179.0, thus removing all doubt about the correlation.

The antigens of the depressed series include those against which haemolytic auto-antibodies act, which suggests that another common factor affecting these antigens may be a propensity to undergo changes resulting in the body failing to recognize them as part of itself, and treating them as foreign antigens.

The antigenic status of the Indonesian and Malaysian ovalocytic bloods is not yet known, but when ascertained should immediately either confirm or rebut the hypothesis that these arise from the same hereditary condition as exits in P.N.G.

The I$ strength of cells of individuals from 6 different families with (sporadic) elliptocytosis, both haemolytic and non-haemolytic, has been found to be normal (Booth et al., 1977; Woodfield, D.G., Amato, D., unpublished data), thus providing a further distinguishing feature between the two conditions.
THE MALARIAL HYPOTHESIS

Geographical location rather than ethnic or linguistic group appears to determine the occurrence of ovalocytosis/antigenic depression in P.N.G. Also, the incidence of the condition is notably constant from population to population, which is in contrast to the very variable distribution of blood group alleles in the same populations. These considerations suggested (Booth, 1975; Amato and Andrews, 1975) that some selective mechanism might apply, though as the incidence of ovalocytosis seemed not to exceed 20%, it might be that the condition conferred advantage at some period of life, and disadvantage at another, supposing that equilibrium gene frequencies for the hereditary condition have been attained in coastal regions and that ovalocytosis is not neutral in effect. If ovalocytics were advantaged during childhood and disadvantaged in utero or in adulthood, a balanced polymorphism could result.

The congruent distribution of ovalocytosis and malaria in P.N.G. has prompted some preliminary investigations, which have provided results tantalizingly suggestive, but not, in general, statistically significant of an increased resistance to malaria in ovalocytic children. The main difficulty arises from the relative paucity of ovalocytic compared to normal subjects in any random series, and, of course, this is compounded by the need to sub-divide the subjects into those with and without malarial parasites present.

The data of Serjeantson, Bryson, Amato, and Babona (1977), on children aged 2-14 years from Kar Kar Island and Gogol Valley, show that the likelihood of infection in ovalocytic children is about 75% that in normocytic children for Plasmodium falciparum, P. vivax and for all species combined. Of 397 children examined, 52 were ovalocytic, and of these only 15 had demonstrable parasites. These workers emphasize the very large sample size needed to demonstrate significant differences in parasitaemia rates between normocytics and ovalocytics.

In an attempt to overcome this problem, Babona and Amato (1976) studied 255 children aged 6 months to 5 years presenting at Madang Hospital with fever (> 38°C). In this way, it was hoped to secure a greater proportion of malarious subjects. However, a possible disadvantage emerged, as only 14 ovalocytics (5.5%) were found in the series, while among 84 afebrile children (controls) the rate was 8.3%. Even so, 119 of 241 normocytic children had malarial parasitaemia, compared with 3 of the 14 ovalocytics, which is a significantly lower rate (p < 0.05). When the analysis was restricted to those with falciparum malaria, there was a lower, but non-significant rate of parasitaemia among the ovalocytics.

Baer et al. (1976) have reported resistance to higher grades of malarial parasitaemia among ovalocytic Temuan people in Malaysia (two-thirds of malaria seen in the region is due to P. falciparum). They also found a higher frequency of ovalocytosis among adults than among children, which would be expected if ovalocytics possessed a selective advantage. However, Serjeantson et al. (1977) found no significant difference in the incidence of ovalocytosis between adults and children in P.N.G.

It is noteworthy that the protection afforded by the sickle-cell trait (Hb S trait) against malaria is most obvious when the deficiency of sicklers among children dying of malaria is treated statistically (Motulsky, 1964). Whether an analogous study would prove feasible in regard to ovalocytosis and malaria in P.N.G. is doubtful.

Clearly, an apparently relatively minor change in red cell membrane composition can profoundly affect susceptibility to malaria. In the absence of the Duffy blood group antigens (Fy\^a and Fy\^b), as occurs in 80-90% of West Africans, P. vivax cannot gain entry to the erythrocytes (Miller, Mason, Clyde, and McGinniss, 1976), presumably because in this situation the receptor normally activated by this parasite is also absent. Fy (a-b-) cells have normal morphology and survival.

If ovalocytosis confers any resistance to malaria, then the mechanism for this protection seems likely to occur after entry into the red cells by the parasites, as ovalocytic subjects can be seen with para-
parasitaemia, and more specifically, parasites can be seen in oval cells.

COMPARISON OF 'ELLIPTOCYTOSIS' AND 'OV ALOCYTOSIS'

The main features which help to differentiate these two conditions are summarized in Table 1.

### TABLE 1

**Summary of Differences between 'Elliptocytosis' and 'Ovalocytosis'**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Elliptocytosis</th>
<th>Ovalocytosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occurrence on world scale</td>
<td>Worldwide</td>
<td>Apparently limited to parts of Southeast Asia and Melanesia</td>
</tr>
<tr>
<td>Geographic restriction</td>
<td>None</td>
<td>Lowland tropical areas, congruent with regions of malarial endemicity</td>
</tr>
<tr>
<td>Incidence</td>
<td>0.02 - 0.05%</td>
<td>2 - 20%</td>
</tr>
<tr>
<td>Inheritance</td>
<td>Autosomal dominant</td>
<td>Autosomal recessive</td>
</tr>
<tr>
<td>Morphology of red cells</td>
<td>Mainly elongated oval</td>
<td>Mainly oval (often with stomatocytes, knizocytes, oval macrocytes, and 'bacillary' shapes); lack of rouleaux formation.</td>
</tr>
<tr>
<td>Haemolysis on basis of red cell defect</td>
<td>Occurs in minority of cases</td>
<td>Probably does not occur</td>
</tr>
<tr>
<td>Effect on ESR</td>
<td>Probably none</td>
<td>Expected rise of ESR in inflammatory and other states not seen</td>
</tr>
<tr>
<td>Selective antigenic depression</td>
<td>Absent</td>
<td>Present</td>
</tr>
</tbody>
</table>

NATURE OF THE MEMBRANE DEFECT

Very little is known about the nature of the red cell membrane defect(s) in either of these two abnormalities. No consistent differences between patients with the haemolytic and non-haemolytic forms of hereditary elliptocytosis have been found.

It is probable that the defect in ovalocytosis associated with antigenic depression involves the portions of the membrane where the depressed antigens are normally expressed. One might assume either that the antigens subject to depression all depend, for their full expression, upon the same membrane component(s), or alternatively that the membrane anomaly in some way physically obscures the antigenic sites. The series of depressed determinants would thus be associated by structure and/or spatial orientation on the red cell membrane.

ADDENDUM

Professor Sir John Dacie has recently brought to our attention an article (Honig, G.R., Lacson, P.S., and Maurer, H.S. (1971) A new familial disorder with abnormal erythrocyte morphology and increased permeability of the erythrocytes to sodium and potassium. *Pediatric Research* 5:159), in which the authors describe ovalocytosis without anaemia or evidence of haemolysis in several members of a Filipino family. From their description and photomicrographs, it appears that the condition is identical with the one seen in P.N.G. The significance of the report with respect to this type of ovalocytosis is twofold:

1. Several in vitro abnormalities (without apparent clinical significance) are identified in this condition, including decreased osmotic fragility, increased autohaemolysis after 48 hr incubation, increased glucose consumption by red cells, and decreased intracellular potassium;

2. The disorder is documented in yet another country of the Southeast Asia-Melanesia region (though we are not aware of any reports bearing on its incidence in the Philippines).
ACKNOWLEDGEMENT

We are grateful to Mrs D. Skelton for secretarial assistance.

REFERENCES


TRENDS IN SEXUALLY TRANSMITTED DISEASE INCIDENCE IN PAPUA NEW GUINEA

Candy K. Lombange

Papua New Guinea Institute of Medical Research

SUMMARY

A retrospective study of gonorrhoea and syphilis from Health Department records was carried out in Papua New Guinea. During the ten-year period (1974-1983) 101,636 new cases of gonorrhoea and 34,422 of syphilis were reported among the general population of Papua New Guinea. The incidence of both sexually transmitted diseases have significantly (P < 0.005) increased over the decade despite the introduction and implementation of the National Sexually Transmitted Disease (STD) Control Programme. Some which contribute to the present increase in sexually transmitted diseases are segregation of health and non-health services, insufficient staff training and increased immigration to urban centres.

INTRODUCTION

Venereal diseases did not exist in Papua New Guinea before contact with Western civilization. In 1874 early in the medical history of this country Rev. Lawes reported that no syphilis was seen among Papuans (1). Similarly, in the same century there was no record of reported cases of venereal disease in German New Guinea (2).

In 1902, Wenland first reported sexually transmitted disease in New Guinea (3) while in 1908 Bellamy reported a 5% prevalence of STD in Papua (4). After World War II sexually transmitted disease was noticed as prevalent in the Trust Territory of Papua and New Guinea. The first case of syphilis in Papua New Guinea was reported in 1960. Subsequently, an epidemic of syphilis was reported in the New Guinea highlands region in 1969 (4). By 1970-1972 gonorrhoea was prevalent throughout the country whereas syphilis was more prevalent along the highlands highway.

Ten years ago the five-year National Health Plan was introduced. The objectives of the 1974-1978 National Health Plan (5) in respect to sexually transmitted disease control were to reduce the incidence of the disease through:

1. readily available, free and confidential treatment;
2. contact tracing and treating sexual partners;
3. training of health personnel;
4. health education;
5. coordinated efforts of all agencies important in the control of the disease.

The targets of the plan were to have by 1978:

A. 50% of STD patients naming and locating sexual partners and 50% of these contacts being treated;
B. 95% of all patients coming for treatment notified and reported to National Disease Control Headquarters;
C. established STD clinics staffed by HEOs or nurses at most centres;
D. at national level a specialist appointed in venereal diseases; and
E. the teaching of venereology to all health personnel.

The proposals of the plan recommended some important changes to improve the management and control programme of venereal disease. Among these proposed changes was the need to direct and evaluate the control measures and the recommendation that the venereologist co-ordinate action at national and provincial levels.

Evidently the STD Control Programme which ended five years ago had not been
evaluated. It is important that health planners and responsible organizations know the outcome of the implemented programme.

MATERIALS AND METHODS

The method used was a retrospective record research of gonorrhoea and syphilis morbidities in Papua New Guinea. The reported morbidities of both diseases and contact-tracing activities throughout the country for the last ten years were studied. The incidences of both gonorrhoea and syphilis are reported in the EPINT system which monitors monthly morbidities of the diseases at the provincial level. The provincial disease surveillance agents collate statistics from special STD clinics and peripheral health establishment units into the provincial total. These provincial total case morbidity figures are submitted to the National Disease Control statistics section for final reference.

There was a total of 120 EPINT records studied from the National Disease Control statistics unit. The case morbidities for gonorrhoea and syphilis were analysed over a ten-year period. Specific information regarding the operation of the sexually transmitted disease control programme was obtained from the national STD control coordinator by interviewing him. The sister-in-charge of the PMGH STD clinic was also interviewed for supplementary information in regard to the operation of the STD programme.

<table>
<thead>
<tr>
<th>Year</th>
<th>Estimated Population</th>
<th>Gonorrhoea Morbidity</th>
<th>Rate Per 100,000</th>
<th>Syphilis Morbidity</th>
<th>Rate Per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1974</td>
<td>2,641,209</td>
<td>6,333</td>
<td>239.77</td>
<td>1,847</td>
<td>69.93</td>
</tr>
<tr>
<td>1975</td>
<td>2,703,121</td>
<td>6,403</td>
<td>236.87</td>
<td>1,597</td>
<td>59.07</td>
</tr>
<tr>
<td>1976</td>
<td>2,769,033</td>
<td>8,970</td>
<td>323.93</td>
<td>2,257</td>
<td>81.50</td>
</tr>
<tr>
<td>1977</td>
<td>2,826,945</td>
<td>9,105</td>
<td>322.07</td>
<td>1,936</td>
<td>68.48</td>
</tr>
<tr>
<td>1978</td>
<td>2,829,173</td>
<td>12,119</td>
<td>428.35</td>
<td>4,029</td>
<td>142.40</td>
</tr>
<tr>
<td>Subtotal</td>
<td>42,930</td>
<td>11,666</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1979</td>
<td>2,950,769</td>
<td>10,383</td>
<td>351.87</td>
<td>4,808</td>
<td>162.94</td>
</tr>
<tr>
<td>1980</td>
<td>3,012,681</td>
<td>10,945</td>
<td>363.29</td>
<td>4,637</td>
<td>153.91</td>
</tr>
<tr>
<td>1981</td>
<td>3,074,593</td>
<td>9,676</td>
<td>314.70</td>
<td>3,395</td>
<td>110.42</td>
</tr>
<tr>
<td>1982</td>
<td>3,138,505</td>
<td>14,634</td>
<td>466.27</td>
<td>4,161</td>
<td>132.57</td>
</tr>
<tr>
<td>1983</td>
<td>3,200,417</td>
<td>13,070</td>
<td>408.38</td>
<td>5,755</td>
<td>179.82</td>
</tr>
<tr>
<td>Subtotal</td>
<td>58,708</td>
<td>22,756</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>101,638</td>
<td>34,422</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
RESULTS

National Morbidity
In the period 1974-1983 gonorrhoea and syphilis surveillance reported the following.

Gonorrhoea
There was a total of 101,638 new cases reported among the general population of the country, giving an incidence over 10 years of 31.76/1000. Of these, 42,930 cases were from 1974-1978 with a five-year incidence of 15.17/1000 and 58,708 cases for 1979-1983 with a five-year incidence of 18.34/1000. Between the two five-year intervals the disease increased by 26.8%.

Syphilis
A total of 34,422 new cases was reported from the general population of the country with an incidence over 10 years of 10.75/1000. From this there were 11,666 cases in 1974-1978 at a five-year incidence of 4.12/1000 and in 1979-1983 22,756 cases, with a five-year incidence of 7.11/1000. Between these two periods syphilis increased by 48.7%.

Both the diseases have comparatively increased over the decade despite the implementation of the STD Control Programme (Table 1 and Figure 1).

Regional Distribution
Tables 2 and 3 show the regional morbidities for both the diseases and the distribution of incidences between the period of implementation of the National Health Plan and the subsequent five years (6).

It can be seen from the results that there has been a significant increase in the incidences of both diseases in recent years. For the highlands region the incidence of gonorrhoea has come down, which is partly due to poor reporting, especially no reporting from the Eastern Highlands Province since 1982.

There have been very late or even no monthly reports sent in from some provinces. This is indicated in Table 3 and Figure 2, where there are very low numbers in certain provinces compared to their populations. Despite the inconstant reporting, there is no doubt that

Figure 1: Gonorrhoea and Syphilis Morbidity for PNG (1974-1983).
## TABLE 2

REGION-WISE INCIDENCE OF GONORRHOEA AND SYPHILIS IN PAPUA NEW GUINEA

<table>
<thead>
<tr>
<th>Years</th>
<th>Region</th>
<th>Gonorrhoea Morbidity</th>
<th>Rate Per 1000/5yr</th>
<th>% Increase</th>
<th>Syphilis Morbidity</th>
<th>Rate Per 1000/5yr</th>
<th>% Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>1974-78</td>
<td>Southern</td>
<td>6,200</td>
<td>11.26</td>
<td></td>
<td>1,439</td>
<td>2.61</td>
<td></td>
</tr>
<tr>
<td>1979-83</td>
<td>Southern</td>
<td>10,876</td>
<td>17.29</td>
<td>43</td>
<td>4,156</td>
<td>6.60</td>
<td>65</td>
</tr>
<tr>
<td>1974-78</td>
<td>Momase</td>
<td>22,216</td>
<td>27.97</td>
<td></td>
<td>6,772</td>
<td>8.52</td>
<td></td>
</tr>
<tr>
<td>1979-83</td>
<td>Momase</td>
<td>29,434</td>
<td>32.01</td>
<td>24</td>
<td>12,705</td>
<td>13.82</td>
<td>47</td>
</tr>
<tr>
<td>1974-78</td>
<td>Highlands</td>
<td>10,033</td>
<td>9.30</td>
<td></td>
<td>3,355</td>
<td>3.12</td>
<td></td>
</tr>
<tr>
<td>1979-83</td>
<td>Highlands</td>
<td>8,480*</td>
<td>7.19</td>
<td>-15</td>
<td>5,081</td>
<td>4.31</td>
<td>34</td>
</tr>
<tr>
<td>1974-78</td>
<td>N.G. Islands</td>
<td>4,481</td>
<td>10.92</td>
<td></td>
<td>100</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>1979-83</td>
<td>N.G. Islands</td>
<td>9,919</td>
<td>20.93</td>
<td>55</td>
<td>814</td>
<td>1.71</td>
<td>88</td>
</tr>
</tbody>
</table>

Eastern Highlands STD Clinic was closed in 1982

## TABLE 3

REGIONAL DISTRIBUTION OF GONORRHOEA AND SYPHILIS RATES, 1974-1983

### A. Southern Region

<table>
<thead>
<tr>
<th>Year</th>
<th>Estimated Population</th>
<th>Gonorrhoea Morbidity</th>
<th>Rate Per 100,000</th>
<th>Syphilis Morbidity</th>
<th>Rate Per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1974</td>
<td>487,518</td>
<td>978</td>
<td>200.60</td>
<td>91</td>
<td>18.66</td>
</tr>
<tr>
<td>1975</td>
<td>503,285</td>
<td>1,293</td>
<td>246.18</td>
<td>223</td>
<td>44.30</td>
</tr>
<tr>
<td>1976</td>
<td>519,052</td>
<td>1,460</td>
<td>281.28</td>
<td>544</td>
<td>104.80</td>
</tr>
<tr>
<td>1977</td>
<td>534,819</td>
<td>939</td>
<td>275.57</td>
<td>140</td>
<td>26.17</td>
</tr>
<tr>
<td>1978</td>
<td>550,588</td>
<td>1,584</td>
<td>287.69</td>
<td>441</td>
<td>80.09</td>
</tr>
</tbody>
</table>

Subtotal: 6,200, 1,439

<table>
<thead>
<tr>
<th>Year</th>
<th>Estimated Population</th>
<th>Gonorrhoea Morbidity</th>
<th>Rate Per 100,000</th>
<th>Syphilis Morbidity</th>
<th>Rate Per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979</td>
<td>566,353</td>
<td>1,554</td>
<td>274.38</td>
<td>556</td>
<td>98.17</td>
</tr>
<tr>
<td>1980</td>
<td>582,120</td>
<td>1,987</td>
<td>341.33</td>
<td>735</td>
<td>126.26</td>
</tr>
<tr>
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<td>597,888</td>
<td>2,048</td>
<td>342.53</td>
<td>732</td>
<td>122.43</td>
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<tr>
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<td>613,655</td>
<td>2,556</td>
<td>416.52</td>
<td>816</td>
<td>132.97</td>
</tr>
<tr>
<td>1983</td>
<td>629,422</td>
<td>2,730</td>
<td>433.73</td>
<td>1,317</td>
<td>209.23</td>
</tr>
</tbody>
</table>

Subtotal: 10,875, 4,156

Total: 17,075, 5,595
### TABLE 3 contd.

#### B. Momase Region

<table>
<thead>
<tr>
<th>Year</th>
<th>Estimated Population</th>
<th>Gonorrhoea Morbidity</th>
<th>Rate Per 100,000</th>
<th>Syphilis Morbidity</th>
<th>Rate Per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1974</td>
<td>693,903</td>
<td>3,704</td>
<td>533.79</td>
<td>1,459</td>
<td>210.25</td>
</tr>
<tr>
<td>1975</td>
<td>718,942</td>
<td>2,935</td>
<td>408.23</td>
<td>823</td>
<td>128.38</td>
</tr>
<tr>
<td>1976</td>
<td>743,981</td>
<td>4,303</td>
<td>578.37</td>
<td>1,012</td>
<td>136.02</td>
</tr>
<tr>
<td>1977</td>
<td>769,020</td>
<td>4,913</td>
<td>638.86</td>
<td>1,176</td>
<td>152.92</td>
</tr>
<tr>
<td>1978</td>
<td>794,059</td>
<td>6,361</td>
<td>801.07</td>
<td>2,202</td>
<td>277.30</td>
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</table>

Subtotal | 22,216 | 6,772 |

<table>
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<th>Year</th>
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<th>Gonorrhoea Morbidity</th>
<th>Rate Per 100,000</th>
<th>Syphilis Morbidity</th>
<th>Rate Per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979</td>
<td>819,098</td>
<td>5,579</td>
<td>681.11</td>
<td>2,681</td>
<td>327.31</td>
</tr>
<tr>
<td>1980</td>
<td>844,137</td>
<td>5,520</td>
<td>653.92</td>
<td>2,454</td>
<td>290.71</td>
</tr>
<tr>
<td>1981</td>
<td>869,176</td>
<td>4,111</td>
<td>472.97</td>
<td>1,977</td>
<td>227.45</td>
</tr>
<tr>
<td>1982</td>
<td>894,215</td>
<td>6,004</td>
<td>671.42</td>
<td>2,134</td>
<td>238.64</td>
</tr>
<tr>
<td>1983</td>
<td>919,254</td>
<td>8,220</td>
<td>894.20</td>
<td>3,459</td>
<td>376.28</td>
</tr>
</tbody>
</table>

Subtotal | 29,434 | 12,705 |

Total | 919,254 | 51,650 | 19,477 |

#### C. Highlands Region

<table>
<thead>
<tr>
<th>Year</th>
<th>Estimated Population</th>
<th>Gonorrhoea Morbidity</th>
<th>Rate Per 100,000</th>
<th>Syphilis Morbidity</th>
<th>Rate Per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1974</td>
<td>991,340</td>
<td>1,289</td>
<td>130.02</td>
<td>295</td>
<td>29.75</td>
</tr>
<tr>
<td>1975</td>
<td>1,012,088</td>
<td>1,400</td>
<td>138.32</td>
<td>446</td>
<td>44.06</td>
</tr>
<tr>
<td>1976</td>
<td>1,032,836</td>
<td>2,282</td>
<td>220.94</td>
<td>694</td>
<td>67.19</td>
</tr>
<tr>
<td>1977</td>
<td>1,053,358</td>
<td>2,074</td>
<td>196.89</td>
<td>591</td>
<td>65.10</td>
</tr>
<tr>
<td>1978</td>
<td>1,074,312</td>
<td>2,988</td>
<td>278.13</td>
<td>1,329</td>
<td>123.70</td>
</tr>
</tbody>
</table>

Subtotal | 10,033 | 3,355 |

<table>
<thead>
<tr>
<th>Year</th>
<th>Estimated Population</th>
<th>Gonorrhoea Morbidity</th>
<th>Rate Per 100,000</th>
<th>Syphilis Morbidity</th>
<th>Rate Per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979</td>
<td>1,095,060</td>
<td>2,221</td>
<td>202.81</td>
<td>1,513</td>
<td>138.16</td>
</tr>
<tr>
<td>1980</td>
<td>1,115,808</td>
<td>1,879</td>
<td>168.39</td>
<td>1,290</td>
<td>115.61</td>
</tr>
<tr>
<td>1981</td>
<td>1,136,556</td>
<td>1,636</td>
<td>143.37</td>
<td>491</td>
<td>43.20</td>
</tr>
<tr>
<td>1982</td>
<td>1,157,304</td>
<td>2,400</td>
<td>207.37</td>
<td>1,027</td>
<td>64.51</td>
</tr>
<tr>
<td>1983</td>
<td>1,178,052</td>
<td>344</td>
<td>29.20</td>
<td>760</td>
<td>64.51</td>
</tr>
</tbody>
</table>

Subtotal | 8,480 | 5,081 |

Total | 1,178,052 | 18,513 | 8,436 |
both diseases are becoming almost out of control in all regions.

Urban Distribution
The first National Seminar on STD in 1980 requested the operating STD Clinics to submit full details of diseases, particularly on sex, age and laboratory diagnosis. Before this no clinic tabulations had been attempted. The reported cases for the two PNG cities are tabulated from EPINT (6) for 1981-1983 in Tables 4 and 5 and graphed in Figure 3.

There has been an increase in the incidence of gonorrhoea in both cities. The incidence of syphilis has considerably increased in the Port Moresby clinic while there had been a significant decline (P < 0.005) in the incidence of syphilis in the Lae clinic. This discrepancy is probably related to:

A. underreporting;
B. uncertainty of diagnosis of genital ulcers; or
C. cases being treated privately and not reported to the public disease surveillance.

Age and Sex Distribution
Distributions of gonorrhoea and syphilis by age and sex for PNG (1979-1983) are presented in Table 6. These results show that those most commonly affected for both diseases, irrespective of sex, are 15-24 years old. Male patients present to the clinic more often than females, because more females are asymptomatic than their partners.

Contact-Tracing Activities
The contact-tracing activities for 1979-1983 are shown in Table 7. For the whole country 11% of the sexual contacts have been traced and 86.5% of those cases found were treated. This is a very small portion of case-detection activities compared to the National STD Plan target of 50% naming and locating of sexual partners. Each region has done very poorly with contact-tracing activities (Table 8).
Secondary Syphilis

From 1979 to 1983, a total of 848 cases of secondary syphilis have been reported and this accounts for about 3.7% of the known syphilis cases in that period. In Port Moresby General Hospital STD Clinic during 1979-1983 more than half of the secondary syphilis cases have been reported (466 cases), which is 19.2% of the reported syphilis cases in that five-year period from the clinic.

There were no cases of late syphilis reported in the 1979-1983 period but two cases had been reported in 1971-1982 (7,8).

DISCUSSION

The crude rate of gonorrhoea and syphilis (STD) for the country from 1974 to 1983 is 42.5/1000, which is almost identical to the PNG Crude Birth Rate. Incidences of gonorrhoea and syphilis in 1971-1972 were 2.1/1000 and 0.7/1000, respectively (4). In 1974-1983 incidences of gonorrhoea and syphilis were 32/1000 and 11/1000, respectively. This is an eighteen-fold increase compared with 1972 (9).

Despite the introduction and implementation of the National Sexually Transmitted Diseases Control Programme from 1974 to 1978, gonorrhoea and syphilis have become almost out of control. This is not only evident from the significant increase in the national STD incidences but also in all regions the disease control programme has become ineffective.

It must be noted that reported incidences represent only a proportion of the general population who seek treatment through these special STD clinics. There are many patients
who are missed out in the disease surveillance system of the country. For instance, asymptomatic female patients with gonorrhoea, those attending general practitioners' clinics, and patients either being helped out by wantok health workers or those who come for treatment through public outpatient clinics are evidently not reported. With these facts in mind it is apparent that less than the national target of cases is being reported to the National STD Control Programme. It is quite evident from the study that sexual transmitted disease is becoming a serious clinical and psychosocial health problem in Papua New Guinea.

The diseases commonly affect the early reproductive age groups, 15-29 years, especially males. This is closely correlated with the steady migration of this age group into urban centres associated with socioeconomic development.

The transition to a Western socioeconomic lifestyle has been a contributing factor to the spread of venereal diseases. This is quite evident all over the world. The Director-General of WHO in 1964 described the movement of population as one of the most important factors in the spread of venereal diseases (10). In England in 1967, 39% of treated patients with syphilis were immigrants (11). This is true in PNG with increased trends of STD incidences in the two cities and most other towns. It is obvious that gonorrhoea and syphilis are urban diseases and their increase is associated with the rapid growth rate of urban population drift.

This is not only a public health problem of PNG but is a leading disease morbidity problem in the world today. WHO reported that 25% of the world's population are affected by sexually transmitted diseases. The incidences have been...
more or less steady in developed countries, while in developing countries they are increasing rapidly. This can be seen in Africa where 20-40% of females of childbearing age are suffering from STD and there is a close correlation between high rates of infertility and gonococcal endemcity (11). In Sri Lanka both syphilis and gonorrhoea increased by 25% from 1972 to 1973 (11) and there is further evidence of increase in relation to the present socio-economic situation. Studies in PNG have shown that 15% of all gynaecology admissions

### TABLE 4

STD IN TWO URBAN CENTRES OF PAPUA NEW GUINEA, 1981-1983

<table>
<thead>
<tr>
<th>Year</th>
<th>Estimated Population</th>
<th>Gonorrhoea Morbidity</th>
<th>Rate Per 10,000</th>
<th>Syphilis Morbidity</th>
<th>Rate Per 10,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Port Moresby</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1981</td>
<td>127,547</td>
<td>1,402</td>
<td>109.92</td>
<td>432</td>
<td>33.89</td>
</tr>
<tr>
<td>1982</td>
<td>132,337</td>
<td>1,500</td>
<td>113.35</td>
<td>563</td>
<td>42.54</td>
</tr>
<tr>
<td>1983</td>
<td>137,127</td>
<td>2,277</td>
<td>166.05</td>
<td>1,197</td>
<td>87.29</td>
</tr>
<tr>
<td>Total</td>
<td>5,179</td>
<td></td>
<td></td>
<td>2,192</td>
<td></td>
</tr>
<tr>
<td>Lae</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1981</td>
<td>116,432</td>
<td>1,871</td>
<td>160.69</td>
<td>2,569</td>
<td>220.64</td>
</tr>
<tr>
<td>1982</td>
<td>120,802</td>
<td>2,079</td>
<td>172.10</td>
<td>1,080</td>
<td>89.40</td>
</tr>
<tr>
<td>1983</td>
<td>125,172</td>
<td>2,719</td>
<td>217.22</td>
<td>571</td>
<td>45.62</td>
</tr>
<tr>
<td>Total</td>
<td>6,669</td>
<td></td>
<td></td>
<td>4,220</td>
<td></td>
</tr>
</tbody>
</table>

### TABLE 5

INCIDENCE OF GONORRHoeA AND SYPhilIS IN TWO URBAN CENTRES OF PAPUA NEW GUINEA, 1981-1983

<table>
<thead>
<tr>
<th>Year</th>
<th>Gonorrhoea Morbidity</th>
<th>Rate/1000</th>
<th>Syphilis Morbidity</th>
<th>Rate/1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Port Moresby</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1981</td>
<td>1,402</td>
<td>10.99</td>
<td>432</td>
<td>3.38</td>
</tr>
<tr>
<td>1982</td>
<td>1,500</td>
<td>11.33</td>
<td>563</td>
<td>4.25</td>
</tr>
<tr>
<td>1983</td>
<td>2,277</td>
<td>16.60</td>
<td>1,197</td>
<td>8.25</td>
</tr>
<tr>
<td>Total</td>
<td>5,179</td>
<td></td>
<td>2,192</td>
<td></td>
</tr>
<tr>
<td>Lae</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1981</td>
<td>1,871</td>
<td>16.06</td>
<td>2,569</td>
<td>22.06</td>
</tr>
<tr>
<td>1982</td>
<td>2,079</td>
<td>17.21</td>
<td>1,080</td>
<td>8.94</td>
</tr>
<tr>
<td>1983</td>
<td>2,719</td>
<td>21.72</td>
<td>571</td>
<td>4.56</td>
</tr>
<tr>
<td>Total</td>
<td>6,669</td>
<td></td>
<td>4,220</td>
<td></td>
</tr>
</tbody>
</table>
are for pelvic inflammatory disease (PID) and of these 43% have gonococcus present (12).

It is clear that large population movements caused by tourism, training schemes and labour migration as well as socio-economic changes tend to favour the transmission of sexually transmitted diseases.

Contact-tracing activities have gone down throughout the country. Overall activities have been 11%, which is well below the target of the introduced programme. This whole issue of contact-tracing activities seems to be a worldwide problem. The reasons for these failures are multifactorial, the main obvious ones being social, cultural, legal, economic and human habit, which tend to hinder the contact-tracing activities. Direct contact tracing of sexual partners is becoming very complicated.

However, developed countries have begun a

**TABLE 6**

DISTRIBUTION BY AGE OF GONORRHOEA AND SYPHILIS, 1979-1983

<table>
<thead>
<tr>
<th></th>
<th>&lt; 1</th>
<th>1-14</th>
<th>15-24</th>
<th>25-40</th>
<th>&gt; 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonorrhea</td>
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<td>21</td>
<td>253</td>
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</tr>
<tr>
<td></td>
<td>1980</td>
<td>0</td>
<td>15</td>
<td>3,834</td>
<td>2,728</td>
</tr>
<tr>
<td></td>
<td>1981</td>
<td>12</td>
<td>75</td>
<td>4,258</td>
<td>3,154</td>
</tr>
<tr>
<td></td>
<td>1982</td>
<td>8</td>
<td>34</td>
<td>2,167</td>
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</tr>
<tr>
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<td>0</td>
<td>5</td>
<td>848</td>
<td>502</td>
</tr>
<tr>
<td>Total</td>
<td>41</td>
<td>382</td>
<td>1,508</td>
<td>10,059</td>
<td>1,710</td>
</tr>
<tr>
<td>Syphilis</td>
<td>1979</td>
<td>0</td>
<td>15</td>
<td>2,092</td>
<td>1,211</td>
</tr>
<tr>
<td></td>
<td>1980</td>
<td>0</td>
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<td>1,499</td>
<td>1,224</td>
</tr>
<tr>
<td></td>
<td>1981</td>
<td>0</td>
<td>51</td>
<td>2,033</td>
<td>2,286</td>
</tr>
<tr>
<td></td>
<td>1982</td>
<td>0</td>
<td>19</td>
<td>830</td>
<td>545</td>
</tr>
<tr>
<td></td>
<td>1983</td>
<td>0</td>
<td>5</td>
<td>269</td>
<td>183</td>
</tr>
<tr>
<td>Total</td>
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<td>105</td>
<td>6,723</td>
<td>5,449</td>
<td>1,050</td>
</tr>
</tbody>
</table>

**TABLE 7**

CONTACT-TRACING ACTIVITIES IN STD CLINICS IN PAPUA NEW GUINEA, 1979-1983

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of New Contacts</th>
<th>Number of Contacts Found</th>
<th>%</th>
<th>Number of Contacts Treated</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979</td>
<td>10,726</td>
<td>1,989</td>
<td>18.5</td>
<td>1,679</td>
<td>84.4</td>
</tr>
<tr>
<td>1980</td>
<td>9,233</td>
<td>1,629</td>
<td>17.6</td>
<td>1,293</td>
<td>79.4</td>
</tr>
<tr>
<td>1981</td>
<td>15,653</td>
<td>1,571</td>
<td>10.0</td>
<td>1,479</td>
<td>94.1</td>
</tr>
<tr>
<td>1982</td>
<td>16,356</td>
<td>251</td>
<td>1.5</td>
<td>226</td>
<td>90.0</td>
</tr>
<tr>
<td>1983</td>
<td>6,626</td>
<td>1,008</td>
<td>15.2</td>
<td>902</td>
<td>89.5</td>
</tr>
<tr>
<td>Total</td>
<td>58,594</td>
<td>6,448</td>
<td>11.0</td>
<td>5,583</td>
<td>86.5</td>
</tr>
</tbody>
</table>
### TABLE 8

REGION-WISE CONTACT-TRACING ACTIVITIES, 1979-1983

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of New Contacts</th>
<th>Number of Contacts Found</th>
<th>%</th>
<th>Number of Contacts Treated</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979</td>
<td>2,111</td>
<td>79</td>
<td>3.7</td>
<td>57</td>
<td>72.1</td>
</tr>
<tr>
<td>1980</td>
<td>2,643</td>
<td>64</td>
<td>2.4</td>
<td>64</td>
<td>100.0</td>
</tr>
<tr>
<td>1981</td>
<td>489</td>
<td>105</td>
<td>21.4</td>
<td>105</td>
<td>100.0</td>
</tr>
<tr>
<td>1982</td>
<td>4,095</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>1983</td>
<td>1,431</td>
<td>80</td>
<td>5.5</td>
<td>80</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>10,769</td>
<td>328</td>
<td>3.0</td>
<td>306</td>
<td>93.3</td>
</tr>
</tbody>
</table>

**B. Momase Region**

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of New Contacts</th>
<th>Number of Contacts Found</th>
<th>%</th>
<th>Number of Contacts Treated</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979</td>
<td>3,352</td>
<td>579</td>
<td>17.3</td>
<td>438</td>
<td>75.6</td>
</tr>
<tr>
<td>1980</td>
<td>3,233</td>
<td>349</td>
<td>10.8</td>
<td>291</td>
<td>83.4</td>
</tr>
<tr>
<td>1981</td>
<td>3,040</td>
<td>676</td>
<td>22.3</td>
<td>676</td>
<td>100.0</td>
</tr>
<tr>
<td>1982</td>
<td>5,382</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>1983</td>
<td>3,099</td>
<td>357</td>
<td>11.5</td>
<td>286</td>
<td>80.1</td>
</tr>
<tr>
<td>Total</td>
<td>18,106</td>
<td>1,961</td>
<td>10.8</td>
<td>1,691</td>
<td>86.2</td>
</tr>
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</table>

**C. Highlands Region**

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<tr>
<th>Year</th>
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<th>%</th>
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**D. New Guinea Islands Region**

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<th>Number of Contacts Found</th>
<th>%</th>
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<th>%</th>
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<td>11.9</td>
<td>751</td>
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control program based on providing information for increased public awareness of STD. This certainly has had some effect leading to an increase of incidence reporting. For instance United Kingdom and Singapore have reported that increased incidences of STD reporting have resulted from mass health education campaigns about the disease (10). With this health education method, more patients report to clinics for medical check-ups and seek early treatment as soon as symptoms start to develop. This could be the appropriate method that PNG must seriously consider adopting since the direct contact-tracing method has failed.

There are some operational problems which contribute to the present difficulties with the control of sexually transmitted diseases in Papua New Guinea. These are:

A. Segregation of Services
Sexually transmitted disease clinics have apparently been isolated from the main health care system. For example, in many instances medical superintendents and hospital doctors have completely ignored the proper care and management of STD cases. The author has experienced this in the country’s largest city STD clinics. Doctors carry out no regular supervision of sisters and HEOs engaged in STD management activities. These paramedical workers can do what is required for diagnosis and treatment of this serious clinical and psychosocial disease but must be backed up by doctors in the hospital clinics. The best way to integrate and provide effective service is to bring STD services under the general package of health care services. This has been adopted in USA and other developed countries where disease control programmes have thereby become easier in practice and less costly (10).

B. Low Staff Morale
From the interview results regarding staff morale, participating staff feel bored by the repetition of duties with no future for advancement in the field. They are further discouraged by the lack of interest shown by hospital doctors. There is no stimulation or encouragement by the provision of inservice or other short courses for the staff who are actually involved in the delivery of the programme by the Department of Health and its teaching institutions. Some of these factors have caused low staff morale which reflects the present problem of STD in the whole country.

C. Lack of Teaching Interest
The lack of teaching interest in STD at all levels of medical training in the country is becoming evident. This is shown by the lack of professional interest and public awareness of the disease by all health personnel. Training and teaching of venereology must be properly aimed at all levels of health training institutions, from the medical school down to medical aid training.

D. Health Resource Constraints
Constraints of trained manpower, financial resources and specialized technical services are problems everywhere in developing countries. These problems are more political than directly related to health. Therefore health workers can do little to solve them, though one way to help overcome them would be to integrate the STD control services with the general health care system.

There are limitations of funding for transport and other services for special STD activities but this can be solved by proper planning and management of the hospital and provincial resources within its day-to-day services. The current Government NPEP funding must be fully used by the provinces for extension of health education activities rather than contact tracing because it is a misuse of resources to spend them on a method known to be unsuccessful.

Special funding is not warranted at this stage of the country’s economy, but rather the coordination of inter-departmental activities. It has been recommended from a study done in the highlands that the Department of Education can teach sexual and STD education through primary schools, secondary schools and teacher training institutions so that the message can then be disseminated to the community by them (13). There are other Government departments such as the Department of Information Services for public campaigns through the media and distribution of publications, and the Department of Youth and Religion for counseling and public seminars at rallies, etc. which are
needed to help combat this increasing public health problem.

CONCLUSIONS

Sexually transmitted diseases, especially gonorrhoea and syphilis, are becoming major health morbidity problems comparable to pneumonia and gastroenteritis in this country. The vector and host of the diseases are both human and therefore the basic goal of the STD control programme can only be achieved through developing human awareness and modifying human behaviour. This can be done by:

1. Campaign for STD health education
   - at all levels of schools
   - through local and national media
   - through all other non-government coordinating agencies, e.g. churches
   - national and local newspapers.

2. Integration of STD care in the general health care system e.g. STD control becomes part of the overall communicable disease control programme.

3. Permitting the optimal use of existing infrastructures at central, provincial or local health units for prevention of STD.

4. Establishment of a central unit for training and evaluation of the control programme for communicable diseases.

ACKNOWLEDGEMENTS

I thank Mr John Tawai, the National STD Control Co-ordinator, for making the information available for this project. Secondly, I thank the Sister-in-charge of the PMGH STD clinic for contributing her views on current operational problems with STD management and the control programme.

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LARGE surveys of blood pressure among populations in Europe and the U.S.A. have shown that blood pressure tends to rise with age (Master, Garfield and Walters, 1952; Hamilton, Pickering, Roberts and Sowry, 1954; Boe, Humerfelt and Wedervang, 1957). The problem of whether this rise can be regarded as “normal”, or whether it represents the operation of an abnormal condition associated with elevated blood pressure, continues to exercise workers in this field (Pickering, 1961).

Blood pressure tends to rise with age even in populations among whom the disease which we call “essential hypertension” is rare or virtually absent (Maddocks, 1961a). There have been reports of populations in which no appreciable change in blood pressure associated with age was recorded: The Samburu people of Kenya (Shaper, Williams and Spencer, 1961); Ceylonese (Bibble, Cullumbine, Kurtisuge, Watson, and Wikamanayake, 1949); Caroline Islanders (Murrill, 1949); and Kalahari Bushmen (Kaminer and Lutz, 1960); but either because they were somewhat exotic populations, or because techniques of sampling or measurement were not always standard, these reports have not received much prominence.

This paper reports findings among a population in which blood pressure appears to fall with age.

POPULATION.

The Chimbu district lies in the Eastern Highlands of New Guinea, and contains an estimated population of 160,000. The Chimbu people have been described in detail by Brown and Brookfield (1959). The populations represented in this survey were from the areas of Mintima, Wandi and Gumine. It was not possible to measure complete village communities, as has been done in other surveys in the Western Pacific, because the Chimbu are grouped in small family hamlets. In each centre, an attempt was made to gather all the members of several “lines”, and it is thought that these were fairly completely represented. A “line” is a clan or census division, the members of which have common ties of family and of land ownership. Older members of each line were particularly sought, and were traced where possible, to their houses or gardens if they had not come to the survey centre. The three different populations did not differ significantly in any of the parameters measured, and they are therefore presented as a single population, comprising 268 male and 161 female adults.

METHODS

The technique for the measurement of blood pressure has previously been described (Lovell, Maddocks and Rogerson, 1960). Subjects were seated at a table and had been rested for at least 10 minutes before the reading was taken. Height was measured to the nearest centimetre, and weight to the nearest pound on an accurate beam scale. Skinfold thickness measurements were made below the angle of the left scapula using a Harpenden caliper.

Age estimation presented some difficulties. It could be done only by arranging the members of each line in generations and in order of seniority, and then estimating the age of certain key persons in the line by reference to a single memorable event—the first European expedition to the area in 1932. Persons not born at that time were now (December, 1962) under 30 years of age, men who had carried for the expedition were now probably over 50 years of age, and men who were already fathers of several children at the time of the expedition were now probably over 60 years of age.
RESULTS

Findings are grouped in decades of age, and recorded as means for each decade in Table 1. For both males and females, means for height, weight, skinfold thickness, arm circumference and blood pressure tend to fall in groups of increasing age. For systolic pressures of females, however, mean values are highest in the middle age-range, falling only in the oldest age group. (the pattern of blood pressures is illustrated in Figure 1.) “Mean” blood pressure is calculated from the formula:

\[
\text{Mean blood pressure} = \frac{\text{Diastolic} + \text{Systolic} - \text{Diastolic}}{3}
\]

It is close to the physiological mean of blood pressure and provides a way of examining systolic and diastolic pressures together.

The change in mean blood pressure with age may be represented by simple regression equations:

- **Males**—Mean Blood Pressure (mm. Hg.) = 95.5 — 0.2024 age (years).
- **Females**—Mean Blood Pressure (mm. Hg.) = 93.5 — 0.1023 age (years).

For both sexes, the regression coefficient differs significantly from zero as shown by the standard error.

- S.E. (Males) = ±0.02 ;
- S.E. (Females) = ± 0.014.

DISCUSSION

The Chimbu people may be unique in having a pattern of blood pressures which falls with increasing age. Almost identical findings reported by Whyte (1958) and Barnes (1964) in other populations from the same region suggest that this pattern is not an artefact of case selection or technique. A number of factors may be considered in attempting to assess why the Chimbu have such an unusual pattern.

1. **Selective Mortality and Disease Pattern**

The average life expectancy among the Chimbu is probably less than 40 years, though no accurate figures are available. The pattern of blood pressure found among them might be explained if persons with higher blood pressures were dying young. But the common causes of death in the New Guinea Highlands (acute respiratory...
infections, diarrhoeal disease and other infections) are not associated with high blood pressure, and selective mortality does not appear to influence blood pressure.

2. Body Build

A steady fall in the mean values for all measurements concerned with body build is a striking finding for both sexes after the third decade of age. This is not the usual finding in Western populations, where body weight, arm circumference, etc., are greatest in the age range 40-60 years (Maddocks, 1964). This suggests that falling body build may explain falling blood pressures among the Chimbu, since body build has a definite effect on blood pressure (Boe et al., 1957; Miall and Oldham, 1958). The importance of body build can be assessed by calculating partial regression equations in which the separate influence of age and body build on blood pressure are represented. In the following equations, body build is represented by arm circumference, an index which closely parallels body weight and weight/height.

**Males**

Mean Blood Pressure = 64.4 — 0.116 age + 1.14 arm circumference (cm.).

**Females**

Mean Blood Pressure = 59.9 — 0.042 age + 1.49 arm circumference (cm.).

Comparing these with the simple regression equations presented above, it is apparent that even after allowing for the fall in body build with age, blood pressure still falls with age, though the rate of fall is reduced. Some other factor as well as body build must be operating to make pressures fall with age.

3. Dietary Factors—Protein

The diet of the Chimbu people has been studied by Oomen and Malcolm (1958), Venkatachalam (1962) and in two communities by Whiteman (1962). The results of their surveys are similar. They describe an average daily intake of between 25 g. and 30 g. protein, and from 1,850 to 2,883 calories. Such a low protein intake, most of it from vegetable protein, amounts to chronic protein malnutrition, and probably explains the falling body bulk during adult life. Fat is almost absent from the diet of the Chimbu. The women of the area carry a particularly heavy burden of physical labour and a continuous cycle of reproduction, synthesizing foetal and placental protein or producing breast milk over a continuous period of up to 15 years. This has been described as “the maternal depletion syndrome” (Jelliffe and Maddocks, 1964). However, Indonesian populations on even lower dietary intakes of protein have a pattern of blood pressure which rises with age (Bailey, 1963) and protein deficiency does not seem to be a sufficient explanation of the Chimbu pressures.

4. Dietary Factors—Salt

Salt has long been a valuable trade item in the Chimbu area. A small sodium spring in the Wahgi Gorge near Gumine was the site of a flourishing salt-making industry until about 10 years ago. Local missionaries remember when nearly 100 huts clung to the sides of the gorge near the spring, and here the leaves were soaked in spring water, burned, and the salt extracted from the ashes by leaching through bark funnels. Finally the solution was evaporated to dryness to form thin flat cakes about 12 inches across.

This salt, being almost the only good source of sodium in the whole region, was highly prized, and one cake is said to have been worth a pig. Now, however, trade stores sell imported salt throughout the Eastern Highlands, and the old salt industry has collapsed.

The Chimbu were apparently a population with a low intake of salt, and this was probably true of the whole New Guinea Highlands. In West New Guinea, Oomen (1961) reported the mean 24-hour urinary sodium excretion (an accepted measure of sodium intake) as less than 70 mg., lower than most salt-free diets! Even today, with trade-store salt freely available, salt intake is low. In 10 of the adult male Chimbu seen on this survey, the average 24-hour sodium excretion was 1.5 g. about one fifth of the usual European value.

Salt intake is relevant to this discussion because there is a considerable amount of evidence that blood pressure is affected by dietary salt. The evidence falls under three main headings:

(i) Epidemiological. Dahl (1961) has suggested that in societies or groups habitually consuming less than 5 g. of salt daily, essential hypertension will be rare, and in societies
members of “primitive” communities move away from the simple life to take up a competitive wage-earning existence in the cities, hypertension begins to appear. It has not so far been possible, however, to definitely incriminate any specific environmental factors (Scotch, 1960; Maddocks, 1961b; Cruz-Coke, 1963).

We may hope that repeated careful observation of populations like the Chimbu will enable us to record such a change if it is going to occur. Unfortunately, even in such isolated communities, so many other changes in diet, social organization and pattern of activity will occur simultaneously that it is unlikely that the operation of specific environmental factors will be apparent. The answer to the problem of the aetiology of essential hypertension will probably not come from such studies. Nevertheless it would be foolish to neglect the study of populations which have no hypertension, because in a few generations they may have ceased to exist.

SUMMARY

The Chimbu people of the New Guinea Highlands have a pattern of blood pressure in which there is an apparent fall in both systolic and diastolic pressures as age increases. This is not explained by changes in body build with age. It may be influenced by a low dietary intake of salt, and by psychological factors which are difficult to define. Changes may occur in the blood pressure pattern of the Chimbu over the next 10-20 years, and it will be important to observe whether their blood pressures will show a parallel increase.

ACKNOWLEDGEMENTS

We wish to acknowledge with thanks the valuable assistance provided in the field by Dr. R. Barnes, Mr. J. Ross, Mr. Noah Temgue and Mr. Toule Tarabi. Mr. Michael Pemberton did all the basic tedious statistical analysis.

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PUBLICATIONS OF RELEVANCE TO PAPUA NEW GUINEA AND MELANESIA

Bibliographic Citation List generated from MEDLARS


4 Bakker MI, Hatta M, Kwenang A, Van Bentheim BH, Van Beers SM, Klatser PR, Oskam L. Prevention of leprosy using rifampicin as chemoprophylaxis. Am J Trop Med Hyg 2005 Apr;72(4):443-448. An intervention study was implemented on five Indonesian islands highly endemic for leprosy to determine whether rifampicin can be used as chemoprophylaxis to prevent leprosy. The population was actively screened before the intervention and subsequently once a year for three years. In the control group, no chemoprophylaxis was given. In the contact group, chemoprophylaxis was only given to contacts of leprosy patients and in the blanket group to all eligible persons. The cohort consisted of 3,965 persons. The yearly incidence rate in the control group was 39/10,000; the cumulative incidence after three years was significantly lower in the blanket group (P = 0.031). No difference was found between the contact and the control groups (P = 0.93). Whether this apparent reduced leprosy incidence in the first three years in the blanket group is due to a delayed development of leprosy or a complete clearance of infection needs to be determined.

5 Bakker MI, Hatta M, Kwenang A, Faber WR, van Beers SM, Klatser PR, Oskam L. Population survey to determine risk factors for Mycobacterium leprae transmission and infection. Int J Epidemiol 2004 Dec;33(6):1329-1336. Epub 2004 Jul 15. BACKGROUND: Not every leprosy patient is equally effective in transmitting Mycobacterium leprae. We studied the spatial distribution of infection (using seropositivity as a marker) in the population to identify which disease characteristics of leprosy patients are important in transmission. METHODS: Clinical data and blood samples for anti-M. leprae ELISA were collected during a cross-sectional survey on five Indonesian islands highly endemic for leprosy. A geographic information system (GIS) was used to define contacts of patients. We investigated spatial clustering of patients and seropositive people and used logistic regression to determine risk factors for seropositivity. RESULTS: Of the 3986 people examined for lepso, 3271 gave blood. Seroprevalence varied between islands (1.7-8.7%) and correlated significantly with leprosy prevalence. Five clusters of patients and two clusters of seropositives were detected. In multivariate analysis, seropositivity significantly differed by leprosy status, age, sex, and island. Serological status of patients appeared to be the best discriminator of contact groups with higher seroprevalence: contacts of seropositive patients had an adjusted odds ratio (aOR) of 1.75 (95% CI 0.922-3.31). This increased seroprevalence was strongest for contact groups living < or =75 m of two seropositive patients (aOR = 3.07; 95% CI 1.74-5.42). CONCLUSIONS: In this highly endemic area for leprosy, not only household contacts of seropositive patients, but also people living in the vicinity of a seropositive patient were more likely to harbour antibodies against M. leprae. Through measuring the serological status of patients and using a broader definition of contacts, higher risk groups can be more specifically identified.


The degree to which widespread avian blood parasites in the genera Plasmodium and Haemoproteus pose a threat to novel hosts depends in part on the degree to which they are constrained to a particular host or host family. We examined the host distribution and host-specificity of these parasites in birds from two relatively understudied and isolated locations: Australia and Papua New Guinea. Using polymerase chain reaction (PCR), we detected infection in 60 of 105 species, representing 44% of individuals surveyed (n = 428). Across host families, prevalence of Haemoproteus ranged from 13% (Acanthizidae) to 56% (Petroicidae) while prevalence of Plasmodium ranged from 3% (Petroicidae) to 47% (Ptilonorhynchidae). We recovered 78 unique mitochondrial lineages from 155 sequences. Related lineages of Haemoproteus were more likely to derive from the same host family than predicted by chance at shallow (average LogDet genetic distance = 0, n = 12, P = 0.001) and greater depths (average distance = 0.014, n = 11, P = 0.001) within the parasite phylogeny. Within two major Haemoproteus subclades identified in a maximum likelihood phylogeny, host-specificity was evident up to parasite genetic distances of 0.029 and 0.007 based on logistic regression. We found no significant host relationship among lineages of Plasmodium by any method of analysis. These results support previous evidence of strong host-family specificity in Haemoproteus and suggest that lineages of Plasmodium are more likely to form evolutionarily-stable associations with novel hosts.

Becker AE, Gilman SE, Burwell RA. Changes in prevalence of overweight and in body image among ethnic Fijian women in Fiji during a period of rapid social change and the relationship between changes in body image and BMI. Obes Res 2005 Jan;13(1):110-117.

OBJECTIVE: To investigate changes in prevalence of overweight and obesity and in body image among ethnic Fijian women in Fiji during a period of rapid social change and the relationship between changes in body image and BMI.

RESEARCH METHODS AND PROCEDURES: The study design was a multiwave cohort study of BMI and weight, collection of demographic data by written survey, and administration of the Nadroga Language Image Questionnaire. RESULTS: The prevalence of overweight and obesity was significantly different between the cohorts, increasing from 60% in 1989 to 84% in 1998 (p=0.014). In addition, the age-adjusted mean BMI was significantly higher in 1998 compared with 1989 (p=0.011). Finally, there were significant between-cohort differences in multiple measures of body image, which were mostly independent of BMI.

DISCUSSION: At 84%, the prevalence of overweight and obesity in this community sample of Fijian women is among the highest in the world. The dramatically increased prevalence over the 9.5-year period studied corresponds with rapid social change in Fiji and significant shifts in prevailing traditional attitudes toward body shape.

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We aimed to evaluate the annual incidence of influenza in New Caledonia and to identify the circulating viral types and subtypes in order to gather information for the local vaccination programme and regional influenza surveillance. A surveillance network was set up in 1999; it included sentinel practitioners in Noumea and the virology department of the Pasteur Institute. Influenza circulated in New Caledonia every year, regularly during the southern hemisphere winter and occasionally during March-May. Isolates were generally consistent with world surveillance, except in 1999, when a new A/H1N1 variant was identified. This study emphasises the need for regular influenza surveillance, even when performed on a limited scale. Importantly the optimal time for local vaccination was found to be in December or January each year.


Sixty-seven extracts of 30 medicinal plants traditionally used in New Caledonia or Vanuatu by healers to treat inflammation, fever and in cicatizing remedies were evaluated in vitro for their antipROTOzoal activity against Leishmania donovani, Leishmania amazonensis and Trypanosoma cruzi. Among the selected plants, Pagiantha cerifera was the most active against both Leishmania species: four extracts were active against promastigotes of Leishmania donovani at EC(50) values inferior to 5 microg/ml. Garcinia pedicillata extract had an EC(50) value of 12.5 microg/ml against intracellular amastigotes of Leishmania amazonensis. Alone Amborella trichopoda reduced by more than 80% the trypomastigotes of Trypanosoma cruzi in the blood.


Twenty plants, belonging to sixteen families, used in traditional New Caledonian and Vanuatu medicine for treatment of symptoms potentially related to tuberculosis (cough, fever or inflammation) were screened for antimycobacterial activity. We also screened an original endemic plant, Amborella trichopoda, only member of the monogeneric family Amborellaceae and considered the most primitive living angiosperm. In total, 55 extracts were evaluated for inhibitory activity against Mycobacterium bovis BCG strain at a concentration of 100 microg/ml. Methanolic and dichloromethane extracts of Amborella trichopoda, Codiaeum peeltatum, Myristica fatica, and essential oils Myopor um crassifolium showed an activity at this concentration. Methanolic extract of Amborella trichopoda fruits presented a significant activity with a minimal inhibitory concentration included between 1 and 2.5 microg/ml. In the same conditions, this activity was comparable with those of the reference drugs pyrazinamide and ethambutol, at 20 and 2.5 microg/ml, respectively.
Nitric oxide production and nitric oxide synthase activity in malaria-exposed Papua New Guinean children and adults show longitudinal stability and no association with parasitemia.

Individuals in areas of intense malaria transmission exhibit resistance (or tolerance) to levels of parasitemia in their blood that would normally be associated with febrile illness in malaria-naive subjects. The resulting level of parasitemia associated with illness (the pyrogenic threshold) is highest in childhood and lowest in adulthood. Clinical parallels between malarial and bacterial endotoxin tolerance have led to the supposition that both share common physiological processes, with nitric oxide (NO) proposed as a candidate mediator. The hypotheses that NO mediates tolerance and blood stage parasite killing in vivo were tested by determining its relationship to age and parasitemia cross-sectionally and longitudinally in a population of 195 children and adults from Papua New Guinea encountering intense malaria exposure. Despite pharmacological clearance of asymptomatic parasitemia, NO production and mononuclear cell NO synthase (NOS) activity were remarkably stable within individuals over time, were not influenced by parasitemia, and varied little with age. These results contrast with previous smaller cross-sectional studies. Baseline NO production and NOS activity did not protect against recurrent parasitemia, consistent with previous data suggesting that NO does not have antiparasitic effects against blood stage infection in vivo. The NO indices studied were markedly higher in specimens from study subjects than in samples from Australian controls, and NOS activity was significantly associated with plasma immunoglobulin E levels, consistent with induction of NO by chronic exposure to other infections and/or host genetic factors. These results suggest that NO is unlikely to mediate killing of blood stage parasites in this setting and is unlikely to be the primary mediator in the acquisition or maintenance of malarial tolerance.

13. Brown H.
Treating the injured and burying the dead.

14. Cameron J.
Caring for mama and pikinini in Papua New Guinea.

Allele specificity of naturally acquired antibody available in the literature were analyzed. Phylogenetic studies using different algorithms (minimum evolution, neighbour joining, maximum parsimony, and maximum likelihood) gave the same clear-cut results. Newly sequenced HTLV-I isolates described in this report allocated in three well-defined subtypes: Cosmopolitan, Central African, and a new distinct one that we termed 'Maroni' subtype (present in the Maroni Basin, French Guiana, and West Indies). Clearly, the most divergent PTLV-I strains present in Asia-Australo-Melanesia as well as African and Asian STLV-I derived from the same node in the phylogenetic tree as isolates of the Central African subtype. In addition, we showed that within each PTLV-I subtype, groups of isolates may be characterized by nonrandom and systematically associated mutations.

Human T-cell leukemia virus type 1 molecular variants, Vanuatu, Melanesia.

Four of 391 Ni-Vanuatu women were infected with variants of human T-cell leukemia virus type 1 (HTLV-1) Melanesian subtype C. These strains had env nucleotide sequences approximately 99% similar to each other and diverging from the main molecular subtypes of HTLV-1 by 6% to 9%. These strains were likely introduced during ancient human population movements in Melanesia.

Origin and dissemination of chloroquine-resistant *Plasmodium falciparum* with mutant pfcr alleles in the Philippines.

The pfcr allelic type and adjacent microsatellite marker type were determined for 82 *Plasmodium falciparum* isolates from the Philippines. Mutant pfcr allelic types P1a and P2a/P2b were dominant in different locations. Microsatellite analysis revealed that P2a/P2b evolved independently in the Philippines, while P1a shared common ancestry with Papua New Guinea chloroquine-resistant parasites.

18. Cortés A.
A chimeric *Plasmodium falciparum* Pfnbp2b/Pfnbp2a gene originated during asexual growth.

The *Plasmodium falciparum* line 3D7-A has an unusual invasion phenotype, such that it can invade enzyme-treated and mutant red blood cells that are resistant to invasion by other parasite lines. 3D7-A has a chimeric Pfnbp2b gene that contains part of the repeat region of the paralogous gene Pfnbp2a. This chimeric gene originated by spontaneous gene conversion during normal maintenance in culture, indicating that ectopic recombination and gene conversion during asexual growth are potentially important mechanisms participating in the evolution of paralogous genes in Plasmodium. However, the presence of the chimeric Pfnbp2b gene in 3D7-A was not associated with its peculiar invasion phenotype.

Allele specificity of naturally acquired antibody...

Antibody responses against proteins located on the surface or in the apical organelles of merozoites are presumed to be important components of naturally acquired protective immune responses against the malaria parasite *Plasmodium falciparum*. However, many merozoite antigens are highly polymorphic, and antibodies induced against one particular allelic form might not be effective in controlling growth of parasites expressing alternative forms. The apical membrane antigen 1 (AMA1) is a polymorphic merozoite protein that is a target of naturally acquired invasion-inhibitory antibodies and is a leading asexual-stage vaccine candidate. We characterized the antibody responses against AMA1 in 262 individuals from Papua New Guinea exposed to malaria by using different allelic forms of the full AMA1 ectodomain and some individual subdomains. The majority of individuals had very high levels of antibodies against AMA1. The prevalence and titer of these antibodies increased with age. Although antibodies against conserved regions of the molecule were predominant in the majority of individuals, most plasma samples also contained antibodies directed against polymorphic regions of the antigen. In a few individuals, predominantly from younger age groups, the majority of antibodies against AMA1 were directed against polymorphic epitopes. The D10 allelic form of AMA1 apparently contains most if not all of the epitopes present in the other allelic forms tested, which might argue for its inclusion in future AMA1-based vaccines to be tested. Some important epitopes in AMA1 involved residues located in domain II or III but depended on more than one domain.


An outbreak of acute diarrheal disease was reported in Kupang, Nusa Tenggara, Indonesia, in August 2002. An investigative team carried out a retrospective historical review of records, and a case-control study involving data and specimen collections. Etiologic determination involving stool specimens was based on an enzyme-linked immunosorbent assay, with a reverse transcriptase-polymerase chain reaction performed for serotyping purposes. Two thousand six hundred probable cases were identified from hospital records during the outbreak months of June, July, August, and September 2002. Previous enteric outbreaks were recognized from the same months in the preceding years and all annual outbreak episodes following a period of prolonged, low rainfall. In contrast to previous outbreaks described from trend analysis, the overwhelming burden of disease fell upon the pediatric population versus the young and old in previous outbreak instances. Rotavirus was found to be the causative etiology, with serotype 1 predominating.


A study (ISRCTN 77665712) was undertaken to test the effectiveness and the acceptability of vitamin E and low-dose aspirin, alone or in combination, as treatment for prolonged vaginal bleeding induced by Norplant. A total of 486 Norplant users who were requesting treatment for bleeding lasting longer than 7 days were enrolled in five centers: Beijing, China; Jakarta, Indonesia; Santiago, Chile; Santo Domingo, Dominican Republic; and Tunis, Tunisia. They were randomized to one of four daily treatment: 200 mg vitamin E daily, 80 mg aspirin daily, both or a placebo. Treatment packs were designed to ensure blinding of both the subjects and the clinical staff. Neither vitamin E nor low-dose aspirin nor their combination was found to have any effect on reducing the length of the bleeding episode for which treatment was taken or on the vaginal bleeding patterns these women experienced during the year of follow-up.


A review of the literature was carried out to evaluate malaria and its environmental relationships. Research, in 6 parts of Indonesia, addressed the relationship between malaria incidence and physical and socioeconomic factors, using longitudinal and cross-sectional approaches. Physical factors, which are generally important for malaria, included rainfall, mosquito breeding and resting sites, their distance from human habitation, and elevation, though the latter was not statistically significant. Housing conditions were occasionally important. Social and economic factors of importance were income, education, use of bednets and pattern of outdoor activities, especially at night. Use of repellents, mosquito coils and sleeping arrangements were significant in some of the studies.


In cervical cancer, human papillomavirus type 18 (HPV 18) and HPV 16 are predominantly related to adenocarcinomas (ADCs) and squamous cell carcinomas (SCCs), respectively. Here, we studied whether the geographically distributed HPV intratypic variants are also associated with histologically different tumors. A total of 44 HPV 18-positive and 91 HPV 16-positive cervical carcinomas from Indonesia, Dutch and Dutch patients were histologically classified using hematoxinil and eosin, periodic acid Schiff plus and Alcian Blue staining. Samples were sequenced and intratypic variants
were classified into the known phylogenetic branches. The Asian Amerindian HPV 18 variant was observed in 56% of ADCs compared to 15% of SCCs (p < 0.006). The African HPV 18 variant was exclusively found in SCCs. By sequencing the HPV 18 E6 and E7 open reading frames, we found predicted amino acid changes only in 8 samples. Two amino acid changes were consistent throughout the African branch. In HPV 18-positive tumors, we did not find a specific linkage between intratypic variants and histopathology. We conclude that HPV 18 intratypic variants are differentially associated with adenocarcinoma and squamous cell carcinoma of the cervix. The findings described here stress the biologic significance of intratypic HPV variants and might help explain differences in the pathogenesis of cervical ADCs and SCCs.

25 Duke T.
Slow but steady progress in child health in Papua New Guinea.
*J Paediatr Child Health* 2004 Dec;40(12):659-663.

26 Duke T, Oa O, Mokela D, Oswyn G, Hwaihwanje I, Hawap J.
The management of sick young infants at primary health centres in a rural developing country.
*Arch Dis Child* 2005 Feb;90(2):200-205.

AIMS: To investigate the epidemiology of illness among young infants at remote health clinics in a rural developing country and to determine risk factors for mortality that might be used as triggers for emergency treatment or referral. METHODS: Multi-site 12 month observational study of consecutive presentations of infants less than 2 months, and an investigation of neonates who died in one district without accessing health care. RESULTS: Forty per cent of 511 young infant presentations occurred in the first week of life and most of these in the first 24 hours. Twenty five deaths were recorded: 18 in the health facilities and seven in villages. In addition there were eight stillbirths. Clinical signs predicting death were: not able to feed, fast respiratory rate, apnoea, cyanosis, 'too small', 'skin-cold', and severe abdominal distension. Signs indicating severe respiratory compromise were present in 25% of young infants; failure to give oxygen therapy was a modifiable factor in 27% of deaths within health facilities. A high proportion of seriously ill young infants were discharged from health facilities early without adequate follow up. A common reason for not seeking care for fatally ill neonates was the perception by parents that health staff would respond negatively to their social circumstances. CONCLUSIONS: Clinical signs with moderate positive predictive value for death may be useful triggers for emergency treatment and longer observation or urgent referral. The results of this study may be useful in planning strategies to address high neonatal mortality rates in developing countries.

27 Duke T, Tefuaurani N, Baravilala W.
Getting the most out of health education in Papua New Guinea. Report from the 40th Annual Papua New Guinea Medical Symposium.

Expanding southwest pacific mitochondrial haplogroups P and Q.

Modern humans have occupied New Guinea and the nearby Bismarck and Solomon archipelagos of Island Melanesia for at least 40,000 years. Previous mitochondrial DNA (mtDNA) studies indicated that two common lineages in this region, haplogroups P and Q, were particularly diverse, with the coalescence for P considered significantly older than that for Q. In this study, we expand the definition of haplogroup Q so that it includes three major branches, each separated by multiple mutational distinctions (Q1, equivalent to the earlier definition of Q, plus Q2 and Q3). We report three whole-mtDNA genomes that establish Q2 as a major Q branch. In addition, we describe 314 control region sequences that belong to the expanded haplogroups P and Q from our Southwest Pacific collection. The coalescence dates for the largest P and Q branches (P1 and Q1) are similar to each other (approximately 50,000 years old) and considerably older than prior estimates. Newly identified Q2, which was found in Island Melanesian samples just to the east, is somewhat younger by more than 10,000 years. Our coalescence estimates should be more reliable than prior ones because they were based on significantly larger samples as well as complete mtDNA coding region sequencing. Our estimates are roughly in accord with the current suggested dates for the first settlement of New Guinea-Sahul. The phylogeography of P and Q indicates almost total (female) isolation of ancient New Guinea-Island Melanesia from Australia that may have existed from the time of the first settlement. While Q subsequently diversified extensively in New Guinea-Island Melanesia, it has not been found in Australia. The only shared mtDNA haplogroup between Australia and New Guinea identified to date remains one minor branch of P.

Incidence of vaccine-preventable *Haemophilus influenzae* type b pneumonia and meningitis in Indonesian children: hamlet-randomised vaccine-probe trial.

BACKGROUND: Most studies of *Haemophilus influenzae* type b (Hib) disease in Asia have found low rates, and few Asian countries use Hib vaccine in routine immunisation programmes. Whether Hib disease truly is rare or whether many cases remain undetected is unclear. METHODS: To estimate incidences of vaccine-preventable Hib pneumonia and meningitis among children younger than 2 years in Lombok, Indonesia, during 1998-2002, we undertook a hamlet-randomised, controlled, double-blind vaccine-probe study (818 hamlets). Children were immunised (WHO schedule) with diphtheria, tetanus, pertussis (DTP) or DTP-PRP-T (Hib conjugate) vaccine. Vaccine-preventable disease incidences were calculated as the difference in rates of clinical outcomes between DTP and DTP-PRP-T groups. Analyses included all children who received at least one vaccine dose. FINDINGS: We enrolled 55073 children: 28147 were assigned DTP-PRP-T and 26926 DTP. The proportion of pneumonia outcomes prevented by vaccine ranged from less...
than 0 to 4.8%. Calculated incidences of vaccine-preventable Hib disease (per 10(5) child-years of observation) for outcome categories were: substantial alveolar consolidation or effusion, less than zero (-43 [95% CI -185 to 98]); all severe pneumonia, 264 (95% CI less than zero to 629); all clinical pneumonia, 1561 (270 to 2853); confirmed Hib meningitis, 16 (1.4 to 31); meningitis with cerebrospinal-fluid findings consistent with a bacterial etiology, 67 (22 to 112); and admission for suspected meningitis or presenting to a clinic with convulsions, 158 (42 to 273). INTERPRETATION: Hib vaccine did not prevent the great majority of pneumonia cases, including those with alveolar consolidation. These results do not support a major role for Hib vaccine in overall pneumonia-prevention programmes. Nevertheless, the study identified high incidences of Hib meningitis and pneumonia; inclusion of Hib vaccine in routine infant immunisation programmes in Asia deserves consideration.


To study the genetic diversity of Plasmodium vivax in the Republic of Korea, nucleotide sequence variations at the merozoite surface protein-3alpha (PvMSP-3alpha) locus were analyzed using 24 re-emerging isolates and 4 isolates from imported cases. Compared with the well known Belem strain (Brazil), a large number of amino acid substitutions, deletions, and insertions were found at the locus of the isolates examined. The Korean isolates were divided into two allelic types; type I (15 isolates), similar to the Belem strain, and type II (9), similar to the Chesson strain (New Guinea). Isolates from imported cases were classified into three types; type III (1 from Malaysia), similar to type B from western Thailand, type IV (1 each from Indonesia and India), and type V (1 from Pakistan), both being new types. Our results have shown that the MSP-3alpha locus of re-emerging Korean P. vivax is dimorphic with two allelic types coexisting in the endemic area.


A comparative study of the diagnostic value of the ICT-TB test and the TB-Dot test, based on laboratory examination, was carried out in 39 patients suffering from sputum positive pulmonary tuberculosis (25 males and 14 females, aged 16-50 years) and in 48 patients (27 males and 21 females, aged 17-55 years) suffering from non-tuberculosis pulmonary diseases, that had attended the Tembagapura Hospital and the TB Control Health Center Timika-Mimika, Papua. The diagnostic sensitivity of the ICT-TB test was 87.18%, the diagnostic specificity was 81.25%, the diagnostic positive predictive value was 79.07%, the negative predictive value was 88.64%, and the diagnostic efficiency was 83.91%. The diagnostic sensitivity of the TB-Dot test was 93.31%, the diagnostic specificity was 95.83%, the diagnostic positive predictive value was 94.74%, the negative predictive value was 93.85%, and the diagnostic efficiency was 94.25%. The results of the statistical analysis of the data obtained in this study revealed that the diagnostic specificity, the diagnostic positive predictive value and the diagnostic efficiency of the TB-Dot test were significantly higher (p < 0.05) than those of the ICT-TB test. However, the diagnostic sensitivity and the negative predictive value of both tests did not differ significantly (p > 0.05). Viewed from the point of their practicability, it can be justified that the ICT-TB test is a very practicable test, which needs only 15 minutes and does not require special instruments to perform the test, but is more expensive than the TB-Dot test. On the other hand, though the TB-Dot test is not very practicable and relatively time consuming, it has a significantly higher degree of diagnostic value and is much cheaper when compared to the ICT-TB test.


In plasmodia, the dihydrofolate reductase (DHFR) enzyme is the target of the pyrimethamine component of sulfadoxine-pyrimethamine (S/P). Plasmodium vivax infections are not treated intentionally with antifolates. However, outside Africa, coinfections with Plasmodium falciparum and P. vivax are common, and P. vivax infections are often exposed to S/P. Cloning of the P. vivax dhfr gene has allowed molecular comparisons of dhfr alleles from different regions. Examination of the dhfr locus from a few locations has identified a very diverse set of alleles and showed that mutant alleles of the vivax dhfr gene are prevalent in Southeast Asia where S/P has been used extensively. We have surveyed patient isolates from six locations in Indonesia and two locations in Papua New Guinea. We sequenced P. vivax dhfr alleles from 114 patient samples and identified 24 different alleles that differed from the wild type by synonymous and nonsynonymous point mutations, insertions, or deletions. Most importantly, five alleles that carried four or more nonsynonymous mutations were identified. Only one of these highly mutant alleles had been previously observed, and all carried the 57L and 117T mutations. P. vivax cannot be cultured continuously, so we used a yeast assay system to determine in vitro sensitivity to pyrimethamine for a subset of the alleles. Alleles with four nonsynonymous mutations conferred very high levels of resistance to pyrimethamine. This study expands significantly the total number of novel dhfr alleles now identified from P. vivax and provides a foundation for understanding how antifolate resistance arises and spreads in natural P. vivax populations.


To have a very good surveillance system, it is paramount important to have a functional health information system that could be easily used for monitoring and investigation of disease outbreaks. In Papua New Guinea (PNG) a national health
information system was developed, trialed and implemented nationwide. Furthermore to have the system working linked to it must be the local health system for sustainability and control. A public health manual for disease surveillance in PNG was developed and is now being used for surveillance. This paper describes how the health information system, particularly surveillance system was developed and implemented on the national scale, how it was integrated with other management information systems and how information has been used to support management decision-making and informed policy decision. It will highlight some of the hurdles that it has encountered while trying to implement the system. PNG has one of the best national health information systems as compared to many developing countries but limited information generated from the system. There was also less feedback from all levels of the health sector. We need to improve surveillance on the basic principles of integration, focus, and sharing of work. There must be an appropriate and timely response and feedback. We need to improve on the current system rather than building a new one.

AIMS: We assessed the disposition of oral amodiaquine (AQ) and CYP2C8 polymorphism in 20 children with falciparum malaria. METHODS: AQ and DEAQ concentrations were determined with SPE-HPLC method. CYP2C8 genotypes were assessed by PCR-RFLP method. RESULTS: AQ was not detectable beyond day 3 postdose. Cmax for DEAQ was reached in 3.0 days. The mean values for t1/2, MRT, and AUCtotal were 10.1 days, 70.6 days, and 206.7 microg·h·l(-1) day, respectively. All the children were CYP2C8* homozygous. CONCLUSION: Our data are consistent with those previously reported, and the AQ regimen seems pharmacokinetically adequate in the absence of CYP2C8 polymorphism.

35 Kevau IH, Vince JD, McPherson JV.

36 Klapsing P, MacLean JD, Glaze S, McClean KL, Drebott MA, Lanciotti RS, Campbell GL.
We report 2 clinically characteristic and serologically positive cases of Ross River virus infection in Canadian tourists who visited Fiji in late 2003 and early 2004. This report suggests that Ross River virus is once again circulating in Fiji, where it apparently disappeared after causing an epidemic in 1979 to 1980.

37 Kotze AC, Coleman GT, Mai A, McCarthy JS.
A field-applicable assay for testing anthelmintic sensitivity is required to monitor for anthelmintic resistance. We undertook a study to evaluate the ability of three in vitro assay systems to define drug sensitivity of clinical isolates of the human hookworm parasite Necator americanus recovered from children resident in a village in Madang Province, Papua New Guinea. The assays entailed observation of drug effects on egg hatch (EHA), larval development (LDA), and motility of infective stage larvae (LMA). The egg hatch assay proved the best method for assessing the response to benzimidazole anthelmintics, while the larval motility assay was suitable for assessing the response to ivermectin. The performance of the larval development assay was unsatisfactory on account of interference caused by contaminating bacteria. A simple protocol was developed whereby stool samples were subdivided and used for immediate egg recovery, as well as for faecal culture, in order to provide eggs and infective larvae, respectively, for use in the egg hatch assay and larval motility assay systems. While the assays proved effective in quantifying drug sensitivity in larvae of the drug-susceptible hookworms examined in this study, their ability to indicate drug resistance in larval or adult hookworms remains to be determined.

38 Laman M, Ripa P, Vince J, Tefuarani N.
Pulse oximetry was performed on 77 children admitted with acute lower respiratory tract infections (ALRI) to the children’s ward in Port Moresby General Hospital, Papua New Guinea over a 4-month period in 2002. Clinical findings were correlated with different levels of hypoxaemia, <93%, <90% and <85%. Cyanosis, head nodding and drowsiness were good predictors of hypoxia but lacked sensitivity. Decisions to use oxygen based on these signs would therefore result in a significant number of children with hypoxia not receiving oxygen. Pulse oximetry is the best indicator of hypoxaemia in children with ALRI and, although relatively expensive, its use might be cost-effective in controlling oxygen requirements.

OBJECTIVE: To assess the effects of a 3-year programme aimed at controlling scabies on five small lagoon islands in the Solomon Islands by monitoring scabies, skin sores, streptococcal skin contamination, serology and haematuria in the island children. METHODS: Control was achieved by treating almost all residents of each island once or twice within 2 weeks with ivermectin (160-250 microg/kg), except for children who weighed less than 15 kg and pregnant women, for whom 5% permethrin cream was used. Reintroduction of scabies was controlled by treating returning residents and visitors, whether or not they had evident scabies. FINDINGS: Prevalence of scabies dropped from 25% to less than 1% (P < 0.001); prevalence of sores...
from 40% to 21% (P < 0.001); streptococcal contamination of the fingers in those with and without sores decreased significantly (P = 0.02 and 0.047, respectively) and anti-DNase B levels decreased (P = 0.002). Both the proportion of children with haematuria and its mean level fell (P = 0.002 and P < 0.001, respectively). No adverse effects of the treatments were seen. CONCLUSION: The results show that ivermectin is an effective and practical agent in the control of scabies and that control reduces the occurrence of streptococcal skin disease and possible signs of renal damage in children. Integrating community-based control of scabies and streptococcal skin disease with planned programmes for controlling filariasis and intestinal nematodes could be both practical and produce great health benefits.


BACKGROUND: Non-specific beneficial as well as deleterious effects of childhood immunizations have been reported in areas of high mortality. This study aimed to determine the effects of diphtheria-tetanus-whole-cell-pertussis (DTP), BCG, hepatitis B, and measles vaccines on mortality in the highlands of Papua New Guinea (PNG). METHODS: Demographic events for children born in 1989-1994 who were under monthly demographic surveillance in Tari were recorded from birth until age 2 years, out-migration, death, or the end of the study period. Data on BCG, hepatitis B, DTP, measles and pneumococcal polysaccharide vaccination were collected monthly from clinic records. To allow for different characteristics of immunized and non-immunized children, analysis included conditioning on a propensity score for vaccination, adjusting for differences in children’s background characteristics. RESULTS: In all, 101/3502 children (3%) who had at least one vaccine died between ages 29 days and 24 months were compared to 112/546 (21%) who had none. BCG was associated with lower mortality in the 1-5 month age group (hazard ratio [HR] = 0.17, 95% CI: 0.09, 0.34), measles vaccine with lower mortality at age 6-11 months (HR = 0.42, 95% CI: 0.17, 1.01), and pneumococcal polysaccharide vaccine with lower mortality at age 12-23 months (HR = 0.42, 95% CI: 0.19, 0.93). One or more doses of DTP was associated with lower overall mortality (HR = 0.27, 95% CI: 0.16, 0.44), particularly in the 1-5 month age group (HR = 0.19, 95% CI: 0.10, 0.34), and also in those who had had prior BCG (HR = 0.45, 95% CI: 0.22, 0.91). CONCLUSION: Routine immunizations are effective in reducing overall mortality in young children in an area of high mortality. In particular, DTP, whether considered separately or in addition to BCG, was associated with a lowering of overall mortality, in contrast to findings reported from Guinea-Bissau.


HLA class-I and class-II allele frequencies and two-locus haplotypes were examined in 367 unrelated Melanesians living on the islands of Vanuatu and New Caledonia. Diversity at all HLA class-I and class-II loci was relatively limited. In class-I loci, three HLA-A allelic groups (HLA-A*24, HLA-A*34 and HLA-A*11), seven HLA-B alleles or allelic groups (HLA-B*1506, HLA-B*5602, HLA-B*13, HLA-B*5601, HLA-B*4001, HLA-B*4002 and HLA-B*2704) and four HLA-C alleles or allelic groups (HLA-Cw*04, HLA-Cw*01, HLA-Cw*0702 and HLA-Cw*15) constituted more than 90% of the alleles observed. In the class-II loci, four HLA-DRB1 alleles (HLA-DRB1*15, HLA-DRB1*11, HLA-DRB1*04 and HLA-DRB1*16), three HLA-DRB3-5 alleles (HLA-DRB3*02, HLA-DRB4*01 and HLA-DRB5*01/02) and five HLA-DQB1 alleles (HLA-DQB1*0301, HLA-DQB1*04, HLA-DQB1*05, HLA-DQB1*0601 and HLA-DQB1*0602) constituted over 93, 97 and 98% of the alleles observed, respectively. Homozygosity showed significant departures from expected levels for neutrality based on allele frequency (i.e. excess diversity) at the HLA-B, HLA-Cw, HLA-DQB1 and HLA-DRB3/5 loci on some islands. The locus with the strongest departure from neutrality was HLA-DQB1, homozygosity being significantly lower than expected on all islands except New Caledonia. No consistent pattern was demonstrated for any HLA locus in relation to malaria endemicity.


OBJECTIVE: Fatal snakebites at Port Moresby General Hospital (PMGH), Papua New Guinea (PNG), were examined to identify interventions that may improve patient survival. DESIGN: Retrospective case series. SUBJECTS AND SETTING: Inpatients at PMGH who presented with snakebite, had evidence of envenomation, and died as inpatients between 1 January 1992 and 31 December 2001. OUTCOME MEASURES: Number and cause of fatalities; ventilation bed-days; antivenom timing, dose and price. RESULTS: 87 deaths occurred among 722 snakebite admissions to the intensive care unit (ICU). Of these 722 patients, 82.5% were ventilated, representing 45% of all ventilated ICU patients seen in 2000 (3430/7517) of all ICU ventilator bed-days. The median duration of ventilation in fatal snakebite cases was significantly less than in non-fatal cases for children (3.0 v. 4.5 days) and adults (3.0 v. 5.0 days). The case-fatality rate for children (14.6%) was significantly greater than that for adults (8.2%). Sixty fatalities were examined in detail: 75% received blood products; 53% received antivenom (mostly a single ampoule of polyvalent), but only 5% received antivenom c. or = 4 hours post-bite. Major causes of death included respiratory complications (50%), probable intracerebral haemorrhage (17%), and renal failure (10%). Antivenom unit costs increased significantly over the decade; in 2000 an ampoule of polyvalent antivenom was 40-fold more expensive in PNG than in Australia on a gross domestic product (A dollars) per capita basis. CONCLUSIONS: Management of severe snakebite is a major challenge for PMGH. Improved antivenom procurement and use policies (including increased use of appropriate monovalent antivenoms), combined with targeted snakebite education interventions (community- and hospital-based), are
key interventions to reduce the ongoing toll from snakebite.

43 Mosley LM, Sharp DS, Singh S.
Effects of a tropical cyclone on the drinking-water quality of a remote Pacific island.

The effect of a cyclone (Ami, January 2003) on drinking-water quality on the island of Vanua Levu, Fiji was investigated. Following the cyclone nearly three-quarters of the samples analysed did not conform to World Health Organisation (WHO) guideline values for safe drinking-water in terms of chloride residual, total and faecal coliforms, and turbidity. Turbidity and total coliform levels significantly increased (up 56 and 62 per cent, respectively) from pre-cyclone levels, which was likely due to the large amounts of silt and debris entering water-supply sources during the cyclone. The utility found it difficult to maintain a reliable supply of treated water in the aftermath of the disaster. Communities were unaware they were drinking water that had not been adequately treated. Circumstances permitted this cyclone to be used as a case study to assess whether a simple paper-strip water-quality test (the hydrogen sulphide, H(2)S) kit could be distributed and used for community-based monitoring following such a disaster event to better protect public health. The H(2)S test results correlated well with faecal and total coliform results as found in previous studies. A small percentage of samples (about 10 per cent) tested positive for faecal and total coliforms but did not test positive in the H(2)S test. It was concluded that the H(2)S test would be well suited to wider use, especially in the absence of water-quality monitoring capabilities for outer island groups as it is inexpensive and easy to use, thus enabling communities and community health workers with minimal training to test their own water supplies without outside assistance. The importance of public education before and after natural disasters is also discussed.

44 Mueller I, Namuigi P, Kundi J, Ivivi R, Tandrapah T, Bjorge S, Reeder JC.
Epidemic malaria in the highlands of Papua New Guinea.

As part of a larger study into the epidemiology of malaria in the highlands of Papua New Guinea, outbreak investigations were carried out at the end of the 2002 rainy season in 11 villages situated between 1,400 and 1,700 meters above sea level that had reported epidemics. Locations and timing of these epidemics corresponded largely to those reported in the pre-control era of the 1960s and 1970s. On average, 28.8% (range = 10.3-63.2%) of people in each of the 11 villages were found to be infected with malaria. Plasmodium falciparum accounted for 59% of all identified infections and Plasmodium vivax for 34%. The majority (53%) of infections were symptomatic. Although symptomatic infections were most common in children 2-9 years of age (36%), even in adults a prevalence of 20% was observed. A comparison with earlier non-epidemic data in three of the villages without easy access to health care showed markedly increased levels of morbidity, with 6-10-fold increases in parasite prevalence, a 3-fold increase in both measured and reported fevers, and a 12-fold increase in enlarged spleens. The average hemoglobin levels were reduced by 2.3-3.5 g/dL, with a concurrent increase in moderate to severe anemia (hemoglobin level < 7.5 g/dL) from 0.0-3.3% to 3.8-18.4%. These massive increases in morbidity have devastating impact on the affected communities and highlight that malaria epidemics are a serious and increasing public health problem in the highlands of Papua New Guinea.

45 Owen IL.
Parasitic zoonoses in Papua New Guinea.

Relatively few species of zoonotic parasites have been recorded in humans in Papua New Guinea. A greater number of potentially zoonotic species, mostly nematodes, occur in animals but are yet to be reported from humans. Protozoa is the best represented group of those infecting man, with Giardia duodenalis, Cryptosporidium parvum, Cyclospora cayetanensis, Toxoplasma gondii, Sarcozystis spp., Entamoeba polecki, Balantidium coli and, possibly, Blastocystis hominis. The only zoonotic helminths infecting humans include the trematode Paragonimus westermani, the cestodes Hymenolepis nana, H. diminuta and the sparganum larva of Spirometra erinaceae, and the nematodes Trichinella papuae and Angiostrongylus cantonensis and, possibly, Ascaris suum. Other groups represented are Acanthocephala (Macracanthorhynchus hirudinaceus), insects (Chrysomya bezziana, Cimex spp., Ctenocephalides spp.), and mites (Leptotrombidium spp. and, possibly, Sarcopsis scabiei, and Demodex spp.). One leech (Phytodolobus lineata) may also be considered as being zoonotic. The paucity of zoonotic parasite species can be attributed to long historical isolation of the island of New Guinea and its people, and the absence until recent times of large placental mammals other than pig and dog. Some zoonotic helminths have entered the country with recent importation of domestic animals, in spite of quarantine regulations, and a few more (two cestodes, one nematode and one tick) are poised to enter from neighbouring countries, given the opportunity. Improvement in water supplies, human hygiene and sanitation would reduce the prevalence of many of these parasites, and thorough cooking of meat would lessen the risk of infection by some others.

46 Poka H.
Practising in rural Papua New Guinea.

47 Pozio E, Owen IL, Marucci G, La Rosa G.
Inappropriate feeding practice favors the transmission of Trichinella papuae from wild pigs to saltwater crocodiles in Papua New Guinea.

The recent discovery of Trichinella zimbabwensis in farmed crocodiles (Crocodilus niloticus) of Zimbabwe and its ability to infect mammals, and the development of both T. zimbabwensis and Trichinella papuae in experimentally infected reptiles led to an investigation of Trichinella infection in saltwater crocodiles (Crocodylus porosus) and in wild pigs (Sus scrofa) of Papua New Guinea, to see if T. papuae also, is present in both cold- and warm-blooded animals. Of 222 crocodiles examined, 47 animals (21.2%), all from Kikori, Gulf Province, were positive for non-encapsulated larvae in the muscles. The greatest number of larvae was found usually in the biceps, with an average of 7 larvae/g. One
isolate from a crocodile infected successfully both laboratory rats and mice. Of 81 wild pigs examined, 9 from Bensbach river area (Western Province) and 1 from Kikori area (Gulf Province) were positive for non-encapsulated larvae in the muscles. Trichinella larvae from both saltwater crocodiles and wild pigs have been identified by multiplex-PCR analysis as T. papuae. The sequence analysis of the region within the large subunit ribosomal DNA, known as the expansion segment V, has shown the presence of a molecular marker distinguishing T. papuae isolates of Bensbach river area from those of Kikori area. This marker could be useful to trace back the geographical origin of the infected animal. The epidemiological investigation carried out in the Kikori area has shown that local people catch young crocodiles in the wild and keep them in holding pens for several months, before sending them to the crocodile farm in Lae (Morobe Province). They feed the crocodiles primarily with wild pig meat bought at the local market and also with fish. These results stress the importance of using artificial digestion for routinely screening of swine and crocodiles, and of adopting measures for preventing the spread of infection, such as the proper disposal of carcasses and the adequate freezing of meat.

48 Ratu Sade K.
This Perspective reports on the challenges that face a solo doctor in a provincial hospital in the Solomon Islands following the civil disturbances of 1998-2003. The Health Service is seriously constrained by a paucity of funding, supplies and personnel. In spite of that, a rudimentary service can be provided and lives can be saved using simple techniques and basic resources. Further training of nurses, midwives and doctors is required. Emergency medicine, as a generalist discipline, provides a foundation to improve the delivery of care to the acutely ill and injured in these circumstances.

49 Reeder JC.

50 Robertson SE, Roca A, Alonso P, Simoes EA, Kartasasmita CB, Oalaye DO, Odaibo GN, Collinson M, Venter M, Zhu Y, Wright PF.
OBJECTIVE: To assess the burden of respiratory syncytial virus (RSV)-associated lower respiratory infections (LRI) in children in four developing countries. METHODS: A WHO protocol for prospective population-based surveillance of acute respiratory infections in children aged less than 5 years was used at sites in Indonesia, Mozambique, Nigeria and South Africa. RSV antigen was identified by enzyme-linked immunosorbent assay performed on nasopharyngeal specimens from children meeting clinical case definitions. FINDINGS: Among children aged < 5 years, the incidence of RSV-associated LRI per 1000 child-years was 34 in Indonesia and 94 in Nigeria. The incidence of RSV-associated severe LRI per 1000 child-years was 5 in Mozambique, 10 in Indonesia, and 9 in South Africa. At all study sites, the majority of RSV cases occurred in infants. CONCLUSION: These studies demonstrate that RSV contributes to a substantial but quite variable burden of LRI in children aged < 5 years in four developing countries. The possible explanations for this variation include social factors, such as family size and patterns of seeking health care; the proportion of children infected by human immunodeficiency syndrome (HIV); and differences in clinical definitions used for obtaining samples. The age distribution of cases indicates the need for an RSV vaccine that can protect children early in life.

51 Rodgers-Bird QM.

52 Sa JM, Nomura T, Neves J, Baird JK, Wellemes TE, del Portillo HA.
We describe here the sequence of the Plasmodium vivax mdr1 gene from 10 different isolates differing in chloroquine sensitivity. The deduced amino acid sequence of PvMDR1 shares more than 70% similarity with other malarial MDR proteins and it displays consensus motifs of an ABC family transporter including two transmembrane domains and two ATP binding cassettes. Similarity and dendrogram analyses of the encoding sequences could be grouped according to their geographical origin. Within each geographical group however, no correlation was found between chloroquine resistance and specific mutations.

53 Schultz R.

54 Suligoi B, Danaya RT, Sarmati L, Owen II, Boros S, Pozio E, Andreoni M, Rezza G.
To investigate the spread of human immunodeficiency virus (HIV) and other sexually transmitted viruses, two serosurveys (the first in 1999 among 56 adults and the second in 2001 among 351 adults) were conducted in remote villages of the southwestern part of Papua New Guinea. Only one individual was positive for antibodies to HIV. In 2001, the seroprevalence of human herpes virus 8 (HHV-8) was 32.2%, and the seroprevalence of herpes simplex virus type 2 (HSV-2) was 27.4%. Both prevalence rates increased with age, and were lower in the villages near the Bensbach River. The seropositivity of HSV-2 was independently correlated with HHV-8 infection. Our data show that the inhabitants of the southwestern region of Papua New Guinea currently experience an extremely low circulation of HIV. However, the high prevalence of infectious agents that can be sexually transmitted, such as HSV-2 and to a lesser extent HHV-8, indicates the presence of behavioral patterns that may facilitate the spread of HIV in this area of
Iodine deficiency in Papua New Guinea (PNG) is a significant public health concern, with evidence of moderate iodine deficiency. The median urinary iodine concentration for children aged 6-12 years in the Hela Region was 100 mg/l, indicating moderate iodine deficiency. The median daily consumption of salt was 2.62 +/- 1.29 g. The iodine content of salt in households and retail shops was determined; eight had died following hospital discharge and 41 were lost to follow-up. Major neurological sequelae were found in 50 (63 per cent) of surviving children, and 27 (34 percent) had multiple severe complications. In rural Papua New Guinea, meningitis causes high rates of mortality and severe long-term disability in a high proportion of survivors. High-level resistance to chloramphenicol is likely to be a major problem in the future, but widespread availability of third-generation cephalosporins for the treatment of meningitis, although urgently required, will not overcome the other problems of delayed presentation with established complications. There is a need for the introduction of conjugate Haemophilus influenzae vaccine, and affordable vaccination strategies against Streptococcus pneumoniae. Richer countries could sponsor these vaccines in developing countries, and apply pressure on vaccine producers to lower the costs.

Wood DM, Alsahaf H, Streete P, Dargan PI, Jones AL.

Rotenone is a pesticide derived from the roots of plants from the Leguminosae family. Poisoning following deliberate ingestion of these plant roots has commonly been reported in Papua New Guinea. However, poisoning with commercially available rotenone in humans has been reported only once previously following accidental ingestion in a 3.5-year-old child. Therefore, the optimal management of rotenone poisoning is not known. After deliberate ingestion of up to 200 ml of a commercially available 0.8% rotenone solution, a 47-year-old female on regular metformin presented with a reduced level of consciousness, metabolic acidosis and respiratory compromise. Metformin was not detected in premortem blood samples obtained. Despite intensive supportive management, admission to an intensive care unit, and empirical use of N-acetylcysteine and antioxidant therapy, she did not survive. Poisoning with rotenone is uncommon but is potentially fatal because this agent inhibits the mitochondrial respiratory chain. In vitro cell studies have shown that rotenone-induced toxicity is reduced by the use of N-acetylcysteine, antioxidants and potassium channel openers. However, no animal studies have been reported that confirm these findings, and there are no previous reports of attempted use of these agents in patients with acute rotenone-induced toxicity.

Wuster W, Dumbrell AJ, Hay C, Pook CE, Williams DJ, Fry BG.

We analyze the phylogeny of three genera of Australasian elapid snakes (Acanthophis, Oxyuranus, and Pseudechis), using parsimony, maximum likelihood, and Bayesian analysis of sequences of the mitochondrial cytochrome b and ND4 genes. In Acanthophis and Pseudechis, we find evidence of multiple trans-Torresian sister-group relationships. Analyses of the timing of cladogenic events suggest crossings of the Torres Strait on several occasions between the late Miocene and the Pleistocene.
These results support a hypothesis of repeated land connections between Australia and New Guinea in the late Cenozoic. Additionally, our results reveal undocumented genetic diversity in Acanthophis and Pseudechis, supporting the existence of more species than previously believed, and provide a phylogenetic framework for a reinterpretation of the systematics of these genera. In contrast, our Oxyuranus scutellatus samples from Queensland and two localities in New Guinea share a single haplotype, suggesting very recent (late Pleistocene) genetic exchange between New Guinean and Australian populations.


Consumption of the traditional kava preparation was reported to correlate with low and uncustomary gender ratios (more cancer in women than men) of cancer incidences in three kava-drinking countries: Fiji, Vanuatu, and Western Samoa. We have identified flavokawain A, B, and C but not the major kavalactone, kawain, in kava extracts as causing strong antiproliferative and apoptotic effect in human bladder cancer cells. Flavokawain A results in a significant loss of mitochondrial membrane potential and release of cytochrome c into the cytosol in an invasive bladder cancer cell line T24. These effects of flavokawain A are accompanied by a time-dependent decrease in Bcl-x(L), a decrease in the association of Bcl-x(L) to Bax, and an increase in the active form of Bax protein. Using the primary mouse embryo fibroblasts Bax knockout and wild-type cells as well as a Bax inhibitor peptide derived from the Bax-binding domain of Ku70, we showed that Bax protein was, at least in part, required for the apoptotic effect of flavokawain A. In addition, flavokawain A down-regulates the expression of X-linked inhibitor of apoptosis and survivin. Because both X-linked inhibitor of apoptosis and survivin are main factors for apoptosis resistance and are overexpressed in bladder tumors, our data suggest that flavokawain A may have a dual efficacy in induction of apoptosis preferentially in bladder tumors. Finally, the anticarcinogenic effect of flavokawain A was evident in its inhibitory growth of bladder tumor cells in a nude mice model (57% of inhibition) and in soft agar.


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