VOLUME 6, NO. 4

COMMUNICABLE DISEASES SURVEILLANCE BULLETIN

NOVEMBER 2008

NICD NHLS

FOREWORD

A highlight of the November 2008 bulletin is the first report of data on multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis from the NHLS corporate data warehouse (CDW). This article emphasises two important issues. Firstly, the utility of the CDW as a data source to augment more traditional surveillance activities. Secondly, the importance of the laboratory in tracking the burden of XDR tuberculosis which is an emerging pathogen globally is highlighted.

Two articles looking at various aspects of the quality of surveillance systems are the evaluation of predictors of non-reporting to the GERMS-SA surveillance programme and the evaluation of the usefulness of the new measles diagnostic algorithm. Additionally, a descriptive survey of HIV testing algorithms nationally provides useful background information for the interpretation of surveillance data. Lastly, we include a description of an influenza outbreak in the Northern Cape. Such outbreaks are almost certainly more common then would appear from the literature. The documentation of outbreaks is essential to aid in critical review of the response and to facilitate preparedness for future outbreaks.

Cheryl Cohen, Editor

CONTENTS

PREDICTORS OF NON-REPORTING TO A NATIONAL LABORATORY-BASED SURVEILLANCE PROGRAMME

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Background

The Group for Enteric, Respiratory and Meningeal disease Surveillance in South Africa (GERMS-SA) conducts national, laboratory-based surveillance for bacterial and fungal diseases of public health importance at over 270 clinical microbiology laboratories, with additional enhanced surveillance at 23 hospital sites. Surveillance is conducted for invasive disease due to enteric pathogens, including *Salmonella* and *Shigella*, and for invasive disease due to the respiratory and meningeal pathogens *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae*, and *Cryptococcus*. Each unit performs additional characterisation of received isolates, such as serotyping and determination of antimicrobial susceptibility. The completeness of reporting of cases to the surveillance programme is assessed by performing regular audits on all laboratory-confirmed cases of disease reported to GERMS-SA.

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WEB
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Aims

To improve laboratory reporting and isolate submission to the GERMS-SA surveillance programme by identifying predictors of non-reporting of case patients with invasive disease by clinical microbiology laboratories in 2007.

Study Design and Methods

Case data of patients with invasive, laboratory-confirmed disease due to *Salmonella*, *Shigella*, *S.pneumoniae*, *N.meningitidis*, *H.influenzae*, and *Cryptococcus* species in South Africa in 2007, which met the requirements of each unit's case definition, were reported to GERMS-SA by diagnostic laboratories. Cases were reported using standardised laboratory forms, containing specimen and isolate data, and demographic details of patients. In addition, more detailed case report forms, containing additional clinical and epidemiological data, were completed by surveillance officers at enhanced surveillance sites (ESS). Corresponding isolates were also transported to the respective GERMS-SA units for further characterisation. Patient case data were subsequently captured onto databases in *EpiInfo version 6.04d*. At the end of 2007, a complete audit of laboratory-confirmed cases reported to GERMS-SA in 2007 was performed using the National Health Laboratory Service (NHLS) Corporate Data Warehouse (CDW) – a centralised repository from which data on all laboratory tests performed at NHLS laboratories throughout the country (excluding KwaZulu-Natal) can be extracted. Specifically, the NHLS CDW was used to generate line lists of all patients with invasive disease due to *Salmonella*, *Shigella*, *S.pneumoniae*, *N.meningitidis*, *H.influenzae*, and *Cryptococcus* spp. recorded in the eight provinces in 2007. These lists were compared with the cases captured on the GERMS-SA databases in the same year, and any cases found to be missing from the latter databases were subsequently recorded as audit, or non-reported, cases. An analytical cross-sectional study of secondary data obtained from the 2007 audits was conducted, whereby predictors of non-reporting of cases were identified by univariate and multivariate logistic regression.

Results and discussion

In 2007, a total of 11,576 patients with laboratory-confirmed invasive disease due to *Salmonella*, *Shigella*, *S.pneumoniae*, *N.meningitidis*, *H.influenzae*, and *Cryptococcus* spp. were detected from NHLS laboratories by the surveillance programme, 2,890 (25%) of which were not reported to GERMS-SA. The majority of all 11,576 cases were detected in Gauteng province (5,112; 44%), and 66% (7,624) of all cases were detected at non-ESS. Overall, cerebrospinal fluid (CSF) was the commonest specimen type from which patients were diagnosed with invasive disease (7,713; 67%), and 73% (8,497) of patients were aged over 15 years. Of the 794 cases of *Salmonella* and 56 cases of *Shigella*, 168 (21%) and 14 (25%), respectively, were non-reported. A total of 4,017 cases of *S.pneumoniae*, 431 cases of *N.meningitidis*, and 325 cases of *H.influenzae* were detected, of which 804 (20%), 46 (11%), and 85 (26%), respectively, were non-reported. Additionally, of the 5,953 cases of *Cryptococcus* spp. detected by surveillance in 2007, 1,773 (30%) were non-reported to the programme (Figure 1). On univariate analysis, the percentage of cases that were non-reported differed significantly according to the organism, province, specimen type, age, ESS, and month of specimen collection (Table 1).

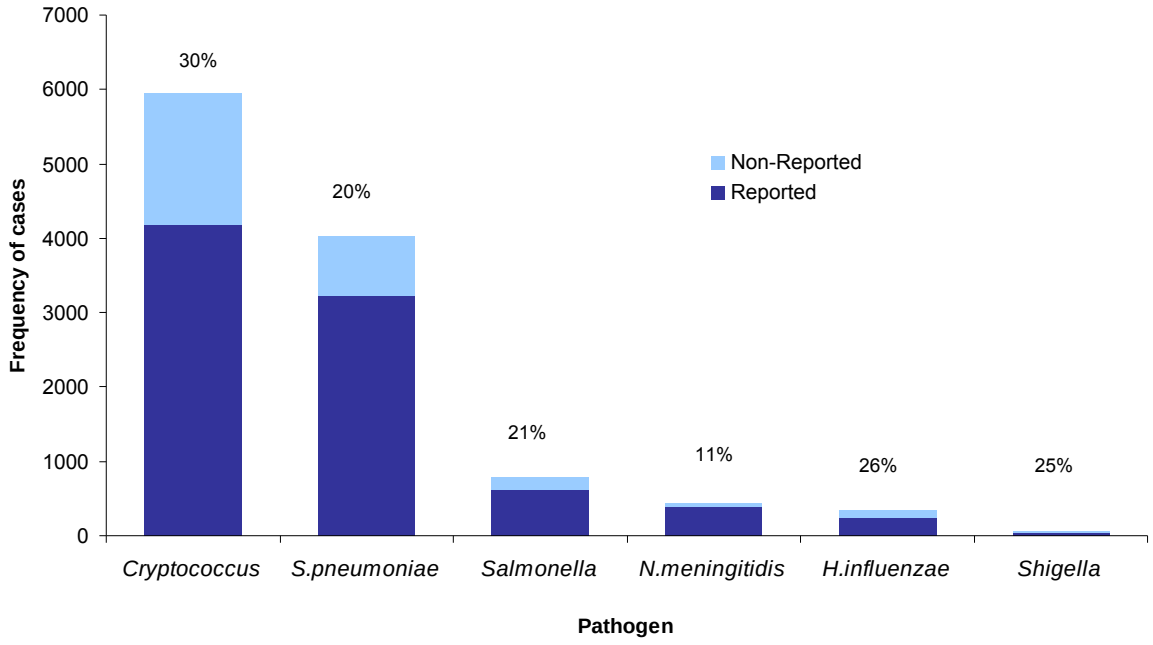

Figure 1: Number of cases reported and non-reported (%) to a national laboratory-based surveillance programme in 2007, by pathogen.

Table 1: Variables associated with non-reporting to the Group for Enteric, Respiratory and Meningeal Pathogens Surveillance - South Africa (GERMS-SA) surveillance programme in 2007.

	Cases Non-Reported		Univariate analysis		Multivariable analysis	
Variable	**n/ N**	**%**	**OR [95% CI]**	**P**	**OR [95% CI]**	**P**
Gender				<0.100		
Male	1,304/ 4,052	24.4	1			
Female	1,547/ 4,479	25.7	1.1 [0.9 - 1.2]			
Organism						
N. meningitidis	46/ 431	10.7	1		1	
Cryptococcus **	1,773/ 5,953	29.8	3.6 [2.6 - 4.8]		2.6 [1.8 - 3.6]	
H. influenzae **	85/ 325	26.2	3.0 [2.0 - 4.4]	<0.001	2.6 [1.7 - 4.0]	<0.001
Salmonella **	168/ 794	21.2	2.2 [1.6 - 3.2]		1.8 [1.2 - 2.7]	
Shigella **	14/ 56	25.0	2.8 [1.4 - 5.5]		2.3 [1.1 - 4.8]	
S. pneumoniae **	804/ 4,017	20.0	2.1 [1.5 - 2.9]		1.6 [1.2 - 2.3]	
Province						
FS	195/ 963	20.3	1		1	
EC **	714/ 1,518	47.0	3.5 [2.9 - 4.2]		3.5 [2.9 - 4.2]	
GA	826/ 5,112	16.2	0.8 [0.6 - 0.9]		1.1 [0.9 - 1.3]	
LP **	257/ 656	39.2	2.5 [2.0 - 3.2]	<0.001	2.6 [2.1 - 3.3]	<0.001
MP **	448/ 1,111	40.3	2.7 [2.2 - 3.2]		2.9 [2.3 - 3.5]	
NC **	40/ 142	28.2	1.5 [1.0 - 2.3]		2.7 [1.7 - 4.1]	
NW	206 /900	22.9	1.2 [0.9 - 1.5]		1.1 [0.9 - 1.4]	
WC	204/ 1,174	17.4	0.8 [0.7 - 1.0]		1.1 [0.9 - 1.4]	
Specimen						
CSF	2084/ 7,713	27.0	1	<0.001	1	<0.001
BC	537/ 3,394	15.8	0.5 [0.5 - 0.6]		1.0 [0.9 - 1.2]	
Other **	269/ 469	57.4	3.6 [3.0 - 4.4]		6.9 [5.5 - 8.8]	
Enhanced Surveillance Site						
Yes	417/ 3,952	10.6	1	<0.001	1	<0.001
No **	2,473/ 7,624	32.4	4.1 [3.6 - 4.6]		3.3 [2.9 - 3.7]	
Age Group						
Adult	2,171/ 8,497	25.6	1	<0.001	1	<0.001
Paediatric **	524/ 2,495	21.0	0.8 [0.7 - 0.9]		1.3 [1.1 - 1.5]	
Unknown	195/ 584	33.4	1.5 [1.2 - 1.7]		1.0 [0.9 - 1.3]	
Month						
Jan	278/ 982	28.3	1		1	
Feb	243/ 900	27.0	0.9 [0.8 - 1.1]		1.1 [0.9 - 1.3]	
Mar **	263/ 886	29.7	1.1 [0.9 - 1.3]		1.3 [1.0 - 1.6]	
Apr **	265/ 910	29.1	1.0 [0.9 - 1.3]		1.3 [1.0 - 1.6]	
May	252/ 1,005	25.1	0.8 [0.7 - 1.0]		1.0 [0.8 - 1.2]	
Jun **	160/ 801	20.0	0.6 [0.5 - 0.8]	<0.001	0.7 [0.6 - 0.9]	<0.001
Jul	258/ 1,089	23.7	0.8 [0.6 - 1.0]		0.9 [0.7 - 1.1]	
Aug	257/ 1,144	22.5	0.7 [0.6 - 0.9]		0.9 [0.7 - 1.1]	
Sep	227/ 1,024	22.2	0.7 [0.6 - 0.9]		0.8 [0.7 - 1.1]	
Oct	246/ 1,014	24.3	0.8 [0.7 - 1.0]		0.8 [0.7 - 1.1]	
Nov	228/ 965	23.6	0.8 [0.6 - 0.9]		0.9 [0.8 - 1.2]	
Dec	213/ 856	24.9	0.8 [0.7 - 1.0]		1.0 [0.8 - 1.3]	

*OR Odds ratio, CI confidence interval
** Statistically significant at the 5% level.

Controlling for potential confounding variables, multivariate analysis showed the following predictors of non-reporting of cases to the surveillance programme: organism, province, specimen, non-ESS, age group, and month (Table 1). As compared to non-reporting of *N.meningitidis*, non-reporting was 2.6 times more likely for *Cryptococcus* spp. and *H.influenzae*, 2.3 times more likely for *Shigella*, 1.8 times more likely for *Salmonella*, and 1.6 times more likely for *S.pneumoniae*. Compared to non-reporting of cases from Free State province, non-reporting was 3.5 times more likely from the Eastern Cape, 2.9 times more likely from Mpumalanga, 2.7 times more likely from the Northern Cape, and 2.6 times more likely from Limpopo. Univariate analysis showed an association between non-reporting and specimen type, with CSF specimens twice as

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likely as blood culture specimens to be non-reported (Table 1). Following the control for confounding variables by multivariate analysis, both specimen types were equally likely to be non-reported. The apparent univariate association may have been due to confounding by organism type and the large number of *Cryptococcus* cases, 97% (5,754/ 5,953) of which were CSF specimens and 30% (1,773/ 5,953) of which were non-reported. Non-reporting by laboratories of case patients diagnosed from "other" specimen types, including pleural, joint, and unspecified fluid types, was 6.9 times more likely than the non-reporting of both CSF and blood culture specimen types. Age group was found to be another predictor of non-reporting – children under the age of 15 years with laboratory-confirmed invasive disease were 1.3 times more likely to be non-reported than adult cases over the age of 15 years. This apparent association with age group may represent confounding by an additional variable that was not controlled for. The same confounding may explain the association between non-reporting and month. Finally, as would be expected, cases from non-ESS were 3.3 times more likely to be non-reported than those from ESS, where cases were actively followed up (Table 1).

Conclusion

Predictors of non-reporting of laboratory-confirmed invasive disease due to *Salmonella, Shigella, S.pneumoniae*, *N.meningitidis*, *H.influenzae*, and *Cryptococcus* spp. to a national laboratory-based surveillance programme, include organism type, specimen type, province, non-enhanced surveillance site, and age group. These factors therefore need to be targeted in order to improve reporting from participating laboratories in the surveillance network.

MEASLES SURVEILLANCE : A NEW MEASLES DIAGNOSTIC ALGORITHM SOUTH AFRICA, 2007

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Introduction

Measles is a highly infectious disease that causes morbidity and mortality in both developing and industrialized countries.[1] The measles vaccine was first introduced in 1963 and progressively introduced across the globe, leading to a decrease in the global measles incidence as immunization coverage improved.[2,3] Despite significant global reduction in measles incidence, measles remains the leading vaccine-preventable killer of children worldwide and is estimated to have caused 454,000 deaths in 2004, almost half of which were in Sub-Saharan Africa.[4, 5, 6]

Global measles control activities can be characterized into different phases: the introduction of routine vaccination against measles through the expanded programme on immunization (EPI); the provision of additional opportunity to vaccination through supplementary immunization activities (SIAs); and reduction of measles associated mortality.[2] Measles became a notifiable disease in South Africa in 1980. In 1995, EPI was launched with a goal of controlling measles through routine immunisation. Since the mid-1990s the Department of Health has been very active in controlling measles through routine immunization services and SIAs.[7]

Within different countries and regions, the goals of measles immunization programmes could be to control incidence, to prevent outbreaks or to eliminate measles.8 Surveillance is a crucial cornerstone of measles control strategies irrespective of the goals for the immunization programmes. There are four strategies recommended for reducing measles associated mortality and for achieving elimination status: providing the first dose of measles vaccine to successive birth cohorts; ensuring that all children have a second opportunity for measles vaccination; enhancing measles surveillance with integration of epidemiological and laboratory information; and improving the management of every single measles case.[8] The success in controlling measles in South Africa has led it to the shift of South Africa's immunization goals from control to elimination of measles.[7] When measles elimination is the goal, surveillance must be case based with the principal objectives of: immediately detecting any suspected cases; confirming cases by laboratory diagnosis; and identifying importations and possible sources of infection. In-depth investigation of each suspected case is critical. [3]

For measles surveillance to be successful it is essential to have appropriate case definitions. Case definitions in use in South Africa include:

- Suspected Measles Case (SMC): Any person in whom a clinician suspects measles infection or any person with fever and maculo-papular rash (i.e. non-vesicular) and cough, coryza (i.e. runny nose) or conjunctivitis (i.e. red eyes).[1]
- Laboratory confirmed case: any suspected case that is laboratory confirmed.[1] The current gold standard, recommended by the World Health Organization (WHO), for laboratory confirmation of measles infection is based on serum detection of measles specific IgM antibodies using enzyme-immuno-assays (EIA).9 Other methods that can be used to confirm measles infection include an immunoglobulin G (IgG) sero-conversion or a four fold rise in the IgG titre on a second specimen, viral isolation and detection of viral specific ribonucleic acid (RNA) by reverse transcriptase polymerase chain reaction (RT-PCR) testing on appropriate specimens (nasopharyngeal specimens, throat swabs, urine or filter paper blood spots).[5, 9, 10, 11]

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- Additional data is essential for understanding the effectiveness of the vaccination system and epidemiologic links between cases. This includes:
- date of occurrence of cases;
- place of occurrence of cases;
- age and vaccination status of cases.[1]

In South Africa, the National Institute for Communicable Diseases (NICD) is accredited by the World Health Organization (WHO) to perform measles and rubella IgM testing for the national case based surveillance and trace the molecular epidemiology of the measles virus.[12] Despite the low incidence of measles in South Africa, outbreaks still occur.[13] To ensure sustained elimination of measles, all aspects of surveillance already mentioned need to be strengthened. Since the early 1980's the NICD has been using a serology test for measles specific IgM (Dade Behring enzygnost anti-measles-virus/IgM) for the diagnosis of measles. Studies suggest that urine RT-PCR is a more sensitive laboratory marker compared to the serology tests.[14, 15] The specificity of RT-PCR methods has been estimated to be as high as 100%.[14] However, the sensitivity and specificity of both these methods are further influenced by the timing of specimen collection in relation to the onset of rash, and disease prevalence as manifested in positive and negative predictive values.[10,11,15] A combination of serology and RT-PCR methods in areas of low measles prevalence may improve the positive predictive values for a diagnosis of measles to 98%.[16]

In 2007, the NICD developed and initiated a new testing algorithm which proposes sequential testing of all serum specimens with measles specific IgM positive and equivocal results, to be confirmed with the RT-PCR on urine specimens. This paper aims to present preliminary results of the evaluation of the new measles testing algorithm and highlight some of the challenges experienced during follow up of SMCs reported to the NICD in 2007.

Specific objectives of the study were to:

- Collect clinical and epidemiological information on all measles IgM positive and equivocal cases
- Categorise measles IgM positive and equivocal cases according to types of specimens submitted and timing of specimen collection in relation to onset of rash
- Classify patients using clinical, epidemiological and laboratory data
- Describe the number of IgM positive and IgM equivocal cases confirmed by the RT-PCR test

Methods

A cross sectional study was conducted at NICD in 2007. Clinical, epidemiological and laboratory information was obtained from the NICD measles surveillance database, case investigation form (CIF), laboratory forms and telephonic record reviews. We developed a new CIF that we used to follow up all measles IgM positive and IgM equivocal cases that had been reported to the NICD from January to December 2007. The information required included: demographic details, date of onset of rash, other presenting symptoms and signs, date of specimen collection, type of specimens collected, vaccination history, contact history, treatment given, presence of complications, and patient clinical outcome. All health institutions in all nine South African provinces are required to notify the health authorities of all suspected measles cases and to submit blood and urine specimens to the NICD for measles and rubella laboratory investigations. All the national provinces, except Free State Province (FSP), submitted specimens from SMC to the NICD for investigation. FSP performed their own laboratory testing and submitted the results to the NICD.

The laboratory investigations performed by the NICD (according to the new algorithm) are as follows:

- Serology test for measles-specific IgM (Dade Behring enzygnost anti-measles-virus/IgM) on all serum specimens of SMC
- RT-PCR test on urine specimens of measles IgM positive and IgM equivocal cases. A positive RT-PCR test result was considered as confirmation of the measles diagnosis. A negative RT-PCR test result on a urine specimen collected within 5 days of onset of the rash was considered as a negative measles result.

Clinical, epidemiological and laboratory information were used to classify cases into 3 groups:

- Probable true measles cases: patients confirmed on RT-PCR or cases with an identified epidemiological link to confirmed case
- Probable false positive cases: cases with a dual rubella positive result, cases with negative urine RT-PCR result on timeously collected urine specimen, cases vaccinated within 6 weeks of the positive IgM result, or cases clinically not compatible with a diagnosis of measles
- Cases not able to classify: cases with no additional essential information obtained, or cases with no urine specimens submitted.

Results

A total of 79 cases were included in the study (32 measles IgM positive cases and 47 measles IgM equivocal cases). Data on gender was available on 76 of 79 cases, of which 42 (55%) were female. Data on age was available for all the cases. The median age was five years (interquartile range of 1 to 9 years).

CIFs were submitted to the NICD from 30% (24/79) of cases and we were able to do telephonic record reviews on 53% (42/79) of the cases. 53% (42/79) of cases had available data on signs and symptoms at presentation with 11 of those cases meeting the SMC case definition. Even though 61% (48/79) of cases submitted both blood and urine specimens, the time period between date of onset of rash and date of specimen collection could be calculated in only 33% (26/79) of cases. Urine was collected within 5

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days of onset of rash for 77% (20/26) of these cases. The mean time period between onset of rash and specimen collection in the 26 patients with these data available was 2 days. Only 7 cases tested urine PCR positive (5 from IgM positive cases and 2 from IgM equivocal cases) for measles virus. One of the IgM positive patients had been vaccinated 5 days before specimen collection and the isolate was shown to be the vaccine strain. Measles vaccination history was recorded for only 35% (28/79) of cases, with 3/28 reporting vaccination within six weeks prior to the onset of rash. This suggested that the positive measles IgM result of 3/28 cases was due to vaccination. A history of contact with SMCs was recorded in 28 of 79 (35%) patients with 13 of those patients reporting to have been in contact with a SMC. Clinical management was recorded in 28 of 79 (35%) cases with only 9 of those cases reported to have been given Vitamin A. We were able to obtain information on outcome in 47% (37/79) of cases. There was one measles associated admission and no measles associated deaths.

42/79 (53%) cases had records of signs and symptoms; with only 11/79 (14%) cases meeting the SMC case definition. (Table 1)

Table 1: Presenting signs and symptoms of the measles IgM positive and equivocal cases investigated by the NICD, South Africa; January to December 2007*

Signs and symptoms	Measles IgM positive [n (%)] N = 23	Measles IgM equivocal [n (%)] N = 19
Fever	12 (52)	6 (32)
Rash	23 (100)	19 (100)
Cough	4 (17)	6 (32)
Coryza	5 (22)	4 (21)
Conjunctivitis	5 (22)	2 (11)
SMC Case Definition met	7 (30)	4 (21)

* Those cases that have the symptoms as reflected on this table are not mutually exclusive. If a symptom was not recorded it was counted as absent.

The following diagrams illustrate the summary of the classification of cases for measles IgM positive and measles IgM equivocal cases. Urine-PCR enabled more accurate classification of 13/79 (16%) cases.

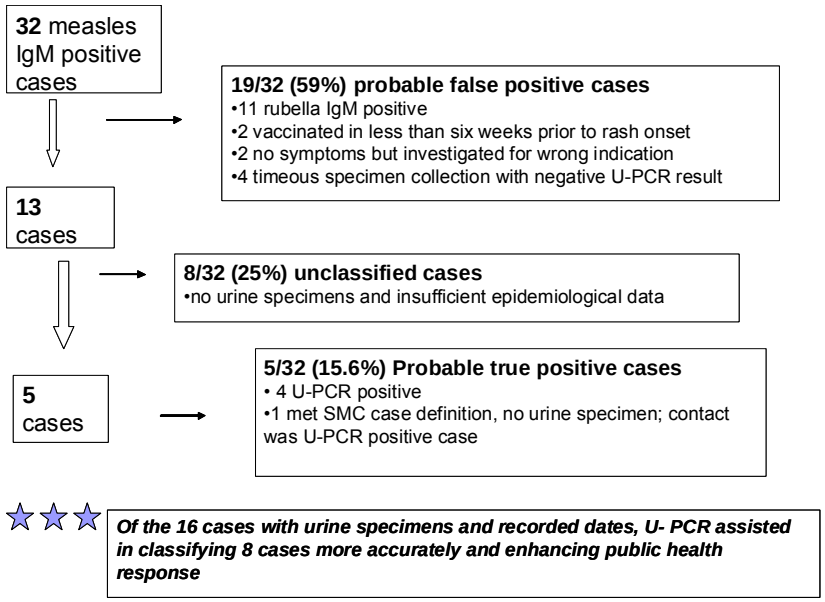
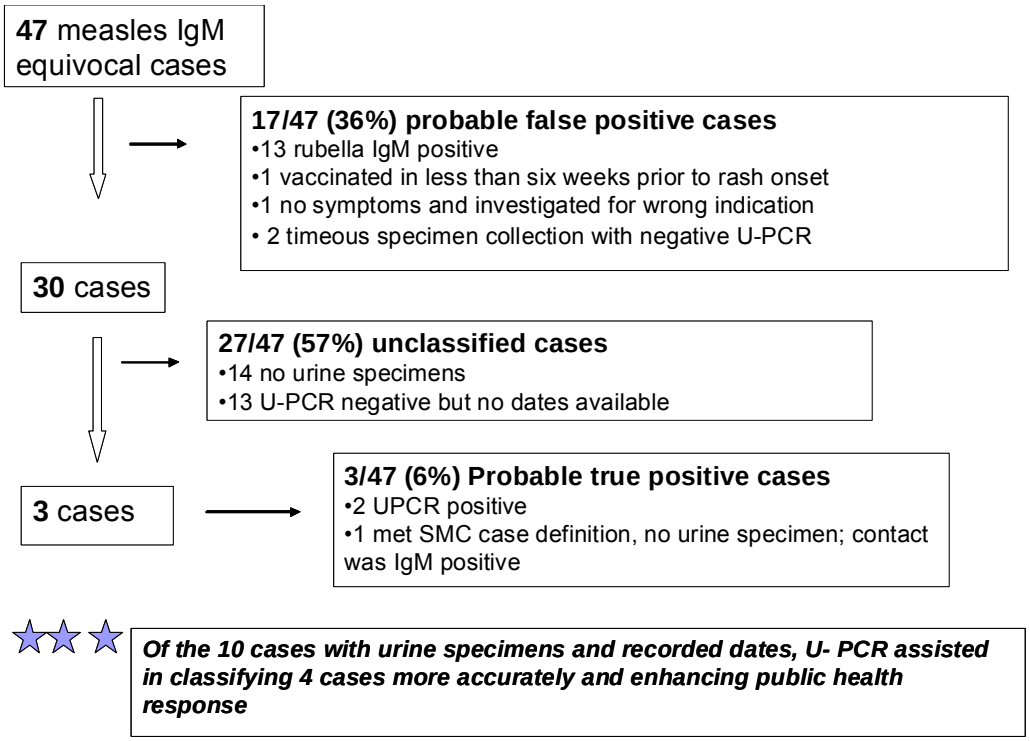


Figure 1 : Flow diagram representing the classification of measles IgM positive cases reported to the NICD, South Africa; January to December 2007

U-PCR—Urine polymerase chain reaction
SMC—Suspected measles case



Flow diagram illustrating the classification of measles IgM equivocal cases reported to the NICD, South Africa; January to December 2007

U-PCR—Urine polymerase chain reaction
SMC—Suspected measles case

Study limitations

The standard CIF used for measles surveillance is used for surveillance of meningitis and neonatal tetanus as well. Therefore, some of the information essential to measles surveillance could not be captured using the form alone. Obstacles to obtaining information through telephonic record review included: lack of contact details for the health facility (e.g. facility name not recorded, mobile clinics and facilities in rural areas) and absence of detailed patient records at the facility. We had no gold standard measles diagnostic test against which to compare our results and thus were unable to fully evaluate the diagnostic algorithm.

Conclusion

The new measles testing algorithm has been useful because urine-PCR enabled more accurate classification of cases, leading to an enhanced public health response. However significant challenges still exist, especially with regards to lack of essential data and proper urine specimen collection and submission. The additional essential data required, is crucial to assist in classification of cases and to better direct public health interventions and resources. Upon completion of this study, a CIF specific to measles surveillance has been piloted this year. South Africa currently requires collection of blood and urine specimens on all SMC, in accordance with WHO recommendations for countries in the elimination phase of measles control.[11] For South Africa to achieve elimination status, there needs to be an improved awareness on the national measles elimination goals, the importance of surveillance, appropriate specimen collection, proper individual case management and completeness of data provided on the CIF.

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MULTIDRUG-RESISTANT AND EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS IN SOUTH AFRICA FROM DATA EXTRACTED FROM THE NHLS CORPORATE DATA WAREHOUSE

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Patients with extensively drug-resistant tuberculosis (XDR-TB) constitute a subset of the multidrug-resistant tuberculosis (MDR-TB) group. Initially XDR-TB was defined as infection caused by *Mycobacterium tuberculosis* resistant not only to isoniazid and rifampicin but also to any 3 of the 6 classes of second-line agents (aminoglycosides, polypeptides, fluoroquinolones, thioamides, cycloserine, and para-aminosalicylic acid) approved for treatment of tuberculosis (TB).[1] Following the KwaZulu-Natal outbreak[2], XDR-TB has been defined by the World Health Organization Global Task Force on XDR-TB in 2006 as MDR-TB patients whose isolates are resistant to both isoniazid (INH) and rifampicin and in addition are resistant to one of the second-line injectable anti-tuberculosis drugs (amikacin, kanamycin or capreomycin), as well as to any of the fluoroquinolones used for the treatment of TB.[3] Prospective surveillance according to the directives of the World Health Organization/ International Union Against Tuberculosis and Lung Disease (WHO/IUATLD) Global Project on Anti-tuberculosis Drug Resistance Surveillance (GPDRS) is the recommended approach for reliable and comparable statistics on drug resistance in *M. tuberculosis* in countries world-wide. The last surveys conducted in South Africa by the South African Medical Research Council's Tuberculosis Epidemiology & Intervention Research Unit according to GPDRS criteria covered the period 2001-2002 and showed percentages of 0.9% to 2.6% primary MDR cases in the provinces of South Africa while the prevalence in re-treated cases was between 1.8% and 4.0%[4]. These seemingly low percentages of MDR-TB could be misleading unless interpreted in the context of the high TB incidence in South Africa driven by the HIV/AIDS epidemic. In terms of absolute numbers, South Africa has been estimated to have one of the highest MDR-TB burdens in the world[5,6].

Comprehensive computerized information captured on the NHLS laboratory information management system (DISA) from 8 provinces have been available on MDR-/XDR-TB for several years and are very useful for monitoring effectiveness of the National TB Control Programme (NTBCP) and establishing strategies for TB management. However, retrospective analysis of computerized data from TB-laboratories is fraught with problems, most importantly, the duplication of patients. Accurate retrieval of data from the Corporate Data Warehouse (CDW) is largely dependent on the initial data input into the DISA laboratory information system. Incomplete patient demographics, spelling mistakes and lack of indication of the stage of programme management on the specimen requisition form make it difficult to identify patient duplication and to distinguish new MDR-TB cases from re-treatment cases. This is further complicated by the frequency of submission of specimens from one patient. However, extensive and meticulous "cleaning" of data was performed in order to provide as reliable information as possible, including useful evidence of the magnitude of drug-resistant TB in South Africa. Data should also be sufficiently reliable to assist with the planning of TB control strategies by provincial and central government health authorities in the country.

Methodology of data retrieval

The DISA-based laboratory data are merged into a central CDW housing demographic data and specimen results from 8 provinces, with KwaZulu-Natal currently outstanding. The figures from KwaZulu-Natal were compiled from computerized data generated by the TB referral laboratory at the Inkosi Albert Lethuli Hospital, the

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only culture and drug susceptibility testing laboratory in that province. Data from this laboratory were transferred to the NHLS CDW. Data from the DISA system update the CDW on a daily basis. Transition from specimen specific to patient specific data is problematic and requires programming algorithms to identify unique patients taking into account incorrectly spelt names and conflicting demographic data. MDR- and XDR-TB data are subjected to additional refinement for patient-based reporting through a manual process to further eliminate duplications.

Results and discussion of present study

The numbers of MDR-TB and XDR-TB over the ~5-year period 2004 to 2nd October 2008 in the various provinces, as well as the mean annual incidence rates per 10000 for MDR-TB and XDR-TB cases per 100000 are given in the Table. Figure 1 features the total number of MDR-TB and XDR-TB cases over the ~5-year period, the projected numbers to cover the full 5-year period and the ratios of XDR-TB cases to MDR-TB cases expressed in percentages. Incidence rates of MDR-TB and XDR-TB cases for the various provinces during this period are given in Figure 2.

MDR-TB profiles

The numbers of MDR-TB cases over the ~5-year period retrieved from DISA totaled 24441 cases with a mean of 5176 p.a. and varied from 519 in Limpopo Province to 6265 in KwaZulu-Natal. The latter province, together with Western Cape, Eastern Cape, and Gauteng all registered well over 3500 cases during this period with estimated incidence rates of 27.5 per 100000 per annum for Western Cape and figures of 13.8, 13.2 and 9.0 per 100000 for KwaZulu-Natal, Eastern Cape and Gauteng respectively (see Table and Figure 1). Northern Province, Mpumalanga, Free State and North West Province recorded between 803 (Northern Province) and 1430 (Mpumalanga) new cases over this period, and their MDR-TB incidence rates were also very high: the Northern Cape figure of 20.2 per 100000 was second only to that of the Western Cape, while the incidence rates for the other 3 provinces were 10.3, 6.7, and 6.2 per 100000 respectively. Limpopo Province recorded 519 MDR-TB cases during this period with an annual incidence rate of 2.2 per 100000.

The DISA-derived incidence rates for the 9 provinces are illustrated in Figure 2. All provinces showed increases in MDR-TB during the survey period. In KwaZulu-Natal the numbers of documented new cases rocketed from 464 in 2004 to 2138 in 2006 and leveled to 2050 in 2007, dropping precipitously to 688 for 2008 up to 2nd October (the projected figure of new MDR-TB cases for the full year is 907). The corresponding incidence rates were 4.9, 22.7 and 21.9 per 100000 for 2004, 2005, 2006 and 2007, while the 2008 incidence was calculated at 9.6 per 100000. All the other provinces recorded marked increases during 2006 and 2007. Further increases were recorded in Eastern Cape, Mpumalanga, Free State and Limpopo in 2008, while in KwaZulu-Natal, Western Cape, Northern Cape, Gauteng and North West Province the figures steadied or dropped during 2008. It is not possible to know to what extent the rises during the period 2006-2008 are real or whether they reflect the intensified laboratory surveillance that followed the XDR-TB outbreak scare in the Tugela Ferry region in KwaZulu-Natal in 2005[2]. The marked rise in cases in KwaZulu-Natal during 2005, 2006 and 2007 may also, at least in part, be attributed to the extensive surveillance exercise which was instituted in this province during this period. Similarly, the differences in incidence rates between the provinces were undoubtedly influenced by the extent to which TB control programmes of the respective provinces utilized the services of TB-laboratories in their region.

Table: MDR- and XDR-TB cases in South Africa 2004-2008*

Province**	Population $X10^6$	MDR Cases	MDR Rates*** $X10^{-5}$		XDR Cases	XDR Rates $X10^{-6}$	Rank***
WC	4.5	5897	27.5	(1)	151	7.2	(4)
NC	0.84	803	20.2	(2)	30	8.1	(3)
KZN	9.4	6265	13.8	(3)	940	20.7	(1)
EC	6.4	3911	13.2	(4)	349	12.5	(2)
MP	3.1	1430	10.3	(5)	20	1.4	(8)
GP	8.8	3672	9.0	(6)	148	3.7	(5)
FSP	2.8	874	6.7	(7)	17	1.4	(7)
NWP	3.7	1070	6.2	(8)	50	2.9	(6)
LP	5.3	519	2.2	(9)	19	0.8	(9)
National	44.8	24441	11.6		1724	7.7	

* Numbers of cases and rates up to 2nd October 2008
* * WC – Western Cape, NC – Northern Cape, KZN – KwaZulu-Natal, EC –Eastern Cape, MP – Mpumalanga , GP – Gauteng Province, FSP – Free State Province, NWP – North West Province, LP – Limpopo Province
*** Ranks of MDR and XDR rates per province are given in brackets.

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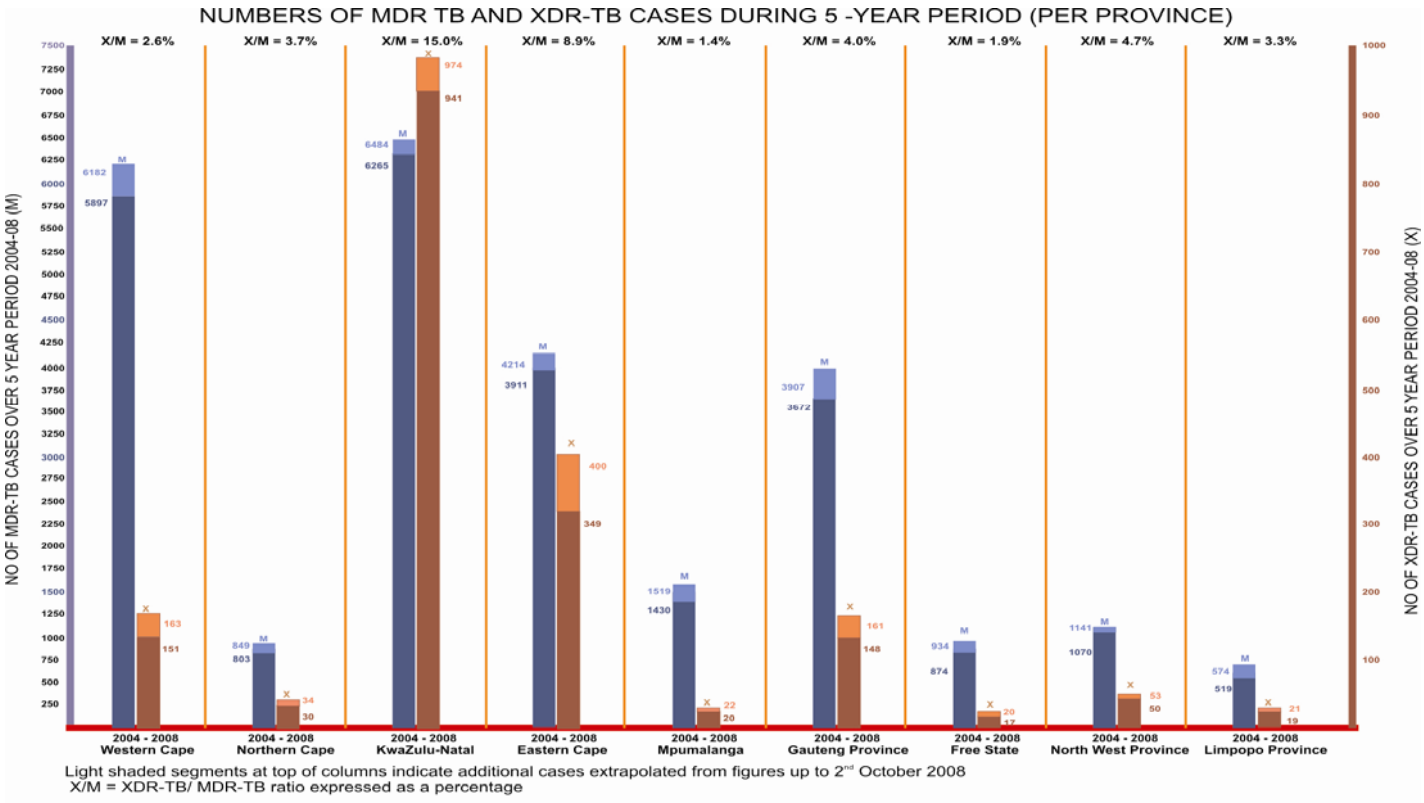

Figure 1: Numbers of MDR-TB and XDR-TB cases in South African provinces during 2004-2008.

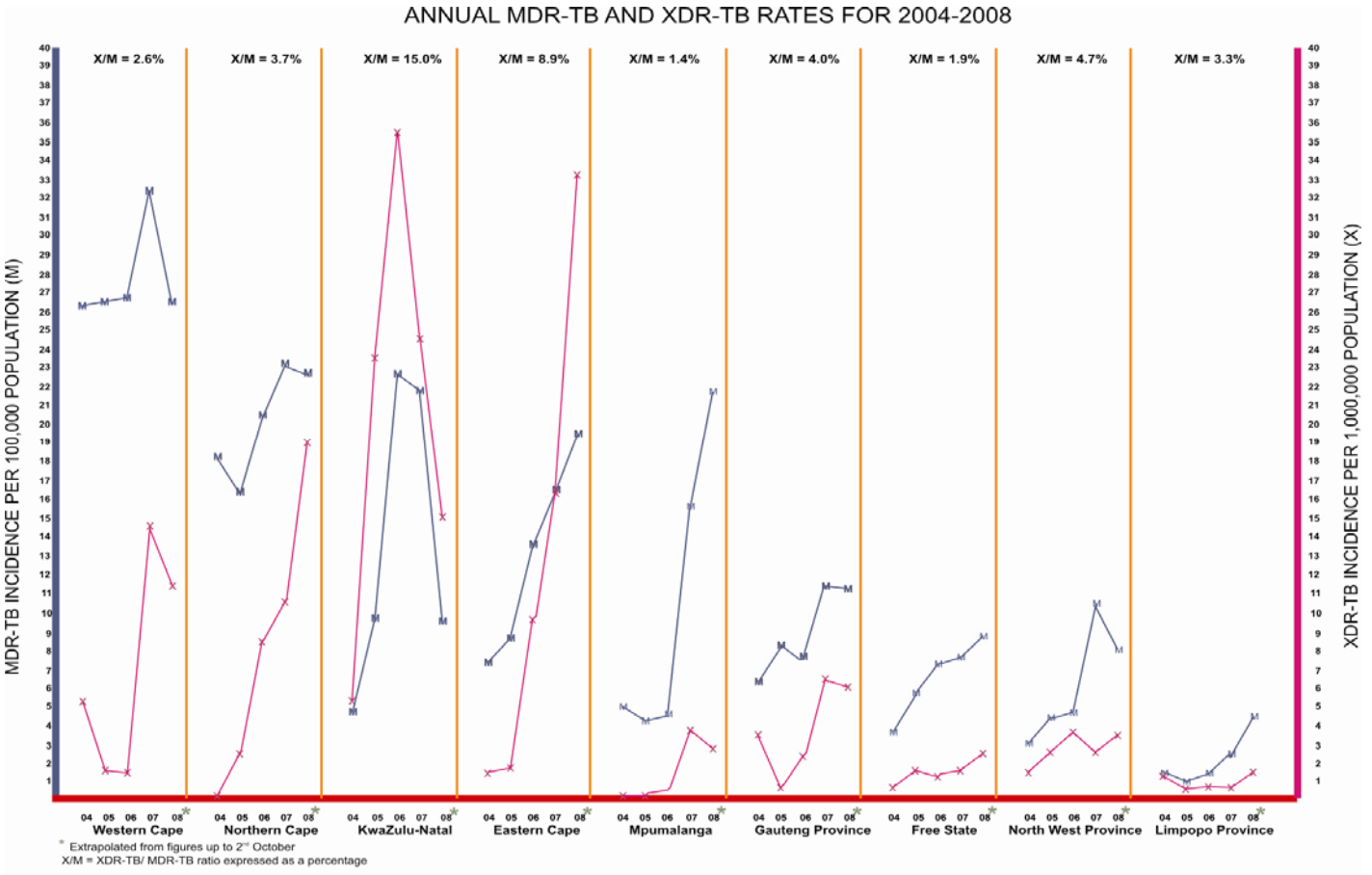

Figure 2: Annual incidence rates of MDR-TB and XDR-TB for the 9 provinces of South Africa

XDR-TB profiles

A total of 1724 XDR-TB cases was recorded during the survey period. The most striking feature of the laboratory-derived XDR-TB statistics is the escalation of XDR-TB cases in KwaZulu-Natal from 48 in 2004 to 221 in 2005, 333 in 2006 and 231 in 2007 dropping to 107 during the first 9 months of 2008 (the extrapolated figure for 2008 is 141 XDR-TB cases). These DISA-derived records coincide with the published findings of the Tugela Ferry outbreak in KwaZulu-Natal[2].The ratios of numbers of XDR-TB cases in relation to MDR-TB (X/Ms), expressed in percentages were 10.3% in 2004 compared to 24.1% in 2005 and are in accordance with the XDR-TB outbreak in that province in 2005. X/M ratios are affected mainly by failure of management of MDR-TB and DOTS-plus resulting in treatment failures and development of XDR-TB during treatment, as well as to increased transmission of XDR-TB due to deficient infection control. The high X/M ratios of 15.6%, 11.2% and 15.5% for the following 3 years suggest continued transmission of XDR-TB cases. The only other province with an X/M ratio of ≥5.0% for the ~ 5-year period is the Eastern Cape with a ratio of 8.9% (see Figure 1 and Figure 2). Apart from KwaZulu-Natal and Eastern Cape, sharp increases in XDR-TB cases were also recorded in the Western Cape, Gauteng, Northern Cape, and Mpumalanga. All these provinces demonstrated increases in X/M ratios (annual fluctuations of X/M ratios are not shown in Figure 2), while modest increases in the numbers of XDR-TB cases were registered in the Free State, North West Province and Limpopo (see Figure 2)

Despite the high prevalence of MDR-TB cases in the Western Cape (highest in the country), the XDR-TB rate is relatively lower than in other high TB prevalence provinces, ranking 4th after KwaZulu-Natal, Eastern Cape and Northern Cape (Table) and this is reflected by its relatively low X/M% ratio of 2.6% compared with other high prevalence provinces (see Figure 1).

Surprisingly, based on DISA-derived data, both the MDR-TB and XDR-TB rates of Gauteng (ranked 6th and 5th by province respectively) appear to be relatively low. However, compared with the Western Cape where, as is the case in Gauteng, comprehensive laboratory monitoring of MDR-TB treatment is practiced, the X/M ratio is 4.0% as opposed to 2.6% for the Western Cape, suggesting superior management of MDR-TB in the latter province. The validity of such a comparison is however, questionable.

The limitations accorded to MDR-TB statistics derived from DISA also apply to XDR-TB cases. The increasing trends shown here may have been influenced substantially by intensified surveillance since 2005, while the relatively low numbers in some provinces may be as a result of under utilization of laboratory services, including testing for susceptibility to second-line anti-TB agents which are essential for XDR-TB detection.

General Discussion

Drug resistance world-wide

TB drug resistance results from inadequate therapy, allowing for selection and growth of resistant organisms or by spread of resistant strains to close contacts leading to primary drug resistance. MDR-TB and XDR-TB are a growing public health problem world-wide, resulting largely from deficiencies in case and management programmes. XDR -TB has for many years been a recognised but poorly defined problem in South Africa. As early as 1997 an outbreak involving six patients infected with an MDR-TB strain resistant to isoniazid, rifampicin, ethambutol and pyrazinamide as well as ofloxacin and three other second-line drugs was reported at Sizwe Hospital for Tropical Diseases[7]. Highly resistant strains have also been reported from Asia, Europe and the Middle East [8-12]. In 2005, an outbreak of highly lethal XDR-TB in a rural area in KwaZulu-Natal, focussed attention on the problem of drug resistance in South Africa.[2] In this study, out of 1539 patients tested, of 554 TB culture-positive patients 221 were MDR-TB and of these 53 were extensively drug resistant. All patients with XDR-TB that were tested for serological evidence of HIV infection were co-infected with HIV. Most of the XDR patients were not previously treated and on genotyping, 85% of the isolates tested belonged to the same family, suggesting nosocomial transmission.

The data presented here indicate sharp increases in XDR-TB cases in all the provinces with the exception of North West Province (50 cases)), Limpopo (19 cases) and Free State (17 cases), where the numbers of XDR-TB cases detected in each of these provinces were fairly evenly distributed over 5 years. In Mpumalanga, 19 of the 20 cases from that province were detected during 2007 and 2008 and of the 30 cases from Northern Cape, 21 were diagnosed during these latter 2 years while the other provinces showed escalation of cases to 148 in Gauteng, 151 in Western Cape 349 in Eastern Cape and 940 in KwaZulu-Natal (Figure 2).

In a survey conducted by the Centers for Disease Control and Prevention and the World Health Organization, of 17690 isolates collected from 25 supranational TB reference laboratories between 2000 and 2004, 3520 (19.8%) were MDR-TB and 10% of the MDR-TB cases were XDR-TB (compared with 7.1 in South Africa). This survey showed that XDR-TB has a wide geographic distribution and is associated with worse outcomes.[13] In February 2008, the WHO indicated that XDR-TB had been found in 45 countries.[14]

Unfortunately drug resistance surveillance is limited by poor health infrastructure and a paucity of laboratory facilities capable of performing drug susceptibility testing (DST), thus many cases are likely to go unreported. In addition, existing tests for resistance to second-line drugs are not standardised and are less reproducible.

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HIV co-infection with MDR- and XDR-TB

The HIV epidemic has impacted severely on the burden of TB in Africa.[15-17] Populations with latent TB that acquire HIV infection are at increased risk of reactivation of TB. In addition, patients immunocompromised as a result of HIV infection are at high risk of developing active TB if exposed to new infections. These risks are exacerbated by the interaction of patients with active TB and HIV-infected patients in outpatient clinics, crowded hospital wards and the community as a whole.[16] The increased burden on the health systems may also lead to increased risk of treatment failure and development of resistant strains.[15]

MDR- and XDR-TB can cause devastating nosocomial outbreaks in HIV-infected populations as demonstrated in New York[18] in the 1990s and in 2005 in KwaZulu- Natal.[2] However, it remains unclear whether HIV infection represents an independent risk factor for the development of MDR-TB. Several studies show increased rates of drug-resistant TB among HIV-infected patients[19-21] while other studies fail to support the findings.[22-25] No significant difference in the prevalence of HIV infection in patients with drug-susceptible and new drug-resistant TB was reported in the 2001 South African national TB survey.[6]Andrews et al.[15] suggest that HIV-infected individuals may be disproportionately represented in the early stages of outbreaks as they are likely to manifest disease more quickly and recently circulating strains are more likely to be drug resistant. This may account for the higher rates of drug resistance found in smaller studies. Other factors, such as malabsorption of anti-tuberculosis drugs may also increase the risk of acquiring drug resistance in HIV-infected patients.[26,27] It is also possible that the specific genotype family of drug-resistant strains of *M. tuberculosis* may play a role in transmission of M/XDR-TB. Studies have suggested that the Bejing genotype family is more virulent and may be associated with anti-TB drug resistance in certain geographical settings.[28,29]

Diagnostic tests

Rapid diagnosis of TB and identification of drug resistance is critical to implement early treatment and reduce disease transmission. While some diagnostic tools have remained unchanged for decades, a number of exciting new technologies are being developed, including the line probe GenoType MTBDR *plus* assay (Hain Lifescience GmbH, Nehren, Germany) which has recently been evaluated in South Africa[30]. This PCR-based method which can detect the presence of *M. tuberculosis* as well as MDR-TB has now been recommended for use in developing countries by the World Health Organization and will be introduced into the national TB control programme in the near future.

The tuberculin skin test is still utilised in the diagnosis of latent TB and active TB in children. Recently detection of interferon-γ (INF-γ) in the blood following exposure to specific TB antigens[31] has been proposed as an alternative or adjunct for skin tests. INF-γ release assays detect both latent and active TB but cannot distinguish between the two. Lack of cross reactivity with BCG vaccine strains improves specificity of INF-γ-release assays (IGRAs). Research is needed to assess the value of these tests in high burden settings but in a Cape Town study, HIV infection did not appear to affect INF-γ substantially as measured by the T-Spot.TB test (Oxford Immunotec, Oxford, UK).[32]

Since Koch discovered the tuberculosis bacilli in 1882, TB microscopy has remained an essential component of TB diagnosis. Smear microscopy of sputum is rapid and cheap but sensitivity remains an issue particularly in sub-Saharan Africa with its burden of HIV/AIDS which affects the sensitivity smear microscopy. Fluorescence and iLED microscopy increases sensitivity but is limited by equipment costs.

Mycobacterial culture remains the gold standard for TB diagnosis from clinical specimens. *M. tuberculosis* replicates slowly and solid media cultures require 2-8 weeks incubation to generate visible colonies. This process can be accelerated by detecting immature colonies microscopically. Automated liquid culture methods e.g. the MGIT 960 system that detect bacterial oxygen consumption can halve time to detection, but are more costly and have a higher rate of contamination.

Drug susceptibility testing

In most developing countries, DST is performed on solid media causing delays of 8-18 weeks before results are available. DST performed in liquid culture media can reduce this delay to 1-3 weeks. The microscopic observation drug susceptibility assay for direct detection of *M. tuberculosis* drug resistance relies on microscopic observation of early *M. tuberculosis* colonies in liquid media with or without incorporated antibiotics within 1 week.[33] This method correlates well with standard methods for susceptibility to rifampicin, isoniazid, streptomycin and ethambutol. Performance is less good on sputum samples that are negative on smear microscopy.

Conclusion

The data presented here emphasise and put in perspective the extent and gravity of MDR-TB and XDR-TB in the various provinces and highlight the consequences of deficient DOTS-plus management. High XDR-TB: MDR-TB ratios strongly suggest increased transmission of XDR-TB in some provinces which may be linked to the HIV/AIDS epidemic. Under-utilization of laboratory monitoring, especially with regard to second-line anti-TB drugs by some provinces has undoubtedly resulted in missing XDR-TB cases. The magnitude of the drug resistance problem underscores the importance of improved infection control and treatment management of TB patients in this country.

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OUTBREAK OF ACUTE UPPER RESPIRATORY DISEASE IN MARYDALE, NORTHERN CAPE, JULY 2008

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Background

Influenza is a highly contagious, acute respiratory disease and can occur as pandemics (rare), annual epidemics, localised outbreaks and sporadic cases. Localised outbreaks are mostly described in institutionalised groups but are known to occur in geographically isolated towns.

On 18 July 2008, the Marydale clinic professional nurse reported an increase in the number of patients presenting with flu–like illness. An outbreak investigation was initiated to establish the existence and magnitude of the outbreak, identify the cause and make recommendations for management and control.

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Methods

The Communicable Disease Control (CDC) Unit of the Northern Cape Provincial Department of Health ensured sufficient supplies and personnel to manage the increased number of patients at the clinic. Resources were mobilised from the district and local authority. A line list of individuals meeting the suspected case definition (any person, presenting with a sore throat and fever, with or without cough, resident in Marydale during July 2008) was compiled. Five children were sent to the doctor in Prieska to assess the severity of illness and he diagnosed an acute, uncomplicated upper respiratory illness. A team consisting of members of the Northern Cape provincial and district Departments of Health (CDC, Environmental Health, Quality Assurance), the professional nurse and Community Health Workers from Marydale Clinic, the matron of Prieska Hospital and the SAFELTP investigated the outbreak.

Active case finding was instituted at neighbouring clinics and hospitals and all were contacted to establish if they had seen an increased number of case with acute respiratory illness. The available clinic data for 2007 and 2008 were reviewed to determine total number of patients and total cases of pneumonia seen per month. The Environmental Health Practitioner evaluated environmental conditions at the clinic, school and school hostel. The outbreak team was divided into four groups and cases were interviewed in four locations near the clinic. Two throat and/or nasal swabs, for viral and bacterial culture respectively, were collected from cases with onset of illness of ≤48 hours. One swab from each patient was put in Amies transport medium for microbiological investigation and the other in Viral Transport Medium (VTM) for detection of respiratory viruses. Specimens were submitted to the NHLS laboratory in Kimberly and the Respiratory Virus Unit at the NICD respectively.

Results

Marydale is a small, relatively isolated town in the Karoo District Municipality, Pixley ka Semme District. Nearby towns include Prieska, Kennard, Groblershoop and Upington. The climate is very dry with an average annual rainfall of 189mm. The economy is sustained mainly through livestock farming, mostly sheep and cattle. The total population in Marydale and the district is about 3 476 with an unemployment rate of 54%.

The outbreak started on 18 July and peaked on 20 July (Figure 1). The last case was reported on 2 August 2008. No increase in cases was seen in the surrounding clinics or Prieska hospital. There was no increase in the proportion of patients presenting with pneumonia. The clinic, school and hostel were not overcrowded and were well ventilated and clean. A total of 210 cases were reported that met the case definition (estimated prevalence = 6%, 210/3476). Of these cases, 69% (144/210) reported a sore throat and 14% (30/210) had fever (Table 1). Other reported symptoms included “myalgia, cough and a runny nose. Of 209 patients with available data on gender, 109 (52%) were female. Ages ranged from 4 months to 66 years with a median age of 9 years. Children aged 0-14 years were the most affected, with the highest number of cases, 68 (32%) in the 5-9 year age group. Of these 90 (43%) attended the primary school .

Twenty-eight specimens were tested immediately on receipt for the presence of influenza by real time PCR. Of these, 79% (22/28) were positive for influenza A and were further subtyped as H1N1 . The remaining six specimens

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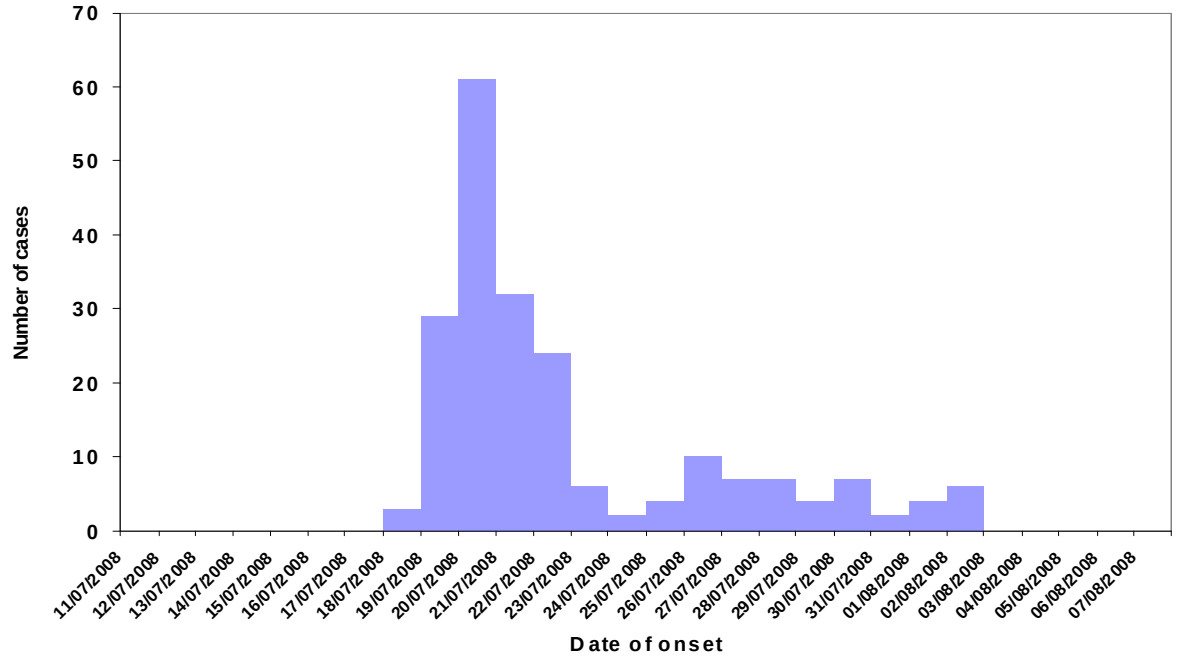

Figure 1: Epidemic curve of acute upper respiratory disease cases by date of onset, Marydale, Northern Cape, 18 July to 2 August 2008 (n= 208)

were subsequently shown to be positive for H1N1 by virus isolation. Three specimens were selected randomly and further characterized by sequencing to determine which strain was circulating in the community. The outbreak virus strains were identical to each other and were closely related to H1N1 viruses circulating in other parts of South Africa.9 Microbiological culture yielded no bacterial pathogens.

Table1: Frequency of signs and symptoms during the acute upper respiratory disease outbreak in Marydale, Northern Cape, July 2008 (n=210)

Signs and symptoms	Number of Patients	%
Sore throat	144	69
Fever	30	14
Cough	29	14
Headache	26	12

Table 2: Frequency of cases by sex and age group, during the acute upper respiratory disease outbreak in Marydale, Northern Cape, 2008

Characteristic	Number of Patients	%
Sex (n = 209)		
Male	100	48
Female	109	52
Age group (years) (n = 210)		
<1	6	3
1-4	48	23
5-9	68	32
10-14	42	20
15-19	9	4
20-24	9	4
25-29	4	1
30-34	1	1
35-39	19	9

Discussion

Seasonal influenza outbreaks are expected throughout South Africa during the winter period. Localised outbreaks of influenza in isolated communities are well described[4, 5]. This was the first of such influenza outbreaks that was detected and investigated in the Northern Cape Province. School children were the most affected group. The attack rate was lower than expected in such a community and could be due to many factors. These may include late recognition of the outbreak (an earlier peak of cases may have been missed), and incomplete case finding as surveillance activities were restricted to healthcare facilities and did not include household tracing. Illness was mild with no complications reported which is consistent with influenza A H1N1 infection.

Conclusion

Early detection and rapid response is the key to outbreak control. Seasonal outbreaks of influenza will continue to occur in South Africa and the impact of such outbreaks can be mitigated by the use of influenza vaccine for high risk groups, health education in schools and communities and early detection and management of complicated cases. Investigation of such outbreaks provides a valuable opportunity to better define the epidemiology of influenza in various geographical areas in SA and assists local outbreak response teams in building capacity for effective outbreak response .

Acknowledgements

Staff of Marydale Clinic, Karoo District Municipality, Pixley ka Semme District, Northern Cape Department of Health, Kimberley NHLS laboratory, NICD Epidemiology Division, Respiratory Virus Unit and Viral Diagnostic Unit.

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A DESCRIPTION OF HIV TESTING STRATEGIES AT 21 LABORATORIES IN SOUTH AFRICA

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Introduction

In 2003, a national laboratory-based surveillance network was established by the National Institute for Communicable Diseases (NICD), to provide surveillance information on 9 pathogens of public health importance in South Africa. GERMS-SA (Group for Enteric, Respiratory and Meningeal Disease Surveillance in South Africa) collected basic demographic information on patients diagnosed with the specific infections, at all health centers involved in the surveillance effort. At selected enhanced sites additional demographic and clinical data were collected on patients meeting the surveillance case definitions, to add background and context to the surveillance data obtained.

In the South African health milieu data on the HIV-serostatus of the patients is essential for interpretation of trends in disease burden and evaluation of risk factors for illness and poor outcome. The case-report form thus incorporated a comprehensive list of questions concerning the patients' HIV-serostatus, their willingness to have an HIV test, their reasons for refusal, and clinical markers of HIV as well as treatment received. These data have over the years proved useful in adding to the interpretation of surveillance data.

Ongoing evaluation of the surveillance programme however, revealed a few unanswered questions regarding laboratory HIV testing strategies across the country. Questions were asked regarding the tests used for adult patients and for children, the practice of confirmatory testing and the diagnostic devices used for such testing. The most important query surrounded the standardization of HIV testing practices in the different provinces, as GERMS-SA data was eventually combined into a single comprehensive dataset that was purported to be representative of the entire country.

South Africa has an HIV prevalence amongst its antenatal attendees of 29%, one of the highest HIV rates in the world.[1] Screening and diagnosis of HIV is traditionally done by testing for anti-HIV antibodies in suspected cases.[2] The common methods are using enzyme-linked immunosorbent assay (ELISA) peformed in a laboratory or as a rapid test or Western Blot tests. The Western Blot is more labour intensive, and therefore, ELISA's are more frequently used. A screening ELISA followed by a confirmatory ELISA using different test kits or one screening ELISA followed by a Western Blot test is required to label a result positive on the first specimen. In the case of an HIV positive result on a first specimen, a second specimen is recommended to confirm the identity of the first specimen and to confirm reactivity of the result.[2]

With the advent of Rapid HIV tests, the Department of Health has promoted the use of Voluntary Counseling and Testing Services to combat the HIV epidemic.[3] Central to this service is the use of Rapid HIV tests in adults, to ensure that patients receive their results at the same visit, in order to minimize loss to follow-up. Rapid HIV tests use ELISA technology and are defined as "those tests used outside the normal or existing laboratory infrastructure or those performed using a rapid ELISA device, not requiring an analyzer or routine test kit system".[2]. The use of rapid tests is advised by the Department of Health in the following circumstances:

1. Within the field setting e.g. Health Care Centres/Clinics
2. As part of surveillance or sero-prevalence studies
3. In clinical settings where urgent results are required for clinical decisions
4. In resource constrained conditions
5. As part of the HIV management approach and treatment procedures, that may include a second type of HIV Rapid test for confirmatory diagnostic purposes

If a Rapid HIV test is positive, it is recommended that a second confirmatory test be performed, either using another Rapid test kit or an ELISA performed in a laboratory.[4] In children less than 18 months, the test of choice for diagnosis of HIV is the HIV DNA PCR.[5] HIV-PCR is performed on a child if the mother is known to be HIV-infected or if the child's ELISA is positive suggesting exposure to HIV infection.

Methods

In order to determine the HIV testing strategies at various laboratories, we designed a telephonic survey. Laboratory managers at all enhanced site laboratories participating in the GERMS-SA surveillance programme were selected to participate. This yielded a sample of 23 laboratory managers. If a laboratory manager was not available, then the laboratory technician responsible for the HIV testing in that laboratory was determined to be an appropriate replacement. The staffing (numbers and skill levels) and resources of the laboratories in the sample varied. Eight laboratories were based in large academic hospitals and therefore had large staff compliments with different degrees of skill and access to greater resources. Other laboratories were situated in rural areas with a far smaller staff compliment and access to fewer resources.

A questionnaire was designed with 3 sections consisting of laboratory details, laboratory HIV testing practices for adults and laboratory HIV testing for children (defined as

(Continued on page 17)

individuals less than 18 months of age). The majority of the questions were close ended with respondents being given a choice of options. Among other questions, the respondents were asked what test was done on the first specimen sent to the laboratory for HIV testing, what test kit was used and whether a second confirmatory test was performed. Similar questions were asked for children, with HIV-PCR being added on as an additional response option.

Results

Over a period of one month in 2008, 21 of the 23 selected laboratories were contacted. We attempted to interview at least one laboratory in every province. However, we were unable to contact the selected laboratory in the North West Province.

Of the 21 laboratories surveyed, all except 3 laboratories in KwaZulu-Natal, performed on-site testing for HIV. For testing of specimens from adults, all laboratories performed a screening and then a confirmatory HIV test on the blood specimen received. For 16 of the 21 laboratories (76%), the screening and the confirmatory tests were standard ELISA's performed in a laboratory. Four laboratories used a rapid test as the screening test followed by a standard ELISA, while one laboratory used the rapid test as a confirmatory test with the standard ELISA for screening. The most common diagnostic devices used to process ELISA tests in the laboratory were the Abbott Axsym and the Roche Elecsys. The rapid test used was the Abbott Determine HIV 1, now distributed by Inverness.

For children less than 18 months of age, the HIV test performed depended in most cases, on the request by the treating physician. Commonly, the screening test used was reported to be the standard ELISA, and if positive, an HIV-PCR was then done for confirmation. HIV-PCR tests were generally processed at large academic hospital laboratories, using the Roche Amplicor. Five laboratories used rapid HIV tests for either screening or confirmation of HIV infection in children less than 18 months of age.

Discussion

In South Africa, with its high prevalence of HIV, a culture of Voluntary Counseling and Testing (implying the use of rapid testing) has been encouraged. This ensures that patients receive their test results immediately without the need for return visits, where many patients are lost to follow-up. As a result, laboratories in South Africa receive far fewer specimens to process than in previous years where all HIV testing was done by the laboratories. Only discordant specimens, where results of the rapid tests are inconclusive, as well as some inpatient specimens are sent to the laboratories for HIV testing.

This survey has shown that for laboratory testing of HIV in adults, an ELISA-based algorithm was generally used with a second confirmatory test performed on the same specimen if the screening test was positive. The investigator could not determine if two separate specimens were sent by clinicians for HIV testing, as the respondents interviewed were laboratory technologists, and as such, would have been the inappropriate study population for such a question. Nevertheless, HIV testing for adults in South Africa was in line with international recommendations. The World Health Organisation advocates the use of serial HIV testing if an ELISA-based algorithm is being used. This implies that if the screening test is HIV sero-positive, the specimen should be tested with a second test that uses a different antigen from the first. A second positive test is considered to be a true positive result in populations with a prevalence of HIV of 5% or more.[6]

HIV testing amongst children less than 18 months was, appropriately, dependent on the treating clinician's request. Many laboratories were unable to perform HIV-PCR on-site, and specimens were sent to tertiary care facilities, sometimes in other provinces, for analysis. However, the referral pathways for HIV-PCR testing are well established and this should not pose obstacles to HIV diagnosis in babies in South Africa.

In summary, for adult HIV testing, there was considerable uniformity regarding HIV testing strategies. For the paediatric population, the choice of a screening test is more complex with such factors as clinical features and lack of knowledge of maternal HIV status compounding the issue. Data are inconclusive as to the utility of rapid testing in the paediatric population. The fact that several laboratories routinely use rapid tests in this population requires further investigation, which is beyond the scope of this survey.[7]

This study was limited by the fact that it was a telephonic survey with a small number of laboratories included, although the sample did include laboratories at large academic hospitals as well as smaller laboratories in rural settings. In addition, only enhanced site laboratories were surveyed and their participation in the GERMS-SA surveillance, which entails regular supervisory visits of these laboratories, may have biased the findings.

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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 September 2007/2008*

Disease/Organism	Cumulative to 30 June, year	EC	FS	GA	KZ	LP	MP	NC	NW	WC	South Africa
Anthrax	2007	0	0	0	0	0	0	0	0	0	0
	2008	0	0	0	0	0	0	0	0	0	0
Botulism	2007	0	0	0	0	0	0	0	0	0	0
	2008	0	0	0	0	0	0	0	0	0	0
Cryptococcus spp.	2007	989	523	1986	1246	464	734	58	577	415	6992
	2008	1054	439	1387	1110	288	496	36	560	486	5856
Haemophilus influenzae, invasive disease, all serotypes	2007	23	21	156	51	3	16	1	4	52	327
	2008	23	22	130	30	3	19	4	5	66	302
Haemophilus influenzae, invasive disease, < 5 years											
Serotype b	2007	1	2	20	10	0	2	0	2	12	49
	2008	5	7	18	5	1	3	2	2	10	53
Serotypes a,c,d,f	2007	1	1	13	2	0	0	0	0	5	22
	2008	1	1	11	0	0	1	0	0	5	19
Non-typeable (unencapsulated)	2007	0	1	27	7	0	1	0	0	3	39
	2008	2	3	14	1	0	1	0	0	8	29
No isolate available for serotyping	2007	11	5	36	12	2	5	1	0	15	87
	2008	10	1	33	6	1	7	0	2	13	73
Measles	2007	5	1	7	1	1	5	0	1	1	22
	2008	4	1	7	3	1	1	2	4	3	26
Neisseria meningitidis, invasive disease	2007	12	26	178	20	7	17	7	27	57	351
	2008	20	18	177	25	4	30	8	12	57	351
Novel Influenza A virus infections	2007	0	0	0	0	0	0	0	0	0	0
	2008	0	0	0	0	0	0	0	0	0	0
Plague	2007	0	0	0	0	0	0	0	0	0	0
	2008	0	0	0	0	0	0	0	0	0	0
Rabies	2007	4	0	0	4	1	0	0	0	0	9
	2008	7	0	0	5	3	0	0	0	0	15
**Rubella	2007	134	10	62	147	64	35	21	29	69	571
	2008	258	3	134	244	103	118	8	62	22	952
Salmonella spp. (not typhi), invasive disease	2007	29	33	286	72	11	14	2	19	48	514
	2008	44	23	353	77	5	31	12	12	51	608
Salmonella spp. (not typhi), isolate from non-sterile site	2007	108	22	172	90	22	73	8	19	57	571
	2008	140	25	279	124	14	73	8	15	98	776
Salmonella typhi	2007	9	1	10	7	2	8	0	2	5	44
	2008	9	1	17	9	2	17	0	0	8	63
Shigella dysenteriae 1	2007	0	1	0	0	0	0	0	0	0	1
	2008	0	0	0	0	0	0	0	0	0	0
Shigella spp. (Non Sd1)	2007	99	48	239	99	13	32	27	12	225	794
	2008	119	48	343	89	8	39	18	8	293	965
Streptococcus pneumoniae, invasive disease, all ages	2007	254	248	1758	425	116	225	44	161	427	3658
	2008	233	204	1680	424	78	171	56	133	412	3391
Streptococcus pneumoniae, invasive disease, < 5 years	2007	94	82	476	161	31	58	17	34	168	1121
	2008	72	73	475	142	15	53	21	24	148	1023
Vibrio cholerae O1	2007	0	0	0	0	0	0	0	0	0	0
	2008	0	0	2	0	0	32	0	0	0	34
Viral Haemorrhagic Fever (VHF)											
Crimean Congo Haemorrhagic Fever (CCHF)	2007	0	0	0	0	0	0	0	0	0	0
	2008	1	2	0	0	0	1	2	0	0	6
Other VHF (not CCHF)***	2007	0	0	0	0	0	0	0	0	0	0
	2008	0	0	4	0	10	4	0	0	0	18

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

***For 2008 all cases 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 September 2007/2008*

Programme and Indicator	Cumulative to 30 Sept, 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	2007	33	22	47	33	36	19	8	14	21	233
	2008	45	15	48	45	43	32	4	10	30	272
Laboratory Programme for the Comprehensive Care, Treatment and Management Programme for HIV and AIDS											
CD4 count tests											
Total CD4 count tests submitted	2007	157707	64866	298690	349898	85236	96275	58200	80348	107446	1298666
	2008	216199	90389	398140	592883	141196	130771	76022	104807	136294	1886701
Tests with CD4 count < 200/µl	2007	59111	25600	116316	120302	37886	35603	18629	28035	26895	468377
	2008	82926	31656	152103	165422	50814	48693	24860	34359	39476	630309
Viral load tests											
Total viral load tests submitted	2007	61093	24096	118185	156621	30804	28544	21602	30028	34575	505548
	2008	91323	39190	180367	206377	61467	46192	31477	42811	45346	744550
Tests with undetectable viral load	2007	24784	12483	64194	73308	14934	14269	12067	16235	27692	259966
	2008	44962	22940	107002	118207	35721	25108	19199	26123	36523	435785
Diagnostic HIV-1 PCR tests											
Total diagnostic HIV-1 PCR tests submitted	2007	12080	3827	28868	29501	5808	5114	4248	5493	10591	105530
	2008	18123	7323	39034	47162	11153	7545	2320	10534	12551	155745
Diagnostic HIV-1 PCR tests positive for HIV	2007	2249	983	5496	6135	1348	1304	809	1258	1164	20746
	2008	2374	1325	5649	7711	2033	1511	332	1818	1180	23933

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.
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

The Communicable Diseases Surveillance Bulletin is published by the National Institute for Communicable Diseases (NICD) of the National Health Laboratory Services (NHLS), Private Bag X4, Sandringham, 2131, Johannesburg, South Africa.

Suggested citation: [Authors' names or National Institute for Communicable Diseases (if no author)]. [Article title]. Communicable Diseases Surveillance Bulletin 2008; 6 (3): [page numbers]. Available from http://www.nicd.ac.za/ pubs/ survbull/2008/ CommDisBullAug08.pdf