## Communicable Diseases Surveillance Bulletin

## March 2005

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Cytoarchitectural and histopathological changes in a liver sample from a Marburg patient who was treated in Johannesburg, South Africa in 1975.
CDC/Dr J Lyle Conrad, source : Public Health Image Library
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[^0]| EPIDEMIC PRONE DISEASE SURVEILLANCE : JANUARY-FEBRUARY |  |  | CUMULATIVE | ECP | FSP | GAP | KZP | LPP | MPP | NCP | NWP | WCP | RSA |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AFP, cases from whom specimens have been received | < = 15 years |  | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 2 \\ & 3 \end{aligned}$ | $\begin{aligned} & 0 \\ & 4 \end{aligned}$ | $\begin{aligned} & 3 \\ & 3 \end{aligned}$ | $\begin{aligned} & 3 \\ & 8 \end{aligned}$ | $\begin{aligned} & 10 \\ & 1 \end{aligned}$ | $\begin{aligned} & 3 \\ & 1 \end{aligned}$ | $\begin{aligned} & 1 \\ & 1 \end{aligned}$ | $\begin{aligned} & 0 \\ & 3 \end{aligned}$ | $\begin{aligned} & 4 \\ & 1 \end{aligned}$ | $\begin{aligned} & 26 \\ & 25 \end{aligned}$ |
| Measles, IgM positive results | All ages |  | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 0 \\ & 15 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 20 \\ & 16 \end{aligned}$ | $\begin{aligned} & \text { U } \\ & 28 \end{aligned}$ | $\begin{aligned} & 0 \\ & 1 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 10 \end{aligned}$ | $\begin{aligned} & 20 \\ & 70 \end{aligned}$ |
| Rubella, IgM positive results from measles IgM negative patients | All ages |  | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 18 \\ & 4 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 11 \\ & 6 \end{aligned}$ | $\begin{aligned} & U \\ & 7 \end{aligned}$ | $\begin{aligned} & 2 \\ & 1 \end{aligned}$ | $\begin{aligned} & 5 \\ & 6 \end{aligned}$ | $\begin{aligned} & 2 \\ & 0 \end{aligned}$ | $\begin{aligned} & 3 \\ & 4 \end{aligned}$ | $\begin{aligned} & 0 \\ & 3 \end{aligned}$ | $\begin{aligned} & 41 \\ & 31 \end{aligned}$ |
| CCHF | All ages |  | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 1 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 1 \\ & 0 \end{aligned}$ | $\begin{aligned} & 2 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 4 \\ & 0 \end{aligned}$ |
| Rabies, human | All ages |  | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 0 \\ & 1 \end{aligned}$ | $\begin{aligned} & 0 \\ & 1 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 6 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 1 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 7 \\ & 2 \end{aligned}$ |
|  | All ages | All serotypes | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 0 \\ & 2 \end{aligned}$ | $\begin{aligned} & 2 \\ & 0 \end{aligned}$ | $\begin{aligned} & 14 \\ & 11 \end{aligned}$ | $\begin{aligned} & 3 \\ & 3 \end{aligned}$ | $\begin{aligned} & 0 \\ & 1 \end{aligned}$ | $\begin{aligned} & 1 \\ & 4 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 1 \end{aligned}$ | $\begin{aligned} & 12 \\ & 3 \end{aligned}$ | $\begin{aligned} & 32 \\ & 25 \end{aligned}$ |
|  |  | Serotype b | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 1 \\ & 0 \end{aligned}$ | $\begin{aligned} & 2 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 3 \\ & 0 \end{aligned}$ |
| Haemophilus influenzae, invasive | Age < 5 years | Non-serotype b | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 2 \end{aligned}$ | $\begin{aligned} & 1 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 2 \\ & 0 \end{aligned}$ | $\begin{aligned} & 3 \\ & 2 \end{aligned}$ |
|  |  | Non-typable | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 0 \\ & 1 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 4 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 3 \\ & 0 \end{aligned}$ | $\begin{aligned} & 7 \\ & 1 \end{aligned}$ |
|  |  | Unknown serotype | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 0 \\ & 1 \end{aligned}$ | $\begin{aligned} & 1 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 3 \end{aligned}$ | $\begin{aligned} & 0 \\ & 2 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 1 \\ & 1 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 3 \\ & 0 \end{aligned}$ | $\begin{aligned} & 5 \\ & 7 \end{aligned}$ |
| Meningococcal disease | All ages |  | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 4 \\ & 0 \end{aligned}$ | $\begin{aligned} & 3 \\ & 2 \end{aligned}$ | $\begin{aligned} & 10 \\ & 16 \end{aligned}$ | $\begin{aligned} & 1 \\ & 1 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 1 \\ & 2 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 3 \\ & 1 \end{aligned}$ | $\begin{aligned} & 7 \\ & 7 \end{aligned}$ | $\begin{aligned} & 29 \\ & 29 \end{aligned}$ |
|  | All ages |  | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 11 \\ & 25 \end{aligned}$ | $\begin{aligned} & 12 \\ & 18 \end{aligned}$ | $\begin{aligned} & 178 \\ & 212 \end{aligned}$ | $\begin{aligned} & 35 \\ & 46 \end{aligned}$ | $\begin{aligned} & 14 \\ & 7 \end{aligned}$ | $\begin{aligned} & 16 \\ & 24 \end{aligned}$ | $\begin{aligned} & 2 \\ & 5 \end{aligned}$ | $\begin{aligned} & 9 \\ & 10 \end{aligned}$ | $\begin{aligned} & 67 \\ & 55 \end{aligned}$ | $\begin{aligned} & 344 \\ & 402 \end{aligned}$ |
|  | Age < 5 years |  | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 6 \\ & 10 \end{aligned}$ | $\begin{aligned} & 5 \\ & 7 \end{aligned}$ | $\begin{aligned} & 78 \\ & 52 \end{aligned}$ | $\begin{aligned} & 14 \\ & 18 \end{aligned}$ | $\begin{aligned} & 4 \\ & 2 \end{aligned}$ | $\begin{aligned} & 5 \\ & 7 \end{aligned}$ | $\begin{aligned} & 1 \\ & 1 \end{aligned}$ | $\begin{aligned} & 5 \\ & 5 \end{aligned}$ | $\begin{aligned} & 23 \\ & 28 \end{aligned}$ | $\begin{aligned} & 141 \\ & 130 \end{aligned}$ |
|  | Penicillin, nonsusceptible, all ages |  | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 1 \\ & 8 \end{aligned}$ | $\begin{aligned} & 4 \\ & 4 \end{aligned}$ | $\begin{aligned} & 65 \\ & 57 \end{aligned}$ | $\begin{aligned} & 9 \\ & 12 \end{aligned}$ | $\begin{aligned} & 2 \\ & 2 \end{aligned}$ | $\begin{aligned} & 4 \\ & 3 \end{aligned}$ | $\begin{aligned} & 0 \\ & 1 \end{aligned}$ | $\begin{aligned} & 3 \\ & 2 \end{aligned}$ | $\begin{aligned} & 21 \\ & 7 \end{aligned}$ | $\begin{aligned} & 109 \\ & 96 \end{aligned}$ |
|  | Susceptibility unknown, all ages |  | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 1 \\ & 0 \end{aligned}$ | $\begin{aligned} & 2 \\ & 3 \end{aligned}$ | $\begin{aligned} & 16 \\ & 36 \end{aligned}$ | $\begin{aligned} & 6 \\ & 16 \end{aligned}$ | $\begin{aligned} & 2 \\ & 1 \end{aligned}$ | $\begin{aligned} & \hline 0 \\ & 3 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 4 \end{aligned}$ | $\begin{aligned} & 4 \\ & 13 \end{aligned}$ | $\begin{aligned} & 31 \\ & 76 \end{aligned}$ |
| Salmonella species - invasive isolates | All ages | All serotypes excl. <br> S. typhi | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 2 \\ & 12 \end{aligned}$ | $\begin{aligned} & 5 \\ & 2 \end{aligned}$ | $\begin{aligned} & 105 \\ & 99 \end{aligned}$ | $\begin{aligned} & 8 \\ & 13 \end{aligned}$ | $\begin{aligned} & 2 \\ & 4 \\ & \hline \end{aligned}$ | $\begin{aligned} & 2 \\ & 4 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 1 \\ & 0 \\ & \hline \end{aligned}$ | $\begin{aligned} & 11 \\ & 15 \end{aligned}$ | $\begin{aligned} & 136 \\ & 149 \end{aligned}$ |
| Salmonella species - enteric isolates | All ages | All serotypes excl. S typhi | $\begin{array}{r} 2004 \\ 2005 \\ \hline \end{array}$ | $\begin{aligned} & 18 \\ & 36 \\ & \hline \end{aligned}$ | $\begin{aligned} & 8 \\ & 4 \\ & \hline \end{aligned}$ | $\begin{aligned} & 41 \\ & 58 \\ & \hline \end{aligned}$ | $\begin{aligned} & 5 \\ & 16 \\ & \hline \end{aligned}$ | $\begin{aligned} & 2 \\ & 2 \\ & \hline \end{aligned}$ | $\begin{aligned} & 1 \\ & 12 \\ & \hline \end{aligned}$ | $\begin{aligned} & 0 \\ & 1 \\ & \hline \end{aligned}$ | $\begin{aligned} & 9 \\ & 7 \\ & \hline \end{aligned}$ | $\begin{aligned} & 30 \\ & 25 \\ & \hline \end{aligned}$ | $\begin{aligned} & 114 \\ & 161 \\ & \hline \end{aligned}$ |
| Salmonella typhi | All ages |  | $\begin{array}{r} 2004 \\ 2005 \\ \hline \end{array}$ | $\begin{aligned} & 1 \\ & 7 \\ & \hline \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \\ & \hline \end{aligned}$ | $\begin{aligned} & 5 \\ & 1 \\ & \hline \end{aligned}$ | $\begin{aligned} & 3 \\ & 2 \\ & \hline \end{aligned}$ | $\begin{aligned} & 2 \\ & 1 \\ & \hline \end{aligned}$ | $\begin{aligned} & 2 \\ & 10 \\ & \hline \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \\ & \hline \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \\ & \hline \end{aligned}$ | $\begin{aligned} & 2 \\ & 6 \\ & \hline \end{aligned}$ | $\begin{aligned} & 15 \\ & 27 \\ & \hline \end{aligned}$ |
| Shigella species | All ages | All serotypes | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 29 \\ & 32 \end{aligned}$ | $\begin{aligned} & 13 \\ & 5 \end{aligned}$ | $\begin{aligned} & 42 \\ & 39 \end{aligned}$ | $\begin{aligned} & 21 \\ & 23 \end{aligned}$ | $\begin{aligned} & 4 \\ & 5 \end{aligned}$ | $\begin{aligned} & 2 \\ & 6 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 2 \\ & 2 \\ & \hline \end{aligned}$ | $\begin{aligned} & 64 \\ & 48 \end{aligned}$ | $\begin{aligned} & 177 \\ & 160 \end{aligned}$ |
| Vibrio cholerae 01 | All ages | All serotypes | $\begin{aligned} & 2004 \\ & 2005 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 122 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 4 \\ & 0 \end{aligned}$ | $\begin{aligned} & 0 \\ & 0 \end{aligned}$ | $\begin{aligned} & 126 \\ & 0 \end{aligned}$ |

$U=$ unavailable, $0=$ no isolates received $\quad$ Note: The above are NICD laboratory data and do not nececessarily reflect a quantitative measure of disease in the country.

# INFLUENZA VACCINE RECOMMENDATIONS: 2005 

Barry D Schoub, NICD

Official recommendations for annual influenza vaccination are published in the February issues of the South African Medical Journal. These recommendations are based largely on those of the World Health Organization and the Advisory Committee for Immunisation Practices (ACIP) of the USA. The most frequently asked questions regarding influenza vaccinations are:

- Who should be immunised?
- Who should not be immunised?
- When should vaccine ideally be administered?


## WHO SHOULD BE IMMUNISED?

Category 1 - At risk persons (i.e. at risk for complications of influenza)
$\sqrt{ }$ All persons over the age of 65 years
$\sqrt{ }$ Persons with chronic pulmonary or chronic cardiac disease
$\sqrt{ }$ Immunosuppressed persons e.g. chronic renal disease, metabolic disorders such as diabetes, HIV infected persons if CD4 count is above 200 per ~I (below that the vaccine is not likely to be effective)
$\sqrt{ }$ Pregnancy - women who will be in the second or third trimester during the winter season should be immunised because of reduced air entry increasing the risk of influenza-related pneumonia. However, the vaccine is contraindicated in the first trimester because of the unknown effects during the early development of the foetus.
$\sqrt{ }$ Children with medical conditions of chronic pulmonary or chronic cardiac diseases as well as immunosuppressed children should be immunised as in the case of adults. Children on aspirin therapy should also be immunised because of the risk of Reye's syndrome.

## Category 2 - Contacts of high-risk persons

$\sqrt{ }$ This includes healthcare workers, caregivers of the elderly and high-risk patients and persons living under the same roof as highrisk persons.

## Category 3 - Workplace vaccination

$\sqrt{ }$ The cost benefit and cost savings of immunising employees has been clearly demonstrated in many studies and shown to reduce absenteeism and medical costs.

## Category 4 - Personal protection

$\sqrt{ }$ Although not medically mandated as in the case of categories 1 and 2 , persons who wish to avoid a rather miserable and often debilitating illness due to influenza should be encouraged to be immunised.

## WHO SHOULD NOT BE IMMUNISED?

$\sqrt{ }$ Severe egg hypersensitivity - modern influenza vaccines contain only extremely minute traces of egg protein and hypersensitivity reactions are consequently very rare and are mainly directed against preservatives in the vaccine rather than the egg protein. Therefore, only a history of severe anaphylactic hypersensitivity to egg protein would be a contraindication.
$\sqrt{ }$ First trimester of pregnancy - see above
$\sqrt{ }$ Febrile illness

## WHEN TO VACCINATE?

The ideal timing is close enough to winter to capitalise on the height of the antibody response, but not too late to have "missed the boat" once the influenza season has started. Antibody responses usually commence about 2 weeks after vaccination and reach a peak in about a month. The ideal time is therefore in April as the influenza season seldom commences before middle to late May. However, the vaccine could still be profitably administered late, provided there is still about two weeks or more before the influenza season commences.

## VACCINE FORMULATION:

The recommended strain composition for the vaccine for 2005 is as follows:

- A/New Caledonia/20/99 $\left(\mathrm{H}_{1} \mathrm{~N}_{1}\right)$-like virus
- A/Wellington/1/2004 $\left(\mathrm{H}_{3} \mathrm{~N}_{2}\right)$ - like virus
- B/Shanghai/361/2002 - like virus

The packaging must stipulate that the formulation corresponds to the 2005 recommendations and practitioners must ensure that the current 2005 vaccine is used for maximal efficacy.

# INFLUENZA VACCINATION SYMPOSIUM 

Barry D Schoub, NICD. Reproduced with kind permission of Modern Medicine, SA

A highly successful one-day symposium on influenza, organised by the National Institute for Communicable Diseases (NICD), was held on Wednesday 16 February 2005 in Johannesburg. The symposium had 2 interrelated themes - influenza surveillance and influenza vaccination. Surveillance for influenza, centred mainly in the Johannesburg area, plays a very significant public health role in the diagnosis of winter epidemics of acute respiratory infection and also provides valuable information to the WHO Global Influenza Programme on the influenza strains to be incorporated annually into the southern hemisphere vaccine formulation. Networks of sentinel general practitioners have been established in many centres throughout the world. Dr Jean-Marie Cohen, himself a general practitioner for 12 years and one of the founders of the GROG surveillance programme in France, one of the earliest and most successful surveillance programme, presented the elements of what makes for a successful network, which is not only highly important for public health but equally benefits the subscribing general practitioners.

Much of the symposium was devoted to presentations highlighting the need to improve awareness that influenza is one of the most important causes of vaccine-preventable mortality and morbidity in the world. Data presented by Dr Kristin Nichol, Professor of Medicine at the University of Minnesota and a world authority on the cost-benefit of influenza vaccination, demonstrated that influenza is the number one cause of vaccine-preventable deaths in the USA. In that country, with a population of 280 million, influenza is responsible for up to 50 million cases annually, resulting in 34000 to 51000 deaths and 100 to 200 million days of illness costing billions of dollars. She also showed that the vaccine is 70 to $90 \%$ effective in preventing laboratory confirmed illness and 25 to 34\%
effective in preventing upper respiratory tract infections from all causes, thereby reducing acute respiratory related sick leave by 32 to $43 \%$. Countries throughout the world have shown that the vaccine reduces allcause mortality by 20 to $75 \%$ in the elderly. Unfortunately, South Africa is progressively lagging behind the rest of the developed world in influenza vaccination. Dr David Fedson, the co-ordinator of Macro-epidemiology of Influenza Vaccination, showed how South Africa influenza vaccination figures have declined from 55 per 1000 population in 2000 to only 21 per 1000 in 2004. In contrast, virtually every developed country has steadily increased their coverage with Canada leading the world with 344 per 1000 followed by Korea with 311 per 1000 and the USA with 288 per 1000. A number of reasons for the poor utilisation of vaccine in this country were analysed. In the main, it appears to be due to misunderstanding the efficacy of the vaccine to specifically prevent influenza infection and not other respiratory infections, as well as unwarranted fears of the side effects of the vaccine. South Africa still has some way to go to catch up to the rest of the world, especially as influenza is likely to be a more severe disease in the poorer sections of our population as well as those who are immunologically compromised, for example as a result of HIV infection.

The grave threat of an influenza pandemic was discussed in several presentations in the light of the human infections with avian influenza in South East Asia. The unavailability of licensed methodologies to rapidly produce adequate amounts of protective vaccine is seen as a major obstacle to an effective response to the coming pandemic. In the meantime, an important component of pandemic preparedness is the annual immunization programmes in the interpandemic period.

# UPDATE ON HIGHLY PATHOGENIC AVIAN H5N1 INFLUENZA 

Terry G Besselaar, Vaccine Preventable Virus Infections Unit, NICD

## OUTBREAKS AND IMPACT ON HUMAN CASES AND DEATHS

Prior to the Asian outbreaks which began late in 2003, highly pathogenic avian influenza (HPAI) was considered a rare disease. More than 120 million birds died or were destroyed within the first 3 months in the Asian outbreaks of influenza A H5N1. These massive control efforts had an impact as the outbreaks declined sharply during March 2004 except in Thailand, where sporadic outbreaks were reported throughout April. Likewise, new human cases declined, then ceased, with the last occurring case in Vietnam in mid-March.

During this first phase of the HPAI, from January to March, 35 human cases were reported, of which 24 were fatal. These figures were far more than those in the 1997 Hong Kong H5N1 outbreak and the mortality rate much higher.

The second phase of the HPAI began in late June 2004, when outbreaks in poultry were reported in Cambodia, China, Indonesia, Thailand, and Vietnam. A month later, Malaysia also reported its first poultry outbreaks. The outbreaks were much smaller, but nevertheless were followed by renewed sporadic reporting of human cases of H5N1 infection in Vietnam
and Thailand beginning in August, 2004 and continuing into 2005. Most cases occurred in rural areas, suggesting a community-wide threat to health in large and remote areas. On February 2, 2005, the first human case of avian influenza A H5 infection from Cambodia was reported.

The first probable case of human- to- human transmission in a family cluster was reported in Thailand in September. Another cluster that suggests the virus passed from person to person has also occurred more recently. Here a 14 -year-old girl fell ill on 14 February, her 21-year-old brother on 21 February, and a 26-year-old male nurse who cared for the brother, on 26 February.

The total number of human cases of avian H5N1 from January 2004 to 28 February 2005 reported officially by WHO were 55 , of which 42 were fatal. Of these, 37 cases occurred in Vietnam, 17 in Thailand and one in Cambodia. There is, however, a discrepancy in the official (WHO) and the unofficial number of cases. The University of Minnesota is compiling up to date unambiguous figures of avian influenza cases and deaths in East Asia, which are 65 with 46 deaths compared to the WHO's figures of 55 with 42 deaths.

## NEW FEATURES OF THE H5N1 OUTBREAKS

Looking at the human cases in 2004 and early 2005, two features are striking. The first one is the overwhelming concentration of cases in previously healthy children and young adults. The second is the very high mortality, which could not be easily explained scientifically.

Evidence strongly suggests that H5N1 is now endemic in parts of Asia, having established a permanent ecological niche in poultry. Studies comparing virus samples over time show that H5N1 has become progressively more pathogenic in poultry and in the mammalian mouse model. It also has been shown to survive several days longer in the environment. Further evidence suggests that H5N1 is expanding its mammalian host range. The virus, for example, has been shown to cause severe disease and death in species not previously considered susceptible to disease by influenza A. An example is the large outbreak in October in captive tigers in Thailand, many of whom developed high fevers, usually progressing to severe pneumonia as a result of H5N1 infection from eating chicken carcasses.

Disturbing new evidence suggests that domestic ducks are now excreting H5N1 in its highly pathogenic form without showing signs of illness. A recent laboratory study of domestic ducks infected with several 2004 H5N1 viruses showed that, when compared with infections caused by viruses from 2003, domestic ducks shed more virus for longer periods.

The study found that the quantities of virus excreted by healthy-looking ducks approach those excreted by diseased and very ill chickens. This suggests that domestic ducks might now be acting as a "silent" reservoir for the H5N1 virus, which is highly pathogenic for chickens. To date, no evidence has linked human H5N1 cases to exposure to asymptomatic domestic ducks. However, the laboratory findings came at a time when some human cases could not be traced to contact with diseased or dead poultry.

The new findings expand on recent evidence, based on characterization of H5N1 viruses from southern China, that domestic ducks have played a central role in generating and maintaining H5N1, in its highly pathogenic form, in parts of Asia.

## AVAILABILITY OF H5N1 PROTOTYPE STRAINS FOR INFLUENZA PANDEMIC VACCINE DEVELOPMENT

An effective vaccination system is one key to fighting a pandemic. Genetic and antigenic characterization of representative H5N1 viruses have revealed significant drift in the 2004/2005 viruses relative to the 1997 strains from the Hong Kong outbreak. The recent Asian viruses isolated from both humans and animals are genetically highly similar to the A/ Vietnam/1194/04 and A/Vietnam/1203/04 strains which are the prototype vaccine strains recommended by WHO for pandemic influenza production. The prototype vaccine strains have been modified by means of reverse genetics to remove the stretch of polybasic amino acids that are associated with high virulence in the haemagglutinin cleavage site.

These H5N1 influenza pandemic vaccine prototype strains have already been made available to a number of institutions and companies and several different vaccines have been produced for clinical testing. There are however a number of problems with the H5 vaccines. While there are no intellectual property issues restricting the use of reverse genetics for pandemic vaccine research, it is anticipated that licences must be negotiated before commercial use of such vaccines. Another hurdle is that in some countries, the reassortant may be viewed as a genetically modified organism and approval will be needed for virus cultivation. In addition, in some countries, although the reassortant is derived from a human H5N1 virus, it may be subject to an import licence from veterinary authorities.

## ANTIVIRALS DRUGS

The worst effects of a pandemic could be lessened by stockpiling anti-viral medications. The H5N1 viruses continue to show resistance to amantadine. Oseltamivir phosphate (Tamiflu) has been used with some measure of success against influenza H5N1. Should governments have enough antivirals to treat 25 percent of the population, they will keep a country's
frontline services running. The cost of such medication, however, is very high and there is currently a limited supply of the drug.

## PANDEMIC PLANNING

The WHO has been urging its member states for a number of years to invest in pandemic preparedness for two main reasons:

1. Preparation will mitigate the direct medical and economic effects of a pandemic, by ensuring that adequate measures will be taken and implemented before the pandemic occurs.
2. Preparing for the next influenza pandemic will provide benefits now, as improvements in infrastructure can have immediate and lasting benefits, and can also mitigate the effect of other epidemics or infectious disease threats.

Currently, South Africa is ill prepared for an influenza pandemic. A pandemic preparedness meeting will be held at the NICD in April 2005 to try to address some of the most critical issues for the contingency of a major global pandemic.

## MARBURG DISEASE OUTBREAK IN ANGOLA

## Robert Swanepoel, Felicity Burt, Lucille Blumberg, Janusz Paweska, Special Pathogens Unit, NICD

An outbreak of viral haemorrhagic fever (VHF) caused by Marburg virus was confirmed in Uige Province in northern Angola on 21 March 2005. During the period 1 October 2004 to 5April 2005, there have been 181 cases clinically identified, including 156 deaths (case fatality rate 86\%) reported from Uige, Luanda, Cabinda, Malanje and Cuanza Norte Provinces. All cases reported outside Uige Province are reportedly epidemiologically linked to Uige. Out of 14 cases subjected to laboratory confirmation in CDC Atlanta, 10 were positive for Marburg virus.

Haemorrhagic fever caused by the Marburg virus that is closely related to the Ebola virus (filoviruses), first emerged almost simultaneously in August 1967 in Marburg and Frankfurt in Germany and in September 1967 in Belgrade in former Yugoslavia. The first 25 patients all had contact with African green monkeys (Ceropithecus aethiops) or were involved in processing organs or cell cultures derived from these animals, which were imported to Europe from EastAfrica. There were five secondary cases among medical care and laboratory personnel and one patient appears to have transmitted infection via semen to his wife some seven weeks after he had recovered from the disease. Seven of the 32 patients died.

Subsequently Marburg disease was recognized early in 1975 in a young Australian hitch-hiker who become ill in Marburg, on the Natal coast in South Africa and was admitted to hospital in Johannesburg. His travelling companion become ill one week later and a nurse who attended them become ill a further week later. Before coming to South Africa, the Australian couple had been travelling in Zimbabwe. The index patient succumbed and the other two patients survived. In 1982, a young man who had come from Zimbabwe to South Africa 11 days previously developed febrile illness with haematemesis. Although this case has been reported as being confirmed Marburg infection based on results of indirect immunofluorescence antibody test, no virus could be recovered from the patient serum and semen samples.

The last outbreak occurred in the DRC in 1998-2000 resulting in 126 deaths. The victims were gold miners in Durba close to the town of Watsa. In this outbreak, genetic characterization of strains suggested multiple introductions of the virus into the human population. Despite extensive ecological investigations, the source host of Marburg virus, as is the case with Ebola virus, remains unknown. Non-human primates are highly susceptible to filoviruses and therefore they are unlikely to be a reservoir host of these viruses.

After an incubation period of 4-10 days, which can extend up to 21 days, the onset of disease is sudden with fever, myalgia, sore throat and fatigue. Gastrointestinal symptoms are common, notably profuse diarrhoea, nausea and vomiting and abdominal pain. A maculopapular rash is common, appearing on about day 5 of illness. Haemorrhagic manifestations occur from about days 5-7 of illness in about 50\% of patients. A poor prognosis is marked by haemorrhagic signs as well oliguria, metabolic acidosis, shock and respiratory distress. Laboratory findings show an early lymphopaenia, leukopaenia or leucocytosis, and thrombocytopaenia.

Since the signs and symptoms of Marburg are very non-specific, and the differential diagnosis is very broad, the epidemiological context of the case is of utmost importance. It is critically important to exclude other treatable causes of febrile conditions, especially malaria which is common in areas in which Marburg has been reported, and may progress rapidly. Specific diagnostic tests for Marburg can be performed by a limited number of highly skilled laboratories globally with BSL 4 facilities. Molecular tests (PCR), antigen and antibody detection, and culture are used for laboratory diagnosis.

Management of cases is largely supportive. Infection control, using strict barrier nursing and protective equipment is essential. The virus may be transmitted from infected patients through contact with body fluids and infected needles.

Predominant symptoms during the current Angolan outbreak of Marburg disease include fever, haemorrhage, vomiting, cough, diarrhoea and jaundice and the majority of the cases have occurred in children <5 years of age. Several health care workers have been affected, and some of these have died, including a paediatrician in Luanda. Patients have been managed in health care facilities in Uige, Cabinda and Luanda. International health teams have been deployed to the area to assist with infection control, case management, laboratory diagnostics, epidemiological investigations, social mobilization activities and surveillance of contacts.

Clinicians should consider the diagnosis of Marburg VHF among febrile patients who within 21 days before onset of fever, have either travelled in northern Angola, had direct contact with blood, other body fluid, secretions or excretions of a person or animal suspected of having VHF, or worked in a laboratory or animal facility that handles specimens from haemorrhagic cases. The likelihood of acquiring VHF is considered extremely low in persons who do not meet any of these criteria. The cause of fever in persons who have travelled to VHF endemic areas is more likely to be due to infection with other infectious agents. Notably malaria is one to be first considered.

## Guidelines for laboratories handling suspected Marburg specimens IT IS ESSENTIAL THAT THIS PROCEDURE IS FOLLOWED FOR ALL SUSPECTED CASES

1) Immediately contact the NICD to discuss the case BEFORE sending any specimens:
a. Dr Lucille Blumberg - 0113866337 OR 0828076770
b. Dr Gillian de Jong - 0113866409 OR 0833698014
c. Outbreak hotline - 0828839920
2) If it is agreed on discussion that specimens should be processed for suspected Marburg disease, transport specimens to the Special Pathogens Unit, NICD, Sandringham as follows:
a. USE APPOPRIATE PRECAUTIONS AT ALL TIMES WHEN HANDLING BLOOD OR OTHER BODY FLUIDS.
b. Wrap blood specimen tubes separately in absorbent material e.g. cotton wool.
c. Then place the specimens in a secondary container, preferably made of sturdy plastic or stainless steel with a well fitting lid.
d. Wrap them again in absorbent material and place in another container.
e. Put the patient details on the OUTSIDE of this container including:
i. Patient name and hospital number
ii. Doctor and contact no.
iii. Lab name and contact person
iv. Clinical details
v. Results of any tests already performed
f. Address the package to: The NICD Special Pathogens Unit, 1 Modderfontein Road Sandringham Johannesburg. For Attention: Dr Burt or Dr Paweska.
3) Please note: the BSL4 laboratory at the NICD Special Pathogens Unit (SPU) is not operational currently. If it is decided that testing for Marburg disease should be done on a particular case, specimens will be sent on by the unit to the CDC Atlanta for processing.

# INFLUENZA SURVEILLANCE PROGRAMME 

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## VIROLOGICAL SURVEILLANCE

Virological surveillance is the foundation on which national and international influenza surveillance systems are built. The global influenza surveillance network was established by the WHO in 1947 and provides information on epidemiological trends and circulating strains of influenza virus from 116 national influenza centres in 86 counties, and 4 WHO collaborating centres for Reference and Research on Influenza (Atlanta, London, Melbourne and Tokyo). Influenza surveillance systems are generally based on sentinel general practitioner networks e.g. the USA network is comprised of over a 1000 sentinel sites.

South Africa is part of the Southern Hemisphere network, which includes New Zealand and Australia. Before the expected start of the influenza season, national influenza centres are provided with a kit of laboratory diagnostic reagents to determine the type and subtype of influenza viruses circulating during the season.

Molecular characterisation of influenza isolates gives an indication of the genetic drift of the circulating strains. This is critical in assessing the efficacy of the current vaccine and in the selection of appropriate strains for inclusion in the vaccine for the following season. National reference centres report viral strain
information to the WHO via the web based reporting system, FluNet. A subset of the isolates is submitted to WHO Influenza Collaborating Centres for complete antigenic characterisation. Ideally, countries seek to send shipments corresponding to the beginning, peak and end of the influenza season. Local data is critical for making informed vaccination policy decisions. Since epidemics of influenza occur at different times of the year in different parts of the world and the virus is constantly changing, there is need to review vaccine recommendations twice a year. Consultation for the vaccine formulation for following winter, is held in mid February for the northern hemisphere (November to April), and September for the southern hemisphere (May to October).

## SOUTH AFRICAN VIRAL WATCH

In South Africa the Viral Watch Programme was established in 1984 at the former National Institute for Virology (NIV, now incorporated into the NICD) where the national influenza reference laboratory is sited. The programme has comprised 12-20 sites: general medical practitioners, specialist paediatric practices in the private and public sectors, university and school clinics and the NIV/NICD staff clinic. Up to two throat or nasal swabs per week can be taken by each site throughout the year from patients with acute respiratory infections of recent onset i.e. within 24 hours, and without obvious bacterial cause, and transported to the NICD in viral transport medium for virus isolation.

During 2004, 320 specimens were received for detection of respiratory virus, of which the Viral Watch programme collected 107. It was a very quiet season with comparatively low school absenteeism, showing a peak rising above the mean absentee rate calculated over a five year period starting at week 26 (Fig 1). However, this was the week that winter school holidays started in government schools, and the independent
schools were on a mid-term break. Influenza virus was isolated from 26 patients attending Viral Watch sites. The first isolate was made from a specimen taken on 14 May and the last from a specimen taken on 4 August. Twenty-five isolates were influenza A, 19 of which have been further identified as A H3N2 (A/ Fujian/411/2002(H3N2)-like). Only one influenza B isolate was made. Patients' ages ranged from 3 to 46 years (median 21). In addition influenza A was confirmed in 12 specimens sent by private laboratories, 7 of which have been further identified as A H3N2. Other respiratory virus isolates made were 16 para-influenza virus, 49 respiratory syncytial virus, 11 adenovirus, and 5 untyped respiratory virus. The Viral Watch accounted for $33,4 \%$ of all respiratory specimens with an isolation rate of $26,3 \%$.

## EXPANSION OF NETWORK

The South African network has recently been expanded to approximately 73 sites in Gauteng, predominantly general medical practices but also including occupational health clinics and pharmacies, which have increasingly become important primary health care sites. Participating sites will be asked to report epidemiological data to give some indication of the burden of respiratory diseases in the community and will earn continuing professional development (CPD) awards, receive WHO/NICD collaboration certificates, have regular communications with NICD staff and participate in a dynamic network as 'Watch Docs'. A national surveillance system may be considered in the future.

Conclusion: Surveillance is a critical component of a national pandemic preparedness plan. It is essential for every country to have an early warning system to detect an unusual cluster or number of human influenza cases that may be due to a new influenza virus and to strengthen and expand the global surveillance network to allow for timely detection of pandemic strains.


Influenza isolates and school absenteeism : 2004


[^0]:    This bulletin is available on the NICD website : http://www.nicd.ac.za
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