Melioidosis: Continuing High Mortality in the Top End of the Northern Territory

Bart Currie, Royal Darwin Hospital and Menzies School of Health Research

Between October 1989 and February 1993 there have been 68 confirmed cases of melioidosis from the Top End of the Northern Territory, with 20 (29%) deaths.

Significant risk factors for disease have been diabetes, alcohol abuse and Aboriginality. Only one fatal case has had no evident underlying medical condition. Four cases were children, the youngest being 3 years old. Both urban and rural cases have occurred, with a wet season (November till April) predominance. The majority of cases have been considered to have a newly acquired infection, usually with percutaneous inoculation from soil or water harbouring Pseudomonas pseudomallei. However inhalation or ingestion of P. pseudomallei may have occasionally occurred. A small number of cases were reactivation of latent disease.

The commonest presentation of melioidosis has been pneumonia, with or without septicemia. Genito-urinary foci, such as prostatic abscesses, and localised cutaneous ulcers have also been common. Abdominal CT scan has revealed splenic abscesses and other focal collections in some patients and is now performed on all melioidosis cases at Royal Darwin Hospital.

The current drug of choice for melioidosis (excluding localised cutaneous disease) is IV ceftazidine. In most cases we have added IV rolitetracycline. After initial IV therapy of usually 7-14 days, maintenance oral therapy with doxycycline or cotrimoxazole is used for around 3 months. A number of the fatalities have been
from relapsed disease, usually associated with poor compliance with maintenance therapy.

Melioidosis is the commonest cause of fatal community-acquired bacteraemic pneumonia in the Top End. Priority measures for control are:

1. Targeting prevention and control of the two commonest risk factors for disease and mortality - diabetes and alcoholism;
2. Limiting exposure of skin to wet season soils by encouraging use of protective footwear and gloves where appropriate, such as in gardening and in occupational exposure;
3. Avoiding delay in starting appropriate antibiotics in suspected melioidosis; and
4. Emphasising compliance and follow up of maintenance antibiotic therapy to prevent disease relapse.

### Update on Ross River Virus Infections for 1992/3

![Graph showing the number of Ross River Virus (RRV) infections by month in 1992 and 1993.](image)

Between 1 July 1992 and 28 February 1993 CDC in Darwin received 145 laboratory notifications of patients with positive IgM serology for Ross River Virus (RRV).

Of these 145 laboratory notifications, we received 106 completed Arbovirus Surveillance questionnaires from medical practitioners and/or patients. This allowed us to identify the probable date of infection of the 106 patients, and this is shown in figure 1.

The locality of infection where 4 or more subjects were affected is shown below:

<table>
<thead>
<tr>
<th>Locality</th>
<th>No. of cases</th>
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<tr>
<td>Katherine</td>
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<td>Mandorah</td>
<td>4</td>
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<td>Humpty Doo</td>
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<td>Howard Springs</td>
<td>13</td>
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<tr>
<td>Northern Suburbs</td>
<td>28</td>
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</table>

Medical practitioners are returning a greater proportion of the Arbovirus Surveillance questionnaires promptly this year. This allows the Medical Entomology Branch to identify localities where there may be a high rate of transmission of infections, and to investigate reasons for this transmission. This will allow prioritization of mosquito control requirements and public education. In the larger towns, this information assists in deciding the location and frequency for both larval and/or adult mosquito control.
Haemophilus Meningitis in Katherine  
Jan Bullen, Katherine CDU

Since January 1992, there have been nine cases of invasive Haemophilus disease in the Katherine district. Five of them had meningitis and of these four were caused by *Haemophilus influenzae* type *b* (Hib). The remaining four cases had other forms of invasive *H. influenzae* disease, and two of these were type *b*.

The four cases with Hib meningitis were from different areas of the Katherine district, and all had primary infections, with no secondary spread. Two were Aboriginal children, aged 7 and 14 months. The other two were non-Aboriginal children aged 10 and 25 months.

The average household size ranged from 3 to 17 (mean 8.5) with the larger households in the Aboriginal families (mean 13). The number of older siblings ranged from 0 to 4, again with the higher figures in Aboriginal families. Both of these are considered possible risk factors for the transmission of air-borne infections. All household contacts were given rifampicin prophylaxis.

The clinical presentation was similar for all four cases with Hib meningitis. The duration of illness prior to admission varied from 24 to 72 hours; all had vomiting, two were irritable and one was drowsy. Diarrhoea was also noted in 3 children. Neck stiffness was noted in 3 children. None of the cases was comatose on admission. The average duration of the illness was 11.5 days, with a range of 8 to 14 days.

The fifth case with meningitis had *H. influenzae* that was positive to latex a, c, f. This Aboriginal child was comatose on admission after a three day history of diarrhoea and malaise and remained comatose for a further three days. He has residual ataxia and sensori-neural deafness.

Two of these children were transferred to the Royal Darwin Hospital for more intensive treatment.

Whilst these figures are too low for a meaningful interpretation, they support the findings reported by Jeff Hanna for Central Australia. In particular, the younger age of the Aboriginal children is relevant in the choice of vaccine that is effective at an early age.

The number of cases with Hib disease in Katherine has emphasised the need for using an effective vaccine once it becomes available. We will start our immunisation program in March. Our local General Practitioners have implemented an active Hib immunisation programme for older children since 1992.

Acknowledgements:  
Jo Hagger, Microbiologist, KDH, Dr David Brookes.

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The Haemophilus influenzae b Vaccine  
Nan Miller, Darwin CDC

The Federal Government plans to fund the States/Territories for the *Haemophilus influenzae* type *b* (Hib) vaccine program from July 1993 onward. This vaccine will then be incorporated into the routine childhood vaccination schedule across Australia.

The Northern Territory has funds to start the program before July. Health Services across the NT are developing appropriate plans and a timetable to introduce the Hib vaccine.

An early feature of the plan in the NT is to change the hepatitis B vaccine schedule. At present, the hepatitis B vaccine is given at birth, 2 and 6 months of age. This will be changed to the new schedule: at birth, 1 and 6 months of age.
The NT has selected the Hib-OMP vaccine (Pedvax HIB, made by Merck, Sharpe & Dohme and distributed by Commonwealth Serum Laboratories). This vaccine is highly immunogenic after the first injection at 2 months of age. This early response is particularly important for protecting very young Aboriginal infants.

The Hib-OMP vaccine is given at 2 and 4 months of age, with a booster dose at 12 months of age.

A study conducted in the NT by Jeff Hanna showed that Aboriginal children under the age of 5 years had a very high incidence of invasive Hib disease. The rate in Central Australia was among the highest in the world. The rate in non-Aboriginal children in Central Australia was similar to that for Aboriginal children in the Top End, and this was fourfold higher than the rate in other centres in Australia. Between 1985 and 1988, 3 Aboriginal children and 1 non-Aboriginal child died from invasive Hib disease.

Health services in the various districts of the NT will conduct in-services for staff. Information pamphlets for Health Professionals and for parents will be distributed. The official starting date for the program will be announced by the District Health Service.

New legislation will add invasive Haemophilus influenzae disease to the NT notifiable diseases list.

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**Change in Hepatitis B Vaccination Schedule for Infants in the NT**

*Nan Miller, Darwin CDC*

The Department plans to introduce a *Haemophilus influenzae type b* (Hib) vaccine into the childhood immunisation schedule soon (see above). The first dose of the vaccine will be offered to children at the same time as the first triple antigen ie. at 2 months of age.

Many infants have had their first dose of hepatitis B vaccine in hospital and will be due for their second at two months. This means three injections at 2 months of age ie. triple antigen, hepatitis B and Hib; this is unacceptable to most parents and to health staff.

To limit the number of injections at any one visit, the Hepatitis B vaccination schedule will be changed. Your local Communicable Diseases Centre will notify you of the date on which this change will become effective in your area. The new schedule will be the same as the adult schedule:

- first injection - birth (in hospital);
- second injection - 1 month; and
- third injection - 6 months.

The third injection coincides with the Triple Antigen and Polio schedule.

All printed information for parents will be amended to reflect this change. Detailed information on the new Hib vaccine will be available shortly.

If you have any questions please contact the Communicable Disease Centre in your area.
Will Your Phone Notification Prevent a Hepatitis A Outbreak?

Nan Miller, Darwin CDC

Twenty nine cases of hepatitis A were reported from the Palmerston area between August 1992 and January 1993. All cases were in children, staff or family members of children who attended the same child care facility. The first case became symptomatic on 3 August; the second case presented two months later on 5 October. The outbreak gained momentum in early November when three adults and three children in two families became ill. The source of their infection was traced back to younger children in each family who attended the child care facility. Overall, seven children, three care-givers and 19 family members were notified during the outbreak. Contact tracing suggested that another seven children at the day care facility were asymptptomatically infected and were responsible for transmission within their families. The outbreak ended with the last reported case on 13 January.

Early detection of the outbreak was possible because of notifications from doctors and laboratories. We were able to conduct contact tracing and recommend normal human immunoglobulin (IG) prophylaxis for care givers and household contacts within the 7-10 days of exposure required to prevent or control infection. Some doctors preferred to do their own contact tracing and administering of IG, others referred their patients to the community health centre for IG.

To contain this outbreak we implemented the following public health measures:

1. Education

We conducted a workshop for the caregivers on transmission and prevention of hepatitis A with emphasis on general hygiene practices, in particular hand washing.

The Environmental Health Officer visited the child care centre to assess facilities and advise on strengthening hygiene practices. It is likely that the paddling pool contributed to the outbreak. New water quality guidelines for swimming, diving, water slide and paddling pools have been developed.

We provided parents/guardians with information on transmission, signs and symptoms for active surveillance and prevention. Parents were encouraged to watch their families for signs and symptoms of hepatitis and to consult with a medical practitioner and to notify the Child Care Centre.

2. Prophylaxis

We recommended IG to the full time and regular part time staff at the day care centre.

3. Surveillance

The staff at the Centre maintained active surveillance. Children presenting with symptoms suggestive of hepatitis A were excluded until cleared by a medical practitioner. Cases in families were notified to the Communicable Diseases Centre for further investigation in consultation with the attending medical practitioner. We maintained regular contact with the child care facility to identify potential cases. All notified cases were investigated promptly.

Conclusions

Hepatitis A can spread quickly in a day care setting, particularly when there are infants in nappies and/or children in trainers. Although hepatitis A is usually a mild or asymptomatic infection in young children, morbidity in adults can be serious with a case fatality rate of 0.1%, hospitalisation and time off work which has the potential for economic hardship.

Early notification can contain and/or minimise
an outbreak with timely implementation of public health measures. This outbreak did not extend beyond the children, caregivers and families of children attending the day care facility.

**Recommendations**

- Medical practitioners notify cases with acute hepatitis A early by phone.
- Maintain close liaison between all health care providers during an outbreak.
- IG can only be obtained through a community care centre after approval by the Director of the Communicable Diseases Centre.
- IG is available to General Practitioners directly from the Royal Darwin Hospital Pharmacy.

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**EDITORIAL COMMENT**

**Hepatitis A Outbreak**

This outbreak demonstrates that Hepatitis A remains an important disease in the Northern Territory. There were 156 cases of acute hepatitis A notified in the NT in 1992, which represents an incidence of 89.7/100,000 (c.f. N.S.W. 17.4/100,000 and Vic 10.3/100,000 in 1991). Although serious complications are rare and chronic disease does not occur, the virus is responsible for a great deal of morbidity and has a significant economic impact on the community.

Hepatitis A is spread by the faecal-oral route and outbreaks occur where sanitation and hygiene standards are less than optimal. Infection in infancy and early childhood is usually mild, without jaundice and leads to life-long immunity. The disease in older children and adults is more severe. Once endemic in Australia, Hepatitis A is now an uncommon childhood disease. Since a large, susceptible (non-immune) adult population exists there is always the possibility of an outbreak. An epidemic in homosexual men in N.S.W. and Victoria is now diminishing after nearly two years and has been a major public health problem in those states. The NT has a high rate of notified infection due, in part, to the number of susceptible non-Aboriginal adults working in Aboriginal communities. Infection in Aboriginal populations almost always occurs in childhood and is asymptomatic.

The current practice of using normal human immunoglobulin for prophylaxis is well established. Disease is prevented (or modified) in the majority of recipients but immunity is passive and only short-lived. Repeat administrations may be required for on-going protection. Fortunately, if contact with the virus has indeed occurred, immunoglobulin does not prevent the development of active immunity. As icteric disease is very uncommon in children, it is not usually recommended for those under 8 years of age.

Human immunoglobulin is expensive to prepare and is always in short supply. Later in 1993 a new Hepatitis A vaccine will be licensed for use in Australia. The vaccine is highly immunogenic and safe. Its use in high risk adult populations will be a major advance in the prevention of Hepatitis A in our community. Further details of the vaccine will be published in a later bulletin.
Pertussis: Should We Be Concerned?

Nan Miller, Darwin CDC

In Australia, whooping cough outbreaks occur in 3 or 4 year cycles with increased notifications in the summer months. Data from the National Diseases Returns indicate that the summer-autumn of 1989-90 was an epidemic season in most areas of Australia. This was also the experience in the NT with 20 cases notified. Western Australia reported 223 cases and Queensland also experienced an epidemic.

In 1992, 702 cases were reported across Australia compared to 336 cases in 1991, but no cases were reported in the NT. In New South Wales 75 cases were reported by the end of August 1992, a two-fold increase over the same period for 1991. Ninety percent of the cases in NSW were in children over six months of age.

Fifty three cases have been notified across Australia in January 1993 with the NT having its first case, a three year old girl whose diagnosis was laboratory confirmed. She had not been vaccinated against pertussis.

The pertussis vaccine is effective and safe. As with other vaccines, it is associated with minor transient side-effects. Health care providers should check the immunisation status of children aged less than four years, particularly if they are in contact with babies less than six months of age.

In anticipation of an outbreak in the NT we distributed guidelines for the management and control of pertussis. Please contact the Communicable Diseases Centre in your area if you have not received a copy.

Leptospirosis in the Northern Territory

Angela Merianos, Darwin CDC

The Communicable Diseases Centre in Darwin has been notified of a patient who developed acute renal failure secondary to infection with *Leptospira interrogans var australis*. 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.

1. Epidemiology

*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, rabbits, 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 serovars in the NT 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.

2. Clinical Features

The milder, non-icteric form of leptospirosis can be a subclinical or self-limiting illness. It can be missed if not considered in the differential diagnosis of pyrexia of unknown origin and aseptic meningitis. 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 haemoptysis. The incubation period is usually 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 5-10%.

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 surveillance and prevention strategies for this disease. There is no information on the size of the animal reservoir in the NT and 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 unidentified high risk areas.

Care in the Interpretation of Dengue Virus Serology Results

Angela Merianos, Darwin CDC

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 being detected in the Northern Territory until the mid 1950s, and the last locally acquired case of dengue fever occurred in about 1956. Since then 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. A single NT-breeding site, probably initiated with an imported mosquito, was eradicated in 1980.

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, so it can be used as a flavivirus group screening test. However, HI antibody is very nonspecific and cross-reacts with other flaviviruses. Previous immunisation against yellow fever modifies the HI antibody response to other flaviviruses, including Dengue virus.

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 viruses is called the anamnestic response and can result in high titres for all flaviviruses tested. The closer two viruses are antigenically related, 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 approaches the sensitivity of HI.

We have 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 nearly 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 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 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 residence 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.
# Pamphlets/Guidelines Produced in the Northern Territory

## For Health Care Professionals

- AIDS A Story in our Hands to Share (manual for Aboriginal AIDS educators).
- Minimum period of exclusion for children or staff with infectious diseases at day care & schools.
- Prevention of secondary cases of Haemophilus influenzae type b disease.
- Guidelines for the control of Hepatitis A, B, and C & the Hepatitis B vaccination policy.
- Malarial case management protocol.
- Measles outbreak control protocol.
- Prevention of secondary cases of pertussis.
- Tuberculosis Screening program for NT Schools.

## Pamphlets for the Public

(Information on the disease, signs, symptoms, treatment, risk factors and prevention.)

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<th>STD/AIDS</th>
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<td>AIDS the Facts</td>
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<td>AIDS and your Workplace</td>
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<td>Sex-Playing Safe</td>
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<td>Shigella</td>
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<td>Whooping Cough</td>
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### TUBERCULOSIS:

- A Counselling Aid (booklet for TB patients and carers on disease, outcome and treatment)
- General information (guide to Mantoux testing, reading and direction after results: English, Portuguese, Vietnamese, Creola, Tagalog, Greek)
- Contacts (community)
- Extended family screening
- What it means to new arrivals (English, Portuguese, Vietnamese, Chinese, Thai, Tagalog, Greek)
- Advice to visitors and contacts of patients (hospital)