FIELD PLACEMENT IN THE NORTHERN TERRITORY

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Table of contents

Acknowledgements

1 AN OVERVIEW OF THE FIELD PLACEMENT WITH THE NORTHERN TERRITORY DEPARTMENT OF HEALTH AND COMMUNITY SERVICES 1-54

2 SURVEILLANCE 55-91

3 REPORT OF AN OUTBREAK INVESTIGATION 92-137 EPIDEMIC BARMAH FOREST AND ROSS RIVER VIRUS DISEASE IN EAST ARNHEM, NORTHERN TERRITORY

4 ARTICLES APPEARING IN THE COMMUNICABLE DISEASES INTELLIGENCE 138-153

5 MANUSCRIPTS PREPARED FOR SUBMISSION TO PEER REVIEW JOURNALS 154-242

REFERENCES 243-245
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Special thanks to my cohort of MAE students for making it a fun experience.
# Chapter 1

## 1. Background

1.1 AN OVERVIEW OF THE FIELD PLACEMENT WITH THE NORTHERN TERRITORY DEPARTMENT OF HEALTH AND COMMUNITY SERVICES 1-54

1.2 Organisational structure and programs of the Northern Territory communicable diseases network 1-3

1.3 Networking 3-6

1.4 Leading communicable diseases in the NT 6-9

1.5 Field epidemiology - a range of experiences 9-16

1.5.1 Letter written in response to a public inquiry 17-54

1.5.2 Example of a radio interview 18-21

1.5.3 Scrub typhus in the Northern Territory 21-29

1.5.4 A case of diphtheria in Alice Springs 30-31

1.5.5 Pertussis (whooping cough) vaccination 32-33

1.5.6 Tutorial handout - questionnaire design 34

1.5.7 Leptospirosis in the Northern Territory The interpretation of dengue virus serology 35-41

1.5.8 Outline for a Grand Rounds presentation 42-43

1.5.9 A case of diphtheria in Alice Springs 43-45

1.5.10 Tutorial handout - questionnaire design 46-54
AN OVERVIEW OF THE FIELD PLACEMENT WITH THE NORTHERN TERRITORY DEPARTMENT OF HEALTH AND COMMUNITY SERVICES

1.1 Background

I was very fortunate to begin my field experience prematurely at the Communicable Diseases Centre (CDC) in Darwin to assist in the investigation of melioidosis, an uncommon but potentially fatal infection endemic in northern Australia. When a cluster of urban cases occurred in Darwin from November to January 1991, Dr Aileen Plant, then Chief Health Officer of the Northern Territory Department of Health and Community Services (NT DH&CS), contacted the National Centre for Epidemiology and Population Health for assistance. I was about to complete my year as the medical officer at the communicable diseases unit in Alice Springs and prepare myself for the Master of Applied Epidemiology (MAE) coursework, when I found myself seconded to the melioidosis investigation. That was my first experience with a case-control investigation and the difficulties surrounding the selection of appropriate controls. On a more personal level, this outbreak gave me a preview of the intensity of field investigation, the importance of networking with local experts and the single minded commitment that is required to provide answers quickly - in this case, whether we were witnessing a point source outbreak of melioidosis.

Most of my time during the two year placement was spent in outbreak investigations. Outbreaks occurred with surprising regularity in the 12 months following the melioidosis investigation, and included outbreaks of Ross River virus infection, gonococcal conjunctivitis in children, ciguatera (an intoxication caused by eating contaminated fish), Haemophilus influenzae b meningitis, measles and Barmah Forest virus infection. Two of these outbreaks took me to central Australia and East Arnhem and involved liaising with a wide cross-section of health professionals.
My main contribution to the notifiable diseases surveillance system was as co-editor of the *NT Communicable Diseases Bulletin* which we started in November 1991 as part of the feedback loop in our notification system. We are currently in the process of reviewing the notifiable diseases surveillance system and have had a number of meetings to allocate responsibilities to the various medical officers at CDC. Our plan is to incorporate many of the initiatives adopted in New South Wales; rationalising the list of notifiable diseases, reducing the number of diseases requiring doctor notification and improving the quality of laboratory-based notification. My role has been to draft a proposal for activities towards this end and to develop a computer generated reports system.

Dr Mahomed Patel, Director, NT Disease Control Program, encourages a team approach at the Communicable Diseases Centre in Darwin. All drafts of disease control protocols and pamphlets developed by the Department are circulated to all medical officers for comments, as are many of the reports prepared for the Secretary of Health, Mr Ray Norman. I was strongly encouraged to become "expert" in one or more diseases while in the Unit; circumstances focused my research on arboviruses (mainly mosquito-borne viruses) and melioidosis. Although all medical officers at CDC answer inquiries by health professionals, the media and the public, questions about melioidosis and arboviruses were usually directed to me, as were inquiries on sexually transmitted diseases when doctors in the AIDS Unit were unavailable. My experience in central Australia (1990) and the networks I developed during my visits to Nhulunbuy, East Arnhem, also meant that I was usually the first doctor contacted in Darwin by the Communicable Diseases Officers (CDOs) and laboratory staff in Alice Springs, Tennant Creek and Nhulunbuy for all their concerns on surveillance and outbreak control measures. The frequency and informality of my communication with the Communicable Diseases Officers in Nhulunbuy increased dramatically after I worked with them for 10 days during the initial stage of the Barmah Forest virus outbreak investigation.
The field trip gave both sides the opportunity to develop trust and an appreciation of each others skills.

The transition into the role of an epidemiology registrar was facilitated by Dr Patel's knowledge of my level of expertise and limitations in this field; we agreed at the beginning of my MAE placement that I would take on and work up all disease control inquiries from central Australia and start appropriate action. I was instructed to use my discretion on whether to report on the incident and our public health action retrospectively, or consult with him immediately after establishing the nature of the problem if it was new, complex or politically sensitive.

Field placement in the Northern Territory provides dynamic and varied involvement in communicable disease control and acute epidemiology - an experience that I highly recommend. This chapter is a composite of my observations on the existing program of communicable disease control, my perception of disease control priorities and an overview of my epidemiological and public health experience over the two years.

1.2 Organisational structure and programs of the Northern Territory communicable diseases network

The Northern Territory, total area 1,346,200 square kilometres or one sixth of Australia, has a population of 173,000 people. The NT is divided into two ecologically distinct regions, the arid zone of central Australia and the tropical north, each with its own health problems. It contains the highest proportion of indigenous Australians of any state in Australia (22.4% of the NT population), whose major health problems include infectious diseases, alcohol abuse, diabetes, cardiovascular diseases, and trauma.

The NT is also divided into five health districts (Figure 1): Alice Springs and the Barkly Tablelands districts in the central Australia, and the Darwin, East Arnhem and Katherine districts in the north (the Top End). The organisational tree of the NT Department of Health and Community Services is presented in Figure 2.
Figure 1

HEALTH AND COMMUNITY SERVICES OUTLETS IN THE NORTHERN TERRITORY

DARWIN

EAST ARNHEM

REGION

KATHERINE

REGION

Alice Springs and Barkly Region

LEGEND

- Hospital
- Clinic
- General Practitioner
- Dental Clinic
- optometrist
- Health Centre
- Community Health Centre
- Community Health Service
- School Clinic
The Disease Control Program is one of 11 programs of the Community Care Division of the NT DH&CS. The mission statement of the Disease Control Program is to minimise morbidity and mortality from communicable diseases. The program operates in all health districts with staffing levels varying with the population in the district, and in some instances, by special disease control requirements. The objectives of the mission are to be achieved through a number of sub-programs with include:

- communicable disease control and surveillance, including preventative education of health professionals and the public;
- implementation of childhood immunisation policies and the promotion of adult immunisation;
- screening and clinical services to investigate, contact trace and treat clients with selected diseases, specifically tuberculosis, leprosy, sexually transmitted diseases (STD), Human Immunodeficiency Virus (HIV) and the Acquired Immunodeficiency Syndrome (AIDS).

The current medical officers in charge of the sub-programs are Mahomed Patel (disease surveillance and control and immunisation), Vicki Krause (tuberculosis control), John Hargrave (leprosy control) and Frank Bowden (STD/AIDS control). Communicable Disease Officers (CDOs) from each health district have met annually since 1990 for a three day inservice, which is a forum for discussion of communicable diseases issues in their areas and the NT overall.

1.3 Networking

The small size of the public health fraternity in the Northern Territory means that it is relatively easy to identify key people and allied disciplines necessary for effective communicable disease control. Throughout the NT, Communicable Disease Officers liaise closely with: general practitioners; medical and allied health staff of the regional hospitals in Darwin, Alice Springs, Tennant Creek, Katherine and Nhulunbuy, community controlled health services and Rural and Urban Health Services of DH&CS; hospital Infection Control nurses; hospital laboratories, the Western Diagnostic,
Peverill's and Gribble's private pathology services; the Environmental Health, Medical Entomology and Statistics Branches of DH&CS; and the Community Relations Branch which co-ordinates all Departmental public relations activities. Other government and non-government organisations include the Menzies School of Health Research, state reference laboratories, mainly in Perth, Adelaide, Brisbane and Melbourne, the AIDS Council NT and the AIDS Council of Central Australia, the NT Department of Education, Children's Services, Migrant Services and the Immigration Department, the Department of Primary Industries and Fisheries, and the media.

Networking is also frequent with the State Health Departments of Western Australia, South Australia and Queensland. Outbreaks of meningococcal meningitis, gonococcal conjunctivitis and measles have necessitated control measures across state borders since the beginning of my placement in Darwin.

Extensive consultation is essential for the success of any control strategy which involves the community controlled Aboriginal health services. This is especially true for the Central Australian Aboriginal Congress in Alice Springs and the Anyinginyi Congress in Tennant Creek. Co-operation is rarely problematic between the Health Department and the Nganampa Health Council, Pijantjatjara Homelands in northern South Australia, Kalano Community Association in Katherine, the recently established Danila Dilba in Darwin, and the Laynhapuy Homelands Health Project in East Arnhem.

Doctors at CDC in Darwin are often used as mediators to facilitate co-operative disease control action in central Australia when there have been personality clashes between regional CDC staff, Rural Health Services, the Alice Springs Hospital and the community controlled health services. For example, Dr Patel and I were actively involved in the planning and drafting of the research proposal for a serosurvey of antibodies to *Neisseria meningitidis* in Aboriginal children vaccinated with serogroup A and C vaccine ("Mencevax AC") at the end of the meningococcal meningitis outbreak of 1987-91. More recently, I was asked by the Alice Springs Hospital microbiologist and Infection Control Officer to discuss measles control measures with the attending
paediatrician during a nosocomial outbreak. These examples emphasise the need for newly appointed MAE students to develop an understanding of the political climate and at times conflicting agendas of the different health care providers in their state of appointment.

In my two years in Darwin, I have observed the strengthening of collegial ties between CDC and the physicians (principally Drs Bart Currie, Jim Burrows and Diane Howard) and paediatricians of the Royal Darwin Hospital (Drs Alan Walker and Paul Bauert); the Menzies School of Health Research including Prof. John Mathews (Director), Dr Tarun Weeramanthri (PhD student), Dr Valerie Asche (microbiologist) and Ms Jennifer Powers, statistician; the Medical Entomology and Environmental Health Branches of DH&CS (Mr Peter Whelan and Mr Mike Thompson respectively); and the Department of Primary Industries and Fisheries (Drs Lorna Melville and Jim McInerney and Mr Richard Weir). There are now three physicians in Darwin with backgrounds in infectious diseases. All are readily accessible for consultation and are actively involved in research - Drs Bart Currie, Frank Bowden and Jim Burrows who has done research in marine toxins in Fiji.

Dr Weeramanthri and I started the "Epidemiology Interest Group" in 1991 to provide a forum for discussion of epidemiological theory and its practical application. The group meets each fortnight and has attracted people interested in epidemiology outside CDC and the Menzies School, including resident staff at the Royal Darwin Hospital (RDH) and veterinary surgeons. Recently we have encouraged members of the group to present research projects in the planning stages so we can critically evaluate strengths and weaknesses in methodology, thereby improving the quality of the proposal. Our criticisms of a proposed drug trial on ear disease in Aboriginal infants resulted in a meeting of the principal investigators, the District Medical Officer of one of the communities involved in the study, Dr Peter Thorn, Dr Alan Ruben and myself to clarify the case definitions and definitions of the endpoints suggested in the proposal, assessment of outcome and some of the ethical considerations before it was submitted to
the Joint Institutional Ethics Committee of the Royal Darwin Hospital and the Menzies School of Health Research.

My interaction with the Department of Primary Industries and Fisheries veterinary surgeons has been both mutually educational and fun. They have been involved in some of our investigations, namely melioidosis and leptospirosis, and I have presented two epidemiological exercises to them in 1992. I had the opportunity to go out with one of the veterinarians on his routine visit to one property for tuberculosis screening, and on another occasion to a piggery which had reported an infertility problem. Richard Weir (PhD student) and his co-workers at the Berrimah Agricultural Research Laboratory carried out the viral isolations during the Barmah Forest virus investigation and routinely for entomological surveillance purposes.

1.4 Leading communicable diseases in the Northern Territory

Reducing morbidity and mortality from communicable and other infectious diseases in Aboriginal people remains a significant challenge for health professionals in the Northern Territory. Devanesen et al in 1986 highlighted the areas in which the health of Aboriginal people in the NT fell short of that of non-Aboriginal residents. The expectation of life and age-specific mortality data clearly reflect the extent of Aboriginal health disadvantage. Infectious and parasitic diseases are respectively the fourth and fifth leading cause of death in female and male Aborigines in the Northern Territory, although national mortality statistics for 1985 included only 124 female and 136 male deaths from infectious diseases.

The current NT Notifiable Diseases list is presented in Table 1. The enteric diseases (1165 notifications) and sexually transmitted diseases (1889 notifications) together accounted for 81% of the 3774 notifications in 1992. Other important notifiable diseases are measles, malaria, meningococcal meningitis, tuberculosis, arboviruses (principally Ross River and Barmah Forest viruses), diphtheria, pertussis, and acute glomerulonephritis. Regional differences in infectious disease morbidity include:
donovanosis, HTLV-1\textsuperscript{4} and periodic outbreaks of group A meningococcal meningitis and non-sexually transmitted gonococcal conjunctivitis in central Australia; sporadic group C meningococcal meningitis in central Australia and the Top End, with a localised outbreak in East Arnhem; endemic and epidemic arbovirus disease north of the Barkly Tablelands, sporadic cases only occurring in the southern region during particularly heavy monsoonal rains; the high rates of tuberculosis in Katherine; and outbreaks of nephritogenic streptococcal infections in Top End communities.\textsuperscript{5}
### Table 1

#### NOTIFIABLE DISEASES IN THE NORTHERN TERRITORY

<table>
<thead>
<tr>
<th>Sexually Transmitted Diseases</th>
<th>Other: Common Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>Arbovirus (other§)</td>
</tr>
<tr>
<td>Chancroid</td>
<td>Campylobacter</td>
</tr>
<tr>
<td>Chlamydia neonatal conjunctivitis</td>
<td>Dengue Fever¶</td>
</tr>
<tr>
<td>Donovanosis</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td>Genital herpes simplex virus infection</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td>Gonococcal infections</td>
<td>Hepatitis C</td>
</tr>
<tr>
<td>Gonococcal conjunctivitis*</td>
<td>Hepatitis (unspecified)</td>
</tr>
<tr>
<td>Human Immunodeficiency Virus</td>
<td>Malaria*¶</td>
</tr>
<tr>
<td>Lymphogranuloma venereum</td>
<td>Measles*</td>
</tr>
<tr>
<td>Non-specific urethritis</td>
<td>Meningococcal infection*</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Ross River virus</td>
</tr>
<tr>
<td></td>
<td>Salmonella</td>
</tr>
<tr>
<td></td>
<td>Shigella</td>
</tr>
<tr>
<td></td>
<td>Tuberculosis</td>
</tr>
<tr>
<td></td>
<td>Whooping cough</td>
</tr>
</tbody>
</table>

#### Other: Unusual Diseases

| Amoebiasis                    | Poliomyelitis*          |
| Anthrax                       | Psittacosis             |
| Brucellosis                   | Q Fever                 |
| Cholera*                      | Rabies*                 |
| Congenital rubella syndrome (CRS) | Rheumatic fever         |
| Diphtheria*                   | Tetanus                 |
| (Acute) glomerulonephritis    | Typhus                  |
| Hydatid disease               | Vibrio parahaemolyticus|
| Legionella infections*        | Viral haemorrhagic fevers* |
| Leptospirosis                 | Yellow Fever*           |
| Leprosy                       | Yersinia                |
| Plague*                       |                         |

* Diseases requiring urgent notification by phone or facsimile.

§ Arbovirus (other) includes the alphavirus Barmah Forest virus, and the flaviviruses Murray Valley encephalitis virus and kunjin virus.

¶ The NT is receptive to malaria. Dengue fever cases are all imported; active entomological surveillance is maintained for *Aedes aegypti* and *Aedes albopictus*. 
1.4.1 Enteric disease notifications

Enteric disease notifications (campylobacteriosis, hepatitis A, salmonellosis, shigellosis and yersiniosis) accounted for 34% of all notifications for 1991 and 31% in 1992. The highest attack rates for all enteric diseases occur in children under 5 years of age, with a second peak in the 20-29 age group probably reflecting transmission to adults of child rearing age. The highest age specific attack rate for salmonellosis was in infants 0-11 months (2828 per 100 000) and the highest rates for campylobacteriosis, hepatitis A and shigellosis occurred in children aged 1-4 years.

One of the causes of ascertainment bias in our enteric disease notification system is the lack of standardisation between laboratories in the list of pathogens for which they routinely attempt culture. The Alice Springs Hospital laboratory was involved in an investigation of campylobacteriosis in 1987-88, and has maintained a high level of awareness of this organism. In contrast, there are no notifications of campylobacteriosis for the East Arnhem health district. Since 1990, all but two of 35 yersinia isolates have been in residents of the greater Darwin area (metropolitan Darwin, Palmerston and the Litchfield Shire), and this appears to be a true difference in incidence between the regions. The enteric disease survey in Alice Springs detected yersinia in very low numbers so the regional laboratories routinely culture for campylobacter, shigella species, salmonella species and perform a latex agglutination test for rotavirus. They look for yersinia and aeromonas if blood or leucocytes are detected in the stool. In Nhulunbuy Katherine and Darwin, plates for yersinia are prepared when specifically requested and when non-lactose fermenting colonies grow on their standard culture media. The Gove District Hospital laboratory conducted a six month survey of enteric pathogens in 1991; campylobacter was isolated three times and there has been only one yersinia isolate in four years. The main enteric pathogen in the East Arnhem region is rotavirus, but Mr Gabe Schraven, the laboratory Director, believes that enteropathogenic E. coli and adenoviruses are also important causes of
diarrhoeal disease in the district. The Tennant Creek Hospital laboratory only cultures for shigella and salmonella routinely and for campylobacter when indicated.

The system relies almost exclusively on laboratory notification of disease thereby excluding cases in which no pathology specimen is collected, and is limited by the poor sensitivity of (usually) single stool microscopy and culture to detect the infective agent. Outbreaks of shigellosis in 1990 and hepatitis A in 1990 and 1992 have shown that the existing surveillance program for enteric diseases is an insensitive system for detecting outbreaks.

At present we do not carry out surveillance for viral or parasitic diarrhoeal diseases in the community eg rotavirus. This deficiency is recognised and will be addressed by Dr Ruben (MAE 1992) will be focusing his attention on this area in 1993.

1.4.2 Sexually transmitted diseases

The control of sexually transmitted diseases in the NT (chlamydia, donovanosis, gonorrhoea, herpes simplex virus, and syphilis) is one of the priority programs in the NT. Problems in control include: the asymptomatic nature of many STD; late presentations or failure to present for treatment; difficulties with contact tracing compounded by alcohol and substance abuse; cultural taboos, "shame", surrounding sexuality and genital examinations which may impede the examination of a client by a health care provider of the opposite sex; the predominance of female health providers in rural clinics resulting in fewer presentations of infected men; community and personal perceptions about the importance of STD to health; and poor compliance with prolonged oral antibiotic regimens for some of the STD eg 10-14 days of treatment required for non-gonococcal urethritis and cervicitis, and weeks to months of antibiotics required for effective treatment of donovanosis. The incidence of HIV and AIDS has remained low, and sentinel screening suggests that there has been no transmission within Aboriginal communities.
Although most incidence cases of syphilis in the NT are detected serologically, the clinical case definition will be modified to more accurately reflect the stage of disease (primary, secondary, latent, tertiary and congenital) as chronicity determines treatment and follow-up requirements (Dr Frank Bowden, personal communication). Congenital syphilis will become a separate notification category. Another STD requiring review is non-specific urethritis (NSU). The current reporting practices for NSU result in a meaningless statistic in the NT; only 12 cases were reported in 1992. We need to re-evaluate the importance of this disease complex in the notification system, and either rely on a laboratory based case definition or remove it from the Notifiable Diseases list.

1.4.3 Arbovirus infections and malaria surveillance

Intensive epidemiological and entomological surveillance programs are maintained for the mosquito-borne viruses and malaria. Northern Australia is receptive to malaria, although Australia was certified free of malaria by the World Health Organisation in 1981. None of the cases of dengue fever notified in the NT are locally acquired, but the disease was endemic until eradication of *Aedes aegypti* was achieved in the 1950s. The last recorded case of indigenous dengue was in 1955-56. Examination of tyres imported from South East Asia by the NT Quarantine and Inspection Service has detected *Ae albopictus*, another important vector of dengue fever. Similar concerns now exist for the re-introduction of *Ae aegypti* through the importation of larvae in spare tyres of vehicles entering the NT from north Queensland. The CDC in collaboration with the Medical Entomology Branch and the Royal Darwin Hospital maintain active surveillance for both diseases.

In 1980 the Medical Entomology Branch established the NT Arbovirus Disease Surveillance program with the aim of providing timely data on geographical or temporal clustering of cases of Ross River virus (RRV) infection and other arboviruses for vector control. Data entry and follow-up of laboratory confirmed
cases were taken over by CDC in 1992; the questionnaire includes demographic, entomological, serological and a number of clinical questions. Specific questions include movements in the three weeks preceding onset of symptoms and the possible location of infection. The system is based on stimulated surveillance through the pathology services which send out arbovirus notification forms to the requesting doctor with each positive result. It is labour intensive, usually requiring telephone interviews of cases to identify the probable place of infection.

Barmah Forest virus was recognised as a human pathogen in the NT following an outbreak in 1992 of 42 serologically confirmed and four probable cases in Nhulunbuy on the Gove Peninsula. The flaviviruses Murray Valley encephalitis (MVE) virus and kunjin virus rarely cause human disease in the NT. Only five cases of encephalitis attributed to MVE were reported during the Australia-wide outbreak in 1974\textsuperscript{10}, and there have been no confirmed cases of kunjin virus disease although the virus is frequently isolated from pools of mosquitoes (Richard Weir, Berrimah Agricultural Research Laboratory, NT Department of Primary Industries and Fisheries, personal communication). Our failure to detect kunjin virus-associated human disease may in part be due to inadequate surveillance; cases of clinical polyarthritis and flu-like illness are not routinely tested for kunjin virus infection. Screening for kunjin is only requested for clarification of flavivirus serology in cases diagnosed with dengue fever who deny history of travel outside the NT during the incubation period.

1.4.4 Tuberculosis

Tuberculosis control was reassessed in 1984/85 after 65 cases were reported in 1984, a 50% increase over notifications in 1983. Active surveillance and extensive contact tracing have reduced incidence from 46.8 per 100,000 in 1984 to 17.9 per 100,000 in 1991 and 18.6 in 1992. Most cases occur in Aborigines (60.0 per 100,000) and recent immigrants from hyperendemic areas. Although improving, these incidence rates are significantly higher than the Australian tuberculosis
incidence rate in 1990 of 3.4 per 100,000. The program aims to reduce tuberculosis incidence by 24% per year.\textsuperscript{2}

1.4.5 Changes to the notifiable diseases list

In keeping with the recommendations of the Communicable Diseases Standing Committee in July 1992, the NT will be adding non-neonatal botulism, \textit{Haemophilus influenzae} b, mumps, rubella and listeriosis to the list of NT Notifiable Diseases.

1.4.6 Important non-notifiable infectious diseases in the NT

There are also some non-notifiable diseases which cause considerable morbidity and mortality in parts of the NT. The incidence of invasive \textit{Haemophilus influenzae} b in central Australian Aboriginal children is among the highest reported.\textsuperscript{11} Attack rates in non-Aboriginal children are also higher than those reported in the Top End.

Melioidosis, first diagnosed in a male diabetic presenting with atypical pneumonia in 1960, is endemic in the Top End. An outbreak of 34 cases which started during the near record wet season of 1990/91, resulted in 12 deaths (35% case fatality rate). \textit{Pseudomonas pseudomallei}, the bacterium causing melioidosis, is the most common cause of fatal community-acquired pneumonia referred to the Royal Darwin Hospital.\textsuperscript{12} Active surveillance established during the outbreak, November 1990 to June 1991 detected 33 cases. Retrospective review of discharge diagnoses of patients admitted to the Darwin Private Hospital by Dr Bart Currie identified one additional case of very mild cutaneous melioidosis.

A focus of scrub typhus has been identified in Litchfield Park, a nature reserve near Darwin which has been accessible to tourism only since about 1985. There have been five cases of scrub typhus in visitors to the park. In 1991, CDC in collaboration with the Conservation Commission of the Northern Territory and the Community Relations Branch of DH\&CS developed a disease prevention message for display on billboards at the entrances to the Park.
1.5 Field epidemiology - a range of experiences

The following section aims to present a selection of written material I have prepared in the last two years. These include an example of a response to a public inquiry on mosquito-borne virus infections, a transcript of a live radio interview with the Australian Broadcasting Corporation (ABC) in Darwin, a letter circulated to medical practitioners in the NT informing them of a focus of scrub typhus, a press release describing a case of diphtheria, an article for the regular health feature in the *Sunday Territorian* newspaper, the handout which accompanied my tutorial on questionnaire design prepared for the NCEPH Introductory Course in March 1992, two recent draft reports for the *NT Notifiable Diseases Bulletin* on leptospirosis and the interpretation of flavivirus serology and the outline of a presentation for the Royal Darwin Hospital Grand Rounds. I have also included a critical review of some of these examples with the benefit of experience (January 1993).
13 July 1992

Ms Win Kent
Arthritis Foundation of the Northern Territory
PO Box 37582
WINNELLIE NT 0821

Dear Ms Kent

I refer to your inquiry about modifying the recent Ross River virus information pamphlet published by the Department of Health in Western Australian. As we discussed on the phone, the clinical and public health information is excellent and needs no modification.

My only suggestion is that mention should also be made about the Barmah Forest virus (BF) which has been isolated from mosquitoes in the NT for several years, and since the large outbreak in Nhulunbuy this year we now consider another important arbovirus (mosquito-borne virus) causing human disease. We have actively encouraged doctors to screen patients for BF when they suspect an arbovirus infection. BF infections are similar to Ross River virus infections clinically, although our preliminary analysis suggests that it is probably a milder disease of shorter duration. The main symptoms are fatigue, joint pain, rash, muscle aches and pains, and headache. Some people also complain of respiratory symptoms such as earache, disturbance of balance, sore throat, runny nose and cough, while others also experience gastrointestinal symptoms such as nausea and diarrhoea. These symptoms also accompany Ross River virus infection. An interesting feature of the rash in BF infection is that it can be vesicular (blister-like) and very itchy. The rash seems to be more common in BF than Ross river virus infection, while the reverse is true for joint involvement.

Peter Whelan, medical entomologist for the Northern Territory, has also reviewed the pamphlet and makes the following suggestions:

**Insert 1 - When and where**

In the Top End of the NT, the main risk season is from December to March inclusive, with the highest risk period in January when large numbers of mosquitoes result from
both tides and rainfall. Humid conditions enable mosquitoes to live longer, and other environmental factors allow virus to pass back and forth from mosquitoes to animals and sometimes humans.

If there are higher than normal tides in October or November followed closely by an early onset of extended rain, human infections can occur earlier (October to November), and under favourable conditions, throughout the year.

The lowest risk for Ross River virus infections is in the Alice Springs area, while disease occurs in Katherine to Tennant Creek after extended and widespread rain. The highest risk area is north of Larrimah. In the Top End, most cases of Ross River virus are reported from rural communities in close proximity to mosquito breeding sites (Katherine, Jabiru and Nhulunbuy). In Darwin, suburbs bordering Leanyer Swamp have higher infection rates than the inner suburbs.

**Insert 2 - Mosquitoes**

The "salt marsh mosquito", *Aedes vigilax*, is thought to spread Ross River virus in coastal areas during the early wet season. The "common banded mosquito" *Culex annulirostris* spreads the virus over most of the NT from December to April, and probably during other favourable periods. *Aedes normanensis* the "flood water mosquito" may also spread the virus in the subcoastal areas as far south as Tennant Creek from December to February.

You may also wish to say that both *Aedes vigilax* and *Culex annulirostris* carry the Barmah Forest virus. The other minor changes that Peter suggests are written on the accompanying photocopy of the pamphlet.

I hope this information will be of use, and apologise that my response was delayed. Please contact me if you have any other questions about Northern Territory arboviruses.

Yours sincerely

Dr Angela Merianos  
Epidemiology Registrar  
Communicable Diseases Centre, Darwin  
for  
Director, Disease Control.
Comments:

Ms Kent contacted me to obtain some information on Ross River virus as part of the display the NT Arthritis Foundation were planning for the Darwin Show Day. She was also considering a new RRV pamphlet for the NT targeting people infected with Ross River virus, as our existing publication focuses on prevention. In the course of a telephone conversation we had before I wrote this letter, she requested information on the chronicity of RRV, its relationship to degenerative arthritis and whether RRV results in long term disability. Some of these questions were answered in the Ross River virus pamphlet produced by the Western Australian Health Department. The purpose of my letter was to address issues relevant to arbovirus disease in the Northern Territory which were not adequately covered in the literature that Ms Kent had already accessed. As the general public and people infected with RRV were the main targets of her stall, I had simplified the entomological text suggested by Peter Whelan.

In retrospect, I could have simplified the letter further by omitting some of the unnecessary medical jargon and entomological details. The latter is also a criticism of the Western Australian pamphlet. My description of the clinical presentation of Barmah Forest virus in paragraph 2 can be condensed to read "The illness caused by Barmah Forest virus is similar to that caused by the Ross River virus, but we believe that it is probably milder and less prolonged. The main symptoms are tiredness, joint pains, rash, muscle aches and pains and headache. Some people also complain of a flu-like illness with any of the following symptoms: earache; disturbance of balance; sore throat; runny nose; cough; nausea; vomiting and diarrhoea". Similarly I would now substitute "joint pain and arthritis" for "joint involvement".

I would also make the following changes to the entomological section: "In the NT Ross River virus is mainly a disease of the Top End although cases can occur as far south as Alice Springs after heavy rains. Most people become infected with the virus from December to March, but infection can occur throughout the year. Special care should be taken to avoid mosquito bites in Katherine, Jabiru, Nhulunbuy and suburbs
bordering Leanyer swamp in Darwin". I would omit all reference to the vector species and focus on disease prevention strategies.

1.5.2 Example of a radio interview

The following is a transcript of a live interview with Tony Walker on the "Drive Time" Program, ABC, Darwin, November 1991. This interview was typical of an number of radio and newspaper interviews I was invited to give on Ross River virus disease, Barmah Forest and melioidosis. The second answer for each question or comments in brackets is the revised version.

TW Well, the wet season is virtually upon us, bringing with it all manner of dreaded diseases. You may remember the last wet when almost 200 people were diagnosed with Ross River Fever, and 12 people died from melioidosis, or "Nightcliff gardeners' disease" as it's sometimes known. Well, with the wet season more or less here again, and fears starting to arise about wet season illness, you might be pleased to know there are simple steps you can take to keep yourself healthy. Joining me in the studio now is Dr Angela Merianos from the Communicable Diseases Centre here in Darwin.

AM Thank you for inviting me.

TW Pleasure. Melioidosis and Ross River Fever - they were the main diseases during the last wet. Are they the principal worry, the principal problems?

AM They're certainly the diseases that we'll be focusing most of our health promotion activities on this wet season, because they're both eminently preventable diseases.

TW Well, let's talk about both of them, perhaps Ross River Fever, the most common, first. How is that contracted?
AM It's a mosquito borne virus, so it entails someone being bitten by a mosquito, which then makes it pretty obvious that the way to avoid this disease is to maximise your protection against mosquito bites. And that would include using personal insect repellent, avoiding being exposed to mosquitoes in the peak biting times, which are often between dusk and dawn; when people go outside, particularly in the evenings, to remember to wear light weight, light coloured clothing that covers up most of their exposed body parts to avoid bites, to use mosquito coils when outside, and mosquito nets if necessary, making sure they've got screens on their windows. And most importantly, remembering to slap on the insect repellent.

AM Infection with Ross River virus occurs when a person is bitten by a mosquito carrying the virus. The way to prevent this disease is to protect yourself against mosquito bites. Simple measures you can take to avoid bites are applying personal insect repellent containing DEET such as "Rid" or "Tropical Strength Aerogard" when outdoors, especially between dusk and dawn when mosquitoes are most likely to bite, covering up with light coloured long sleeved shirts and trousers and burning mosquito coils when outside, using mosquito nets if necessary when sleeping, and making sure fly screens on windows and doors are well maintained. Emptying out and wiping dry the drip trays of plants and disposing of empty containers will stop mosquitoes from breeding near living areas.

TW Now, last year we had a very big wet, people that were here would remember, and it also seemed as though a large number of people were diagnosed with Ross River Fever, larger than usual. Is the incidence of the disease normally reflected in the extent of the wet? In other words, if we get a lot of rain, do we get a lot of Ross River Fever?
AM That appears to be what has happened in the Territory, and certainly there’s a lot of evidence to suggest that mosquito numbers will increase if you’ve had a particularly wet season, because it does aid the natural reproductive cycle of mosquitoes, so that you increase your numbers. Hence, there are more mosquitoes around to bite people.

AM Ross River virus is mainly a wet season disease in the NT although it can occur throughout the year under certain conditions. Mosquito eggs require moisture to hatch, so mosquito numbers increase after rain, high tides and when humidity is high. As mosquito numbers increase so does the chance of being bitten by a mosquito carrying the virus.

TW I mentioned we had over 200 people diagnosed last year, but I think there were quite a few members of the health fraternity who thought that might be only a small number of those who actually had the disease. Is that feeling prevailing in the Communicable Diseases Unit, that there were probably many more suffering from it than were officially notified?

AM That’s always a problem with the notification system which depends on a number of different sources to get reports coming in, but one of the important things to remember about something like Ross River virus is that it’s really a spectrum of disease, so sometimes, if for instance someone presents with a mild illness which mimics a flu-like illness, they may not be investigated for Ross River virus. And so the diagnosis can be missed.

AM Large studies throughout Australia have shown that most people who become infected with Ross River virus remain well. This virus causes a range of illness from a mild flu-like infection to severe and prolonged illness. People with the milder forms of Ross River virus may not be investigated with a blood test, so the diagnosis is missed. The number of officially notified cases is the number of people with an illness recognised by
their doctors to be Ross River virus disease and which was confirmed with a blood test. In other words, people with more severe disease.

TW It is a notifiable disease?

AM Yes, it is in the Territory.

TW What are the symptoms you should be looking out for with Ross River Fever?

AM The common one, is of course joint pain in a number of joints, which we call polyarthritis. It's usually associated with fevers, and probably, in about 50% of cases, a fleeting rash as well. But often the disease starts off as a transient flu-like illness, which of course can mimic any other causes of a flu-like illness. Long term effects can also include things like chronic tiredness and depression. Some people also suffer quite badly from headaches initially, and muscle aches and pains as well as the joint pains.

AM The common one is joint pain in a number of joints, which we call polyarthritis. Ross River Virus is usually associated with fevers, and in about 50% of cases, a fleeting rash as well. Some people also suffer quite badly from headaches initially, and muscle aches and pains as well as the joint pains. The disease often starts off as a flu-like illness, and then progresses to the more characteristic illness. Long term effects include tiredness and depression or feeling low.

TW So, if you exhibit any of those symptoms, it's worth while going to see your doctor.

AM Yes.

TW Are children more at risk than adults?

AM That's an interesting question. Certainly the cases that occur in children are very small, it's an unusual disease in children. But part of that may be that, in
fact, children have such mild disease, or a subclinical infection, they don't even present with clinical symptoms. Or something so mild that it goes unrecognised. That in fact it may be a problem, but we're just not seeing it. Certainly it doesn't appear to be a problem in terms of disease; the kids may be infected but they're not coming down with the symptoms the adults come down with.

AM That's an interesting question. Certainly few of the cases notified to the Communicable Diseases Centre are children. Most children don't develop symptoms or have very mild and unrecognised Ross River virus disease. The kids may be infected but as they don't come down with the symptoms the adults complain of we don't regard it as a health problem.

TW Can you tell us simply why that might be the case? Why it mightn't affect children as much as adults?

AM There are a number of diseases where the disease in childhood is much milder.

TW And this might be one of them. Alright. Well, let's go on to the other headline grabbing disease of last wet season, one that grabbed national headlines in fact. Melioidosis, or "Nightcliff gardeners' disease" as many people like to more romantically regard it. How much of a problem's that?

AM It certainly can be a problem in people in certain risk groups such as diabetics, people who abuse alcohol, people with an impaired immune system for any number of reasons. And some other reasons why people have impaired immune systems include cancers and other malignancies, and people that have to take steroid therapy for whatever reason over a long period of time. So these people are the ones that are most likely to develop the disease melioidosis, if they come in contact with the organism.
It certainly can be a problem in people in certain risk groups such as diabetics, people who abuse alcohol and other substances, people with underlying medical conditions such as lung, liver and kidney disease - all people with an impaired immune system. Some of the other reasons the immune system may be impaired are cancers, leukaemia, long term treatment with steroids, and other infections. So it is these risk groups that are most likely to develop the disease melioidosis, if they come in contact with the organism.

So people with underlying disease. And it's one that can be fatal, as we saw last wet season, with a dozen or so people dying.

That's correct.

That's definitely one that seems to, the incidence seems to increase with the amount of rain that we have. It's an organism that lives under the ground, isn't it?

What's believed to happen is that the organism remains in the deeper layers of the soil, and with heavy rains, as the water table rises, so does the organism. So it reaches the surface, and then is present in surface soil and standing surface water.

So what measures should we take to avoid contact with melioidosis?

One of the things we want people to recognise is that we're not expecting them to stop going out during the wet season, but when they are doing things that may put them at risk of exposure to either soil or standing water, they should wear appropriate clothing. So, for instance, particularly if you are in one of those risk groups, if you go out gardening you wear waterproof shoes and you wear protective gloves when you're gardening. Similarly, people that are occupationally exposed to soil and standing water should just remember simple
things like wearing protective footwear and gloves if they're doing something that could possibly expose them to small cuts on their hands or feet.

AM ... So, for instance, if you go out gardening you should always wear waterproof shoes and protective gloves. It's very common for people who are in frequent contact with soil and standing water at work to get small cuts on their hands and feet; along with the high risk groups I mentioned previously, people working outdoors should always remember their protective hand and foot wear.

TW And it seems one of the problems with the melioidosis outbreak here last wet season was that quite a section of the medical fraternity wasn't absolutely familiar with the disease, and that it's fairly difficult to diagnose. Was that the case?

AM It is an uncommon disease, luckily. The diagnosis really depends on a laboratory diagnosis in most cases. There is a blood test that we sometimes use in conjunction with a clinical picture of melioidosis.

TW So an effort has been made to familiarise the local medical fraternity with the symptoms?

AM That is actually done every year. Each new intake of residents and registrars at the Royal Darwin Hospital are brought up to date with the diseases that are prevalent [common] in the Territory.

TW OK. Any other particular health warnings for the wet season that we should take account of?

AM I think people should remember the basic, common sense precautions that they take in hot climates anyway, but certainly our preventative health efforts will go towards these two disease in this wet season.
TW I understand there is an information kit on melioidosis coming out.

AM That's correct. And on Ross River virus.

TW And the other thing that so many of us do at this time of the year is head off on holidays, particularly over to South East Asia, and it's worth reminding people about the importance of checking what sort of inoculations, if any, they need too.

AM We're really trying to promote adult tetanus-diphtheria vaccine, which we call ADT, that people should remember to have every 10 years. And that basically updates their vaccination status against diphtheria and tetanus. For people travelling to some of the more exotic countries, a polio booster may also be an appropriate thing, and that's just a syrup that you take orally [by mouth]. In terms of antimalarials [medication against malaria], it's very important that each person consult their doctor about the specific areas they're travelling to, because antimalarial requirements do change quite dramatically between different regions. [Antimalarial tablets do not guarantee protection against malaria, so travellers should always see a doctor if they become unwell on their return from a malarious country. As malaria is also spread by mosquitoes, all the ways to avoid mosquito bites that we discussed earlier, insect repellent, appropriate clothing, mosquito coils, sleeping nets and fly screens, also apply to prevention of malaria].

TW All right. Thanks for all that information.

AM You're welcome.
Comments:

The key points that I wanted to bring out in this interview were:

1. Both Ross River virus disease and melioidosis are preventable, and preventative measures won't disrupt daily life.

2. To be infected with RRV you must be bitten by mosquitoes.

3. Preventative measures against infections with Ross River virus are the use of an effective insect repellent, appropriate clothing when outdoors, mosquito coils, sleeping nets and fly screens. These measures also apply to prevention of malaria.

4. Melioidosis is usually a disease of immunocompromised people (diabetics, alcoholics, people with malignancies, people with chronic diseases and people on immunosuppressive treatment).

5. *Pseudomonas pseudomallei* is present in the soil and muddy water.

6. Waterproof shoes and gloves should be worn when exposed to soil and standing water.

7. Occupational exposure to soil and muddy water may put healthy people at risk of melioidosis.

It is difficult to evaluate the effectiveness of media releases and interviews for either of these diseases on the short term as the impact of environmental conditions on incidence is likely to mask the effect of behavioural changes due to preventative education. Both organisms cause subclinical infections which can only be identified by serological surveys, and the incubation or latency period in melioidosis ranges from weeks to years. In spite of the shortcomings of interview, the feedback I received at the time from the Community Relations Branch and the ABC staff was very positive.
1.5.3 Scrub typhus in the Northern Territory

9 July, 1991

Dear colleague,

RE: RECENT CASES OF SCRUB TYPHUS IN DARWIN AND KATHERINE

Since August 1990, 4 cases of scrub typhus (Tsutsugamushi Disease; mite-borne typhus) have been confirmed in visitors to Litchfield Park. Scrub typhus is a new disease to the NT, but its importance is likely to increase as tourism expands in nature reserves such as Litchfield. It is endemic in Queensland, central, eastern and SE Asia and northern Japan. It will be important to consider the diagnosis of scrub typhus among residents and tourists who have been to Litchfield Park.

Scrub typhus is a zoonosis caused by *Rickettsia tsutsugamushi*, and is transmitted by trombiculid mites (Leptotrombidium deliensis) which infest some species of native rodents and marsupials.

Human infection follows a mite larva (chigger) bite. There is no direct person-to-person transmission. The incubation period ranges from 6-21 days, but averages 10-12 days.

Scrub typhus is characterised by an acute onset of fever, chills, headache and a non-productive cough, and is followed within a week by generalised lymphadenopathy and a maculopapular rash in over half of the cases. In approximately 70% of cases an eschar develops at the site of the bite, which later vesiculates, ruptures and becomes covered with a black scab. Regional lymphadenitis is usually present.

If left untreated complications include encephalitis, pneumonitis, and interstitial myocarditis. The case fatality rate varies from 5-60% depending on area, strain of rickettsia, previous exposure to disease, and pre-existing medical conditions. Clinical recovery is prompt with specific chemotherapy; defervescence usually begins within 36 hours. The antibiotic of choice is doxycycline, and a loading dose is required.
Diagnosis is based on the serological detection of specific rickettsial antigens, usually on paired sera. Treatment should not be delayed while awaiting laboratory confirmation. As multiple serotypes exist that display only limited cross-immunity, re-infection is possible.

Visitors to areas potentially endemic for scrub typhus should use DEET (N,N-diethyl-m-toluamide) containing personal insect repellents. Permethrin impregnated clothing, bedding etc may be indicated when exposure is expected to be prolonged.

If you suspect a case of scrub typhus or require more information, please contact Dr Bart Currie, RDH, or myself at CDC on 228 560.

Yours sincerely,

Dr Angela Merianos
Epidemiology Registrar
COMMUNICABLE DISEASES CENTRE
for REGIONAL DIRECTOR
SUBJECT: A CASE OF DIPHTHERIA IN ALICE SPRINGS

AN 11 YEAR OLD CHILD LIVING IN ALICE SPRINGS WAS DIAGNOSED WITH DIPHTHERIA YESTERDAY. THE ORGANISM WAS GROWN FROM A NOSE SWAB COLLECTED WHEN THE CHILD PRESENTED TO THE ALICE SPRINGS HOSPITAL WITH A PERSISTENT NASAL DISCHARGE. SHE IS OTHERWISE WELL.

THE COMMUNICABLE DISEASE CONTROL CENTRE, DEPARTMENT OF HEALTH AND COMMUNITY SERVICES, IN ALICE SPRINGS IS UNDERTAKING CONTACT TRACING AMONG THE CHILD'S HOUSEHOLD AND COMMUNITY CONTACTS, INCLUDING HER CLASSROOM CONTACTS. AS HER SCHOOL ATTENDANCE HAS BEEN POOR IN THE LAST WEEK, THE RISK OF DIPHTHERIA IN HER CLASSMATES IS VERY LOW.

PARENTS IN ALICE SPRINGS ARE ADVISED TO CHECK THEIR CHILDREN'S IMMUNISATION STATUS AGAINST DIPHTHERIA, AND UPDATE THEIR VACCINATIONS IF INCOMPLETE. THE RELEVANT VACCINATIONS ARE THE "TRIPLE ANTIGEN" (DTP - DIPHTHERIA, TETANUS AND PERTUSSIS) FOR CHILDREN AGED 5 YEARS AND UNDER, AND CDT (DIPHTHERIA AND TETANUS) FOR CHILDREN AGED 6 - 8 YEARS. ADULTS SHOULD ALSO BE VACCINATED WITH ADT (ADULT DIPHTHERIA AND TETANUS VACCINE) AGAINST DIPHTHERIA AND TETANUS EVERY 10 YEARS.

CHILDHOOD IMMUNISATIONS ARE AVAILABLE AT INFANT HEALTH CLINICS. IMMUNISATION OF OLDER CHILDREN AND ADULTS SHOULD BE ARRANGED THROUGH COMMUNITY HEALTH CENTRES.

ALL ENQUIRIES SHOULD BE DIRECTED TO DR ROSIE BRENNAK AT THE COMMUNICABLE DISEASES CENTRE ON 50 2426.
Comments:

The aims of this press release were to:

1. assure parents of children attending the same school as the index case in Alice Springs that their children were not at risk of diphtheria;

2. remind the community of the importance of immunisation for all age groups as diphtheria is an endemic disease in central Australia.

I doubt that I successfully communicated the first message to the public as my style of writing was too scientific and depersonalised. I would revise the first two paragraphs accordingly:

"An 11 year old child living in Alice Springs was diagnosed with diphtheria yesterday. She has a mild form of the disease and complained only of a persistently runny nose. She is otherwise well."

"Diphtheria can be prevented by immunisation. The Communicable Disease Control Centre, Department of Health and Community Services, in Alice Springs is contacting parents of the child's classmates to check immunisation records and to offer vaccination to children who are not fully immunised against diphtheria. As the child's school attendance has been poor in the last week, there is little risk of infection with diphtheria among her classmates."
PERTUSSIS (WHOOPING COUGH) VACCINATION

Is your child up to date with pertussis vaccinations?

Two infants have recently been diagnosed with whooping cough in Cairns. The father of one of the children may have been infected before his child became ill. Travel to Cairns over the school holidays may mean that some Territorians have come into contact with this disease.

Pertussis is a bacterial infection of the respiratory tract which can be very serious, especially in infants. Pertussis can also affect older children and adults who then pass the infection to children under 5 years of age in the family. It starts as a "flu-like" illness with runny nose, fever and cough. Severe coughing "fits" which end with a characteristic high pitched whoop and often vomiting, start within 1 - 2 weeks of infection. The infection can last for several months.

Pneumonia is the most common cause of death from whooping cough. Coughing fits can cause brain damage in a small number of children. Infants may also fail to thrive because of repeated vomiting.

Pertussis can be prevented by a vaccination with DPT (diphtheria, pertussis, tetanus vaccine) given at 2, 4, 6 and 18 months of age in the NT.

If your child is not fully immunised for age, contact your Infant Health Clinic or Community Health Centre. For further information contact the Communicable Diseases Centre in your region.
Questionnaire Design

"Scientists never collect data, they create data". Babbie p 119.

Introduction

A well researched, constructed and administered questionnaire is a powerful research tool, especially in social research.

The focus of questionnaires is information that a group of individuals possesses.

Questionnaires may be administered in a number of ways, each with advantages and disadvantages.

eg self-administered questionnaires (group, mailed, computer-assisted)
personal interview (individual or group)
telephone interview.

Exercise: Name a number of advantages and disadvantages of questionnaires.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheap to produce/administer</td>
<td>Question validity</td>
</tr>
<tr>
<td>Quick distribution in self-administered form.</td>
<td>Biases eg measurement, recall.</td>
</tr>
<tr>
<td>Can elicit information not available by other means.</td>
<td>Crude measure.</td>
</tr>
<tr>
<td>Can have high external validity.</td>
<td>Researcher has little control over self-administered questionnaires.</td>
</tr>
</tbody>
</table>

Basic Principles

The questionnaire is based on our conceptual framework. As many social research models use abstract indices with no ultimate definition eg social class, our conceptual framework and the way we ask questions will determine whether we make useful and unbiased measurements.

Goals of questionnaire design

To obtain information relevant to the purpose of the study.
To collect this information with maximum reliability and validity.
To make the process of coding and analysis as easy as possible.
To avoid wasting respondents and interviewers time.

**Methods**

- Define the aims and objectives of your research project. Be clear and precise. These define your analysis.

Is a survey the best method? Has similar research been carried out before? Is an instrument available for use/adaptation? What local expertise is available for consultation?

- Clarify your frame of reference. Develop clear definitions of the variables to be used in your questionnaire. Identify types and values. Decide in detail what information is required.

What are the attributes contained within a concept? What are the conceptual endpoints of the attributes/dimensions that describe the concept? Are your definitions useful measures of the concept?

**Exercise:** Define socioeconomic status.

*What activities can we use to determine an individual’s religiosity?*

eg Charles Glock’s definition of religiosity - ritual involvement, ideological involvement, intellectual involvement, experiential involvement, consequential involvement. Also consider the other end of the spectrum (anti-religiosity).

- Prior dummy analysis. Think about expected results eg expected shapes of frequency distributions, relationships in scatter plots and two-way tables.

- Then design the questions (and pre-coded answers whenever possible). Question format will differ depending on whether you are on a fishing expedition or you are expanding on existing knowledge.

- Format the questionnaire.
MEASUREMENT AND ANALYSIS

The survey research format generates many types of useful data.

**Facts** Data that both the respondent and you generally accept as true eg demographic characteristics.

**Beliefs** eg Does God exist?

**Attitudes** eg prejudice.

**Levels of measurement**

- **Nominal** Distinguishes categories in a given variable eg F / M. The categories are mutually exclusive and bear no other relationship to one another.

- **Ordinal** Qualitative rank order of data along a scale. eg 1 upper class, 2 middle class, 3 lower class. There are no absolute values.

- **Interval** The distance between points have a true meaning eg age, weight, height.

You must determine which type of analysis you will conduct after data collection, and format questions in a way that you use the right kind of measurement.

**Measurement quality**

- **Precision** Not always desirable nor necessary. If the degree of precision required is initially unknown, you can always collapse categories later.

- **Accuracy** Is the information correct.

- **Reliability** Repeated measurements yielding the same result. In order to maximise reliability remember:
  - competency to answer
  - relevance
  - clarity.

- **Validity** Refers to the extent that a measure adequately reflects the real meaning of the concept under consideration.
  eg Does passing a Driver’s Licence written test measure ability to drive?
QUESTION CONSTRUCTION

Questions and statements
The issue is summarised, and the respondents agree or disagree eg Yes/No, Likert scale - scaling of levels of agreement or disagreement.

Open- and closed-ended questions
Open ended questions allow the respondent to develop their own answers.

Advantages
- Useful for eliciting new information.
- Good for complex issues.
- Diversification of questionnaire.
- Format is more creative.
- Shows that you care about what the respondent really thinks.
- Safety valve.

Disadvantages
- Irrelevant information included.
- Greater detail in the responses.
- Answers are not standardised so analysis is more difficult.
- Coding difficult/subjective.
- Requires literacy if not an interview.
- Time consuming ?higher non-response rate.

In closed-ended questions, respondents are asked to select their answer from the list provided.

Advantages
- Very popular and easy to use.
- Greater uniformity of answers.
- Easily processed.
- Coded directly on questionnaire.
- Answers provide clues about intent.
- Can help elicit sensitive information.

Disadvantages
- Response categories must be exhaustive.
- "Other" category required.
- "Appropriate" answer bias.
- Random answering.
- Answers must be mutually exclusive.
- Loss of information.
- Questionnaire looks longer.

Most outbreak investigation questionnaires will attempt to elicit facts in the form of closed-ended questions.

Nested, contingency or hierarchical questions
If a series of questions apply only to a subset of the study population eg pregnancy outcomes, they can be made contingent on an earlier response.

eg If yes, then...
Flow charts etc.
Matrix questions
Several questions that have the same set of categories can be formatted as a group. An inherent danger is a "response set" eg all "yes" answers.

Indexes and scales

HELPFUL HINTS AND MISTAKES TO AVOID

. A clear and concise summary of the objectives of the survey should accompany the questionnaire.

. Always include a unique personal identifier eg ID number. Unique identifiers are very useful in relating files.

. Know your study population! Ensure respondents' competency to answer. Don't include questions that the majority of the study population can't answer.

. Ask relevant questions. Avoid topics which your study population neither knows about/cares about/makes up answers on the spur of the moment about eg in one study, 9% of the respondents stated that they knew about a fictitious electoral candidate, 4.5% stated that they had seen him on TV.

. Don't assume that the respondent will know what you want. Avoid ambiguous questions/instructions. Give instructions each time you change the question format, or make it clear that the instructions apply to the whole questionnaire.

. Divide complex issues into a series of short questions.

. Avoid jargon unless dealing with a specific interest group or when jargon is appropriate eg group idioms.

. Unless otherwise indicated, assume an age 12 reading age (most newspapers are written at this reading level).

. Avoid double-barrelled questions. eg Do you think that the defence budget should be cut and the money spent on low budget housing?

. Avoid negative statements, especially double negatives. People read over negatives, such as "not prohibited" eg Australia should not discontinue uranium mining.
Avoid biased items and terms ie leading questions. Remember, data is created and you need to be continually aware of the effect of question wording on the results that you will obtain.

Bias may be due to:

1. identification of an attitude or position with a prestigious/notorious person/official agency
   eg Do you agree or disagree with the PM's/NHMRC's/Supreme Court's etc stand on...positive bias
   eg Do you agree or disagree with PM's/Iraq's/Fred Nile's etc stand on... negative bias;

2. unintended bias to positive/negative associations eg terms such as atheist, liberal, conservative, communist, feminist, gay;
   eg Government assistance to "poor people" is more acceptable to the general public than assistance to "people on welfare";

3. question ordering.

FORMATTING

General rules

- Spread out and uncluttered.
- Avoid abbreviations.
- Clear, unambiguous instructions. For an interview questionnaire, the interviewer should have a script to follow verbatim.
- Keep the questionnaire as short as possible.
- Boxes are best.
- Be creative! Make the questionnaire interesting and attractive.

Question ordering

- The presence of one question may affect subsequent answers. Be aware of the problem and account for it eg pilot alternative formats of the questionnaire to see whether ordering makes a difference.
  eg ordering may introduce positive and negative biases;
  the respondent will attempt to be consistent;
  the respondent may refer to a previous concept in an open-ended question.
In self-administered questionnaires, it is usually best to begin with the most interesting, non-threatening questions and to end with the demographics. The reverse is true for personal interviews.

OUTBREAK INVESTIGATIONS

During an outbreak investigation, you won't have the time to carefully plan near perfect questionnaires! A "quick and dirty" working questionnaire can be developed very quickly as most of the questions will focus on the facts required for a line listing, not on attitudes/beliefs.

You should still make the time to discuss the outbreak with local experts, and check whether a template questionnaire suitable for adaptation exists.

Always elicit a contact phone number/address etc for recall purposes.

NB. ALWAYS PILOT YOUR QUESTIONNAIRE!

REFERENCES


Comment:

My aim in preparing this tutorial was to summarise the important elements of questionnaire design in a practical way, by including lessons learnt through my own experience with surveys. My approach was influenced by the information I had expected and did not receive when my intake of MAE students covered this topic in March 1991. It was accompanied by a short exercise on questionnaire preparation in the field when faced with an outbreak.
1.5.7 Drafts of two articles prepared for the NT Communicable Diseases Bulletin January 1993.

Leptospirosis in the Northern Territory

The Communicable Diseases Centre in Darwin has been notified of a case of acute renal failure secondary to infection with *Leptospira interrogans* var *australis*, a serotype of the icteric group of leptospires which can cause severe disease. The patient was a 56 year old man admitted to the Royal Adelaide Hospital on 3 December 1992, 14 days after lacerating his foot while swimming in the Katherine Gorge. He developed interstitial nephritis after a prodrome of fever, flu-like symptoms and mild confusion. He made an uneventful recovery and was discharged from care.

*L. interrogans* var *australis* has not been identified in South Australia and the patient denied travel to other areas where this serotype is endemic, such as northern Queensland. Circumstantial evidence points to the Katherine Gorge as the site of infection. Transmission is usually by percutaneous or conjunctival inoculation or ingestion of the leptospires which are present in the urine of infected animals. Important animal reservoirs include domestic and native rodents, bandicoots, lagomorphs (rabbits and hares), cattle and feral pigs. Leptospirosis is a disease usually associated with occupational exposure to animal urine, but can also be a recreational hazard in endemic areas. The most important non-icteric NT serovars are *hardjo* and *pomona*. Approximately 8 cases of mainly *Leptospira interrogans* var *hardjo* have been reported in the NT over the last 10 years; two cases were reported in 1992.

The milder, non-icteric form of leptospirosis can be a subclinical or self-limiting illness and can be missed if not considered in the differential diagnosis of pyrexia of unknown origin. Other common symptoms and signs include headache, chills, severe myalgia (calves and thighs), conjunctival suffusion and rash. More severe manifestations are meningitis, haemolytic anaemia, haemorrhage into the skin and...
mucous membranes, hepatorenal failure, confusion and pulmonary involvement which may manifest as haemoptysis. The incubation period is 7-12 days but can range from 2-20 days. Severe leptospirosis (Weil’s disease) with hepatorenal failure occurs in 5-10% of cases and has a case fatality rate of 5-20%.

Leptospirosis is a notifiable disease in the Northern Territory. CDC is collaborating with the Conservation Commission of the Northern Territory, CSIRO and the Department of Primary Industries and Fisheries to develop some surveillance and prevention strategies for this disease. There is no information on the size of the animal reservoir in the NT; more cases may occur as the number of visitors to national parks increase. "Hot spots" of disease have been identified in north Queensland and it is possible that we also have as yet unidentified high risk areas.

**Comment:**

The accompanying report on leptospirosis in Chapter 2 is included to demonstrate the value of networking with local experts in order to obtain detailed and up-to-date summaries of local conditions, problems and resources.

**The interpretation of dengue virus serology**

The four dengue virus serotypes (DEN-1 to DEN-4) belong to the flavivirus group which includes the Murray Valley encephalitis virus, kunjin and Yellow Fever viruses. The principal vector is the mosquito *Aedes aegypti*, but *Ae albopictus* and *Ae polynesiensis* are important vectors in South East Asia and the Western Pacific respectively. *Ae aegypti* is an urban mosquito which breeds in containers such as the drip trays of plants; it is responsible for the recent large outbreak of dengue fever in northern Queensland (over 4000 cases). *Ae aegypti* was last detected in the Northern Territory in the mid 1950s, and the last locally acquired case of dengue fever occurred
in about 1956. Since then diligent entomological surveillance by the Medical Entomology Branch, NT Department of Health and Community Services, and the NT Quarantine and Inspection Service, Department of Primary Industry and Fisheries, has prevented re-introduction of this vector.

Because we are confident that dengue fever does not occur in the NT, we urge doctors to include a detailed history of travel and exposure to mosquitoes on the laboratory request form when ordering dengue serology. Serological diagnosis of dengue infection depends on four tests: haemagglutination inhibition (HI); complement fixation (CF); the plaque reduction neutralisation test (PRNT); and IgM capture enzyme-linked immunosorbent assay (MAC-ELISA). Some laboratories also use an indirect fluorescent antibody test (IFA) to detect IgM. In primary infections HI antibody is detected as early as 4-5 days after the onset of illness. It is sensitive in detecting low levels of antibody but is very nonspecific and cross-reacts with other flaviviruses, so it is used as a flavivirus group screening test. Previous immunisation against Yellow Fever also modifies the HI antibody response to other flaviviruses.

For example, following primary infection with Murray Valley encephalitis virus which may have occurred many years earlier, HI antibodies to MVE will rise again after Yellow Fever vaccination or infection with another flavivirus. This boosting of antibody titres to other flaviviruses is called the anamnestic response and can result in high titres for all flaviviruses tested. The closer two viruses are antigenically, the greater the similarity in antibody titres produced by cross-reacting antibodies. This can result in a confusing serological picture which is open to misinterpretation unless a clinical history is provided.

IFA-IgM slide microscopy depends on the skill of the technician reading the test and is also subject to false positive results. Neutralisation Inhibition is the "gold standard" but is labour intensive and is usually reserved for research purposes. IgM class capture ELISAs are regarded as relatively specific in distinguishing between flaviviruses and approach the sensitivity of HI.
CDC in Darwin has recently investigated a number of cases of "laboratory confirmed" dengue infections in people who denied travel outside the NT within the incubation period for dengue fever (1-12 days; average 7 days). In all cases the laboratory involved retested their sera using more specific methods and confirmed that the original dengue result was incorrect. A confirmed case of locally acquired dengue infection has important implications for vector control as it implies that either *Ae aegypti* or *Ae albopictus* has been introduced into the NT. *Ae albopictus* was detected in car tyres imported from South East Asia in the past and similar concerns exist for the reintroduction of *Ae aegypti* from northern Queensland.

We recommend the following measures to assist the laboratories in their interpretation of flavivirus serology, especially dengue:

1. provide details of travel outside the Northern Territory, history of mosquito bites and date(s) of Yellow Fever vaccination when requesting flavivirus serology;

2. if the patient denies travel outside the NT, record their country of origin and history of past residence or travel in areas where dengue is endemic and exclude previous known infection with other flaviviruses.

Cross-reactions can also occur between the alphaviruses Ross River virus, Barmah Forest virus and sindbis, but are less common than with the flaviviruses.
1.5.8 An unusual outbreak in Nhulunbuy, East Arnhem


Aims:
1. to present the process of outbreak investigation to non-epidemiologists in an interactive way, based on the format of "Hypotheticals";
2. to raise the profile of CDC with RDH staff and reinforce the importance of disease notification to the new RDH residents and registrars.

Speakers:
Mahomed Patel and I - epidemiology of the outbreak and the role of CDC;
Peter Whelan - entomology and animal studies;
Bart Currie - clinical aspects.

Timing:
35 - 40 mins with 5-10 minutes of discussion at the end of the presentation.

OUTLINE
Overhead 1 - Background

- Nhulunbuy is a mining community of approximately 3600 people on the Gove Peninsula. Approximately 1/3 of the population is aged 0 - 14 years.
- Most town residents are non-Aboriginal.
- The aluminum mining company, Nabalco, is the biggest employer.
- The closest Aboriginal community, Yirrkala, has a population of approximately 250. Its distance from Nhulunbuy is about 12 km. Most other Aboriginal people live in outstations.
Overhead 2 - CDC alerted to the outbreak

7 Feb 1992 Dr Paul Spillane at Gove District Hospital notified CDC of 6-7 cases of acute onset of lethargy, fatigue, rash and fever.

A phone call on the same day to the single private practice in Nhulunbuy confirmed another 5-6 patients.

All cases were non-Aboriginal.

All but one were adults.

Most cases lived in the north part of town.

Comment: Bart Currie was conveniently in Nhulunbuy on a routine clinic visit and we asked him to examine the patients seen in A&E.

Bart to present initial clinical findings and to give the differential diagnosis.

List of investigations.

Question 1 Is this an outbreak?

Question 2 What would you do next?

CDC faxed a preliminary questionnaire to the Communicable Disease Officers (CDOs) the same afternoon and to the private practice in Nhulunbuy.

Question 3 What questions would you include in the questionnaire?
Overhead 3 - The initial questionnaire

- Demographics.
- Date of illness onset.
- Clinical questions appropriate to the differential diagnosis.
- History of travel in East Arnhem and outside Nhulunbuy for the month before onset of symptoms.
- History of mosquito exposure.
- The names of symptomatic contacts and their relationship to the index case eg household contacts, contact in the work place.

The field investigation

Comment:

12 Feb Formal epidemiological and entomological investigations started.

The initial aims of the CDC investigation were to confirm the epidemic, develop a case definition, and commence active case finding and specimen collection to determine the aetiology.

Question 4 Suggest a working case definition.

Overhead 4 - Components of a case definition and our case definition

The main components of any epidemiological case definition:
- when
- where
- who
- what - main symptoms and signs.
We used a clinical case definition of:

- rash ± acute joint pain, swelling or tenderness ± unexplained fever;
- Time - from 1 January 1992 ongoing. (We later changed this to 1 December 1991);
- Place - Nhulunbuy and surrounds;
- Person - residents of Nhulunbuy and surrounds since at least 1 January 1991.

Comment:
Discuss reasons behind a sensitive case definition.

Question 5 How do we find out about other cases?

Overhead 5 - Surveillance

- Active versus passive case finding.
- Retrospective audits and prospective case finding.

Sources of information:

1 Prospective

- hospital doctors
- liaison with the general practice
- A & E - new cases
- clinic staff of the community controlled health service
- school nurses (absenteeism)
- Nabalco occupational health officers (absenteeism)
- by word of mouth "dob in a mate"
- the media
2 Retrospective
- A & E log book of reasons for presentation / admission list
- hospital pathology services log book
- private pathology services
- existing surveillance data if available

Overhead 6 - The epidemic curve of the entire outbreak

Question 6 How would you interpret this epidemic curve?

Discuss expected differences in the shape of an epidemic curve showing person to person transmission.

- Consistent with a common source or simultaneous exposure.
- Data collected in the first three days of the field investigation (12 - 14 February) strongly supported an arbovirus outbreak.

Our contact tracing showed no evidence of person to person spread:

- there was no significant household clustering;
- very few symptomatic children, unusual in an outbreak of adenovirus or enterovirus infections;
- anecdotal evidence against droplet spread (symptomatic school teacher and no transmission in her class).

Comment:

21 Feb 5 of 18 sera positive for BF IFA-IgM. Both acute and convalescent cases were tested.
Other sera were RRV IFA-IgM positive.
Attempted viral isolation from nasopharyngeal swabs, stool and urine and serum cultures was unsuccessful.

**Entomological studies**

*Comment:*

Meanwhile the entomology team had trapped approximately 2000 mosquitoes and were coming up with some interesting findings of their own.

Peter to present background on BF, entomological studies, epidemic curves of mosquitoes (superimposed on human disease epidemic curve) and control measures.

**Overhead 7 - Age-specific attack rates.**

**Question 7** We have confirmed a Barmah Forest virus outbreak. *What other epidemiological investigations might you consider now and why?*

**Overhead 8 - Secondary objectives/studies**

Our secondary objectives were:

1. broaden our knowledge of this virus including the spectrum of disease severity;
2. to estimate the size of the problem;
3. determine the inapparent infection rate.

*Methods:*

- a prospective study of seropositive cases (this gives us information about the spectrum of disease);
- a representative serosurvey (provides background rates, detects mild cases who failed to present, permits estimation of symptomatic to asymptomatic attack rates;
- animal trapping to identify reservoirs.
22-26 Feb We collected blood from 247 mainly adult volunteers who were either asymptomatic, or had minor symptoms which did not fulfil our case definition.

22-27 Apr We collected second serum samples from 178 people (72%).

- Participants completed clinical questionnaires on both occasions.
- Demographic data, including duration of residence in Nhulunbuy, were included in the first questionnaire.

Overhead 10 - Summary of the key features of BF disease.

Overhead 11 - Results of the serosurveys and symptomatic: asymptomatic infection rates.
Overhead 12 - Summary of main findings

- BF has outbreak potential and may have been the cause of some of the seronegative polyarthritis cases of the 1990/91 wet season outbreak.

- The age specific attack rates are similar to those seen with RRV.

- The disease is similar to RRV but appears to be of shorter duration in most cases.

- BF appears to be a relatively new virus in Nhulunbuy.

- The asymptomatic to symptomatic attack rate is approximately 2:1.

- BF and RRV share an ecological niche.

- There may have been a third unidentified arbovirus causing a clinically indistinguishable illness in Nhulunbuy.

- BF should always be considered in the differential diagnosis of arbovirus disease in the NT.
Overhead 13 - Preventative measures including logistics

The output loop - public health action

- Feedback and preventative health messages were given to doctors and to the community throughout the outbreak.
- Newspaper articles and radio interviews in Nhulunbuy and Darwin;
- All serosurvey volunteers received arbovirus avoidance messages with their results;
- The results were presented at a public meeting in August.
- We have regular updates on mosquito-borne disease activity in our NT Communicable Diseases Bulletin.

Co-presenters to add last thoughts.

Questions.
Chapter 2

2 SURVEILLANCE 55-91

2.1 Background 55-56

2.2 Notifiable disease surveillance in the NT 56-61

2.3 Areas requiring review in the NT Notifiable Diseases surveillance system (discussion paper) 62-68

2.4 Surveillance of melioidosis 69-78

2.5 A telephone investigation of leptospirosis 79-85

2.6 Post-vaccination immunity to Neisseria meningitidis in central Australia 86-91

Copies of the NT Communicable Diseases Bulletin
2.1 Background

Most of my involvement in communicable diseases surveillance during the last two years has been in setting up active surveillance during outbreaks, familiarizing myself with the existing system and infrastructure, forming my own networks, following up notifications of disease, communicating with medical officers, drafting research proposals for seroepidemiological investigations and as co-editor of the Northern Territory Communicable Diseases Bulletin. I have included three examples of specific disease surveillance in this section: melioidosis; leptospirosis and meningococcal meningitis. I have also drafted a discussion paper for the review of the existing notification system. As co-editor of our Bulletin I was responsible for commissioning people throughout the NT to write specific articles, writing many of the regular features, editing submitted articles, proof reading drafts and supervising format and setting deadlines. I also negotiated with the Publications Branch of DH&CS to print copies and set up the distribution list. Examples of the Bulletin are included at the end of this section.

At the beginning of my placement in Darwin, Mahomed Patel and I took a decision to develop a feedback loop in the surveillance system as a priority. In the past there was no regular contact between CDC and the medical practitioners, and Darwin CDC did not provide any summary statistics for the regional units, except for the summary of Disease Control activities in the Annual Report. Doctors were alerted to outbreaks by urgent letters and by the media, and the Communicable Disease Officers by telephone and facsimile. Doctors would also receive protocols for disease control such as the NT Measles Control Protocol. These documents tended to be long and detailed and of
questionable relevance to general practitioners. It was apparent from a number of outbreaks of diseases which required urgent doctor notification that these protocols were not being read nor used as references. In the first copy of the Bulletin in November 1991, we described the aims of the publication - "... to provide feedback from the Communicable Diseases Centre to all participants in the NT communicable diseases surveillance system ... in recognition of the invaluable contribution made by participants, and to enhance control efforts for the communicable diseases in the NT." Our decision was consistent with the definition of surveillance adopted by the 21st World Health Assembly in 1968 which described surveillance as the "systematic collection and use of epidemiological information for the planning, implementation, and assessment of disease control."  

2.2 Notifiable disease surveillance in the NT

At present, each health district has its own system of collating and reporting on surveillance data. Most districts send handwritten or computer-generated hard copies to Darwin in various formats for entry onto the NT-wide Epi Info notification record file. Although the Alice Springs CDC has been computerised for a number of years and has attempted to provide Darwin CDC with discs rather than written reports, differences in the data collected between the two regions has meant that re-entering the data is more expedient than downloading the relevant variables and merging the two files. Most of the other districts are in the process of computerising their notification data. The districts are usually punctual in providing Darwin CDC with fortnightly statistics for transmission to the Communicable Diseases Branch, Commonwealth Department of Health, Housing and Community Services.

The notification system in the Northern Territory is based on passive surveillance of communicable diseases through doctor and laboratory notifications. Doctors and pathology services have been instructed to notify diseases with outbreak potential immediately by telephone or facsimile. Diseases requiring urgent notification are marked on the notifiable diseases list which is periodically sent out to all doctors and is
included in the notification booklet. However, CDC still relies almost exclusively on the informal network between health services for outbreak alerts. In January 1993, I conducted an informal telephone survey of a convenience sample of 34 of the 57 private surgeries in all health districts and found that only eight surgeries had a current Notifiable Diseases list or notification booklet. An additional five surgeries had old lists which did not include measles (notifiable in the NT since 1990). The doctors rely on the pathology services to indicate notifiable diseases on the hard copies of results so they fail to notify diseases requiring notification on clinical suspicion. In Darwin region only 24.5% (359/1464) of notifications in 1992 were doctor notifications. Distribution of the new notification forms and literature, and education of medical practitioners in the use of the notification system is a recognised priority in CDC (refer to “Proposal for areas of review of the current NT Diseases Surveillance System.”)

In September 1991, I conducted a small survey among the CDOs on their perceptions of the efficiency of the surveillance system and their sources of notification data (Attachment A), and presented the main findings at our annual meeting. The response by all CDOs for the questions “Do doctor notifications generally add any more information to the laboratory reports (except onset date)?” was that they contributed nothing at all or were only useful for some diseases. In most regions the CDOs were alerted to disease outbreaks by urgent laboratory notifications, by routine surveillance data or via informal networking (“the grapevine”). All regions gave examples of missed outbreaks which could have been averted by earlier notification and systematic analysis of notification data. None of the regional Communicable Diseases Centres systematically analysed their surveillance data although several CDOs stated that one of the purposes of surveillance was program planning and evaluation. Summary statistics were produced in some regions upon request for administrative purposes only.
Most of the active surveillance that occurs in the NT is stimulated by the occurrence of outbreaks or alerts to potential outbreaks. There are a small number of state-wide projects in which active surveillance is ongoing. CDC in collaboration with the Medical Entomology Branch carries out continual active surveillance for mosquito-borne diseases in the NT (discussed in Chapters 1 and 3). The Tuberculosis Control Program maintains active surveillance by Mantoux testing high risk groups such as contacts of known cases, health care professionals, school aged children, refugees and immigrants from hyperendemic areas, gaol inmates and staff, residents and staff of nursing homes and clients of alcohol rehabilitation units.

The Leprosy Control Program provides regular follow-up examinations of leprosy patients discharged from treatment. The Katherine region CDC has made a commitment to conduct community-wide leprosy surveys after three indeterminate cases were diagnosed.

The Communicable Diseases Officers in the East Arnhem region have been computerising the immunisation records of all children aged 0-5 years by validating records in the field. Until recently serosurveys for syphilis were conducted regularly in this health district and contributed to the fluctuations seen in the annual incidence rates for syphilis over the last decade.
SURVEILLANCE SYSTEM QUESTIONNAIRE - CDOs MEETING SEPT 1991

Region

(1) How many hrs/wk does your unit spend on the surveillance data ________
hrs

(2) Roughly what percentage of your time is this? ____ %

(3) What are your main sources of surveillance data?

(4) What does your region do with the data (apart from sending it to Darwin)?

(5) How efficient do you think your current system is for identifying changes in
disease activity? (circle answer)

  (1) inefficient
  (2) adequate
  (3) very efficient

If you've circled option (1), please give reasons below

(6) Do you think the system is easy to use? Yes / No

If no, please give reasons

(7) How do you find out about outbreaks? (circle most important source only)

  (1) routine surveillance data
  (2) urgent doctor notification(s) eg phone call
  (3) urgent lab notification(s)
  (4) the "grape vine"
  (5) the public
  (6) the media
  (7) other

If you've circled options (4), (6) or (7), please elaborate
Attachment A

(8) Do doctor notifications generally add any more information to the laboratory reports (except onset date)?

(1) not at all
(2) only for some diseases
(3) usually receive a doctor's notification for each lab report

If you've circled option (2), list relevant diseases

(9) How is information fed back to participating doctors/health staff? (circle one answer only)

(1) no feedback except during an outbreak
(2) informal discussion with individual doctors/health staff
(3) written update circulated
(4) other __________________________

(10) What sort of follow-up does your CDU do for the following diseases?

Hep A __________________________
Hep B __________________________
RRV __________________________
salmonella ______________________
mumps __________________________
morbilliform rash __________________
pertussis _________________________

(11) How many outbreaks have you been aware of in your region in the last 12 months? _______ (approx)

(12) Were any detected through the surveillance system early enough to prevent cases? Y / N

If yes, list the relevant outbreaks and state how quickly they were recognised.

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
Attachment A

If no, where do you think the system falls down?

________________________________________________________

(13) Does your region produce reports of summary statistics?  Yes / No
If yes, how frequently?  ____________________________
To whom do you circulate your reports?

________________________________________________________

(14) At present you receive no feedback from Darwin.
What sort of feedback would be helpful?

________________________________________________________

(15) How often would you like feedback?

(1) every month
(2) every 3 months
(3) every 6 months

Thank you for your assistance!
2.3 Discussion paper on the areas requiring review in the current NT Notifiable Diseases Surveillance system

I was asked to draft and present a discussion paper for CDC staff towards reviewing the existing surveillance system. Following is a summary of the key points.

Presented at a meeting on 8 September 1992 to relevant CDC staff.

Present: M Patel, V Krause (TB), J Wright (TB), F Bowden (AIDS/STD), K Sheppard (AIDS/STD), N Miller (CDC general), K Piper (CDC general), A Ruben (NCEPH), A Merianos (NCEPH)

1 Notifiable diseases list

Rationalisation of the existing list and identification of priority diseases. Review the relative importance of the notifiable diseases along the lines of the Canadian model which uses 12 criteria to rank each disease on a 5 point scale for each category. The final rank is the sum of scores in each category. They use the following criteria: WHO/international quarantine requirements; primary industry/federal food regulatory agency interests; incidence; morbidity; mortality; case fatality rate; communicability; potential for outbreaks; socioeconomic impact; public perception of risk; vaccine preventability; and necessity for an immediate public health response.

Doctor versus laboratory notifications - review the existing list, all of which legally requires doctor notification at present. Our surveillance of the enteric diseases (campylobacteriosis, salmonellosis, shigellosis and vibrio infections) and some of the sexually transmitted diseases (gonorrhoea, sporadic gonococcal conjunctivitis, chlamydia) is already essentially laboratory based, mainly requiring doctor notification to alert us to suspected outbreaks. Identification of diseases for which doctor notification is essential, and diseases for which both doctor and laboratory notification are equally important. Which disease notifications are almost exclusively hospital-based?

New national requirements - inclusion of Haemophilus influenzae b, non-neonatal botulism, listeriosis, mumps and rubella to the NT list.
Can we identify any diseases with no relevance in the NT which can be dropped from the list?

2 The notification form
Revision of the format of the existing notification form to make it more user friendly. Separate forms for the laboratories and doctors.

Logistics of distribution to doctors and laboratories.

Issues that need addressing include:

   How many doctors in the NT have a copy of the current Notifiable Diseases list?

   What proportion of all notifications are doctor notifications?

   What is the quality of routine doctor notifications? How much extra information is obtained from the doctor's notification when laboratory notification is also available? How can we improve the quality of doctor notifications?

3 Legislation issues
Legislative changes to the Notifiable Diseases Act to increase the flexibility of the system, particularly the inclusion of new diseases and deletion of irrelevant diseases.

Clarification of legal notification requirements - the existing wording on the legal requirements of pathology services to notify is limited to the sexually transmitted diseases chancroid, donovanosis (granuloma inguinale), genital herpes, gonorrhoea, lymphogranuloma venereum and syphilis, and is open to interpretation. Section 16 of the NT Notifiable Diseases Act (1981) refers to pathology investigations and states that "where a pathology investigation indicates that a person is an infected person in relation to a disease specified in Schedule 5 [STD], the person conducting the investigation shall give to the Chief
Medical Officer a written notice in the prescribed form containing the details of the results of that investigation." The ambiguity creates problems with contact tracing when laboratories refuse to provide names, and in some situations, demographic details.

4 General surveillance and/or "special" systems of surveillance
What information do we need to extract from the notification system?
How do we best obtain that information? (Michael Levy - "Who does what best?")
How do we best obtain risk factor information eg for hepatitis B or C?

Passive versus active surveillance.

Periodic active surveillance eg for post-streptococcal glomerulonephritis, surveys, serosurveys.

Sentinel surveillance systems and surveillance networks eg influenza surveillance in hospitals, nursing homes, industry, schools, hospital based surveillance, day care centres etc. Our experience is that general practitioner interest and participation in the ASPREN network has been poor in the NT, so routine sentinel practice surveillance might not be feasible. Private practitioner involvement has usually been very good during recognised outbreaks eg measles.

How do we make better use of the informal notification network eg hospital infection control sisters, school and tertiary level student health services, community controlled health services, children’s services.

5 Case definitions
Advantages and disadvantages including logistics (resource and staff allocation to validate cases).

Preparation of national case definitions is in progress.
Use of existing case definitions eg Centers for Disease Control, Atlanta, Canadian Communicable Diseases Surveillance System Disease-specific case definitions, Benenson's *Control of Communicable Diseases in Man*, case definitions already used by other states.

6 Protocols for notification and for outbreak control

We need to develop a "Notification Requirements" package to be included in the literature given to all doctors (and relevant allied health professionals) when they are first registered as medical practitioners in the Northern Territory. The package should include a brief overview of the role of CDC and the important communicable and other infectious diseases in the NT, the list of Notifiable Diseases, sample copies of correctly filled notification forms and a notification booklet, and relevant excerpts from the (revised) Notifiable Diseases Act. CDC should also hold workshops for each new intake of residents and registrars in all health districts to impress upon them the importance of good quality surveillance data.

We are already working on a number of disease control protocols and revising existing protocols.

7 Evaluation of the surveillance system

Refer to the Centers for Disease Control document on surveillance system evaluation based on the following criteria: simplicity of structure and usage; flexibility; acceptability; sensitivity of routine surveillance and the system's ability to detect outbreaks; positive predictive value; representativeness; and timeliness.
No formal evaluation of the surveillance system has been carried out, although some of the more obvious limitations have been addressed in an ad hoc manner. I have listed some of these limitations below.

7.1 Computerised surveillance data are only available since mid-1989. Surveillance data can be extracted from the Annual Reports at least as far back as the 1970s (Central Library), but the Reports only include annual totals for selected diseases and crude attack rates in some editions. There is no consistency in the health region divisions eg northern and southern regions versus the current health districts. There is no readily available data on the age and sex distribution of these cases for the plotting of long term trends. The earlier version of the computerised database is incompatible with the format of the surveillance system used since 1991. Disease name, age, sex, region, community and ethnic group can be extracted from the 1989-90 system, but the accuracy of the data is questionable because of internal problems affecting data entry at that time. Checks for duplication have been set up for the current program. Missing demographic data continues to be a problem.

7.2 Analysis of the data is carried out on an ad hoc basis. Report generating models are available for adaptation in Epi Info. The system has the capability to compare notification data for successive years as long as the recfile structure is identical. Regular (weekly) reports will assist in the detection of disease outbreaks and will help to monitor the effectiveness of outbreak control measures.

7.3 Laboratory notifications of chlamydial STD have increased since discussions with the Royal Darwin Hospital. The microbiology unit does not keep a log of unusual pathogens such as leptospirosis and the rickettsioses. We need to emphasise the importance of non-notifiable disease surveillance and maintain rapport with the physicians. Dr Burrows is concerned that laboratory reports
returned from reference laboratories after patients have been discharged are filed in the case notes before the attending physician has sighted the result.

8 Timeliness

How long are we taking at each stage in the loop and how can we improve performance?

Input stage

- Data entry

Data retrieval and analysis

- Action

Feedback local and national

Once we are alerted to an outbreak, mobilisation of the surveillance network is quick and efficient. Doctors are alerted through the courier services of the private laboratories (often same day distribution in Darwin). CDOs throughout the NT also receive facsimiles and are then expected to notify local doctors if appropriate.

The *NT Communicable Diseases Bulletin* has been supported by recipients interstate but we have received very little feedback within the NT. Except for Alice Springs and Darwin, we have had few contributions from the other health districts. We have to reassess our aims in producing this newsletter because the irregularity of publication means that it is no longer a timely report of communicable disease activity in the NT.

9 Logistics

Time: How long does it take to confirm a notification diagnosis and institute appropriate action?

Staffing requirements.

Prioritisation of diseases for labour intensive follow-up and contact tracing. Who does what best?
Territory-wide continuing education of the Communicable Diseases Officers (and STD/AIDS educators) in basic epidemiological principles and biostatistics. A possible forum is one of the annual CDOs meetings which could be dedicated to epidemiologic principles and the surveillance system, structured as an interactive workshop.

Organisational changes.

Hierarchy of responsibility for disease surveillance.

Identify and address areas where duplication of surveillance occurs.

Publicity and education of the system users, principally doctors, the CDOs and the laboratories.
2.4 Melioidosis surveillance.

The following section contains: the draft outline for the stimulated surveillance of melioidosis and the investigation of high risk patients during the outbreak period in the 1990-91 wet season; the melioidosis surveillance form; and the proposal for a seroepidemiological study of *Pseudomonas pseudomallei* antibodies submitted to the Joint Institutional Ethics Committee of the Royal Darwin Hospital and the Menzies School of Health Research.

2.4.1 This guideline was prepared for circulation to doctors and allied health professionals throughout the Top End.

MELIOIDOSIS SURVEILLANCE AND INVESTIGATION OF SUSPECTED CASES DARWIN REGION, JANUARY 1991

1 Background and rationale for surveillance

There have been 11 bacteriologically confirmed cases of *Pseudomonas pseudomallei* in the urban Darwin region since December, 1991. Historically the incidence of clinical melioidosis has been 1-2 cases/month during the rainy season, so the current clustering of cases has prompted an epidemiological investigation.

Melioidosis is an opportunistic infection and the cases admitted to the Royal Darwin Hospital have all been immunocompromised. However, these severe clinical cases are only part of a spectrum of disease ranging from asymptomatic to acute fulminant infection. Serosurveys from endemic areas in South East Asia and Northern Queensland have reported infection rates as high as 29% in rural communities. The current situation in urban Darwin is unique and raises concerns of continued transmission, possibly through skin inoculation, although the route(s) of spread have not been
clearly defined. In rural outbreaks of melioidosis there has been a clear association with unusually heavy rainfall.

The following guidelines for the surveillance of *Pseudomonas pseudomallei* have been developed by the Communicable Disease Centre, Darwin.

2 Active case finding

Retrospective - general practitioners and DMOs

All immunocompromised patients who have presented with lower respiratory tract infections, abscesses, septic arthritis, urinary tract symptoms or signs, including sterile pyuria, or pyrexia of unknown origin should be reviewed and screened for *Pseudomonas pseudomallei*. Patients most at risk appear to be diabetics, alcoholics and patients with lung malignancies. A preceding viral upper respiratory tract infection may prime the respiratory mucosa for opportunistic bacterial infection.

Culture and antibiotic sensitivities

Including blood cultures prior to the administration of antibiotics.

*Pseudomonas pseudomallei* serology

- HI (IgG) titres 1:40 or higher indicate past infection.
- A positive IFA-IgM titre is consistent with current infection and recrudescence.
- Acute and convalescent sera (IgM) to monitor disease progress.

Radiology

Early referral for CXR in high risk patients even if the principal symptoms are not respiratory.

Respiratory virus serology (optional).

Prospective - general practitioners, RDH staff, DMOs

- As above for all newly presenting high risk patients.
Arterial blood gases deteriorate early in the course of pulmonary melioidosis and should be considered as part of the septic workup.

3 Epidemiological studies

Community based

- Sentinel general practices.

- Screening of untagged stored sera (last 3 months) for both IgM and IgG antibodies to *Pseudomonas pseudomallei*. Collection of demographic data (age, sex, suburb, ethnicity).

- Prospective serological study of low risk patients presenting with an infection. Duration 1 month. Informed consent to be obtained. Request for *Pseudomonas pseudomallei* culture if specimen(s) sent off for routine MCS. Short questionnaire to include demographic data and exposure risk.

Hospital based surveillance

- Active surveillance among all high risk patients. Melioidosis to be considered in the differential diagnosis of all patients presenting with sepsis.

- Prospective serological study of low risk patients presenting with an infection through Accident and Emergency, medical wards and when routine bloods are sent off from Outpatient Clinics. Duration 1 month. Informed consent to be obtained. Short questionnaire to include demographic data and exposure risk.

4 Preventative education of risk groups

High risk patients should be made aware of risk factors for melioidosis and prevention strategies eg. wearing shoes and protecting extremities from cuts and superficial infections such as tinea pedis which would facilitate inoculation with soil pathogens; early medical attention to infected skin lesions and other
infective symptoms etc. Patients should be counselled to adopt a healthy lifestyle to minimise immunosuppression etc.

5 Development of a melioidosis database

As a latent infection with recrudescence is known to occur with melioidosis, often many years after the primary infection, a register of cases found to be seropositive and/or culture positive should be considered to assist in the early diagnosis of recrudescence.
MELIOIDOSIS SURVEILLANCE QUESTIONNAIRE

Date __/__/__  HRN _______________
Surname ______________________  First name ______________________
Address ________________________  Suburb/Town ____________________
Phone (w) ______________  (h) ______________
DOB __/__/__  or Age ____ yrs  Sex M/F  Ethnicity A/O

Main occupation ______________________________________________________
Place employed ______________________________________________________
Other occupations ____________________________________________________
Place employed ______________________________________________________

Frequency of occupational exposure to soil, mud, or standing water.
(1) frequent  (2) infrequent  (3) nil  (4) N/A

HISTORY OF THE PRESENTING ILLNESS (IF APPLICABLE)
Onset date __/__/__
Admission date __/__/__
or date of outpatient visit __/__/__
Outcome of illness Living / Died
Date of separation __/__/__
Serology positive Y/N
Culture positive Y/N
Culture sites ______________________

Other symptoms ______________________

SYMPTOMS  DURATION
Fever/chills  Y/N __________
Cough  Y/N __________
Abdominal pain  Y/N __________
Painful urination  Y/N __________
Weight loss  Y/N __________
Skin lesions  Y/N __________
CXR changes  Y/N __________

PAST MEDICAL HISTORY
Diabetes  Y/N
Lung disease  Y/N
Type of lung disease  (1) COAD
(2) TB
(3) old CXR abnormality
(4) other
Leprosy  Y/N
Pregnancy  Y/N

Alcohol use  Y/N
No/size of drinks/day ______________________
Malignancy  Y/N
Steroid use  Y/N
Preparation/duration ______________________
Illicit drug use  Y/N
Preparation/ route ______________________
Other ______________________

Cigarette smoking  Y/N
No of cigs/day as a smoker ______________________
If now a non-smoker, state number of years stopped ______________________
Other relevant medical history ____________________________

EXPOSURE FACTORS
Number of years resident in the NT ________________
Place(s) of residence in the NT ____________________

History of residence in, or travel to Nth Qld, Nth WA, SE Asia, or other tropical countries? Y / N
If yes, where? _____________________________ When? _______

History of penetrating injury or unhealed skin lesion (including infected bites & ingrown toenails) within 3 months of the illness? Y / N
If yes, site & nature of injury ____________________________ How was it sustained? ____________________________
Date of the injury ______/____/____
Treatment required ____________________________

Any recreational activities with heavy soil/mud/standing water exposure eg gardening, digging for shellfish, boating, swimming in waterholes? Y / N
If yes, state activity ____________________________

Type of footwear worn at work when exposed to soil/mud/standing water:
(1) waterproof shoes/boots
(2) open sandals/thongs/canvas shoes
(3) barefeet
(4) N/A

Protective gloves worn at work Y / N or N/A

Type of footwear worn recreationally when exposed to soil/mud or standing water:
(1) waterproof shoes/boots
(2) open sandals/thongs/canvas shoes
(3) barefeet
(4) N/A

Protective gloves worn gardening Y / N or N/A

Any contact with the following farm animals?
goats Y / N
pigs Y / N
sheep Y / N

Disease Control Centre notified Y / N
Dept of Primary Industries & Fisheries notified Y / N
Environmental Health notified Y / N

Investigations:

________________________________________________________________________
2.4.2 Proposal for a cross-sectional and prospective serosurvey of antibodies to *Pseudomonas pseudomallei* antibodies in Darwin.

Submitted to the Joint Institutional Ethics Committee of the Royal Darwin Hospital and the Menzies School of Health Research, 30 October 1991.

THE JOINT INSTITUTIONAL ETHICS COMMITTEE OF THE ROYAL DARWIN HOSPITAL AND THE MENZIES SCHOOL OF HEALTH RESEARCH

Application for Ethics Clearance for Research Procedures Involving Human Beings

Applicants should read the NHMRC Statement on Human Experimentation before completing this application. Answers to questions must be typed and expressed in a manner that is meaningful to an informed layperson.

Applications should be lodged with the Committee Secretary in Medical Administration, Royal Darwin Hospital.

Eighteen copies of this Application and two copies of the full scientific protocols are to be furnished by the applicant.

1 **TITLE OF THE PROJECT**

   (a) Formal title: A serosurvey of antibodies to *Pseudomonas pseudomallei* in Darwin - occupation as a risk factor for seroconversion.

   (b) *Pseudomonas pseudomallei* serosurvey.

2 **INITIAL OR RENEWAL APPLICATION:** Is this a continuation of an existing project already given Ethics Committee approval? **ND**

3 **CHIEF INVESTIGATOR**
   Name: Dr Angela Merianos
   Professional qualifications: MBBS MPH, FAFPHM
   Position: Epidemiology Registrar
   Department/Faculty: Disease Control
   Phone: 089 228560

4 **CO-INVESTIGATORS**
   Name: Dr Mahomed Patel
   Professional qualifications: MBBS FRACP FAFPHM
   Department/Faculty: Disease Control

   Name: Dr Bart Currie
   Professional qualifications: MBBS FRACP FAFPHM
   Department/Faculty: MSHR

5 **DURATION OF PROJECT:** From November 1991 To April 1993

6 **FUNDING:** Is this protocol the subject of a grant application? **ND**
   If yes, what is the Agency? **NA**
   Has it been funded? **NA**

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**NOTE:** In completing the following sections, please respond in a way that is meaningful to the informed layperson. Be concise and address the ethical issues that are implicit in each question.
SCIENTIFIC AND EDUCATIONAL AIMS OF PROJECT. SPECIFIC HYPOTHESES SHOULD BE STATED CLEARLY:

Aims:
1. To measure the seroprevalence of antibodies to *Pseudomonas pseudomallei* in the working population at the beginning of the 1991/92 "wet season".
2. To measure the risk of seroconversion to *Pseudomonas pseudomallei* attributable to occupational exposure.
3. To develop appropriate guidelines for the prevention of exposure to *Pseudomonas pseudomallei* in the workplace.

JUSTIFICATION OF THE PROPOSAL AND OF THE INVESTIGATORY POPULATION

The epidemic of melioidosis which occurred in the 1990/91 wet season was associated with a mortality rate of approximately 36%. Interview of cases or their proxies indicated that occupational exposure to soil may be an important risk factor in melioidosis, especially in patients without underlying medical risk factors i.e., in patients with a normal immune system. A recent successful workers' compensation claim has set a precedent for compensation following work-related melioidosis.

We propose a serosurvey of employed Darwin residents to measure the risk attributable to occupation in the development of *Pseudomonas pseudomallei* antibodies. The Darwin Statistical Division has been chosen as the study population as environmental studies in 1991 proved the presence of *Pseudomonas pseudomallei* in the soil.

SUMMARY OF THE ETHICAL CONSIDERATIONS

Informed written consent will be obtained from all participants. Two self-administered questionnaires will be filled out by all subjects, and will include questions on demographic details, past medical history, work history, and travel history.

Counselling about the implications of a positive antibody test will be made available to all participants, and appropriate follow-up with Work Health, NT, will be arranged.

We are negotiating with a medical representative of Work Health, NT, for his participation as a co-investigator.

(a) DETAILS OF EXPERIMENTAL PROCEDURES/METHODOLOGY INCLUDING SAMPLING PROCEDURES, INVASIVE TESTS (VENEPUNCTURE, RADIOGRAPHY ETC)

The study includes two self-administered questionnaires to be filled out at the time of both venepunctures for *Pseudomonas pseudomallei* antibody testing. The venepunctures will be carried out at the beginning and at the end of the wet season.

(b) WHICH OF THE ABOVE PROCEDURES ARE UNRELATED TO THE CARE OF THE INDIVIDUAL PATIENT?

Seropositive patients will receive long-term benefits by closer monitoring. There is no immediate benefit of this study to subjects who are seronegative. Our improved understanding of the epidemiology of *Pseudomonas pseudomallei* infection will direct public health policy in the workplace.
11 **IS THE RESEARCH TO BE CARRIED OUT ON:**

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<th>Volunteers</th>
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12 **JUSTIFICATION OF SAMPLE SIZE:** State whether a biostatistician was consulted on calculating sample size, or in any other aspects of study design (eg randomisation procedures).

From the 1986 ABS classification of occupational groups we have estimated that in the Darwin Statistical Division the ratio of indoor to outdoor occupations is approximately 2:1. Sample size was calculated using the epidemiological software Epi Info Version 5. No biostatistician was consulted.

We estimate that 1023 subjects are required for a cohort study of 95% CI with 90% power, ratio of unexposed (indoor workers) : exposed (outdoor workers) = 2:1, if the frequency of antibodies to *Pseudomonas pseudomallei* in the exposed is 10% vs 5% in the unexposed. We know from a serosurvey in 1991 of a convenience sample of 300 blood bank sera and sera from patients attending the Royal Darwin Hospital, that the seroprevalence rate of *Pseudomonas pseudomallei* antibodies in Darwin is of the order of 5% (Dr Bart Currie, personal communication), and rates of approximately 15% have been reported for diabetic patients, alcoholics and other high risk groups in Queensland (ref).

We propose a pilot study of seroprevalence through the Department of Transport and Works, which has expressed interest since the successful compensation claim by one of its employees, and will adjust our sample size estimate accordingly.

13 **CONSENT STATEMENT:** Please attach your consent form and any other written statements to be given to the participants. If verbal or no consent being given, please state. Have you provided the participants in this study with a means of contacting you urgently in case of emergency?

Refer to attached consent form.
PROPOSED REVIEW OF PROGRESS, PARTICIPANT CARE AND WINDING UP PROCEDURES

As previously stated, participants will be informed of their test result and counselled appropriately about the implications of the test and about medical risk factors such as alcohol abuse and diabetes which may precipitate melioidosis. A written explanation of their results will also be given to all participants.

PROPOSED STORAGE AND ACCESS OF FILES AND DISPOSAL/STORAGE AT CONCLUSION: Please include what steps are being taken to ensure confidentiality of patient information.

Subject records will be kept at the Communicable Diseases Centre and entered into a computerised database. At the conclusion of the study, the hard copies will be destroyed. The computerised records will be kept at CDC as a reference point for a long term follow-up of the cohort.

HAS THE PROPOSED RESEARCH BEEN DISCUSSED WITH LEADERS OF ANY ABORIGINAL COMMUNITIES WHICH MIGHT BE INVOLVED?

This study is urban based and doesn't involve any Aboriginal communities.

DECLARATION: I certify that the information given above is correct to the best of my knowledge. I acknowledge that I must notify the Committee if there is any ethically relevant variation. I have read and agree to abide by the relevant parts of the NHMRC Statement on Human Experimentation.

Signed __________________________ Dated ____________

SIGNATURE OF DIRECTOR/MEDICAL SUPERINTENDENT

Signed __________________________ Dated ____________
Disease Control, Darwin and the Menzies School of Health Research, are conducting a study on the risk of infection with *Pseudomonas pseudomallei*, the germ causing melioidosis, in the Darwin community.

During the 1990/91 "wet season", an outbreak of melioidosis occurred in Darwin. The aim of this study is to measure the presence of antibodies to this germ in people living and working in Darwin so that we can identify the groups that come into contact with the germ most frequently. This will help us advise people how to prevent contact with *Pseudomonas pseudomallei* in the future. The presence of antibodies means that the person has been in contact with the germ. It does not mean that the person has the disease melioidosis, nor that melioidosis will occur in the future.

The study will take place during the "wet" season because we know that the germ is found in soil and muddy water after heavy rain.

If you agree to take part in the study, you will be required to fill out two (2) questionnaires and have blood taken on two (2) occasions, one at the beginning and one at the end of the "wet" season. Your blood will be tested for antibodies to *Pseudomonas pseudomallei*. The questionnaire will focus on factors in your lifestyle which may bring you into contact with this germ, for example the type of work you do, and the number of years you have lived in the Northern Territory.

All participants in the study will receive a copy of their results. If your result is positive, Disease Control staff will discuss the meaning of the result with you in detail.

Participation in this study is voluntary. Disease Control will answer any questions you have about this study (contact Dr Angela Merianos on 228 560 or Mrs Chris Noonan on 228 898).

I have understood the above information and am willing to take part in the study. I understand that the results of this study may be published and my identity will not be revealed.

Name: _______________________________ Date ___/___/___

Signature: ________________________________

Witness's Signature: _______________________________ Date ___/___/___
2.5 A telephone investigation of leptospirosis in the NT

[I have included in parentheses telephone numbers which may be useful to CDC staff in the future].

At approximately 13:30 on Friday 22 January 1993, I accepted a telephone call from Dr Scott Cameron, Director, Communicable Diseases Branch, South Australian Department of Health, about a case of leptospirosis acquired in the Northern Territory. The patient was a 56 year old retired male resident of South Australia who was admitted to the Royal Adelaide Hospital on 3 December 1992 in acute renal failure. He gave a history of cutting his foot while swimming in Katherine Gorge on 20 November. Serological testing was strongly positive for *Leptospira interrogans* var *australis*, a serotype not found in SA. The patient's attending physician in Adelaide was Dr Tony Clarkson. He had not presented for treatment while in the NT.

Benenson states that leptospirosis is a zoonosis affecting mainly agricultural workers especially rice and sugar cane-field workers, farmers, abattoir workers, veterinarians, sewer workers, military troops and others exposed to infected animal urine. The disease can also be a recreational hazard through exposure to contaminated water. The incubation period is 7-12 days but can range from 2-20 days. Severe leptospirosis (Weil's disease) occurs in 5-10% of cases and has a case fatality rate of 5-10%. The laboratory diagnosis is based on leptospire isolation from blood cultures, CSF or any other clinical specimen in the first 10 days of illness, or a 4-fold rise in antibody titre. A presumptive diagnosis can be made on a single microagglutination titre of greater than or equal to 1:100.

From my experience in Darwin I felt that the following people/agencies would be most likely to know whether *Leptospira interrogans* var *australis* had been previously described in the NT either as a cause of human disease or in serosurveys of potential animal reservoirs: the physicians at the Royal Darwin Hospital, Kay Withnall in the RDH microbiology department, the government veterinary surgeons of the Department.
of Primary Industries and Fisheries (DPI&F), and the project officer of the NT Conservation Commission's Wildlife Management/Research Programs division. I asked our secretary Veronica Barrett to search the computerised notification database (January 1990-January 1993) for cases of leptospirosis, and placed a call to the Royal Adelaide Hospital to speak to Dr Clarkson.

I first spoke to Morton Bell, the veterinarian for the DPI&F Quarantine and Inspection Service (818 733) because the regional veterinary officer was unavailable. He suggested that I speak directly to Graham Davis at the Conservation Commission (894 561) and to David Pritchard (892 310) or Frank Corcoran in the DPI&F OIC Veterinary laboratory about animal trapping and serological testing for leptospira species. Morton believed that a project involving rodent trapping and serological testing had been carried out in East Arnhem region, and the veterinary laboratory staff would be aware of any results.

David Pritchard stated no serosurvey for leptospirosis in native and domestic animals had been conducted in the NT. Lagomorphs (rabbits and hares), and marsupial and domestic mice and rats were probably the most important reservoirs in the NT. His laboratory had recently set up a microagglutination test for a number of leptospira species but did not test for the \textit{australis} serotype. The microagglutination test is regarded as quite specific as an adsorption step removes cross-reacting antibodies. He offered his assistance in testing sera for CDC in the future, and would look up the telephone numbers of colleagues at reference laboratories interstate.

Bart Currie (infectious diseases physician) knew of approximately 7-8 cases of leptospirosis in the NT over the last 10 years and was interested in a list of NT serovars if available. Most if not all clinical cases had been associated with \textit{L. interrogans var hardjo}. When we discussed the history of exposure, Bart commented that the most important routes of transmission of leptospirosis described in the medical literature from South East Asia were ingestion and percutaneous inoculation.
Wildlife Officer who may also have come from the Katherine region and had a definite history of contact with rodents.

NT sera are sent to Brisbane for leptospirosis serology. Kay Withnall provided the names of the two key people at the Queensland State Health Reference Laboratory, which is the World Health Organisation reference laboratory for the Western Pacific, but stated that her laboratory did not keep a register of positive serology for leptospirosis. There had been a case of *L. interrogans* var *hardjo* on 29 December. Kay also confirmed that sera for leptospirosis serology from the regional hospitals would be sent to Brisbane via the RDH laboratory so she would be aware of any recent cases in Katherine. She did not know whether the two private laboratory services had received any positive results. When we rang Western Diagnostic Pathology and Dr Peverill's pathology service we were assured that as a Notifiable Disease, CDC would automatically receive a copy of any positive leptospirosis serology.

My original call to DPI&F was then returned by Jill Milan, the current veterinary officer for the Darwin region (892 034). Although Jill did not know of any animal studies, her colleague Colin McCool remembered a study of leptospirosis in feral pigs possibly conducted in the Northern Territory in the 1970s and would examine his records for a reference. Jill provided a reference for a study on feral pigs in Queensland.

I next spoke to Michael Donht at the Queensland State Health Laboratory (07 224 5420) who has been collecting leptospirosis serosurveillance data on Queensland serovars over the last 18 months. His laboratory tested the sera on the Adelaide patient using a microagglutination test. Although there is no data available for the NT, Michael felt that the serovars present in northern Queensland above Mackay would be comparable to the situation in the Top End of the Northern Territory. Eighteen serovars have been identified in northern Queensland, particularly from areas of rainforest. His laboratory uses a panel of 14 serovars, including *australis*. Although leptospires readily multiply in pools of infected water when the ambient temperature
is 25-35°, they are difficult to culture from water and other environmental samples so surveillance depends on serology. The farthest south *australis* is thought to occur is just over the NSW-Queensland border. The organisms has been identified in Queensland cattle. The organism doesn't survive in temperatures below 13°C.

He was confident of the diagnosis as the microagglutination test is very specific and the direct agglutination titre to the *australis* serovar was 1:1600. It was negative for all other serovars. The IgM-ELISA was also positive, but can cross-react with CMV and Q fever. Michael also stated that the distribution of disease is patchy in common with the "islands of endemicity" in scrub typhus. In Cooktown, Queensland, 12 cases were diagnosed from 2 December 1991 to May 1992 from a population of approximately 800 people, when the local medical officer queried leptospirosis in patients presenting with pyrexia of unknown origin. Five cases were blood culture positive during the acute phase. Leptospirosis as the cause of aseptic meningitis was confirmed in a child from Mt Isa when it was established that he had visited his uncle, who also developed clinical leptospirosis, in Cooktown. Michael said that serology for leptospirosis is not part of the routine viral screen, so it may be a cause of meningitis of unknown aetiology. His laboratory tests for leptospirosis if there is a history of animal contact, bushwalking, or the patient belongs to an occupational risk group.

Bandicoots and other small marsupials are the most important animal reservoirs in tropical Queensland. Feral pigs are also being tested. In cattle, *hardjo* lives in a "symbiotic" relationship in the renal tubules and continues to be excreted into the environment for long periods of time. In Queensland, dairy cattle are vaccinated every two years as *hardjo* causes mid- and third trimester abortions and leaves the cow infertile for 2-3 years.

He described two main forms of disease, icteric and non-icteric, and stated that conjunctival inoculation is another important route of transmission, especially among cattle. *L. interrogans var australis, copenhagen, icterohaemorrhagiae* and *pyrogenes*
are all icteric serotypes and cause the more severe forms of leptospirosis. *L. interrogans* var *hardjo* and *pomona* are non-icteric serotypes and cause a flu-like illness which usually resolves in 3-4 weeks without specific treatment. Renal complications are the result of immune complex deposition in the renal tubules.

Graham Davis of the NT Conservation Commission was next to return my call. He asked that CDC brief him on the implications of leptospirosis in national parks and possible preventative strategies when we knew more. He was unaware of any research on leptospirosis through the Commission but suggested that I contact the Senior Wildlife Officers Peter Whitehead (221 758) and Jeff Dyne (221 759); they confirmed that serological testing of feral pigs using a panel of antigens had been carried out in the NT but were unaware of the results.

Dr Tony Clarkson could not provide details of his patient's travel itinerary in the NT, but denied travel to known endemic areas. The patient's lacerated foot became infected and he presented to the Royal Adelaide Hospital with clinical symptoms and signs "typical of leptospirosis" 14 days after the suspected exposure. His illness began with a prodrome of fever, flu-like symptoms and mild confusion and progressed to renal failure secondary to interstitial nephritis. His liver function tests remained normal throughout. He made an uneventful recovery and was discharged. Dr Clarkson was willing to provide further details on written request.

Meanwhile, our secretary had identified another case of leptospirosis (serotype *hardjo*) notified in March 1992. The case was a wildlife officer who had handled crocodile eggs. The laboratory confirmed case from 29 December had not been notified and we are chasing up demographic and risk factor details. There were no cases in 1990 and 1991.

I rang Jim Burrows to clarify whether the patient Bart had mentioned was the same case confirmed on 29 December. He thought that the patient Bart Currie alluded to was a confirmed case of endemic typhus with a history of rodent contact while demolishing
his house. We later confirmed with the laboratory that there had been two unreported cases of endemic typhus (caused by *Rickettsia prowazeki*) since March 1992 which we are following up.

I contacted Michael Donht again on 29 January for further information about any human serosurveys involving people at occupational risk of leptospirosis. In 1982 his laboratory was involved in the prospective program to screen all meat workers for leptospirosis, Q Fever and brucellosis. They tested 4000 meat workers and detected a few cases of leptospirosis, but the program fell through and was never reported in the literature. In approximately 1990 there was an outbreak of over 35 cases of *L. interrogans var hardjo* in meat workers in Inverell, NSW. They send out questionnaires to doctors with positive results to record the patient’s demographic details, occupation, history of travel overseas, outdoor activities, animal contact and major symptoms and signs. If we considered a serosurvey of wildlife officers in the Katherine region he would be pleased to collaborate as the WHO reference laboratory for the region.

From this series of discussions, it is apparent that there is no hard data about the serotypes of leptospirosis in animals in the NT and that the majority of human cases have been caused by serotype *hardjo*. Our surveillance data suggest that severe disease is rare in the NT. We have no information on the sensitivity of surveillance for self-limiting, mild disease.

**Prevention of leptospirosis**

Prevention of leptospirosis is extremely difficult because of the nature of the animal reservoir and the vehicle of transmission (urine). In the NT, preventative strategies are further complicated by our lack of data on the nature and size of the animal reservoir and its distribution. At this stage alerting the medical community both in the NT and interstate of the probable presence of *L. interrogans var australis* in the Katherine region seems a reasonable first step considering the large number of
visitors to the area and the apparent lack of cases. Serological testing of wildlife officers and possibly animal trapping should be considered in the Top End, beginning in the Katherine Gorge National Park.

REPORT OF THE TELECONFERENCE ON RABIES IN CENTRAL AUSTRALIA

PRESENT: M. Patel, A. Hatherell, CMC. Thomas, S. Jervis, COID. Allen Smart
W. Lane, MCDP, ADY
J. Worrall, Meat and Livestock Australia

The proposal was distributed to the following for review prior to the teleconference:
Dr. Sara Kay, QMRA, Canberrra, ACT; Dr. Fred Brown, Farmers' Health Services, SA; Dr. Paul Toovey, Canberrra, ACT; Dr. Robert Health, NSW.

Action:
1. To review the monitoring of movements and trade with Australia.
2. To discuss the draft protocol for the investigation of outbreaks and control of rabies and more vaccination policy.
3. To discuss the practical aspects and logistical feasibility.
2.6 Post-vaccination immunity to Neisseria meningitidis in central Australia

Central Australia experienced an outbreak of serogroup A meningococcal meningitis from 1987 to 1991. The following is the proposal for the investigation of post-vaccination immunity presented for consideration to the Rural Health Services, the Central Australian Aboriginal Congress (CAAC) and the Nganampa Health Council in central Australia. The proposal is based on minutes I took during the teleconference involving the Communicable Diseases Centres in Darwin and Alice Springs, NCEPH and Dr Jay Wenger of the Special Pathogens Branch, Centers for Disease Control in Atlanta, Georgia. It replaced an earlier draft proposal submitted to NCEPH which was modified after the teleconference.

REPORT OF THE TELECONFERENCE ON MENINGOCOCCAL MENINGITIS IN CENTRAL AUSTRALIA 11 June 1991

PRESENT: M. Patel, A. Merianos, CDC, Darwin.
S. Jayathissa, CDCC, Alice Springs.
M. Lane, NCEPH, ACT.
J. Wenger, Meningitis & Special Pathogens Branch, CDC, Atlanta.

This proposal was distributed to the following health service representatives in Alice Springs: Dr Sisira Jayathissa, Community Physician; Dr John Wakeman, Director, Rural Health Services; Dr Ben Bartlett, Central Australian Aboriginal Congress; and Dr Paul Torzillo, Consultant, Nganampa Health Council.

AIMS:

1. To review the epidemiology of meningococcal meningitis (MM) in central Australia.

2. To discuss the draft proposal for the investigation of MM in relation to epidemic prediction and future vaccination policy.

3. To discuss the methodological and logistical considerations of such a study.
SUMMARY OF THE DISCUSSION

**Epidemiology**

The recent adult case of group A MM confirms the persistence of the organism in central Australia. The pattern of disease over the last 3 years hasn't improved (attack rates of 1.6/1000, 1.8/1000 and 1.3/1000 in 1988, 1989 and 1990 respectively), although the last case reported from the Pitjantjatjara Lands occurred in July, 1990. It is premature to predict that the epidemic has ended in the Pitjantjatjarra Lands, or whether the Northern Territory will experience a similar drop in cases.

There is a clear increase in the rate of group C MM. Three of the 9 patients were non-Aboriginal; 67% were in children 0-15 years. At this time there is no justification for widening the vaccination age range to prevent group C disease.

**Host factors**

Why is group A MM exclusively a disease of central Australian Aboriginals in Australia? Why are urbanised Aboriginal children susceptible to group A MM when their non-Aboriginal classmates remain well?

Host factors which should be considered independently of environmental and socioeconomic include genetic susceptibility, complement and/or properdin deficiencies, other immunologic differences.

**Vaccine development**

New polyvalent conjugate meningococcal vaccines have been developed, 1-2 of which are currently being tested in adult trials. These vaccines should be more immunogenic than the polysaccharide vaccines in younger children and will supersede the current vaccines. They will probably be available within 5 years.
Carriage rates

As known from the literature, a cross-sectional study of carriage rates in countries with recurrent disease (e.g. sub-Saharan Africa) has no predictive value of a future epidemic. Carriage rates have not been found to vary much between epidemic waves or between seasons. The highest carriage rates are often seen at the end of the epidemic because a larger proportion of the population has had a chance to be exposed.

As virulent strains usually account for a small proportion of all strains carried in a community, the logistical problems of a longitudinal study long enough to detect any meaningful difference in carriage rates of these virulent strains would be prohibitive. Their value in epidemic prediction must take into account host and environmental factors. The real value of nasopharyngeal swabbing of contacts when a case of MM has occurred is for monitoring antibiotic sensitivities.

Serology

There is still confusion about what is a protective antibody titre, although a bactericidal antibody level of 2mcg/ml is usually quoted. There are no serological markers in a community that can predict the duration of epidemic disease.

Overall vaccine efficacy in Aboriginal children has been much higher than that reported from African countries. However, we do know that 22 of the 53 patients aged 1-15 years with group A or C MM had been immunised (41.5%), so waning immunity and other host factors must be examined. A study of antibody levels before revaccination this year will give one measure of vaccine effectiveness, but needs to be interpreted in the context of clinical vaccine efficacy.

CONCLUSIONS

In view of the difficulties in predicting the course of an MM epidemic, the following key issues were identified. Some of the following questions can be answered by a
limited study of antibody levels, antibiotic sensitivities and host factors associated with meningococcal disease.

- Who is susceptible to disease and why?
- How do we determine susceptibility?
- Is an antibody fall-off occurring in the population and how bad is it?
- Is this why cases are occurring in the vaccinated group?
- How much of the population is still benefiting from vaccination?
- What is the best way of monitoring rifampicin resistance?
- What investigations will help development of a rational vaccination policy?

Dr Wenger suggested that in view of the availability of conjugate vaccines in the foreseeable future, the value of longitudinal data may be limited, and the effort involved unwarranted. Instead, the following limited cross-sectional study is proposed, requiring "one-off" collection of specimens.

**Antibiotic sensitivities**

**Aim:** To determine whether rifampicin should remain our first-line antibiotic for prophylaxis in contacts of MM.

The contacts of all new cases of MM should be offered a nasopharyngeal swab prior to rifampicin administration, and approached for consent of a follow-up swab within 2 weeks of administration. This is an efficient way of maintaining antibiotic sensitivity surveillance in a group with known exposure, who will be offered treatment.

**Antibody study**

**Benefit:** The important immediate value of this study is that it will clarify the age group(s) that should be re-vaccinated in future if the virulent strain of group A meningococcus remains endemic in CA, and the re-vaccination schedule.
Pre-vaccination age-stratified bactericidal antibody survey using 4 age strata in previously vaccinated children (Aboriginal and non-Aboriginal).

Sample size: The strata should contain 30-40 children in the following age groups: 2-3.9 (n=40), 4-7.9 (n=40), 8-14.9 (n=30), 15-18.9 (n=30). At least 10 children aged 2 years should be selected to estimate the size of the immune response to vaccination at age 12-23 months. Venepuncture or capillary blood collection of 1-2 ml of serum, to be stored for transportation to CDC, Atlanta.

Data to be analysed by age group, ethnicity, and time since original vaccination. Although we won't be able to determine the peak antibody level or the rate of fall-off, it will indicate what proportion of the population is still protected, and whether age at vaccination does influence antibody persistence in central Australia.

*Host factor study*

Aim: This would be a clinical study to identify possible causes of previous vaccine failures.

Benefit: C4 is crucial to the activation of the classical complement pathway, and patients with C4 deficiency are at risk of recurrent bacteraemia with a variety of capsulated bacteria including *N. meningitidis*, *H. influenzae* and *S. pneumoniae* and some viruses. Identification of these patients will enable provision of appropriate vaccination and antibiotic prophylaxis. (Refer Ranford et al., 1987; Bishof et al., 1990)

Case-control study of host factors predisposing to MM. Patients to be tested for antibody levels, convalescent phase complement levels and function, properdin and complement deficiency alleles. Retrospective (stored sera) and prospective arm.

Two control groups, both age-matched. One race-matched and one race-unmatched. Children in the antibody study would be appropriate age-matched controls for some of
the cases. A family member control is necessary for genotyping. Control blood (except family controls) for host factor studies to be untagged for confidentiality. Although of no direct advantage to the controls, their participation will determine the contribution that host factors MM susceptibility.

REFERENCES


Addendum November 1992

The District Medical Officers of the Division of Rural Health in central Australia have accepted the task of analysing these data, so the results have been forwarded to the Director of Rural Services in Alice Springs. The results indicate that most of the children tested in all age groups and both sexes did not have "protective" levels of antibody at the time of the serosurvey.
INTRODUCTION

The “Wet Season” edition is the first NT Communicable Diseases Bulletin. It presents epidemiological data on two important “wet season” diseases, epidemic polyarthritis and melioidosis. A summary of research projects and control strategies relating to these infections is also included. This edition is targeting Top End diseases due to their epidemic potential over the next few months, but future publications will be relevant to all regions in the Northern Territory.

AIMS OF THE BULLETIN

The main aim of the Bulletin is to provide feedback from the Communicable Diseases branch of Disease Control (formerly the Communicable Diseases Centre) to all participants in the NT communicable diseases surveillance system. It is published in recognition of the invaluable contributions made by participants, and to enhance control efforts for the communicable diseases in the NT.

Throughout Australia, public health units have recognised the need to review surveillance networks in order to set new agendas for disease control. Our immediate concerns for communicable disease control include the improvement of the quality of collected data, rationalisation of the list of notifiable diseases, incorporation of an ongoing evaluation process and improvement of the output arm of the surveillance system.

Every month, updates will appear on the notifiable diseases, with comments on epidemics or clustering of cases. A cumulative profile of infectious disease notifications by region will be included in the June and December editions. A series of feature articles will focus on the long term trends of important NT communicable diseases. Reader contributions are welcome. This publication will be an adjunct to the outbreak alerts that the Department has distributed in the past.

The Bulletin will be available to all health professionals in the NT. The address for copies appears below. Your feedback and suggestions will help us develop a newsletter that will best address your needs.

EPIDEMIOLOGICAL UPDATES

ROSS RIVER VIRUS

Epidemiology of the outbreak

The near record rainfall of the 1990/91 “wet” season resulted in an epidemic of Ross River virus disease, with 466 notifications from laboratories for the period December 1990 to October 1991. A
more detailed analysis of the cases for which doctors provided detailed notifications directly to the Medical Entomology Branch will be presented separately. Figure 1 shows the epidemic curve for the outbreak, and Figure 2 shows the age distribution of the patients. As expected, the curve follows the seasonal variation in rainfall. Most cases occurred in the 20–39 age group; there was no significant gender-related difference in case numbers. The highest attack rates per 100,000 population occurred in Jabiru, Katherine and rural Darwin.

**The retrospective study**

We are currently conducting a retrospective study of patients with RRV in 1990/91. Questionnaires have been distributed to the doctors who reported cases during the epidemic, and will be forwarded to their patients. The main aims of the study are a better understanding of the natural history of RRV in the NT, and an assessment of the information needs of both patients and doctors. The questionnaire focuses on the chronicity, severity and psychosocial aspects of epidemic polyarthritis (EPA). Preliminary results indicate that symptoms commonly persist for between 3-6 months, and that most patients are unprepared for the impact that EPA can have on their daily lives. We take this opportunity to encourage doctors to return questionnaires and updated patient lists as soon as possible so we can mail the questionnaires to patients.

**Other arboviruses causing epidemic polyarthritis**

It is evident that Ross River virus accounts for only some of the cases consistent with arbovirus infection. The Menzies School of Health Research (MSHR) tested sera for anti-RRV antibodies as part of the diagnostic workup on a group of patients presenting with acute polyarthritis from January 1989 to August 1990, and found that only 16% (40 cases) had a positive result (Dr Keat Song Tai, personal communication). MSHR is planning a serological study of anti-RRV negative sera from cases of EPA, in order to identify the other arboviruses endemic in the NT. Sera will be tested for the presence of antibodies to five Flaviviruses (including MVE, Kunjin, and Kokobera), two alpha viruses (Sindbis and Barmah Forrest), and to the important Bunyaviruses (Gan Gan and Trubanaman).

**Health promotion**

Ross River virus infections will be the focus of a health promotion campaign this "wet season". The Medical Entomology Branch, Department of Health and Community Services (DH&CS), will run its annual campaign against mosquito-borne diseases. The Health Promotions Branch, DH&CS, in collaboration with the Disease Control Centre (DCC) is also working on a multi-media campaign of arboviral disease prevention. Further details will be found in the next edition of the Bulletin.
Pathology request procedures

Doctors are reminded to specifically request anti-RRV IgM on pathology request forms. At present, unpaired sera sent via the Royal Darwin Hospital to the WA State Health Laboratory in Perth will not be tested for RRV antibodies unless a convalescent sample is also received. A request for anti-RRV IgM will prevent delays and difficulties in diagnosis. Private laboratories in the NT usually perform this test when unpaired sera are submitted.

MELIOIDOSIS

Epidemiology of the outbreak

From November 1990 to June 1991, 33 cases of melioidosis were referred to Royal Darwin Hospital. The case fatality rate was 36% (12 cases). All but four patients were infected during the last "wet". The endemic rate of melioidosis in the NT over the last 20 years was 2-3 cases/year. As most cases occurred in the Darwin urban and Palmerston area, an epidemiological investigation was carried out.

Age 50 years and over, male gender, diabetes, and/or alcohol abuse were all independent predictors of melioidosis in the epidemic period. Diabetes and alcohol abuse were the most important risk factors for disease. Diabetics were 13 times more likely to develop melioidosis than non-diabetics, and abusers of alcohol increased their risk of disease sevenfold. The diagnosis should be considered in immunosuppressed patients presenting with pyrexia of unknown origin, pneumonia, acute genitourinary symptoms and unusual skin lesions. At risk patients should be advised to wear waterproof, closed footwear during the "wet season", and gloves when gardening. Melioidosis is uncommon in people with normal immune systems.

Health promotion

This Department plans comprehensive health promotion activities over the next few months to heighten awareness about the risk factors for melioidosis. The campaign will target people in the recognised high risk categories, but a push will also be made for safer working practices in outdoor occupations during the "wet".

THE COLD CHAIN

Cold Chain for vaccine potency
(Nan Miller, Senior Project Officer, DCC)

Vaccines are delicate biological products that can be destroyed by exposure to sunlight and extremes of temperature. The cold chain is the system of transporting and storing vaccines within the recommended temperature range (2°-8 °C) during transport and storage. Repeated or prolonged exposure to temperatures above 10°C can cause loss of potency in heat labile vaccines such as measles.

Other perishables (eg drugs and sometimes food & beverages) are frequently stored with vaccines in the same refrigerator. It may, therefore be difficult to maintain optimum temperatures for vaccines with frequent opening and closing. Temperatures can fluctuate from below 0°C to as high as 14°C in a day with normal usage, particularly in the door of the refrigerator.

Some simple practices can protect the vaccines stored in your refrigerator:

- monitor & adjust refrigerator temperatures with the aid of a min/max thermometer placed on the middle shelf;
- only store vaccines on the middle shelves of the refrigerator, never on the door; and
- never store beverages or food in the refrigerator with vaccines.

Please maintain
the
Refrigerator
Temperature at
2-8°C.
Vaccine potency depends on you.

AVAILABILITY AND DISTRIBUTION OF IMMUNOGLOBULIN
(Nan Miller, Senior Project Officer, DCC)

Immunoglobulin is prepared from pooled human blood. The decision to use it should not be taken lightly. Normal human immunoglobulin is available from the hospital pharmacy at no charge. It can be obtained for your patient's contacts by:
1. Telephone request to the pharmacy for pickup by your staff and administration in your surgery.*

2. Prescription for patient to pickup and return to your surgery for administration.*

3. Prescription for patient to pickup for administration at a Community Health Centre.*

Please do not send patients and or contacts to Accident & Emergency for administration of immunoglobulin.

*Alice Springs hospital pharmacy should be advised by phone before sending a patient over with a prescription.

CIGUATERA IN DARWIN FOLLOWING A MEAL OF CORAL TROUT

Angela Merianos¹, Jim Burrows², and Mahomed Patel³.

(¹ NCEPH Epidemiology Registrar, NT Dept of Health and Community Services; ² Physician, Royal Darwin Hospital; ³ Director, Communicable Diseases Centre, NT Dept of Health and Community Services)

Two cases of ciguatera were reported by a general practitioner to the DCC, Darwin, on 18/9/91. The intoxication followed a meal of locally purchased coral trout.

Both patients experienced nausea, vomiting, mild diarrhoea, abdominal cramps, and paraesthesia in the face and extremities. Temperature reversal, manifested as burning of the mouth and skin on contact with cold water, was a prominent and early feature in both cases. It is considered pathognomonic of ciguatera.

The first case developed facial tingling within one hour of eating the fish. Her flatmate, who ate a smaller portion, become symptomatic with vomiting and diarrhoea within 3 hours. She complained of severe myalgia in addition to her other symptoms.

A further case of ciguatera intoxication was identified at the Royal Darwin Hospital in July, 1991. A 23 year old Darwin man was admitted semi-comatose after complaining of a headache and ataxia for one day. He had suffered a head injury 4 days beforehand and a provisional diagnosis of head injury was made. CT scan was normal. His conscious state rapidly improved over 24 hours, as did the hypotension (BP 90/50) and bradycardia (40-50 beats/minute) recorded on admission. No specific treatment was required.

He then complained of oral and extremity temperature reversal, visual blurring and visual hallucination. The ataxia resolved over 5 days. He later recalled a brief bout of diarrhoea and vomiting before onset of the neurological symptoms.

On further questioning he admitted to having spent two weeks living off the land, and his diet had consisted mainly of coral reef fish caught off the Cobourg Peninsula, NT. He had last eaten fish 12-24 hours and chicken 2 hours prior to the onset of his illness.

COMMENT

Ciguatera is a distinctive food intoxication which follows the ingestion of some species of tropical fish. Ciguatoxin is probably produced by the dinoflagellate Gambierdiscus toxicus, an organism at the base of the coral reef food chain. It is a heat-stable toxin which is not destroyed by cooking or freezing.

Clinical disease follows consumption of the larger carnivorous fish such as mackerel, barracuda and coral trout in which the toxin is concentrated. Coral trout (Plectropomus species) was implicated in 27 cases of ciguatera in Queensland between 1965 and 1984 (Gillespie et al., 1986).
Symptoms usually appear between 2 and 12 hours post-consumption, but the delay may be as long as 24 hours. Mild intoxications can occur. The number of unreported cases is unknown. Serious sequelae which can develop quickly include respiratory distress, bradycardia and hypotension, and acute depression. Hospital admission for observation is recommended in the first 24 hours of ciguatera. Marked improvement in symptoms has been reported after early administration of mannitol (Palafox et al., 1988; Pearn et al., 1989).

In the Northern Territory, ciguatera has been associated with fish caught in the Gulf of Carpentaria near Nhulunbuy (Gove), Borroloola, and Groote Eylandt. The principal ciguateric species include Spanish mackerel, barracuda, coral trout, red emperor and some varieties of cod. Ciguateric fish usually weigh over 2.5 Kg. Seven to 10 cases occur each year following consumption of fish caught in these waters.

Physicians in non-endemic areas should consider the diagnosis of ciguatera in patients presenting with acute gastroenteritis associated with neurological symptoms in patients who have recently eaten fish caught in the tropics or northern Australia.

REFERENCES


Editorial Comment

Since publication of this article, two further cases of ciguatera were reported to DCC by another general practitioner. They had bought frozen coral trout fillets from the same outlet as the earlier cases. Environmental Health Officers have taken appropriate action to prevent further intoxications. DCC is interested in hearing about any future cases of ciguatera.

INFORMATION ON COMMUNICABLE DISEASES

DCC has a large collection of educational material for health professionals, community members and patients on most communicable diseases and aspects of control. These are available to all health professionals and the public. The Publication & Research Branch of DH&CS also keeps a catalogue of these publications. For further information, contact Ms Chris Noonan on 228 898.

UPDATE ON HEPATITIS A IN VICTORIA (Attached)

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Editorial Comment

Eastern and Southern State figures reflect a changing pattern and incidence of hepatitis A which is not apparent in the Northern Territory. We are concerned that hepatitis A is underreported, possibly because disease occurs in an earlier age-group than in the other States, and causes non-specific symptoms. Hepatitis A statistics for the Territory will be reported in the next issue.

STOP PRESS: Several reports of cryptosporidiosis have been received recently. Please notify DCC about any unusually high diarrhoeal disease activity in your area.
DIPHTHERIA IN ALICE SPRINGS
Dr Rosie Brennan and Sr Dianne Brookes,
Communicable Disease Control Centre, Alice Springs

16 diphtheria isolates were detected in central Australia between 1/7/91 and 11/6/92. All were Corynebacterium diphtheriae var mitis; 10 wound isolates (not routinely tested for toxigenicity); 4 throat isolates (2 toxigenic); and 2 nasal isolates (both non-toxigenic). Contact tracing is carried out for cases of nasopharyngeal diphtheria.

On 20 May, an 11 year old child presented to the Alice Springs Hospital with a 6 week history of bilateral, purulent and offensive nasal discharge which yielded C. diphtheriae var mitis on culture. She had a past medical history of persistent C. diphtheriae var gravis in 1986.

Initial contact tracing involved taking nose and throat swabs from all household members, classmates, and several teachers. Diphtheria vaccination records were checked and vaccinations updated when required. The girl's mother was a nasal carrier of C. diphtheriae, but none of the other contacts were positive. We then excluded carriage of the organism among the mother's workmates.

The case and carrier had records of primary immunisation with Triple Antigen, including the 18 month vaccination, but neither had a record of subsequent diphtheria boosters.

The index case was given Bicillin AP 2ml IMI on 25 May, and her mother had Bicillin 4ml IMI on 28 May. C. diphtheriae was again isolated from nasal swabs of both cases on 2 June, and we then prescribed a 7 day course of oral erythromycin. The mother's nasal swab was negative on 10 June, but it was still positive in the index case. Further results are pending. On 9 June, CDCC was informed that the original isolates were non-toxigenic.

EDITORIAL COMMENT
C. diphtheriae toxigenicity studies take approximately 10 days, so outbreak control measures must begin while awaiting results. Early recognition of diphtheria is important as the case fatality rate of 5-10% has not changed appreciably in the last 50 years (Benenson, 1990). These recent cases in Alice Springs in which primary diphtheria vaccination was complete, support the need for the 5 year CDT and regular adult immunisation with ADT every 10 years.

Although immunisation against diphtheria confers protection against clinical disease in the majority of people and is strongly recommended.
a recent diphtheria fatality in Darwin in a previously immunised case (NT Communicable Disease Bulletin 1(4):5) demonstrates the need to offer chemoprophylaxis to all contacts regardless of immunisation status; there are other examples in the literature of cases of diphtheria in people with serum antitoxin levels well above the "protective" level of 0.01 units/ml.

What constitutes adequate chemoprophylaxis is unclear. A review of the literature has shown a wide range of recommended antibiotic regimens, eg single dose benzathine penicillin, 14 days of intramuscular procaine penicillin, and erythromycin for 5 to 10 days.

The role of diphtheria in wounds is also unclear, especially when toxigenic strains are found. CDC in Darwin is trying to collect as much information as possible on diphtheria, and would like information on all new cases. Following a comprehensive review on the subject new recommendations for chemoprophylaxis will be published.

REFERENCE

MEASLES IN ALICE SPRINGS
Dr Rosie Brennan, CDC and Dr Peter Tait
CAAC, Alice Springs

Measles cases continued to be reported in Alice Springs during April-June 1992. There were five cases among Aborigines in one town camp (cases 1-5) and two cases among non-Aborigines (cases 6 and 7). Table 1 gives the line listing of the cases.

DISCUSSION
The index case was vaccinated in 1978 when a less temperature-stable vaccine was available, so she may represent either primary or secondary vaccine failure. Her 3 week old infant is a probable case, on epidemiological and clinical grounds.

Case 3 eluded the second measles vaccine but would like chemoprophylaxis will be demonstrated the need to offer chemoprophylaxis to all contacts regardless of immunisation status; there are other examples in the literature of cases of diphtheria in people with serum antitoxin levels well above the "protective" level of 0.01 units/ml.

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DISCUSSION
The index case was vaccinated in 1978 when a less temperature-stable vaccine was available, so she may represent either primary or secondary vaccine failure. Her 3 week old infant is a probable case, on epidemiological and clinical grounds.

Case 3 eluded the second measles vaccination which is the standard measles control measure followed by the Central Australian Aboriginal Congress (CAAC). She also visited a rural Aboriginal community during the infectious period, but due to prompt notification by CAAC, Rural Health staff were able to implement the Measles Protocol quickly and no secondary cases were reported in the rural community.

Case 4 is either a vaccine failure or a coincident mild measles-like illness, with the raised measles IgM due to vaccination.

The severity of Case 5's illness suggested that it was measles, but may have been vaccine-induced measles which is non-communicable, and usually occurs up to 12 days post-vaccination. Measles serology can't distinguish between wild measles and vaccine-induced illness.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Date of Onset</th>
<th>Vaccination</th>
<th>Measles IgM</th>
<th>Communicable with other cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18 yrs</td>
<td>F</td>
<td>1/6/92</td>
<td>MMR 1/3/92</td>
<td>+</td>
<td>Case 2</td>
</tr>
<tr>
<td>2</td>
<td>2 yrs</td>
<td>F/M</td>
<td>5/6/92</td>
<td>NA</td>
<td>NA</td>
<td>Case 1 (mother)</td>
</tr>
<tr>
<td>3</td>
<td>6 yrs</td>
<td>F</td>
<td>16/6/92</td>
<td>MMR age 9/12</td>
<td>+</td>
<td>Cases 1 &amp; 2</td>
</tr>
<tr>
<td>4</td>
<td>8/12</td>
<td>M</td>
<td>3/6/92</td>
<td>MMR 3/6/92</td>
<td>+</td>
<td>Cases 1 &amp; 2</td>
</tr>
<tr>
<td>5</td>
<td>11/12</td>
<td>M</td>
<td>18/6/92</td>
<td>MMR 6/5/92</td>
<td>NA</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>Infant</td>
<td>M</td>
<td>28/4/92 (notified 19/5/92)</td>
<td>NA</td>
<td>LUR</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>15/12</td>
<td>M</td>
<td>7/6/92</td>
<td>MMR IgM</td>
<td>+</td>
<td>No</td>
</tr>
</tbody>
</table>

LUR: unknown
NA: not applicable
ND: not done
MM: measles, mumps, rubella vaccine
MMR: measles, mumps, rubella vaccine
Case 7 serves to emphasize the importance of serology in guiding the extent of measles control measures. On the grounds of contact with case 7, we excluded an unvaccinated 10-month-old child attending the same playgroup, while awaiting his serology result. He proved to be measles IgG positive (ie immune), and this result meant that the contact could return to playgroup within 4 days rather than the recommended exclusion period of 14 days.

ENTERIC DISEASE NOTIFICATIONS IN THE NORTHERN TERRITORY

Epidemiology
Notifications for campylobacter, hepatitis A, salmonella and shigella accounted for 34% of all notifiable disease notifications in 1991 (1320/3838 reports). Salmonella was the most commonly reported enteric infection with an incidence rate of 270 cases per 100,000 (473 reports).

The following tables show case numbers by disease, age group and region, and stratified incidence rates per 100,000. We were unable to stratify by race with any confidence because 41% of notifications failed to specify ethnic group. The figure on page 4 shows the long term trends of salmonellosis in the NT and Australia for the period 1976-90 on a logarithmic scale.

In 1990 the incidence of salmonella, shigellosia and campylobacter infections was 257, 133 and 206 per 100,000, respectively in the NT and 27, 4, and 33 per 100,000 in Australia. The NT rates were 9.5, 33.3 and 6.2 times the national rate for the corresponding infections. There has been little change in the local trends of salmonellosis and shigellosis in the last 12 years; the lower rates in 1976-77 reflect less consistent reporting practices (data not shown for shigella).

56.5% of all notifications for campylobacter, salmonella and shigella involved children aged 0-4 years, and infants aged 0-11 months (2% of the NT population) accounted for 9.5% of reports. The highest incidence rates also occurred in the under 5 year age group (Table 1). Failure to thrive, growth retardation and chronic malnutrition are sequelae of this enteric disease burden in the NT. The second peak in the 20-29 year age group reflects adult infection while rearing young children. The sex ratio in this age group is F: M 1.7:1.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Campylobacter</th>
<th>Hepatitis A</th>
<th>Salmonella</th>
<th>Shigella</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-11 mths</td>
<td>34 (1172)</td>
<td>0 (0)</td>
<td>82 (2828)</td>
<td>9 (310)</td>
<td>125</td>
</tr>
<tr>
<td>1-4 yrs</td>
<td>251 (2083)</td>
<td>13 (108)</td>
<td>187 (1552)</td>
<td>140 (1162)</td>
<td>591</td>
</tr>
<tr>
<td>5-9</td>
<td>25 (179)</td>
<td>5 (36)</td>
<td>20 (143)</td>
<td>24 (171)</td>
<td>74</td>
</tr>
<tr>
<td>10-14</td>
<td>8 (56)</td>
<td>5 (36)</td>
<td>4 (30)</td>
<td>6 (43)</td>
<td>23</td>
</tr>
<tr>
<td>15-19</td>
<td>7 (54)</td>
<td>5 (38)</td>
<td>8 (61)</td>
<td>11 (84)</td>
<td>31</td>
</tr>
<tr>
<td>20-29</td>
<td>28 (850)</td>
<td>20 (61)</td>
<td>29 (880)</td>
<td>47 (143)</td>
<td>124</td>
</tr>
<tr>
<td>30-39</td>
<td>24 (83)</td>
<td>17 (59)</td>
<td>26 (90)</td>
<td>45 (156)</td>
<td>112</td>
</tr>
<tr>
<td>40-49</td>
<td>6 (35)</td>
<td>0 (0)</td>
<td>17 (99)</td>
<td>17 (99)</td>
<td>40</td>
</tr>
<tr>
<td>50 and over</td>
<td>13 (75)</td>
<td>7 (40)</td>
<td>91 (522)</td>
<td>39 (224)</td>
<td>150</td>
</tr>
<tr>
<td>Unknown</td>
<td>14</td>
<td>2</td>
<td>9</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>410 (234)</td>
<td>74 (42)</td>
<td>473 (270)</td>
<td>363 (207)</td>
<td>1320</td>
</tr>
</tbody>
</table>

*The numbers in parenthesis are the incidence rates per 100,000.

Regional differences (Table 2) may reflect true differences, eg. unrecognized local outbreaks, but are influenced by laboratory and doctor notification practices, different laboratory protocols, eg. the Alice Springs Hospital laboratory routinely plates all faecal specimens for Campylobacter, criteria for stool collection, and patient recognition of and attitudes towards milder forms of diarrhoea.
Hepatitis A

Hepatitis A is under-reported in the Northern Territory (42 per 100,000). This probably results from earlier acquisition of the virus, and missed diagnoses of very mild clinical and subclinical disease in young children. Conversely, the transient nature of the NT adult population means that we have a constant influx of non-immune adults from low prevalence states, with the potential for large scale outbreaks. The national rate for hepatitis A in 1990 was 3 per 100,000.

Hospital with diarrhoeal disease and tested on 3 consecutive days, 75% of stool cultures were negative (Dr A Ruben, unpublished data).

As part of our activities to improve the control of communicable diseases in the NT, Communicable Disease Officers (CDOs) are contacting doctors to collect further information on the contact tracing carried out for priority diseases with outbreak potential (eg. the enteric and vaccine preventable diseases) and/or which require counselling (eg. hepatitis B, hepatitis C, and the sexually transmissible diseases).

Key issues in enteric disease control

Does the patient work as a food handler, health care or child care provider?

If a young child, is the child toilet trained, and does the child attend a creche, day care centre, pre-school or play group?

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**Table 2: Case numbers and incidence per 100,000* of the notifiable enteric diseases by region, NT 1991.**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Alice Springs</th>
<th>Barkly</th>
<th>Darwin</th>
<th>East Arnhem</th>
<th>Katherine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campylobacter</td>
<td>245 (958)</td>
<td>19 (546)</td>
<td>143 (183)</td>
<td>0 (0)</td>
<td>3 (32)</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>1 (4)</td>
<td>7 (201)</td>
<td>48 (61)</td>
<td>5 (106)</td>
<td>13 (139)</td>
</tr>
<tr>
<td>Salmonella</td>
<td>80 (313)</td>
<td>15 (431)</td>
<td>294 (376)</td>
<td>41 (868)</td>
<td>43 (459)</td>
</tr>
<tr>
<td>Shigella</td>
<td>151 (590)</td>
<td>31 (891)</td>
<td>126 (161)</td>
<td>21 (444)</td>
<td>34 (363)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>477</strong></td>
<td><strong>72</strong></td>
<td><strong>611</strong></td>
<td><strong>67</strong></td>
<td><strong>93</strong></td>
</tr>
</tbody>
</table>

*The numbers in parentheses are the incidence rates per 100,000.*

**Surveillance**

Our enteric disease notifications under-estimate the true diarrhoeal disease problem in the NT, focusing only on some bacterial pathogens. Asymptomatic carriage and excretion of enteric pathogens are important in maintaining transmission. Single stool examinations are insensitive in diagnosis, and the early use of antibiotics further reduces isolation rates. In a survey of children admitted to the Royal Darwin Hospital with diarrhoeal disease and tested on 3 consecutive days, 75% of stool cultures were negative (Dr A Ruben, unpublished data).
Does the patient attend an institution (educational or residential)?

Has the patient travelled overseas or interstate?

Is there known contact with other cases of diarrhoea?

(Recent outbreaks of hepatitis A in gay men in NSW, Victoria and SA may make sexual preference/practices relevant when investigating HAV).

Guidelines for the period of exclusion of children from day care and educational facilities and adults from high risk occupations have been circulated to all doctors, Community Health Centres and the Education Department in the NT. CDC recognises the difficulties doctors and parents confront when a child is excluded from their day care centre or school, but our data clearly indicate the need for adherence to exclusion guidelines.

We are also planning to adopt the initiatives introduced in NSW where doctors notify “food borne illness in two or more related cases” and “gastroenteritis among people of any age in an institution”.

We request that doctors indicate on the notification form the patient’s risk group for enteric disease transmission, and whether they have carried out contact tracing and hygiene education or prefer that a CDO is involved. These details will prevent duplication of control efforts and unnecessary phone calls to doctors.

GONOCOCCAL CONJUNCTIVITIS OUTBREAK IN AN ABORIGINAL COMMUNITY

Kate Monger RN and Dr Rosie Brennan

20 cases of clinical gonococcal conjunctivitis occurred in a central Australian Aboriginal community from 21 April - 11 May. Active surveillance commenced in the community, all cases had a swab and smear taken and were treated with procaine penicillin or oral amoxycillin according to the CARPA (Central Australian Rural Practitioners Association) protocol for gonococcal conjunctivitis, and with tetracycline ointment.

18 cases were in children less than 15 years, with a range of 6 months - 9 years. At least 50% of cases occurred in children aged 0-4 years. There was no gender-related difference in case numbers. Eight cases were culture-confirmed N. gonorrhoeae, with one bacteriologically proven reinfection after treatment.

Early implementation of control measures prevented further cases after 11 May.

In the figure, "clinical cases" include cases in which culture yielded another organism which may or may not have caused the conjunctivitis.

EDITORIAL COMMENT

Control measures include screening of affected families, especially children. Comprehensive contact tracing including history of travel to other communities, community gatherings and significant social events; hygiene education; and possible use of insect repellants/flyscreens.

Epidemiological treatment of household contacts with an appropriate antibiotic is effective in localised outbreaks.

Clinic staff should collect a conjunctival smear and swab for culture from all patients presenting with purulent conjunctivitis. STD screening of adults should also be considered especially if cases are sporadic.

Table 1

<table>
<thead>
<tr>
<th>Conjunctivitis outbreak: central Australia</th>
<th>21 April - 11 May 1992</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>---------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>culture +</td>
<td>clinical cases</td>
</tr>
<tr>
<td>N. gonorrhoeae</td>
<td></td>
</tr>
</tbody>
</table>

21 22 23 24 25 26 27 28 29 30 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
INFECTIONOUS DISEASE UPDATES

Meningitis in Nhulunbuy
Harley Dentith and Jane Donaldson,
Communicable Disease Officers,
East Arnhem Region

Two further cases of serogroup C meningococcal meningitis have occurred in Aboriginal communities near Nhulunbuy. This brings the total to 6 cases since 30 September 1991 (NT Compr Dis Bull 1 (4): 6); and the number of confirmed serogroup C isolates to four. There was no confirmed contact between these last 2 cases, though they lived on adjoining beach camps, nor with earlier cases.

The first case was a 3 year old child admitted to the Gove District Hospital on 18 May, with a history of fever, tiredness and irritability. Her clinical condition deteriorated rapidly, and she was transferred to the RDH on the following day. Her blood culture subsequently grew Neisseria meningitidis. She made an uneventful recovery.

The second child, aged 10 years, was admitted on 20 May after a two day history of fever and malaise. His level of consciousness was clouded on admission with signs of cerebral irritation, he was shocked and required ventilator support. He died of overwhelming meningococcal infection within 48 hours of admission.

Chemoprophylaxis with either rifampicin or ceftriaxone was given to all contacts, and Mencevax AC vaccine was administered to children aged 1-15 years in the affected communities. There have been no further cases.

REFERENCES


RDH INVESTIGATION OF UNDIAGNOSED FEVER
Dr Dale Fisher, Infectious Diseases Registrar, Royal Darwin Hospital

The Royal Darwin Hospital Department of Medicine is attempting to better elucidate causes of undiagnosed fever in patients presenting to the public or private hospital Accident and Emergency Departments or to general practitioners. It is of particular interest if the patient gives a history of recent tick or mosquito bite. Please contact Dr Dale Fisher or Dr Bart Currie at the Royal Darwin Hospital, telephone 22 8888, who will help arrange for appropriate specimens to be taken and a short questionnaire to be completed. Over the next 6 months we hope to better understand the spectrum of disease and the incidence of various viruses, rickettsia, leptospira etc and the possible existence of lyme disease and ehrlichiosis in the Northern Territory.

In the next edition of the Bulletin, we will publish details of the current viral meningitis outbreak in Darwin.

VISITING LECTURER
Dr Michael Lane, a WHO consultant with the National Centre for Epidemiology & Population Health at the Australian National University, will be visiting Darwin in July. He will be giving the following talk.

"Expert Error in the Third World or Why Not to Trust Professors"
(RDH Auditorium
Monday 20 July at 12.00 PM.)

All are welcome.

NOTIFICATION OF HEPATITIS C

CDC received 10 laboratory reports of positive Hepatitis C (HCV) serology in 1991, and 17 from 1 January - 18 June this year (6 in June). Recent media attention has increased public
awareness of HCV, and we anticipate the increase in pathology requests to escalate.

HCV is a notifiable disease in the NT (formally reported as "hepatitis - other"). The NT blood transfusion service maintains a database on HCV positive donors, but in order to establish surveillance of HCV in the NT community, CDC would appreciate the following patient history on notification forms.

* **risks category**  
  - post transfusion  
  - haemophilia  
  - injecting drug user  
  - homosexual contact  
  - heterosexual contact  
  - biohazard injury  
  - perinatal transmission  
  - other/unknown

* **evidence of acute hepatitis**  
  - clinical  
  - biochemistry  
  - liver biopsy

* **reason for HCV testing**  
  - acute hepatitis  
  - screening including partner notification  
  - self referral  
  - biohazard injury  
  - unexplained abnormal LFT's

For the purposes of patient confidentiality, the patient identification system used for HIV/AIDS notifications may be preferable to doctors.

**Personal identifiers:**

* first two letters of the last name and first two letters of the first name;  
* date of birth;  
* gender;  
* and postcode or suburb

This will enable us to exclude patients previously notified.
Chapter 3

3 EPIDEMIC BARMAH FOREST AND ROSS RIVER VIRUS DISEASE IN EAST ARNHEM NORTHERN TERRITORY

3.1 Aims of the report

3.2 Arbovirus surveillance in the NT

3.3 The Barmah Forest virus

3.4 Transmission cycle

3.5 The Nhulunbuy outbreak

3.5.1 Background

3.5.2 Topography and mosquito control measures

3.5.3 Events leading to the field investigation

3.5.4 The field investigation

3.5.5 Logistics

3.5.6 Conclusions

3.5.7 Reports written during the outbreak investigation

Attachments A-E
Chapter 3

EPIDEMIC BARMAH FOREST AND ROSS RIVER VIRUS DISEASE IN EAST ARNHEM, NORTHERN TERRITORY

AN OUTBREAK INVESTIGATION

3.1 Aims of the report

The aims of this report are to:

1. chronicle an outbreak investigation of an initially unknown disease;
2. provide insight into the "behind the scenes" administrative and logistical issues that accompany such an investigation; and
3. discuss lessons learned during the investigation.

3.2 Arbovirus surveillance in the Northern Territory

Outbreaks of disease caused by mosquito-borne viruses have resulted in considerable morbidity in the Northern Territory. The northern region is receptive to a number of mosquito vectors and arboviruses which have been implicated in human disease. The Disease Control Program and the Medical Entomology Branch of the NT Department of Health and Community Services in collaboration with the Berrimah Agricultural Research Laboratory and the NT Quarantine and Inspection Service of the Department of Primary Industries and Fisheries, have set up active and passive surveillance systems to monitor disease incidence, local and imported vectors, and mosquito-borne viruses.

CDC maintains passive surveillance through the laboratory based notification system, but has recently taken over the follow-up of cases notified by medical officers through the NT Arbovirus Disease Surveillance Program established by the Medical Entomology Branch in 1980. Cases are contacted to determine as accurately as possible the probable site and date of infection to facilitate vector control measures. In 1992, Drs Patel and Currie, Mr Peter Whelan and I met to discuss the surveillance program and
ways to improve its efficiency. Medical Entomology recorded only cases of Ross River virus infection for which the attending medical officer had returned an Arbovirus Reporting Form while CDC also included cases in which only laboratory reports were available. This resulted in a discrepancy of almost 200 cases between the two systems and an obvious duplication of services. The Communicable Diseases Officer who has taken over data entry and follow-up consults with me about any case in which the history of exposure and illness onset is contradictory and in all cases of dengue fever (refer to Chapter 1 "The interpretation of dengue virus serology").

The Medical Entomology Branch also carries out a number of regular entomological surveys in Darwin, in the vicinity of the principal towns and in important recreation areas. The Berrimah Agricultural Research Laboratory carries out the viral isolations from mosquito pools sorted to species by the entomologists. The NT Quarantine and Inspection Service monitors potential routes of vector importation to prevent the re-introduction of *Aedes aegypti* from northern Queensland or the introduction of *Ae albopictus* larvae in tyres imported from South East Asia.

Ross River virus infections cause most human disease (epidemic polyarthritis, EPA) in the NT. During the 1990-91 wet season a record 499 cases were reported by doctors and laboratories as far south as Alice Springs. Approximately 40% of sera tested at the Menzies School of Health Research laboratory from patients who presented with acute polyarthritis during this outbreak were negative for RRV antibodies (Dr Keat Song Tai, Menzies School of Health Research; MPH treatise). These sera have now been sent to a reference laboratory interstate for testing by a panel of arbovirus antigens. Over 100 arbovirus isolates cultured at the Agricultural Research Laboratory remain unidentified (Mr Richard Weir, Agricultural Research Laboratory; personal communication), and their role in seronegative polyarthritis is unknown.

The flaviviruses Murray Valley encephalitis virus, kunjin and dengue fever virus, are potentially important arboviruses in the NT. Sporadic cases of Australian Encephalitis, caused by central nervous system infection with either MVE virus and
possibly kunjin virus, have occurred in the northern region; all were attributed to MVE. None of the cases of dengue fever reported in the NT are locally acquired; the last indigenous case of dengue occurred in 1955.17

### 3.3 The Barmah Forest virus

The Barmah Forest virus (BF) is a little known mosquito-borne alphavirus, first isolated from the mosquito *Culex annulirostris* (the "common banded mosquito") in northern Victoria in 1974. The virus was first reported as a human pathogen in 1988, and has been successfully cultured from the blood of a patient. Clinical and sub-clinical infections occur, but clinical and epidemiological information is limited.18-19 The ratio of subclinical:clinical infections is unknown. The largest case series reported in the literature describes only 29 patients.

The duration of symptoms is unknown, but infection with BF is thought to be generally mild. Long term sequelae have not been reported, but 10 of 19 patients reviewed eight weeks after the onset of symptoms in the Queensland study continued to report symptoms.19

The serosurveys in NSW and Queensland have found seropositivity rates of 2-13%. In Queensland, an estimated 0.23% of the resident population becomes infected with BF annually. Both studies report a male:female ratio of 1.5:1.18,19

In the Northern Territory, testing polyarthritis patients for BF was not started until the Nhulunbuy outbreak in February 1992.

The mosquitoes *Culex annulirostris* and *Aedes vigilax* (the "salt marsh" mosquito) are the common vectors of Ross River virus in the Northern Territory. Barmah Forest virus has been isolated from both vectors, suggesting a common ecology and distribution. The first BF isolation in the NT was from mosquitoes caught in Mataranka in 1986. Since then there have been isolations most years (Mr Richard Weir, personal communication).
3.4 Transmission cycle

The sylvatic cycle of RRV involves native mammals such as macropods and native rodents. Domestic animals, especially dogs, can also act as reservoirs of infection. Occasionally transmission can occur as mosquito-man-mosquito cycles, as believed to have occurred in the epidemic of RRV which started in Fiji and swept across the western Pacific. Mammals are also thought to be the reservoirs of Barmah Forest virus.

3.5 THE NHULUNBUY OUTBREAK

3.5.1 Background

Nhulunbuy is the largest community on the Gove Peninsula in the East Arnhem region of the Northern Territory. It is a mining community of approximately 3600 people, most non-Aboriginal. The largest Aboriginal community of 250 people is Yirrkala situated approximately 12 kilometres outside of Nhulunbuy. A small number of non-Aboriginals also live in Yirrkala. Residents are mainly employees of the Nabalco alumina mine, public servants, or are self-employed in small business. The Gove District Hospital (GDH) is the regional hospital for the East Arnhem health district. Three full-time Communicable Disease Officers work out of GDH and are ultimately responsible to the East Arnhem District Manager, Mr Ted Hobson and to the Disease Control Program.

3.5.2 Topography and mosquito control measures

The town is surrounded by salt marshes and swamps; the mosquito monitoring and control program is jointly funded and staffed by the Nhulunbuy Town Council and Nabalco.
Weekly mosquito trapping using CO₂ traps is conducted throughout the year in four sites at the periphery of the town. These mosquitoes are counted and pooled by species. Monitoring is intensified during high tides and after heavy rains.

3.5.3 Events leading to the field investigation

On Friday 7 February 1992, Dr Paul Spillane at Gove District Hospital alerted Dr Patel in Darwin of a cluster of 6-7 patients presenting with an acute onset of lethargy, fatigue, rash and fever. Dr Spillane knew about CDC’s involvement in the investigation of measles and melioidosis in 1991. He was concerned that Nhulunbuy was experiencing an outbreak of measles but as all the cases were adults, Dr Patel thought this highly unlikely. As Dr Patel was tied up in a workshop that afternoon he delegated the responsibility of making further inquiries to me. I called the single private practice in Nhulunbuy and spoke to Dr Max Chalmers who is also the medical officer for Nabalco. He had seen another 5-6 cases with similar histories and clinical features, which he described as a “quite severe viral illness” with fever, severe malaise, headache, myalgia and rash. The rash was not pruritic and consisted of discrete red papules on the dorsum of the hands and feet, sometimes with a white halo. None of his patients complained of arthralgia, nor did they complain of respiratory symptoms. Dr Chalmers also stated that he had seen a case of confirmed Ross River virus and two other patients who complained of prodromal symptoms similar to RRV. He commented that mosquitoes were biting voraciously throughout the day.

All of the early patients were non-Aboriginal; all but one were adult. Dr Bart Currie was conveniently in Nhulunbuy on a routine clinic visit and was able to examine four of the patients. Bart gave a differential diagnosis of enterovirus, adenovirus or arbovirus infections and instructed the Gove District Hospital Outpatients’ staff to collect nasopharyngeal or throat swabs, urine, faeces and serum for viral studies.

I developed and faxed a preliminary questionnaire (Attachment A) to the Communicable Disease Officers (CDOs) and to the private practitioners in Nhulunbuy that afternoon.
This questionnaire included demographics, clinical questions appropriate to the
differential diagnosis, the names of symptomatic contacts, and history of travel and
mosquito exposure. Before finalising the questionnaire, I called Peter Whelan to brief
him on the events in Nhulunbuy and to obtain a list of questions relevant to a
mosquito-borne virus outbreak.

I rang Dr Spillane on Monday 10 February; he was unaware of any new cases but
had reviewed some of the patients whose rash had become florid. None of the cases
had required hospital admission.

3.5.4 The field investigation

Confirmation of the outbreak

By 11 February approximately 20 cases had presented to GDH. Mahomed Patel and
I held a teleconference with Mr Hartley Dentith, the Senior CDO, who confirmed that
there had been an explosive increase in the number of mosquitoes and that residents
complained of being bitten throughout the day. Hartley also stated that some of the
more recent cases were complaining of arthralgia.

Even at this early stage, there was mounting evidence that this was an arbovirus
outbreak. I checked the January 1991 Nhulunbuy notifications for mosquito-borne
viruses and found that only four cases had been reported (12 only for January
through March 1991). There had been a small outbreak of 16 cases of RRV in 1988-89.
Mahomed Patel and I invited Bart Currie and Peter Whelan to a meeting that
afternoon to discuss a plan of action. Peter had already made arrangement to fly to
Nhulunbuy the next day to conduct an entomological survey. Bart had made
arrangements with Dr David Smith, Director, State Health Laboratory Services in
Perth to screen acute and convalescent phase sera using a rapid IgM test for a panel
of mosquito-borne viruses (Ross River virus, Barmah Forest virus, Murray Valley
encephalitis virus, kunjin, sindbis, chikungunya and Semliki Forest virus). Mahomed
and I agreed that I would take on the responsibilities of principal investigator for the
epidemiological investigation and that I would visit Nhulunbuy the next day to make a rapid assessment of whether a large scale investigation was necessary. Nhulunbuy's small population meant that word of the unexplained illness was already circulating in the town, so public concern was an incentive to quickly determine the cause.

Case ascertainment

Once in Nhulunbuy my initial aims were to produce a line listing of cases who had completed the questionnaire, develop a case definition, and commence active case finding and specimen collection. I used a sensitive case definition of rash, fever, arthralgia or arthritis to identify both cases of arbovirus infection and respiratory viruses.

Nursing administration assigned Sr Anne Marie McFarland to assist me with the preliminary investigation as the CDOs were short-staffed. We agreed that Anne Marie would assist the Accident and Emergency staff to assess patients presenting with compatible symptoms, ensure that all new cases completed the questionnaires and collect all pathology specimens. We identified cases prospectively through the Accident and Emergency unit of GDH and retrospectively from audits of the logs of pathology requests at the GDH and the private pathology service. Dr Chalmers gave me permission to send his patients' stored sera to the Perth State Health Laboratory. We asked school nurses at the Nhulunbuy Primary and High schools about any increase in absenteeism, and the nursing staff of the Laynhapuy Homelands Health Project, who also provide health care in Aboriginal outstations, about any increase in attendance, especially of patients presenting with rash, unexplained fever, arthralgia or arthritis. There had been no increase in absenteeism in the primary school. Some high school students were symptomatic and were referred to GDH for examination. There was no suggestive illness in the Aboriginal communities, but a small number of young children under five years of age presented with a febrile illness which settled on antipyretics. No sera are available from these
children. We also contacted the health services in Groote Eylandt and Elcho Island to examine their records for patients fulfilling the case definition.

Data collected in the first three days of the field investigation (12 - 14 February) strongly supported an arbovirus outbreak. By 12 February we knew that cases started to appear at the end of January. All were non-Aboriginal, some were children (median age 31 years, range 2-58) and the sex distribution was equal (nine females and 11 males). Most cases lived in the north end of town near the swamps. A history of mosquito bites was universal. Our contact tracing showed no evidence of person to person spread; there was no significant household clustering, very few symptomatic children, unusual in an outbreak of adenovirus or enterovirus infections, and we learnt that there were no cases in the class of a symptomatic teacher. The age distribution and season was against classical enterovirus disease which occurs in the dry season in the NT.

I attempted to estimate the incubation period by identifying cases who had travelled outside Nhulunbuy. We knew of one child whose family had moved to Nhulunbuy three weeks before he became ill, but questioned whether the illness in the children was the same disease as that of adults.

By 13 February I had established that there were two main presentations: acute arthralgia or arthritis with or without an upper respiratory tract infection; or a milder flu-like illness. A rash was present in most cases but ranged in appearance from a faint macular rash to papulovesicular. The vesicular rashes were usually pruritic or painful. There was no desquamation, no enanthem, and involvement of the palms and soles was variable. The weight bearing joints and hands were most commonly affected, but clinical improvement was quite rapid. Some patients complained of extreme fatigue. The frequency of symptoms in the first 20 cases was: fever 45%; fatigue 80%; rash 90%; arthralgia 55%; arthritis 30%; and pharyngitis 30%.
Entomological studies

The aims of the entomological investigation were to:

1. trap and pool mosquitoes by species (an additional four traps were set up for this purpose);
2. prepare the mosquito pools in liquid nitrogen for viral isolation studies;
3. review the mosquito surveillance program in Nhulunbuy in consultation with the Town Council's environmental health officer and the Nabalco representative;
4. step up fogging and larviciding activities to reduce mosquito density rapidly.

Approximately 2000 mosquitoes were trapped and sent to the Berrimah Agricultural Research Laboratory. The team identified breeding sites, including a large man-made pool used as a run-off by the mine which required a landfill, initiated larviciding and fogging and recommended improvements in the surveillance system. *Aedes vigilax*, considered to be at pest levels at 60 mosquitoes per trap, was the dominant species. A later significant rise in *Culex annulirostris* contributed little to the epidemic as it occurred after the peak period of transmission. The extremely high mosquito numbers were attributed to coincident "king" tides and heavy rainfall.

Developing a plan of action - Monday 15 February

After I discussed the preliminary findings with Dr Mike Lane on 13 February, Dr Tony Watson, MAE student in Hobart, was seconded to CDC to assist in the investigation. Drs Mahomed Patel, Bart Currie, Mike Lane, Tony Watson, Mr Peter Whelan (Senior Medical Entomologist) and I participated in a teleconference on 15 February to discuss the epidemiological and entomological data and formulate investigation priorities and strategies. Peter reported that *Aedes vigilax* had peaked during the interval 29 January to 5 February and *Culex annulirostris* numbers had also increased to pest
levels. The hatch in January was a result of high tides and the recent hatch was due entirely to rain. He expected another hatch to reach adulthood on 19 February. Results of the live cell culture from the mosquito pools were expected in two weeks.

We had lengthy discussions about the collection, storage and transportation of sera for viral isolation and serology, which in the early stages was co-ordinated by Dr Currie. He advised us on the type and number of sera aliquots needed for the various tests. It quickly became apparent that we would need laboratory support in Darwin and supernumerary laboratory staff in Nhulunbuy which I was to organise with Ted Hobson and Mr Gabe Schraven, the GDH laboratory Director. The stored sera made available through Western Diagnostic Pathology had not been tested as the laboratory was waiting for the convalescent phase specimen.

Working on the assumption that this was a mosquito-borne virus outbreak, we agreed upon the need for a serosurvey of adults to determine the prevalence of arboviral diseases, seroconversion rates, the clinical spectrum and estimate asymptomatic transmission rates. Mike Lane stated that a convenience sample of volunteers could be used as the mosquito exposure appeared universal. We agreed upon animal trapping to identify reservoirs. We also discussed the possibility of a serosurvey in Yirrkala, or the testing of historical sera to date the introduction of BF into Nhulunbuy. Blood collection from healthy Aborigines was felt to be unjustified on ethical grounds at the time. An important reservation to the serosurvey was the possibility that the panel of arboviruses used in Perth would fail to identify the causative agent, injuring the Department’s credibility with the community.

Testing of the historical sera, some collected from patients presenting with seronegative acute polyarthritis, is likely in the foreseeable future. We conducted the first serosurvey from 22 - 26 February.

Dr Patel had informed media that the outbreak was probably mosquito-borne and stressed the importance of preventing mosquito bites.
Confirmation of a Barmah Forest virus outbreak - Friday 21 February

Mosquito-borne disease was confirmed on 21 February when 5 of 18 sera tested from both acute and convalescent cases proved positive for BF, and other sera were RRV IFA-IgM (Immunofluorescent Antibody) positive. Attempted viral isolation from nasopharyngeal swabs, stool and urine cultures was unsuccessful; collections of these specimens stopped after the first week of the investigation. BF was later isolated from a pool of Aedes vigilax and RRV from Culex annulirostris.

Developing a more specific case definition

We identified a total 187 cases with a rash, arthralgia and/or polyarthritis from 1 December to 31 March.

Once serological results became available I sought to categorise cases as confirmed, probable or suspected. Barmah Forest virus is regarded as antigenically distinct from other alphaviruses so we assumed that HI (Haemagglutination Inhibition) and IFA-IgM (indirect fluorescent antibody-IgM) tests had adequate specificity for this virus.\(^\text{18}\) RRV is antigenically related to sindbis. I initially classified cases as confirmed cases of Barmah Forest virus or Ross River virus if there was a four-fold rise in HI titre and/or a positive IFA-IgM, and all other adult cases as probable. Symptomatic children from whom we did not collect blood were regarded as suspected cases. The antigenic uniqueness of BF was challenged when neutralisation tests conducted by the State Health Laboratory Services in Perth on sera positive to sindbis virus and BF and/or RRV on IFA-IgM and HI proved that cross-reactions between BF and sindbis virus and RRV and sindbis had occurred against expectation. Another shortcoming in defining an acute infection on the basis of circulating IgM was the paucity of data on the persistence of antibody. Some of our IgM-negative cases with an high HI titre gave illness histories consistent with infection during the outbreak.
After a fortuitous meeting and tutorial in the interpretation of alphavirus and flavivirus serology with Dr Charlie Calisher from the Division of Vector-Borne Diseases, National Center for Infectious Diseases, Centers for Disease Control, Fort Collins, Colorado, I have reclassified cases on the basis of IgM positivity and HI titre levels. I also arranged ELISA (enzyme-linked immunosorbent assay) testing of a cross-section of our stored sera at Westmead Hospital in Sydney.

**Patient follow-up**

Since 7 February, most patients suspected of arboviral infection completed the basic questionnaire. Sr McFarland was seconded to the investigation until October to continue active case finding, collect acute and convalescent sera, and follow patients up weekly for the first month and then as often as possible until they became asymptomatic. Assigning a local research officer with whom patients could identify proved invaluable in ensuring continuing co-operation and providing timely feedback to the community.

In July I sent a follow-up questionnaire to all patients, with a letter explaining the redundancy of some of the questions (Attachments B1 and B2). Sr McFarland contacted most patients by phone to tell them about the questionnaire, and to ask them whether they would consider a third blood test during my visit on 19 - 22 August. The response to this follow-up was disappointing as only 49% of patients returned questionnaires. Most of the respondents did agreed to venepuncture, and all but one of the persistently symptomatic people were willing to complete another questionnaire in 2-3 months time. Collecting blood from children using finger prick on this occasion meant that some mothers agreed to return for a first or convalescent sample.

**The serosurvey**

From 22 - 26 February, we collected blood from 247 mainly adult volunteers who were either asymptomatic, or had minor symptoms which did not fulfil our case
definition. From 22 - 27 April we collected second serum samples from 178 people (72%) and first sera from another five volunteers. Participants completed clinical questionnaires on both occasions. Demographic data, including duration of residence in Nhulunbuy, were included in the first questionnaire.

3.5.5 Logistics

Publicity

CDC adopted a proactive role in dealing with the NT press throughout this outbreak. In Darwin, an NT-wide press release on 21 February announced the serological confirmation of a concurrent Barmah Forest and Ross River virus outbreak, and the intention of CDC to undertake active surveillance of BF disease in Darwin.

In Nhulunbuy we used the local newsletter, Arnhem Courier, which is distributed weekly, to call for the serosurvey volunteers, provide updates of the analysis, and to notify patients of the follow-up study in August (Attachment C). I collaborated closely with Hartley Dentith over publishing deadlines of the Arnhem Courier to ensure that our advertisements and updates were in general circulation well before proposed follow-up visits. During my August visit, the Alice Springs office of the ABC broadcasting to Nhulunbuy also interviewed me about the objectives of the trip and our findings.

Before each field trip I prepared poster-size notices giving details of the venue and hours during which we would be available to interview people and collect blood. These were posted on the public notice boards around the town, in the various social clubs (the Yacht and Surfing Clubs, Rotary and Apex) and in the hospital. Ted Hobson approved a mail drop to all private post boxes of letter sized copies of the notice asking for serosurvey volunteers. This occurred within 24 hours of request. The Occupational Health Officers at Nabalco posted the serosurvey notices in the company's buses, and in the tea rooms at the mine and refinery; they invited us to collect blood in their office during the second serosurvey.
Feedback

Cases

We notified the earliest confirmed BF and RRV cases of their results by phone on 21 February before the media were informed. As later results reached Darwin, I entered them in a computerised database and informed Sr McFarland by telephone or facsimile. I also sent her updated hard copies of results upon request. She gave patients their results by phone or during follow-up visits, and sent them a written interpretation of the result which I prepared. The letter was especially useful when notifying patients who were seronegative on paired sera. When most of the results were available, I generated individual reports of serology for placement in the patients' medical records.

During my field trip in August, Sr McFarland arranged interviews with patients whose concerns she felt unable to address.

Volunteers

All volunteers received their result in writing, with an appropriate interpretation, and an arbovirus disease prevention message (Attachments D1-4). I included a photocopy of the pathology form in the letter if the result indicated recent or past infection with BF, RRV (or sindbis virus), and I sent out a follow-up questionnaire to volunteers in whom infection was recent. As we tried to provide results in a timely fashion, a small number of false positive sindbis results were mailed. The acceptability of this system of notification was evident by the small number of inquiries for clarification directed at the CDOs.

We also organised a public meeting during the August visit in the form of a short presentation followed by an open forum; this was poorly attended but useful as an indicator of waning public interest, and more importantly, waning concern by patients themselves.
Health care providers and administrators in Nhulunbuy

Reports were distributed to the District Manager, GDH Medical Superintendent, CDOs, and Director, CDC, before leaving Nhulunbuy on the first two occasions, and after returning to Darwin in September. I visited the Nabalco plant in April to meet with the Occupational Health Officers and discuss my findings. They were also interested in the relationship between the incidence of musculoskeletal symptoms among employees and Ross River virus as their data for 1990-91 indicated increases during the wet season. Mr Joe Coope subsequently provided me with data on absenteeism during the outbreak and the corresponding time in 1991.

Other oral and written presentations

We published a preliminary report in the *Communicable Diseases Intelligence* 1992; 16(6):110-111. I presented the clinical and entomological findings to the staff of the virology and serology laboratories during a visit to the Perth State Health Laboratories in June. This visit was funded by the National Communicable Diseases Network as an opportunity to see the process of serological testing first-hand, to meet our collaborators and to present the data to the laboratory staff. Prof John Mackenzie, Department of Microbiology, QE II Medical Centre, WA, asked our permission to present our preliminary findings at an arbovirus symposium in St Petersburg in July. These data have also been presented by Drs Mike Lane and Aileen Plant in the ACT.

Staffing and consumables

Staffing issues were discussed at the planning stage of the serosurvey. Nursing Administration in Nhulunbuy released Sr McFarland to act as research assistant for the duration of the investigation. We negotiated a limited tenure position for a laboratory technician in Nhulunbuy to process sera for transportation to Darwin. Both these positions were CDC funded. CDC laboratory staff agreed to aliquot sera for testing in Perth and storage at -70°C in Darwin. Gove District Hospital administration also
provided clerical support for the two serosurveys and for the third blood collection from patients. Dr Patel encouraged me to take the administrative role in Nhulunbuy, and to decide on the level of staffing required. This meant liaising with the CDC Administrative Officer to organise their payment.

I attempted to take all blood collection consumables with us on each occasion, as well as an adequate supply of questionnaires. During the first serosurvey we were unprepared for some of the supplies required by the laboratory to aliquot sera; we developed a comprehensive list of consumables for the repeat serosurvey.

**Problems encountered and lessons learned**

**Co-ordination of activities and the role of the principal investigator**

One of the most important lessons I have learnt from this investigation is the need to carefully brief all members of the research team about the objectives of the study and their specific role, especially if they have had no previous experience in research methodology. I failed to adequately instruct our research assistant in Nhulunbuy of her priorities when interviewing patients, so she misinterpreted the focus of the follow-up interviews which was to establish the duration of Barmah Forest virus symptoms, and instead adopted a more clinical and service delivery role. This has slowed collection of crucial data, resulted in lost data as a number of patients have left the community or are lost to follow-up, and caused dissatisfaction in both parties.

We had some significant delays (months) in the testing of both acute and convalescent sera collected from some patients because we failed to chase missing results. We assumed that the sera had arrived in Perth, only to find them stored in both Nhulunbuy and Darwin. The investigation team has lost some credibility with these cases, and this may have resulted in their refusal to be further involved.
Problems with questionnaires

Because the original questionnaire was produced in a few hours and included non-specific questions, we omitted important questions in arbovirus surveillance. An important omission was a postal address, as there is no mail delivery to residential addresses in Nhulunbuy. Unfortunately, the senior CDO who normally briefs us about local conditions and requirements in this region was unavailable on the day. We have attempted to rectify these deficiencies in subsequent interviews. Conversely, some of our questions proved irrelevant. Our haste also meant that we failed to proof read the first serosurvey questionnaire, and missed errors in the format of entry fields. These errors were not detected until I began to analyse the data, and could only be corrected by editing the questionnaire and then re-entering all data in those fields eg fields requiring a numeric format created as alphanumeric variables.

We were unable to supervise patients as they completed the questionnaire, so some of the data were missing and some answers required clarification.

We failed to co-ordinate our allocation of unique identification numbers between the cases and serosurvey volunteers. Both groups started at number one, and caused some initial concern to the laboratory staff. This didn't prove to be a real problem because each blood collection tube was labelled with the person’s full name, allocated number, date of collection, and whether they were a case or part of the serosurvey. These details were repeated on the individual pathology request forms for patients, and the list of names of serosurvey volunteers.

How far can we trust serology?

This investigation has challenged some universally accepted assumptions of arbovirus serology, namely that Barmah Forest virus is antigenically unique and serological tests for BF are therefore highly specific. Cross reactions with sindbis virus antigens were elicited with both HI and IFA-IgM tests, and attributed to a polyclonal anamnestic
response between alphaviruses using the neutralisation inhibition test. In one case, an adolescent investigated for measles but found to have an BF HI titre of 1:1280 and a positive IFA-IgM was retested using a more specific method; the IgM result was revised as a false positive by this test. There have also been a number of cases where there has been a four-fold difference in HI titre when sera from the same patient were tested separately and in parallel. Dr Smith admitted that in apparent dual infections with BF and RRV it may be difficult to distinguish between a true recent dual infection, and a synergistic response between acute antibodies and IgG from a previous arbovirus infection. The highest dilution positive result on HI testing was reported as 1:≥640.

Failure to titre to an endpoint meant that in some cases it was impossible to detect seroconversion or a 4-fold drop in titre at high antibody levels. Repeat testing of these sera using ELISA may clarify some of these findings. At present we can only interpret these results as alphavirus infections.

Another concern is the definition of acute and past arbovirus infections. Some of our cases with histories highly suggestive of an acute infection have been IFA-IgM negative. As the duration of circulating IgM for both BF and RRV is unknown but is believed to last several months, the distinction between acute/recent and past infection has been problematic. In only two of the 12 positive survey volunteers was recent infection diagnosed on the basis of a 4-fold rise in HI antibody titre; both were BF infections and both had a characteristic illness and were reclassified as cases. The remaining 10 asymptomatic volunteers were IgM positive but their HI titres were fixed at levels ranging from 1:40 to 1:320. It can be argued that the volunteers with low HI titres were infected before the outbreak and were exhibiting persistence in IgM.

Prioritising work load and time management

Prioritising work load and time management
the disease both clinically and in relation to the quality of daily life; the nature and chronicity of symptoms; and patient information needs. This study was linked to a smaller study on the educational material currently available to medical practitioners on Ross River virus and on other important arboviruses causing human disease. We attempted to recruit doctors into the study first, and obtain their permission to contact their patients. The low response rate among doctors (approximately 30%) resulted in a biased sample of RRV cases.

Being aware of the limitations of the study before starting detailed analysis and knowing of the comprehensive study undertaken by Condon et al in Western Australia, I expressed my concerns to Dr Patel and we decided that more useful information could be obtained from a prospective study in Nhulunbuy. Having made commitments to the participants to provide feedback on the analysis, I found it difficult to consider completing the project of secondary importance. The data were eventually handed over to the senior project officer at CDC for preliminary analysis.

Learning to prioritise activities in communicable disease control, such as completing elective projects while investigating disease outbreaks, without succumbing to crisis management has been an important challenge over the two years. It has been very instructive to observe the way senior colleagues rank their work commitments and to gain some insight into their thought processes when appraising new situations.

One of the benefits of developing a questionnaire for the Ross River virus study was that I had a easily adapted prototype for the Nhulunbuy follow-up questionnaire which had been used in the field (Attachment E). I was able to reword or omit some of the ambiguous or unnecessary questions when I developed the new questionnaire.

3.5.6 CONCLUSIONS

In spite of these problems and shortcomings, the Nhulunbuy investigation has been very successful. I attribute the relative ease with which we carried out the investigation to our recognition of the importance of communication. We established
good rapport with the East Arnhem District Manager, Medical and Nursing Administrations, the Communicable Diseases Officers and the pathology staff at Gove District Hospital, and the Perth State Health Laboratory Services. Most importantly, the residents of Nhulunbuy received timely feedback which emphasized our recognition of their contribution and support, and ownership of the investigation. Sr McFarland's caring attitude personalised the data collection process and gave patients the opportunity to discuss their concerns at length. These observations are supported by the excellent response to our requests for serial blood collections, and the positive feedback we have received from the Communicable Disease Officers.
OUTBREAK INVESTIGATION, NHULUNBUY FEBRUARY 1992

<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>YES/NO</th>
<th>DATE OF ONSET</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever and/or chills</td>
<td>Y / N</td>
<td>_____ / _____</td>
<td>_____</td>
</tr>
<tr>
<td>Tiredness</td>
<td>Y / N</td>
<td>_____ / _____</td>
<td>_____</td>
</tr>
<tr>
<td>Headache</td>
<td>Y / N</td>
<td>_____ / _____</td>
<td>_____</td>
</tr>
<tr>
<td>Neck stiffness</td>
<td>Y / N</td>
<td>_____ / _____</td>
<td>_____</td>
</tr>
<tr>
<td>Muscle aches and pains</td>
<td>Y / N</td>
<td>_____ / _____</td>
<td>_____</td>
</tr>
<tr>
<td>Rash</td>
<td>Y / N</td>
<td>_____ / _____</td>
<td>_____</td>
</tr>
<tr>
<td>If you do/did have a rash, what parts of your body did are/were affected?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Joint pain</td>
<td>Y / N</td>
<td>_____ / _____</td>
<td>_____</td>
</tr>
<tr>
<td>Swollen joints</td>
<td>Y / N</td>
<td>_____ / _____</td>
<td>_____</td>
</tr>
</tbody>
</table>

If you do/did suffer from painful or swollen joints, which joints are/were affected?
<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>YES/NO</th>
<th>DATE OF ONSET</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(day and month)</td>
<td>days or hours</td>
</tr>
<tr>
<td>Sore throat</td>
<td>Y / N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swollen glands</td>
<td>Y / N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Runny nose</td>
<td>Y / N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Painful red eyes</td>
<td>Y / N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>Y / N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>Y / N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>Y / N</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Any other symptoms? ____________________________

Do you know of anyone else complaining of the same symptoms? Yes / No
If yes, please state names / contact phone numbers.

Have you seen a doctor about this problem? Yes / No Date ______/______
Did you require admission to hospital? Yes / No Date ______/______

**Office use only**

INVESTIGATIONS | RESULTS
---|---
Throat swab | 
Stool culture | 
Serology | 
Other | 

Diagnosis | Confirmed
---|---
Probable
Suspected
**Section 1 - Illness symptoms**

Did you have any of the following symptoms? (Please tick ONE answer only)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Yes / No</th>
<th>For how long?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever and / or chills</td>
<td>Yes / No</td>
<td>7 days or less / 1 - 2 weeks / 3 weeks / 4 weeks / 1 - 2 months / 2 - 3 months / more than 3 months</td>
</tr>
<tr>
<td>Muscle aches or pains</td>
<td>Yes / No</td>
<td>7 days or less / 1 - 2 weeks / 3 weeks / 4 weeks / 1 - 2 months / 2 - 3 months / more than 3 months</td>
</tr>
<tr>
<td>Headache</td>
<td>Yes / No</td>
<td>7 days or less / 1 - 2 weeks / 3 weeks / 4 weeks / 1 - 2 months / 2 - 3 months / more than 3 months</td>
</tr>
<tr>
<td>Rash</td>
<td>Yes / No</td>
<td>7 days or less / 1 - 2 weeks / 3 weeks / 4 weeks / 1 - 2 months / 2 - 3 months / more than 3 months</td>
</tr>
<tr>
<td>Joint pain</td>
<td>Yes / No</td>
<td>7 days or less / 1 - 2 weeks / 3 weeks / 4 weeks / 1 - 2 months / 2 - 3 months / more than 3 months</td>
</tr>
<tr>
<td>Swollen or hot joints</td>
<td>Yes / No</td>
<td>7 days or less / 1 - 2 weeks / 3 weeks / 4 weeks / 1 - 2 months / 2 - 3 months / more than 3 months</td>
</tr>
</tbody>
</table>
Which joints were swollen or hot? (list below)

Which joints were painful? (please tick one or more boxes)

- hips
- knees
- ankles
- toes
- ball of feet
- shoulders
- elbows
- wrists
- knuckles
- thumbs
- jaw
- neck
- back

Please tick ONE answer only for each question below.

**Morning stiffness**

If yes, for how long?
- 7 days or less
- 1 - 2 weeks
- 3 weeks
- 4 weeks
- 1 - 2 months
- 2 - 3 months
- more than 3 months

**Depression or feeling low**

If yes, for how long?
- 7 days or less
- 1 - 2 weeks
- 3 weeks
- 4 weeks
- 1 - 2 months
- 2 - 3 months
- more than 3 months

**Tiredness**

If yes, for how long?
- 7 days or less
- 1 - 2 weeks
- 3 weeks
- 4 weeks
- 1 - 2 months
- 2 - 3 months
- more than 3 months

**Disturbed sleep**

If yes, for how long?
- 7 days or less
- 1 - 2 weeks
- 3 weeks
- 4 weeks
- 1 - 2 months
- 2 - 3 months
- more than 3 months

Any other symptoms?

Are you now completely well? Yes / No If no, go to Section 2.

If yes, when did you first feel completely well _____/_____/92

If you can't remember the exact date, how long did it take before you felt completely well?
- 7 days or less
- 1 - 2 weeks
- 2 - 3 weeks
- 4 weeks
- 1 - 2 months
- 2 - 3 months
- more than 3 months
Section 2 - How is/was your daily life affected by this virus
(If you found any of the following activities very difficult, please tick No for that question)

When your illness was at its worst, were you:

- able to use the toilet, or bathe/shower without help? Yes □ No □
- able to tie your shoes or button your clothes without help? Yes □ No □
- able to walk without a walking stick, crutches or help from another person? Yes □ No □
- able to carry out your normal home duties eg shopping, housework, cooking, gardening etc? Yes □ No □
- able to play sport, do aerobics, swim etc? Yes □ No □

Did you need pain killers?

Were your symptoms present all the time Yes / No or did they come and go? (circle answer)

Were you able to go to work / school when you first became unwell? Yes □ No □ or Not applicable □

If no, how long were you off work / school? ____________ days (roughly)

When you did return to work / school, were you well enough for:

- full duties Yes □ No □
- light duties Yes □ No □ For how long? ____________
- part-time work only Yes □ No □ For how long? ____________

Section 3 - What you'd like to know about mosquito-borne viruses
On which topics would you like more information? (Tick one or more boxes).

- What common symptoms to expect
- How you caught the virus
- Whether any one can catch the virus from you
- The length of illness
- How troublesome the virus can become
- Whether the virus leads to long term disability
- The effect the virus can have on daily life

Last name ____________________________ First name(s) ____________________________
Postal address _________________________
Phone (work) _________________________ (after hours) _________________________
How long have you lived in Nhulunbuy? ____________
How long have you lived in the NT? ____________

If you are still sick, would you be willing to help us by completing a questionnaire in 3 months? Yes / No
Dear

It is now four months since the peak of the mosquito-borne virus (arbovirus) outbreak in Nhulunbuy. As you are aware, Sr Anne Marie McFarland and I have been collecting information on the illness produced by the Barmah Forest and Ross River viruses from as many symptomatic people as possible. Your co-operation and interest to date have been greatly appreciated!

With your help we have already learnt a great deal about the illness caused by the Barmah Forest virus, but some of the most important unanswered questions relate to the length of the illness. The only way to collect information on duration of illness is to contact people a number of times. As reported in The Arnhem Courier (17 July), we know that a number of people who develop a Ross River virus-like illness with joint and muscle pain, rash, tiredness, fever and headaches have negative blood tests for this virus. We now know that some of these patients have Barmah Forest virus infections, but our investigation in Nhulunbuy leads us to believe that there may be yet another unidentified virus spread by the same mosquitoes in the Top End. We want to know how long Barmah Forest virus causes symptoms, and how long those patients with completely negative blood tests remain ill. If mosquito-borne viruses are causing real problems for people in Nhulunbuy, such as interfering with work performance, then we can direct public health resources to arbovirus prevention.

I now invite you to complete a follow-up questionnaire about your symptoms, and how infection with an arbovirus has affected your working and home life. We’ve asked you many of these questions before, but we’re now trying to fill the gaps in key issues which became clearer as we interviewed more patients. Sr McFarland may also ask you to attend the Gove District Hospital for a third blood test.

We realise that filling out another questionnaire may be inconvenient for you, but this information is vital for the health and well being of all people in Nhulunbuy.

Yours sincerely

Dr Angela Merianos
Epidemiology Registrar
Communicable Diseases Centre, Darwin
for
Director, Disease Control.
UPDATE ON THE MOSQUITO-BORNE VIRUS OUTBREAK IN NHULUNBUY

Throughout Australia, specialists in the field of mosquito-borne viruses (arboviruses) are closely following the events in Nhulunbuy because of the unique and important opportunity this outbreak affords for the study of the little known Barmah Forest virus. We will be updating information as our analysis proceeds.

Studies at the Menzies School of Health Research in Darwin, showed that approximately 40% of people tested for Ross River virus infection had a negative result. Barmah Forest virus infection may have been responsible for disease in many of these undiagnosed people! The outstanding co-operation of Nhulunbuy residents in our investigation has already helped our understanding of important mosquito-borne viruses in the Northern Territory, with implications for the rest of Australia.

Since the start of the investigation in February, approximately 180 people have been seen by health staff in Nhulunbuy with symptoms which may have been caused by a mosquito-borne virus. Of these people, one third have laboratory evidence of either Barmah Forest virus infection, Ross River virus infection, or both. These people have developed antibodies to the virus which are detected by blood tests.

What we know so far

Nhulunbuy has experienced the largest outbreak of Barmah Forest virus infection ever described in Australia. From our preliminary analysis, we believe that Barmah Forest virus causes symptoms very similar to Ross River virus (rash, fever, muscle and joint pain, headaches and tiredness), but is a milder infection. Patients with Ross River virus are more likely to complain of joint involvement, particularly swollen, hot joints, than patients with Barmah Forest virus. A rash, which is sometimes itchy, occurs more commonly in Barmah Forest infection.
Questions which require more research

We know that most people infected with Ross River virus do not get sick. Unlike Ross River virus infections, we don't know what proportion of people infected with Barmah Forest virus become ill. Of those who do develop symptoms of Ross River virus infection, about one quarter will complain of symptoms for longer than six months, and some for several years. We don't know if Barmah Forest persists, so this is one of the most important questions we are investigating in Nhulunbuy. Another important question is how long it takes for the body to respond to the virus and produce antibodies which we can measure with a blood test.

Better understanding of the diseases caused by mosquito-borne viruses will enable us to direct preventative public health measures and allocate health resources more effectively.

Results of the volunteer survey

Unforeseeable urgent pathology requests at the Perth State Health Laboratory Services has delayed the large scale testing of the blood collected from volunteers in February and April. The laboratory has now started to release some results, and these will be mailed to all participants with an explanatory note to help with interpretation. The volunteer survey should tell us whether Barmah Forest virus is newly introduced into Nhulunbuy, and what proportion of people remain well after infection with these viruses. We again extend our thanks to all volunteers for their enthusiasm and support.

Follow-up of patients

Sr Anne Marie McFarland has been conducting patient follow-ups of patients in Nhulunbuy. We will be approaching those patients whose blood tests so far have been negative, and some patients with a positive result whose symptoms are ongoing, to attend the Gove District Hospital for a third blood test. We will also be following
consenting patients until their illness settles so that we can establish how long these infections cause symptoms, and how they affect daily life and work performance. We will be sending a follow-up questionnaire to people with proven Barmah Forest virus or Ross River virus. Their participation is voluntary but will be greatly appreciated!

Preventative measures

Unfortunately, mosquito-borne viruses will continue to be a fact of life in northern Australia. Each of us can take preventative measures for personal protection against mosquito bites.

- Maintain fly screens on windows and doors.
- Use personal insect repellent containing DEET (e.g. "Rid", "Tropical Strength Aerogard").
- Wear lightweight, light coloured clothing with long sleeves when outside between dusk and dawn.
- Use mosquito coils and nets when necessary.
- Eliminate mosquito breeding sites around the home. Mosquitoes can breed in water-filled cans, car tyres, drip trays of potted plants, blocked drains etc.

Remember, make a mozzie miserable!

For further information, please contact Sr Anne Marie McFarland or Mr Hartley Dentith at the Gove District Hospital on 870 211, or Dr Angela Merianos at the Communicable Diseases Centre, Darwin, on 228 560.

Dr Angela Merianos
Epidemiology Registrar
Communicable Diseases Centre, Darwin
for
Director, Disease Control.
Dear

Thank you for your participation in the mosquito-borne virus (arbovirus) survey. Your blood was tested for the three most common arboviruses carried by mosquitoes in the Top End - Ross River virus, Barmah Forest virus and sindbis virus.

The results of your blood tests, which measure antibodies to these viruses, are negative. This means that you have not come into contact with these viruses. It also means that you have no immunity to infection with Ross River virus, Barmah Forest virus or Sindbis virus, and may become infected in the future.

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The results of your blood test, which measure antibodies to these viruses, are negative. Because we normally require two blood tests taken at least 10-14 days apart to confirm infection with an arbovirus, your negative result may be misleading. It may just mean that at the time your blood was taken, your body had not yet produced antibodies against the virus. It also means that in February 1992, you had no immunity to infection with Ross River virus, Barmah Forest virus or Sindbis virus, so you may become infected in the future. You may wish to show this result to your doctor for future reference and further explanation.

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The results of your blood tests, which measure antibodies to these viruses, show that you have been infected with the following virus(es) at some time in the past (highlighted below). You may wish to show this result to your doctor for future reference.

Virus(es): Barmah Forest virus    Ross River virus    Sindbis virus

These results mean that you now have immunity to infection with Ross River virus / Barmah Forest virus / Sindbis virus, and probably won’t become infected with the same virus again. You can still become infected with the other mosquito-borne viruses in the future. You cannot pass the virus to other people. Many people who become infected with an arbovirus remain completely well. If you have had symptoms such as fever, rash, joint and muscle pains, joint swelling or persistent tiredness, and would like more information, contact your local doctor or the Communicable Disease Officers at the Gove District Hospital on 870 211.

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The results of your blood tests, which measure antibodies to these viruses, are positive and show that you have recently been infected with the following virus(es) (highlighted below). You may wish to show this result to your doctor for future reference. I have included a follow-up questionnaire about the duration of symptoms, which will be very important in describing the disease caused by these viruses.

Virus(es): Barmah Forest virus   Ross River virus   Sindbis virus

These results also mean that you now have immunity to infection with Ross River virus / Barmah Forest virus / Sindbis virus, and probably won't become infected with the same virus again. You can still become infected with the other mosquito-borne viruses in the future. You cannot pass the virus to other people. Many people who become infected with an arbovirus remain completely well. If you have had symptoms such as fever, rash, joint and muscle pains, joint swelling or persistent tiredness, and would like more information, contact your local doctor or the Communicable Disease Officers at the Gove District Hospital on 870 211.

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!. Wear lightweight, light coloured clothing with long sleeves when outside between dusk and dawn.
!. Use mosquito coils and nets when necessary.
!. Eliminate mosquito breeding sites around the home. Mosquitoes can breed in water-filled cans, car tyres, drip trays of potted plants, blocked drains etc.

Remember, make a mozzie miserable!

Yours sincerely

Dr Angela Merianos
Epidemiology Registrar
Communicable Diseases Centre
for
Director, Disease Control, Darwin.
PATIENT QUESTIONNAIRE
NT ROSS RIVER VIRUS INFECTION 1990/91

Today's date ______________________

Sex (Please circle) M F Age (in years) ______

Surname _____________________________ First name _____________________________

Suburb _____________________________ or Town _____________________________

State _____________________________ (if not the NT)

Phone no. (Work) ____________ (Home) ____________ (optional)

Section 1 - Details of your exposure to the Ross River Virus

1. What is your usual occupation?

2. Do you work outdoors at least half of the time? Yes ☐ No ☐
   If yes, please state your employer _____________________________

3. How long have you lived in Darwin? ______ in years

4. How long have you lived in the NT? ______ in years

5. Date when you first felt unwell with Ross River Virus _____________________________

6. Where were you in the 3 weeks before becoming unwell?

7. Were you bitten by mosquitoes before your illness? Yes ☐ No ☐

8. Did you use personal insect repellent when outside? Yes ☐ No ☐

Section 2 - Illness symptoms

9. Did you have any of the following symptoms? (Please circle ONE answer only for each question)

Fever and/or chills
☐ If yes, for how long?
☐ (1) less than 2 weeks
☐ (2) 2 to 6 weeks
☐ (3) more than 6 weeks

Headache
☐ If yes, for how long?
☐ (1) less than 2 weeks
☐ (2) 2 weeks to 3 months
☐ (3) 3 to 6 months
☐ (4) more than 6 months

Joint pain
☐ If yes, for how long?
☐ (1) less than 2 weeks
☐ (2) 2 weeks to 3 months
☐ (3) 3 to 6 months
☐ (4) more than 6 months

Muscle aches and pains
☐ If yes, for how long?
☐ (1) less than 2 weeks
☐ (2) 2 weeks to 3 months
☐ (3) 3 to 6 months
☐ (4) more than 6 months

Rash
☐ If yes, for how long?
☐ (1) less than 2 weeks
☐ (2) 2 weeks to 3 months
☐ (3) 3 to 6 months
☐ (4) more than 6 months

Swollen Joints
☐ If yes, for how long?
☐ (1) less than 2 weeks
☐ (2) 2 weeks to 3 months
☐ (3) 3 to 6 months
☐ (4) more than 6 months
**Attachment E**

Which joints were affected? (Please tick appropriate boxes)

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**Morning Stiffness**

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**Tiredness**

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<td>(3) 3 to 6 months</td>
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<td></td>
<td>(4) more than 6 months</td>
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**Depression, crying, feeling low**

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<tr>
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<td>(3) 3 to 6 months</td>
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<tr>
<td></td>
<td>(4) more than 6 months</td>
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</table>

**Other symptoms**

Section 3 - How did Ross River Virus affect your life

(If you had difficulty with any of the suggested activities within each question please tick No)

10. Were you able to use the toilet or bathe/shower without help? Yes | No
11. Were you able to tie your shoes or button clothes without help? Yes | No
12. Were you able to walk without a walking stick/crutches or help from another person? Yes | No
13. Were you able to carry out your normal household activities eg shopping, housework, cooking, gardening, play sport? Yes | No
14. Did you need pain killers? Yes | No
15. Were you able to go to work when you first became unwell? Yes | No

If no, how long were you off work?

|        | (1) 1 - 2 weeks |
|        | (2) less than one month |
|        | (3) 1 - 3 months |
|        | (4) 3 - 6 months |
|        | (5) longer than 6 months |

16. Date you first saw your doctor for Ross River Virus
17. What made you go to your doctor?
18. What was the single most distressing symptom you experienced?
19. Please list below anything that made your symptoms worse or brought the joint pain back again.

Section 4 - The length of your illness

20. How long did it take before you felt completely well?

|        | (1) less than one month |
|        | (2) 1 - 3 months |
|        | (3) 3 - 6 months |
|        | (4) longer than 6 months |
21. If you're not completely well, are you still getting joint
pains now? Yes □ No □
   If no, go to question 22.
   If yes, how often do you get joint pains each month?
   ____________________________
   If yes, have you needed time off work or help with
your household duties when the joint pains return?
   Yes □ No □

22. What was your total time off work or the total time you needed help at home?
   □ (1) less than one month
   □ (2) 1 - 3 months
   □ (3) 3 - 6 months
   □ (4) longer than 6 months

23. How has Ross River Virus affected you in your daily life?

Section 5 - Your past medical history

24. Did you suffer from arthritis before this illness? Yes □ No □
   If no, go to question 25.
   If yes, which joints were affected?

   ____________________________________________________________
   If yes, was a specific diagnosis made (eg gout,
rheumatoid arthritis, osteoarthritis)? Yes □ No □
   If yes, what was the diagnosis?______________________

Section 6 - Your knowledge about Ross River Virus

25. What did you know about Ross River Virus before becoming infected?

26. Where did you get most of your information about Ross River Virus?
   □ (1) TV
   □ (2) radio
   □ (3) Newspapers
   □ (4) pamphlets
   □ (5) other______________________________

27. If you read a pamphlet on Ross River Virus, where did you find it?
   □ (1) doctor's surgery
   □ (2) Community Health Centre
   □ (3) from a friend
   □ (4) other______________________________
Attachment E

28. Do you think that the information available on Ross River Virus answered your questions on the following:

a. how the virus would make you feel
   Yes ☐ No ☐
b. how you caught the virus
   Yes ☐ No ☐
c. whether anyone else could catch the virus from you
   Yes ☐ No ☐
d. the length of illness
   Yes ☐ No ☐
e. how troublesome the virus could become
   Yes ☐ No ☐
f. whether the virus would leave you disabled
   Yes ☐ No ☐
g. the effect the illness would have on your daily life
   Yes ☐ No ☐

29. Are there any other comments you wish to make about your illness with the Ross River virus?

------------------------------------------------------------
------------------------------------------------------------
------------------------------------------------------------
------------------------------------------------------------

1.3. The Ross River virus

The Ross River virus (RRV) is a small virus member's name assigned to a virus isolated from the blood of a patient with a febrile illness. The virus was first reported as a human pathogen in 1955, and has since been isolated from the blood of a number of acaetas. Clinical and laboratory investigations have been carried out and information has been recorded in the literature since then.

Patients may remain asymptomatic for several weeks. Knowledge obtained with the virus is then to be expected with the virus being isolated at Ross River virus. Infection can be seen without the onset of symptoms. The disease may be mild and for some months after the onset of symptoms, in the case of some cases may continue to report symptoms.

Surveys have shown the Ross River virus is a common infective agent in Australia, and in Queensland alone, estimates of 2.3% of the population have been infected with the virus. This is a significant difference from other parts of the world, where the virus is less common.

1.5. The mosquito vector

The common mosquito vector of Ross River virus is the "St. Mary's" mosquito and the common vector of Ross River virus in the Northern Territory is the "Flinders" mosquito. Both mosquitoes are found in tropical regions.
To: Mr Ted Hobson, District Manager, East Arnhem.
From: Drs Angela Merianos and Anthony J Watson.
Date: 23 February 1992.

1 BACKGROUND

1.1 The Barmah Forest virus

The Barmah Forest virus (BFV) is a little known mosquito-borne alphavirus, first isolated from the mosquito Culex annulirostris (the "common banded mosquito") in northern Victoria in 1974. The virus was first reported as a human pathogen in 1988, and has been successfully cultured from the blood of a patient. Clinical and sub-clinical infections occur, but clinical and epidemiological information is limited. The ratio of subclinical:clinical infections is unknown. The largest case series reported in the literature describes only 29 patients.

Patients may remain symptomatic for several weeks, although infection with this virus is thought to be generally mild. Long term sequelae of Barmah Forest virus infection have not been reported, but 10 of 19 patients reviewed eight weeks after the onset of symptoms in the Queensland study continued to report symptoms.

Serosurveys from NSW and Queensland report a seropositivity rate of 2-13%. In Queensland, an estimated 0.23% of the resident population becomes infected with BFV annually. Both studies report a male:female ratio of 1.5:1.

1.2 The mosquito vectors

The mosquitoes Culex annulirostris and Aedes vigilax (the "salt marsh" mosquito) are the common vectors of Ross River virus in the Northern Territory. Barmah Forest virus has been isolated from both vectors, suggesting a common ecology and distribution.
2.1 Background

On 7 February 1992, Dr Paul Spillane, Gove District Hospital, notified Dr Mahomed Patel, Disease Control Centre, Darwin, of a cluster of 6-7 patients presenting with an acute onset of lethargy, fatigue, rash and fever. A phone call on the same day to Dr Max Chalmers revealed that he had seen another 5-6 patients. All were non-Aboriginal patients; all but one were adults. By 11 February, approximately 20 cases had presented to GDH. Four patients had been examined by Dr Bart Currie who made a differential diagnosis of enterovirus, adenovirus or arbovirus infections. On 21 February, a serologic test for the mosquito-borne virus Barmah Forest was reported positive from 5 of 18 tested sera from both acute and convalescent cases.

2.2 Case definition and investigation

At present, we are investigating any patient presenting with a rash or joint pain/swelling and/or unexplained fever for suspected Barmah Forest virus infection.

Since 7 February, all patients suspected of BFV infection have completed a questionnaire recording: their demographic information; travel history for the month preceding their illness; date of onset of symptoms; and a description of their symptoms. Some of the earliest patients have also completed a follow-up questionnaire which may need to be administered on more than one occasion if symptoms persist. We have attempted to collect blood for acute serological testing, and will recall patients in 10-14 days for a convalescent specimen. The convalescent collection is particularly important in the diagnosis of Barmah Forest virus infection because the development of antibodies may be delayed for up to six weeks post-infection.

2.3 The epidemic curve

Since December 1991, 88 patients have presented to the Gove District hospital with symptoms consistent with BFV infection (Fig 1). A further 15-20 were seen privately. An unknown number of mild clinical cases remain unrecorded. The minimum crude attack rate (cases / total population) based on hospital cases only is 23.2 per 1000. In contrast, we have only received four Ross River Virus notifications from Nhulunbuy for 1992.

Case numbers rose abruptly in the first week of February, and continued to rise exponentially until the week ending 18/02/92. It is too soon to conclude that the fall in patient presentations over the last few days heralds the end of the outbreak, but it
appears to be tapering off. The high level of community awareness and support for the serosurvey suggest that symptomatic people will continue to present for investigation. A second peak in the epidemic curve may follow the expected mosquito hatching around 13 February.

2.4 Mosquito densities

Figure 2 also shows that the epidemic was preceded by an explosive increase in mosquito density. Mosquito trapping around Nhulunbuy from mid-December 1991 to mid-February 1992 showed a dramatic rise in the numbers of both species. Ae. vigilax numbers started to increase around 18 December and peaked at the end of January. Very few C. annulirostris were caught until 5 February, when 200-350 mosquitoes per trap were recorded. Although numbers were falling by the second week of February, another wave is expected with the hatching.

2.5 Symptoms and signs

The Table presents the most common symptoms and signs of the 86 patients whose data has been entered:

Table

| Symptoms and signs of patients with suspected BFV infection, Nhulunbuy, Dec 1991 - Feb 1992 |
|---------------------------------|-------------------------|
| SYMPTOMS/SIGNS                                                                 | PERCENT |
| Fatigue                        | 84.7                   |
| Rash                           | 76.5                   |
| Muscle aches & pains           | 63.5                   |
| Joint pain                     | 60.0                   |
| Headache                       | 56.5                   |
| Fever                          | 55.3                   |
| Respiratory*                   | 40.4                   |
| Gastrointestinal               |                         |
| Diarrhoea                      | 18.8                   |
| Nausea/vomiting                | 17.6                   |

* Respiratory symptoms included sore throat, runny nose, enlarged lymph nodes, painful or irritated eyes, and cough.

A small number of patients have also complained of intensely itchy skin, with or without the rash, dizziness, and "pins and needles".

A consistent laboratory finding is a lymphocytosis, sometimes associated with a fall in the white cell count. This is a non-specific finding in viral infections.
2.6 Age distribution of suspected cases

Figure 2 shows the age distribution of cases. An unusual finding in this outbreak is the relatively high proportion of paediatric cases. The experience with Ross River virus infection is that infection in children is usually asymptomatic, and that among symptomatic children, the symptoms and signs are so non-specific that the diagnosis is rarely made. In this outbreak, 11.7% (13/88) of cases are aged 0-9 years and 8.2% (7/88) are under 5 years. Assuming 1000 children aged 0-14 years in Nhulunbuy, the age-specific attack rate for this group is 16/1000, and 25.7/1000 for the 15 and over age group.

School absenteeism has not increased above the expected rate for this time of the school year.

2.7 Sex distribution

The male:female ratio is 1:1.

2.8 Race distribution

All reported cases have occurred in the non-Aboriginal population. We have made enquiries about clinic attendances at the Yirrkala Clinic and in the outstations, and nothing unusual has been noted except for a number of Aboriginal children aged less than 5 years presenting with fever. These children were treated symptomatically and no blood was collected for viral studies. If the Aboriginal population has been previously exposed to Barmah Forest virus, then young children would be the most likely non-immune group.

3 THE SEROSURVEY

Over 230 Nhulunbuy residents have participated in the seroprevalence phase of the serosurvey. The follow-up survey is due at the end of March. Most volunteers learned of the survey through the mail drop, and some by word-of-mouth. We will send out reminder notices before the second survey.

4 ONGOING SURVEILLANCE

Sr Anne Marie McFarland has been of invaluable assistance in this investigation. She has interviewed most of the patients and has begun to organise their recall for review and convalescent sera collection.
We have obtained permission from Dr Schreuder to continue passive surveillance through Casualty. Copies of the questionnaire are available for self-administration by patients presenting with suspected Barmah Forest virus infection. A protocol for blood collection has also been posted for Casualty Staff.

It is hoped that Anne Marie will be available 1-2 days per week to act as the local Project Officer to ensure appropriate follow-up of patients.

Dr Liz Chalmers has been informed of the diagnosis and will continue surveillance through the surgery. She has arranged aliquots of sera collected by Western Diagnostic Pathology to be forwarded to the GDH laboratory for BFV serology.

**Epidemic curve of BFV outbreak by week**

**Nhulunbuy, NT, 1992**

*Case numbers vs mosquito counts*

Finally, we would like to thank you and your staff for your hospitality, support and patience. In particular, Hartley Dentith, Anne Marie McFarland, Bob Wintle, and the Laboratory and Casualty staff.
REFERENCES


ARBOVIRAL DISEASE IN NHULUNBUY
SEROLOGY RESULTS AND FOLLOW-UP SEROSURVEY, APRIL 1992

To: Mr Ted Hobson, District Manager, East Arnhem Region.
From: Dr Angela Merianos, Communicable Diseases Centre, Darwin
Date: 27 April, 1992.

1 SEROLOGY RESULTS
1.1 Patients
Blood has been collected from a 163 symptomatic cases to date, from a total 184 suspected cases (89%). As expected, most of the patients on whom serology is available are adults. Acute Barmah Forest virus infection has been confirmed in 27 patients, acute Ross River virus infection in 22, and a further 6 patients have serological evidence of mixed infection with both arboviruses. This is the largest confirmed outbreak of Barmah Forest virus in Australia.

A number of patients have had two negative results on sera collected two weeks apart in the presence of persistent symptoms. These are either true negative results, or reflect delayed seroconversion, ie the convalescent serum was taken before an adequate antibody response had occurred. These patients should have a third sample collected approximately six weeks after the onset of their symptoms. The State Health Laboratory Service in Perth has started testing some of the blood for sindbis virus, and will eventually run a panel of tests for the important Australian arboviruses. It is possible, though unlikely, that a third arbovirus is involved in this outbreak.

1.2 Serosurvey 22 - 26 April 1992
We have collected paired sera on 168 volunteers, 68% of the total 247. Five people who did not take part in the original study have also presented for testing on this occasion.

The results of the serosurvey will not be available until June. We have arranged to urgently test blood collected from serosurvey participants who have developed the symptoms and signs of acute Ross River virus or Barmah Forest virus disease.

2 PATIENT FOLLOW-UP
Relatively little is known about the chronicity of Barmah Forest virus disease. Anne Marie McFarland is attempting to communicate regularly with the patients in order to describe the natural history of this disease, and to determine its impact on daily life and productivity. Once all the data has been collected, we will try to develop a model of symptoms and signs predictive for this infection.
3 MOSQUITO STUDIES

Peter Whelan has reported that Barmah Forest virus was successfully isolated from an *Aedes vigilax* and Ross River virus from a *Culex annulirostris* mosquito, confirming the importance of these vectors in the transmission of arboviruses in the NT.

4 ROUTINE ARBOVIRAL SEROLOGY

The Barmah Forest virus has also caused disease in Darwin (approximately 8 cases). BF serology should now be considered as part of the routine investigation of any patient presenting with a suspected arbovirus infection in the NT.

I'd again like to thank Anne Marie, Bob Wintle, Gabe Schraven, Cindy Ellis, Caroline Brunker, Rod Meyer, Hartley Dentith, and Jane Donaldson, for their enthusiasm and invaluable assistance in this investigation.
Date: 1 September 1992

To: Mr Ted Hobson, District Manager, EAR

From: Dr Angela Merianos, CDC, Darwin

Subject: FOLLOW-UP OF ARBOVIRUS CASES, 19 - 21 AUGUST 1992

As you know, the purpose of this visit was to follow up patients with confirmed or suspected Barmah Forest or Ross River virus disease, to collect a further blood sample wherever possible, and to give the residents of Nhulunbuy the opportunity to ask questions about the investigation in the community meeting.

Although I am very pleased with the number of blood samples collected, 79 samples from cases and a few from survey volunteers, fewer people than expected have completed the follow-up questionnaire even after considerable publicity and reminder phone calls. Anne Marie McFarland and I will attempt to increase the response rate by a second reminder call/telephone interview, but it is clear that as more people recover from their illness, interest in the investigation fades.

Among the 25 people with BF virus disease who have completed the latest questionnaire, 36% complained of ongoing joint pains, swollen joints and tiredness i.e. symptoms lasting longer than 3 months and some as long as 6 months. It appears that for a proportion of people infected with this virus, the duration of symptoms will be similar to that of Ross River virus. The presence of a rash was significantly more common in BF, but is unhelpful in distinguishing the two infections clinically.

I will be contacting individuals who have agreed to complete a further follow-up questionnaire in 2 - 3 months. These will be sent directly to me in Darwin. Anne Marie’s involvement should be finished by the end of this month.

I thank you again for your support, and support of the CDOs, clinical and laboratory staff at the GDH.

Yours sincerely

Angela Merianos

cc. Dr Mahomed Patel
    Mr Hartley Dentith
## Chapter 4

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<td>Gonococcal conjunctivitis in central Australia</td>
<td>138-143</td>
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<td>Ciguatera intoxication in Darwin</td>
<td>144-145</td>
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<td>Barmah Forest in Nhulunbuy</td>
<td>146-148</td>
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<td>4.4</td>
<td>Haemophilus influenzae meningitis in rural Darwin</td>
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4.1 Gonococcal conjunctivitis Volume 15 Number 16 12 August 1991

AN OUTBREAK OF NON-SEXUALLY TRANSMITTED GONOCOCCAL CONJUNCTIVITIS IN CENTRAL AUSTRALIA 31 JANUARY TO 6 JUNE 1991

A Merianos¹, G Mulvey³, S Jayathissa², J Stewart², P Linehan⁴, R Matters²
1 National Centre for Epidemiology and Population Health, Australian National University
2 Northern Territory Department of Health and Community Services
3 Nganampa Health Council, Pitjantjatjara Homelands, South Australia
4 Western Diagnostic Pathology, Alice Springs

From 31/1/91-6/6/91 251 cases of gonococcal conjunctivitis were reported to the Communicable Disease Control Centre (CDCC) in Alice Springs. All but one case occurred in Aboriginal people. Most cases (122) have been reported from the Alice Springs and Barkly Tablelands region of the Northern Territory, 118 have been diagnosed among the communities of the Pitjantjatjara Lands in northern South Australia and 9 cases from Western Australian communities near the NT border. Two further cases were reported from Oonadata and Coober Pedy in SA (Figures 1 and 2).

Figure 1
Epidemic curve of non-sexually transmitted gonococcal conjunctivitis in the Northern Territory

No. of cases

31 14 28 14 28 11 25 9 23 6 20 4 18 1 15
Jan Feb Mar Apr May Jun Jul Aug
Fortnight of onset
This is the third outbreak of non-sexually transmitted gonococcal conjunctivitis in Central Australia since 1981. The outbreaks have occurred in approximately 5 year intervals.

**Sociodemographic characteristics of the affected population**

The Central Australian Aboriginal population is divided into several tribal and language groups, and is highly mobile between related communities. Each tribal group is represented among the “town camps” of Alice Springs where inter-tribal mixing is frequent. The Pitjantjatjara people in South Australia, who live in 8-9 communities with associated out-stations, have traditional ties and sociological homogeneity with their relatives in the Northern Territory, and regard Alice Springs as their administrative and health referral centre.

This mobility, and the extended family structure, facilitate the rapid spread of highly infectious diseases such as gonococcal conjunctivitis in situations of overcrowding and poor hygiene.
Case definition

We have accepted a clinical case definition of acute gonococcal conjunctivitis in communities with at least one other microscopy proven case. A pus swab from the conjunctival sac was collected from most patients for microscopy and culture.

Epidemiology

For the purposes of this report, any reference to South Australian cases will only include cases which occurred in the Pitjantjatjara Home Lands, and the Western Australian cases will be excluded from the analysis.

The outbreak was investigated by the Communicable Disease Centre, Darwin, in association with C.D.C.C., the medical officers of the Nganampa Health Services (Pitjantjatjara Lands), and District Medical Officers of the NT Department of Rural Health. The principal investigator (AM) carried out a field investigation in the Pitjantjatjara Lands, reviewed surveillance data collected by C.D.C.C. and the microscopy and culture results of both the private and hospital-based microbiology laboratories in Alice Springs. The review of over 700 eye swabs processed at the Alice Springs Hospital since December, 1989 revealed only 2 cases of gonococcal ophthalmia neonatorum, and no other cases of gonococcal conjunctivitis had been reported to C.D.C.C. in that period.

Cases occurred sporadically throughout the region since January until the first week of April when 27 patients were diagnosed. The epidemic curve peaked in the week ending 18/4/91 in both the NT and the Pitjantjatjara Lands. Case numbers have consistently fallen in SA, but a second smaller peak occurred in the week ending 16/5/91 in the NT, reflecting disease transmission to previously unaffected communities (Figure 2). The crude attack rates (AR) were 10.4/1000 and 60.9/1000 for the Central Australian Aboriginal population and the Pitjantjatjara Lands communities respectively. The outbreak has not been associated with an increased incidence of anogenital gonorrhoea.

Table 1 shows the age distribution of cases and age-specific attack rates for the NT and the Pitjantjatjara Lands combined. The highest attack rates occurred in children aged 0-4 years in both areas, who make up 13.8% of the total population (linear trend test p<<0.001). This finding is consistent with the age distribution of cases during the 1987 outbreak. Although ages were not available for 12.9% of cases, clinic staff have stated that most are children less than 10 years of age. There is no sex-related difference in attack rates.
Table 1. 
Age-specific attack rates of gonococcal conjunctivitis, central Australia, 31 January - 6 June 1991 (n=240)

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<th>Age gp (yrs)</th>
<th>Cases</th>
<th>% of total</th>
<th>Attack Rate /1000</th>
<th>RR*</th>
<th>95% CI of R.R.</th>
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<td>29</td>
<td>12.1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* NT denominators based on 1986 census data (N=11698).
** SA denominators based on Nganampa Health Council population files (N=1939).
+ Relative Risk calculated using age 15 and over as referent.

Attack rates in the Pitjantjatjara Lands were significantly higher than those calculated for the NT communities in children 14 years and under (Table 2). The difference in attack rates may be due in part to the greater frequency of contact between the Pitjantjatjara communities who belong to the same tribal group and the relatively shorter distances travelled, but may also reflect the different age structure between the regions. The sudden increase in cases in both regions followed a large social event in SA attended by Pitjantjatjara people from both the NT and SA.

Table 2. 
Age-specific attack rates stratified by region

<table>
<thead>
<tr>
<th>Age gp (yrs)</th>
<th>NT Cases</th>
<th>AR/100</th>
<th>NT AR/100</th>
<th>SA Cases</th>
<th>AR/100</th>
<th>SA AR/100</th>
<th>RR*</th>
<th>95% CI of R.R.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 4</td>
<td>49</td>
<td>2.9</td>
<td>56</td>
<td>26.5</td>
<td>9.1</td>
<td>6.4&lt;RR&lt;12.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 - 9</td>
<td>30</td>
<td>2.1</td>
<td>30</td>
<td>13.3</td>
<td>6.4</td>
<td>4.0&lt;RR&lt;10.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 - 14</td>
<td>15</td>
<td>0.9</td>
<td>16</td>
<td>8.0</td>
<td>9.5</td>
<td>4.8&lt;RR&lt;18.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 &amp; over</td>
<td>10</td>
<td>0.1</td>
<td>5</td>
<td>0.4</td>
<td>3.1</td>
<td>0.9&lt;RR&lt;8.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>18</td>
<td>1.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

+ Relative Risk calculated as age-specific AR (Pitjantjatjara Lands, South Australia)/age-specific AR (Northern Territory).

CLINICAL FEATURES

Most children have presented with acute, usually bilateral, purulent conjunctivitis and periorbital cellulitis which has settled rapidly with penicillin or amoxycillin (see
The important sequelae which have been associated with gonococcal ophthalmia neonatorum and genitally acquired gonococcal ophthalmitis in adults (corneal scarring, ulceration and prolapse, and pan-ophthalmitis) have not occurred. The only complications reported were disseminated gonococcal infection with arthritis in a 3 year old child, and transient large joint arthralgia in 4 other children.

INVESTIGATIONS

 Conjunctival swabs for gram stain and culture were collected from 220 cases. Swabs for culture were placed in either Stuart's or charcoal media for transportation to the regional laboratories in Alice Springs, but delays of up to 5 days between collection and processing occurred. The air-dried smears were positive for intracellular gram-negative diplococci in 208 cases (94.5%), and \textit{N. gonorrhoeae} was cultured in 90 cases (40.1%). In only two cases where the microscopy findings were negative did the swab yield a positive culture. A sample of conjunctival and genital gonococcal isolates have been forwarded to the Gonococcal Reference Laboratory in Sydney for serotyping, auxotyping and determination of penicillin MICs.

TREATMENT

 All isolates have been sensitive to penicillin by disc diffusion testing. Single dose treatment with either procaine penicillin or oral amoxycillin with probenecid was recommended as standard treatment, as it proved effective in the 1987 outbreak. We are collecting data on treatment regimens used, and the incidence of recrudescence and re-infection.

CONTROL MEASURES

 Control measures included active case finding by contact screening in affected communities and education of health professionals. Clinic staff were responsible for community education. Cross-border networking facilitated the adoption of a standard treatment regimen and improved notifications.

 Screening of household contacts of known cases was undertaken as a priority in order to determine the role, if any, of asymptomatic transmission and atypical disease. In a review of 10 affected families (93 people), there were 8 secondary cases (9.6%), one re-infected case and a case with both conjunctival and genital gonorrhoea. All but one secondary case occurred among children aged 0-9 years. Screening of 171 asymptomatic contacts, however, only yielded one additional case of gonococcal conjunctivitis (0.6%) and is not a cost-effective strategy.
COMMENT

Epidemic gonococcal conjunctivitis\textsuperscript{1,2} appears to differ from both gonococcal ophthalmia neonatorum and adult gonococcal eye infections associated with anogenital gonorrhoea in severity and the development of sight-threatening sequelae.\textsuperscript{3,4} The reasons for this are unclear, but it is hoped that typing of genital and conjunctival isolates from this outbreak will help to clarify this question. Effective single dose treatment has proven acceptable to the Aboriginal communities in Central Australia, and reduces the logistical problems of follow-up for multidose treatment in a highly mobile population.

This outbreak also highlights the importance of the air-dried smear in the diagnosis of gonococcal infections in remote communities where transportation of specimens to the regional laboratories is often delayed, and culture is unsuccessful.

Our preliminary findings suggest that asymptomatic transmission is not of epidemiological importance, but secondary spread to child household members is relatively common and screening should be targeted at this group.

Personal hygiene, environmental and living conditions such as over-crowding probably predispose to this disease. Vector transmission (flies) may be a feature of these outbreaks as observers in the field commented on the unusually large fly populations during the current and the 1987 outbreaks. An entomological study may resolve this issue. At present, early case detection and effective standardised treatment are the easiest interventions for control.

REFERENCES

\begin{enumerate}
\end{enumerate}
Two cases of ciguatera were reported to the Communicable Diseases Centre, Darwin, on 18 September 1991. The intoxication followed a meal of locally purchased coral trout.

Both patients experienced nausea, vomiting, mild diarrhoea, abdominal cramps, pruritis and paraesthesia in the face and extremities. Temperature reversal, manifested as burning of the mouth and skin on contact with cold water was a prominent and early feature in both cases. It is considered pathognomonic of ciguatera. The first case developed facial tingling within an hour of eating the fish. Her flatmate who ate a smaller portion, became symptomatic with vomiting and diarrhoea within 3 hours. She complained of severe myalgia in addition to her other symptoms.

A further case of ciguatera intoxication was identified at the Royal Darwin Hospital in July, 1991. A 23 year old man was admitted semi-comatose after complaining of a headache and ataxia for one day. He had suffered a head injury 4 days beforehand and a provisional diagnosis of head injury was made. CT scan was normal. His conscious state rapidly improved over 24 hours, as did the hypotension (BP 90/50) and bradycardia (40-50 beats/minute) recorded on admission. No specific treatment was required. He then complained of oral and extremity temperature reversal, visual blurring and visual hallucination. The ataxia resolved over 5 days. He later recalled a brief bout of diarrhoea and vomiting before onset of the neurological symptoms. On further questioning he admitted to having spent two weeks living off the land, and his diet had consisted mainly of coral reef fish caught off the Cobourg Peninsula, NT. He had last eaten fish 12-24 hours and chicken 2 hours prior to the onset of his illness.

COMMENT

Ciguatera is a distinctive food intoxication which follows the ingestion of some species of tropical fish. Ciguatoxin is probably produced by the dinoflagellate Gambierdiscus toxicus, an organism at the base of the coral reef food chain. It is a heat-stable toxin which is not destroyed by cooking or freezing. Clinical disease follows consumption of the larger carnivorous fish such as mackerel, barracuda and coral trout in which the toxin is concentrated. Coral trout (Plectropomus species) was implicated in 27 of the 527 ciguatera cases in Queensland between 1965 and 1984.1
Symptoms usually appear between 2 and 12 hours post-consumption, but the delay may be as long as 24 hours. Mild intoxications can occur. The number of unreported cases is unknown. Serious sequelae which can develop quickly include respiratory distress, bradycardia and hypotension, and acute depression. Marked improvement in symptoms has been reported after early administration of mannitol.  

In the Northern Territory, ciguatera has been associated with fish caught in the Gulf of Carpentaria near Nhulunbuy (Gove), Borroloola and Groote Eylandt. The principal ciguateric species include Spanish mackerel, barracuda, coral trout, red emperor and some varieties of cod. Ciguateric fish usually weigh over 2.5Kg. Seven to 10 cases occur each year following consumption of fish caught in these waters. Many of these cases become symptomatic after returning with their frozen catch to Queensland (Dr G Broadbent, Townsville, personal communication).

Physicians in non-endemic areas should consider the diagnosis of ciguatera in patients presenting with acute gastroenteritis associated with neurological symptoms in patients who have recently eaten fish caught in the tropics of northern Australia.

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4.3 Barmah Forest virus Volume 16 Number 6 23 March 1992

A CONCURRENT OUTBREAK OF BARMAH FOREST AND ROSS RIVER VIRUS DISEASE IN 
NHULUNBUY, NORTHERN TERRITORY

Angela Merianos¹,³, Anne Marie McFarland², Mahomed Patel³, Bart Currie⁴, Peter 
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4 Royal Darwin Hospital and the Menzies School of Health Research. 
5 Medical Entomology Branch NT Department of Health and Community Services.

Background

The Barmah Forest virus is a little-known mosquito-borne alphavirus first isolated 
from the mosquito Culex annulirostris in northern Victoria in 1974.¹ Human 
infection was first diagnosed in 1986², and the virus was successfully cultured from a 
symptomatic patient in 1988.³

The Nhulunbuy outbreak

On 7 February 1992, a District Medical Officer at the Gove District Hospital notified 
the Disease Control Centre in Darwin of a cluster of 12 patients presenting with an 
acute onset of fever, rash, headache, fatigue and lethargy. All were non-Aboriginal 
residents of Nhulunbuy (Gove) township, a community of approximately 3800 people 
in the East Arnhem region of the Northern Territory.

By 11 February, 20 cases had presented to the Gove District Hospital. We began a field 
investigation the following day using a working differential diagnosis of infection with an 
adenovirus, enterovirus or arbovirus. On February 21, the State Health Laboratory 
Service in Perth, using a rapid IgM test, reported that 5 of 18 sera tested positive for 
antibodies to the Barmah Forest virus, and two sera were Ross River virus IgM 
positive.
Figure 1
Cases of arbovirus-like disease by date of onset of symptoms
Nhulunbuy, Northern Territory.
25 December 1991 to 20 February 1992 by week of diagnosis

Figure 2
Numbers of Aedes vigilax and Culex annulirostris females
per CO₂ trap per night: totals for 4 sites at Nhulunbuy
December 1991 to February 1992 by date of collection
Case definition and investigation of cases

In collaboration with the Gove District Hospital and the town's private medical practitioners, we are investigating any patient presenting with an acute onset of rash or arthralgia/joint swelling and/or unexplained fever for suspected Barmah Forest or Ross River virus infections. Since 7 February, we have interviewed most patients suspected of an arboviral infection, recording their demographic data, travel history outside Nhulunbuy, duration of residence in Nhulunbuy, illness onset date, and a description of their symptoms. Some of the earliest cases have also completed a follow-up questionnaire at the time of their recall for convalescent sera collection.

We are attempting to collect acute and convalescent phase sera from all suspected adult cases, and from paediatric cases whenever possible. We have also collected sera on approximately 250 volunteers who do not meet our case definition. They will be recalled in six weeks time for paired sera collection.

All cases seen at the Gove District Hospital will be followed prospectively until symptoms subside.

The epidemic curve

Through active case finding and an audit of Accident and Emergency Unit presentations at the Gove District Hospital, we have identified approximately 140 cases with suspected acute arboviral infection from December 1991 - 3 March 1992. The epidemic curve (Figure 1) represents the first 95 cases to 18 February 1992. Case numbers rose abruptly in the first week of February, and continued to rise exponentially until the week ending 18 February. The fall in patient presentations in week 8 may herald the tapering off of the outbreak.

This outbreak followed an explosive increase in mosquito density (Figure 2). Mosquito trapping around Nhulunbuy from mid-December 1991 to mid-February 1992 showed a dramatic rise in the numbers of both *Aedes vigilax* and *Culex annulirostris*, the main vectors of Ross River virus transmission in the Northern Territory (Figure). We are investigating the role and importance of host, vector and pathogen factors in this outbreak.

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### 4.4 Haemophilus influenzae b meningitis Volume 16 Number 9 24 April 1992

**A CLUSTER OF HAEMOPHILUS INFLUENZAE MENINGITIS CASES IN RURAL DARWIN**

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Three children with *H. influenzae* serotype b (Hib) meningitis were admitted to the Royal Darwin Hospital between 31 October - 12 November 1991. The second case presented within two days of the first. All were non-Aboriginal children aged 2 years and under and residents of the same outer suburb of Darwin. Symptoms of meningitis developed acutely in the youngest child aged 9 months, but the older children had upper respiratory tract symptoms for a week prior to admission. Clinical recovery was satisfactory in all cases.

The Litchfield Shire (the Darwin outer suburb and a number of rural communities) has a population of approximately 8000 people, mainly young families. The spatial and temporal clustering of cases prompted an epidemiological investigation by the Communicable Diseases Centre in Darwin.

The three children were linked epidemiologically through their four year old siblings, all of whom attended the suburb’s pre-school. We could not establish any other common exposure among the cases. Only the last child in the series attended day care. During parent interviews, we obtained a history of a recent or current upper respiratory tract infection (URTI) for each of the 3 siblings attending the pre-school. Two of the pre-schoolers were friends, and played together daily. The children attended the pre-school for approximately 10 hours per week. Only one of the
children with meningitis had prolonged contact with a non-sibling who also attended the pre-school.

The Investigation and control measures

Initially the attending medical staff limited rifampicin chemoprophylaxis to the family of the first case, which included a second child under the age of 4 years. After the third case, the attending paediatricians in consultation with the Communicable Diseases Centre decided to offer rifampicin to all children and staff attending the pre-school.

Before administering rifampicin 20mg/Kg daily for 4 days\(^1\), we sought parental consent for throat swabs, and distributed a short self-administered questionnaire to parents to determine the prevalence of URTI among the children and their families. We also offered screening and prophylaxis to three children less than 2 years of age who were attending the same family day care as the last patient. The pre-school contacts received prophylaxis 14-15 days after the diagnosis of the first case, but the infants attending family day care started rifampicin within 48 hours of known exposure.

We defined primary contacts as those exposed to the index case for at least 4 hours per day for 5 successive days during the week before the onset of symptoms, or for 24 hours in that week.\(^2\) This category included 9 untreated household contacts of the later 2 cases, and the infants at the family day care facility. Secondary contacts were contacts of siblings attending the pre-school. We identify 33 secondary contacts; 29 pre-schoolers and 4 teachers. Throat swabs for *H. influenzae* culture were taken from 40 of the total 45 contacts (89%) of which only one grew *H. influenzae* serotype b (2.5%). The positive result was from one of the pre-schoolers. None of the primary contacts of a meningitis case were oropharyngeal carriers of Hib.

Among the pre-schoolers, 83% (25/30) were either symptomatic of an URTI at the time of interview or had recovered from a recent URTI. At least one other household member in the families of 15 pre-schoolers also had a history of URTI. All but one parent agreed to prophylaxis for their children, and there were no further cases.

DISCUSSION

*H. influenzae* type b is an important cause of childhood morbidity, especially in children under the age of 2 years, because the immature immune system of infants is poor at mounting a protective immune response against polysaccharide antigens.\(^3\) Worldwide Hib is the commonest cause of meningitis in children under the age of 5 years.\(^4\) In a study of 113 episodes of invasive Hib infection in the NT from 1985-88, the most frequent diagnoses were meningitis (37%) and pneumonia (33%).
The incubation period of Hib is unknown, but is probably between 2-4 days.\(^6\) Chemoprophylaxis with rifampicin has been shown to reduce nasopharyngeal carriage by 95% following the recommended dosage regimen.\(^1\) As young children have the highest carriage rates (2-5%) and the greatest risk of invasive disease, we decided to offer chemoprophylaxis usually recommended for day care centre contacts to the preschool contacts as well.\(^2,6\) The American Academy of Paediatricians\(^2\) currently recommends rifampicin prophylaxis when two or more cases of invasive Hib infection occur within 60 days in a day care centre or nursery, although the results of some prospective studies of Hib in day care centres do not support this recommendation.\(^7,8\) In 1991, the NHMRC recommended that careful observation of day care and preschool contacts was preferable to rifampicin prophylaxis.\(^9\)

Day care centre contacts have a low throat carriage rate, but up to one third of child household contacts are colonised at the time of the onset of disease in the index case.\(^10\) The household contacts of the third case who were swabbed on the day of the child’s admission did not grow Hib, but a single swab is insensitive for detecting carriers. Rifampicin prophylaxis should not be withheld while awaiting culture results.

Viral or mycoplasma respiratory tract infections may facilitate invasive bacterial disease.\(^11\) The association between infection with a respiratory virus and meningococcal meningitis has been noted in Chad\(^12\) and Britain.\(^13\) In our investigation, a history of acute respiratory infections was very common in both household and community contacts of the meningitis cases. The two older cases themselves had a prodrome of coryza before Hib meningitis. The implications of these concurrent infections are unclear.

The low Hib carriage rate detected in our investigation is consistent with published observations.\(^14\) This “outbreak” may have been the result of spatial and temporal clustering of sporadic cases, which by chance alone implicated the preschool. In a small community of young families, we would expect that most children under 5 years of age attend preschool or a day care facility, and have siblings in the high risk age group.

Our report highlights the problems of management of day care centre contacts of children with invasive Hib and meningococcal disease. We found it a reassuring exercise to have detected only one Hib carrier among these preschool children, but we are left not knowing whether our intervention actually prevented further cases.
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Chapter 5

MANUSCRIPTS PREPARED FOR SUBMISSION TO PEER REVIEW JOURNALS 154-242

THE 1990-91 OUTBREAK OF MELIIOIDOSIS IN THE NORTHERN TERRITORY OF AUSTRALIA. 154-176
I. EPIDEMIOLOGY AND ENVIRONMENTAL STUDIES.

CONTROL OF A COMMUNITY OUTBREAK OF MEASLES WHICH STARTED IN A POORLY IMMUNISED HIGH SCHOOL POPULATION. 177-196

EPIDEMIC NON-SEXUALLY TRANSMITTED GONOCOCcal CONJUNCTIVITIS IN CENTRAL AUSTRALIA. 197-214

A CONCURRENT OUTBREAK OF BARMAN FOREST AND ROSS RIVER VIRUS INFECTIONS IN NHULUNBUY, NORTHERN TERRITORY. 215-242
(Late draft of the manuscript)
THE 1990-91 OUTBREAK OF MELIOIDOSIS IN THE NORTHERN TERRITORY OF AUSTRALIA.
I. EPIDEMIOLOGY AND ENVIRONMENTAL STUDIES.

Short title: Risk of melioidosis in the Northern Territory of Australia.

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ABSTRACT

From November 1990 to June 1991 33 acute cases of melioidosis occurred in the Northern Territory of Australia; 25 cases were reported in the capital city, Darwin. We carried out an epidemiological investigation to exclude a common source outbreak, describe the risk factors for disease, and develop and institute appropriate control measures. We compared population-based attack rates among various risk groups using logistic regression, and the demographic, medical and behavioral risk factors for melioidosis by a matched case-control study. Environmental Health Officers collected soil, surface water and cooling tower water specimens for *Pseudomonas pseudomallei* culture. The crude attack rate of melioidosis during the outbreak was 52 per 100 000. Age, gender, race, diabetes and alcohol abuse were independent risk factors for disease. The relative risk of disease in diabetic patients was 12.9 (95% CI 5.1 - 32.7; p< 0.001) and 6.7 in alcoholic patients (95% CI 2.9 - 15.2; p< 0.001). We found no significant difference between cases and controls in matched pair analysis for any of several exposure factors studied. We isolated *Pseudomonas pseudomallei* from 4% of soil samples and 9% of surface water samples. Our study confirms the importance of host factors in the development of melioidosis, and attempts to quantify the risk of disease during the Darwin epidemic. *Pseudomonas pseudomallei* is widespread in the soil of urban Darwin.
INTRODUCTION

Melioidosis is a bacterial disease of humans and animals caused by the soil saprophyte *Pseudomonas pseudomallei*, and is endemic in northern Australia above latitude 20°S (Crotty et al., 1963; Woods et al., 1992; Rode et al., 1981; Thomas et al., 1979; Ashdown et al., 1980; Guard et al., 1984; Ketterer et al., 1986; Thomas, 1981; Loyd et al., 1988). Although the incidence of disease is low, the high case fatality rate and significant morbidity associated with the infection make it an important disease clinically. The first case of human melioidosis reported from the Northern Territory (NT) of Australia was in 1960 (Crotty et al., 1963). The patient was a 40 year old male diabetic who presented with pneumonia, and died three weeks later of *P. pseudomallei* septicaemia. Woods et al. reported 52 NT cases of culture confirmed or serologically diagnosed cases of melioidosis from January 1984 to October 1990, a mean incidence of eight cases annually. Most presented during the northern Australian "wet season", November through April. The majority of these cases lived in rural and semi-rural communities remote from Darwin, and many had outdoor occupations which brought them into frequent contact with soil. In contrast, from 1 November 1990 to 30 June 1991, 33 cases of melioidosis were confirmed in the region.

The incidence of melioidosis in humans and in veterinary practice has a seasonal periodicity in endemic areas (Woods et al., 1992; Rode et al., 1981; Thomas et al., 1979; Ashdown et al., 1980; Guard et al., 1984; Ketterer et al., 1986; Strauss et al., 1969), peaking during the months of heaviest rainfall and after flooding (Ketterer et al., 1986). The near record rainfall experienced by the NT in January 1991 was associated with a considerable increase in the number of patients presenting with melioidosis in the same month, clustering in the capital city, Darwin. The temporal clustering of urban cases necessitated urgent exclusion of a common source outbreak. We were particularly concerned about the environmental contamination and possible aerosolisation in a public access facility. Previous studies identified inoculation (Rode et al., 1981; Ashdown et al., 1980; Thin et al., 1970; De Buse et al., 1975), inhalation of dust (Ashdown et al., 1980;
De Buse et al, 1975) or aerosols (Ketterer et al, 1986; Thin et al, 1970; Clayton et al, 1970), and ingestion (Thomas et al, 1979) as possible routes of transmission of *P. pseudomallei* in both humans and animals. Strauss et al (1969a,b) found a positive correlation between recovery rates of *P. pseudomallei* from soil and ground water samples and *P. pseudomallei* antibody prevalence in Malaysia. Serosurveys of military personnel who served in Vietnam suggested that helicopter crewmen were infected by inhaling aerosols produced by helicopter rotors (Clayton et al, 1970). These studies also suggested that *P. pseudomallei* was ubiquitous in soil in these countries.

We began epidemiological and environmental investigations in January 1991. This paper presents the outbreak investigation results of the 25 acute cases of melioidosis in the greater Darwin region from November 1990 to June 1991. The accompanying article also includes eight additional cases reported during the observation period which did not fulfil the case definition used in this study.

**SUBJECTS AND METHODS**

Interview of the first cases or their proxies quickly excluded a common source outbreak within Darwin. Most gave a history of frequent exposure to wet soil or pooled surface water during the rains, and the early cases reported pre-morbid trauma to the feet or infected in-grown toenails.

We conducted a matched case-control study and environmental sampling to test three hypotheses suggested by the descriptive epidemiology and clinical features of the first 15 cases; first, that soil samples and standing water from the greater Darwin region harboured *P. pseudomallei*; second, that *P. pseudomallei* infected cases through exposure to contaminated soil or water; and third, that laceration or maceration of the skin of the extremities, particularly the feet, facilitated transmission. Demonstration of environmental contamination would be used to guide the nature and extent of a proposed prevention campaign. We also compared attack rates for various groups using population denominators enumerated from published sources.
Case definition
The eligible case subjects were 25 patients with acute melioidosis; 24 were admitted to the Royal Darwin Hospital (RDH), or attended the medical outpatient clinic at the Royal Darwin Hospital from November 1990 to June 1991, and one patient was diagnosed with melioidosis at autopsy. All lived in the Darwin Statistical Division during the 1990/91 "wet season", an area of 303 square kilometres and a population of approximately 73 000 people. All but two were bacteriologically confirmed. The two culture negative patients presented with clinical signs of acute melioidosis, and had IFA-IgM (Ashdown, 1981; Khupulsup et al, 1986) or IgM-ELISA (Ashdown et al, 1989) antibodies to P. pseudomallei, with no other causative pathogens identified.

We maintained active surveillance for cases during the "wet season" by reviewing acute admissions to the RDH, the principal hospital of two in the Darwin Statistical Division. We asked physicians, laboratory staff at the RDH and private laboratories, and rural clinic staff to notify all cases of melioidosis to the Communicable Diseases Centre. General practitioners reported cases on a voluntary basis. We distributed a newsletter to all private practitioners informing them of the outbreak and defining the clinical features and patients at risk of melioidosis (Rode et al, 1981; Ashdown et al, 1980; Guard, 1987; Leelarasamee et al, 1989). They were encouraged to review susceptible patients who had presented with pneumonia, pyrexia of unknown origin, genitourinary symptoms or unusual skin infections in the preceding month, to request P. pseudomallei serology when clinically indicated during the "wet season", and to maintain heightened surveillance. Although the study began in January 1991, we also carried out an audit of the case notes of patients diagnosed with melioidosis in November and December 1990, and interviewed the patient or a suitable proxy.

Selection of controls
Because 88% of our cases (22 patients) had a recognised medical risk factor for melioidosis, we selected controls from among diabetic, alcohol abusing, oncology or steroid
dependent patients in whom clinical melioidosis had been excluded. They were not screened for the presence of *P. pseudomallei* antibodies. We intended to select two control subjects matched to each case from consecutive admissions to the general medical or surgical wards of the RDH. We reduced this target to one control per case as the study progressed because of the paucity of suitable in-patient controls. We also extended selection of controls to patients attending the RDH medical out-patient clinics, clients of the RDH Detoxification Unit, and diabetic patients registered with Diabetes Australia Northern Territory.

Eligible controls included 7 female and 27 male Darwin residents, matched to the cases by age (to plus or minus 6 years for patients aged less than 30 years, and to plus or minus 10 years for older patients), gender, and race (Aboriginal or other). The number of controls per case ranged from one to three; 17 cases were matched to one control, 7 to two, and one case to three controls. The final number of controls selected was 34.

**Interviews**

All cases or their proxies, and all of the control subjects agreed to be interviewed. We interviewed proxies if the patient was deceased or too ill to talk to us. Informed verbal consent was obtained from all participants or their proxies. One of the investigators (CMN) conducted the interviews unblinded to the case-control status of the study population, and aware of the risk factors for melioidosis under investigation. Questions were asked in a standard manner. The cases or their proxies were interviewed within two weeks of the diagnosis. We attempted to obtain exposure histories for the three month period before the onset of illness among the cases, and for the same period before the day of the interview for the controls. The exposure variables included occupation; frequency of occupational and recreational exposure to soil, mud or standing water; type of footwear most commonly worn at work and recreation (waterproof shoes or boots, open footwear or bare feet); history of injury to the extremities, including surgical procedures and cutaneous infections such as infected insect bites; severity of the skin trauma graded by a
specialist physician (BC) as mild, moderate or severe; past medical history and intercurrent illness; alcohol use and smoking history. We considered exposure to soil to be frequent if the subject worked outdoors, or spent at least half of their leisure time outdoors each week. We specifically asked about activities such as gardening, digging for molluscs and crustaceans in the mud flats around Darwin, fishing, and camping.

Environmental studies

Environmental Health Officers from the Public Health Branch of the NT Department of Health and Community Services obtained a convenience sample of surface soil and water specimens from the gardens of patients, controls and popular recreational areas. They generally sampled wet shady areas, reported in the medical literature to yield the highest isolation rates of *P. pseudomallei* (Thomas *et al*, 1981; Strauss *et al*, 1969a). Soil was collected from around the residences of the first 22 cases and eight control subjects. They collected topsoil with stainless steel spoons, which were wiped clean and sterilized with heat between collections. No attempt was made to sample deeper soil layers. They also collected water from the cooling towers of the main public access buildings in Darwin, and from the private air conditioning units of two cases. Surfaces of the domestic air conditioning units were swabbed.

Laboratory methods

We prepared culture plates for *P. pseudomallei* from 68 soil and 11 surface water samples, and 7 water samples and 3 surface swabs from the cooling towers and air-conditioning systems tested.

Soil: Each 1kg sample of soil was divided into 4 portions each weighing 250g, apportioned into 4 containers, and 300ml of Ashdown modified broth was added to each container (Ashdown, 1979a). These containers were to have been incubated at 35°C for a minimum of 48 hours, but the smell in the laboratory was prohibitive after 14-18 hours. The specimens were moved outside, where the ambient temperature of 27-34°C would have
been adequate to sustain the growth of *P. pseudomallei*. 50 ml of supernatant was removed from these specimens on day 2, 3, 4 or 5, centrifuged at 3000 rpm for 15 minutes, the supernatant discarded, and the pellet plated onto Pp (*P. pseudomallei*) selective plates.

**Water:** Water samples were filtered through Whatman® number 1 filter paper (W & R Balston Ltd, UK), and then through 0.45 mm millipore filters. The filter papers were incubated in 30 ml of Ashdown modified broth for 48 hours at 35°C.

All inoculated plates were incubated for a minimum of 48 hours, and Pp colonies were identified by their characteristic macroscopic and microscopic morphology, and confirmed with API 20E (Ashdown, 1979b).

### Statistical analysis

We obtained denominators for calculating population-based attack rates (AR) from the Australian Bureau of Statistics (ABS) 1986 population census. We excluded residents of the Darwin Statistical Division less than 20 years of age from all denominators.

We used two methods to estimate the number of diabetics in Darwin, because the true prevalence of diabetes is unknown. We applied the age- and sex-specific diabetes rates reported in the prevalence study in Busselton, Western Australia (Glashaar *et al*, 1985) to the Darwin population to estimate the prevalence in non-Aboriginals, and the corresponding rates described in central Australia (Phillips *et al*, 1990) for the prevalence in Darwin Aborigines. We adjusted both estimates by the ratios of undiagnosed to diagnosed diabetics in each racial group reported in the two studies. This ratio varied with age for non-Aboriginal diabetics, but we used a fixed ratio of one undiagnosed case for each known case in all Aboriginal age categories. The denominator for each racial group was the sum of diagnosed and undiagnosed diabetics.

We used the 1990 ABS survey of alcohol and tobacco consumption in Darwin to estimate the age- and sex-specific denominators of alcohol drinkers in the "moderate" and "high
risk consumption categories, at least 50ml of pure alcohol per day in men and at least 25ml per day in women. These rates also enabled us to estimate denominators for diabetics drinking alcohol at these levels, assuming that the proportions of moderate and high risk drinkers among diabetics and among Aborigines are the same as reported for the general Darwin population.

We estimated the population engaged in outdoor work using the following occupation classifications used by the ABS: farmers and farm managers; natural scientists; building professionals and engineers; electrical, building and vehicle tradespersons; police officers; road and rail transport drivers; mobile plant operators; amenity horticulturalists; and agricultural, construction and mining, and miscellaneous labourers.

We calculated descriptive statistics, relative risks (RR) and their 95% confidence intervals (CI) for the incidence data using the epidemiological program Epi Info Version 5 (Dean et al, 1990), and matched odds ratios (ORM) and their 95% CI (Robins et al, 1986) for the case-control study. Because of small sample size, we collapsed all categorical data into a maximum of three categories for the matched-pair analysis. For example, we recoded the five levels of severity of pre-morbid injury or skin lesions (nil, minor, moderate or severe injury, and non-traumatic heavy soil exposure) into "nil", "minor injury or heavy soil contact" and "moderate to severe injury or existing lesion" categories.

We used logistic regression on our incidence data to estimate the predictors of melioidosis with GLIM statistical software (Baker, 1985). The odds ratios derived from the model approximate relative risk estimates in this study, since the outcome is rare. We selected a subset of predictors based on initial univariate analysis (α=0.05), and employed logistic regression to select the final set of significant predictors (p<0.05). The predictors fitted to the final model were age, gender, race, and history of diabetes and
alcohol abuse. The adjusted relative risks and 95% CIs were calculated from the logistic regression using the formula $\exp(\beta \pm 1.96 \times SE)$, where $\beta$ and SE are the estimated regression coefficient and the standard error respectively (Kleinbaum et al, 1982).

**RESULTS**

**Attack rates**

The epidemic curve of the outbreak is presented in Figure 1. The mean age of the case subjects was 52.1 years (SD 13.5 years), with a range of 20-80 years. Six were female; 8 were Aboriginal. Table 1 presents the risk factors of the cases and controls. The clinical data of the cases will be presented elsewhere. Eighty percent of cases (20 patients) had a history of diabetes and/or current alcohol abuse. Seven patients had two, and two cases had three or more risk factors for melioidosis. One patient had a 15 year history of topical steroid use for psoriasis as his only recognised risk factor, and another had a past history of mastectomy for carcinoma of the breast. Only three patients had no relevant medical histories; two cases in this latter group had frequent occupational exposure to soil. They were males aged 63 and 44 years, and both worked in the building trade. The former had sustained a welding spark burn over his right tibia; he required daily dressings for approximately five weeks and oral antibiotics to control secondary cellulitis. The second patient was a tiler who frequently injured his hands. Seven of the 10 cases with outdoor occupations, and both cases working indoors, described frequent recreational exposure to soil.

Table 2 presents the attack rates stratified by various demographic and risk factors. The crude attack rate of melioidosis in Darwin residents aged 20 years and over was 52 per 100 000. The highest attack rate (2128 per 100 000) occurred in diabetic patients abusing alcohol. Age 50 years and over, Aboriginality, male gender, diabetes and alcohol abuse are significant univariate exposure factors, and infrequent occupational exposure to soil was protective in this analysis.
The similarity in attack rates between cases frequently exposed to soil at work, and those outside the workforce, may be explained by the high proportion of Aboriginal patients in the latter group (7/8 cases compared to 6/17 non-Aboriginal cases; Fisher exact two-tailed p=0.03). Six Aboriginal patients admitted to heavy soil exposure from activities such as fishing and collecting shellfish (75%), while 47% of non-Aboriginal patients (8/17) engaged in frequent outdoor recreation; this difference was not statistically significant ($\chi^2_{1 \text{df}} = 0.81$). Age, gender, history of trauma to the extremities, and the presence of intercurrent medical risk factors were similar between racial groups. The difference between the racial groups in the rate of heavy occupational exposure to soil, 13% for Aboriginal and 53% non-Aboriginal patients, is not statistically significant.

The adjusted relative risks from the logistic regression are shown in Table 3. Age, gender, race, the presence of diabetes and alcohol abuse remain significant predictors of melioidosis after adjustment. The relative risks of melioidosis for Darwin residents are approximately 8, 13 and 7 in the presence of age 50 years and over, history of diabetes, and alcohol abuse respectively. There is no interaction (effect modification) between alcohol and diabetes and the relationship with melioidosis in this population ($\chi^2_{1 \text{df}}=0.011; \ p = 0.91$).

The case-control study

We found no significant difference between cases and controls for any of the predictor variables tested by univariate matched pair analysis (Table 1), so we did not proceed to multivariate analysis. The only significant finding was that more cases than controls were employed at the time of interview (OR$_{M}=5.0$; 95% CI 1.0 - 24.2; $p<0.05$).

The ecological study

One ground water specimen (9.1%) and three soil samples (4.4%) yielded *Pseudomonas pseudomallei* on culture. The Environmental Health Officers collected the positive water sample on the property of one of the cases. Soil collected from the stockpile of a
commercial topsoil distributor in Darwin, the garden of a volunteer outside the investigation, and an area of water seepage on a vacant lot, all yielded *P. pseudomallei*. We failed to isolate the organism in soil samples from the other commercial topsoil distribution sites, and from the cooling towers and air-conditioning systems examined.

**DISCUSSION**

This epidemic of melioidosis in urban Darwin provided a unique opportunity for an analytic study of the epidemiology of the disease. This unusual outbreak is probably associated with the heavy summer rainfall recorded in northern Australia from November 1990 to April 1991 (Woods *et al.*, 1992). A similar increase in case numbers was observed in northern Queensland during the same season, where 28 cases were reported over a six month period (Allen, 1991).

Growth of *Pseudomonas pseudomallei* in the environment requires temperatures between 18-42°Celsius, humidity and consistent rainfall. During heavy rainfall, the rising water table may leach the organism out of the lower soil layers to the surface where favourable environmental conditions facilitate growth and replication (Thomas *et al.*, 1979). The highest levels of environmental contamination with *P. pseudomallei* have been reported in Thailand and Malaysia. The organism is found widely in the soil and surface water of rice paddies, cleared fields, marshes and monsoon drains in endemic areas. Strauss *et al.* isolated *P. pseudomallei* in 28% of soil samples from cleared fields, and in 33% of ground water samples collected in wet rice fields in West Malaysia, although the crude rates of contamination across 10 states were 3.8% and 7.6% for soil and water samples respectively. Finkelstein *et al.* (1966) found isolation rates ranging from 30 - 50% in southern Thailand. Piggott and Hochholzer (1970) observed that discrete areas of hyperendemicity occur within endemic areas. In Australia, Thomas *et al.* sampled a paddock implicated in melioidosis in sheep over a two year period, and cultured *P. pseudomallei* from 10% of 30 water samples and from 1% of 700 soil samples. They
suspected that the high isolation rate from the water samples was a result of sampling mostly muddy water from bore holes rather than surface water.

Our crude isolation rate of 5% from a small number of surface water and soil samples, the lack of geographical clustering of cases within urban Darwin during the epidemic, and their apparent lack of common source exposure suggest that *Pseudomonas pseudomallei* is widely distributed in the soil of Darwin. Anecdotal evidence from long term residents suggests that following Cyclone Tracy which devastated Darwin in 1974, topsoil from a local source was used to landscape severely affected suburbs. Soil yielding cultures of *P. pseudomallei* collected in the garden of the volunteer who lived in one of the re-landscaped suburbs, and from a commercial distributor of topsoil, were linked to this source of topsoil. This supplier delivered soil to a building site where one of the melioidosis cases worked as a concreter. These anecdotes suggest widespread distribution of *P. pseudomallei* contaminated soil in Darwin. Failure to culture the organism from soil collected from the other commercial distributors of topsoil does not preclude its presence, so we did not recommend any specific action against the implicated outlet.

The case-control study did not identify any behavioural factors predisposing to melioidosis. The almost universal exposure of Darwin residents to wet soil and standing water during the 1990/91 "wet season" supports the importance of medical risk factors in the development of disease. The wide confidence intervals for the matched odds ratios do not exclude the possibility of either a positive or a negative (protective) effect. We attribute these results to small numbers, and possibly to lack of specificity of the questionnaire for the relevant soil contact behaviours, or to unequal levels of soil contamination with *P. pseudomallei*.

We had to conduct this study rapidly, so we selected easily accessible controls, most of whom were unemployed; 66.2% of the Darwin population aged 20 years and older were part of the workforce during the 1986 census compared to only 23.5% of the control
subjects in this study. The employment status of cases also differed significantly from that of their matched controls at the time of interview. Our assessment of the role of occupational exposure in the development of melioidosis is therefore invalid.

The risk of melioidosis in cases with heavy occupational exposure to soil was approximately 10 times that of cases who worked indoors in the univariate population-based analysis, even though their recreational exposure was similar. Two of the three patients without predisposing medical risk factors for melioidosis were engaged in outdoor work. Fifty percent of the cases from 1960 - 1990 also worked outdoors; most of the remaining cases were rural Aborigines (Woods et al, 1992). These data suggest that occupational exposure was an important risk factor in this outbreak.

Elsewhere melioidosis is a rural disease, affecting mainly men aged 40 - 50 years, but cases occur in all age groups (Guard et al, 1984; Guard, 1987). Although urban Aborigines in Darwin live less traditional lifestyles, 75% of the Aboriginal cases in this study had engaged in activities with heavy soil exposure, such as gathering sea foods from mangrove swamp areas.

Our investigation supports existing evidence that skin inoculation with soil or water contaminated with *Pseudomonas pseudomallei* is an important route of transmission, although inhalation of aerosols containing the bacteria has not been excluded. The adjusted relatives risks indicate that underlying medical risk factors are more important than demographic variables and environmental exposure in the development of disease. Clinical melioidosis is known to be associated with conditions causing immunosuppression such as diabetes mellitus and chronic alcohol abuse (Rode et al, 1981; Ashdown et al, 1980, Guard, 1987, Leelarasamee et al, 1989; Ashdown et al, 1984). A serosurvey in north Queensland involving 9047 residents found that seroprevalence rates in people with alcoholism and chronic infections (15%), liver disease (13%), and diabetes (9%), were higher than the crude seroprevalence rate of 5.7% (Ashdown et al, 1984). The high
attack rates of melioidosis in diabetics and alcoholics in our study support these observations. A prospective study of seronegative, "high risk" individuals would theoretically improve our understanding of the risk of infection and the natural history of the disease in the immunocompromised. The low incidence of melioidosis, the long latency between infection and disease, sometimes measured in decades, the small size and transient nature of the NT population, and the logistical problems inherent in cohort studies, hinder such an investigation (Rode et al, 1981; Guard, 1987; Morrison et al, 1988).

Although most patients in our series were diagnosed after admission to hospital or at post mortem, close contact with the laboratories in Darwin, and referral of all patients to physicians for treatment, meant that our case ascertainment was very high. Only one additional case of mild cutaneous melioidosis was detected by one of the authors (BC) during an retrospective audit of the admission log books of the private hospital in Darwin. Our methods of estimating risk factor-specific denominators may be inexact, but the orders of magnitude of the attack rates and adjusted relative risks are large enough to remain robust against sizable variations in the denominator populations.

The degree of recall bias of both cases and control subjects in this study may have been considerable, especially after extensive media coverage of the epidemic. We anticipated bias towards recollection of a pre-morbid exposure event, such as minor trauma to the extremities, when interviewing relatives or friends of deceased patients. The data do not show a significant difference in the frequency of pre-morbid events between the deceased patients and surviving cases. The validity of the case-control study is compromised by our reliance on self-reported data of behavioural risk factors, the small number of cases, problems in finding suitable control subjects, and possible over-matching of cases and controls. A control group selected from patients with a malignancy, diabetes, or alcoholism may be inappropriate for the study of melioidosis risk factors in "low risk" cases. We considered a second, population-based, control group, but time and resource constraints prevented such additional analytic study. However, our control group was appropriate for the investigation of a common source outbreak.
Our current melioidosis awareness campaigns advise the public with recognised risk factors, including outdoor occupations, to avoid exposure to soil and untreated water during the "wet season" by using protective foot and hand wear when indicated (Morrison et al., 1988; Johnson, 1967). We also emphasize the need for a high level of clinical suspicion of melioidosis among health care professionals, especially when dealing with patients at risk of the disease. Long term surveillance will be needed to evaluate the effectiveness of these prevention strategies.

ACKNOWLEDGEMENTS
We wish to acknowledge Dr Aileen Plant, Professor Robert Douglas and Professor John Mathews for their input into the initial planning of this investigation, and Ms Jenny Powers for her statistical input. We wish to thank the physicians of the Royal Darwin and Darwin Private Hospitals for their notification and referral of melioidosis patients, Valerie Asche and Kay Withnall for laboratory support, and the Environmental Health Officers Mike Thompson, Christopher Clark, Mary Adam and Paul Csizmadia who collected the environmental samples in Darwin.
Epidemic curve of melioidosis in the Northern Territory
1990–1991

Cases

- Rainfall in mm
- All other cases
- Darwin study cases

Month and year of onset or diagnosis

1990
1991
Table 1
MATCHED-PAIR ANALYSIS OF 25 CASES WITH MELIOIDOSIS AND 34 CONTROL SUBJECTS, DARWIN, 1990 - 91.

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>ORM</th>
<th>95% CI</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OCCUPATIONAL EXPOSURE TO SOIL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not in the workforce</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequent soil / water contact</td>
<td>undefined</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infrequent soil / water contact</td>
<td>0.8</td>
<td>0.1 - 6.3</td>
<td>0.73</td>
</tr>
<tr>
<td><strong>RECREATIONAL EXPOSURE TO SOIL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other eg digging for molluscs</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gardening</td>
<td>0.5</td>
<td>0.2 - 1.8</td>
<td>0.49</td>
</tr>
<tr>
<td><strong>HISTORY OF PRE-MORBID INJURY OR HEAVY SOIL / WATER EXPOSURE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.3</td>
<td>0.4 - 4.0</td>
<td>0.84</td>
</tr>
<tr>
<td><strong>SEVERITY OF THE PRE-MORBID INJURY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor injury or heavy soil contact</td>
<td>3.0</td>
<td>0.7 - 13.2</td>
<td>0.22</td>
</tr>
<tr>
<td>Moderate to severe injury or existing lesion</td>
<td>0.8</td>
<td>0.1 - 10.0</td>
<td>0.63</td>
</tr>
<tr>
<td><strong>FOOTWEAR AT WORK</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Closed shoes</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bare feet or open shoes</td>
<td>2.0</td>
<td>0.2 - 22.1</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>FOOTWEAR DURING RECREATION</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Closed shoes</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bare feet or open shoes</td>
<td>0.8</td>
<td>0.2 - 4.5</td>
<td>0.83</td>
</tr>
<tr>
<td><strong>MEDICAL RISK FACTORS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nil known or other risk factors¹</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes or alcohol abuse, alone or in combination with other risk factors</td>
<td>0.4</td>
<td>0.1 - 2.3</td>
<td>0.49</td>
</tr>
<tr>
<td><strong>SMOKING HISTORY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.0</td>
<td>0.3 - 3.3</td>
<td>0.80</td>
</tr>
</tbody>
</table>

¹ Other medical risk factors includes a patient with a past history of carcinoma of the breast, and another on long term treatment with topical steroids for psoriasis as their only known medical risk factors for melioidosis.
### Table 2

**POPULATION BASED ATTACK RATES OF MELIOIDOSIS**
**BY RISK CATEGORY, DARWIN, 1990 - 91**

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>CASES</th>
<th>POPULATION</th>
<th>AR per 100,000</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AGE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 - 49 years</td>
<td>8</td>
<td>39020</td>
<td>21</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>50 years &amp; over</td>
<td>17</td>
<td>8670</td>
<td>196</td>
<td>9.6</td>
<td>4.1 - 22.11</td>
</tr>
<tr>
<td><strong>GENDER</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>6</td>
<td>22720</td>
<td>26</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>19</td>
<td>24970</td>
<td>76</td>
<td>2.9</td>
<td>1.2 - 7.22</td>
</tr>
<tr>
<td><strong>RACE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Aboriginal</td>
<td>17</td>
<td>45090</td>
<td>38</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Aboriginal</td>
<td>8</td>
<td>2600</td>
<td>307</td>
<td>8.1</td>
<td>3.5 - 18.81</td>
</tr>
<tr>
<td><strong>OCCUPATIONAL SOIL EXPOSURE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not in workforce</td>
<td>13</td>
<td>16130</td>
<td>81</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Infrequent</td>
<td>2</td>
<td>21330</td>
<td>9</td>
<td>0.1</td>
<td>0.0 - 0.53</td>
</tr>
<tr>
<td>Frequent</td>
<td>10</td>
<td>10230</td>
<td>97</td>
<td>1.2</td>
<td>0.5 - 2.84</td>
</tr>
<tr>
<td><strong>MEDICAL RISK FACTORS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nil &amp; other</td>
<td>5</td>
<td>33760</td>
<td>15</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>8</td>
<td>12530</td>
<td>64</td>
<td>4.3</td>
<td>1.4 - 13.21</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6</td>
<td>1120</td>
<td>535</td>
<td>36.0</td>
<td>11.0 - 118.01</td>
</tr>
<tr>
<td>Alcohol &amp; diabetes</td>
<td>6</td>
<td>280</td>
<td>2128</td>
<td>142.0</td>
<td>43.5 - 462.01</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>25</td>
<td>47690</td>
<td>52</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. p<0.001
2. p<0.05
3. p<0.01
4. Not significant

5. Other medical risk factors includes a patient with a past history of carcinoma of the breast, and another on long term treatment with topical steroids for psoriasis as their only known medical risk factors for melioidosis.
### Table 3

**POPULATION BASED ADJUSTED RELATIVE RISKS FOR MELIIOIDOSIS RISK FACTORS FROM MULTIPLE LOGISTIC REGRESSION, DARWIN, 1990 - 91**

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>ADJUSTED RELATIVE RISK</th>
<th>95% CI</th>
<th>P VALUE OF RR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AGE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 - 49 years</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 years &amp; over</td>
<td>8.1</td>
<td>3.3 - 19.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>GENDER</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.8</td>
<td>1.1 - 6.9</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>RACE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Aboriginal</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aboriginal</td>
<td>3.2</td>
<td>1.2 - 8.8</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>DIABETES</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>12.9</td>
<td>5.1 - 32.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>ALCOHOL ABUSE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>6.7</td>
<td>3.0 - 15.2</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

The relative risks for the 5 risk factors were adjusted for each other. There was no interaction (effect modification) between diabetes and alcohol abuse, and the relationship with melioidosis (χ²₁df = 0.011).
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CONTROL OF A COMMUNITY OUTBREAK OF MEASLES WHICH STARTED IN A POORLY IMMUNISED HIGH SCHOOL POPULATION

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ABSTRACT

An outbreak of measles occurred in Darwin from February to March 1991. The first case was in a 13 year old high school student who had returned from a holiday overseas. She was symptomatic on the second day of the new school term. She infected an infant while both waited in a doctor's surgery. Outbreak control measures were instituted 18 days later when the Communicable Diseases Centre was first alerted of cases through the laboratory notification scheme. Through active surveillance, we identified 76 cases of measles, of whom 92% (70 cases) were less than 20 years of age. Of these, 46 were students at the index high school in which the attack rate was 39.2 per 1000. They transmitted the disease to six unvaccinated siblings aged 11 to 18 years, resulting in a secondary attack rate of 113 per 1000 in this age group (relative risk of disease in siblings 2.8; 95% CI 1.2 - 6.2). The outbreak affected one other high school, a number of primary schools, one tertiary institution, and 9 children under 5 years. Only four of the cases had a verified history of previous immunisation against measles. The outbreak was arrested within two weeks of instituting community wide control measures. Inadequate immunisation coverage among school age children and delays in notification were responsible for this outbreak. Improved measles surveillance systems including telephone notification of clinical cases are needed so that control measures can be instituted immediately within the household and in the community.
INTRODUCTION

Measles is a highly infectious disease and can spread rapidly in susceptible populations. Although live measles vaccine became available in Australia in 1965, acceptance and uptake have been impeded by the myth that measles is a minor childhood illness.1

In the recent school outbreak in Port Stephens, NSW, inadequate immunisation coverage was seen as the main cause of the outbreak.2 The attack rate at the worst affected primary school was 9.4%. Similarly, an outbreak from February to April 1991 affecting mainly school aged children in the Central Sydney Health Area resulted in 46 confirmed and nine suspected cases; 67% of cases were unimmunised.3 Vaccine coverage in five affected schools ranged from 4% to 50%.

The periodicity of measles outbreaks and vaccine coverage rates, particularly for the urban centres, have not been adequately documented in the Northern Territory (NT). Before March 1990, when measles became a notifiable disease in the NT, measles surveillance relied exclusively on the informal communication network between health services.

On 18 February 1991, the Communicable Diseases Centre (CDC), Darwin, received laboratory reports confirming two cases of measles. The index case had become symptomatic on 30 January and presented to her local medical officer the following day, a delay of 18 days before CDC was alerted to the outbreak. Telephone calls to general practitioners and laboratories in urban Darwin revealed two more clinical cases. All four cases were students at one high school.

This paper describes the epidemiological investigation and measures that were instituted to control the outbreak. It also identifies surveillance and control issues that
require greater attention if we are to belatedly achieve the target set at the 97th session of the NHMRC in 1984, which aimed at "measles control by 1988".

SUBJECTS AND METHODS

Case definition

We applied the clinical case definition of measles based on the following criteria: 1) history of generalised maculopapular rash lasting 3 or more days; 2) history of fever, equal to or greater than 38°C; and 3) history of cough, coryza or conjunctivitis.4

A confirmed case met the clinical case definition and was either positive for measles-specific IgM antibodies or had been in known contact with a laboratory confirmed case. A probable case met the clinical case definition but was not tested serologically and was not epidemiologically linked to another case.

Case finding and surveillance

We notified all medical practitioners, accident and emergency departments and community health centre staff in the Top End of the NT of the first four cases of measles on 19 February 1991. They were asked to start active surveillance for more cases, to notify all new cases by phone or facsimile, and ensure that all age-eligible, unimmunised children attending their surgery for any reason were encouraged to accept the measles vaccine. The NT Measles Outbreak Protocol, which described policies for the diagnosis and management of cases and contacts, as well as community control measures, was distributed to assist in surveillance and control. We also encouraged medical officers to review their appointment books and identify probable clinical cases retrospectively for the preceding three weeks.

A media release was issued informing the general community of the outbreak. Parents were advised to check their children's immunisation status and get them immunised if there was any doubt. Parents of children with signs and symptoms of measles were
advised to contact their doctor, school nurse, or the CDC, to notify the case and to obtain information on how to prevent the disease spreading to siblings and other children. Two letters about the outbreak and immunisation campaigns were also distributed to parents of all school aged children throughout Darwin.

Nurses at all schools checked the absentee list daily and contacted the student's family if the child was absent for more than two consecutive days. Students with signs and symptoms consistent with measles were excluded from school, and parents were advised to keep unimmunised siblings/contacts away from school.

We maintained daily telephone contact with school nurses and laboratories to identify new cases, and completed a case/contact investigation questionnaire by telephone interviews. The information included demographic details, clinical details - date of onset of symptoms, visits to the doctor, history of previous immunisation against measles, history of household and/or community exposure to measles. The nurse at the index high school also provided details of the number of days the students with measles had taken off school.

We also conducted immunisation coverage surveys at the two high schools, obtaining demographic data and details of immunisation history from students. We accepted a history of previous immunisation only if documentation of immunisation was available, or if immunisation was verified by a medical practitioner or health facility. We made no attempt to corroborate immunisation histories of students immunised interstate; to expedite control measures, they were classified as unimmunised.

The immunisation program

We offered Measles-Mumps-Rubella vaccine (MMRII, Merck, Sharp and Dohme, Pty Limited) to all children over 12 months of age with no record of previous measles immunisation. At the two affected high schools, we initially recommended
immunisation only for unimmunised students. In other schools with at least one confirmed case, we offered immunisation to unimmunised classroom contacts only. Other unimmunised children at the school were advised to attend a Community Health Centre for immunisation. Immunoglobulin was offered to infants less than one year of age who had contact with a confirmed or probable case. Two community health centres in the greater Darwin area remained open on the weekend of 24-25 February 1991 to allow easy access for immunisations to the general community.

We revised these recommendations when two cases were reported in children under 12 months of age during the third week of the outbreak. We lowered the immunisation age for all infants in Darwin to 6 months. Cases also continued to occur at the two high schools, and included students who were previously immunised. In the third week of the outbreak we therefore recommended re-immunisation of high school students who had been immunised before 1989. Re-immunisation was also extended to all students at other schools with a confirmed case of measles.

At the index high school, we followed up each incomplete or unreturned "consent for immunisation" form with a phone call to the parents. School nurses contacted students in all classes and specifically encouraged any who were not immunised. We immunised students at the school on 21 and 22 February, and offered re-immunisation on 1 March. Efforts directed at mass immunisation were less aggressive in the second high school.

Liaison with the media

The Community Liaison Branch of the NT Department of Health and Community Services which is responsible for all Departmental public relations activities, solicited the help of the media as soon as the outbreak was detected. The media was instrumental in stimulating community responsibility for outbreak control by keeping the public informed of the case count and control strategies, publicising the immunisation
campaigns, stressing the importance of immunisation, and emphasizing the preventable, serious sequelae of measles.

**Statistical analysis**

We used the statistical program Epi Info Version 5.01a for data manipulation and descriptive statistics, and Confidence Interval Analysis Version 1.1 software to calculate rates, relatives risks (RR), and 95% confidence intervals of the relative risks and difference in proportions between independent samples. Adults aged 20-64 years are the referent population in the calculation of relative risks in Table 1.

We obtained student population data for the two affected high schools from lists provided by the Education Department, and population data for the Darwin Statistical Division from the Australian Bureau of Statistics 1986 census. Because of the uncertainty of immunisation coverage at the index high school, with a student population of 1172, we carried out sensitivity testing to estimate vaccine efficacy. Vaccine efficacy (VE) was calculated using the formula VE(%)=(1-Relative Risk)*100. Our estimate of highest vaccine efficacy assumes that only students stating that they were unimmunised on the returned "consent for immunisation" form were the denominator population for the attack rate of measles in the unimmunised (n=415). Our estimate of lowest vaccine efficacy assumes that only students who provided documentation of immunisation (n=107) were the denominator population for the attack rate in the immunised. For each denominator, we estimated VE using numerators of four and 10 cases of measles respectively in the immunised population to allow for the level of uncertainty of past immunisation.

**RESULTS**

Figure 1 shows the epidemic curve of the outbreak, and Figure 2 shows the distribution of cases by demographic characteristics. A total of 76 cases (46 females, 30 males)
were reported from 30 January 1991 - 13 March 1991. The mean age was 14 years (range five months to 36 years). The sex difference is the result of a greater number of female cases at the two high schools; the female to male ratio was 28:18 at the index high school and 7:1 at the second high school. The index cases at both high schools were female.

Of the 76 cases, 15 were serologically confirmed and 41 were epidemiologically linked to a seropositive case. Twenty other patients were classified as probable cases. We received conflicting information on the duration of the rash from parents and doctors for four of the probable cases aged less than one year, lessening our confidence in the diagnosis. Paediatricians in Darwin reported seeing children aged between six and 12 months of age with roseola infantum during the measles outbreak.

**Attack rates**

Table 1 shows the age-specific attack rate of measles. The relative risk of measles in the 0-19 age group compared to the Darwin residents 20 years and over was 20.9 (95% CI 9.1 - 48.0). Children aged 1-9 years had the lowest attack rates. The sex-specific attack rates were 1.4 and 0.8 per 1000 for females and males respectively, and the relative risk of measles in females was 1.7 (95% CI for RR 1.1 - 2.6; p=0.036). Sixty one percent of the cases attended the index high school which had an attack rate of 39.2/1000 (46/1172 students), and eight cases (11%) attended the second high school which had an attack rate of 5.8/1000 (RR for the index high school = 6.5; 95% CI 3.1 - 13.8; p<10^{-7}).

**Morbidity**

None of the cases in this outbreak required hospitalisation for measles. At the index high school, measles associated absenteeism resulted in 310 lost student days for the 41 of 46 students for whom accurate information was available. The mean number of days lost was 7.6 (SD 2.7), with a range of 3-15 days.
Source and spread of the outbreak

The source of the outbreak was a 13 year old girl who had returned 8 days earlier from a holiday in Bali. She attended school on 29 January, the first day of the new term and developed a fever the following day. She remained home from school on 31 January when she developed a rash. Her family was not aware of contact with measles cases while travelling. The next two cases were affected nine days into the new term, and the outbreak peaked in the index high school on day 11 of the term. A 14 month old unimmunised child was also infected by the index case while attending the same doctor's surgery on 31 January. Both children were in the waiting room at the same time. This was the infant's only known contact with a case of measles.

Six patients with measles who did not attend the index high school were also infected by its students; four were siblings attending three separate primary schools and a tertiary institution, and two were students at the other affected high school who attended dancing classes with students from the index school.

Sibling studies

Table 2 presents the number of secondary cases by immunisation status in 82 siblings of the cases with measles. Measles was transmitted to six siblings resulting in a crude attack rate of 73.2 per 1000. None of the six were immunised, they were all siblings of students from the index high school and aged between 10 and 18 years. Two of the siblings also attended the index high school and the other four are described above. The age specific attack rate for siblings aged 10-18 years was 113.2 per 1000. The relative risk of measles in older siblings compared to students at the index high school was 2.8 (95% CI for RR 1.2 - 6.2; Fishers exact test p = 0.02)

Immunisation coverage

Four cases of measles at the index high school had a documented history of immunisation; two were serologically confirmed, two were not tested, and six other
patients gave a history of immunisation that could not be verified. Only one of the six cases reported from the primary schools had a documented history of previous immunisation.

The immunisation consent form was returned by 910 of the 1172 students at the index high school (77.6%). Of the 910 respondents, 12% (107 students) provided documentation of previous measles immunisation, 14% (126 students) gave a history of previous measles immunisation that could not be corroborated, and 29% (262 students) were uncertain or did not know their immunisation status. The remaining 415 students denied past measles immunisation. We were unable to determine whether the immunisation status of students who returned consent forms differed from the non-respondents.

Sensitivity testing did not allow for a meaningful interpretation of vaccine efficacy at the index high school. When our numerator was the four cases who produced documentation of previous immunisation, vaccine efficacy ranged from 5.2% to 94.8%. When we included the six measles cases with an unverified history of past immunisation, the range of vaccine efficacy was -176.5% to 84.8%.

As only 14% of the 1379 students at the second high school completed the questionnaire, their results were not analysed further. The level of immunisation coverage of the respondents did not differ significantly from that at the index high school.

Immunisation campaign
A total of 972 students (83%) were immunised at the index high school as part of the measles control strategy; 774 students were immunised during the initial two day immunisation campaign, 137 during the second campaign at the school and 61 students were immunised at community health centres. Ten students developed measles within 1
to 5 days of being immunised, and were probably incubating the disease at the time of immunisation.

At the other high school, where mass immunisation was less intensively promoted and followed up, only 43% of students were immunised during the immunisation campaign. None developed measles. There was a significant difference in the overall immunisation uptake rate between the two schools at the end of the campaigns (95% CI for the difference in proportions 36%-43%; p<10^{-7}).

DISCUSSION

Unlike the pattern of recent measles outbreaks in the USA, which affected mainly unimmunised pre-school children and highly immunised school-aged children, the Darwin outbreak involved predominantly high school children with low levels of immunisation coverage. We attribute the low clinical attack rate in children aged 1-9 years to a higher measles immunisation coverage rate than in high school students. For the 1-9 year old siblings of cases, the immunisation coverage rate was 94%. Spread of measles to the wider community was rapidly contained by the control measures which were instituted once the earlier cases were notified. The predominance of cases among females is most probably due to greater exposure within same sex peer groups; both the index case and the first two cases at the second high school were females.

Notification of the first cases at the second high school on the day of diagnosis, and the early intervention, limited the spread of measles at the school. Other factors which may have reduced transmission included: the right to leave school without permission when ill, which may have resulted in early removal from school and less opportunity to transmit measles to contacts, outdoor study areas, and no regular school assemblies.

The highest attack rate of 113 per 1000 occurred in the 10-18 year old siblings of high school cases. The risk of disease transmission between siblings was 2.8 times
greater than that observed in unrelated high school contacts. None of the family contacts who received age appropriate immunisation developed measles in this outbreak. Higher attack rates in household contacts have been reported previously\textsuperscript{11,12}, and have been attributed to greater intensity of transmission within the home. In the USA, McCormick et al. reported a secondary attack rate of 15.5\% in mainly immunised siblings aged 0-59 months (9/58 children), and Hope Simpson reported secondary attack rates of 76.5\% in susceptible siblings aged 0-15 years and 14.9\% in siblings aged over 15 years in England. This emphasizes the need to prioritise control measures in unvaccinated household contacts, such as exclusion from school and day care facilities when the first case is diagnosed in a household.

The efficacy of measles vaccine is 92-96\%.\textsuperscript{13} We were unable to calculate vaccine efficacy in this outbreak by the case control method because it was not possible to confidently determine the proportion of immunised children in the Darwin area or even at the index high school. Sensitivity testing of vaccine efficacy using maximum & minimum estimates of both numerators and denominators, resulted in vaccine efficacy ranging from no protective effect to 95\%. These results are unhelpful in determining whether vaccine failure contributed to this outbreak. Vaccine coverage at the index high school was at best 65\% and at worst 9\%. These estimates of vaccine efficacy are further complicated by our lack of knowledge of naturally acquired immunity in this age group.

Measles outbreaks have a rapid evolution requiring early recognition for effective control. In the Darwin outbreak, the first 60 cases occurred from 6-27 February 1991, a mean of almost three new cases per day. Measles immunisation of contacts within 72 hours of exposure to a case can prevent new cases of infection.\textsuperscript{14} Notification of the first case by telephone on the day of clinical diagnosis would have enabled early intervention to prevent or significantly limit further spread; the index case was notified through the laboratory notification system 18 days after clinical
diagnosis. However, once the outbreak was recognised, school and community based control measures, guided by an electively prepared measles outbreak protocol, halted transmission within two weeks. Other timely action that may have prevented some secondary transmission was preemptive mass immunisation of all susceptible school aged children and adolescents at the beginning of the outbreak. This could have included a policy to re-immunise children with a record of only one previous immunisation attending the affected schools.

The contact between the first case and the infant in the doctor's surgery was not recognised by the attending doctor. Droplet nuclei generated in an examining room can be dispersed across the entire office suite, and the airborne virus can survive at least one hour. Ideally, patients with suspected measles should not be referred to a clinical practice or to hospital without prior arrangement to ensure respiratory isolation. In private practice, children with uncomplicated measles can be given the last appointment of the day. More commonly, the attending medical officer has no prior warning of the patient's presenting illness; on suspicion of clinical measles the patient should be assessed quickly and sent home. Immunisation should be offered to all susceptible patients subsequently visiting the facility on the same day.

Corroborating immunisation histories during the outbreak was extremely time consuming and labour intensive. New initiatives which are to be implemented in the NT include centralised computerised databases of immunisation and documentation of immunisation status at school entry. The validity of parental reporting of the child's immunisation needs critical assessment. A study in NSW concluded that the reporting of immunisation status by parents appeared to be reliable, but Hawe et al. expressed concern about its validity in Victoria. They suggested that the trend towards over-reporting of immunisation status may lead us to incorrectly conclude that interventions to promote compliance have been successful, and that satisfactory levels of population compliance for eradication have been achieved. In New Zealand, Soljak
found that the proportion of children stated by parents to have received measles immunisation was 33% higher than could be confirmed by their doctors.19

We attribute the success of our control measures to the rapid and co-ordinated mobilisation of public health and private health care providers including pathology services, the Education Department, and other children's services organisations. Communication between the Communicable Diseases Centre and other service providers occurred on a daily basis, and the public was encouraged to telephone CDC with any inquiries. Persistent attempts at immunisation and intensive follow-up of non-respondents including telephone calls to parents at the index high school were also very successful control strategies. Vaccination uptake after two immunisation campaigns was 83% compared to only 43% at the second high school where efforts were less aggressive.

The proactive role of the media in collating and disseminating timely information to the community was facilitated by its early involvement through press releases of the Community Relations Branch of the NT Department of Health and Community Services. Media personnel saw the outbreak as dramatic and newsworthy, but also recognised their community service role in publicising control activities and informing parents of the more serious sequelae of measles. Attention to details by the Community Relations team, such as meeting publication deadlines for press releases, ensured ongoing co-operation.

Outbreaks of vaccine preventable diseases continue to occur because of inadequate immunisation coverage, challenging public health officers to develop new approaches to this deficiency. We need a sustained commitment to improve surveillance of vaccine preventable diseases, educate health care providers to minimise missed opportunities to immunise susceptible children ie to check immunisation status irrespective of the reason for attending a health care facility, identify groups at risk of low immunisation...
coverage, be aware of "consumer" attitudes to immunisation, and improve marketing strategies to "sell" immunisation to the community.
Acknowledgements

Chris Noonan (Research Officer, CDC) researched and developed the NT Measles Outbreak Protocol. Eileen Collard, Nurse co-ordinator, Department of Education, directed the school immunisation campaigns and provided immunisation data. We acknowledge the close collaboration of Department of Education and their nursing staff, Community Health Centres, especially Palmerston & Casuarina, Peverill's Pathology, Western Diagnostic Pathology, medical practitioners, Children Services Bureau, child care centres and parents.
Figure 1 Epidemic curve of measles cases by exposure category, Darwin, 30 January - 13 March 1991

No. of cases

<table>
<thead>
<tr>
<th>CDC notified</th>
<th>All other</th>
</tr>
</thead>
</table>

Jan | Feb | Mar

Date of onset of fever

CDC notified

Index high school

192
Figure 2  Measles notifications by age group or student status

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Population</th>
<th>Cases</th>
<th>Attack Rate</th>
<th>Relative Risk</th>
<th>95% CI of RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary School</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2 years</td>
<td>634</td>
<td>17</td>
<td>2.7</td>
<td>1.1</td>
<td>0.7 - 2.2</td>
</tr>
<tr>
<td>2-4 years</td>
<td>589</td>
<td>15</td>
<td>2.6</td>
<td>1.0</td>
<td>0.6 - 3.0</td>
</tr>
<tr>
<td>under 1 year</td>
<td>414</td>
<td>31</td>
<td>7.5</td>
<td>3.2</td>
<td>2.0 - 5.1</td>
</tr>
<tr>
<td>High School</td>
<td>students</td>
<td>54</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>adults</td>
<td></td>
<td></td>
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</tbody>
</table>
| 193

Table 2  Number of cases and attack rate by age group and student status.
Table 1.  
**Age specific attack rates of measles in Darwin, 30 January to 13 March, 1991.**

<table>
<thead>
<tr>
<th>Age group</th>
<th>Population Estimate</th>
<th>Cases</th>
<th>Attack Rate per 1000</th>
<th>Relative Risk</th>
<th>95% CI of RR</th>
</tr>
</thead>
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<td>&lt;1</td>
<td>1346</td>
<td>5</td>
<td>3.7</td>
<td>27.9</td>
<td>8.5 - 91.4</td>
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<tr>
<td>1 - 4</td>
<td>5220</td>
<td>4</td>
<td>0.8</td>
<td>5.8</td>
<td>1.6 - 20.5</td>
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<td>5 - 9</td>
<td>6345</td>
<td>2</td>
<td>0.3</td>
<td>2.4</td>
<td>0.5 - 11.8</td>
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<td>10 - 14</td>
<td>6459</td>
<td>35</td>
<td>5.4</td>
<td>40.7</td>
<td>17.1 - 96.6</td>
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<td>15 - 19</td>
<td>5878</td>
<td>24</td>
<td>4.1</td>
<td>30.7</td>
<td>12.5 - 75.0</td>
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<td>20 - 64</td>
<td>45259</td>
<td>6</td>
<td>0.1</td>
<td>1.0</td>
<td></td>
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<tr>
<td>0 - 19</td>
<td>25248</td>
<td>70</td>
<td>2.8</td>
<td>20.9</td>
<td>9.1 - 48.0</td>
</tr>
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</table>

Table 2.  
**Number of secondary cases by immunisation status in 82 siblings of cases with measles.**

<table>
<thead>
<tr>
<th>Age Group (years)</th>
<th>Vaccinated (number ill)</th>
<th>Unvaccinated (number ill)</th>
<th>Total (number ill)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 9</td>
<td>25 (0)</td>
<td>4a (0)</td>
<td>29 (0)</td>
</tr>
<tr>
<td>≥ 10</td>
<td>31 (0)</td>
<td>22 (6)</td>
<td>53 (6)</td>
</tr>
</tbody>
</table>

a: Three of these children were not age-eligible for routine measles vaccination, nor did they receive prophylactic immunoglobulin.
REFERENCES


Epidemic gonococcal conjunctivitis in central Australia.

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ABSTRACT

In 1991, an outbreak of non-sexually transmitted gonococcal conjunctivitis occurred among central Australian Aborigines.

Objectives: To describe the epidemiology of the outbreak; characterise the strains of Neisseria gonorrhoeae; identify factors facilitating spread; and assess treatment efficacy.

Methods: We identified cases by surveillance, laboratory notifications, and active case finding. A community survey identified risk factors for this disease. Meteorological data were compared to epidemic curves of the current and previous outbreaks.

Results: We identified 430 cases. The highest attack rate occurred in the 0-4 year age group (85.3/1000), with a linear decrease in attack rates with increasing age (p<0.001). Secondary infections occurred 13.5 times more commonly among household than community contacts (p<0.002; 95% CI for the relative risk 1.7 to 108.0). Disease was less common in children with clean faces (p<0.001) and hands (p=0.002). The outbreak occurred after heavy rainfall in the region, during a period of high fly density, and shortly after large community gatherings. Isolates were predominantly serogroup IA, unusual among central Australian serovars.

Conclusions: Outbreaks of gonococcal conjunctivitis in children occur in communities experiencing poverty and poor hygiene. Age is a significant risk factor for transmission. Sociological and ecological factors may also contribute to outbreaks.
INTRODUCTION

Gonococcal ophthalmia occurs in neonates born to mothers with genital tract *Neisseria gonorrhoeae*. In adults, gonococcal conjunctivitis is uncommon, although the incidence has been increasing in parallel with the rising incidence of sexually transmitted gonorrhoea worldwide. Spread by direct contact or fomites via fingers, towels, bed clothes or flies have been postulated. The application of urine to the eyes as a folk remedy for haemorrhagic viral conjunctivitis was associated with outbreaks of gonococcal conjunctivitis in rural Africa.

Several outbreaks of gonococcal conjunctivitis have occurred in Aboriginal communities in central Australia since 1934 when 91 cases occurred in Alice Springs. Outbreaks in 1981 and 1986-87 affected mainly children under 5 years of age. The 1986-87 outbreak featured rapid transmission within communities and between related communities, an excellent response to single dose parenteral penicillin or oral amoxycillin, and an absence of severe sight-threatening sequelae affecting neonates and adults with sexually acquired gonococcal conjunctivitis.

The first cases of the 1991 outbreak in central Australia were reported in late January. We carried out an investigation to describe the epidemiology of the outbreak, characterise the causative strains of *Neisseria gonorrhoeae*, identify personal and environmental risk factors, and assess treatment efficacy.

SUBJECTS AND METHODS

Approximately 15,000 Aboriginal people live in an area of 800,000 square kilometres in central Australia. There is a high degree of mobility and social interaction between related communities in the Northern Territory (NT), South Australia (SA) and Western Australia (WA). Alice Springs is the health referral centre for the region. The Alice Springs Hospital microbiology unit and Western
Diagnostic Pathology provide pathology services for central Australia. The Alice Springs Communicable Disease Control Centre (CDCC) receives all laboratory-based communicable disease notifications from the entire region, and physician notifications for the southern region of the NT.

We identified cases of gonococcal conjunctivitis by reviewing surveillance data collated, by active case finding in affected communities, and by reviewing all conjunctival pathology reports. We alerted all medical and rural nursing staff in the region of the outbreak, provided treatment advice, and asked clinic staff to produce lists of clinically diagnosed cases and their household contacts. Two of the authors (AM and RC) carried out field investigations in isolated communities in South Australia and Western Australia.

We consulted clinic staff about patients whose microscopy or culture results were positive on more than one occasion to determine whether their conjunctivitis was due to re-infection or to failed treatment. We included re-infected patients only once in the final case count.

We reviewed the Northern Territory surveillance data of sexually transmitted genital and ocular gonorrhoea for 1989-91 to determine whether this outbreak was associated with an increased incidence of genital infection, and whether childhood gonococcal conjunctivitis occurred in the inter-epidemic years. We also examined eye swab isolate records from the Alice Springs Hospital laboratory from December 1989 to April 1991.

Case definition

We accepted a clinical case definition of acute gonococcal conjunctivitis, (purulent conjunctival discharge with or without conjunctival injection and periorbital oedema), in communities where at least one other case had been proven by microscopy and/or culture. We excluded neonates with gonococcal conjunctivitis.
Laboratory investigations

The laboratories received conjunctival swabs from 387 cases and 496 contacts. Residents of the Ngaanyatjarra community chosen for the behavioural risk factor study also had oropharyngeal swabs taken for Neisseria culture. Conjunctival smears were air-dried for gram staining and examined for the presence of intracellular gram negative diplococci. Swabs for culture were placed in either Stuart's or charcoal media for transportation to the laboratories in Alice Springs. Swabs were then plated onto oxoid Thayer-Martin medium and incubated in either a 5% or 10% CO₂ jar at 35.0°C or 36.3°C for 12-24 hours. A convenience sample of 43 conjunctival, 7 genital and one blood culture gonococcal isolates were subcultured and forwarded to the coordinating laboratory of the Australian Gonococcal Surveillance Programme, Prince of Wales Hospital, Sydney, for serotyping, auxotyping, and determination of antibiotic sensitivity.

Delays of up to 7 days occurred between specimen collection and receipt in the laboratory. Most specimens with a transit time of three days or more were only examined by microscopy.

Community survey

One of the investigators (RC) interviewed and examined 87 of the 126 residents of the community in Western Australia which had a particularly high attack rate (191/1000). He identified risk factors which might have facilitated disease transmission in this outbreak by interview, and made a subjective assessment of personal hygiene based on a clean face and hands at the time of interview. He recorded family size, usual type of dwelling, and travel to other communities before the onset of conjunctivitis.
Statistical analysis

We obtained population denominators from three sources: the 1986 Australian Bureau of Statistics census; the 1991 population lists of the Nganampa Health Services, Pitjantjatjara Homelands, SA; and the 1991 population files of the Ngaanyatjarra Homelands Health Service, WA.

We tested contingency tables for significance by the Yates corrected chi square or Fisher exact test. We calculated the standard normal deviate to compare two proportions\. We used the epidemiological program Epi Info Version 5.01 to calculate chi square for trend, relative risk (RR), p values and 95% confidence intervals (CI) for the relative risk.

RESULTS

Attack rates

The epidemic curve is presented in Figure 1. Over the period 31 January-15 August 1991, 430 cases of gonococcal conjunctivitis were identified. The crude attack rate was 25.4 per 1000. There had been no reports of non-neonatal gonococcal conjunctivitis during 1988-90, and no change in the epidemiology of genital gonorrhoea during 1988-91.

Cases occurred sporadically throughout the region until the first week of April when 27 patients were diagnosed. The epidemic reached its peak in late April and May. Three communities reported either their first cases or a sudden increase in patient numbers within two weeks of festivals attended by symptomatic members of related communities. The bimodal tendency reflects transmission to previously unaffected communities throughout this sparsely populated region in the later stages of the epidemic.
Table 1 presents the age-specific attack rates. Sixty-eight percent of cases occurred in children aged 0-9 years. The highest attack rate occurred in children aged 0-4 years. There was a significant inverse relationship between attack rates and increasing age (linear trend test \( p<0.001 \)). Age was unavailable for 11\% of cases, but clinic staff stated that most of these patients were less than 10 years old. There was no difference in attack rates by sex.

**Clinical features**

All affected children presented with acute, usually bilateral, purulent conjunctivitis. Symptoms usually resolved quickly after a single dose of either procaine penicillin or amoxycillin. The only complications reported were disseminated gonococcal infection with arthritis in a three year old boy, transient large joint arthralgia in four other children, and a severe secondary ocular infection with *Staphylococcus aureus* in one child. The complication rate was 6/430 (1.4\%).

**Laboratory results**

Microscopy and culture were performed on 364 conjunctival specimens (85\% of cases). The air dried smears were positive for intracellular gram negative diplococci in 309 cases (84.9\%). *N. gonorrhoeae* was cultured in 134 cases (36.8\%). Culture was positive in only 11 cases with negative microscopy. Review of 95\% of pathology reports (345/364) revealed that 22 of 165 (13.3\%) children aged 0-4 years grew coliforms on conjunctival culture compared to only 7 of 180 (3.9\%) patients aged 5 years and over. The relative risk of conjunctival contamination in the 0-4 age group was 3.1 (95\% CI 1.4 to 7.2; \( \chi^2=8.78; \ p<0.01 \)).

Oropharyngeal *N. gonorrhoeae* was detected in 9 of the 84 residents (10.7\%) of the Ngaanyatjarra community from whom both conjunctival and oropharyngeal swabs were collected. Three of these cases had laboratory confirmed gonococcal conjunctivitis, and
three others had clinical conjunctivitis. The remaining three oropharyngeal carriers had no evidence of conjunctivitis.

The serotypes and auxotypes of 50 conjunctival, genital and blood culture isolates were determined. This outbreak was not caused by a single clone of *N. gonorrhoeae*. All but one conjunctival isolates were IA serovars, and were either non-requiring strains or proline requirers. Two auxotype/serovar (A/S) classes, Pro IA16 and Wt IA4, accounted for 19 of 42 conjunctival isolates each. Only one of these A/S classes, Wt IA4, was found in the sample of 7 genital tract strains. The blood culture isolate from the child with disseminated gonococcal infection was also Wt IA4. Of the sixteen conjunctival isolates obtained during a similar outbreak in 1986-87, three were serogroup IA, and 13 were IB serovars. None of the serovars found in the 1987 outbreak were identified in the current epidemic.

All isolates were "less sensitive" to penicillin (MIC 0.06 - 0.25 mg/L), and fully sensitive to spectinomycin, ciprofloxacin and ceftriaxone. All strains responded to standard penicillin regimens, and treatment failure was implicated as the cause of recurrent symptoms in only one patient. No penicillinase-producing isolates occurred in this outbreak.

Re-infection

Most cases improved within 12-24 hours of treatment. Re-infection in 15 successfully treated children (3.7% of patients aged 0-14 years) was confirmed by re-swabbing. The mean interval between episodes was 23.2 days (SE 2.4 days) with a range of 5 - 40 days.

The community risk factor survey

A single observer (RC) assessed personal hygiene in 84 individuals during a community survey. Residents with gonococcal conjunctivitis were more likely to have unwashed faces and/or hands at the time of examination than those without disease.
(p<0.001 and p=0.002 respectively). An unwashed face had a positive predictive value of only 58% when used as a test for gonococcal conjunctivitis, but the negative predictive value for facial cleanliness was 92%. Clean hands had a positive predictive value of 55% and a negative predictive value of 83%. Mothers were frequently seen to wipe their children's faces with their shirts, and then repeat the procedure on another child. The type of dwelling, household size and travel to other communities were not associated with the presence of conjunctivitis.

Contact screening

Multiple cases occurred within infected households. In 10 affected families of 93 people in one Pitjantjatjara community, there was one co-primary infection and 7 secondary cases for a secondary household attack rate of 8.5%. All but one secondary case occurred in children less than 10 years of age. Screening 171 asymptomatic community contacts in three related communities yielded only one additional case for an attack rate of 0.6%. Secondary infections occurred 13.5 times more commonly among household than community contacts (p<0.002; 95% CI for the relative risk 1.7 to 108.0).

Ecological factors

Review of meteorological data from January 1981 to July 1991 indicated that unseasonably heavy summer rain and humid conditions occurred in some areas of the region before the outbreak. Anecdotes from communities throughout central Australia describe an explosive increase in fly density in January and February 1991, and during the 1986-87 gonococcal conjunctivitis outbreak.

DISCUSSION

Epidemic gonococcal conjunctivitis differs from gonococcal ophthalmia neonatorum and adult gonococcal eye infections associated with anogenital gonorrhoea in severity, lack of sight-threatening sequelae, and response to treatment.
Factors which trigger an epidemic of paediatric gonococcal conjunctivitis are unknown. Gonorrhoea is one of the most common sexually transmitted diseases among Aboriginal adults in central Australia, and untreated adult disease is the most likely reservoir of infection. Gonococcal surveillance data did not indicate an increase in anogenital gonorrhoea preceding or concomitant with this outbreak. Individuals were extremely reluctant to consent to genital examination for cultural reasons, so we cannot compare the prevalence of anogenital gonorrhoea with conjunctivitis attack rates in time and place.

Cases had not experienced more recent non-gonococcal eye infections, such as trachoma, than uninfected children. There had been no increase in the number of eye swabs processed at the Alice Springs Hospital over the 15 month period preceding the outbreak, nor had the percentage which were culture positive increased. Thus we doubt that compromised conjunctival integrity was a major factor in this outbreak.

The epidemic curve of this and previous outbreaks are consistent with person-to-person conjunctival inoculation. Contaminated clothing used to wipe the faces of successive children may be an important vehicle of transmission. The rapid spread of gonococcal conjunctivitis between geographically isolated communities, the sudden appearance of cases in unaffected communities and the peaking of case numbers a short time after large gatherings attended by symptomatic children, further support person-to-person transmission.

The importance of personal hygiene in transmission is supported by the age-specific attack rates, the significant age-related difference in conjunctival contamination with faecal organisms, and by the increased attacks rate in individuals with unwashed faces or hands. Facial cleanliness had a high negative predictive value for clinical and laboratory confirmed conjunctivitis in our study; only 8% of individuals with clean faces had gonococcal conjunctivitis compared to 58% of those with unwashed faces. A large outbreak in Ethiopia in 1987-88, had similar epidemiologic and clinical
features to the central Australian experience. In a case control study of 362 households, the investigators found that a 'clean face' at the time of examination was associated with lower rates of conjunctivitis in the children examined.

Behavioural and life-style factors such as mobility, extended family patterns, crowding, availability of clean water, and environmental hygiene may be concomitants of epidemic gonococcal conjunctivitis. Child care in these communities extends beyond the immediate family. Young children come into close contact with a large number of related adults and their children, and are often minded by slightly older children who may be infected. Frequent travel to related communities, and overcrowding in host communities during festivals, may facilitate transmission.

The overwhelming predominance of serogroup IA strains in this outbreak is interesting, given the greater isolation of IB strains in the Northern Territory for a number of years. Gonococcal serogroups have different pathogenicity; IA strains occur more frequently in disseminated infections. The IA strains involved in this outbreak and the IB strains which were common in the 1986 outbreak, may have undetermined characteristics which enable them to colonise the eye. Gonorrhoea exists as a series of microepidemics, in which the prevalent strains may change quite rapidly. The number of genital isolates examined was too small to exclude the presence of IA16 strains in concurrent genital infections. Host factors or the transmission pattern, rather than virulence of the organism, probably determined the dominant serovar in this outbreak.

Most cases presented with florid conjunctivitis. Asymptomatic infection and oropharyngeal carriage were of no epidemiological importance. In children, infection of the oropharynx was probably secondary to retrograde infection via the lacrimal duct. Screening household contacts of cases proved an efficient approach to early case detection during this outbreak. Although transmission to young children probably does not occur exclusively within the household, the attack rate among household members was significantly higher than among community contacts. Epidemiological treatment of
family contacts was followed by a rapid decline in incidence in the Ngaanyatjarra communities, and may prove an effective control measure in the early stages of an epidemic. We did not undertake mass treatment in all affected communities because of the possibility of increasing resistance to penicillin.

Circumstantial and anecdotal evidence exists for a role of flies in transmission. Community members and health staff reported that fly density had increased noticeably at the beginning of this outbreak. Young children are less likely to swat flies away from their eyes, and flies may be mechanical vectors of transmission. Outbreaks of “pink eye”, a rickettsial infection of sheep, have been associated with high fly density (personal communication, Dr William Vogt, CSIRO, Canberra, ACT). The Australian bushfly, *Musca vetustissima* Walker, is anthropophilic, and feeds from the face, eyes, sores and abscesses. Flies may be mechanical vectors of viral, bacterial, protozoal and helminthic infections.16,17

The reported increase in fly numbers was preceded by above average rainfall. Weather patterns vary greatly across the region and rainfall is only monitored in selected communities, so that the role of rainfall remains speculative. Increased humidity may have prolonged the viability of *Neisseria gonorrhoeae* in fomites.

Effective control measures included early detection through active case finding, networking between health services and communities, and prompt standardised treatment. Health and hygiene education, and a comprehensive sexually transmitted diseases control program, are important for the long term control of gonococcal conjunctivitis. Single dose treatment with a suitable penicillin seems reliable, and reduces logistical problems of follow-up for multidose treatment. Strains involved in individual outbreaks should be examined to ensure their sensitivity to penicillin.
Acknowledgements

The authors wish to thank the following for their invaluable assistance during this investigation: CDCC, Alice Springs, NT; Mr Paul Linehan, Western Diagnostic Pathology, Alice Springs; Mr Rex Matters, Alice Springs Hospital laboratory; the Nganampa Health Services, which partially funded the field investigation in the Pitjantjatjara Homelands, SA; the Royal Flying Doctor Service, which provided transport for the field investigation in the Ngaanyatjarra Homelands, WA; Sonja Thomas and Ian Butterworth of the Bureau of Meteorology, Northern Territory Regional Office; Veronica Barrett, CDC Darwin; and rural clinic staff in central Australia.
Figure 1.

Epidemic curve of gonococcal conjunctivitis in central Australia
31/1/91 - 15/8/91

No. of cases

100
80
60
40
20
0

Jan  Feb  Mar  Apr  May  Jun  Jul  Aug
31  14  28  14  28  25  11  28  23  20  18  4  1  15

Fortnight of onset
Table 1

AGE SPECIFIC ATTACK RATES OF EPIDEMIC GONOCOCCAL CONJUNCTIVITIS IN CENTRAL AUSTRALIA, 1991.

<table>
<thead>
<tr>
<th>Age group (yrs)</th>
<th>Population Estimate</th>
<th>Cases</th>
<th>Attack Rate/1000</th>
<th>Relative Risk</th>
<th>95% CI of RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 4</td>
<td>2110</td>
<td>180</td>
<td>85.3</td>
<td>27.6</td>
<td>18.7 - 40.8</td>
</tr>
<tr>
<td>5 - 9</td>
<td>1900</td>
<td>114</td>
<td>60.0</td>
<td>19.4</td>
<td>13.0 - 39.1</td>
</tr>
<tr>
<td>10 - 14</td>
<td>1830</td>
<td>59</td>
<td>32.3</td>
<td>10.5</td>
<td>6.7 - 16.3</td>
</tr>
<tr>
<td>15 and over</td>
<td>9390</td>
<td>29</td>
<td>3.1</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Age unknown</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>15230</td>
<td>430</td>
<td>25.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Linear trend test of attack rates p<0.001.
REFERENCES


This is a late draft of the BF epidemiology paper which has not yet been distributed to the co-authors.

draft only

EPIEMIOLOGY PAPER

A CONCURRENT OUTBREAK OF BARMH FOREST AND ROSS RIVER VIRUS INFECTIONS IN NHULUNBUY, NORTHERN TERRITORY

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ABSTRACT

Introduction: The Barmah Forest virus (BF) has not been previously associated with human disease in the Northern Territory. We report an outbreak of BF and Ross River virus (RRV) infections in the East Arnhem region.

Objectives: Our initial objective was to identify the cause of a case cluster characterised by fever, rash, arthralgia and lethargy. Our secondary objectives became to describe the epidemiology and seroepidemiology of the outbreak; describe the natural history of the disease; estimate the ratio of subclinical infection to disease; and identify clinical features associated with BF infection.

Methods: We identified 187 cases of clinical illness compatible with arboviral disease and followed them prospectively until symptoms subsided. We collected acute and convalescent phase sera for arboviral serology from 73% of cases and from 227 asymptomatic volunteers who also completed detailed questionnaires during both serosurveys.

Results: The crude attack rate for acute compatible illness during the outbreak was 52 per 1000. We identified 42 serologically confirmed cases of BF, 28 cases of RRV, and 3 cases in which HI and IFA-IgM were positive for both BF and RRV resulting in crude attack rates of 12, 8 and 1 per 1000 respectively. Attack rates for all diagnostic categories increased with age. BF was isolated from Aedes vigilax mosquitoes and RRV from a pool of Culex annulirostris collected during the peak of the outbreak. Our serosurvey findings suggest that 97% of the adult Nhulunbuy population were susceptible to BF and 86% to RRV infection. The asymptomatic to symptomatic ration in residents aged 30 years and over was approximately 1.5:1 for BF and 2.6:1 for RRV.
Conclusion: We report the first documented outbreak of coincident Barmah Forest virus and Ross River virus disease in a defined population. BF is capable of causing outbreaks of illness similar to RRV.
INTRODUCTION

Barmah Forest virus (BF) is a little-known mosquito-bourne alphavirus first isolated from Culex annulirostris in northern Victoria in 1974 and has since been isolated from several mosquito species in eastern Australia. BF is serologically closer to Sindbis virus than to Ross River virus (RRV) the best known agent of epidemic polyarthritis. Current serological tests for BFV are both sensitive and specific. BF was first isolated in the Northern Territory (NT) in 1986 from a pool of Culex annulirostris trapped in Mataranka. It has been isolated annually since from both Aedes vigilax and Culex annulirostris, the principal vectors of Ross River virus transmission in the NT and probable vectors of BF transmission to humans.

Human infection was first diagnosed in 1986, and the virus was successfully cultured from a symptomatic patient in 1988. Human disease diagnosed as infection with Barmah Forest virus is uncommon, but few clinicians are aware of BF. Phillips et al reported 29 unrelated clinical cases diagnosed in eastern Australia from July 1988 to March 1989. Hawkes et al found antibodies to BF in blood donors throughout New South Wales. The illness most commonly associated with infection includes fever, rash, myalgia, arthralgia, and other symptoms consistent with a viraemia.

On 7 February 1992, medical staff at the Gove District Hospital (GDH) notified the Communicable Diseases Centre in Darwin of 12 patients presenting with acute onset of fever, rash, headache, fatigue and lethargy. By 11 February 20 cases had presented to GDH, and the NT Department of Health and Community Services committed resources to a formal epidemiological and entomological investigation of the outbreak. On 21 February, the State Health Laboratory Services in Perth reported that 5 of 18 sera from these patients had antibodies to BF using a rapid immunofluorescence IgM test. Another two sera were positive for RRV.
We report the first outbreak of BF disease investigated prospectively and coincident with an outbreak of RRV. The outbreak consisted of at least 187 clinical cases in a remote population of approximately 3600 people.

SUBJECTS AND METHODS

Nhulunbuy is a mining town on the sparsely populated Gove Peninsula of East Arnhem Land. Most Aboriginal people in the region live in remote outstations. The nearest Aboriginal community of approximately 250 people is located 12 kilometres from the town.

The town is situated within close proximity of tidal marshlands, and within the flight range of the "salt marsh mosquito" *Aedes vigilax*. Mosquito density surveillance is carried out by weekly trapping around Nhulunbuy. During the "wet season" November through March, and following tidal peaks, rapid increases in the number of *Ae vigilax* and *Cx annulirostris* commonly occur. From mid-December 1991 to mid-February 1992, vector monitoring activities in Nhulunbuy detected a dramatic rise in the numbers of both *Ae vigilax* and *Cx annulirostris* (Figure 1), and townspeople reported considerable biting activity. Rainfall and high tides in mid-December were responsible for the initial wave of *Ae vigilax*, 3.9 metre tides from 21 - 24 January preceded the increase in *Cx annulirostris*, and coincident rains and high tides from 15-18 February resulted in a second wave of both mosquito species.

We detected cases by: interviewing and examining all patients with compatible symptoms presenting through the GDH Accident and Emergency ward; liaising with the doctors at the town's single private practice, the Occupational Health Officers of the mining company and the health care staff of the Aboriginal community and outstations; enquiring about absenteeism at the primary and secondary schools; and by publicising the outbreak through the media, notices in community bulletin boards and by word of mouth to actively encourage self-reporting of illness. We also reviewed the GDH outpatient log and the hospital’s pathology request log from 1 December 1991 to
identify patients who presented with unexplained rash, musculoskeletal symptoms or fever, and/or for whom Ross River virus serology had been ordered, and obtained samples of sera collected by the private practitioners from Western Diagnostic Pathology.

We interviewed 97% of patients suspected of an arboviral infection, recording their demographic characteristics, travel history outside Nhulunbuy, duration of residence in Nhulunbuy, date of illness onset, history of serologically confirmed RRV infection, and a description of their symptoms. We collected at least one serum sample from 176 cases (94%) during the observation period. We obtained paired sera from 130 adult cases and from 7 children under age 14 years, third samples from 64 cases in August 1992, and unpaired sera from 13 children and 26 adults. We classified the remaining eight children and two adults as compatible cases on clinical grounds only. We attempted to follow all cases seen at the Gove District Hospital for approximately six months. One of the authors (AMM) based at GDH interviewed patients on a weekly basis until case numbers became prohibitive; in late August, we distributed a self administered follow-up questionnaire to all patients. We validated clinical details in the follow-up questionnaire by referring to the first interview, and corrected errors of recall accordingly. When new symptoms occurred after the date of first interview, we compared the details to the records kept by AMM.

Case definitions

We used a sensitive case definition of polyarthritis/arthralgia, rash or fever during the acute phase of the outbreak. We later reclassified all cases using a more specific clinical case definition which incorporated the symptoms and signs consistently associated with seropositive cases in the preliminary analysis. "Major" signs and symptoms were rash, acute polyarthritis and arthralgia; "minor" symptoms were morning stiffness, myalgia, fatigue, headache and sustained depression of mood in a previously well person. A compatible case of acute illness with an arbovirus required a minimum of two major, or one major and two minor signs or symptoms during the
outbreak period 1 December 1991 to 31 March 1992. There were four exceptions to this case definition; all were symptomatic cases with confirmatory serology but were never interviewed by the investigators.

We diagnosed BF disease in a clinically compatible case if they showed a fourfold or greater rise or fall in HI antibody titres in paired sera tested in parallel, and/or Barmah Forest IgM antibody was detected by IFA. A probable case of BF was a clinically compatible case with any of the following serological profiles: (1) an unpaired, acute phase HI titre of 1:80 or higher with an equivocal BF IFA-IgM; (2) a stable HI titre of 1:80 or higher in acute and convalescent phase sera without detectable IFA-IgM antibodies; and (3) a single convalescent phase HI titre of at least 1:320 without detectable IgM. We diagnosed cases of Ross River virus infection in the presence of RRV-specific serology. We used the term "alphavirus" infection when acute and convalescent phase HI titres for both BF and RRV were equivalent, and IFA-IgM was positive for both viruses. Serum collected 30 days or more after the onset of symptoms is regarded as convalescent. When providing results to patients and clinicians, we described confirmed and probable cases as definite cases of BF or RRV.

We considered patients with compatible clinical symptoms on whom serology was unavailable or inconclusive on unpaired sera to be possible cases of BF or RRV. Using the proportion of BF and RRV cases among patients in whom complete serology is available, we have estimated the number of BF and RRV cases in the former group. We used this total estimate of total BF and RRV infections only when calculating asymptomatic to symptomatic infection rates. Because of the difficulty of making a definitive diagnosis, we have included them, along with the seronegative cases, in the epidemic curve, but have excluded them from the comparison of clinical signs and symptoms in BF and RRV disease in the accompanying article.
Seroepidemiology

We conducted serosurveys in February and April. We publicised both extensively by advertisements in the local newspaper and on community bulletin boards, postal drops to all post office boxes in Nhulunbuy, announcements at meetings of community organisations, and by word of mouth. We collected sera from 244 volunteers from 18-24 February; 17 developed a characteristic illness and were reclassified as cases. The remaining 227 volunteers provided seroprevalence data and were the denominator population for the calculation of asymptomatic infection rates. 68% of the volunteers (165/244) participated in the second serosurvey eight weeks later. On both occasions, they completed questionnaires similar to those developed for the clinical cases. The first questionnaire focused on illness in the preceding month and history of previous RRV disease, and the follow-up questionnaire on new symptoms in the intersurvey period. In this way we were able to confidently determine the date of onset of a compatible illness in most symptomatic participants.

Subclinical infection with BF or RRV was diagnosed among asymptomatic serosurvey volunteers in the presence of confirmatory serology. IFA-IgM negative asymptomatic volunteers with HI titres of 1:40 or higher on initial testing were considered to be immune because of infection prior to this outbreak. Volunteers who were seronegative at initial testing but failed to present for follow-up serology were excluded from the denominator of “conclusive” diagnoses, and added to the population at risk. We have used the estimated number of BF and RRV cases in determining the asymptomatic to symptomatic infection ratios.

Specimen collection and laboratory methods

David Smith to elaborate and correct these details.

Sera referred to the State Health Laboratory Services in Perth were aliquoted and transported to the laboratory on dry ice. A convenience sample of 25 acute phase sera
was centrifuged immediately after collection and stored in liquid nitrogen for virus isolation studies. In order to identify the aetiologic agent initially, sera from the earliest cases were screened with a panel of IFA-IgM antigens which included the alphaviruses BF, RRV, Sindbis, Chikungunya and Semliki Forest virus, and the flaviviruses Murray Valley encephalitis virus and Kunjin. Subsequently all sera were tested by HI for BF, RRV and Sindbis virus, and sera with HI titres of 1:40 or higher were also tested by IFA-IgM. A small number of adolescent females were also tested for rubella IgM.

We also collected 9 nasopharyngeal swabs, 5 urine and 10 faeces from the first 13 patients to exclude disease associated with enteroviruses and adenoviruses. Nasopharyngeal swabs were placed in viral transport medium (Brand details etc) for transportation to the Royal Darwin Hospital.

**Entomological investigations and isolation of virus from mosquitoes**

Working on the assumption of an arbovirus outbreak in Nhulunbuy, the Medical Entomology Branch, NT Department of Health and Community Services, in collaboration with local vector monitoring and control authorities, mounted an entomological field investigation on 12 - 13 February. Using carbon dioxide baited mosquito monitoring traps, approximately 2830 mosquitoes were caught and sorted by species into pools of 50 mosquitoes per pool, and transported in liquid nitrogen to the Berrimah Agricultural Research Centre in Darwin for viral isolation. Sentence on viral isolation technique (Richard Weir).

**Animal reservoir studies**

The Conservation Commission of the Northern Territory and the North Australian Quarantine Service in conjunction with the Medical Entomology Branch and the Berrimah Agricultural Research Centre conducted a limited animal and bird trapping and bleeding study to identify possible animal reservoirs of alphaviruses in Nhulunbuy and surrounding bushland. Mammal traps were laid out on three consecutive nights for
a total of 390 traps. A convenience sample of 23 domestic dogs was also tested for arbovirus antibodies.

Statistical methods

The 1991 Australian Bureau of Statistics preliminary estimates of the Nhulunbuy population provided denominator data for the calculation of attack rates. ABS occupational groupings used in this analysis are managers and administrators, professionals, para-professionals, tradespeople, clerks, sales and personal services, plant and machine operators, and labourers and related workers. We used Epi Info Version 5.01b for questionnaire development, data entry and manipulation, and descriptive statistics, the Microsoft Excel spreadsheet for calculation of attack rates, and Confidence Interval Analysis, Version 1.1 software to determine relative risks (RR), 95% confidence intervals (CI) of the attack rates and relative risks, and to run survival time analyses for two independent samples and calculate Cox proportional hazard ratios.

We calculated two observation periods in person months for each case. The total time observed was calculated by subtracting the date of onset from the date of last presentation. We estimated the duration of illness for 162 cases in three ways: if the patient was still symptomatic at the last follow-up, the duration of illness equalled the total person months of observation; if s/he recorded the date on which they first felt completely well, it was subtracted from the date of onset; and if s/he was well but could only approximate the length of illness, we used the midpoint of the range given, for example, 2 - 3 months is approximated to 2.5 months, and "over three months" to 3.5 months. This method of estimating disease chronicity may have resulted in an underestimation of prolonged illness, as only 17 patients recorded the date they first felt well.

We estimated the inapparent infection rate for adults aged 30 years and over by extrapolating the observed rate of each serological category in the volunteer group to
the general population. Our first serosurvey included 9.1% of residents aged 30-39 years (86/943), 19.3% of residents aged 40-49 years (83/430) and 8.7% of residents aged 50 years and over. Our sample of 0-29 year olds was insufficient (35 volunteers) to extrapolate the inapparent infection rate to the entire age group.

RESULTS

Attack rates

Figure 1 presents the week of onset of the 187 cases with illness compatible with an arbovirus infection and the counts of *Aedes vigilax* and *Culex annulirostris* trapped at the site nearest to human habitation during the outbreak. The crude attack rate of illness compatible with an arbovirus infection was 52 per 1000. We identified 42 confirmed cases of BF, 28 of RRV, and 3 cases in which HI and IFA-IgM were positive for both BF and RRV, resulting in attack rates of 12, 8 and 1 per 1000 respectively. In addition, we made a diagnosis of probable BF in three cases and probable RRV in seven cases, and estimated three cases of BF and two of RRV in the clinically diagnosed group. Our total estimate was 48 cases of BF infection and 37 of RRV infection.

The outbreak began in December, peaked in mid-February, and tapered off in early March. Cases of Barmah Forest virus and Ross River virus infection started to appear at the same time. The beginning of the outbreak was preceded by a rapid build-up of numbers of *Aedes vigilax*, and the peak coincided with the appearance of large numbers of *Culex annulirostris*. Case numbers fell consistently during the second wave of *Ae. vigilax*.

Table 1a presents the breakdown of the 187 compatible cases by age group and diagnostic category, and the corresponding attack rates are presented in Table 1b. The attack rate of confirmed and probable BF in patients aged 25 years and over (20.5 per 1000) was significantly higher than that of cases 0-24 years (3.0 per 1000; RR of BF in the older age group=6.7; 95% CI 2.6 to 16.8; \( \chi^2 = 20.73; p<10^{-4} \)). The corresponding attack rates of Ross River virus were 13.8 and 4.8 per 1000
respectively (RR=2.8; 95% CI 1.3 to 6.2; $\chi^2=13.32; p<0.001$). RRV cases were distributed more evenly across age groups than BF, but within age groups the attack rates of BF and RRV were similar. There was no significant difference in attack rates by sex.

Of the 11 patients aged 0-14 years from whom we obtained acute and convalescent sera, three had a confirmed arbovirus infection and two had probable infections. The two probable infections were BF in adolescents aged 11 and 13 years; the former was negative for BF-lgM on sucrose gradient testing but her paired HI titres were 1:1280, and the second case has an HI titre of 1:80 and an equivocal IFA-lgM result. RRV was confirmed in a 10 and 14 year old, and a 9 year old child with high HI titres was IFA-lgM negative.

This outbreak was confined to the non-Aboriginal population of the Gove peninsula. The attack rate in adult Aboriginals was apparently nil, although a number of the non-Aboriginals living or working in Aboriginal communities became ill. Clinic staff in Yirrkala informed us of an unusual number of Aboriginal children under 5 years of age who presented to the clinic in early February with a febrile illness. They were successfully treated with anti-pyretics and no blood was collected for arbovirus serology, so the cause of their symptoms remains speculative. There was no increase in clinic presentations among older children and adult Aboriginals.

Plotting cases by street of residence provided no evidence of clustering in space, and given the ubiquity of mosquitoes, we would not have expected any. Multiple cases among the 167 patients who provided full addresses occurred at 21 locations; 18 private homes yielding 15 pairs and three households of three patients each, and a further 11 cases from three different locations. Their diagnoses were 10 cases of BF, six of RRV, two of past infection with RRV, and 32 clinically compatible cases. Concordant diagnoses of two RRV infections occurred only in one household, and discordant BF and RRV infections were confirmed in two other households. Viral culture results of stool, urine and nasopharyngeal specimens, and serological evidence
from cases attending the primary and secondary schools failed to support a concurrent outbreak of an agent transmitted by the respiratory or faecal-oral route.

There was no significant difference in attack rates when cases of confirmed arbovirus infection were analysed by ABS occupational groups ($\chi^2$ for trend = 0.254, $p = 0.061$).

The mining company did record a 37% increase in person hours lost by absenteeism during the outbreak (9767/429 000 rostered hours), compared to 1 December 1990-31 March 1991 when 7129 person hours were lost. This increase of 615 missed hours per 100 000 rostered hours was statistically significant (95% CI for the difference in proportions 556 - 674 person hours lost per 100 000 rostered hours).

Duration of residence in Nhulunbuy

Table 2 presents quartiles of duration of residence in Nhulunbuy by diagnostic category for 125 cases. There was no significant difference in residence history between serologically confirmed and compatible cases, nor between BF and RRV cases ($\text{Kruskal-Wallis } H_{6\text{df}}=5.921; p=0.432$). Similarly, there was no difference in length of residence by serological diagnosis among the serosurvey volunteers, nor between cases and volunteers. The median length of residence for volunteers was six years, with a range of 0-35 years.

The incubation period in BF

Six serologically confirmed cases of BF infection provided enough detail in travel itineraries outside Nhulunbuy for the month before onset of their symptoms to permit an estimate of the incubation period. An adult who returned from holidays in Italy and Bali became unwell three days after returning home. Two patients had onset dates 12 days, another two 18 days, and one case 20 days after returning to Nhulunbuy, for an mean incubation period of 13 days (SD 6.6 days).
Clinical presentation

The details of the clinical illness are presented in the accompanying paper. We followed 183 cases for a total 790.6 person months; 50% for at least 4.9 months and 25% for between 6.2 and 8.0 months. Thirty patients (14%) were lost to follow-up within 30 days of diagnosis. We were able to determine the duration of symptoms for 68 of the 77 serologically confirmed patients, and 94 compatible cases. 60% (25/42) of patients with BF, 29% (8/28) with RRV, one of the three "alphavirus" cases and 48% (55/114) of compatible cases stated that they were well before, or on the date, of last consultation. The rest were still symptomatic at last contact. Table 3 presents the observed and expected number of BF cases who became symptom free each month of observation. Patients with Barmah Forest virus and the clinically compatible cases for whom we failed to make a serological diagnosis, had a similar symptomatic period which was significantly shorter than that of RRV, but 45% of confirmed and probable BF cases were still symptomatic after 6 months of observation. Age did not influence the duration of illness in cases who recovered during the observation period ($r=0.10$, 95% CI -0.10 to 0.30).

Rash was a prominent feature in confirmed and probable cases of Barmah Forest virus infection (43/44 cases, 97.7%); 70% of RRV infections (21/33) were also associated with a rash (RR of rash in BF=1.5, 95% CI 1.2 to 2.0; $\chi^2=13.28$; $p<0.001$). RRV appeared to be more arthritogenic than BF, but the rates of arthralgia and arthritis were not significantly different between the infections. Arthralgia was present in 32 RRV infections (97.7%) and acutely inflamed or swollen joints in 20 (60.6%). The corresponding rates of arthralgia and arthritis for BF were 86.4% (38 cases) and 38.6% (17 cases). All three "alphavirus" cases presented with arthralgia; two also complained of rash and one had arthritis. There was no difference in the proportion of patients presenting with fever, fatigue, headaches, myalgia, or depression of mood.
Table 4 presents the serological results of the 227 asymptomatic volunteers by age. We identified 16 asymptomatic cases from the serosurvey; 6 BF, 9 RRV and 1 alphavirus infection. The background rate of HI antibodies to Barmah Forest virus was 2.6% in the volunteer group. The prevalence was 3.5% when we included the two volunteers with HI antibodies to both BF and RRV as BF infections. As expected, past infection with Ross River virus was more common than with BF (14.1%, 32 subjects). The prevalence of RRV-HI antibodies increased significantly with age in volunteers (X^2 test for trend=4.055; p<0.05). Conversely, we observed the highest rate of BF-HI antibodies in the 0-19 age group (X^2 test for trend=6.831; p<0.01); the rates of BF-HI antibodies were 13%, 8%, 0%, 2% and 0% for the 0-19, 20-29, 30-39, 40-49 and 50 years and over age groups respectively. This is probably a spurious finding due to small sample size and self-selection of the serosurvey group.

There was no significant difference in the age distribution or results of serology by sex. We estimated the inapparent infection rate for adults aged 30 years and over by applying the infection rate of BF (4.1%) and RRV (4.8%) in the volunteer group of the same age to the general population. An estimated 54 residents were infected with BF and 50 with RRV, suggesting inapparent infection to clinically ill ratios of about 54:35 (1.5:1) for BF and 50:19 (2.6:1) for RRV in this age group.

Seroconversion occurred in only two volunteers, and both were symptomatic cases of Barmah Forest virus disease. They have been analysed in the case series. There were no seroconversions to Ross River virus. Of the remaining 15 volunteers who developed a compatible illness, two were BF-IgM positive and two were RRV-positive on the first specimen, three patients had elevated RRV HI titres with negative IFA-IgM results, seven were seronegative for BF and RRV on paired sera, and one failed to present during the second serosurvey.
Laboratory evidence for Barmah Forest virus

The details of the laboratory work characterising the virus responsible for this outbreak are presented elsewhere. Of the 137 patients with paired sera submitted for laboratory work, 20.4% (28 cases) seroconverted on Barmah Forest HI antibody testing and 5.1% (7 cases) seroconverted to RRV. Sera from three of five patients in whom dual infection with BF and RRV could not be differentiated from an anamnestic response by HI and IFA-IgM were re-tested using Neutralisation Inhibition. In two, the results of neutralisation were consistent with recent BF infection on a background of past RRV. The serological findings of the third case remain equivocal and may indicate a true dual infection. We have identified sequential infection with these alphaviruses in a 29 year old woman who seroconverted to BF in late February. She was noted to have later seroconverted to RRV sometime between the second blood collection on 10 March and a third sample collected on 21 August. Her RRV HI titre of 1:160 coincided with the appearance of RRV-IgM which had been negative on the previous two occasions.

Sera were negative for acute infection with Sindbis (n=83), Chikungunya (n=26), Kunjin (n=9), Murray Valley encephalitis (n=28) and Semliki Forest (n=13) viruses and rubella (n=3).

Viral isolation

Attempts at viral isolation from the 25 acute phase sera placed in liquid nitrogen were unsuccessful. Only one of 9 nasopharyngeal specimens yielded an adenovirus, and proved to be a concurrent infection in a patient with BF who complained of upper respiratory tract symptoms. Viral isolation from stool and urine specimens was also unsuccessful.
Barmah Forest virus was isolated from one pool of 50 *Aedes vigilax* mosquitoes and Ross River virus from one pool of *Culex annulirostris* collected on 12 - 13 February. No other arboviruses were cultured from the remaining pools.

Attempts at viral isolation from the 5 native mammals (two grassland Melomys and three domestic agile wallabies), a black rat, three water birds (two sacred ibis and a white-faced heron), and the 23 domestic dogs were all unsuccessful. Antibody studies have also been unhelpful.

**DISCUSSION**

The first documented outbreak of Barmah Forest virus disease occurred in an isolated community in the Northern Territory in December 1991 through March 1992. During the outbreak 187 cases of an illness compatible with acute arbovirus infection were identified through active surveillance, resulting in a crude attack rate of 52 per 1000. Although we are unable to provide a costing of the Nhulunbuy outbreak, the mining company recorded an increase in absenteeism of 37%, an increment of 2638 person hours lost during the outbreak compared to the same time interval in 1991. We attribute rapid decline in case numbers in late February to early recognition of the outbreak, intensive fogging and larviciding activities, and a well publicised mosquito bite prevention campaign.

The incidence rate of symptomatic BF infection was 12 per 1000. This rate is much lower than that reported by Vale et al. (80 per 1000) in a group of 97 unselected surgical patients and 65 outpatients investigated for polyarthritis from coastal areas of southern New South Wales. Serologically confirmed cases of BF disease accounted for 22% of all presentations (42 cases), and 15% (28 cases) were RRV infections. Both infections were less common in the 0-24 years age group than in residents aged 30 years and over, but cases of Ross River virus were distributed more evenly across age groups than Barmah Forest virus infection. The highest attack rates were recorded in the 40-49 age group for both viruses.
The clinical picture of BF in Nhulunbuy is consistent with that found in the case series reported by Hawkes and Phillips. The illness was characterised by rash, arthralgia, myalgia, headache, fatigue and fever. Almost 98% of the BF cases in this series presented with a rash; in contrast, Phillips et al. reported a rash in only 47% of their cases. Although BF may exist as a number of topotypes with differences in pathogenicity and clinical expression, errors in patient recall may also have contributed to the lower frequency of rash in the Queensland study. When we compared patient responses in our follow-up questionnaire with details given in the acute phase of illness, we identified fever and rash as the symptoms most often forgotten because of their transience.

Our longitudinal data suggest that infection with Barmah Forest virus results in a milder illness than Ross River virus. A significantly larger number of BF cases than expected became well in each month of observation when compared to the rate of convalescence in Ross River virus disease. However, 45% of confirmed and probable BF cases were still symptomatic after 6 months of observation. The seronegative cases with clinically compatible illness had a similar symptomatic period to BF cases which leads us to postulate that a third, as yet unidentified pathogenic arbovirus, may have been responsible for illness in these patients. We are confident of the completeness of case ascertainment during the outbreak investigation, and our epidemiological, laboratory and anecdotal data make a missed concurrent outbreak of an agent transmitted by the respiratory or faecal-oral route unlikely. A large number of uncharacterised mosquito-borne viruses have been isolated in the Northern Territory (Mr Richard Weir, Berrimah Agricultural Research Laboratory, NT Department of Primary Industry and Fisheries, personal communication).

We detected a background rate of BF HI antibodies of 2.6-3.5% in the serosurvey volunteers. Duration of residence in Nhulunbuy did not appear to influence clinical attack rates or seroprevalence. Serosurveys from various regions in New South Wales have reported similar rates. Phillips et al. in Queensland detected HI antibody to BF
in 6.5% of 2010 consecutive serum samples, but prevalence was higher in men (7.8%) than in women (5.0%). There was no gender-related differences in either BF incidence or prevalence rates in our study. These sera were drawn from volunteers rather than a representative sample of the community, but we believe that the ubiquitous nature of the mosquito biting during the outbreak make the volunteers a reasonable group from which to estimate serological incidence. Our low asymptomatic to clinically apparent disease ratio of 1.5:1 for Barmah Forest virus and 2.6:1 for Ross River virus are consistent with ratios observed in New South Wales and Fiji during epidemics.

There are several possible explanations for this outbreak. First, similar outbreaks may have occurred in the past, remaining unrecognised because of the relatively mild nature of the illness, or inadequate surveillance. Cases investigated for epidemic polyarthritis in the Northern Territory were not routinely screened for Barmah Forest virus infection before this outbreak. Second, epidemiologic or laboratory facilities to investigate such outbreaks fully are not readily available in isolated parts of northern Australia. Third, some as yet unknown change may have occurred in the vectors present in this area, and made them more competent to transmit this virus. Fourth, the virus itself may have had some genetic change which has rendered it more pathogenic to man. Fifth, ecologic changes may have occurred in the as yet unknown intermediate hosts which have increased the infection rate in the vectors in the area.

These possibilities will require considerable coordinated field work to unravel, but it seems clear that BF is not an innocuous infection, and research should continue to define its ecologic and epidemiologic characteristics. We are negotiating testing of an historical serum bank of non-Aboriginal and Aboriginal sera so that we can determine whether Barmah Forest virus infection is new to the region. This outbreak underscores the difficulty of studying arbovirus activity in the tropical areas of Australia. The Northern Territory is vulnerable to the introduction of both viruses and vectors from interstate and overseas, so intensive entomological surveillance and
preventative education are ongoing public health measures for arbovirus disease control.
Fig 1. Compatible cases of arbovirus infection
Nhulunbuy, NT, 1 December 1991 - 31 March 1992

Week of onset
Table 1a


<table>
<thead>
<tr>
<th>Age Group</th>
<th>Population</th>
<th>BF</th>
<th>RRV</th>
<th>Alpha</th>
<th>Compatible</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denominators</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-4</td>
<td>379</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>8</td>
<td>114(104)</td>
</tr>
<tr>
<td>5-9</td>
<td>412</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>9</td>
<td>187</td>
</tr>
<tr>
<td>10-14</td>
<td>415</td>
<td>0</td>
<td>(2)</td>
<td>8</td>
<td>(6) 11</td>
<td>11</td>
</tr>
<tr>
<td>15-19</td>
<td>228</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>20-24</td>
<td>220</td>
<td>2</td>
<td>1</td>
<td>(3)</td>
<td>5</td>
<td>(3) 8</td>
</tr>
<tr>
<td>25-29</td>
<td>329</td>
<td>7</td>
<td>4</td>
<td>9</td>
<td>(7) 20</td>
<td>20</td>
</tr>
<tr>
<td>30-39</td>
<td>943</td>
<td>16(17)</td>
<td>7 (8)</td>
<td>34 (32)</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>430</td>
<td>10</td>
<td>9(11)</td>
<td>18</td>
<td>(16) 39</td>
<td>39</td>
</tr>
<tr>
<td>50 and over</td>
<td>253</td>
<td>6</td>
<td>1</td>
<td>12</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>3609</td>
<td>42(45)</td>
<td>28(35)</td>
<td>3</td>
<td>114(104) 187</td>
<td></td>
</tr>
</tbody>
</table>

* The numbers in parentheses are the total BF, RRV and compatible cases in each age group when probable cases are also included.
Table 1b

Age-specific attack rates per 1000* by diagnostic category,


<table>
<thead>
<tr>
<th>Age Group</th>
<th>BF</th>
<th>RRV</th>
<th>Alpha</th>
<th>Compatible</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>5-9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>10-14</td>
<td>0 (5)</td>
<td>7</td>
<td>0</td>
<td>19 (14)</td>
<td>27</td>
</tr>
<tr>
<td>15-19</td>
<td>4</td>
<td>9</td>
<td>0</td>
<td>35</td>
<td>48</td>
</tr>
<tr>
<td>20-24</td>
<td>9</td>
<td>5 (14)</td>
<td>0</td>
<td>23 (14)</td>
<td>36</td>
</tr>
<tr>
<td>25-29</td>
<td>21</td>
<td>12 (18)</td>
<td>0</td>
<td>27 (21)</td>
<td>61</td>
</tr>
<tr>
<td>30-39</td>
<td>17 (18)</td>
<td>7 (8)</td>
<td>1</td>
<td>36 (34)</td>
<td>62</td>
</tr>
<tr>
<td>40-49</td>
<td>23</td>
<td>21 (26)</td>
<td>5</td>
<td>42 (37)</td>
<td>91</td>
</tr>
<tr>
<td>50 and over</td>
<td>24</td>
<td>4</td>
<td>0</td>
<td>47</td>
<td>75</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>8 (10)</td>
<td>1</td>
<td>32</td>
<td>52</td>
</tr>
</tbody>
</table>

* The numbers in parentheses are the rates per 1000 of BF and RRV and compatible cases in each age group when probable cases are also included.
Table 2

Patients' years of residence in Nhulunbuy at the time of first presentation by serological diagnosis (n=126*).

<table>
<thead>
<tr>
<th>Serological Diagnosis</th>
<th>Cases</th>
<th>Quartiles of years of residence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Minimum</td>
</tr>
<tr>
<td>Alphavirus</td>
<td>3</td>
<td>1.0</td>
</tr>
<tr>
<td>BF</td>
<td>31</td>
<td>1.0</td>
</tr>
<tr>
<td>RRV</td>
<td>21</td>
<td>0.5</td>
</tr>
<tr>
<td>IgM negative RRV</td>
<td>9</td>
<td>0.0</td>
</tr>
<tr>
<td>Seronegative§</td>
<td>52</td>
<td>0.0</td>
</tr>
<tr>
<td>Clinical only &amp; ~</td>
<td>9</td>
<td>0.8</td>
</tr>
</tbody>
</table>

* One patient with the diagnosis of IgM negative BF had lived in Nhulunbuy for 16 years.

§ Seronegative patients to BF and RRV HI and IFA-IgM on paired sera.

~ Inconclusive serology includes patients who were negative on BF and RRV HI and IFA-IgM testing of acute phase sera, and on whom convalescent sera are unavailable.
Table 3
Cox proportional hazard analysis of duration of illness in Barmah Forest infection.

<table>
<thead>
<tr>
<th>Time (mo)</th>
<th>Survival</th>
<th>BF outcome (well cases)</th>
<th>Hazard</th>
<th>95% CI of Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>11</td>
<td>7.6</td>
<td>4.14</td>
<td>1.3 - 13.4</td>
</tr>
<tr>
<td>2.0</td>
<td>13</td>
<td>8.1</td>
<td>4.42</td>
<td>1.5 - 13.0</td>
</tr>
<tr>
<td>3.0</td>
<td>20</td>
<td>12.3</td>
<td>4.57</td>
<td>1.9 - 10.9</td>
</tr>
<tr>
<td>4.0</td>
<td>24</td>
<td>15.7</td>
<td>3.43</td>
<td>1.6 - 7.3</td>
</tr>
<tr>
<td>5.0</td>
<td>24</td>
<td>16.2</td>
<td>3.10</td>
<td>1.5 - 6.4</td>
</tr>
<tr>
<td>6.0</td>
<td>24</td>
<td>16.2</td>
<td>3.10</td>
<td>1.5 - 6.4</td>
</tr>
<tr>
<td>7.0</td>
<td>24</td>
<td>17.4</td>
<td>2.44</td>
<td>1.2 - 5.0</td>
</tr>
</tbody>
</table>

* RRV is the comparison group in the calculation of the hazard ratio.
Table 4

Results of serology by age group of 227 asymptomatic volunteers.

<table>
<thead>
<tr>
<th>Serological Diagnosis</th>
<th>Age Group in years</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 - 19</td>
<td>20 - 29</td>
</tr>
<tr>
<td>Alphavirus</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>BF</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>RRV</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>IgM negative alpha</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IgM negative BF</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>IgM negative RRV</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Seronegative§</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Inconclusive</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>24</td>
</tr>
</tbody>
</table>

* The age of one seronegative patient is unknown.

§Seronegative for BF, RRV and Sindbis viruses on HI and IFA-IgM testing.
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