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COMMUNICABLE DISEASES SURVEILLANCE BULLETIN

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NICD NHLS

FOREWORD

As of 17 August 2009, there had been 2844 patients and 6 deaths with laboratory confirmed infection due to pandemic influenza A H1N1 in South Africa reported to the National Institute for Communicable Diseases (NICD) of the National Health Laboratory Service. Cases have been reported from all 9 provinces with the majority reported from Gauteng and the Western Cape[1]. The current bulletin thus has a focus on influenza, with articles dealing with the treatment and prevention of influenza as well as a commentary on the local implications of the pandemic. We also include an article focusing on a newly introduced influenza sentinel surveillance programme for patients with Severe Acute Respiratory Infection (SARI). The pandemic virus continues to circulate widely in the community and we anticipate that numbers of laboratory confirmed cases will increase for a number of weeks to come. The NICD monitors progression of the pandemic through several surveillance programmes. Weekly updates on findings of these programmes can be found on the NICD webpage at www.nicd.ac.za.

Cheryl Cohen, Editor

Reference

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CONTENTS

TREATMENT AND PREVENTION OF INFLUENZA

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Background

South Africa experiences annual seasonal influenza epidemics between May and August each year[1]. There are two types of seasonal influenza viruses; influenza A and B. At present two subtypes (H1N1 and H3N2), designated on the basis of two surface antigens: haemaglutinin and neuraminidase, are circulating in humans. Seasonal influenza viruses experience regular progressive antigenic change ("antigenic drift"). For this reason the annual seasonal influenza vaccine is updated each year. In contrast, antigenic shift occurs when a completely new subtype of influenza of influenza virus appears and can result in the emergence of a new virus with the potential to cause a pandemic. In April 2009 a new influenza virus was identified circulating in human populations and on 15 July 2009 had been identified from more than 100 000 patients from more than 100 countries[2]. This novel virus is named pandemic influenza A (H1N1) 2009 to distinguish it from seasonal influenza viruses. Because it is a completely new virus in human populations it is referred to as a pandemic virus.

The pandemic H1N1 virus has so far generally been associated with relatively mild illness but a small number of patients may develop severe illness or death as with seasonal influenza.

(Continued on page 2)

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

WEB
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Clinical presentation and spectrum of illness
Infection due to influenza virus can give rise to a wide range of clinical presentations ranging from asymptomatic infection to severe illness and death[3]. Uncomplicated influenza illness is generally characterised by sudden onset of constitutional and respiratory symptoms such as fever, myalgia, cough, sore throat, rhinitis and headache. Uncomplicated illness typically resolves in 3-7 days. Influenza may be associated with more severe complications and these include: viral pneumonia, secondary bacterial or viral infections (including pneumonia, sinusitis and otitis media), exacerbations of underlying illnesses (e.g. pulmonary and cardiac illness). Rare complications include encephalopathy, myocarditis, transverse myelitis, pericarditis and Reyes syndrome. Certain individuals are at increased risk for severe complications of influenza (Table 1). Clinically it is very difficult to distinguish illness due to influenza from that due to other respiratory viruses. However, during the influenza season approximately 79% of adult patients with fever and cough will be due to influenza[4].

This article will focus on the use of pharmacologic agents for the treatment and prevention of influenza. A discussion of non-pharmacologic measures for influenza control is beyond the scope of this article. Detailed updated South African guidelines related to pandemic influenza A H1N1 are available from www.nicd.ac.za[13].

Options for treatment and prevention
Vaccine
Influenza vaccines are updated each year on the basis of global influenza surveillance data. The annual seasonal influenza vaccine contains strains corresponding antigenically as closely as possible to the 3 seasonal influenza strains prevalent in human populations: influenza A H1N1, influenza A H3N2 and influenza B. Several formulations of seasonal influenza vaccine are available and licensed for use in South Africa. Vaccines should contain 15µg of each haemagglutinin antigen in each 0.5ml dose[5]. Currently there is no vaccine available against pandemic influenza A H1N1 2009. Available data suggest that seasonal influenza vaccines are unlikely to induce an antibody response against pandemic influenza A H1N1 infection[6].

Who should be vaccinated?
Influenza vaccine remains the primary means for preventing seasonal influenza infection and updated recommendations for influenza vaccination in South Africa are published annually[5]. Individuals for whom influenza vaccination is recommended are listed in table 2.

Administration of vaccine
Vaccines should be given sufficiently early to provide protection for the winter[5,7]. A protective antibody response takes about 2 weeks to develop. The dose in adults is one 0.5 ml dose intramuscularly of the whole, split-product or subunit vaccine. In children aged < 12 years one dose of the split-product or subunit vaccine may be used. Children <9 years who have never been vaccinated should receive 2 doses 1 month apart. Children < 3 years of age should receive half the adult dose on two occasions separated 1 month apart. Contraindications to vaccination are listed in table 3.

Antiviral Agents
Antiviral drugs may be used for the treatment and prophylaxis of influenza. The decision as to which antiviral drug to use should include the indication (treatment or prophylaxis), patient characteristics (age and presence of underlying conditions) and resistance patterns of circulating influenza viruses. Updated information on the frequency of circulating influenza viruses and dominant circulating strains in South Africa can be obtained from the National Institute for Communicable Diseases (NICD) webpage www.nicd.ac.za. Recommendations for use of antiviral agents in South Africa may change as data on antiviral susceptibilities and currently circulating virus strains become available.

There are two classes of antiviral drugs licensed for the therapy of influenza. The older adamantanes, amantidine (Symmetrel®) and rimantidine (Flumadine® - not registered for use in South Africa) and the newer neuraminidase inhibitors oseltamivir (Tamiflu®) and zanamavir (Relenza®).

Antiviral resistance
In recent years, the majority of influenza A H3N2 viruses detected have been resistant to the adamantane class of drugs and this class of antivirals are not active against influenza B[7,8]. In addition, currently circulating strains of pandemic influenza A H1N1 are resistant to this class of agents[9]. For this reason these agents are not currently routinely recommended for the treatment or prophylaxis of influenza in South Africa during seasons when influenza A H3N2 or pandemic influenza A H1N1 predominates[8]. Adamantanes may have a role in the management of patients with disease due to seasonal influenza A H1N1 as described below.

Oseltamivir and zanamivir are active against seasonal influenza A H3N2 and influenza B viruses. Currently circulating strains of pandemic influenza A H1N1 remain susceptible to this class of agents[9]. However, widespread resistance to oseltamivir has been described amongst circulating strains of seasonal H1N1 globally. In the 2008 influenza season in South Africa 100% of tested isolates displayed high level resistance to oseltamvir [10]. Oseltamivir resistant isolates currently remain susceptible to zanamivir and this agent may be considered for patients with severe infection due to resistant strains. In patients in whom zanamivir is contraindicated, and who have severe infection due to probable oseltamivir resistant strains, combination therapy with oseltamivir and amantidine may be used[8].

Antiviral treatment is most effective when initiated within 48 hours of the onset of illness. Antiviral therapy may reduce the duration of illness by approximately 1 day, reduce

(Continued on page 3)

nasal shedding of virus and may reduce the rate of serious illness and death[11,12]. Oseltamivir (Tamiflu®) is orally administered and is registered for use in individuals aged ≥1 year of age. Zanamivir (Relenza®) is administered through an inhaler and is registered for use in individuals aged ≥ 12 year of age.

Who should be treated?

Persons with an uncomplicated febrile illness due to seasonal or pandemic influenza typically do not require treatment unless they are at higher risk for influenza complications[7,13,3]. Use of antiviral agents should be limited to persons with suspected, probable or confirmed influenza infection with the following indications:

- Individuals with moderate or severe influenza-related illness
- Hospitalised patients
- Any individual at high risk for serious complications of influenza (Table 1)

When should treatment be started?

Treatment should be initiated as soon as possible after the onset of symptoms ideally within 2 days of onset of illness. Although benefit is likely to be greatest when therapy is initiated within 48 hours, some benefit may still be obtained in patients whose therapy is started later in the course of illness. Recommended duration of treatment is five days. Antiviral doses recommended for treatment of seasonal influenza A H3N2, seasonal influenza B and pandemic influenza A/H1N1 virus infection are described in Table 4.

Prophylaxis

Influenza vaccination is the primary means of preventing influenza infection. Chemoprophylaxis may be indicated in situations where there is no influenza vaccine available (such as for prevention of pandemic influenza A H1N1 infection) or in persons at high risk of influenza complications (Table 1) in whom influenza vaccination is contraindicated. In addition, where influenza viruses are currently circulating in the community chemprophylaxis may be considered in high risk persons during the 2 weeks after vaccination before and adequate immune response develops (6 weeks for children who have not been previously vaccinated and who require 2 doses of vaccine 4 weeks apart). Antiviral chemoprophylaxis may also be useful in conjunction with other control measures in institutional influenza outbreaks[3]. Antiviral post-exposure prophylaxis should be offered to high risk close contacts of suspected, probable or confirmed cases of infection due to pandemic influenza A H1N1 (Table 1). Dosage of agents for antiviral prophylaxis are described in table 5. Duration of antiviral chemoprophylaxis post-exposure is 10 days after the last known exposure to a suspect or confirmed case of pandemic influenza A/H1N1 virus infection. In high risk patients in whom influenza vaccination is contraindicated chemoprophylaxis may be indicated throughout the period of sustained community influenza activity[3].

Table 1: Individuals at high risk for serious complications of influenza

1. Persons (adults or children) with underlying medical conditions and who are receiving regular medical care for conditions such as chronic pulmonary disease (including asthma) and cardiac disease (excluding hypertension), chronic renal and hepatic diseases, diabetes mellitus and similar metabolic disorders, sickle cell anaemia and other haemoglobinopathies
2. Individuals who are immunosuppressed (including HIV infected persons and persons on immunosuppressive medications);
3. Adults and children who have any condition (e.g., cognitive dysfunction, spinal cord injuries, seizure disorders, or other neuromuscular disorders) that can compromise respiratory function or the handling of respiratory secretions or that can increase the risk for aspiration;
4. All persons over the age of 65 years*;
5. Children and adolescents who are receiving long-term aspirin therapy and who might be at risk for experiencing Reye's syndrome after influenza virus infection;
6. Residents of nursing homes and other chronic-care facilities
7. Pregnant women
8. Obesity**

*Persons aged > 65 years are at increased risk of severe disease due to seasonal influenza but may not be at increased risk of severe disease due to pandemic influenza A H1N1[2,16]

**Preliminary reports suggest that obese individuals may be at increased risk of severe or fatal illness due to pandemic influenza AH1N1. Obesity is not generally regarded as a risk factor for severe disease due to seasonal influenza[2]

Pregnant Women

Pregnant women have an increased of hospitalisation during the influenza season. This risk is greatest during the second half of pregnancy[14]. Pregnant women may also be at increased risk of complications of pandemic influenza A H1N1 infections[15]. Thus early treatment for pregnant women with influenza should be considered. No clinical studies have been conducted to assess the safety of oseltamivir and zanamivir for pregnant women. Oseltamivir or zanamivir should be used during pregnancy where the potential benefit justifies the potential risk to the embryo or fetus. The manufacturers' package inserts should be consulted. However, no adverse effects have been reported among women who received oseltamivir or zanamivir during pregnancy or among infants born to women who have received oseltamivir or zanamivir. Pregnancy should not be considered a contraindication to oseltamivir or zanamivir use[8]. Because zanamivir is an inhaled medication and has less systemic absorption, some experts prefer zanamivir over oseltamivir for use in pregnant women when feasible.

Table 2: Individuals in who seasonal influenza vaccination is recommended[5]:

1. Persons (adults or children) who are at high risk for influenza and its complications because of underlying medical conditions and who are receiving regular medical care for conditions such as chronic pulmonary and cardiac disease, chronic renal diseases, diabetes mellitus and similar metabolic disorders, and individuals who are immunosuppressed (including HIV infected persons with CD4 counts above 200/ml);
2. Residents of old-age homes, chronic care and rehabilitation institutions;
3. Children on long-term aspirin therapy;
4. Medical and nursing staff responsible for the care of high-risk cases;
5. Adults and children who are family contacts of high-risk cases;
6. All persons over the age of 65 years;
7. Women who would be in the second or third trimester of pregnancy during the influenza season. Pregnant women with medical conditions placing them at risk for influenza complications should be immunized at any stage of pregnancy;
8. Any persons wishing to protect themselves from the risk of contracting influenza, especially in industrial settings, where large-scale absenteeism could cause significant economic losses.

Table 3: Contraindications to influenza vaccination[5]

1. Persons with a history of severe hypersensitivity to eggs;
2. Persons with acute febrile illnesses should preferably be immunized after symptoms have disappeared;
3. The vaccine should be avoided in the first trimester of pregnancy unless there are specific medical indications - see above indication no. 7.

Adverse events and contraindications

Oseltamivir
Nausea and vomiting are the commonest reported adverse effects. Transient neuropsychiatric events have rarely been reported in persons taking oseltamivir[8].

Zanamivir
Zanamivir is only licensed for use in people without underlying cardiorespiratory disease and is not recommended for persons with underlying airways disease[8].

Clinicians should consult manufacturers' package inserts for further information on adverse events and contraindications for these agents.

Table 4: Recommended dosage of antiviral agents for treatment of patients with severe infection due confirmed, probable or suspected novel influenza A/H1N1 or seasonal influenza A H3N2 or B*

Age Group	Weight	Oseltamivir dosage*	Zanamivir dosage*
Adults		75 mg twice per day	Two 5 mg inhalations (10 mg total) twice per day
Children	15 kg or less	30 mg twice per day	Two 5 mg inhalations (10 mg total) twice per day (only in children aged 12 years or older)
	15–23 kg	45 mg twice per day	
	24–40 kg	60 mg twice per day	
	>40 kg	75 mg twice per day	

*Recommended duration of treatment is 5 days. Oseltamivir is not currently licensed for use in <1 year old and zanamivir is only registered for children ≥ 12 years of age. Currently circulating strains of seasonal influenza A H1N1 are resistant to oseltamivir but remain susceptible to zanamivir.

Table 5: Recommended dosage of antiviral agents for prophylaxis of influenza infection*

Age Group	Weight	Oseltamivir dosage*	Zanamivir dosage*
Adults		75 mg once per day	Two 5 mg inhalations (10 mg total) once per day
Children	15 kg or less	30 mg once per day	Two 5 mg inhalations (10 mg total) once per day (only in children aged 12 years or older)
	15–23 kg	45 mg once per day	
	24–40 kg	60 mg once per day	
	>40 kg	75 mg once per day	

*Recommended duration of prophylaxis is 10 days. Oseltamivir is not currently licensed for use in <1 year old and zanamivir is only registered for children ≥ 12 years of age. Currently circulating strains of seasonal influenza A H1N1 are resistant to oseltamivir but remain susceptible to zanamivir.

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SWINE FLU—IMPLICATIONS FOR SOUTH AFRICA

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Wednesday, 17th June 2009, the first case of pandemic Influenza H1N1 2009 ("swine influenza") was confirmed in South Africa and indeed Sub-Saharan Africa, about a week after the WHO declared a global pandemic. Within 3 weeks over a 100 cases were detected. Introduction of the virus to South Africa was surprisingly delayed given that the country was in the peak of the influenza season as substantiated by a high isolation rate of the predominantly seasonal influenza H3N2 strain. Why there was this unusual delay is difficult to pinpoint – it could well be the relatively low traveller traffic from countries with high levels of community transmission such as Mexico and later, USA.

Where did the virus come from?

With a world anticipating the next pandemic to be due to avian influenza H5N1, pandemic H1N1 took all by surprise. Where did this virus come from? Its original forebear, classical H1N1 swine influenza virus, was introduced into the pig population from an avian source at about the same time that H1N1 entered the human population causing the 1918 Spanish influenza pandemic. In humans H1N1 became the regular seasonal influenza virus undergoing continual drift and causing relatively mild winter outbreaks of influenza. In contrast, classical swine influenza, while causing a similar disease in pigs (with occasional sporadic transmission to humans), remained antigenically static, resulting in a substantial antigenic gap with human H1N1. In 1995 the swine virus reassorted with a human and an avian virus to produce triple reassortant swine virus, (which was also responsible for a few sporadic human cases of an influenza-like illness). The present pandemic H1N1 virus

(Continued on page 6)

arose following a further reassortment event with the triple reassortant swine virus and an Eurasian virus, the latter adding a matrix gene specifying resistance to the M2-ion channel blocking drugs such as amantadine. The virus, however, still retains sensitivity to the neuraminidase blocking drugs, Oseltamivir (Tamiflu) and Zanamivir (Relenza). This sequence of events is shown in figure 1.

Characteristics of pandemics

Pandemics are rare events occurring only 2 or 3 times per century (about at 15- to 50-year intervals). Some of the typical characteristics of past pandemics, which have now also been seen in the current 2009 pandemic are as follows:-

Characteristics of pandemics

Pandemics are rare events occurring only 2 or 3 times per century (about at 15- to 50-year intervals). Some of the typical characteristics of past pandemics, which have now also been seen in the current 2009 pandemic are as follows:-

i. **Novel virus:** Past pandemics have generally ushered in a new subtype of influenza replacing the preceding subtype and then settling in to become a regular seasonal influenza virus. The pandemic H1N1 virus has behaved like a new subtype of influenza because of the substantial antigenic gap between the classical swine flu virus and human H1N1.

ii. **Increased transmissibility:** Antigenic novelty, whether due to the advent of a new subtype or a radical antigenic distance within an existing subtype will circulate rapidly in an immunologically naïve human population. So, for example, the R values (basic reproductive number) in past pandemics in 1918, 1957 & 1968 were 2.1, 1.6 & 1.8 respectively, compared to 1.2 to 1.3 for seasonal influenza. R values in the current 2009 pandemic have varied from 1.24 to 1.58 for Mexico, but as high as 2.3 for Japan. Secondary household attack rates of 22 to 33% have been found with pandemic H1N1 compared to only 5 to 15% for seasonal influenza.

iii. **Increased virulence:** As at 22nd June some 231 deaths have occurred out of the 52,160 cases detected globally – giving a case fatality rate (CFR) of 0.4%. However this is certainly artificially high at this relatively early stage of the pandemic given that detected cases may well only be the tip of the true iceberg of infection. Similarly in Mexico the CFR was 0.4% and 0.2% for the USA. The CFR for seasonal influenza is 0.04 to 0.08% (the 1918 Spanish flu pandemic the CFR was 5%).

iv. **Age shift:** While seasonal influenza typically affects the extremes of age most severely (very young and elderly), the 1918 Spanish flu pandemic demonstrated a W-shaped mortality curve reflecting that young adults bore the brunt of the morbidity and mortality of that pandemic. Similarly in the 2009 pandemic, the median age of patients in countries throughout the world was between 10 and 20 years. This may be due to some residual cross-immunity from past exposures to H1N1 infection in older persons.

v. **Multiple waves:** The 3 Influenza pandemics of the last century came in 2 to 3 waves – the initial wave being the mildest, followed by severe 2nd or 3rd waves. The reason for this counter-intuitive behaviour is not known.

vi. **Relative non-seasonality**: Unlike seasonal influenza, the current pandemic (as was also the case in past pandemics) started in the spring/ summer of the Northern Hemisphere.

What does the future hold?

a. **Short-term:** South Africa has now well passed 500 confirmed cases with a number of cases having had no contact with imported cases. It will be most surprising if South Africa does not now experience a rapid and extensive outbreak given the winter milieu which has promoted the widespread H3N2 outbreak in South Africa earlier this winter. How pandemic H1N1 will express itself clinically in the developing world is one of the important and as yet unanswered questions.

b. **Long-term:** Historical examination of past pandemics may provide only limited clues given the great difference in so many conditions. On the one hand air travel has vastly increased and thereby greatly accelerating the spread of the virus – what the Spanish influenza pandemic took six months to reach, H1N1 pandemic influenza has accomplished in less than six weeks. Also urbanisation with informal squatting, over-crowded living conditions, immunosuppression, such as from HIV infection, may all contribute to a bleaker picture of a modern pandemic. However, vast improvements in medical management, diagnostic technologies, early detection and more efficient and rapid outbreak response have radically improved our ability to respond effectively to this new pandemic. What remains as imponderables are whether pandemic H1N1 will also come in multiple waves, and if so if the second or third wave will be more severe as in past pandemics? Will the virus develop the kind of explosive mutational resistance to oseltamivir as seen in seasonal H1N1 or could it reassort with seasonal H1N1 and thereby incorporate the resistance mutation? Perhaps the most concerning of all is the possibility that pandemic H1N1 could reassort with avian H5N1 and thereby resulting in a reassortant with greatly increased virulence (CFR of H5N1 is currently over 60%).

Prevention

Vigorous efforts are being made by vaccine manufacturers to produce a vaccine against pandemic H1N1. Indications are that licensed vaccines should be available towards the latter part of 2009. Equally important are basic hygiene practices applicable equally to influenza and other

(Continued on page 7)

respiratory and gastrointestinal infections. These need to be widely publicized so that they become engrained as a behavioural habit:-

a. Cough and sneeze etiquette – coughing into the forearm or elbow instead of into the hand or using a tissue to cover nose and mouth and adequately disposing of used tissues.

b. Regular hand washing with soap (preferably an antimicrobial soap) and water.

c. Social distancing, avoiding close contact with an infected patient– a distance of at least 6 feet. Patients need to be preferably nursed at home if not too ill, to minimize risk of transmission to health care workers.

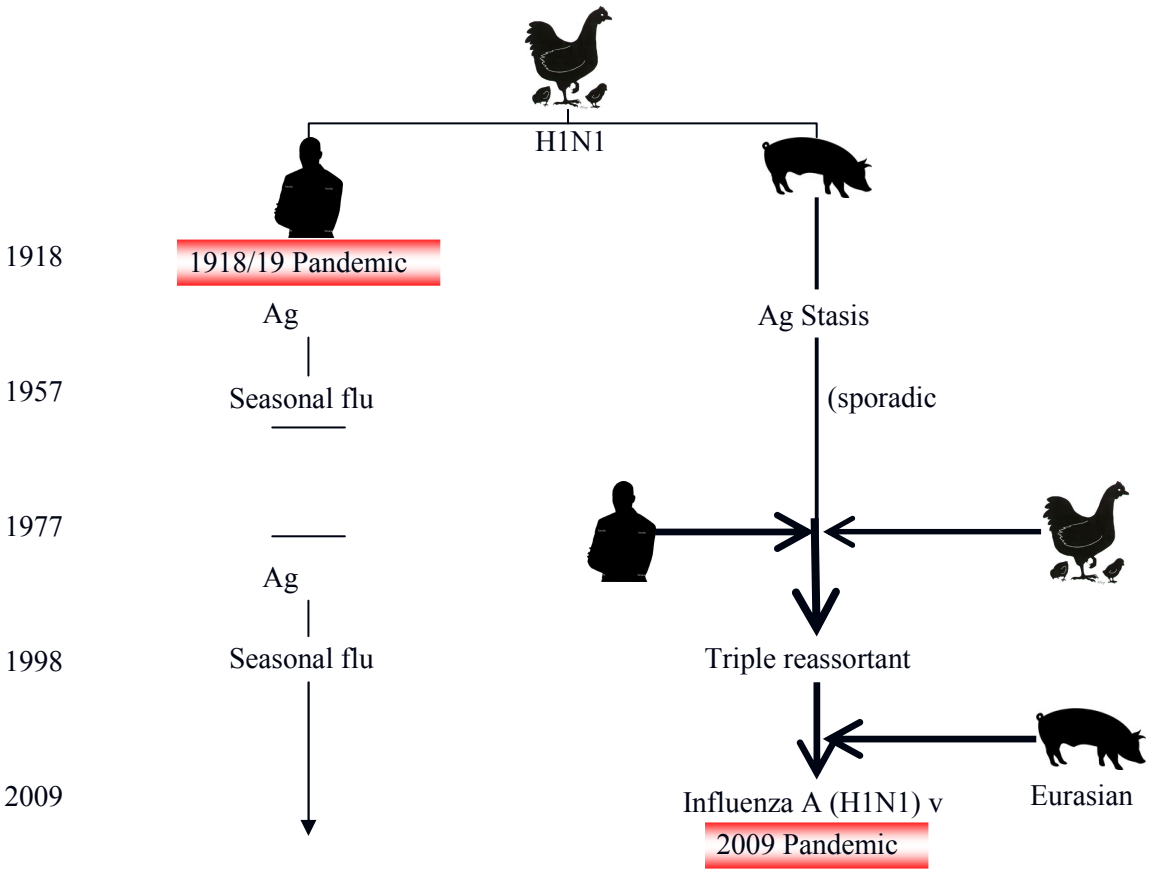

Figure 1: The origins of pandemic influenza A (H1N1)

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SEVERE ACUTE RESPIRATORY TRACT INFECTION SURVEILLANCE - A NEW INFLUENZA SURVEILLANCE PROGRAMME

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Introduction

In 2005 in South Africa, influenza and pneumonia was the leading underlying cause of death in children aged 1-4 years, accounting for 24% of all deaths in this age group, and the second commonest cause of death in adults (10% of all deaths). Similarly, in infants less than 1 year, perinatal respiratory and cardiovascular disease was the leading cause of death (33% of all deaths)[1]. In South Africa, childhood community-acquired pneumonia (CAP) is responsible for approximately 30-40% of hospital admissions. Case-fatality rates in these hospitalized pneumonia cases range from 15-28%[2-5].

In February 2009, a sentinel surveillance programme for severe acute respiratory illness (SARI) was initiated. This report aims to describe the main characteristics of the SARI surveillance programme and present preliminary results of testing for influenza and respiratory syncytial virus from the first 6 months of surveillance ending 24 July 2009.

Aims and objectives of the surveillance programme

The aim of the SARI surveillance program is to describe trends in numbers of patients with SARI at sentinel surveillance sites and determine the relative contribution of influenza and other respiratory viruses (respiratory syncytial virus (RSV), Enterovirus (EV), parainfluenza virus 1, 2 and 3 (PIV1, 2, 3), human metapneumovirus (HMPV), rhinovirus (RV) and adenovirus (AV)) to this disease presentation in a setting with a high prevalence of Human Immunodeficiency Virus (HIV) infection. In addition we aim to determine the proportion of SARI cases that have evidence of invasive infection due to *Streptococcus pneumoniae*.

The programme has multiple objectives. The primary objectives include the following: to estimate the proportion of SARI cases that have a positive laboratory diagnosis of influenza, to describe trends in the incidence of SARI including case fatality ratios, to provide data on the seasonality of influenza and other respiratory viruses, to characterise circulating influenza strains and other respiratory viruses and to detect novel influenza viruses.

Secondary objectives include comparison of the epidemiology, causal agents and clinical presentation of SARI in HIV-infected and uninfected individuals, description of the numbers of SARI cases with evidence of co-infection with viral and invasive bacterial pathogens and monitoring trends in antiviral resistance amongst influenza virus isolates from SARI cases.

Data from the SARI programme will serve to better inform public health policy regarding pneumonia and influenza management, prevention and control in South Africa. In addition, it will assist in monitoring the progression of pandemic influenza and planning for future influenza pandemics.

Methods

The sites that are presently participating in the programme are Chris Hani Baragwanath Hospital, Gauteng (urban site), Mapulaneng and Matikwana hospitals, Mpumalanga (rural site) adjacent to the University of the Witwatersrand Agincourt Health and Demographic Surveillance Site and Edendale Hospital in Pietermaritzburg, KwaZulu-Natal, (periurban site). Matikwana and Mapulaneng hospitals are situated approximately 42 kilometers apart and cover a similar population and are thus considered as one surveillance site (Agincourt) for the purposes of analysis of seasonality data.

The criteria for selecting sentinel sites included the following:

- Capacity at the surveillance site (including willingness to participate in the programme), interested clinicians, capacity for specimen storage and transport
- Geographic location with the aim to include areas with a variety of climatic zones and to include urban and rural sites
- Settings with a defined service population allowing for calculation of disease rates
- Sufficient admissions to justify the expense of employing surveillance officers

The SARI programme is a prospective hospital-based sentinel surveillance programme. The study population includes people who live in the geographic area served by each of the hospitals. All patients admitted to sentinel hospitals and meeting the SARI case definition (excluding weekends) are approached for enrolment into the surveillance programme. At Chris Hani Baragwanath Hospital (CHBH) a convenience sample of adult patients is enrolled due to the large numbers of adults admitted to the hospital on a daily basis. This sample is selected by enrolling patients into the programme from the admission ward every 5th day (excluding weekends). In addition, adult cases presenting to CHBH and transferred to Selby hospital are eligible for enrolment.

Hospital admissions are screened daily from Monday to Friday to identify patients meeting surveillance case definitions (Table 1). Detailed demographic and clinical history information is collected by structured interview following consent from the patient or from parent or caregiver if patient is a minor. Data on relevant laboratory investigations performed during hospitalization such as bacterial culture, investigations for tuberculosis diagnosis and HIV testing are collected through record review and

(Continued on page 9)

Table 1: Case definitions for inclusion in surveillance

Severe acute respiratory infection (persons 2 days to < 3 months old)	Any child with diagnosis of suspected sepsis or physician diagnosed lower respiratory tract infection (LRTI) irrespective of signs and symptoms. Patient presenting within 7 days of the onset of illness
Physician diagnosed LRTI (Children ≥ 3 months old to < 5 years old)	Any child ≥ 3 months to < 5 years with physician-diagnosed acute LRTI including bronchiolitis, pneumonia, bronchitis and pleural effusion. Patient presenting within 7 days of the onset of illness
Severe acute respiratory infection (persons ≥ 5 years old)	Any person presenting with manifestations of acute LRTI with: Sudden onset of fever (>38ºC) AND Cough or sore throat AND Shortness of breath, or difficulty breathing with or without clinical or radiographic findings of pneumonia.) Patient presenting within 7 days of the onset of illness

review of laboratory databases. Details of management during hospital admission and outcome are also collected.

Following enrolment, nasopharyngeal aspirates (for children less than 5 years) and throat and nasopharyngeal swabs (for patients 5 years of age or older) are collected and stored in viral transport medium for transport to National Institute for Communicable Diseases (NICD) of the National Health Laboratory Service (NHLS) for testing. Unlinked anonymous HIV ELISA (in patients aged > 18 months) or PCR (in patients aged <= 18 months) testing is performed using a dried blood spot or whole blood specimen for patients who did not have an HIV test as part of routine care.

Testing for the presence of respiratory viruses is done by multiplex PCR for influenza, adenovirus, enterovirus, rhinovirus, human metapneumovirus, respiratory syncytial virus, parainfluenza virus type 1, 2 and 3. All samples that have been identified as influenza A positive are subtyped using a one step qualitative RT PCR real time assay. All samples are also characterised using the novel A/H1N1 one step RT PCR real time assay to identify the 2009 pandemic virus (CDC realtime RTPCR protocol for detection and characterization of influenza)[6]. A blood sample of 0.5 ml minimum volume is collected in an EDTA (purple-topped) vacutainer tube and transported to the Respiratory and Meningeal Pathogens Research Unit at the NICD for processing for a single-target (*lytA*) TaqMan quantitative real-time PCR assay based on an adaption of a previously described method by Carvalho et al[7]. This test will determine the presence of pneumococcal DNA in the blood.

Clinical and laboratory data collected on case investigation forms are sent to NICD for data entry into an MS access database and analysis. Feedback of aggregated data is provided weekly to the sentinel sites.

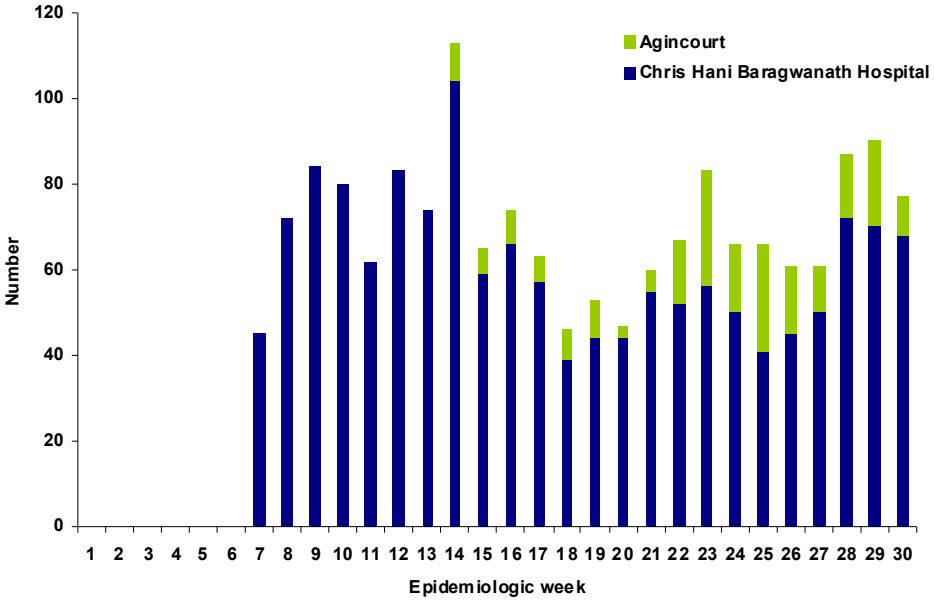

Figure 1: Number of samples collected from patients with Severe Acute Respiratory Infection by epidemiologic week and surveillance site, 2009.

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Results

The programme was initiated in February 2009 and the sites were rolled out starting at CHBH (February 2009, week 7) followed by Mapulaneng and then Matikwana hospitals (April 2009, week 14). Edendale Hospital will start recruiting patients in August 2009.

Between 9th February 2009 (week 7) and the 26th July 2009 (week 30), 1526 samples were tested and 1364 case investigation forms were entered into the database. The majority of enrolled SARI cases to date, 89% (n=1351/1526), were from CHBH, 76% (n=1044/1364) of the patients were under 5 years of age and 47% (638/1356) of patients with available data on gender were female.

Figure 1 illustrates the number of samples collected by surveillance site over the program period.

Of the 1526 samples tested, 442 (29%) were positive for respiratory syncytial virus (RSV) and 166 (11%) were positive for influenza virus. Detection rate of respiratory syncitial virus increased from week 8 of the year and peaked in week 11 (Figure 2). In the peak RSV season the detection rate of RSV was between 60% and 70%. The rate of detection of influenza virus started increasing from week 18 and peaked in week 26. The detection rate of influenza at the peak of the season was between 35% and 40%. Of the 166 influenza virus isolates identified 162 (99%) were influenza A H3N2, 3 were influenza B and 1 was pandemic influenza A H1N1 (Figure 3).

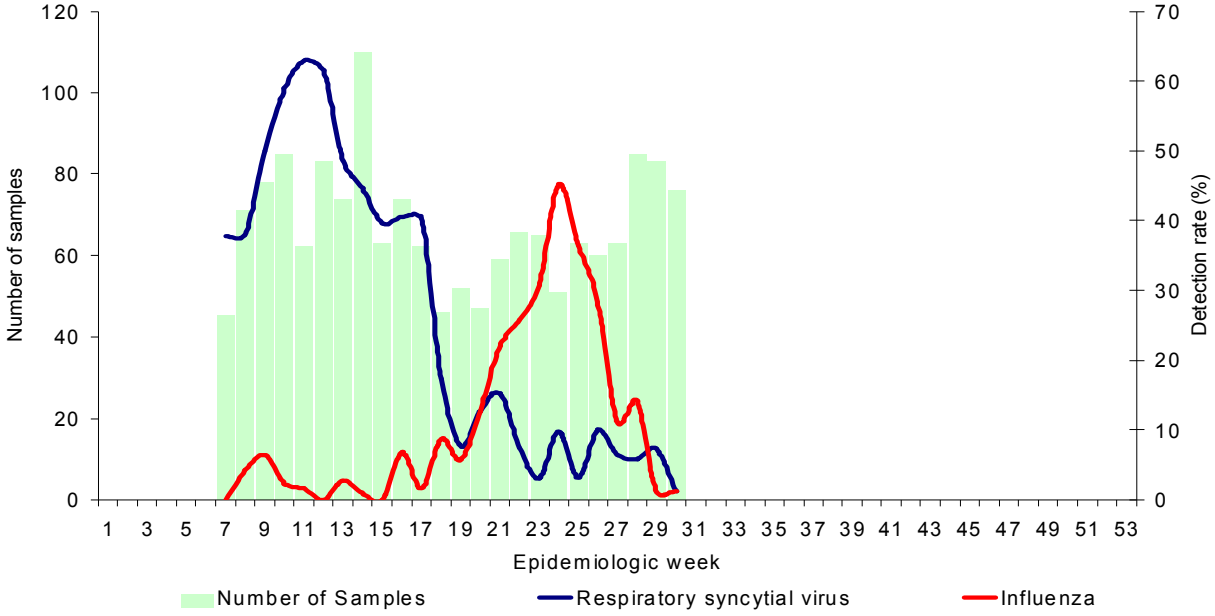

Figure 2: Number of specimens received and detection rate for influenza virus and respiratory syncytial virus by epidemiologic week, SARI surveillance sites, 2009

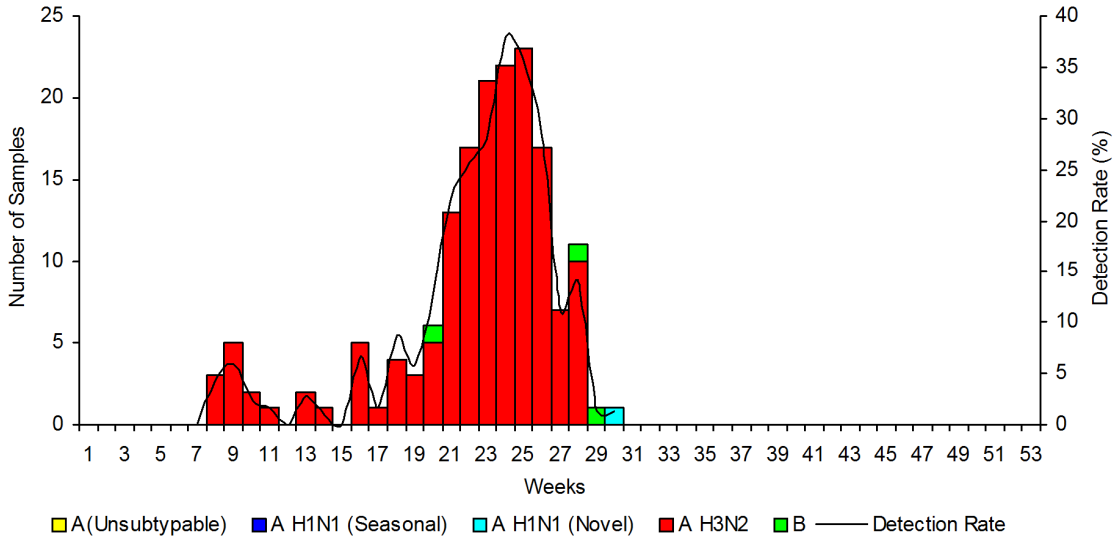

Figure 3: Number of specimens testing positive for influenza by virus type and subtype and detection rate for all SARI surveillance sites, 2009

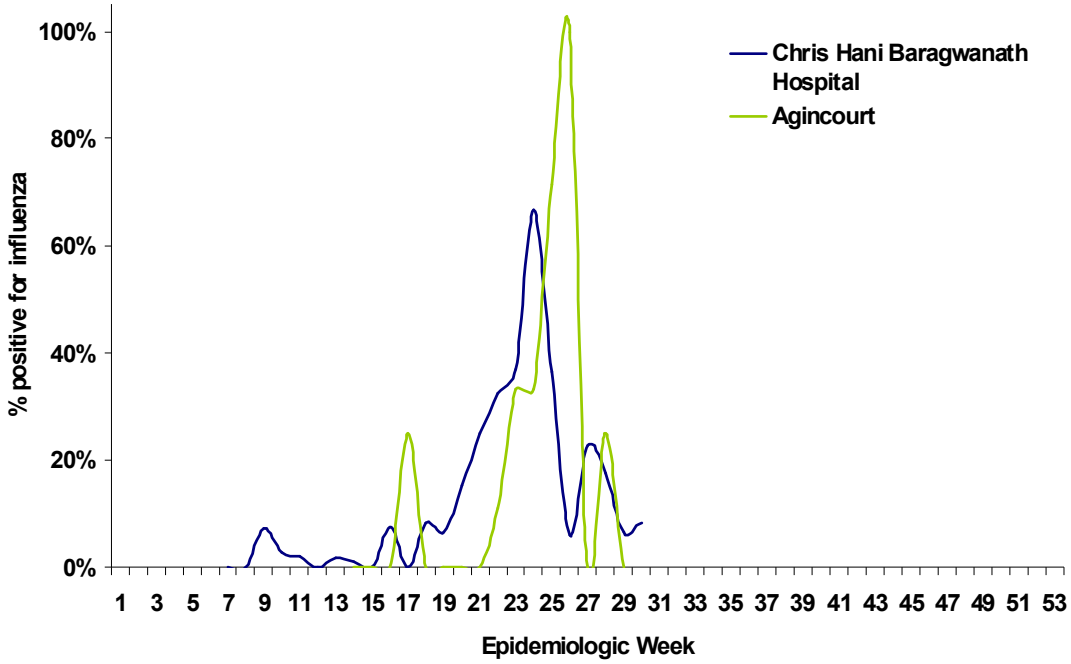

Figure 4 Detection rate for influenza by epidemiologic week Chris Hani Baragwanath Hospital Soweto and Agincourt Mpumalanga, 2009

At CHBH the influenza season began in week 19 and peaked in week 24 while at the Matikwana and Mapulaneng hospitals the season began slightly later in week 22 and peaked in week 26 (Figure 4).

Discussion

The SARI surveillance programme represents a substantial addition to influenza surveillance in South Africa. It complements the existing viral watch programme, which focuses on influenza-like illness, by providing data on hospitalized patients. In addition, the systematic enrollment of eligible patients according to a standardised protocol at differing geographic sites will allow for robust comparisons between settings.

Preliminary data from the SARI surveillance programme has allowed us to describe the seasonality of influenza and RSV in two geographic areas of South Africa. In the peak of the influenza season we were able to identify influenza virus from more than a 3rd of patients with pneumonia presenting to sentinel sites. We have also been able to describe the timing of the RSV season which preceded the influenza season. Only one patient infected with pandemic influenza A H1N1 viruses was identified through SARI surveillance during this reporting period. As the virus spreads more widely the SARI surveillance programme will hopefully allow us to monitor and describe the epidemiology of patients hospitalized with respiratory infection due to pandemic influenza A H1N1.

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Table 1: Provisional number of laboratory confirmed cases of diseases under surveillance reported to the NICD - South Africa, corresponding periods 1 January - 30 June 2008/2009*

Disease/Organism	Cumulative to 30 June, year	EC	FS	GA	KZ	LP	MP	NC	NW	WC	South Africa
Anthrax	2008	0	0	0	0	0	0	0	0	0	0
	2009	0	0	0	0	0	0	0	0	0	0
Botulism	2008	0	0	0	0	0	0	0	0	0	0
	2009	0	0	0	0	0	0	0	0	0	0
Cryptococcus spp.	2008	714	306	1115	757	231	467	28	407	324	4349
	2009	743	257	1270	810	336	461	44	393	342	4656
Haemophilus influenzae, invasive disease, all serotypes	2008	16	14	82	19	2	11	4	4	41	193
	2009	17	10	77	23	1	16	5	6	46	201
Haemophilus influenzae, invasive disease, < 5 years											
Serotype b	2008	3	4	12	3	0	2	2	2	7	35
	2009	3	4	9	9	0	1	1	0	12	39
Serotypes a,c,d,e,f	2008	1	1	8	0	0	1	0	0	3	14
	2009	0	1	12	0	0	1	0	1	5	20
Non-typeable (unencapsulated)	2008	1	3	9	1	0	1	0	0	5	20
	2009	1	0	11	5	0	1	0	0	5	23
No isolate available for serotyping	2008	6	0	25	5	1	5	0	1	10	53
	2009	2	1	13	4	1	4	1	2	5	33
Measles	2008	1	0	4	3	0	1	1	3	2	15
	2009	3	0	29	3	0	5	0	1	4	45
Neisseria meningitidis, invasive disease	2008	11	7	96	7	0	16	4	4	27	172
	2009	14	3	95	15	1	17	2	7	32	186
Novel Influenza A virus infections	2008	0	0	0	0	0	0	0	0	0	0
	2009	0	0	11	0	0	0	0	0	3	14
Plague	2008	0	0	0	0	0	0	0	0	0	0
	2009	0	0	0	0	0	0	0	0	0	0
Rabies	2008	5	0	0	5	3	0	0	0	0	13
	2009	4	0	0	3	1	0	0	0	0	8
**Rubella	2008	72	3	40	59	28	18	0	18	13	251
	2009	89	3	28	45	8	42	24	12	15	266
Salmonella spp. (not typhi), invasive disease	2008	27	21	272	50	4	24	10	10	42	460
	2009	28	16	176	60	1	20	5	11	45	362
Salmonella spp. (not typhi), isolate from non-sterile site	2008	115	17	215	84	9	56	7	9	77	589
	2009	121	20	356	73	3	79	13	32	123	820
Salmonella typhi	2008	3	1	13	4	2	10	0	0	5	38
	2009	4	1	12	2	0	3	0	0	7	29
Shigella dysenteriae 1	2008	0	0	0	0	0	0	0	0	0	0
	2009	0	0	0	0	0	1	0	0	0	1
Shigella spp. (Non Sd1)	2008	79	32	279	64	7	32	11	5	220	729
	2009	129	45	341	87	2	43	10	11	234	902
Streptococcus pneumoniae, invasive disease, all ages	2008	139	130	933	228	41	117	37	74	262	1961
	2009	199	138	1062	249	40	105	40	78	324	2235
Streptococcus pneumoniae, invasive disease, < 5 years	2008	38	54	292	90	11	41	13	15	92	646
	2009	68	37	300	84	10	35	21	16	116	687
Vibrio cholerae O1	2008	0	0	3	0	0	26	0	0	0	29
	2009	0	0	37	0	450	62	0	18	4	571
Viral Haemorrhagic Fever (VHF)											
Crimean Congo Haemorrhagic Fever (CCHF)	2008	0	2	0	0	0	0	2	0	0	4
	2009	0	0	0	0	0	0	1	0	0	1
†Other VHF (not CCHF)	2008	0	0	4	0	10	4	0	0	0	18
	2009	0	0	0	3	0	0	0	0	0	3

Footnotes

*Numbers are for cases of all ages unless otherwise specified. Data presented are provisional cases reported to date and are updated from figures reported in previous bulletins.

**Rubella cases are diagnosed from specimens submitted for suspected measles cases † Other VHF for 2008 and 2009 are Rift Valley fever
Provinces of South Africa: EC – Eastern Cape, FS – Free State, GA – Gauteng, KZ – KwaZulu-Natal, LP – Limpopo, MP – Mpumalanga, NC – Northern Cape, NW – North West, WC – Western Cape

U = unavailable, 0 = no cases reported

Table 2: Provisional laboratory indicators for NHLS and NICD, South Africa, corresponding periods 1 January - 30 June 2008/2009*

Programme and Indicator	Cumulative to 30 June, year	EC	FS	GA	KZ	LP	MP	NC	NW	WC	South Africa
Acute Flaccid Paralysis Surveillance											
Cases < 15 years of age from whom specimens received	2008	31	11	32	17	26	13	3	6	17	156
	2009	28	2	29	49	28	26	6	11	11	190
Laboratory Programme for the Comprehensive Care, Treatment and Management Programme for HIV and AIDS											
CD4 count tests											
Total CD4 count tests submitted	2008	139450	58360	256669	428242	89520	84356	22344	93033	88845	1260819
	2009	176742	63713	312762	394315	102339	1E+05	26386	115004	110587	1421950
Tests with CD4 count < 200/µl	2008	54381	19692	97986	109058	31946	30863	6683	30676	25383	406668
	2009	57521	19153	106637	123775	32996	40114	8065	35946	30842	455049
Viral load tests											
Total viral load tests submitted	2008	58743	25197	114935	131295	38303	29001	9038	37560	29064	473136
	2009	67571	16865	149690	176264	45091	44103	8664	45808	40936	594992
Tests with undetectable viral load	2008	28053	14543	67855	73546	21871	15817	4761	23210	23283	272939
	2009	38453	12928	98470	116576	29103	27509	5132	30328	33597	392096
Diagnostic HIV-1 PCR tests											
Total diagnostic HIV-1 PCR tests submitted	2008	11755	4914	26499	26933	7458	4394	1527	6706	8699	98885
	2009	13434	5247	27876	35226	7697	8613	1784	8535	9051	117463
Diagnostic HIV-1 PCR tests positive for HIV	2008	1523	917	4060	4977	1367	922	224	1250	877	16117
	2009	1470	659	3089	3639	1025	1152	210	1094	768	13106

Footnotes

*Numbers are for all ages unless otherwise specified. Data presented are provisional numbers reported to date and are updated from figures reported in previous bulletins.
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