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FOREWORD

Resistance to the antimicrobial rifampicin is a key marker for multidrug-resistant tuberculosis (MDR-TB) and is an emerging concern. The increasing incidences of MDR-TB and alternative therapy possibilities are discussed in this issue, which also includes details of laboratory confirmed human rabies in South Africa for the period 2012-2013. Cases of rabies occur annually in South Africa despite the availability of effective control and prevention measures.

Surveillance reports for this issue include the four influenza surveillance programmes that are co-ordinated by the NICD. Data on milder influenza-like illness (ILI) and severe acute respiratory (SARI) illness, collated for 2013, show that the 2013 influenza season was initially dominated by circulation of influenza A(H1N1)pdm09 followed by A(H3N2) in the latter part of the season. The surveillance data also show that the 2013 season was unusually protracted. Antimicrobial resistance surveillance is also conducted at the NICD, and aims to determine the extent of resistance amongst the most important disease causing pathogens in South Africa. Data presented in this issue show the extent of antimicrobial resistance by pathogen for 2012.

All contributors are thanked for their inputs, and I trust you will find these reports useful and interesting.

Basil Brooke, Editor

CONTENTS

DEVELOPMENT OF RESISTANCE TO RIFAMPICIN AND OTHER RIFAMYCINS IN MYCOBACTERIUM TUBERCULOSIS AND THE EXTENT OF CROSS-RESISTANCE BETWEEN THESE ANTIMICROBIALS

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Introduction

The rifamycin class of antimicrobial agents was discovered in *Streptomyces mediterranei* (now *Nocardia mediterranei*) in 1957.[1] Rifampicin, first evaluated during clinical trials in 1967[1], is used globally for the treatment of tuberculosis. Together with isoniazid, rifampicin is the cornerstone of combination treatment for drug-susceptible tuberculosis. It is also used in combination

with dapsone for the treatment of paucibacillary leprosy, and these two drugs plus clofazimine are used to treat multibacillary leprosy.[2] Rifampicin combined with doxycycline is recommended by WHO for the treatment of brucellosis while rifampicin combined with either ofloxacin or doxycycline has also been shown to be effective for the treatment of brucellosis with the caveat that fluoroquinolone should not be used on its own.[3] Rifampicin also shows good anti-staphylococcal activity and has been used in combination with an aminoglycoside and/or vancomycin for the treatment of *Staphylococcus epidermidis* endocarditis involving prosthetic valves.[4] Experimental infections in animal models of *S. epidermidis* endocarditis showed that the combination of rifampicin and a fluoroquinolone was superior to treatment with vancomycin alone.[5] Other rifamycins available for clinical use or evaluated in clinical trials are rifabutin, rifapentine and rifalazil.

Mode of action of rifamycins

Rifampicin binds to the β-subunit of the DNA-dependent RNA polymerase enzyme encoded by the *rpoB* gene and in the process inhibits transcription and therefore protein synthesis in rifampicin susceptible organisms.

Genetic basis of resistance to rifamycins

The genetic basis of resistance to rifampicin and other rifamycins in *Mycobacterium tuberculosis,* the causative agent of tuberculosis, involves alterations (insertion, deletion or missense mutations) in the 81-bp rifampicin resistance determining region (RRDR), located in the central part of the *rpoB* gene.[6-10]

Cross-resistance involving rifamycins

Various degrees of rifamycin cross-resistance involving rifampicin, rifabutin, rifapentine or rifalazil (KRM- 1648) can occur.[10,11] Single nucleotide mutations involving codons 531 and 513 confer resistance to all four rifamycins, while mutations in codon 516 are associated with resistance to rifampicin and rifapentine only, leaving susceptibility to rifabutin and rifalazil intact.[6,12] In Australia, low frequency *rpoB* mutations at codon 522 encode resistance to rifampicin but do not appear to affect susceptibility to rifabutin.[13] Mutations in codon 526 confer resistance to rifampicin and rifapentine alone (glutamic acid or leucine substitutions) or to all four rifamycins (tyrosine substitution).[12]

Mutations encoding different levels of rifamycin resistance

Missense mutations in codons 516, 526 (some mutations) or 531 result in high-level rifampicin resistance and mutations at position 514, 517, 521, 526 (some mutations), or 533 are associated with low-level resistance.[6,11-13]

Global extent of rifampicin resistance in *Mycobacterium tuberculosis*

Rifampicin resistance is a key marker of multidrug-resistant (MDR) – tuberculosis and is an emerging concern. Based on reports from countries world-wide, WHO estimated that 83,715 patients were diagnosed globally with MDR-tuberculosis in 2012.[14] This is likely an under-estimate as drug susceptibility testing is not universally applied, especially in the developing world and true estimates are likely above 300,000. In South Africa, a total of 13,915 new MDR cases were diagnosed in 2012. This is slightly higher than the 13,762 new MDR cases reported in 2011.

Discussion

Amongst the armamentarium of drugs used in the treatment of chronic infections, the advent of rifamycins has changed the landscape of antimicrobial therapy, most notably rifampicin for the treatment of tuberculosis and leprosy and, to a lesser extent, rifabutin for the treatment and prophylaxis of *Mycobacterium avium* complex infections in patients with AIDS. However, due

to the increasing incidence of resistance to rifampicin coupled with resistance to isoniazid, leading to multi-drug resistant tuberculosis (MDR-TB), emphasis has shifted towards alternative tuberculosis therapies. Amongst these, at least theoretically following clinical validation, could be drug regimens containing rifabutin or rifalazil for infections caused by strains harbouring *M. tuberculosis* isolates with mutations in codons 516 or 522, as well as some strains with codon 526 mutations in the *rpoB* gene.

Rifampicin is consistently integrated into phenotypic drug susceptibility panels, but other rifamycins are not. Therefore, considerations could be given to the use of *M. tuberculosis* genetic profiles to predict cross-resistance patterns so as to enable the treatment of tuberculosis caused by some rifampicin-resistant strains, including some mono-resistant cases, which carry mutations associated with susceptibility to rifabutin and rifalazil, e.g. isolates with codon 516 or 522 mutations. Treatment with rifabutin has an additional benefit of fewer drug interactions in patients receiving protease inhibitors as part of anti-retroviral therapy. Furthermore, the performance of minimum inhibitory concentration (MIC) testing of strains could aid the interpretation of the genotypic findings for patient management.

Conclusion

Many unanswered questions remain with regard to the use of rifamycins for the effective treatment of resistant strains of tuberculosis. However, the use of phenotypic and genotypic methods to demonstrate levels of resistance and cross-resistance can optimize and prolong their usage.

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HUMAN RABIES IN SOUTH AFRICA, 2012-2013

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Introduction

Rabies is a zoonosis causing fatal encephalitis. The disease is caused by the rabies virus and other so-called rabies-like viruses belonging to the genus *Lyssavirus*. From a public health perspective, the rabies virus is the most important and causes an estimated 55 000 human cases in developing countries annually.

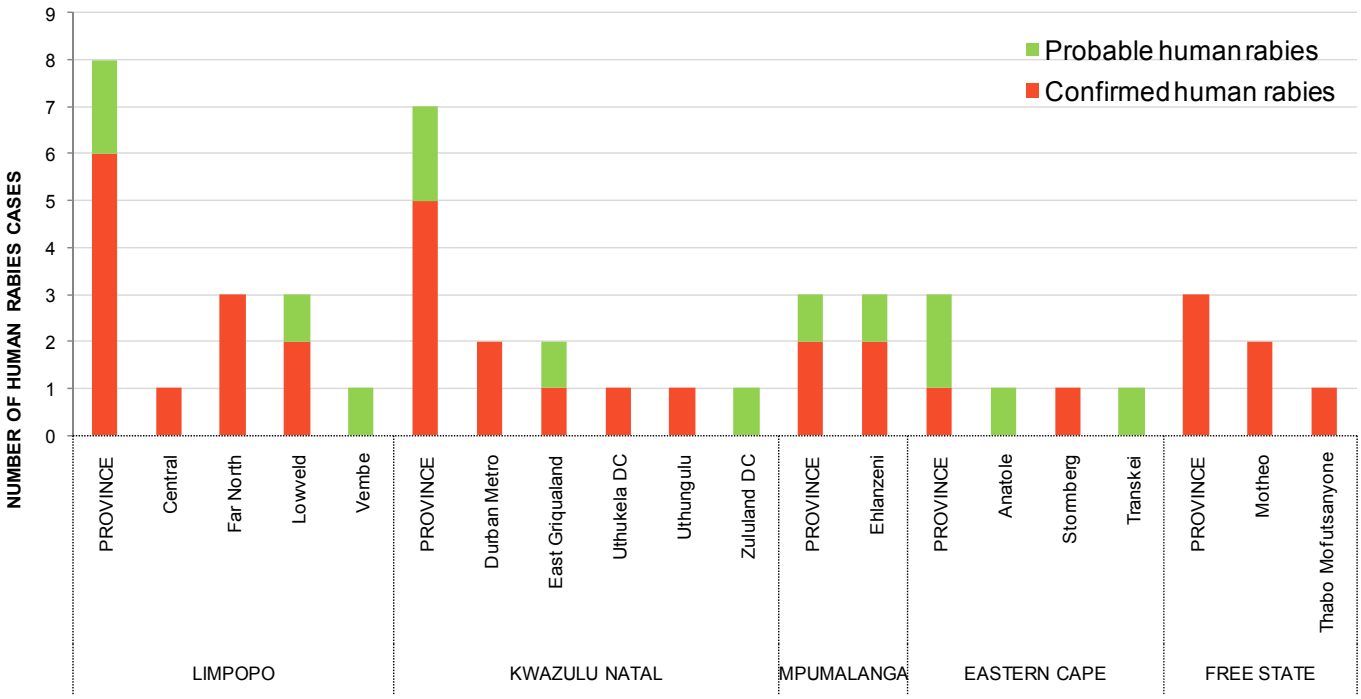
Rabies cases occur widely in Africa, including South Africa, mostly as a result of inadequate control of rabies in domestic dogs. In South Africa, the rabies virus is maintained in complex epizootic cycles involving domestic dogs, black-backed jackals, bat-eared foxes and several species of herpestids (i.e. mongoose and suricates).[1] In South Africa, 85% of laboratory confirmed human cases have been associated with domestic dogs while the remainder are likely the result of exposure to game animals.[2] Historically, the majority of human rabies cases in South Africa have been reported from the KwaZulu-Natal and Eastern Cape provinces but, more recently, an increasing number of cases have been reported from Limpopo Province. In the past decade, rabies has been described from locations where it was previously controlled. This includes the Vhembe district of the Limpopo Province[3] and southern and eastern-southern Mpumalanga.[4] The first report of local transmission of rabies virus in Johannesburg, Gauteng Province, was reported in 2010.[5]

Laboratory confirmed human cases

The National Institute for Communicable Diseases (NICD) has been involved in the laboratory investigation of human rabies cases in South Africa since 1983. From this time to date, a total of 420 human rabies cases has been laboratory confirmed. Of these, 137 have been reported in the past ten years (2003-2013) with an average of 12.45 cases per year (range: 6-31 cases per year). Two thirds of these cases (n=104) were male with an average age of 17.6 (range 1-80). The majority of cases were of the younger age group with 46% aged below 9 years. Cases were reported from the KwaZulu-Natal (n=52), Limpopo (n=39), Eastern Cape (n =32), Mpumalanga (n=6), Free State (n=4), North West (n=2), Northern Cape (n=1) and Gauteng (n=1) provinces.

During 2012 and 2013 a total of 17 cases was recorded. These were reported from the Limpopo (n=6), KwaZulu-Natal (n=5), Free State (n=3), Mpumalanga (n=2) and Eastern Cape (n=1) provinces (figure 1, table 1). A history of dog exposure was described in fourteen of these cases (82.35%).

The NICD has the capacity for ante-mortem and post-mortem investigations of suspected human rabies cases. During 2012-2013, 14 of 17 confirmed cases were tested by the direct fluorescent antibody test on brain impression smears. This test remains the gold standard for laboratory diagnosis of rabies.



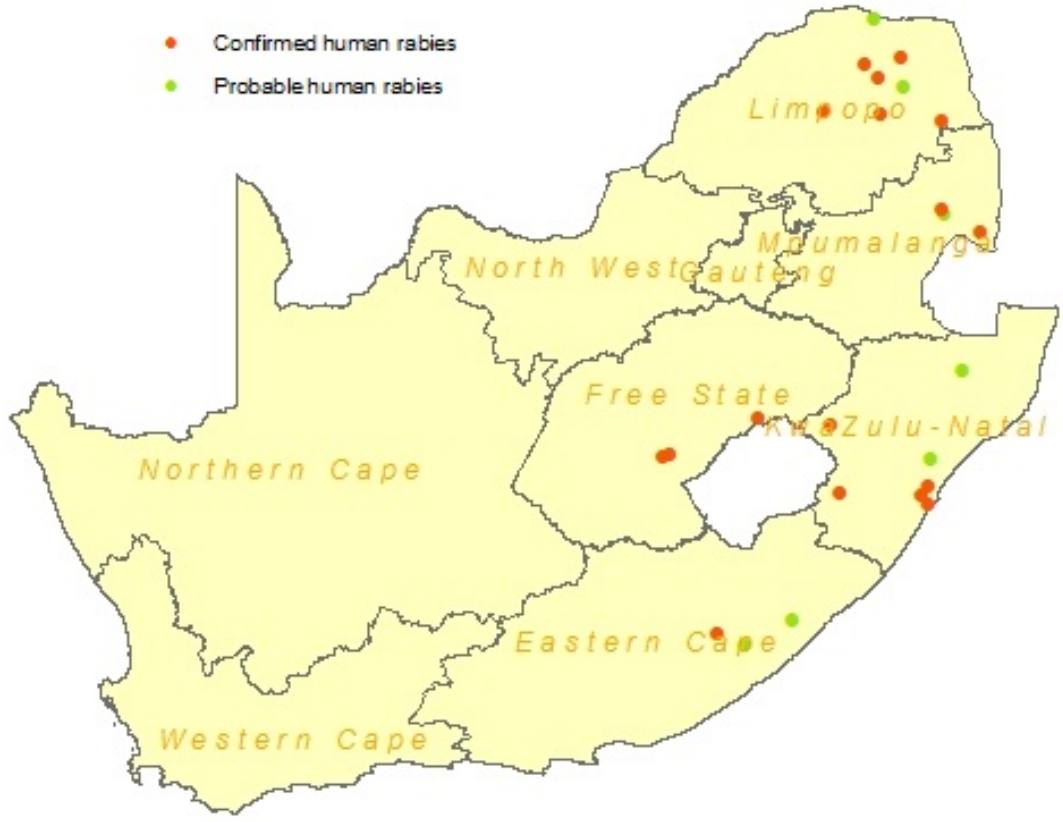


Figure 1: Distribution of laboratory confirmed and clinically diagnosed human rabies cases by province and district in South Africa, 2012-2013.

Table 1: Case details of laboratory confirmed human rabies in South Africa, 2012-2013.

Year	Age/ Sex*	Location residence/ exposure	Source of exposure	Category of exposure	Post exposure intervention	Symptoms
2012	2M	Chebeng, Limpopo	Dog	Below the eye category 3	4 doses rabies vaccine, no rabies immunoglobulin	Fever, confusion, loss of ability to walk
2012	17F	Thohoyandou, Limpopo	Unknown	Unknown	Unknown	Fever, confusion, developed left hemi-paresis
2012	29M	Underberg, KwaZulu-Natal	Dog	Unknown	None	Migratory pain up arm into head, hydrophobia, breathing difficulty, dysphasia, delirium, confusion, agitation, photophobia
2012	52F	Engonyameni, near Umlazi, Kwazulu-Natal	Dog	Bite on right arm category 3	None	Itchiness and pains on the site of the healed wound bite, hydrophobia, hypersalivation, confusion, weakness, vomiting, brain scan showed encephalitis
2012	7M	Bergville, Okhahlamba, Kwa-Zulu-Natal	Dog	Single bite on fore-arm, category 3	None	Malaise, loss of energy, confusion, vomiting, fever
2012	8M	Nkomazi, Mpumalanga	Dog	Unknown	None	Unknown
2012	10M	Mukulamu, kondeni, Nukula, Limpopo	Unknown	Unknown	None	Six days history of fever, confusion, inability to walk or sit
2012	21M	Tshelimnyama, Mariannhill, KwaZulu-Natal	Dog	Palm of left hand category 3	One dose rabies vaccine, no rabies immunoglobulin, wound treatment	Nausea, headache, pain to left shoulder and arms, palpitations, difficulty in swallowing and hydrophobia
2012	10M	Fouriesburg, Free State	Dog	Two bites on face/ nose and arm category 3	Referred for suturing , tetanus vaccination, no rabies post exposure prophylaxis	Difficulty in swallowing, could not swallow water
2012	7M	Ncoaha A/A, Ematheleni Village, Cofimvaba, Eastern Cape	Dog	Wound on left hip category 3	One dose of rabies vaccine, no immunoglobulin	Fever, headache, vomiting, muscle spasm, anorexia, priapism, localised weakness, confusion, agitation, autonomic instability, malaise, anxiety, dysphasia, delirium, aggressiveness, hypersalivation
2013	6M	Malukazi, southern border of Umlazi, KwaZulu-Natal	Dog	Wound right hand, buttock and left wrist, multiple bites category 3	4 doses rabies vaccine, no immunoglobulin	Fever, headache, muscle spasm, coughing, vomiting, malaise, nausea, dysphasia, anorexia, developed pain in the back of her left leg and in her arm, confusion, anxiety and impaired communication
2013	65M	Mvangatini, Kabokweni, Mpumalanga	Dog	Wound index finger, right hand single bite category 3	One dose of rabies vaccine, no immunoglobulin	Headache and pain in hand that sustained wound, aero-and hydrophobia, hypersalivation, confusion, instability and anxiety
2013	21M	Thaba-Nchu, Mangaung, Free State	Dog	Wound, category 3, undescribed	Wound treatment only, no rabies post exposure prophylaxis	Difficulty in swallowing own saliva and water, hydrophobia, increased temperature, confusion, agitation
2013	9F	Elim, Makhado, Limpopo	Unknown	Unknown	None	Neurological syndrome, hyperactivity, coma
2013	5M	Botshabelo, Free State	Dog	Superficial wounds/scratches category 2	Unknown	Confusion, hypersalivation
2013	38M	Mopani, Elim, Limpopo	Dog	Single bite on calf of leg, category 3	None	Fever, muscle spasm, insomnia, anxiety, seizures, hydrophobia, hypersalivation, clenching teeth, WBC normal
2013	38M	Tzaneen, Limpopo	Dog	Undescribed, category 3	None	Severe headache 3 days, painful joints, dizziness, confusion, restlessness, pyrexia, hydrophobia 2 days

*Age is given in years; M=male; F=female

Intervention failure in confirmed human rabies cases

Nearly half of the laboratory confirmed human rabies cases apparently did not seek any medical intervention after exposure to rabid animals (figure 2). This reflects the general lack of awareness of the public of the importance of seeking post-exposure prophylaxis upon contact with suspect animals, especially dogs. It must also be taken in consideration that the majority of confirmed rabies cases are from rural areas and that access to medical care may be problematic. In two cases, the patients presented to health care facilities but were provided only with wound treatment reflecting the lack of awareness of the healthcare workers.

Another important contributing factor to failure in prevention of rabies virus infection was the non-provision of rabies immunoglobulin (RIG) in category 3 exposures. This is a known and well document reason for so-called rabies post exposure prophylaxis failures.[6]

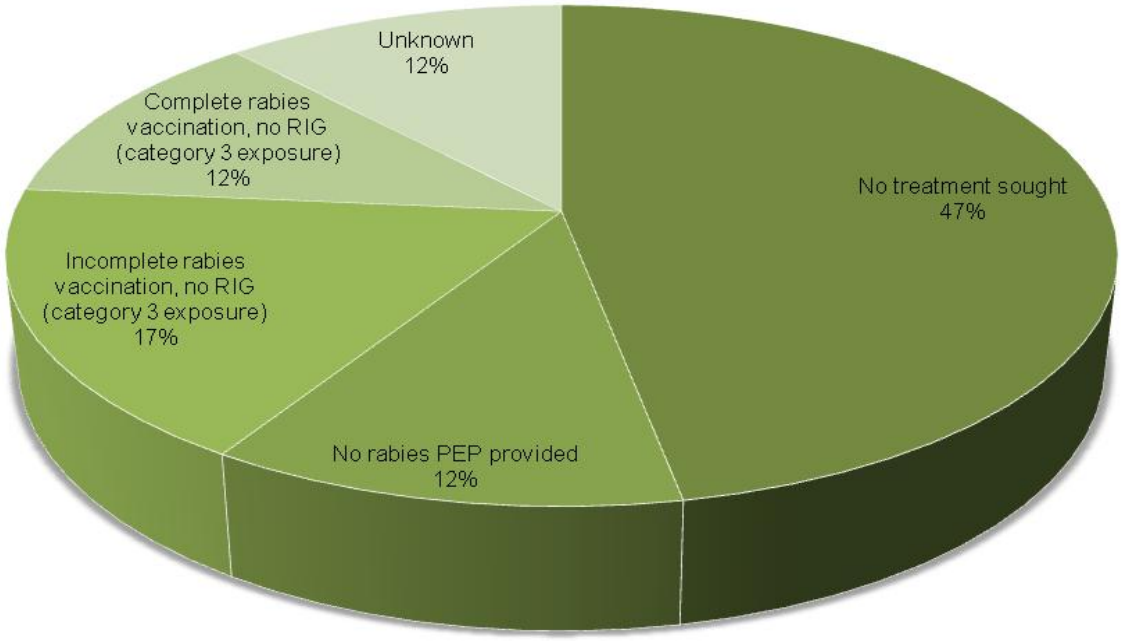


Figure 2: Interventions for rabies prevention in laboratory confirmed human rabies cases, South Africa, 2012-2013

Clinically diagnosed human cases

During 2012 and 2013, a total of seven cases of rabies with clinical diagnosis was recorded. These originated from the Limpopo (n=2), Eastern Cape (n=2), KwaZulu-Natal (n=2) and Mpumalanga (n=1) provinces (table 2). Five of these cases are classified as probable cases as defined by the World Health Organization.[7] The case histories included animal exposure and the clinical progressions and outcomes were compatible with rabies disease. These cases could not be verified by laboratory testing for various reasons: in two cases extensive ante-mortem investigation yielded only negative results and no specimens were available post-mortem for confirmation; all testing, including direct fluorescent antibody performed on post-mortem collected brain tissue, was negative for one case; no tissue samples were submitted for investigation for one of the cases from the Limpopo Province.

Various factors contribute to the failure of laboratory confirmation of cases. Although ante-mortem testing is useful, the direct fluorescent antibody test performed on brain biopsies remains the gold standard for rabies laboratory diagnosis. However, obtaining brain tissue post-mortem from patients that died of suspected rabies disease can be problematic due to cultural and religious beliefs and consent is often denied. Ante-mortem investigations should be based on comprehensive testing of repeat saliva specimens, nuchal biopsies, cerebrospinal fluid and serum. The latter are used for the detection of rabies antibodies which may indicate seroconversion in unvaccinated individuals, whilst the other specimens are screened for the presence of viral RNA. The quality of the specimens and vaccination history of each patient are some of the factors that may influence test outcomes. Negative test results on ante-mortem collected specimens do not exclude a diagnosis of rabies.

Table 2: Case details of clinically diagnosed cases of human rabies, South Africa, 2012-2013.

Year	Age/ Sex*	Location residence/ exposure	Source of exposure	Category of exposure	Post exposure intervention	Symptoms	Out-come	Laboratory investigations for rabies	Classifi-cation[i]
2012	16M	Tafalofefe, Eastern Cape	Dog	A bite on left calf, category 3	3 doses rabies vaccine, no rabies immunoglobulin	Fever, headaches, inability to walk or talk, confusion, coma within a week	Death	saliva & CSF - by PCR, CSF + IgG/M IFA, ante-mortem skin biopsy, saliva - by PCR, no post-mortem	Probable
2012	4M	Ngonyami school, Umlazi, KwaZulu-Natal	Dog	Multiple bites left lower ankle, category 3	3 doses rabies vaccine, no rabies immunoglobulin	Confusion, talking by himself, loss of appetite, incontinence and suffering, seizure, neck stiffness, hyper salivation and unresponsiveness.	Alive	5 x saliva, nuchal biopsy – by IFA	Probable
2013	2M	Botshabelo, Limpopo	Dog	Unknown	1 dose rabies vaccine, no rabies immunoglobulin	Biting infusion line, refusal to eat, talking to himself, unable to walk, weakness, aggres-sion, diarrhoea, meningitis-like illness	Death	No specimens submitted	Probable
2013	7M	Ncwasa, Mqwanduli, Eastern Cape	Unknown	Unknown	Unknown	Refusal of food despite appe-tite, vomiting, weakness, mild wheezing in chest, act in strange manner, looked confused, restless, hypersali-vation, failed resuscitation, itching at vertical side of knee	Death	No specimens submitted	Suspected
2013	40F	Zululand, KwaZulu-Natal	Cat	Scratches, category 2	None	Headache, nausea, vomiting, hypersalivation, hydrophobia, confusion, restlessness	Death	Serum & CSF - by IG/M IFA, saliva, skin biopsy - by PCR & impression smears, brain - by FAT	Probable
2013	22M	Msogwaba, Mpuma-langa	Unknown	Unknown	unknown	Seizures, meningitis, constantly scratching healed wound on his left leg	Death	saliva & CSF - by PCR, blood & CSF + by IG/M IFA, no post-mortem	Suspected
2013	30F	Musina, Limpopo (from Zimbabwe)	Dog	Unknown	None	Abnormal behaviour, hyper-salivation, periods of aggres-sive behaviour alternating with calmness and seizures, healed scars behind left knee	Death	Post-mortem saliva - no post-mortem	Probable

*Age is given in years; M=male; F=female.
[i]Classification of clinical cases according to the WHO Recommended Surveillance Standards, WHO/CDS/CSR/ISR/99.2

Conclusions

Rabies is a preventable but fatal neurological disease of humans and other mammals. Despite the availability of effective interventions for the control and prevention of this disease, cases of human rabies are confirmed in South Africa annually. In the past ten years, rabies has been reported from localities were it was previously controlled highlighting the fact that South Africa should be considered as an endemic site for rabies and that all exposures to suspected animals should be adequately assessed for risk of rabies. Low awareness of the risk of transmission of rabies virus after exposures to suspected animals (however benign the exposure may appear, i.e. small scratches or licks on mucous membranes) in the general public but also in healthcare workers remains an important contributing factor in the failure of interventions to prevent rabies infection in human patients.

Acknowledgements

Laboratory scientists and technologists of the Special Viral Pathogens Laboratory and the medical doctors and pathologists of the Division of Public Health Surveillance and Response, NICD, are thanked for their contributions.

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RESPIRATORY VIRUS SURVEILLANCE REPORT, SOUTH AFRICA, 2013

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Introduction

The National Institute for Communicable Diseases (NICD) coordinates four influenza surveillance programmes. These aim to characterise the influenza subtypes circulating in South Africa, as well as to describe the seasonality and epidemiology of the annual influenza season. These programmes collate data on milder influenza-like illness (ILI) and severe acute respiratory (SARI) illness.

The four influenza surveillance programmes include:

1. Viral Watch and Enhanced Viral Watch
2. Severe acute respiratory illness (SARI)
3. Influenza-like illness (ILI) in public health facilities
4. The respiratory morbidity surveillance system

The principal findings of each programme for the year 2013 are given below:

Viral Watch and Enhanced Viral Watch surveillance programmes

Viral Watch

The Viral Watch (VW) sentinel surveillance programme was initiated in 1984. It aims to provide information on the geographic spread and timing of influenza virus circulation as well as the type and distribution of circulating influenza viruses each year. During 2013, 171 practitioners registered across South Africa submitted a total of 2009 specimens throughout the year. Of these, 1803 were submitted to the NICD, 26 to the Department of Virology at Inkosi Albert Luthuli Central Hospital/ University of KwaZulu-Natal, and 180 to the National Health Laboratory Service, University of Cape Town laboratory, in the Western Cape Province. Positive specimens from these sites were sent to the NICD for confirmation, serotyping and sequencing.

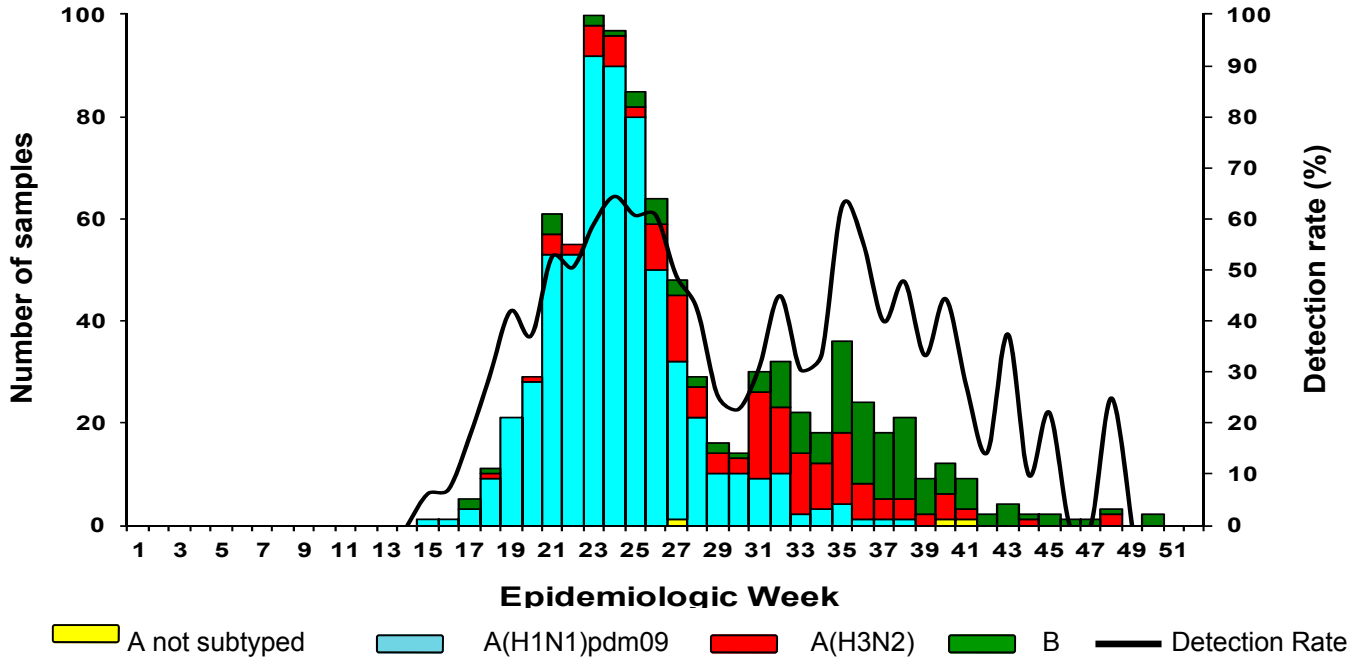
Of the 2009 specimens tested, 877 (44%) were positive for influenza. Dual A(H1N1)pdm09 and A(H3N2) infection was detected in five samples (<1%). Other dual infections included one sample positive for A(H1N1) pdm09 and B, and one for A(H3N2) and B. Of the remaining 870 positive specimens, 578 (66%) were influenza A(H1N1)pdm09, 143 (16%) were A(H3N2), 146 (17%) were B, and 3 (<1%) were A unsubtyped.

The beginning of the influenza season is defined as the first week the influenza detection rate (calculated on specimens tested at the NICD only) rises above 10% and then consistently remains above this level. The end of the season is defined as the week before the detection rate drops below 10%. The first influenza case of the 2013 season was detected in a specimen collected on 22nd April (week 17), and the last from a specimen collected on 13th October (week 41). The onset of the influenza season in week 17 is one of the earliest recorded since the beginning of the Viral Watch. The season peaked in week 24 when the detection rate rose to 64%. While the average duration of the influenza season over the 9 years prior to 2013 is 17 weeks, the 2013 season lasted 25 weeks (figure 1).

A further 565 respiratory virus detections were made from the 486/1132 (43%) patients who tested negative for influenza during 2013. Of these, 112 (23%) were adenovirus (AV), 47 (8%) were enterovirus (EV), 59 (10%) were human metapneumovirus (HMP), 50 (9%) were parainfluenza viruses (PIV) 1-3, 56 (10%) were respiratory syncytial virus (RSV) and 229 (40%) were rhinovirus (RV).

Enhanced Viral Watch

In 2009, in response to the prevailing influenza pandemic, enhanced Viral Watch centres at 12 public hospitals were initiated to detect influenza strains in patients hospitalized with severe respiratory illness. In 2013, 327 specimens were received from six of these centres. Of these specimens, the largest number (287, 88%) came from Gauteng. Influenza was detected in the specimens of 30 (10%) patients of which 23 were A(H1N1)pdm09, two were A(H3N2), and five were influenza B. Two hundred and forty-eight other respiratory viruses were detected in a further 196 patients of which 71 (29%) were RV, 63 (25 %) were RSV and 55 (22%) were AV.



A(H1N1)pdm09 n= 584, A(H3N2) n=143, influenza B n=146, A not subtyped n=3

Figure 1: Numbers of samples and influenza detection rate, by influenza subtype and week, in patients enrolled into the Viral Watch surveillance programme, 2013.

Severe acute respiratory illness (SARI) surveillance programme

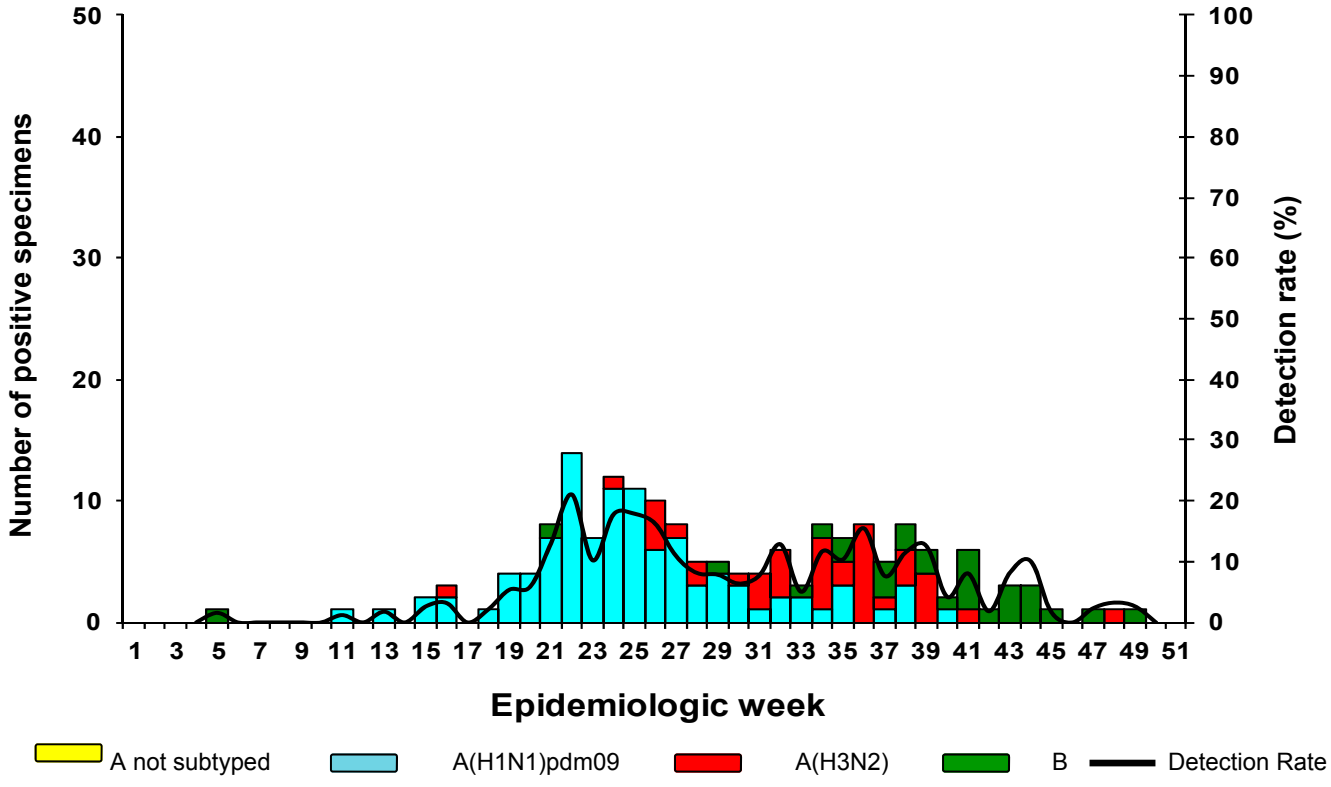
The SARI sentinel surveillance programme was initiated in April 2009 and is presently operational at six public hospitals in four provinces. The primary aims of the programme are to describe trends in the numbers of SARI cases at sentinel sites and to determine the relative contribution of influenza and other respiratory viruses to the SARI syndrome. The SARI sites include: Chris Hani Baragwanath Hospital (CHBH) in Gauteng, Matikwana and Mapulaneng hospitals which form the Agincourt site in Mpumalanga, Klerksdorp-Tshepong hospital (KTH) complex in the Northwest Province and Edendale hospital in KwaZulu-Natal.

Hospitalised patients meeting the clinical case definition of acute respiratory illness were prospectively enrolled. Clinical and epidemiological data were collected using standardized questionnaires. Information on in-hospital management and outcome was also collected. Upper respiratory tract samples (oropharyngeal and nasopharyngeal swabs in patients ≥5 years old or nasopharyngeal aspirates in patients <5 years of age) were collected and tested at the NICD for the presence of influenza and other respiratory viruses using real-time reverse transcriptase polymerase chain reaction (RT-PCR). Blood specimens were tested for the presence of pneumococcal DNA using quantitative real-time PCR for the *lyt*A target. In 2013, due to funding limitations, numbers enrolled at the CHBH site were reduced by systematic sampling of paediatric and adult patients on a 1-2 days per week rotating schedule.

During 2013, 3128 patients were enrolled into the SARI programme, from which 3041 (97%) samples were collected and tested for respiratory viruses. Due to the aforementioned change in enrolment sampling at the CHBH the number of samples collected at Klerksdorp/ Tshepong (KTH) hospitals was higher than that at CHBH for the first time since the introduction of the

programme. A third of the samples were collected at KTH (1012/3037, 33%). Children under 5 years accounted for 51% (1594/3128) of patients and 1650/3124 (53%) were male. Of the 3041 patients with influenza results, 174 (6%) were positive for influenza using RT-PCR. Of these, 101 (58%) were positive for influenza A(H1N1) pdm09, 42 (24%) were positive for influenza A(H3N2), 31 (18%) were positive for influenza B and one was a dual infection comprising A(H1N1) pdm09 and A(H3N2).

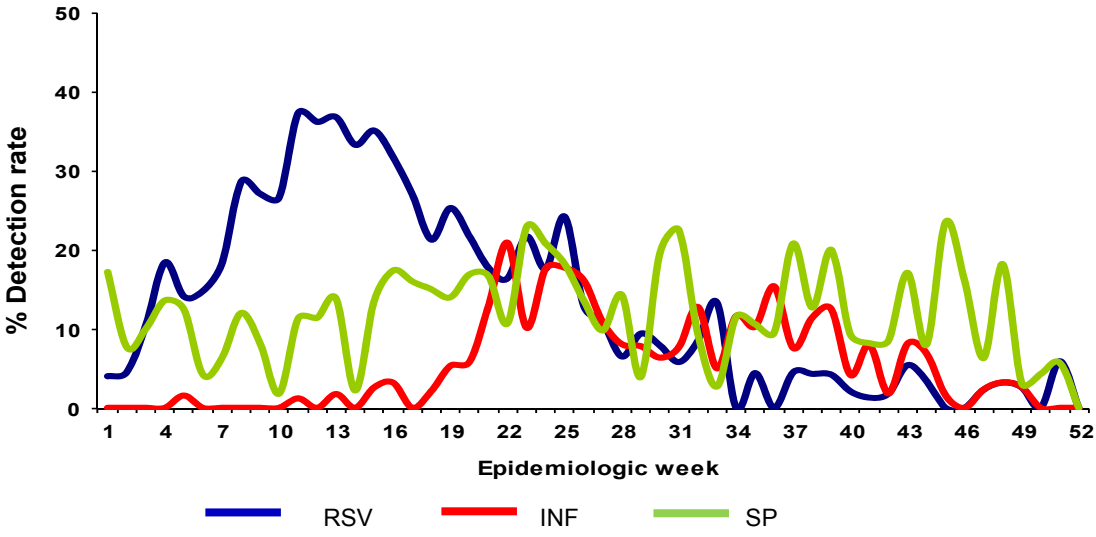
During week 21 (week starting 20th May), the influenza detection rate rose above 10% and remained above 10% until week 28 (week starting 8th July). The peak detection rate of 18% occurred in week 25 (week starting 17th July). A smaller peak of more than 10% occurred between weeks 34 (week starting 19th August) and week 36 (week starting 2nd September) (figure 2).



A(H1N1)pdm09 n=101, influenza A(H3N2) n=42, influenza B n=31, influenza A(H1N1)pdm09 & A(H3N2) n=1

Figure 2: Numbers of samples positive for influenza and influenza detection rate, by subtype and week, in patients enrolled into the Severe Acute Respiratory Illness (SARI) programme, 2013.

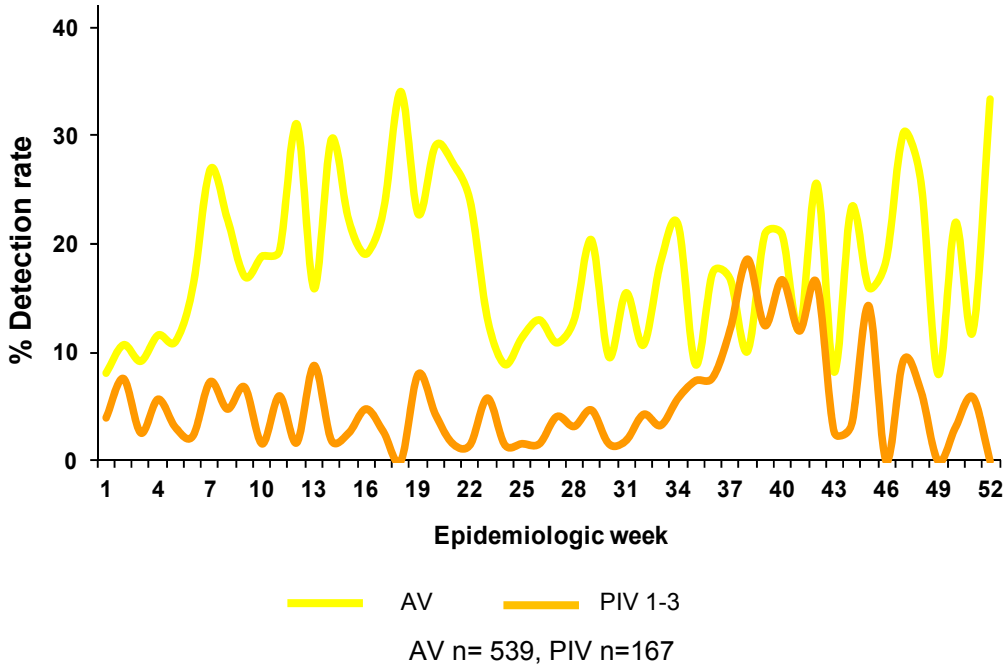
Amongst patients enrolled into the SARI programme, testing for additional respiratory viruses identified RV in 28% (860/3041), AV in 18% (539/3041), RSV in 15% (452/3041), EV in 6% (170/3041), human metapneumovirus (hMPV) in 3% (96/3041), PIV3 in 3% (99/3041), PIV1 in 1% (39/3041) and PIV2 in 1% (29/3041) of samples.



RSV n= 452, influenza n= 175, SP n=285

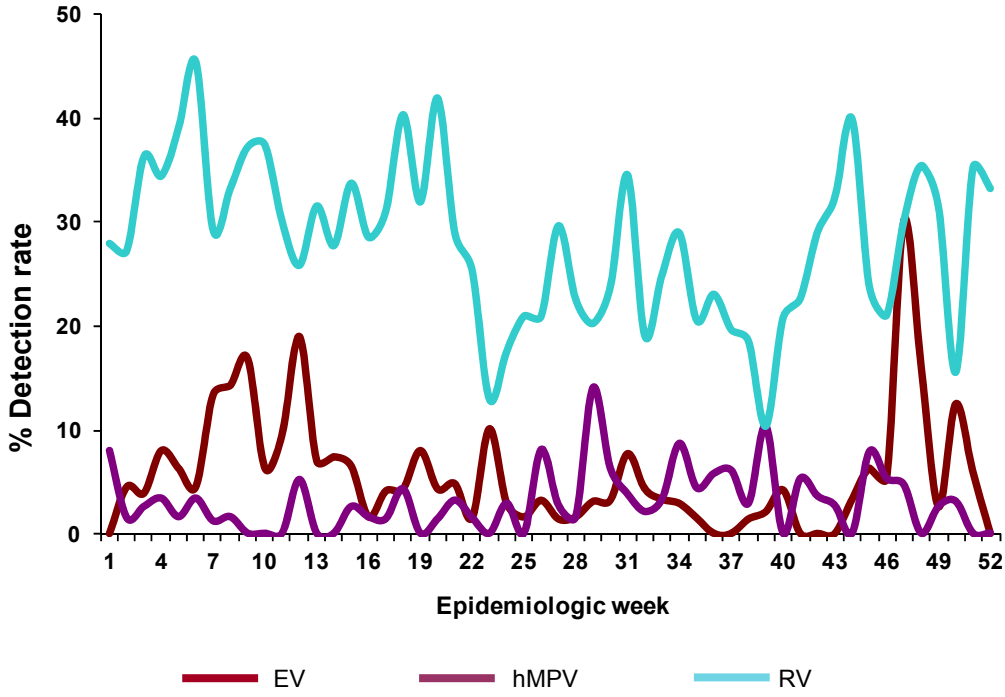
Figure 3: Severe Acute Respiratory Illness (SARI) surveillance programme detection rates for respiratory syncytial virus (RSV), influenza virus (INF) (all subtypes) and S*treptococcus pneumonia* (SP) by week, 2013.

Of the 3128 patients enrolled into SARI, 2382 (76%) had blood specimens tested for the presence of pneumococcal DNA. Of these, 285 (12%) were positive for S*treptococcus pneumonia* (SP) (figure 3). Of the patients with influenza, 143/175 (82%) had blood samples taken and 21/143 (15%) were positive for SP. During 2013, the RSV season preceded the influenza season. The detection rate for RSV remained above 10% from week 3 (week starting 14th January) until week 31 (week starting 22nd July) and reached a peak of 37% in week 11 (week starting 11th March). Figures 4 and 5 show the detection rates for respiratory viruses other than influenza and RSV.



AV n= 539, PIV n=167

Figure 4: Severe Acute Respiratory Illness (SARI) surveillance programme detection rates for adenovirus (AV) and parainfluenza viruses (PIV) (1-3) by week, 2013.



EV n=170, hMPV n=96, RV n=860

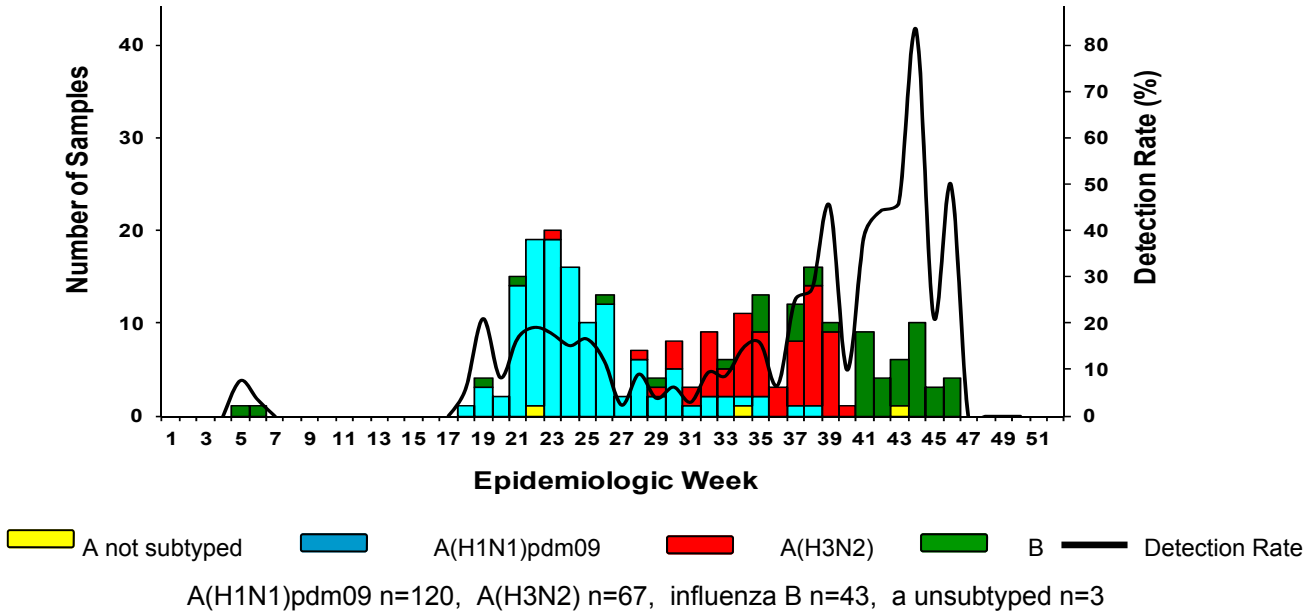
Figure 5: Severe Acute Respiratory Illness (SARI) surveillance programme detection rates for enterovirus (EV), human metapneumovirus (hMPV) and rhino virus (RV) by week, 2013.

Influenza-like illness in primary health care clinics

During 2012, systematic surveillance for ILI was set up at two clinics in two provinces (North West Province and KwaZulu-Natal). An additional four clinics in these provinces were added during 2013. Patients fitting a clinical case definition were prospectively enrolled. Clinical and epidemiological data were collected for each patient. Upper respiratory tract samples (oropharyngeal and nasopharyngeal swabs in patients ≥5 years old or nasopharyngeal aspirates in patients <5 years of age) were collected and tested at the NICD for the presence of influenza and other respiratory viruses using RT-PCR.

During 2013, a total of 1991 specimens was received from all six ILI sites. Of the 243 (12%) positive samples, influenza A(H1N1)pdm09 was detected in 120 (49%), influenza A(H3N2) in 67 (28%), influenza B in 43 (18%) and influenza A (not subtyped) was detected in three patients (<1%). There were two dual infections: one A (H1N1)pdm09 and A(H3N2), and one A(H3N2) and influenza B. The first influenza detection of the season was made from a specimen collected on 29th April (week 18), and the last positive specimen was collected in week 46 (week starting 11th November). Sporadic detections were made both before and after the season.

The influenza season started in week 19 and continued to week 26 (6th May through week starting 24th June). A second peak occurred between weeks 37 and 45 (9th September through week starting 4th November). The peak detection rate of 83% was observed in week 44 (week starting 21st October) (figure 6). The two peaks correspond to the influenza season described by the Viral Watch programme.



A(H1N1)pdm09 n=120, A(H3N2) n=67, influenza B n=43, a unsubtyped n=3

Figure 6: Numbers of samples and influenza detection rate, by influenza subtype and week, in patients enrolled into Influenza-like Illness (ILI) surveillance at public health clinics, 2013.

Respiratory Morbidity Surveillance

In order to describe the influence of the influenza season on the number of pneumonia and influenza (P&I) hospitalizations, the NICD reviews anonymized data from a private hospital group. The numbers of hospitalizations for P&I during the influenza season were compared to those for the periods preceding and following the season. During 2013 there were 1 204 969 consultations reported to the NICD through the respiratory morbidity data mining surveillance system. Of these, 31637 (3%) were due to P&I.

An increase in P&I consultations and admissions with a second peak following the initial peak was observed during the influenza season as reported in the Viral Watch and SARI programmes (figure 7). The smaller peak preceding the influenza season corresponds to the RSV season observed in the SARI programme. Similarly, the number of hospitalizations for P&I corresponds to the peak RSV and influenza seasons (figure 8).

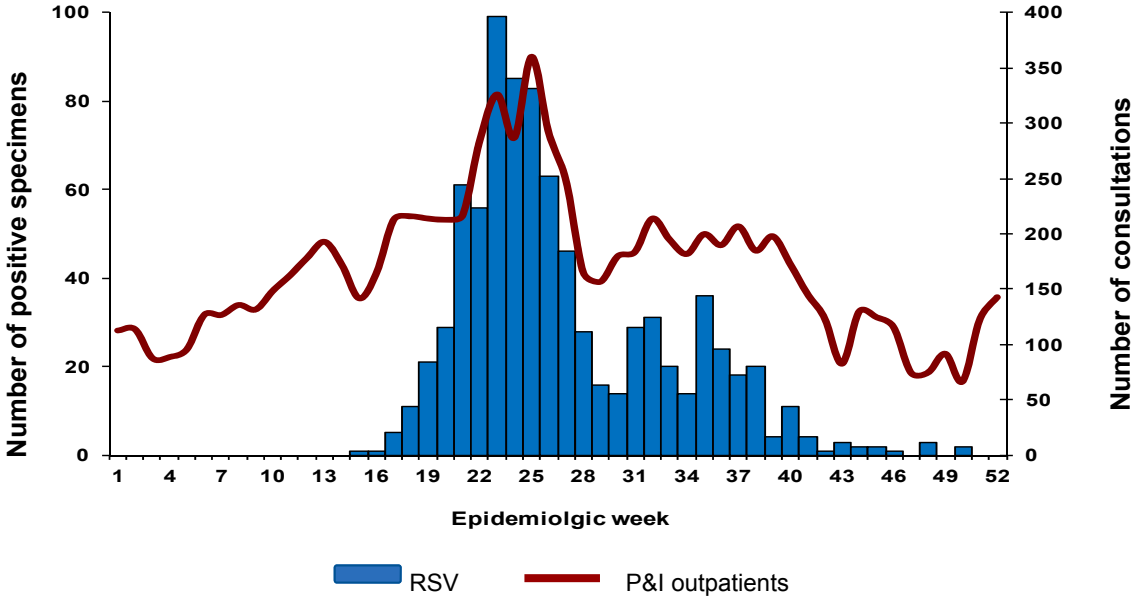


Figure 7: Numbers of private hospital outpatient consultations with a discharge diagnosis of pneumonia and influenza (P&I), and numbers of influenza positive viral isolates (Viral Watch) by week, 2013.

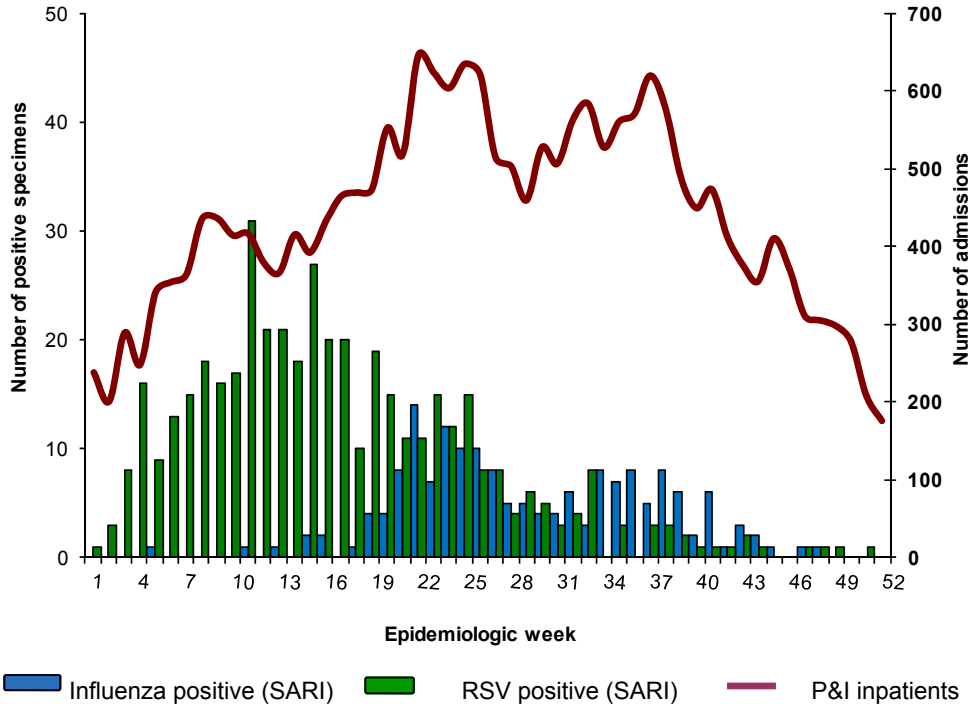


Figure 8: Numbers of admissions for pneumonia and influenza (P&I inpatients), as well as numbers of influenza positive viral isolates (Viral Watch) and respiratory syncytial virus (RSV) positive isolates (SARI) by week, 2013.

Molecular characterizations of influenza virus strains

Genetic characterisations of Influenza A (H3N2), A (H1N1)pdm09 and Influenza B strains are used to monitor genetic drift as well as the emergence of new lineages which are identified by specific amino acid mutations relative to a designated reference strain. The naming of lineages is decided by the WHO Vaccine Consultation Meeting team.

Influenza A(H3N2)

H3N2 HA gene sequences were generated from 9 clinical specimens selected from the 2013 season for both the ILI and SARI surveillance programs. All 2013 strains are within genetic group 3, specifically subgroup 3C, of the seven described lineages. Subgroup 3C is characterised by the following amino acid mutations: Q33R, N145S and N278K relative to A/Perth/16/2009 as reference. Other mutations that can also be occur in subgroup 3C viruses are S45N, T48I, A198S and V223I. The 2013 vaccine strain A/Victoria/361/2011 is also in subgroup 3C.

Influenza A(H1N1)pdm09

In the 2013 season, the HA gene from 70 influenza A (H1N1)pdm09 positive clinical samples was sequenced. Influenza viruses representing 99% of the samples (69/70) were lineage 6 (CDC classification) and one was lineage 7. Influenza A(H1N1)pdm09 strains from five individuals who reported that they received the vaccine are lineage 5 (n=1) and lineage 6 (n=4). The signature amino acid mutation, K283E, characterises the subgroup in lineage 6 containing the 2013 South African viruses.

Influenza B

The HA1 region of the HA genes from a total of seven clinical samples positive for influenza B was sequenced

and characterised. No B/Victoria lineage strains were identified.

B/Yamagata lineage

Seven viruses sequenced belong to clade 2 of B/Yamagata lineage viruses which is characterised by the mutations R48K, P108A and T181A, whereas in 2012 two-thirds of B/Yamagata lineage viruses were in clade 3 which is characterised by the amino acid mutations S150I, N166Y and S230D in reference to the B/Florida/4/2006 strain. In SARI cases positive for influenza B, all samples (n=71/86) subtyped belonged to the B/Yamagata lineage.

Isolation and antigenic characterisations of influenza virus strains

During the 2013 influenza season, a total of 63/91 (69%) influenza virus isolates were successfully obtained from clinical samples that tested positive for influenza on a real-time multiplex PCR assay with a crossing point value ≤30. Of these, 53 were influenza A and 10 were influenza B viruses. The majority of influenza A isolates (89%, n=41/46) were A(H1N1)pdm09 which dominated the season. Of the embryonic egg isolations attempted, 50% (18/36) were successful, of which 14 were influenza A(H1N1)pdm09, three were influenza A(H3N2) and one was influenza B.

A total of 52 virus isolates could be characterised antigenically by hemagglutination inhibition assay (HIA) of which 80% (40/49) were influenza A(H1N1)pdm09 and showed normal reactivity to the A/California/7/2009 reference antiserum. Four influenza A(H3N2) isolates were typed of which three reacted with a 4-fold lower titre and one reacted with a ≤2-fold lower titre compared to the control or reference antiserum, A/Perth/16/2009. Eight influenza B virus isolates reacted with titres similar to the control antiserum for the influenza B/Yamagata lineage, B/Wisconsin/1/2010.

Resistance testing of influenza virus strains

No drug resistant genotypes were detected from a total of 103 influenza A(H1N1)pdm09 positive clinical samples [ILI (Viral Watch)=70 hospitalized cases, (Enhanced Viral Watch)=6; SARI=27] tested for the presence of the H275Y mutation associated with oseltamivir resistance. In addition, 24 influenza virus isolates were tested for phenotypic evidence of reduced susceptibility to the neuraminidase inhibitors oseltamivir and zanamivir. Of these, two showed reduced sensitivity even though both contained the drug-sensitive genotype at position 275.

Discussion

The 2013 influenza season was initially dominated by circulation of influenza A(H1N1)pdm09, mainly in weeks 20-30 (13th May to 22nd July), followed by circulation of predominantly A(H3N2) in weeks 31-40 (29th July to 30th September). The season ended with circulation of mainly influenza B in weeks 41-47 (7th October to 11th November). Although the overall detection rate was higher in the Viral Watch programme (44%) than in the ILI surveillance programme (12%), the season and circulating viral subtypes were similar. The protracted 2013 season is reflected in all surveillance programmes.

The detection rate of 12% for *S. pneumoniae* was somewhat higher than has been recorded in preceding years. This was likely a result of changes to the surveillance programme including improved quality of DNA extraction from blood specimens and changes in the enrolment algorithm at CHBH in 2013.

The A(H1N1)pdm09 strains dominated the season and the majority of viruses were in genetic lineage 6. All viruses showed good antigenic reactivity to antisera raised against the A/California/7/2009 vaccine strain. Genetic drift from the vaccine strains has occurred in the influenza A and B strains. In contrast to 2012 when both

Influenza B lineages co-circulated, the Influenza B/Yamagata-like viruses circulated in 2013. All the B/Yamagata-like virus isolates showed normal reactivity with antisera raised against the B/Wisconsin/1/2010 vaccine strain. Circulating influenza A(H3N2) viruses mainly belonged to lineage 3C. Three A(H3N2) isolates typed showed low reactivity to antisera raised against the A/Victoria/361/2011 vaccine strain. Two isolates from participants with influenza-like illness were identified that showed reduced sensitivity to the neuraminidase inhibitors in the phenotypic resistance assay, yet contained the sensitive genotype for the signature mutation at position 275.

Vaccine recommendations for the 2014 influenza season in the southern hemisphere include a new influenza A(H3N2) strain, A/Texas/50/2012-like, which has antigenic properties similar to the A/Victoria/361/2011 vaccine strain, and a change from the influenza B vaccine strain to a new B/Yamagata/ lineage strain namely B/Massachusetts/2/2012-like.

Acknowledgements

We wish to thank all doctors who participated in the Viral Watch and Enhanced Viral Watch programmes in 2013. Contributors to the SARI and Viral Watch Surveillance programmes are thanked for their inputs. These include: Shabir Madhi, Director, NICD; Amelia Buys, Maimuna Carrim, Cheryl Cohen, Mignon Du Plessis, Orienka Hellferscee, Victoria Magomani, Jo McAnerney, Fahima Moosa, Jocelyn Moyes, Marthi Pretorius, Makatisane Papo, Adrian Puren, Florette Treurnicht, Akhona Tshangela, Marietjie Venter, Anne von Gottberg, Sibongile Walaza and Nicole Wolter of the Centre for Respiratory Diseases and Meningitis, NICD; Mark Goosen and Deidre Greyling of the Centre for HIV and STIs, NICD; Andrew Black of Chris Hani Baragwanath Hospital; Michelle Groome, David Moore and Suzan Nzenze of the Department of Science and Technology / National Research Foundation: Vaccine Preventable Diseases Unit; Meera Chhagan, Halima Dawood, Sumayya Haffejee and Fathima Naby of Edendale Hospital; Keith Klugman of Emory University, Atlanta USA; Erna du Plessis, Omphile Mekgoe and Ebrahim Variava of the Klerksdorp/Tshepong Hospital Complex; Kathleen Kahn, Stephen Tollman and Rhian Twine of the MRC/Wits Rural Public Health and Health Transitions Research Unit (Agincourt); Frew Benson of the South African National Department of Health - Communicable Diseases Directorate; Adam Cohen and Stefano Tempia of the United States Centers for Disease Control and Prevention (CDC); Keitumetsi Baloyi, Ulenta Chetty, Margaret Hlobo, Sandra Kashe, Agnes Koena, Tselane Makgoba, Julia Malapane, Wisdom Malinga, Seipati Matshogo, Annalet Moodley, Myra Moremi, Thulisile Mthembu, Nomathemba Mofokeng, Bekiwe Ncwana, Wendy Ngubane, Maureen Nkosi, Andrina Sambo, Gabisile Senne, Nelly Sigasa and Khadija Shangase of the Surveillance Officers & Research Assistants group; Nireshni Naidoo, Boitumelo Letlape, Debra Mathebula, Venson Ndhlovu, Kelebogile Motsepe, Robert Musetha, Mpho Ntoyi, Shirley Mhlari, Thembinkosi Matiwane and Dimakatso Maraka of the Data management team.

ANTIMICROBIAL RESISTANCE SURVEILLANCE FROM SENTINEL PUBLIC HOSPITALS, SOUTH AFRICA, 2012

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Introduction

Antimicrobial resistance (AMR) is a key public health concern that threatens effective treatment of antimicrobial infections, both locally and globally. Surveillance is conducted to determine the extent and pattern of resistance amongst the most important disease causing pathogens in humans.[1] The objectives of the AMR surveillance programme are to determine the number of cases reported from selected hospitals by month for selected pathogens and to describe antimicrobial susceptibility to the most important treatment regimens by pathogen by hospital.

Methods

All data were sourced from the National Health Laboratory Service (NHLS) Corporate Data Warehouse (CDW). This is a national repository for all public health hospitals in South Africa and contains archived data from two laboratory information systems (LIS), DISALAB and TrakCare.[2]

Bloodstream infections for the period January to December 2012 were extracted for the following pathogens: *Acinetobacter baumannii* complex, *Enterobacter cloacae* complex, *Escherichia coli, Enterococcus faecalis, Enterococcus faecium, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Staphylococcus aureus.* Routine data were collected from sentinel sites (mostly academic sites) (table 1).

Antimicrobial susceptibility test reporting was based on Clinical and Laboratory Standards Institute (CLSI) guidelines.[3] The different laboratory methods used included Microscan, Vitek and disk diffusion. Owing to two different LIS, each with its own coding system of organisms and antibiotics, as well as a lack of standardization across NHLS laboratories on how data were captured, extensive cleaning and recoding of data was necessary. Cleaning of the data involved creating unique patient identifiers, which enabled de-duplication and the generation of patient-level data. Some data may be incomplete due to missing cases not captured on the LIS or non-standardized coding of pathogens and antibiotics.

Table 1: Antimicrobial Resistance Surveillance participating hospitals by province, South Africa, and their characteristics.

Hospital Site	Province	Academic Hospital	No of beds
Charlotte Maxeke Johannesburg Academic Hospital (CMJAH)	Gauteng	Yes	1088
Chris Hani Baragwanath Hospital (CHBH)	Gauteng	Yes	3200
Dr George Mukhari Hospital (DGMH)	Gauteng	Yes	1200
Grey's Hospital (GH)	KwaZulu-Natal	Yes	530
Groote Schuur Hospital (GSH)	Western Cape	Yes	893
Helen Joseph Hospital (HJH)	Gauteng	Yes	700
Inkosi Albert Luthuli Central Hospital (IALCH)	KwaZulu-Natal	Yes	846
King Edward VIII Hospital (KEH)	KwaZulu-Natal	Yes	922
Mahatma Gandhi Hospital (MGH)*	KwaZulu-Natal	No	350
Nelson Mandela Academic Hospital/Mthatha Tertiary (NMAH)	Eastern Cape	Yes	520
RK Khan Hospital (RKKH)*	KwaZulu-Natal	No	543
Steve Biko Academic Hospital (SBAH)	Gauteng	Yes	832
Tygerberg Hospital (TH)	Western Cape	Yes	1310

Results

Data from antimicrobial susceptibility tests are summarised for: *Acinetobacter baumannii* complex (figure 1), *Pseudomonas aeruginosa* (figure 2), *Enterobacter cloacae* complex (figure 3), *Escherichia coli (*figure 4*), Klebsiella pneumoniae* (figure 5)*, Staphylococcus aureus* (figure 6), *Enterococcus faecalis* (figure 7) and *Enterococcus faecium* (figure 8). For each organism, total number of cases by month, and susceptibility to selected antimicrobial agents with numbers and percentages (susceptible or resistant) per site was analyzed (figures 1-8).

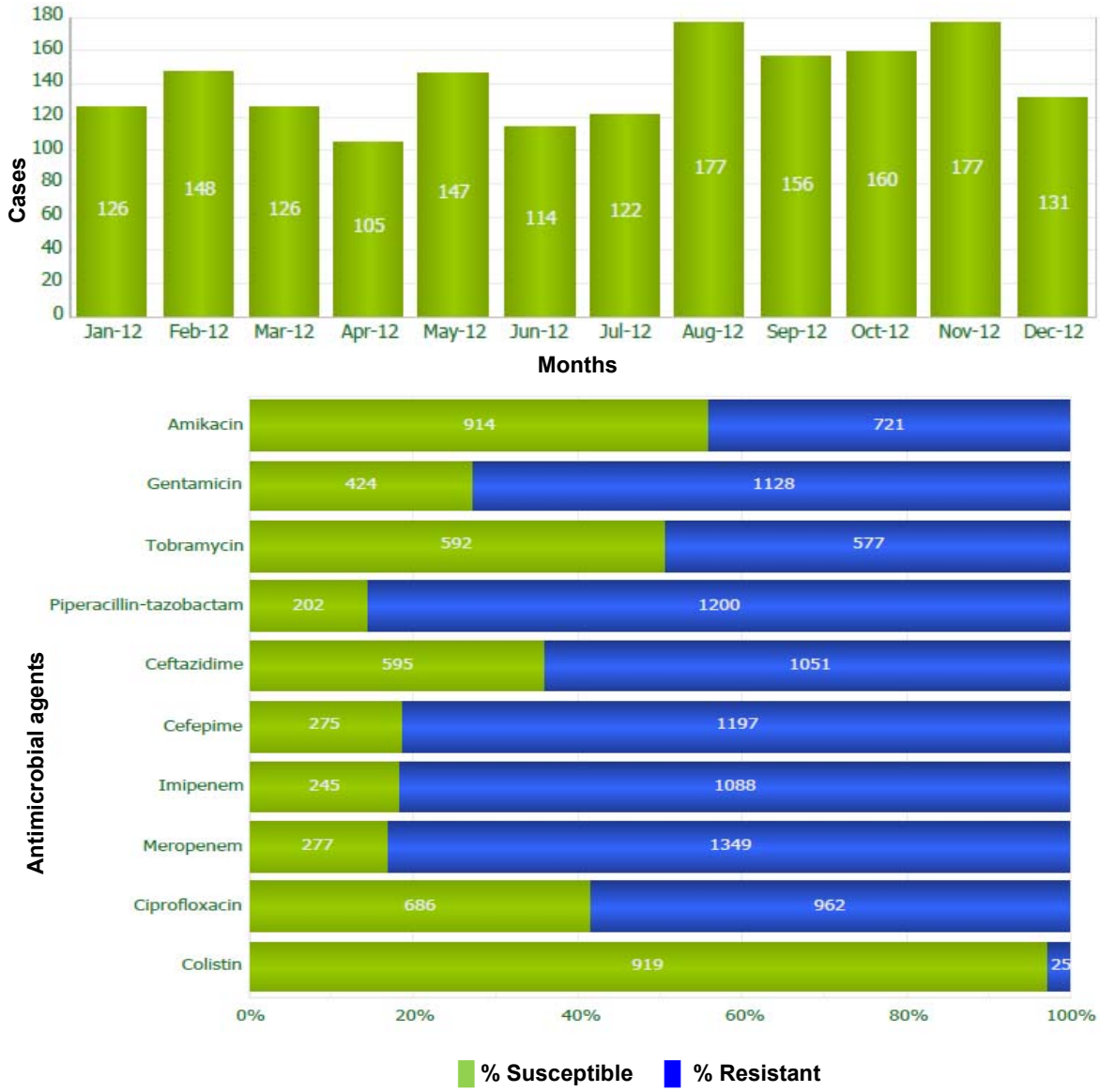

Figure 1: *Acinetobacter baumannii* cases by month, and numbers and percentages of susceptible and resistant *A. baumannii* complex isolates from blood cultures at public-sector sentinel sites, 2012. Total number of isolates analyzed = 1689.

Acinetobacter baumannii is resistant to the majority of antimicrobial agents listed owing to various mechanisms of resistance including: loss of outer membrane porins and permeability, efflux system, Amp C beta-lactamases and others. Resistance was highest to carbapenems, cefepime and ceftazidime, and was lowest to ciprofloxacin and amikacin. Colistin resistance was low for the period under review.

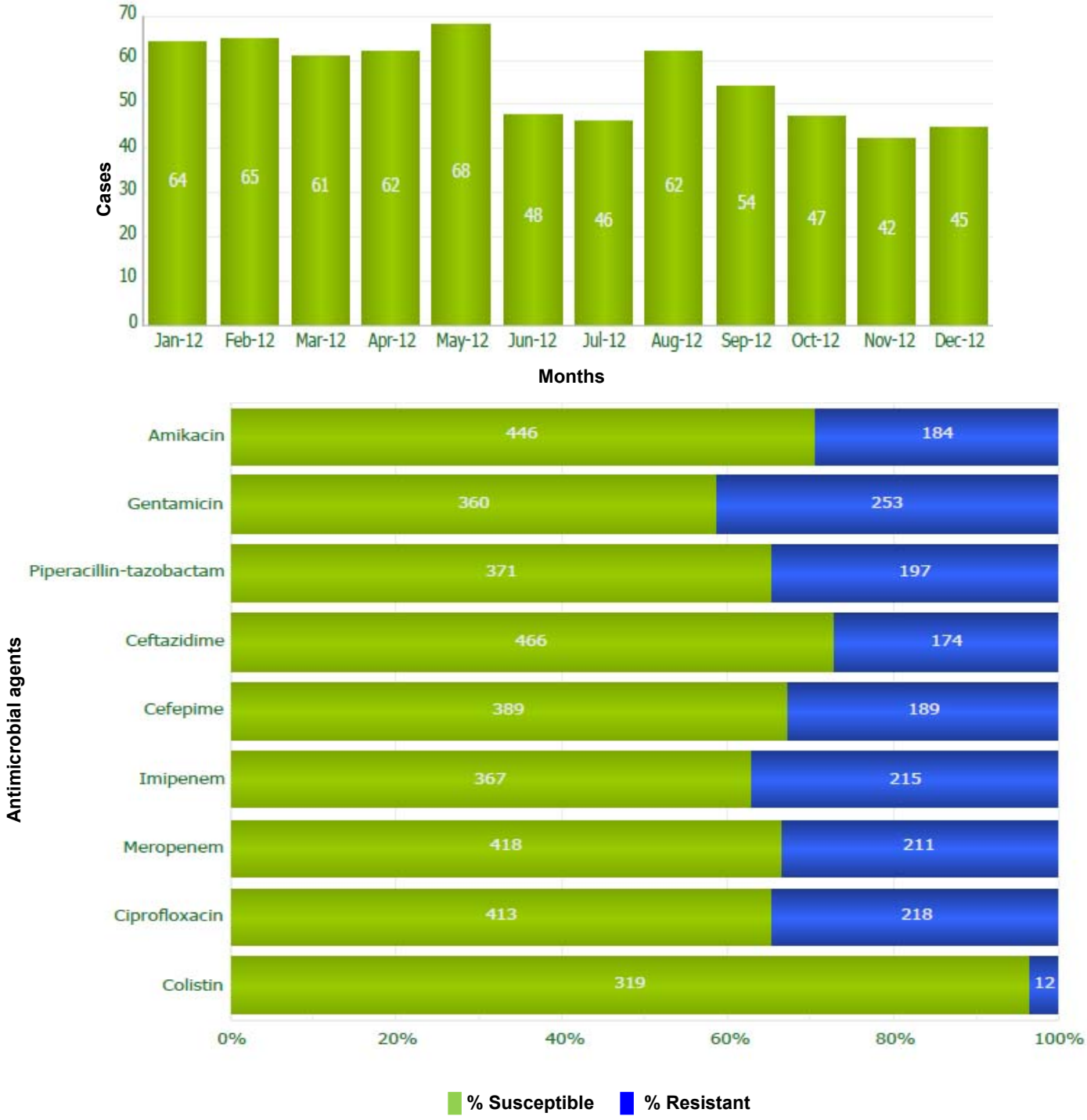

Figure 2: *Pseudomonas aeruginosa* cases by month, and numbers and percentages of susceptible and resistant *P. aeruginosa* isolates from blood cultures at public-sector sentinel sites, 2012. Total number of isolates analyzed = 664.

Pseudomonas aeruginosa isolates were moderately resistant to antimicrobial agents compared to *A. baumannii*. Resistances to ceftazidime, piperacillin-tazobactam and imipenem were highest, while colistin resistance was lowest.

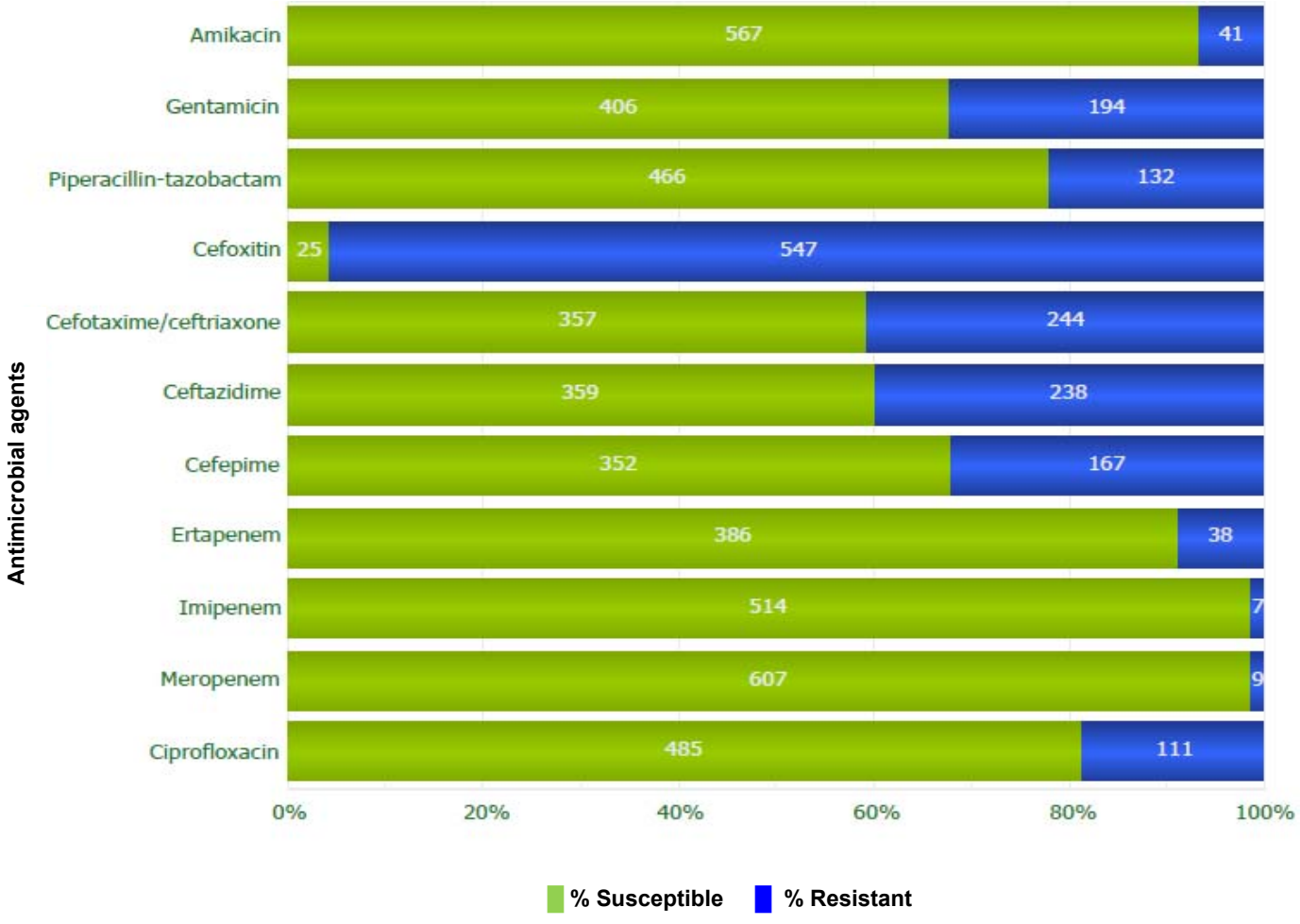

Figure 3: *Enterobacter cloacae* cases by month, and numbers and percentages of susceptible and resistant *E. cloacae* complex isolates from blood cultures at public-sector sentinel sites, 2012. Total number of isolates analyzed = 639.

The high level of resistance of *E. cloacae* complex to ertapenem (38%) is a major concern. Resistance to carbapenems and cefepime indicates the presence of de-repressed mutants resistant to all cephalosporins.

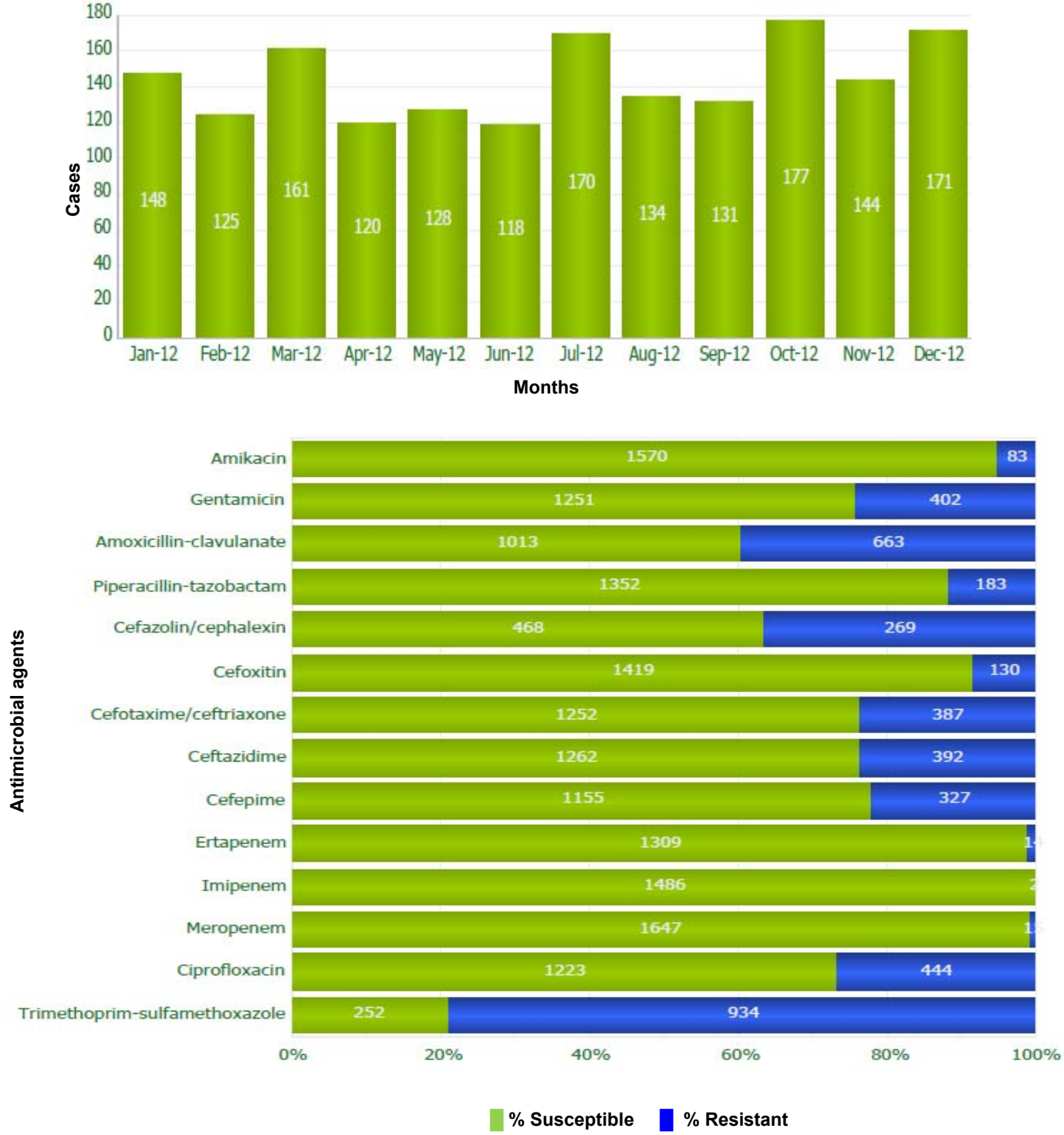

Figure 4: *Escherichia coli* cases by month, and numbers and percentages of susceptible and resistant *E. coli* isolates from blood cultures at public-sector sentinel sites, 2012. Total number of isolates analyzed = 1727.

Resistance to antimicrobials was high in *E. coli.* Resistance to amoxicillin-clavulanate as well as 1st and 3rd generation cephalosporins indicates the presence of extended spectrum beta-lactamases (ESBLs). Ciprofloxacin resistance is also of concern.

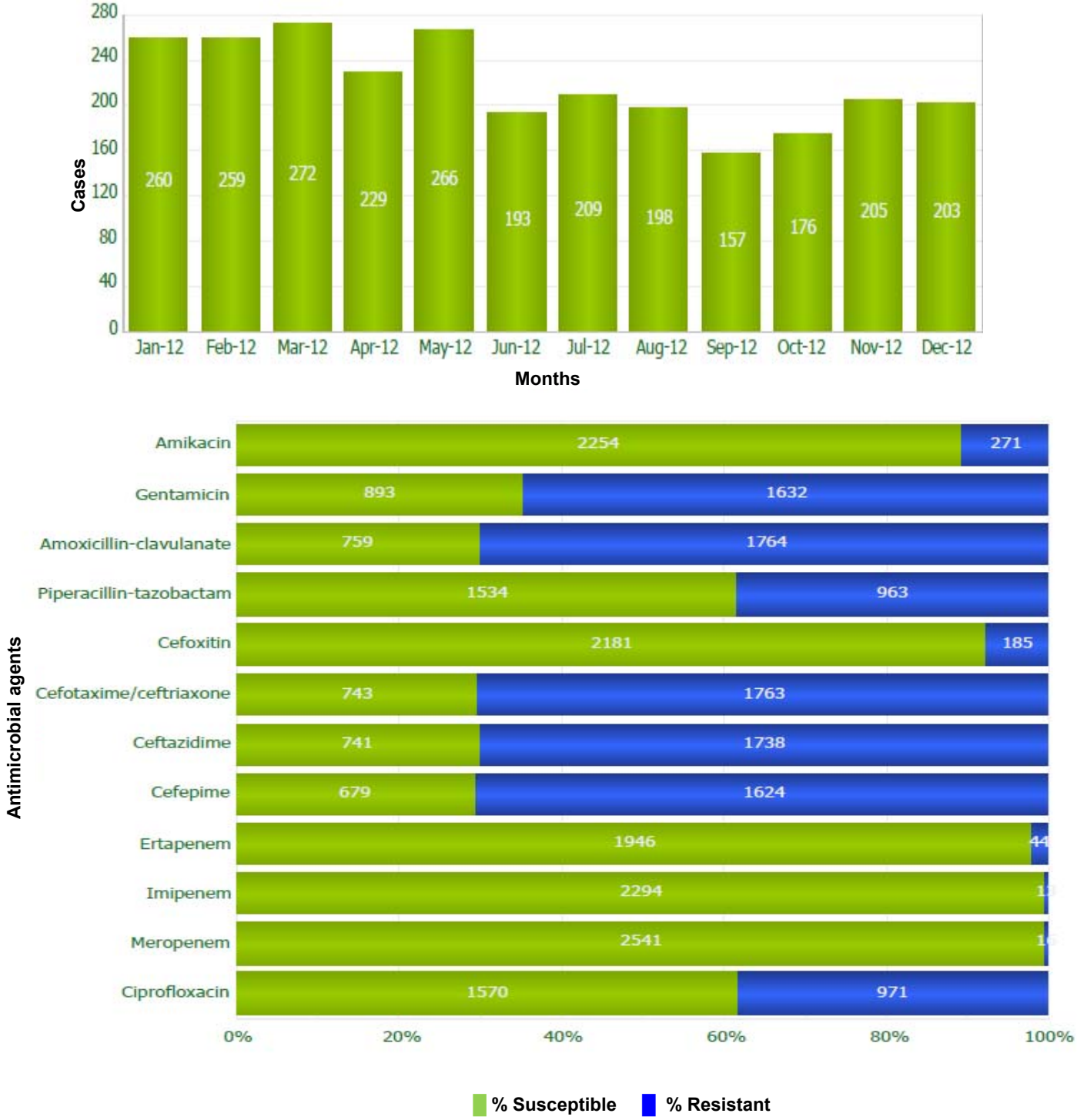

Figure 5: *Klebsiella pneumoniae* cases by month, and numbers and percentages of susceptible and resistant *K. pneumoniae* isolates from blood cultures at public-sector sentinel sites, 2012. Total number of isolates analyzed = 2627.

Klebsiella pneumoniae was resistant to multiple antimicrobials including ESBLs, ciprofloxacin and amikacin. Ertapenem resistance was low. Although resistance to other carbapenemases was very low, the rapid emergence of strains with carbapenemases production threatens the last line of therapeutic options. Thus continuous monitoring of resistance trends needs to be implemented.

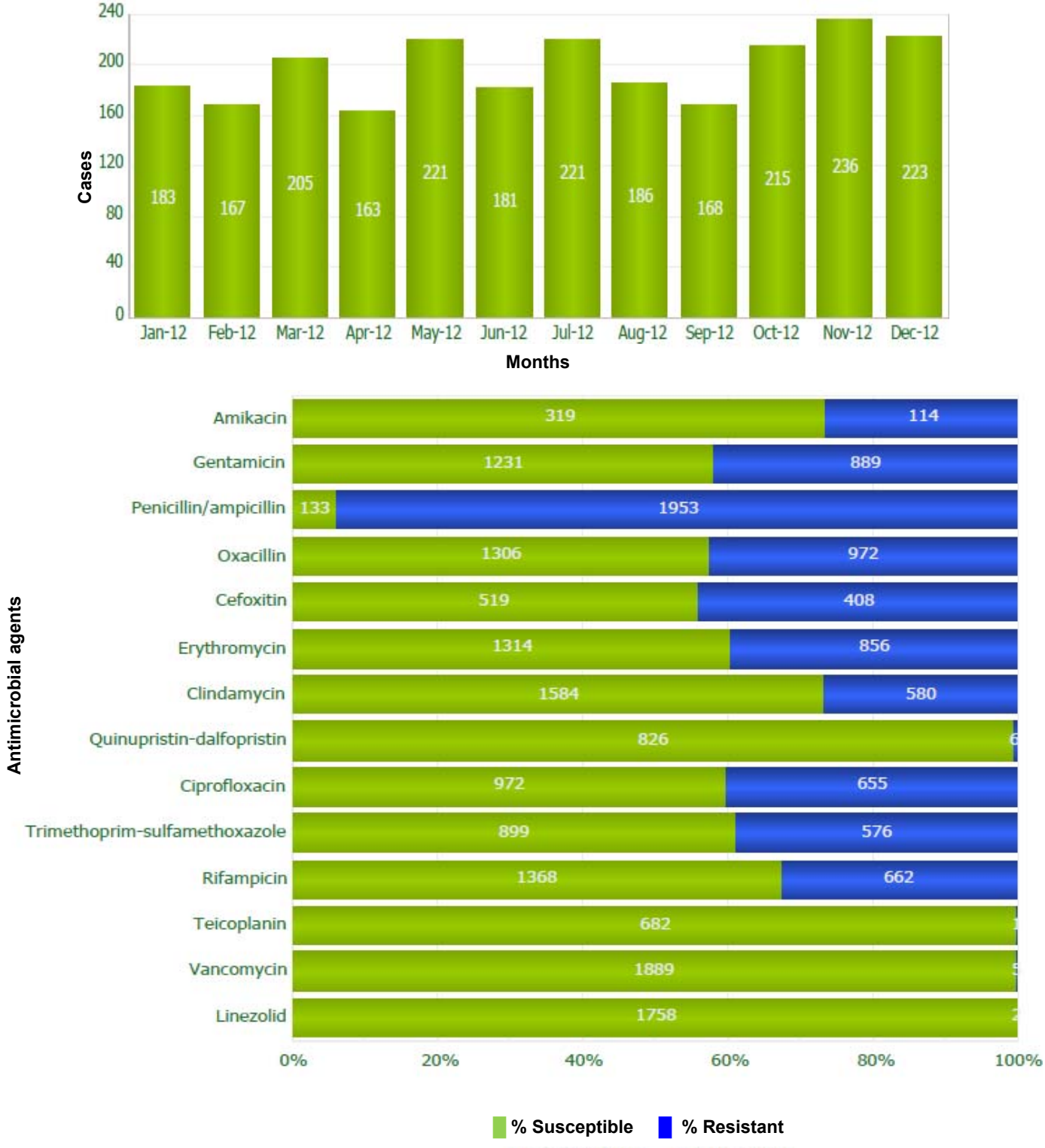

Figure 6: *Staphylococcus aureus* cases by month, and numbers and percentages of susceptible and resistant *S. aureus* isolates from blood cultures at public-sector sentinel sites, 2012. Total number of isolates analyzed = 2369.

Six *S. aureus* isolates were reported to be vancomycin resistant. However, this was not confirmed and data should be treated with caution. Resistances to methicillin and all other beta-lactams, erythromycin and clindamycin were recorded.

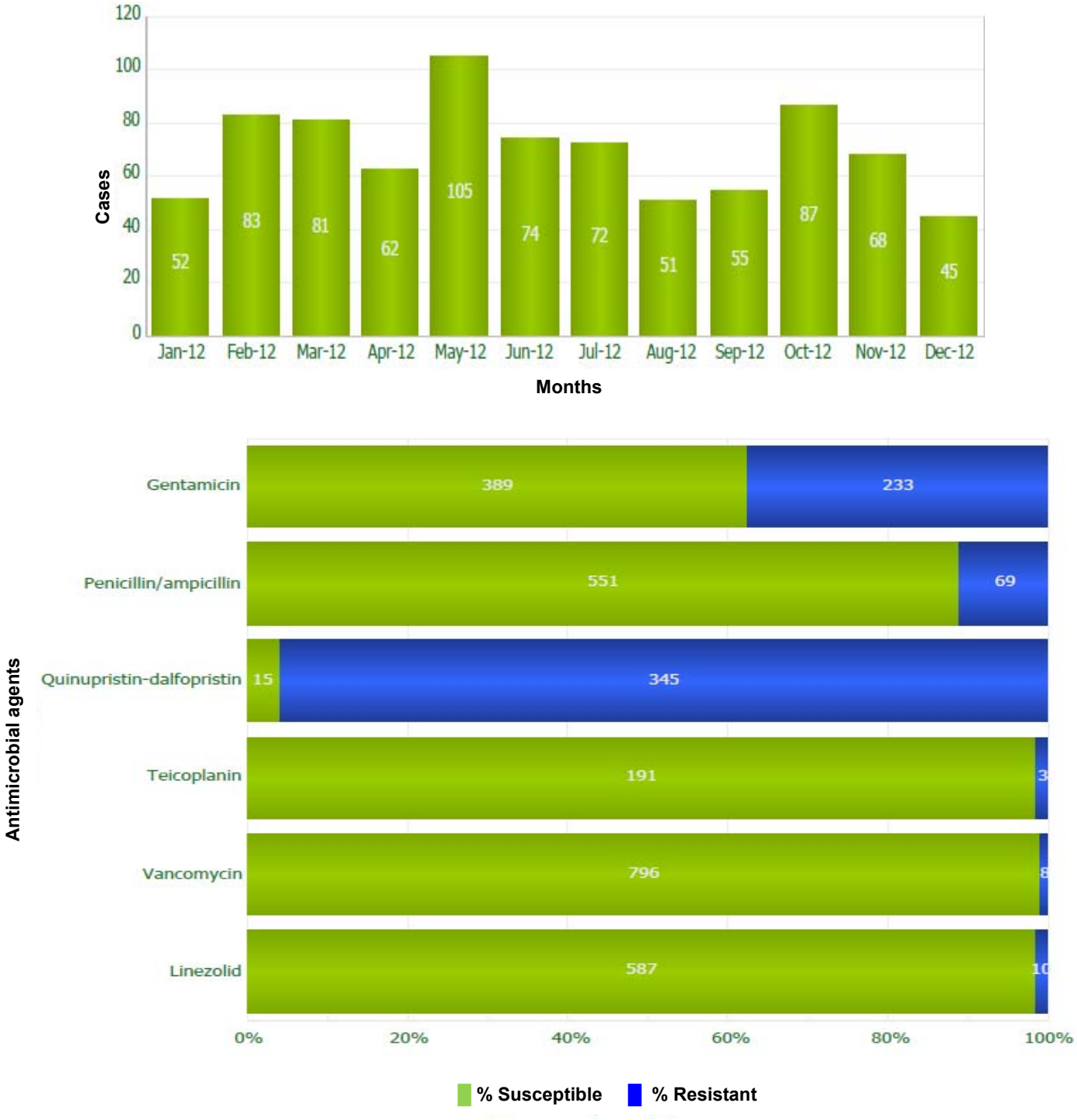

Figure 7: *Enterococcus faecalis* cases by month, and numbers and percentages of susceptible and resistant *E. faecalis* isolates from blood cultures at public-sector sentinel sites, 2012. Total number of isolates analyzed = 835.

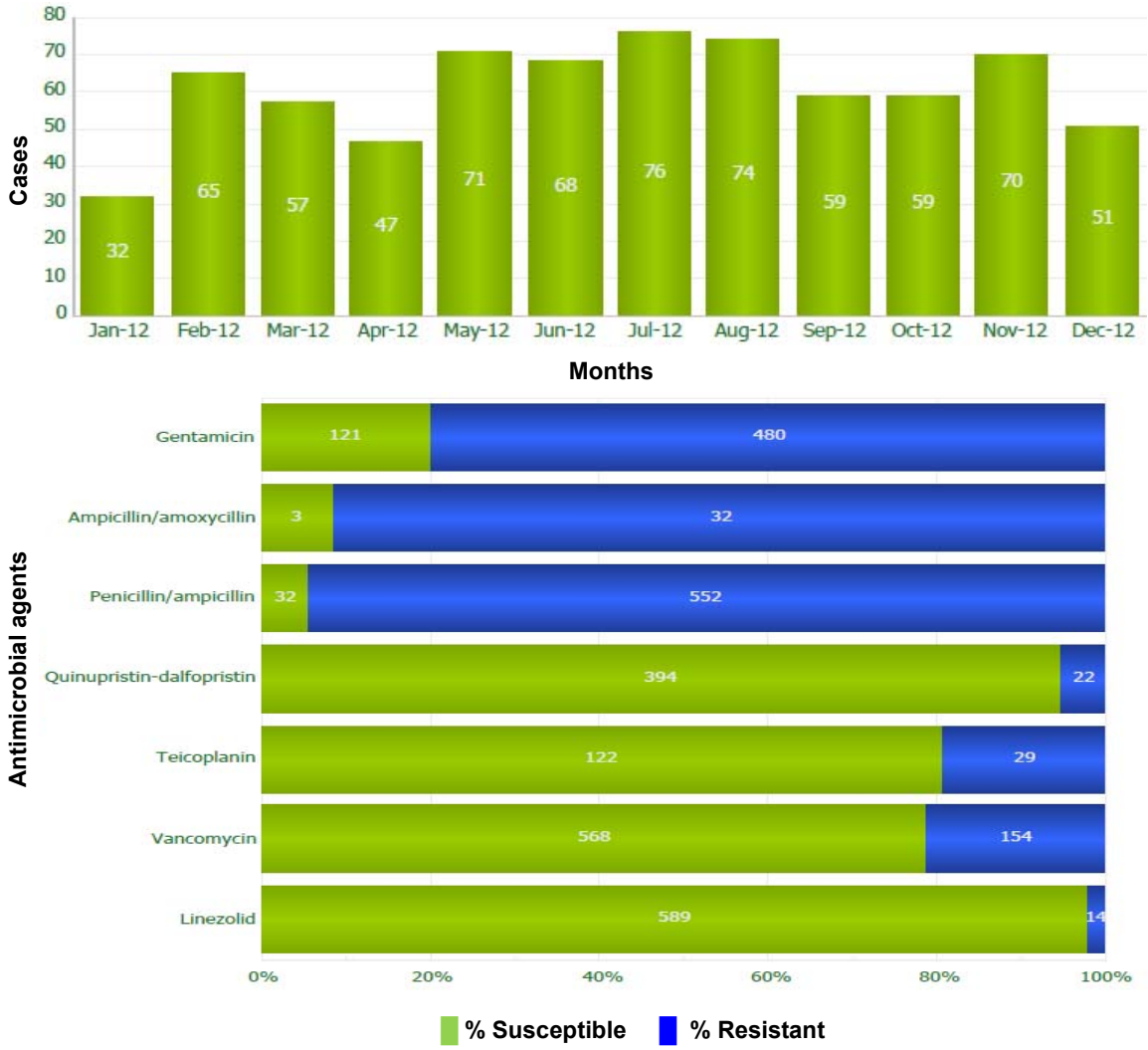

Figure 8: *Enterococcus faecium* cases by month, and numbers and percentages of susceptible and resistant *E. faecium* isolates from blood cultures at public-sector sentinel sites, 2012. Total number of isolates analyzed = 729.

Enterococci are intrinsically resistant to a broad range of antibiotics including cephalosporins, penicillins (*E. faecium*), sulfonamides, and low concentration of aminoglycosides. Vancomycin resistant *E. faecium* was recorded which may indicate an outbreak situation in the hospital setting.

Conclusion

The data presented in this report highlight the importance of surveillance for antimicrobial resistance patterns. Surveillance needs to be ongoing in order to identify trends as well as possible outbreaks.

Disclaimer

Data are reported as received through the CDW. No clinical data or molecular data were available to distinguish between hospital-associated and community acquired infections.

Acknowledgements

The NHLS CDW team is acknowledged for cleaning the data and preparing the table and figures.

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2. Garner JS et al. CDC definitions for nosocomial infections. *Am J Infect Control* 1988; 16:128-140.
3. Cockerill FR. Perfromance Standards for Antimicrobial Susceptibility Testing; Twenty-Second Informational Supplement; CLSI M100-S22 2012.

Table 1: Provisional number of laboratory confirmed cases of diseases under surveillance reported to the NICD - South Africa, corresponding periods 1 January - 31 December 2012/2013*

Disease/Organism	1 Jan to 31 Dec, year	EC	FS	GA	KZ	LP	MP	NC	NW	WC	South Africa
Anthrax	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	0	0	0	0	0	0
Botulism	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	0	0	0	0	0	0
Cryptococcus spp.	2012	1061	311	1955	1879	175	362	59	300	563	6665
	2013	709	247	2024	1687	147	363	53	258	540	6028
Haemophilus influenzae, invasive disease, all serotypes	2012	35	17	105	47	3	13	8	7	92	327
	2013	26	17	114	49	2	14	5	3	105	335
Haemophilus influenzae, invasive disease, < 5 years											
Serotype b	2012	2	5	18	3	1	4	2	2	12	49
	2013	5	1	11	5	0	2	0	0	6	30
Serotypes a,c,d,e,f	2012	2	0	5	0	0	1	0	0	6	14
	2013	0	1	5	2	0	1	1	0	8	18
Non-typeable (unencapsulated)	2012	0	1	18	6	0	0	0	0	14	39
	2013	0	1	5	2	0	1	1	0	8	18
No isolate available for serotyping	2012	6	2	11	8	0	4	2	1	8	42
	2013	1	4	25	9	1	5	1	0	9	55
Measles	2012	0	2	8	6	1	0	0	2	1	20
	2013	2	0	3	1	0	0	0	1	1	8
Neisseria meningitidis, invasive disease	2012	49	12	77	26	3	6	2	8	47	230
	2013	45	14	72	39	1	4	2	6	50	233
Novel Influenza A virus infections	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	0	0	0	0	0	0
Plague	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	0	0	0	0	0	0
Rabies	2012	1	1	0	4	3	1	0	0	0	10
	2013	0	2	0	1	3	1	0	0	0	7
Salmonella spp. (not typhi), invasive disease	2012	39	16	311	118	6	31	10	5	105	641
	2013	44	19	319	121	7	42	5	6	139	702
Salmonella spp. (not typhi), isolate from non-sterile site	2012	185	37	562	238	10	64	14	16	368	1494
	2013	199	72	992	305	18	128	15	57	512	2298
Salmonella typhi	2012	4	0	23	12	1	10	0	1	13	64
	2013	1	2	24	11	0	11	0	1	14	64
Shigella dysenteriae 1	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	0	0	0	0	0	0
Shigella spp. (Non Sd1)	2012	277	65	593	232	5	35	31	9	393	1640
	2013	261	88	679	289	14	64	17	31	314	1757
Streptococcus pneumoniae, invasive disease, all ages	2012	314	218	1293	578	65	161	48	128	419	3224
	2013	301	191	998	497	53	136	80	130	480	2866
Streptococcus pneumoniae, invasive disease, < 5 years	2012	52	34	241	81	6	20	7	17	51	509
	2013	44	41	214	75	6	10	7	32	69	498
Vibrio cholerae O1	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	1	0	0	0	0	1
Viral Haemorrhagic Fever (VHF) Crimean Congo Haemorrhagic Fever (CCHF)	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	2	0	0	0	2	0	1	0	5
Other VHF (not CCHF)	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	0	0	0	0	0	0

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.

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 - 31 December 2012/2013*

Programme and Indicator	1 Jan to 31 Dec, 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	2012	59	29	68	72	45	46	3	18	27	367
	2013	64	19	63	83	49	39	24	7	39	387

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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U = unavailable, 0 = no cases reported

Monitoring for the presence of polio in a country is based on AFP (acute flaccid paralysis) surveillance – the hallmark clinical expression of paralytic poliomyelitis. The clinical case definition of AFP is an acute onset of flaccid paralysis or paresis in any child under 15 years of age. AFP is a statutory notifiable disease and requires that 2 adequate stool specimens are taken as soon as possible, 24 to 48 hours apart, but within 14 days after onset of paralysis, for isolation and characterisation of polio virus. The differential diagnosis of AFP is wide, the most common cause of which is Guillain-Barre Syndrome. The incidence of AFP in a population has been studied in a number of developing countries and WHO have determined, as a result of these studies, that the criterion for adequate surveillance of AFP is 2 cases per 100 000 population of children less than 15 years of age (it was formerly 1 per 100,000 but this was thought to be inadequately sensitive).

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