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Annual Report 2007

NICD

NHLS

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Cover photograph: GERMS-SA Principal Investigator Meeting, 10 October 2007

Foreword

Prof. Anwar Hoosen
Pretoria Academic Hospital

The publication of this Annual Report of the Group for Enteric, Respiratory and Meningeal disease Surveillance in South Africa (GERMS-SA) is coordinated by a group of workers based at the National Institute for Communicable Diseases (NICD), a branch of the National Health Laboratory Service (NHLS), Johannesburg. Good national surveillance data collection and analysis requires the collaborative efforts of partners who are located at various institutions and laboratories throughout the country. Hence, credit for this comprehensive, informative and extremely useful report must be given to the NICD, together with its collaborating partners.

Laboratory-based surveillance was initiated in the late 1990s for some of the pathogens currently under the GERMS-SA umbrella. The formation of the NHLS and establishment of the NICD enabled and facilitated the development of a national laboratory-based surveillance system. The surveillance system has matured, resulting in the compilation of surveillance summaries such as these in recent years. It is envisaged that this system will improve further with greater participation from academic centres and participating laboratories. The development and application of newer molecular technologies for laboratory characterisation and tracking of pathogens promises further enhancement of surveillance data.

Good surveillance data, as documented in this report, has great value for health care professionals and administrators. Monitoring trends in prevalence and incidence of infectious agents in a country with an extremely high HIV/AIDS burden is of utmost importance. Medical microbiologists, public health specialists, infectious diseases specialists and policy makers greatly value information on antimicrobial susceptibility patterns and characteristics of pathogenic micro-organisms. Besides monitoring hospital-acquired pathogens, the detection of antimicrobial resistance in isolates from the community is also of great importance. Furthermore, national laboratory-based surveillance systems will need to be expanded as newer vaccines for rotavirus and HPV are introduced into the public health sector.

Who would have predicted some 10 to 20 years ago that HIV/AIDS would have such an impact? This report contains important information on organisms such as *Cryptococcus neoformans, Streptococcus pneumoniae* and non-typhoidal *Salmonella* which play a significant role in the epidemic. In South Africa, good surveillance systems and relevant data are essential to inform interventions to control this ravaging epidemic.

Introduction

This year's annual report presents a summary of key surveillance findings from GERMS-SA for 2007. A major development in 2007 was the establishment of the National Health Laboratory Services (NHLS) Corporate Data Warehouse (CDW). This is a centralised repository from which data on laboratory tests performed at NHLS laboratories throughout the country (excluding KwaZulu-Natal) can be extracted. The CDW is still in the pilot stages of development but offers great scope for strengthening surveillance. In 2007, the GERMS-SA programme was able to use the CDW to perform a complete audit of laboratory-confirmed cases reported to the National Institute for Communicable Diseases (NICD); this audit encompassed all pathogens under surveillance except *Pneumocystis jirovecii* and diarrhoeagenic *Escherichia coli*.

The inclusion of audit data represents a change to the surveillance system methodology and allows for the inclusion of cases that would have previously been missed into the surveillance database. This creates challenges for the interpretation of trends in burden of disease. For most pathogens, numbers of reported cases in 2007 will be falsely elevated as compared to 2006. This could lead to incorrect interpretations of outbreaks of disease or might mask a true decline in case numbers. It is essential that data in this report be presented with a proviso informing readers of the change in surveillance methodology.

Although presenting challenges in data interpretation, the introduction of the CDW has potential to enhance the quality of surveillance data. The ability to perform complete audits allows GERMS-SA to more accurately estimate numbers of laboratory-confirmed cases of diseases under surveillance diagnosed at NHLS laboratories. It also has future potential for real-time identification of surveillance isolates making it possible for automated reports to be sent out alerting investigators and surveillance officers of a surveillance case. This could allow more timeous case investigation and response.

Continuous review and improvement is an essential component of a successful surveillance system. Changes to the surveillance system must, however, be accompanied by careful consideration of the impact on the system as a whole. GERMS-SA continues to grow from year to year and this year's annual report reflects this process of continuous improvement.

Methods

The methods utilised by the GERMS-SA surveillance programme have been previously described in detail (1).

In brief, approximately 125 South African clinical microbiology laboratories participated in the surveillance programme in 2007. The population under surveillance in 2007 was estimated at 48 million (2). Diagnostic laboratories reported surveillance cases to the NICD using laboratory case report forms, according to standard case definitions. Case isolates, if available, were submitted on Dorset transport media to the NICD for further phenotypic and genotypic characterisation (1). At enhanced surveillance sites (16 sites in 9 provinces), surveillance officers completed case report forms for selected cases, by case patient interview or hospital medical record review, to obtain additional clinical details, including antimicrobial use, vaccination history, HIV status and patient outcome.

Data management was centralised at the NICD. Case data were recorded on an Epi Info version 6.04d (Centers for Disease Control and Prevention (CDC), Atlanta, USA) database. A surveillance audit was performed for NHLS laboratories in 8 provinces (excluding KwaZulu-Natal) between 1 January and 31 December 2007, using the CDW. The audit was designed to detect laboratory-confirmed cases not reported to GERMS-SA by participating laboratories. The audit included all surveillance cases, except *P. jirovecii* and diarrhoeagenic *E. coli*. Cases detected by audit were recorded on the surveillance database. Incidence rates were calculated using mid-year population estimates for 2006 and 2007 from Statistics South Africa (2) (Table 1). HIV/ AIDS incidence rates were calculated for 2006 and 2007 using data from the Actuarial Society of South Africa (ASSA) 2003 model (Table 1) (3). Reported p values were calculated using the Mantel-Haenszel chi-squared test and p values < 0.05 were considered significant.

Ethics approval for the ongoing activities of the surveillance programme was obtained from the Health Research Ethics Committee (Human), University of Witwatersrand (Clearance number M02-10-42). Surveillance activities were funded by the NICD/ NHLS; enhanced surveillance site

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activities continued to be partially funded by a CDC-NICD Cooperative Agreement (U62/ CCU022901).

Table 1: Population denominators used to calculate incidence rates, 2006 and 2007.

Province	General population (2)		HIV-infected population (3)		AIDS population (3)	
	2006	2007	2006	2007	2006	2007
Eastern Cape	7,058,842	7,074,056	666,822	698,699	64,096	70,031
Free State	2,961,843	2,968,607	387,770	391,527	46,249	48,392
Gauteng	9,205,778	9,359,765	1,407,486	1,431,389	156,328	162,429
KwaZulu Natal	9,733,138	9,817,592	1,540,183	1,552,390	193,028	200,628
Limpopo	5,668,602	5,711,471	396,873	415,652	39,474	42,559
Mpumalanga	3,245,356	3,270,896	446,010	450,975	57,470	59,017
Northern Cape	908,614	915,050	61,415	64,610	5,385	6,075
North West	3,851,660	3,876,587	480,387	489,585	54,083	57,718
Western Cape	4,752,960	4,850,324	267,289	283,742	19,736	22,524
South Africa	**47,386,793**	**47,844,348**	**5,654,235**	**5,778,569**	**635,849**	**669,373**

Operational Report

Site visits

In 2007, NICD staff members visited 34 surveillance sites in 7 provinces (Table 2). This provided an opportunity to engage with the laboratories and hospitals participating in the programme.

Table 2: GERMS-SA surveillance site visits between 1 January and 31 December 2007

Date	Province	Laboratory	Hospital
3-4 May 2007	Eastern Cape	NHLS Mthatha	Nelson Mandela Academic Complex
		NHLS Butterworth	Butterworth Hospital
		NHLS East London	Frere Hospital
		NHLS Cecilia Makiwane	Cecilia Makiwane Hospital
12-13 July 2007	Eastern Cape	NHLS Port Elizabeth	-
		Pathcare Port Elizabeth	-
		NHLS Grahamstown	Settlers Hospital
		NHLS Uitenhage	Uitenhage Hospital
18-19 April 2007	Free State	NHLS Manapo	Manapo Hospital
		NHLS Bethlehem	Bethlehem Hospital
31 January 2007	Gauteng	NHLS Helen Joseph	Helen Joseph Hospital
15 March 2007	Gauteng	Ampath Pretoria	-
		Lancet Pretoria	-
25 April 2007	Gauteng	Ampath Metalbox	-
13 September 2007	Gauteng	NHLS DGMH	Dr George Mukhari Hospital
19 September 2007	Gauteng	NHLS CHBH	Chris Hani Baragwanath Hospital
19 September 2007	Gauteng	NHLS Sebokeng	Sebokeng Hospital
4 October 2007	Gauteng	NHLS Johannesburg Hospital	Johannesburg Hospital
17-18 April 2007	KwaZulu Natal	NHLS PMMH	Prince Mshiyeni Hospital
		NHLS IALH	King Edward VIII Hospital
23-24 July 2007	KwaZulu Natal	NHLS GJ Crookes	GJ Crookes Hospital
		NHLS Port Shepstone	Port Shepstone Hospital
15-16 August 2007	Northern Cape	NHLS Upington	Gordonia Hospital
		Ampath Upington	-
		NHLS Springbok	Springbok Hospital
6-7 December 2007	North West Province	NHLS Gelukspan	Gelukspan Hospital
		NHLS Thusong	Thusong Hospital
14-18 May 2007	Western Cape	NHLS Paarl	Paarl Hospital
		NHLS Worcester	Eben Donges Hospital
		Pathcare Cape Town	-
		NHLS Tygerberg	Tygerberg Hospital
		NHLS Greenpoint	-
26 July 2007	Western Cape	NHLS George	George Hospital
		Pathcare George	-

Surveillance audit

The surveillance audit detected more than 3,400 additional cases which had not been reported to the surveillance programme (Table 3).

Table 3: Cases detected by surveillance audit by province, 2007.

Surveillance case		Percentage of cases detected by audit* n_1/n_2 (%)	Number of cases detected by audit									
			EC	FS	GA	KZ	LP	MP	NC	NW	WC	SA
Invasive	Typhoid	1 / 58 (2)	0	0	0	0	0	0	0	0	1	1
	Non-typhoidal salmonellosis	159 / 938 (17)	44	8	67	0	4	10	9	11	6	159
	Shigellosis	10 / 66 (15)	4	1	4	0	0	1	0	0	0	10
	Cryptococcosis	1774/ 7149 (25)	535	114	343	0	212	335	18	127	90	1774
	Meningococcal disease	47 / 507 (9)	3	3	22	0	0	6	1	3	9	47
	Haemophilus influenzae disease	88/ 420 (21)	18	4	41	0	2	8	1	2	12	88
	Pneumococcal disease	811 / 4733 (17)	117	58	346	0	38	89	12	63	88	811
Non-invasive	Salmonella Typhi	0 / 13 (0)	0	0	0	0	0	0	0	0	0	0
	Non-typhoidal salmonellosis	310 / 1144 (27)	56	16	102	0	29	35	13	24	35	310
	Shigellosis	240 / 1425 (17)	34	11	101	0	8	18	5	17	46	240
	Cholera	0 / 0 (0)	0	0	0	0	0	0	0	0	0	0
Total		**3440 / 16448 (21)**	**811**	**215**	**1026**	**0**	**293**	**502**	**59**	**247**	**287**	**3440**

*Percentage of cases detected by audit = number of cases detected on audit (n_1)/ total number of cases detected by GERMS-SA (n_2)*100

EC: Eastern Cape; FS: Free State; GA: Gauteng; KZ: KwaZulu-Natal; LP: Limpopo; MP: Mpumalanga; NC: Northern Cape; NW: North West; WC: Western Cape; SA: South Africa

Coordination meetings

Surveillance Officer meeting, 8-9 March 2007

This meeting, convened at the NICD, was attended by 18 surveillance officers from 8 provinces and 2 site coordinators from KwaZulu-Natal and Western Cape. The meeting included two days of training, and discussion of enhanced surveillance site performance indicators. The meeting focused on patient access to anti-retroviral treatment at enhanced surveillance sites.

Surveillance Officer meeting, 21-22 November 2007

The meeting, convened at the NICD in Johannesburg, was attended by 20 surveillance officers from 8 provinces. Feedback from the Principal Investigators meeting and projects from the 2006-2007 period, data collection issues and presentation of surveillance indicators and the new case report form were covered during the meeting.

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Principal Investigator (PI) meeting, 10-11 October 2007

The 2 day PI meeting, convened at the NICD in Johannesburg, was attended by over 50 local, national and international delegates, including representatives from the Department of Health. Surveillance and research achievements emanating from the GERMS-SA programme were presented by surveillance project leaders. Surveillance and research plans for 3 AIDS-associated opportunistic infections: cryptococcosis, non-typhoidal salmonellosis and pneumococcal disease were discussed in workshops. The inaugural steering committee meeting was convened after the PI meeting.

Surveillance Reports

Salmonella enterica serotype Typhi

Enteric Diseases Reference Unit

Results

Table 4: Number of invasive and non-invasive *Salmonella* Typhi isolates (n =71) reported to EDRU by province, South Africa, 2007.

Province	Invasive *Salmonella* Typhi	Non-invasive *Salmonella* Typhi
Eastern Cape	10	2
Free State	0	1
Gauteng	20	1
KwaZulu Natal	9	1
Limpopo	4	2
Mpumalanga	6	6
Northern Cape	0	0
North West	2	0
Western Cape	7	0
South Africa	**58**	**13**

Table 5: Number of *Salmonella* Typhi isolates reported to EDRU (n =71) by age category, 2007.

Age category (years)	Number of isolates
<1	4
1 - 5	7
6 - 14	18
15 - 64	37
>64	0
Unknown	5
South Africa	**71**

Table 6: Results of antimicrobial susceptibility testing for *Salmonella* Typhi isolates (n = 70) received by EDRU, 2007, excluding isolates identified by audit.

Antimicrobial tested	Susceptible (%)	Intermediate (%)	Resistant (%)
Ampicillin	91.4	0.0	8.6
Cotrimoxazole	91.4	0.0	8.6
Chloramphenicol	97.1	0.0	2.9
Nalidixic acid	92.9	0.0	7.1
Ciprofloxacin	100.0	0.0	0.0
Tetracycline	88.6	1.4	10.0
Kanamycin	100.0	0.0	0.0
Streptomycin	92.9	0.0	7.1
Imipenem	100.0	0.0	0.0
Ceftriaxone	100.0	0.0	0.0

Discussion

The number of *Salmonella* Typhi isolates was regarded as too small to calculate incidence rates (Table 4). These were culture-confirmed cases and thus excluded those patients in whom a serological diagnosis was made without culture. Two

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isolates of *Salmonella* Paratyphi A from the Western Cape and two of *Salmonella* Paratyphi C were received, from the Western Cape and Gauteng respectively. One adult female with *Salmonella* Paratyphi A had travelled to India and the isolate may have been imported. No travel history was elicited from the remaining three adults. *Salmonella* Typhi isolation by month showed seasonality, with increased numbers between October and February (Figure 1). No major outbreaks were detected in 2007. Typhoid fever occurred in children less than five years of age (Table 5). Certain antimicrobials were tested for epidemiological purposes only and should not be used for treatment of typhoid fever. All *Salmonella* Typhi isolates received in 2007 were susceptible to ciprofloxacin (Table 6), the treatment of choice, although the occurrence of nalidixic acid resistance is cause for concern. Nalidixic acid resistance may be used as a marker for quinolone resistance; it is indicative of the potential for an organism to develop fluoroquinolone resistance (4). Response to ciprofloxacin may be poor in the presence of nalidixic acid resistance. The *Salmonella* Paratyphi A isolates were both resistant to nalidixic acid, but susceptible to ampicillin, co-trimoxazole and chloramphenicol. One isolate of *Salmonella* Paratyphi C was fully susceptible to all antimicrobials tested, but the other was resistant to nalidixic acid.

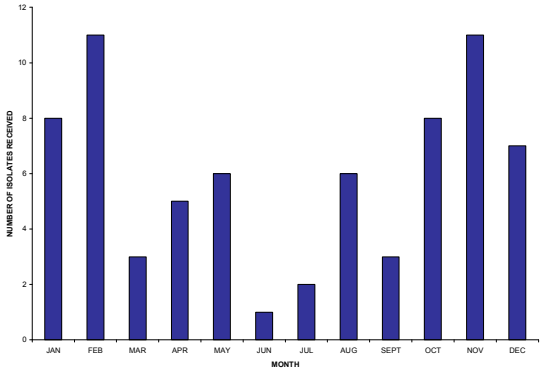

Figure 1: Number of *Salmonella* Typhi isolates reported to EDRU by month of isolation, 2007.

Non-typhoidal *Salmonella enterica* (NTS)

Enteric Diseases Reference Unit

Results

Table 7: Number* of non-invasive and invasive non-typhoidal *Salmonella* isolates (n = 2082) reported to EDRU by province, South Africa, 2007, including those identified on audit.
(province unknown for 3/2085)

Province	Invasive non-typhoidal *Salmonella*	Non-invasive non-typhoidal *Salmonella*
Eastern Cape	87	197
Free State	48	46
Gauteng	478	357
KwaZulu Natal	114	110
Limpopo	28	56
Mpumalanga	37	139
Northern Cape	13	23
North West	43	58
Western Cape	90	158
South Africa	**938**	**1144**

*Incidence rates were not calculated as there may be regional differences in specimen collection practices.

Table 8: Number of non-invasive and invasive non-typhoidal *Salmonella* isolates reported to EDRU by age category, 2007 and incidence rates of invasive NTS by age category.

Age Category (years)	Cases		
	Non-invasive	Invasive	Cases 100,000
<1	261	203	19.11
1 - 5	194	97	1.92
6 - 14	74	54	0.60
15 - 64	486	516	1.71
>64	46	21	0.85
Unknown	86	47	-
Total	**1147**	**938**	1.96

*Incidence rates for non-invasive non-typhoidal *Salmonella* were not calculated because not all cases of gastroenteritis due to non-typhoidal *Salmonella* may be cultured in clinical practice.

Table 9: Number of non-typhoidal *Salmonella* isolates reported to EDRU by anatomical site of isolation*, 2007, including those identified on audit.

Specimen	n	%
CSF	24	1.15
Blood culture	826	39.62
Stool	858	41.15
Other	377	18.08
Total	**2085**	**100**

*Note that many cases had multiple isolates of the same serotype, including those with isolates from an invasive site and a second isolate from stool. Mixed infections with different *Salmonella* serotypes were not identified in 2007.

Table 10: Results of antimicrobial susceptibility testing for all non-typhoidal *Salmonella* isolates (n = 1504) tested by EDRU, 2007, excluding isolates identified on audit.

Antimicrobial tested	Susceptible (%)	Intermediately resistant (%)	Resistant (%)
Ampicillin	62.6	0.1	37.3
Cotrimoxazole	63.4	0.0	36.6
Chloramphenicol	66.7	1.5	31.8
Nalidixic acid	71.6	0.0	28.4
Ciprofloxacin	99.7	0.2	0.1
Tetracycline	54.7	10.9	34.4
Kanamycin	85.5	6.8	7.7
Streptomycin	66.2	0.0	33.8
Imipenem	100.0	0.0	0.0
Ceftriaxone	82.3	0.0	17.7

Discussion

A lack of clear seasonality reflected the nosocomial nature of many of the invasive cases, as well as the burden of disease associated with HIV infection (Figure 2 and Table 8). *Salmonella* meningitis is a significant disease in this population.

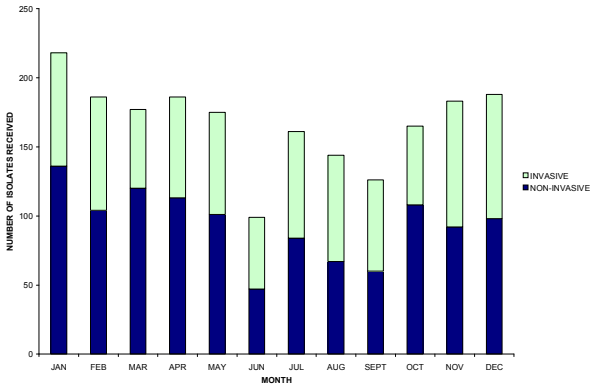

Figure 2: Number of non-invasive and invasive non-typhoidal *Salmonella* isolates reported to EDRU by month of isolation, 2007 - including those identified on audit.

Non-invasive disease appeared to be seasonal. Certain antimicrobial agents were tested for epidemiological reasons only and should not be used for treatment. Of those NTS isolates tested, 266 (17.7%) were noted to be extended spectrum beta-lactamase (ESBL) producers. Nalidixic acid resistance is a cause for concern because it is a marker of increasing resistance to the quinolones and is associated with poor response to fluoroquinolone treatment in clinical cases (4). Nalidixic acid resistance, in combination with ESBL production, was identified in 208 (13.8%) NTS isolates. Pentavalent resistance (resistance to five or more antimicrobials) was observed in 512 (34.0%) isolates. Multi-drug resistant serotypes included primarily *Salmonella* Typhimurium and *Salmonella* Isangi (Table 10).

***Shigella* spp.**
Enteric Diseases Reference Unit

Results

Table 11: Number of invasive and non-invasive *Shigella* isolates (n =1491) reported to EDRU by province, South Africa, 2007.

Province	Invasive *Shigella*	Non-invasive *Shigella*
Eastern Cape	10	196
Free State	4	81
Gauteng	27	432
KwaZulu-Natal	7	123
Limpopo	2	25
Mpumalanga	7	126
Northern Cape	0	52
North West	0	41
Western Cape	9	349
South Africa	**66**	**1425**

Table 12: Case numbers* and incidence rates for *Shigella* (invasive and non-invasive) reported to EDRU by age category, 2007.

Age Category (years)	Cases	
	n	Cases /100,000
<1	164	15.44
1 - 5	587	11.63
6 - 14	149	1.65
15 - 64	466	1.54
>64	50	2.03
Unknown	75	-
Total	**1491**	**3.12**

*Cases may be underreported due to local clinical practices.

Discussion

Invasive shigellosis is not common compared with overall burden of disease (Table 11). The predominant burden of reported disease was in the under five-year age group (Table 12). Higher isolation rates in January and from October to December in 2007 suggest seasonality (Figure 3). During this period, a number of water-borne outbreaks were detected, with numerous enteric pathogens implicated (5). This also resulted in increased numbers of *Shigella* isolates seen during this time period. Quinolone resistance remained low (Table 13). Nine of 1227 isolates tested were ESBL-producers. Certain anti-microbials were tested for surveillance purposes only and should not be used for treatment. *S. dysenteriae* type 1 remains rare, and *S. flexneri* type 2a predominates as the commonest sero-type causing endemic disease (Table 14).

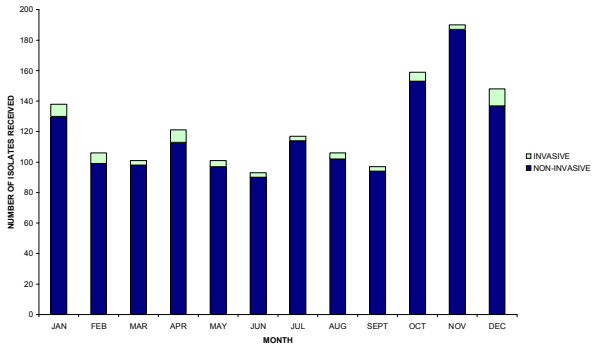

Figure 3: Number of non-invasive and invasive *Shigella* isolates reported to EDRU by month of isolation, 2007, including audit specimens.

Table 13: Results of antimicrobial susceptibility testing for *Shigell*a isolates (n =1227) received by EDRU, 2007.

Antimicrobial tested	Susceptible (%)	Intermediately resistant (%)	Resistant (%)
Ampicillin	50.6	0.1	49.3
Cotrimoxazole	16.9	0.0	83.1
Chloramphenicol	66.1	0.2	33.7
Nalidixic acid	99.0	0.0	1.0
Ciprofloxacin	100.0	0.0	0.0
Tetracycline	50.9	1.2	47.9
Kanamycin	99.4	0.2	0.4
Streptomycin	43.7	0.0	56.3
Imipenem	100.0	0.0	0.0
Ceftriaxone	99.3	0.0	0.7

Table 14: Commonest* invasive and non-invasive *Shigella* serotypes (n = 1227) reported to EDRU by province, 2007. excluding those identified by audit.

Province	*S. dysenteriae* type 1	*S. flexneri* type 1b	*S. flexneri* type 2a	*S. flexneri* type 6	*S. sonnei* phase II
Eastern Cape	0	33	62	10	7
Free State	1	14	19	8	0
Gauteng	0	41	113	44	17
KwaZulu-Natal	0	33	34	5	1
Limpopo	0	2	3	4	3
Mpumalanga	0	17	19	13	1
Northern Cape	0	9	22	5	0
North West	0	3	5	5	0
Western Cape	0	67	109	33	6
South Africa	**1**	**219**	**386**	**127**	**35**

*Including *Shigella dysenteriae* type 1. Although these isolates are rare, the potential for future epidemics remains while these strains are in circulation.

Diarrhoeagenic *Escherichia coli* (DEC)

Enteric Diseases Reference Unit

Results

Table 15: Number of diarrhoeagenic *Escherichia coli* isolates (n = 269) reported to EDRU by province, South Africa, 2007, representing 253 infectious episodes, including those patients which had more that one pathotype (see below). No audits were conducted. (Province unknown for 6/275)

Province	DAEC	EAggEC	EHEC/ STEC	EIEC	EPEC	ETEC
Eastern Cape	5	9	0	0	18	6
Free State	0	0	0	0	3	0
Gauteng	1	13	0	0	44	2
KwaZulu-Natal	0	0	0	0	0	0
Limpopo	0	0	0	0	2	0
Mpumalanga	53	26	2	11	17	20
Northern Cape	1	4	1	0	4	4
North West	7	4	0	2	0	1
Western Cape	4	1	0	0	4	0
South Africa	**71**	**57**	**3**	**13**	**92**	**33**

DAEC, Diffusely adherent *E. coli*; EAggEC, enteroaggregative *E. coli*; EHEC, STEC, Shiga-toxigenic *E. coli* enterohaemorrhagic *E. coli*; EIEC, enteroinvasive *E. coli*; EPEC, enteropathogenic *E. coli*; ETEC, enterotoxigenic *E. coli*.

Table 16: Number of diarrhoeagenic *E. coli* isolates (n = 275) reported to EDRU by age category, 2007.

Age category (years)	DAEC	EAggEC	EHEC/ STEC	EIEC	EPEC	ETEC
<1	12	22	0	0	47	8
1 - 5	15	14	1	3	24	12
6 – 14	7	2	0	3	3	2
15 - 65	34	14	2	6	10	8
>65	1	1	0	0	0	0
Unknown	2	4	6	1	8	3
Total	**71**	**57**	**9**	**13**	**92**	**33**

Discussion

The predominance of isolates received in children under the age of one year may reflect culturing practices; infants are more likely to have stools taken for culture due to the devastating effects of diarrhoea in children of this age. Numbers of isolates through the year were greatly affected by the occurrence of diarrhoeal outbreaks (5), during which a number of patients were identified as having more than one pathogen, including a number of pathotypes of diarrhoeagenic *E. coli* (Table 15). This was particularly notable in adults in whom typically "paediatric" strains of *E. coli* were identified (Table 16). Increased numbers of both DAEC and EAggEC were identified during the diarrhoeal outbreaks. Incidence rates were not calculated as numbers are not viewed as being fully representative. EHEC O26, which has been associated with outbreaks in the past, was identified during the Delmas diarrhoeal outbreak in November 2007 (6-8). Serotypes associated with EPEC included O111, O119, O127 and O55. STEC serotypes were more diverse, diverse serotypes were also noted for other enterovirulent *E. coli* isolates. Identification of both EHEC and STEC was incidental (9). The occurrence of serotype O55 is of interest as it has previously been shown that enterohaemorrhagic *E. coli* O157 evolved from this serotype (10).

Vibrio cholerae O1

Enteric Diseases Reference Unit

No *Vibrio cholerae* O1 isolates from cases in South Africa were received by EDRU in 2007. No imported cases were identified.

Cryptococcus spp.

Mycology Reference Unit

Results

During 2007, 7149 incident cases of cryptococcosis were detected; 1774 cases by surveillance audit. In total, 6105 isolates were received by the Mycology Reference Unit (MRU), of which 5630 (92%) were viable. Of 5588 isolates which were speciated, 5474 (98%) were identified as *Cryptococcus neoformans*; 112 were identified as *Cryptococcus gattii* and the species identification of 2 isolates was inconclusive by phenotypic testing. Eighty nine cases of *C. gattii* infection were identified; most cases were diagnosed in the north-eastern regions of the country (Figure 4). The overall incidence rate in the South African general population was 15/100,000 (2). The incidence of cryptococcosis amongst HIV-infected individuals was 133/100,000 cases, and amongst people sick with AIDS was 12/1000 AIDS cases (2).

In the Eastern Cape, where a surveillance audit was performed for both 2006 and 2007, incidence rates decreased from 19/100,000 to 14/100,000 (Table 17). In KwaZulu-Natal, where no surveillance audits were performed, incidence rates remained stable. In other provinces, the surveillance audit performed solely in 2007 influenced the number of detected cases; hence, trends are more difficult to interpret (Table 17). Most cases of laboratory-confirmed cryptococcosis continue to be diagnosed in urbanised or mining districts (Figure 5). Of 6590/7149 (92%) cases where age was known, 116 cases were identified in children <15 years of age. The highest incidence of cryptococcosis was in the 35-39 year age group (Figure 6). Where gender was known (7016/7149, 98%), 54% of cases occurred in females.

(Continued on page 13)

(Continued from page 12)

Most incident cases (96%) were diagnosed with meningitis (laboratory tests on cerebrospinal fluid positive for *Cryptococcus* species), and 3.4% with fungaemia (Table 18). The remainder of cases (n=17), where specimen type was known, were diagnosed by culture of urine, sputum, pus, pleural fluid and other specimen types.

Of 1549 incident cases presenting to enhanced surveillance sites (tertiary or regional hospitals) and with completed clinical case report forms at the time of analysis, 486 cases (31%) died during the first hospital admission (outcome known for 1539/1549 cases, 99%).

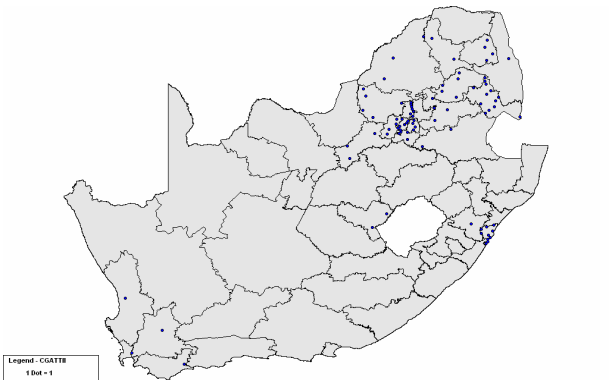

Figure 4: Cases of *Cryptococcus gattii* (n=89) by health district of South Africa, 2007.

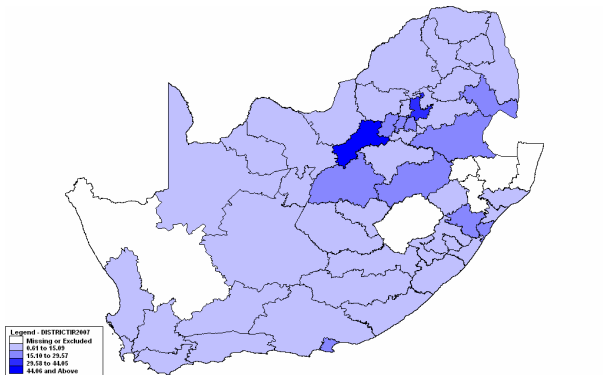

Figure 5: Chloropleth distribution map of incidence of cryptococcosis by health district in South Africa, 2007.

Table 17: Number of cases and incidence rates of *Cryptococcus* spp. as reported to MRU by province, South Africa, 2006 and 2007.

Province	2006*		2007§	
	n	Cases/100,000	n	Cases/100,000
Eastern Cape	1357	19	1017	14
Free State	287	10	524	18
Gauteng	1856	20	2041	22
KwaZulu-Natal	1348	14	1269	13
Limpopo	215	4	471	8
Mpumalanga	439	14	749	23
Northern Cape	63	7	61	7
North West	378	10	588	15
Western Cape	353	7	429	9
South Africa	**6296**	**13**	**7149**	**15**

*In 2006, a surveillance audit was performed for NHLS laboratories only in the Eastern Cape; 953 additional microscopy (India ink) or culture-confirmed incident cases were detected by audit.
§In 2007, a surveillance audit was performed for all NHLS laboratories in 8 provinces (excluding KwaZulu-Natal); 1774 additional microscopy (India ink) or culture-confirmed incident cases were detected on audit.

Table 18: Number and percentage of incident cases of cryptococcal disease as reported to MRU by specimen type, South Africa, 2007.

Site of specimen	n	%
CSF	6860	96
Blood	245	3.4
Other	17	0.2
Unknown	27	0.4
Total	**7149**	

Discussion

Overall, almost 800 more laboratory-confirmed cases of cryptococcosis were detected by GERMS-SA in 2007, compared with 2006. Most patients continue to be diagnosed with meningitis in urbanised centres, and this probably reflects clinician specimen-taking practices. The demographic profile of cases with cryptococcosis continues to mirror the profile of HIV-infected patients in South Africa. Paediatric cryptococcosis remains a relatively uncommon clinical entity, though it must be considered as part of a differential diagnosis. The in-hospital mortality of patients with cryptococcosis remains unacceptably high. It is hoped that the recent publication of Southern African guidelines for the clinical management of HIV-infected patients with cryptococcosis will have an impact on patient survival (11).

The use of highly active antiretroviral treatment (HAART) in developed countries has impacted significantly on incidence of AIDS-associated cryptococcosis (12). In South Africa, where it is estimated that 350,000 HIV-infected people accessed HAART through the National HIV/AIDS Comprehensive Care, Management and Treatment (CCMT) Programme by the end of 2007 (13), similar trends are anticipated. However, the comparison of provincial incidence rates between 2006 and 2007 has been influenced by the surveillance audit performed in 2007, with the exception of the Eastern Cape where a surveillance audit was performed for both years and KwaZulu-Natal, where no surveillance audits were performed at all. Decreased incidence rates in the Eastern Cape in 2007 compared with 2006, and stable case numbers in KwaZulu-Natal in 2006 and 2007 suggest that access to HAART has made an impact. The increase in detected cases in Limpopo (100% increase), Free State (80% increase), Mpumalanga (63% increase) and North West (50% increase) may be explained by more active case-finding (driven by audits) in 2007. Fairly stable case numbers in the Western Cape, Gauteng and Northern Cape, despite active case-finding, may suggest that the CCMT Programme has made an impact in these provinces. These preliminary findings will require further careful investigation and monitoring of incidence rates.

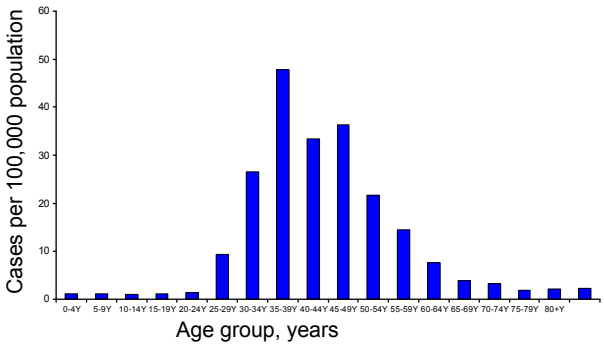

Figure 6: Age-related incidence of cryptococcosis in the general population, South Africa, n= 7149, age unknown: 561/7149 incident cases (8%)

Pneumocystis jirovecii

Parasitology Reference Unit

Results

In 2007, 286 cases of *Pneumocystis* pneumonia (PCP) were reported to the Parasitology Reference Unit through the GERMS-SA surveillance system (Table 19).

The number of cases reported was approximately the same compared to 2006. These numbers do not reflect the true burden of PCP in the country, as PCP is not fully reported, for several reasons. Few laboratories test for *Pneumocystis* pneumonia, bronchoscopy is expensive, and induced sputum requires specialized equipment and trained personnel to obtain adequate samples (14).

Numbers of PCP isolates peaked in children less than one year of age and in the 21 to 60 year age group (Figure 7). Of cases with known gender 59% (144/244) were female. Studies have shown that heterosexual women and women of unknown risk appear more likely than their male counterparts to contract PCP (15).

Sixty four patients presented to enhanced surveillance sites. The discharge diagnosis was known for 48 patients (75%) and 45 had a lower respiratory tract infection. Of the 41 cases with available data on outcome, 18 (44%) died during the admission. Twenty one of 23 patients with data on discharge medications received cotrimoxazole on discharge.

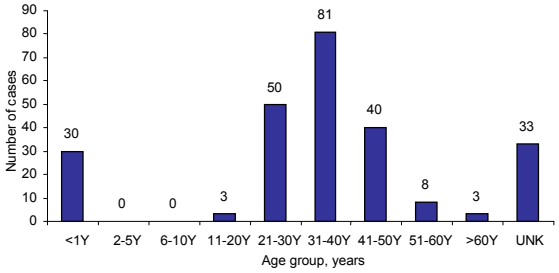

Figure 7: Number of PCP cases reported by age group, South Africa, 2007

Table 19: Number of *Pneumocystis* pneumonia cases reported by province, 2006-2007

Province	2006	2007
Eastern Cape	25	30
Free State	6	16
Gauteng	177	144
KwaZulu Natal	7	20
Limpopo	0	0
Mpumalanga	17	12
Northern Cape	0	0
North West	0	13
Western Cape	52	51
South Africa	**284**	**286**

Discussion

Before the widespread use of prophylaxis, it was estimated that 80% of people with AIDS would eventually develop PCP (16). Trimethoprim-sulfamethoxazole (TMP-SMX, cotrimoxazole) is used for treatment and prophylaxis. Prophylaxis has reduced the incidence of PCP, but has resulted in a significant correlation between the use of sulfa-drugs and point mutations in the dihydropteroate synthase (DHPS) gene (17). US studies have shown that patients with DHPS mutations are three times more likely to die compared to those with wild-type DHPS genes (17). Access to isolates from different areas in the country is useful for monitoring this aspect of cotrimoxazole resistance and the genetic diversity of strains.

Neisseria meningitidis

Respiratory and Meningeal Pathogens Reference Unit

Results

In 2007, 455 cases of meningococcal disease were reported to RMPRU, and an additional 47 cases were identified on audit: a total of 502 cases of laboratory-confirmed meningococcal disease were identified by the surveillance system during the year (Table 20). The number of cases reported increased during the winter and spring months (Figure 8). Of all cases reported to RMPRU, cerebrospinal fluid (CSF) was the most common specimen yielding meningococci (Table 21).

Cases of W135 disease were reported from all provinces. In Gauteng Province, the incidence of meningococcal disease was estimated at 3/100,000 population, and most of that disease was due to W135 (143/194, 74%) (Table 22). The preponderance of serogroup B disease in Western Cape Province was still noted: 25/51 (49%) of all cases serogrouped. Burden of disease was greatest in children less than five years of age. Age and serogroup -specific incidence rates show that infants were at greatest risk of disease for all serogroups (Figure 9).

Preliminary analysis of case fatality rates, as calculated in enhanced surveillance sites where in-hospital outcome is specifically looked for, was 35/183 (19%). This was similar to 2006 (30/224, 13%; p=0.12) (18). Only 6/277 (2%) isolates had penicillin minimum inhibitory concentrations (MICs) > 0.06µg/ml (19), and would be considered non-susceptible.

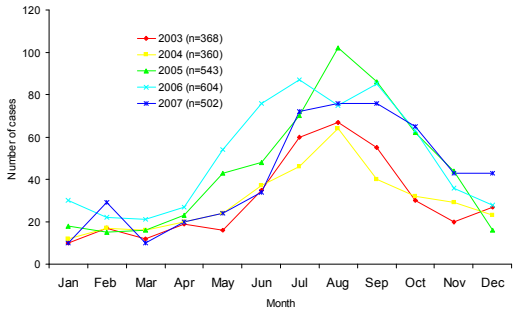

Figure 8: Number of cases of laboratory-confirmed meningococcal disease in South Africa as reported to RMPRU by month and year (2003-2007).

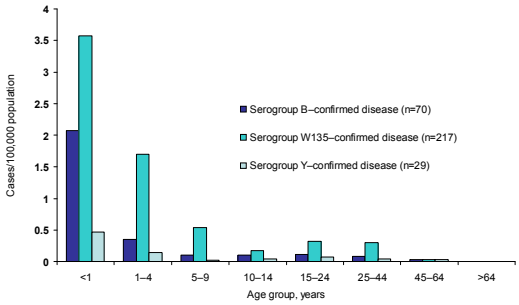

Figure 9: Reported age-specific incidence rates for confirmed serogroups B, W135 and Y, South Africa, 2007 (of 502 cases reported, 485 had known age, and 353 had specimens or viable isolates available for serogrouping).

Discussion

Overall incidence of disease did not change substantially from 2006, but in Gauteng Province, the burden of serogroup W135 disease decreased in 2007 in comparison to 2006 (18;20). The clinical relevance of increasing MICs is unclear, and penicillin is, at present, still being recommended as the drug of choice for therapy for confirmed meningococcal disease.

Table 20: Number of cases and incidence rates of meningococcal disease as reported to RMPRU by province, South Africa, 2006 and 2007.

Province	2006		2007	
	n	Cases/100,000	n	Cases/100,000
Eastern Cape	32	0.45	18	0.25
Free State	46	1.55	39	1.31
Gauteng	364	3.95	254	2.71
KwaZulu-Natal	20	0.21	33	0.34
Limpopo	8	0.14	9	0.16
Mpumalanga	26	0.80	26	0.79
Northern Cape	14	1.54	9	0.98
North West	25	0.65	37	0.95
Western Cape	69	1.45	77	1.59
South Africa	**604**	**1.27**	**502**	**1.05**

Table 21: Number and percentage of cases of meningococcal disease as reported to RMPRU by specimen type, South Africa, 2006 and 2007.

Site of specimen	2006		2007	
	n	%	n	%
CSF	448	74	384	76
Blood	152	25	116	23
Other	4	1	2	0.4
	604		**502**	

Table 22: Number of cases of meningococcal disease reported to RMPRU by serogroup and province (n=502, 353 (70%) with specimens or viable isolates available for serogrouping), South Africa, 2007.

Province	Serogroup								
	No isolate available	A	B	C	W135	Y	Z	Non-groupable	Total
Eastern Cape	8	0	2	2	3	3	0	0	18
Free State	14	0	5	3	12	4	1	0	39
Gauteng	60	5	30	4	143	12	0	0	254
KwaZulu-Natal	15	0	4	4	10	0	0	0	33
Limpopo	2	0	0	0	6	1	0	0	9
Mpumalanga	13	0	1	0	9	3	0	0	26
Northern Cape	2	0	2	3	2	0	0	0	9
North West	9	0	4	1	21	2	0	0	37
Western Cape	26	0	25	7	15	4	0	0	77
South Africa	**149**	**5**	**73**	**24**	**221**	**29**	**1**	**0**	**502**

Haemophilus influenzae

Respiratory and Meningeal Pathogens Reference Unit

Results

The number of cases of *Haemophilus influenzae* invasive disease reported in 2007 to RMPRU was 332, while an additional 88 cases were identified during the national audit (total number of cases available for analysis was 420). Of these, 226 (54%) had isolates or specimens available for serotyping, and 84/226 (37%) were confirmed as serotype b (Table 23). Serotype b isolates were more likely to be isolated from CSF than non-typeable *H. influenzae* (40/84 48% vs. 7/94 7%, p<0.001) (Table 24).

In 2007, a total of 54 cases of Hib were reported in children <5 years (Figure 10); an additional

four cases were identified on polymerase chain reaction (PCR) testing of transport specimens. Serotype b has again become the most important *H. influenzae* causing disease in infants (Figure 11). Since 2003, rates of Hib disease as recorded by our surveillance network in infants <1 year of age have increased, and there seems to be a continued increase in 2007, although not reaching significance (p=0.094, chi-squared test for trend, 2003 to 2007) (Figure 12).

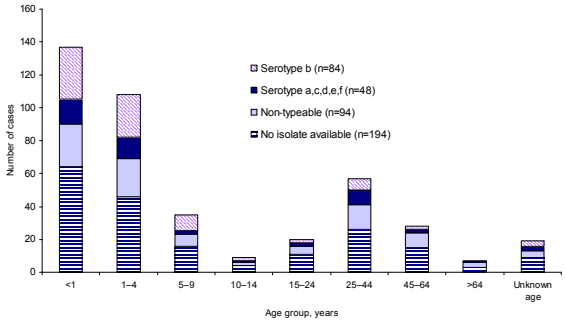

Figure 10: Number of cases of *Haemophilus influenzae* reported to RMPRU by serotype and age group, South Africa, 2007 (of 420 cases reported, 401 had known age, and 226 had specimens or viable isolates available for serotyping).

Twenty-six percent of serotype b strains were resistant to ampicillin (MIC>1mg/L (18) (all producing beta lactamase)), 20 of 77 isolates tested, while 14% (13/94) of non-typeable strains were resistant (p=0.045). Ampicillin resistance of Hib isolates has increased compared with 2006, but this did not reach statistical significance (20/77, 26% in 2007 vs 12/71, 17% in 2006 (21), p=0.181).

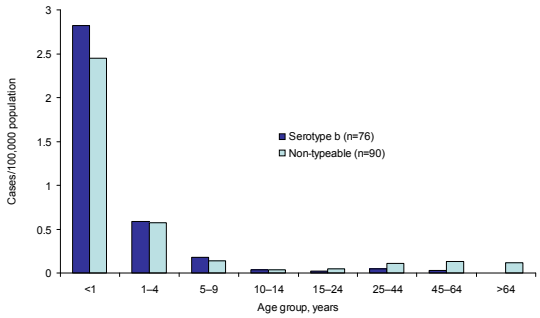

Figure 11: Reported age-specific incidence rates of serotype b and non-typeable *Haemophilus influenzae* disease, South Africa, 2007 (of 420 cases reported, 401 had known age, and 215 had viable isolates available for serotyping).

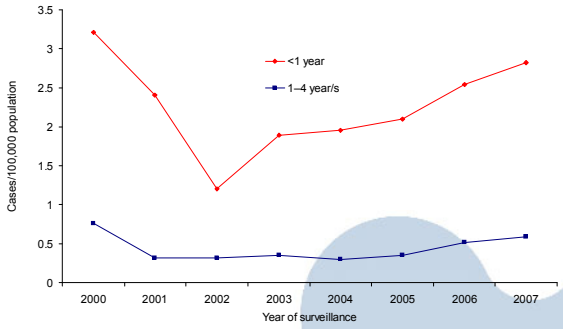

Figure 12: Incidence rates of *Haemophilus influenzae* serotype b disease in children <5 years, South Africa, 2000-2007 (excluding cases identified using polymerase chain reaction (PCR) on specimens – only done in 2007).

Discussion

Since the introduction of the *H. influenzae* serotype b (Hib) conjugate vaccine into the Expanded Programme on Immunisation (EPI) for South Africa in 1999, there has been a reduction in cases reported due to this serotype (22). The recent increase in reported cases of Hib disease in children <1 year needs to be monitored carefully, and further analysis of these cases will follow.

Table 23: Number of cases of *Haemophilus influenzae* disease reported to RMPRU by serotype and province (n=420, 226 (54%) with specimens or viable isolates available for serotyping), South Africa, 2007

Province	Serotype								
	No isolate available	a	b	c	d	e	f	Non-typeable	Total
Eastern Cape	21	0	3	0	0	0	2	2	28
Free State	12	0	6	0	1	1	2	1	23
Gauteng	83	5	34	1	1	2	19	57	202
KwaZulu-Natal	25	0	17	1	0	1	2	20	66
Limpopo	6	0	0	0	0	0	0	0	6
Mpumalanga	10	0	4	0	0	1	2	5	22
Northern Cape	2	0	1	0	0	0	0	0	3
North West	2	0	2	0	0	0	0	0	4
Western Cape	33	4	17	0	1	1	1	9	66
South Africa	**194**	**9**	**84**	**2**	**3**	**6**	**28**	**94**	**420**

Table 24: Number and percentage of cases of *Haemophilus influenzae* disease as reported to RMPRU by specimen type, South Africa, 2007

Site of specimen	No isolate available		Serotype b		Serotypes a, c, d, e, f		Non-typeable	
	n	%	n	%	n	%	n	%
CSF	45	23	40	48	16	33	7	7
Blood	123	63	41	49	31	65	76	81
Other	26	13	3	4	1	2	11	12
Total	**194**		**84**		**48**		**94**	

Streptococcus pneumoniae

Respiratory and Meningeal Pathogens Reference Unit

Results

Incidence of reported invasive pneumococcal disease varied widely by province (Table 25). The age group at highest risk of disease in South Africa was infants <1 year of age (Figure 13). The majority of episodes reported to RMPRU were diagnosed from positive blood culture specimens (Table 26).

Penicillin non-susceptible isolates (MIC>0.06mg/L (18)), have increased from 2006 (1429/3327, 43% in 2007 compared to 1107/3423, 32% in 2006, p<0.0001), and this ranged from 30% to 54% in different provinces (Table 27). Non-susceptible isolates were common in children less than 5 years of age (Figure 14).

The proportion of disease in 2007 in children <5 years due to the seven serotypes in the vaccine (4, 6B, 9V, 14, 18C, 19F and 23F), and serotype 6A (ongoing evidence for cross-protection within this serogroup (23)), in South Africa is more than 70% according to our data (Table 28).

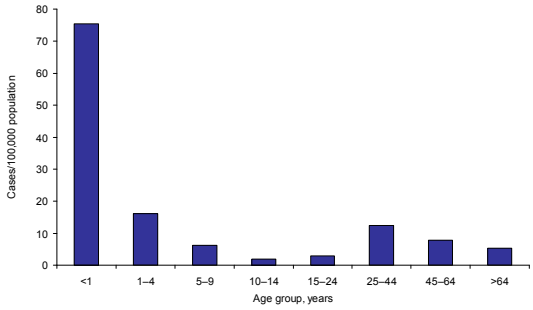

Figure 13: Reported age-specific incidence rates for invasive pneumococcal disease, South Africa, 2007 (4733 cases reported, age known in 4493).

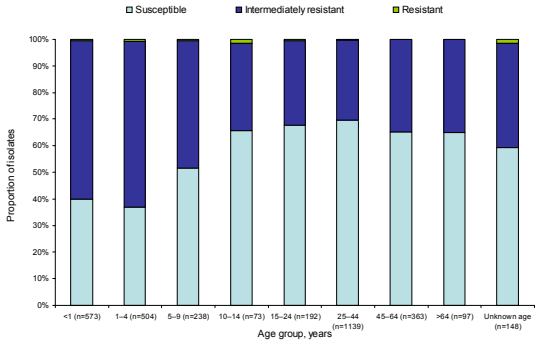

Figure 14: Number of cases of IPD reported to RMPRU in 2007 by age group and penicillin susceptibility (non-susceptible MIC>0.06mg/L(18) to penicillin 4733 cases reported, 3327 with viable isolates).

Table 25: Number of cases and incidence rates of invasive pneumococcal disease reported to RMPRU by province, South Africa, 2006 and 2007.

Province	2006		2007	
	n	Cases/100 000	n	Cases/100 000
Eastern Cape	289	4.09	354	5.00
Free State	227	7.66	313	10.54
Gauteng	2107	22.89	2259	24.14
KwaZulu-Natal	462	4.75	537	5.47
Limpopo	102	1.80	148	2.59
Mpumalanga	209	6.44	277	8.47
Northern Cape	37	4.07	57	6.23
North West	139	3.61	221	5.70
Western Cape	488	10.27	567	11.69
South Africa	**4060**	**8.57**	**4733**	**9.89**

Table 26: Number and percentage of cases of invasive pneumococcal disease reported to RMPRU by specimen type, South Africa, 2007.

Site of specimen	n	%
CSF	1723	36
Blood	2587	55
Other	423	9
	4733	

Discussion

The increased resistance occurred in all age groups (data not shown), and on preliminary analysis may be related to an increase of sero-type 19A and 6A strains that are resistant to penicillin and trimethoprim-sulfamethozaxole. This increase in non-susceptible strains will be investigated further.

PREVENAR® (7-valent conjugate pneumococcal vaccine) was launched in South Africa in the private sector in 2005 by Wyeth South Africa (Pty) Ltd, and is at present the only vaccine for the prevention of pneumococcal disease in children < 2 years. Our data of serotype coverage for this vaccine, support advocacy from clinicians and parents for the vaccine price to be reduced and the possible inclusion of this vaccine in the EPI in the future.

Table 27: Number and percentage of penicillin non-susceptible isolates from invasive pneumococcal disease cases reported to RMPRU by province, South Africa, 2007.

Province	No isolate available	Susceptible		Intermediately resistant		Resistant	
	n	n	%	n	%	n	%
Eastern Cape	135	126	58	93	42		0.0
Free State	84	134	59	95	41		0.0
Gauteng	682	918	58	649	41	10	0.6
KwaZulu-Natal	115	194	46	228	54		0.0
Limpopo	59	62	70	27	30		0.0
Mpumalanga	99	105	59	72	40	1	0.6
Northern Cape	16	23	56	18	44		0.0
North West	78	94	66	48	34	1	0.7
Western Cape	138	242	56	185	43	2	0.5
South Africa	1406	1898	57	1415	43	14	0.4

Table 28: Number and percentage of cases reported in children less than 5 years of age caused by the serotypes contained in the 7-valent vaccine, South Africa, 2007.

Province	7-valent serotypes (4, 6B, 9V, 14, 18C, 19F and 23F)	Serotype 6A	Total isolates available for serotyping	% of IPD due to 7-valent serotypes including 6A
Eastern Cape	41	13	75	72
Free State	51	5	74	76
Gauteng	253	62	457	69
KwaZulu-Natal	104	24	171	75
Limpopo	17	2	22	86
Mpumalanga	37	2	51	76
Northern Cape	9	0	14	64
North West	24	2	35	74
Western Cape	94	27	178	68
South Africa	**630**	**137**	**1077**	

Discussion

This year's Annual Report presents surveillance data in a format similar to the Annual Report 2006. This should facilitate a comparison of trends year on year.

Laboratory-based surveillance systems will inevitably under-estimate the true burden of disease. Case reporting to a public health agency like the NICD requires (a) that the disease under surveillance manifests clinically, (b) that the case patient seeks medical attention, (c) that the health care worker submits an appropriate specimen to the diagnostic laboratory, (d) that the laboratory is able to isolate the pathogen and (e) that the laboratory reports the confirmed case to the surveillance system. There is attrition at each of these steps; hence, this concept has been referred to as a "surveillance pyramid" (24). For the first time, the GERMS-SA surveillance programme has attempted to correct case estimates by performing a comprehensive audit of the NHLS laboratory information system (Disa*lab), accessed through the NHLS corporate data warehouse. The surveillance audit has allowed the system to count cases at the level of the diagnostic laboratory, one step down the pyramid. For invasive cases, where reporting is better, the percentage of additional cases identified on audit ranged from 0% for *Salmonella* Typhi to 25% for *Cryptococcus* spp. The estimates of case reporting for *Neisseria meningitidis* and *Haemophilus influenzae* provided by the comprehensive audit is not very different from the estimates of completeness of approximately 70-90% for *Neisseria meningitidis* and 70% for *Haemophilus influenzae* which had been developed based on incomplete audits in the past (20,22,25). There does, however, seem to be variation in the completeness of reporting from the laboratories between pathogens. Drilling down to the base of the surveillance pyramid to estimate the true burden of disease is possible but requires resources. Previous work performed by GERMS-SA investigators has determined that there is regional variability in specimen-taking practices by clinicians, which influences case-counting (26). Further work of this nature is required to enable a reasonable estimate of the true burden of the diseases under surveillance.

The GERMS-SA programme, in its 5th year, has matured to the point where analysis of accumulated surveillance data is able to generate meaningful information. The system is well placed to evaluate trends in the burden of AIDS-associated opportunistic infections which may provide an indirect measure of the impact of the HIV epidemic. In addition we can evaluate the impact of increasing HIV prevalence, antibiotic use and vaccination programmes on the clinical presentation of cases and serotype distribution and antimicrobial resistance patterns of pathogens under surveillance. Data currently collected from enhanced surveillance sites has allowed for secondary data analyses including the impact of HIV infection on mortality and antibiotic resistance amongst cases of diseases under surveillance (27-29). In addition, where trends detected by analysis of surveillance data require further exploration, the programme can serve as a launching pad for special studies. Such analytic studies are being planned, but are resource-intensive. Surveillance data have directly impacted on clinical management of infectious diseases and public health policy in South Africa. In 2007, cryptococcal surveillance data were provided to support development of national clinical management guidelines for cryptococcosis in HIV-infected patients (11). Surveillance data were also used in the preparation of South African Community-Acquired Pneumonia (CAP) guidelines, published in 2007 (30). Pneumococcal surveillance data, presented to the National Advisory Group for Immunisation (NAGI), were used to motivate for inclusion of the heptavalent conjugate pneumococcal vaccine into the South African Expanded Programme on Immunisation (EPI). This Annual Report includes a list of publications which has emanated from GERMS-SA since its inception.

Publications

Publications in peer-reviewed journals

2003
von Gottberg A, Ludewick H, Bamber S, Govind C, Sturm AW, Klugman KP. Emergence of fluoroquiolone-resistant *Streptococcus penumoniae* in a South African child in a tuberculosis treatment facility. *Pediatr Infect Dis J* 2003;22:1020-1021.

2006
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