

Global Vaccine Preventable Invasive Bacterial Diseases (VP-IBD) Information and Surveillance Bulletin

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The World Health Organization (WHO) produces a twice-yearly global vaccine preventable invasive bacterial diseases (VP-IBD) surveillance bulletin to share information and data with partners at the national, regional, and global levels. This Bulletin presents surveillance data for January through December of 2009, as reported by Member States participating in the WHO coordinated network for VP-IBD sentinel surveillance that targets hospitalized children under 5 years of age.



This second edition of the Bulletin summarizes global VP-IBD data in terms of surveillance network characteristics, Tier 1/meningitis data including information related to bacterial pathogens and serotypes, and Tier 2/meningitis-pneumonia-sepsis information. Moving forward, WHO proposes to present data in this format, and welcomes comments on this method of data presentation. WHO will continue to explore options to best present Tier 3 data, as related to information gathered by population based sites.

Comments on this Bulletin are Welcome. Please Email to Dr. Mary Agócs (agocsm@who.int)

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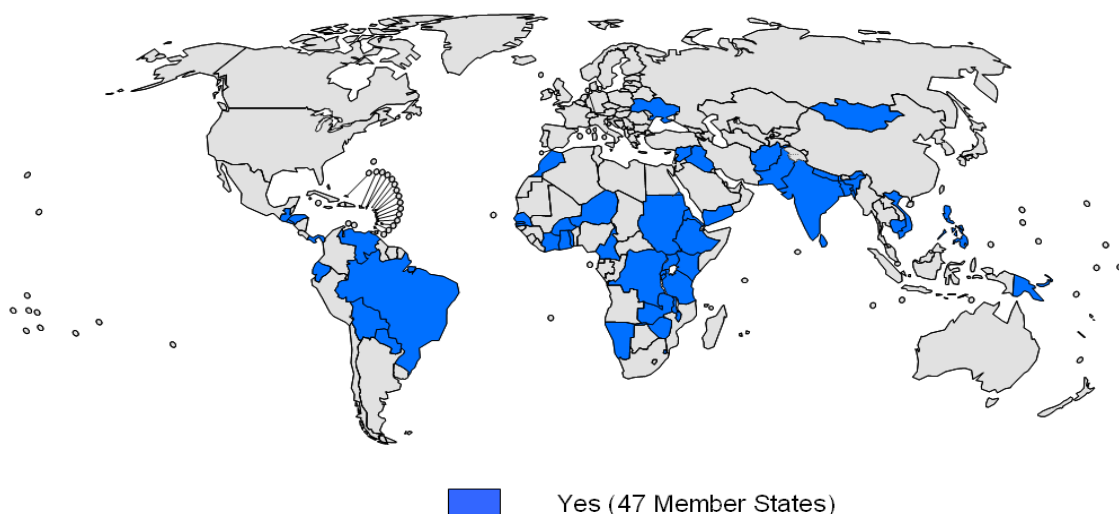
2009 VP-IBD surveillance data

VP-IBD surveillance network characteristics

During 2009, 47 Member States participated in the VP-IBD surveillance network, and reported data to WHO (Figure 1 and Table 1). WHO Regional Offices coordinate all of the regional activities, which include providing training, standard guidelines, quality assurance and technical support. Regional Offices also receive and synthesize data from the individual countries.

Figure 1. Countries reporting Invasive Bacterial Diseases surveillance data to WHO in 2009.

Invasive Bacterial Diseases Surveillance Countries Participating in the WHO Network and Reporting Data for 2009



Data collected from WHO Regions and partners.

Slide date: 14 September 2010

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Overall, 45% of reporting countries were based in the WHO African Region (AFR). Conversely, most sentinel reporting sites (53%) were in the WHO Eastern Mediterranean Region (EMR), as some EMR reporting countries had significantly expanded sites beyond the minimum recommended 1 to 3 sentinel sites per country, and had adopted a more national approach to data collection. GAVI eligible countries were provided financial support using GAVI Alliance funds channelled through WHO. Of the 72 GAVI-eligible countries during 2009, 34 (47%) were supported to establish sentinel sites and report IBD data to WHO.

Table 1. Characteristics of WHO VP-IBD Surveillance Network by WHO Region, 2009

WHO Region	By GAVI eligibility			No.(%) sentinel sites reporting	Total No.(%) countries reporting
	No.(%) GAVI-eligible countries	No.(%) GAVI-eligible countries reporting	Proportion of GAVI-eligible countries reporting		
AFR	36 (50)	19 (56)	53%	28 (15)	21 (45)
AMR	6 (8)	2 (6)	33%	28 (15)	9 (19)
EMR	6 (8)	4 (12)	67%	101(53)	7 (15)
EUR	8 (11)	1 (3)	12%	3 (2)	1 (2)
SEAR	9 (13)	4 (12)	44%	8 (4)	4 (9)
WPR	7 (10)	4 (12)	57%	24 (13)	5 (11)
TOTAL	72 (100)	34 (100)	47%	192 (100)	47 (100)

WHO has adopted a layered approach to IBD surveillance, with 3 reporting tiers conducting increasing levels of surveillance. All countries are recommended to conduct Tier 1/meningitis surveillance at a minimum of 1-3 sentinel sites, depending on country size and population heterogeneity. Fewer sites with the required technical capacity undertake Tier 2 where, in addition to meningitis, cases of pneumonia and sepsis are investigated using blood culture. Finally, Tier 3, which involves surveillance for meningitis, pneumonia and sepsis in a well characterized catchment population that allows estimation of disease incidence, is proposed in at least one site in each WHO region or sub-region. Among the 47 countries reporting data to WHO, all reported meningitis data, 17 (36%) reported additional Tier 2 data, and 2 (4%) were population based sites (Table 2).

Table 2. Number of countries reporting VP-IBD data by surveillance tier and WHO Region, 2009.

WHO Region	Type of IBD surveillance		
	Tier 1 Meningitis	Tier 2 + Sepsis and Pneumonia	Tier 3 +Population-based
AFR	21	0	1
AMR	9	8	0
EMR	7	4	0
EUR	1	0*	0
SEAR	4	4	1
WPR	5	1	0
TOTAL	47	17	2

*Ukraine conducts sepsis surveillance on hospitalized meningitis cases.

Tier 1 - Meningitis Surveillance

During 2009, 25,440 children <5 years of age hospitalized with suspected meningitis¹ were enrolled in the WHO VP-IBD surveillance network (Table 3). This represented a 15% increase over the number of reported suspected meningitis cases during 2008. Most of the increase occurred in the WHO South East Asia (SEAR) and Western Pacific Regions (WPR), with India, Philippines, and Viet Nam joining the surveillance network.

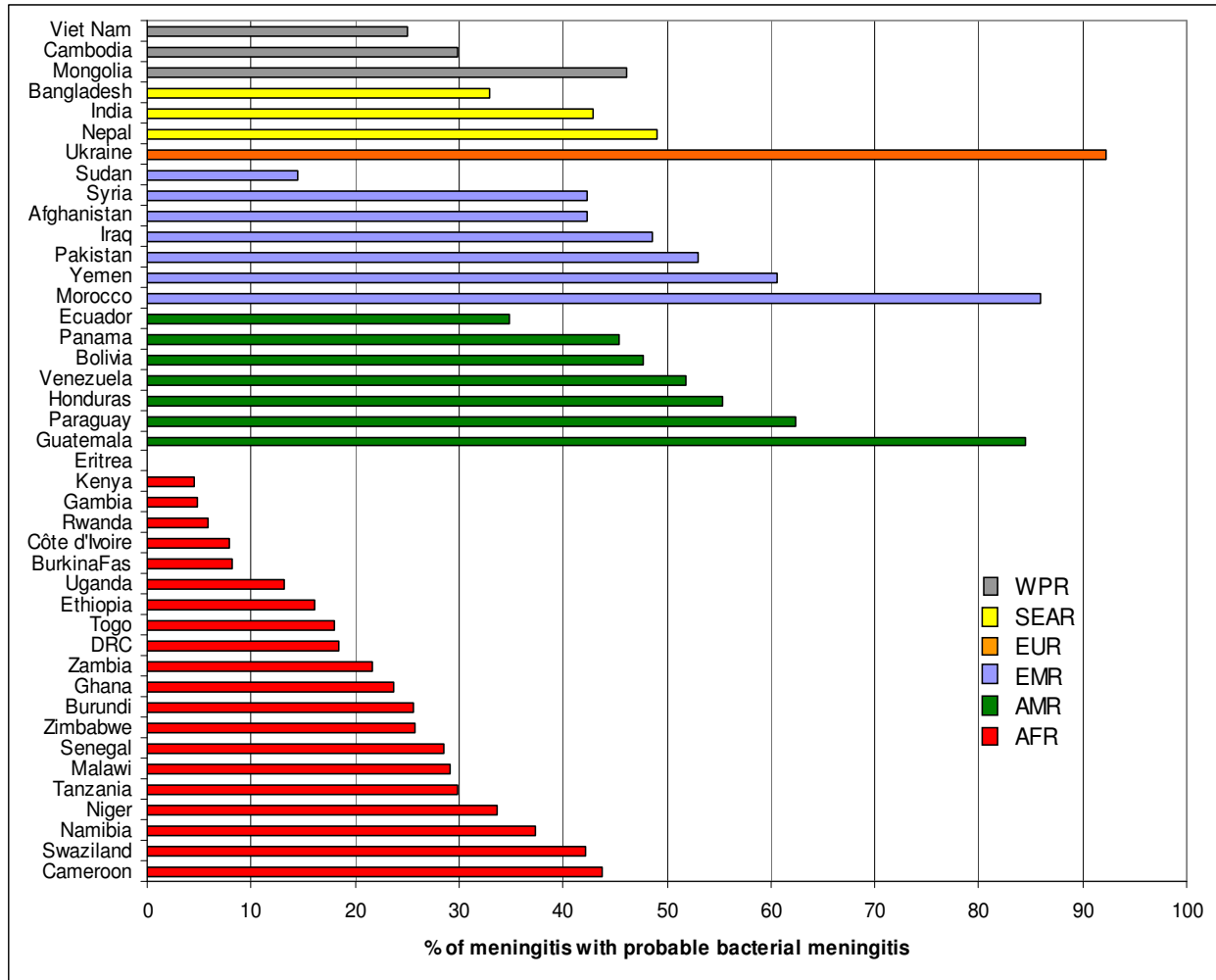
Table 3. Number of children <5 years of age hospitalized with suspected meningitis and enrolled in the WHO VP-IBD surveillance network, by WHO Region, 2008 as compared to 2009.

WHO Region	Year 2008		Year 2009		% change in number of cases from 2008 to 2009
	No.(%) reporting countries	No.(%) suspected meningitis	No.(%) reporting countries	No.(%) suspected meningitis	
AFR	22 (48)	8640 (39)	21 (45)	9634 (38)	+12
AMR	8 (17)	3713 (17)	9 (19)	3743 (15)	+1
EMR	9 (20)	7908 (36)	7 (15)	7787 (31)	-2
EUR	1 (2)	130 (1)	1 (2)	103 (1)	-21
SEAR	3 (6)	1104 (5)	4 (8)	2408 (9)	+118
WPR	3 (6)	602 (3)	5 (11)	1765 (7)	+193
TOTAL	46 (100)	22097 (100)	47 (100)	25440 (100)	+15

¹ Signs and symptoms of bacterial meningitis as defined by the clinician, WHO *Summary Report on Meeting to Standardize New Vaccines Surveillance Data to be Collected, Shared and Reported*, 2008.

Among children with suspected meningitis, the percent with probable bacterial meningitis² varied widely between countries (range 0 to 92%), (Figure 2). Three countries reported probable meningitis constituting over 80% of suspected meningitis; they were Ukraine (92%), Morocco (86%) and Guatemala (85%).

Figure 2. Percent of suspected meningitis cases with probable bacterial meningitis, by country and WHO Region, 2009.

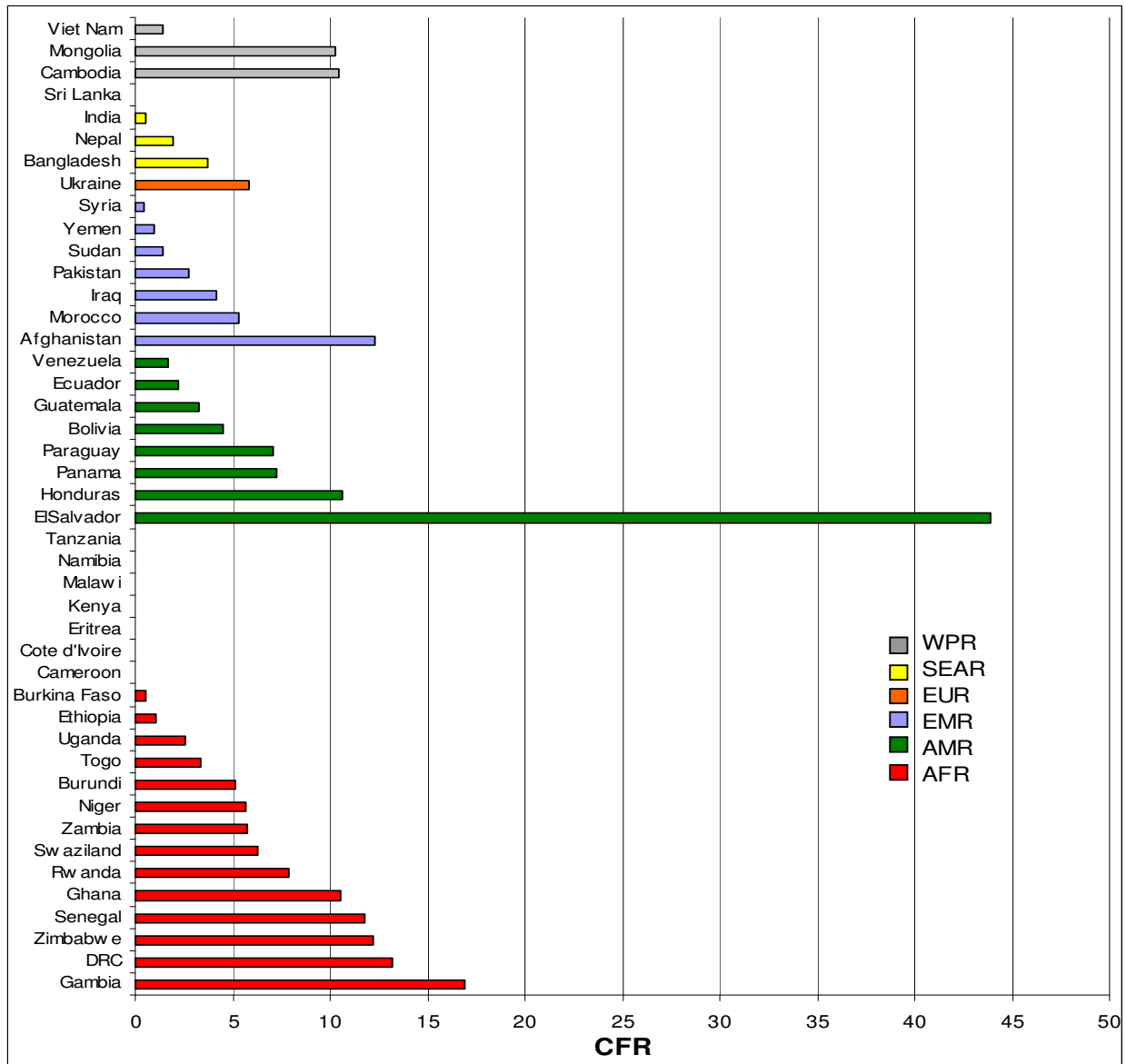


NOTE: Missing data from AMR countries: Brazil and El Salvador, SEAR country: Sri Lanka and WPR countries: Papua New Guinea and Philippines.

Forty-four countries also reported case fatality ratios (CFR) for meningitis (Figure 3). The CFR varied from 0% to 44%, with one country, El Salvador with a CFR of 44%, being an outlier. In all other countries, the CFR was below 20%. The median CFR in AFR, AMR, EMR, EUR, SEAR and WPR were 3%, 6%, 3%, 6%, 1% and 10%, respectively.

² Probable bacterial meningitis: A suspected case of meningitis with examination of cerebral spinal fluid showing at least one of the following: 1) turbid appearance, 2) WCC (>100 cells/mm³), 3) WCC (10-100 cells/mm³) and either an elevated protein (>100mg/dl) or decreased glucose (<40 mg/dl).

Figure 3. Case Fatality Ratio (CFR) of children <5 years of age hospitalized with suspected meningitis, by country and WHO Region, 2009.



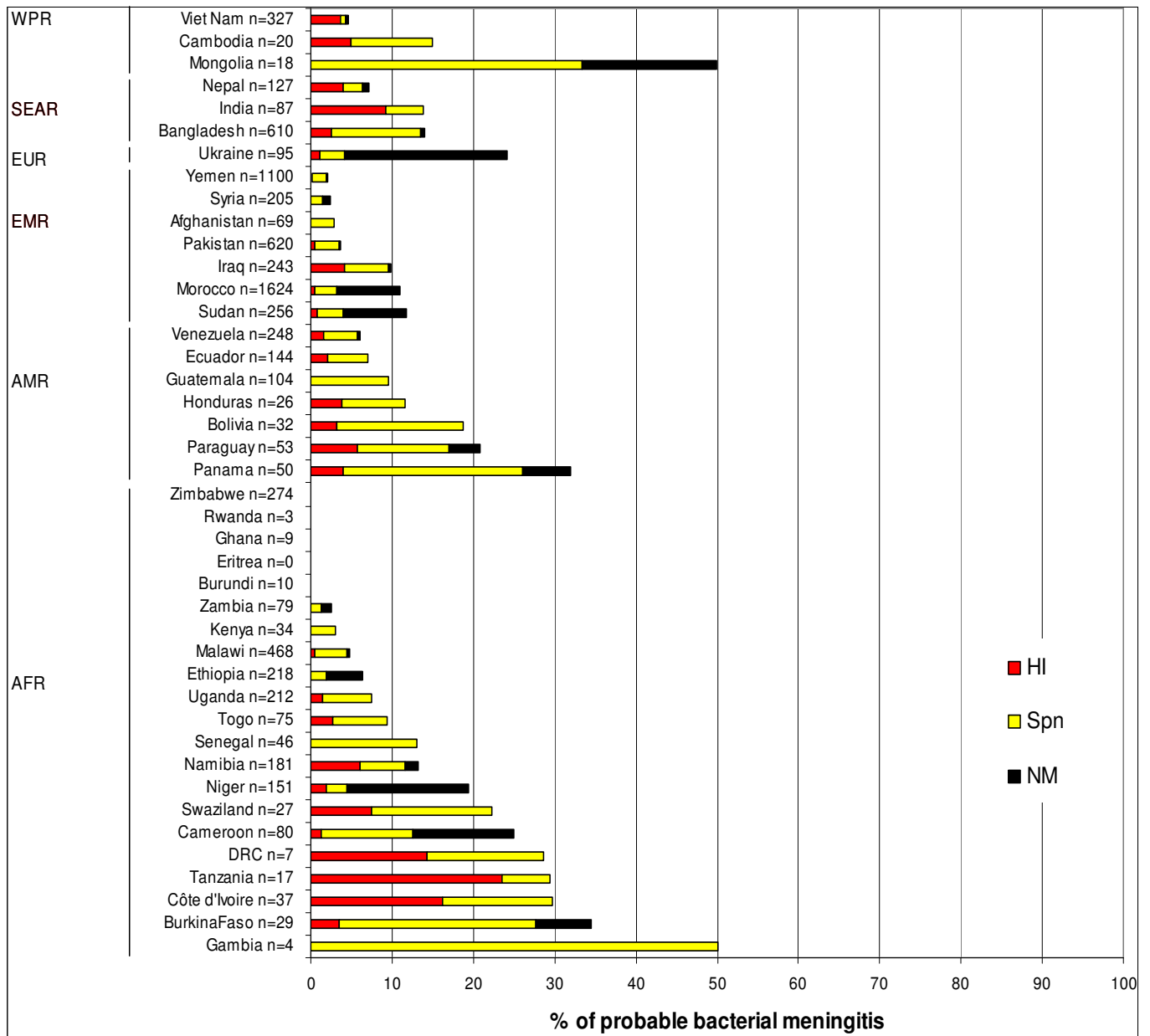
NOTE: No Data from AMR country: Brazil and WPR countries: PNG and Philippines.

Tier 1 - Aetiologic agents of probable bacterial meningitis

The WHO VP-IBD surveillance system only gathers pathogen information as related specifically to detection of one of the three vaccine preventable organisms, *Haemophilus influenzae*, *Streptococcus pneumoniae*, or *Neisseria meningitidis*. Sites varied in the use of antigen detection or PCR for etiologic diagnosis with some sites using them for one or more of the three pathogens and other sites using only conventional culture. Any one of these organisms was detected in 8.6% of children with probable bacterial meningitis, globally. There was a wide variation between countries in the percent of probable bacterial meningitis identified with any one of these pathogens, ranging from 0% to 50% (Figure 4). Among the regions, the median percent detection were 9%, 12%, 4%, 24%, 12% and 15% in AFR, AMR, EMR, EUR, SEAR and WPR, respectively.

The percent due to *Haemophilus influenzae* ranged from 0% in 14 countries, to 24% in Tanzania. The percent of probable bacterial meningitis due to *Streptococcus pneumoniae* ranged from 0% in 6 countries, to 50% in the Gambia. The percent of probable bacterial meningitis due to *Neisseria meningitidis* ranged from 0% in 22 countries, to 20% in the Ukraine. Currently, data is not collected on the percent of probable bacterial meningitis due to other pathogens or where no pathogen was detected.

Figure 4. Percent of probable bacterial meningitis caused by the bacterial pathogens *Haemophilus influenzae* (HI), *Streptococcus pneumoniae* (Spn), and *Neisseria meningitidis* (NM), by country and WHO Region, 2009.



NOTE: Missing data from AMR countries: Brazil and El Salvador, SEAR country: Sri Lanka, and WPR countries: Papua New Guinea and the Philippines. Total number of probable bacterial meningitis (n=) stated next to each country.

Hib vaccine had been introduced into the national immunization programmes of most reporting countries, which allowed for further assessment of meningitis due to *Haemophilus influenzae* as related to national Hib vaccine use (Table 4). Reporting countries were divided into those that had introduced Hib vaccine within time spans of less than 1 year, 1-4 years and over 5 years ago. AFR countries that had introduced vaccine for over 1 year had substantially fewer probable bacterial meningitis cases due to *Haemophilus influenzae* than countries which had introduced vaccine less than 1 year ago (1% versus 14%).

Table 4. Percent of probable bacterial meningitis cases with *Haemophilus Influenzae* (HI), by number of years of Hib vaccine introduction into the national immunization programme and WHO Region, 2009 (regional median with country range).

WHO Region	Number of years of Hib vaccine introduction					
	<1 yr or Hib vaccine not in use		1-4yrs		≥ 5 yrs	
	No. reporting countries with Hib introduced	% of probable bacterial meningitis cases with HI (country range)	No. reporting countries with Hib introduced	% of probable bacterial meningitis cases with HI (country range)	No. reporting countries with Hib introduced	% of probable bacterial meningitis cases with HI (country range)
AFR	6	14 (1-24)	7	1 (0-3)	8	0 (0-1)
AMR	0	0	1	0	8	3 (2-6)*
EMR	3	0 (0-4)	3	0 (0-1)	1	0
EUR	0	0	1	1	0	0
SEAR	3	4 (2-9)	1	Missing Data	0	0
WPR	3	4 (4-5)**	2	0***	0	0
OVERALL	15	5	15	0	17	1

* Missing data from Brazil and El Salvador

** Missing data from the Philippines

*** Missing data from PNG

Tier 2 - Meningitis-Pneumonia-Sepsis Surveillance

During 2009, Tier 2 data was reported by 17 countries in 4 WHO Regions with over 17,000 children < 5 years of age hospitalized with pneumonia³ and enrolled in the WHO VP-IBD surveillance network (Table 5). The number of children enrolled increased by over 250% in the 3 SEAR countries who reported data in 2008 and 2009. Ministries of Health and WHO are working to further standardize Tier 2 data and its reporting.

Table 5. Number of children <5 years of age hospitalized with pneumonia and enrolled in the WHO VP-IBD surveillance network, by WHO Region, 2008 as compared to 2009.

WHO Region	Year 2008		Year 2009		% change in number of enrolled from 2008 to 2009
	No.(%) reporting countries	No.(%) children enrolled with pneumonia	No.(%) reporting countries	No.(%) children enrolled with pneumonia	
AMR	7 (47)	11428 (72)	8 (50)	14546 (82)	+27
EMR	4 (27)	1051 (7)	4 (25)	1634 (9)	+55
SEAR*	3 (20)	1198 (8)	3 (19)	4433 (25)	+270
WPR	1 (7)	2286 (14)	1 (6)	1631(9)	-29
TOTAL	15 (100)	15963 (100)	16 (100)	17811 (100)	+12

* No data from India

³ Any child <5 years of age hospitalized with signs and symptoms of pneumonia as defined by the clinician.

Tier 2 - Aetiologic agents of meningitis-pneumonia-sepsis surveillance

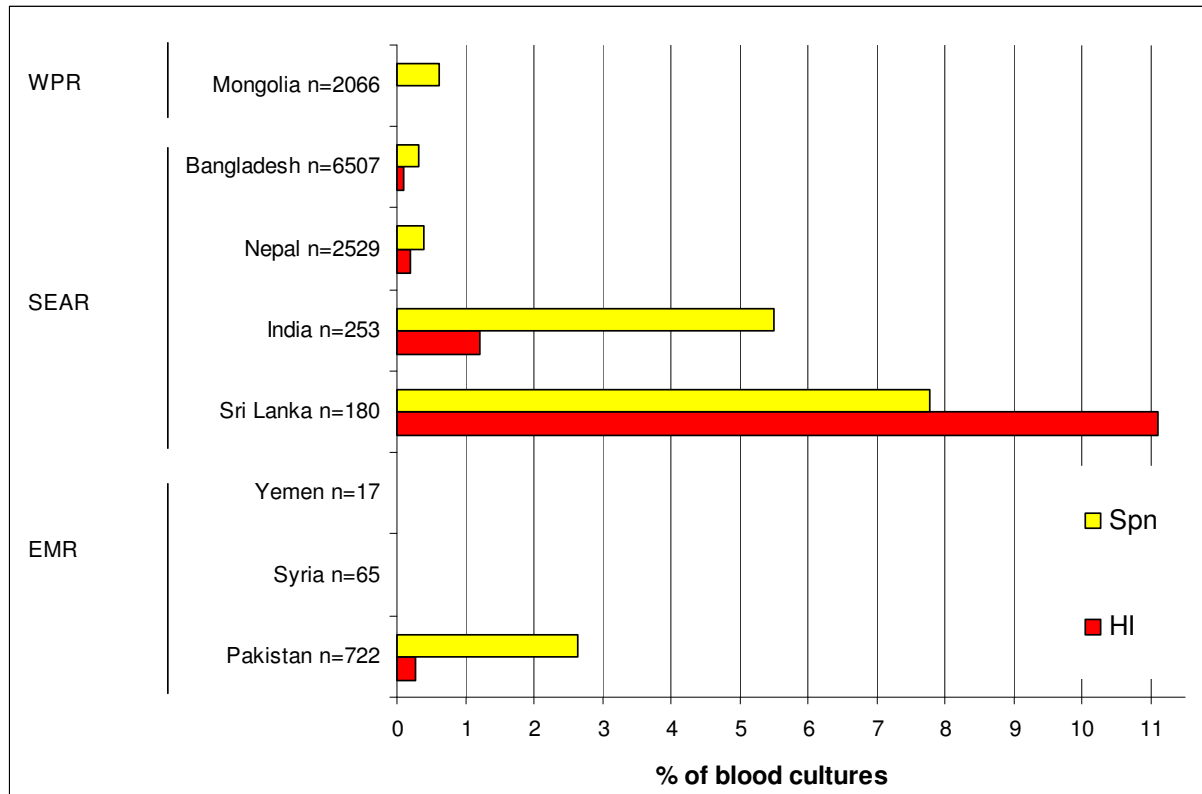
During 2009, 186 children hospitalized with meningitis, pneumonia, or sepsis were found to have *Streptococcus pneumoniae*, with most of the organism isolated in AMR (52%). Most of the children with *Haemophilus influenzae* were detected in SEAR (66%) or AMR (30%), (Table 6). Most countries reporting Tier 2 data had <1% isolation of *Streptococcus pneumoniae* and *Haemophilus influenzae* from blood cultures of children with pneumonia/sepsis (Figure 7).

Table 6. Number of *Haemophilus influenzae* or *Streptococcus pneumoniae* identified by culture, latex or polymerase chain reaction from blood cultures of children with pneumonia/sepsis, by WHO Region, 2009.

WHO Region	No. (%) <i>Haemophilus influenzae</i>	No. (%) <i>Streptococcus pneumoniae</i>
AMR	16 (30)	96 (52)
EMR	2 (4)	19 (10)
SEAR	36 (66)	58 (31)
WPR	0	13 (7)
OVERALL	54 (100)	186 (100)

NOTE: AFR and EUR countries do not conduct and/or report Tier 2 pneumonia/sepsis surveillance at present.

Figure 7. Percent of blood cultures due to *Streptococcus pneumoniae* (Spn) and *Haemophilus influenzae* (HI) taken from children with pneumonia/sepsis, by country and WHO Region, 2009.



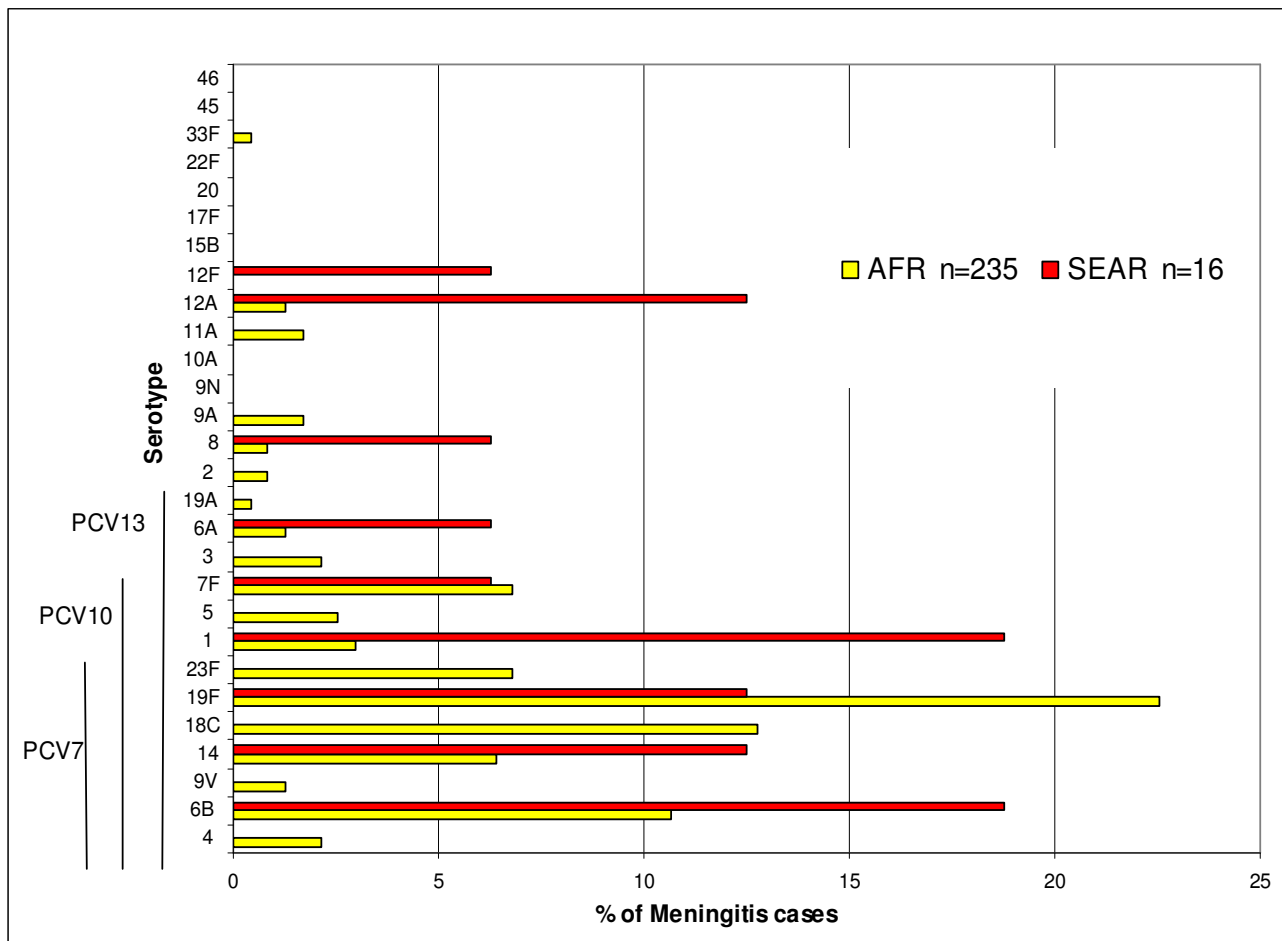
NOTE: Total number of blood cultures taken from children with pneumonia/sepsis (n=), stated next to the country. Countries in AMR were excluded from the analysis due to missing denominator data. Afghanistan in EMR region not shown because country reported zero blood cultures.

Serotype Data

During 2009, serotype data was available for 4 AFR countries (Ethiopia, Kenya, Uganda, Tanzania) and 4 SEAR countries (Bangladesh, India, Nepal, and Sri Lanka). In both AFR and SEAR regions, over 60% of cases of meningitis as well as other invasive diseases caused by *Haemophilus influenzae* were due to type b serotype.

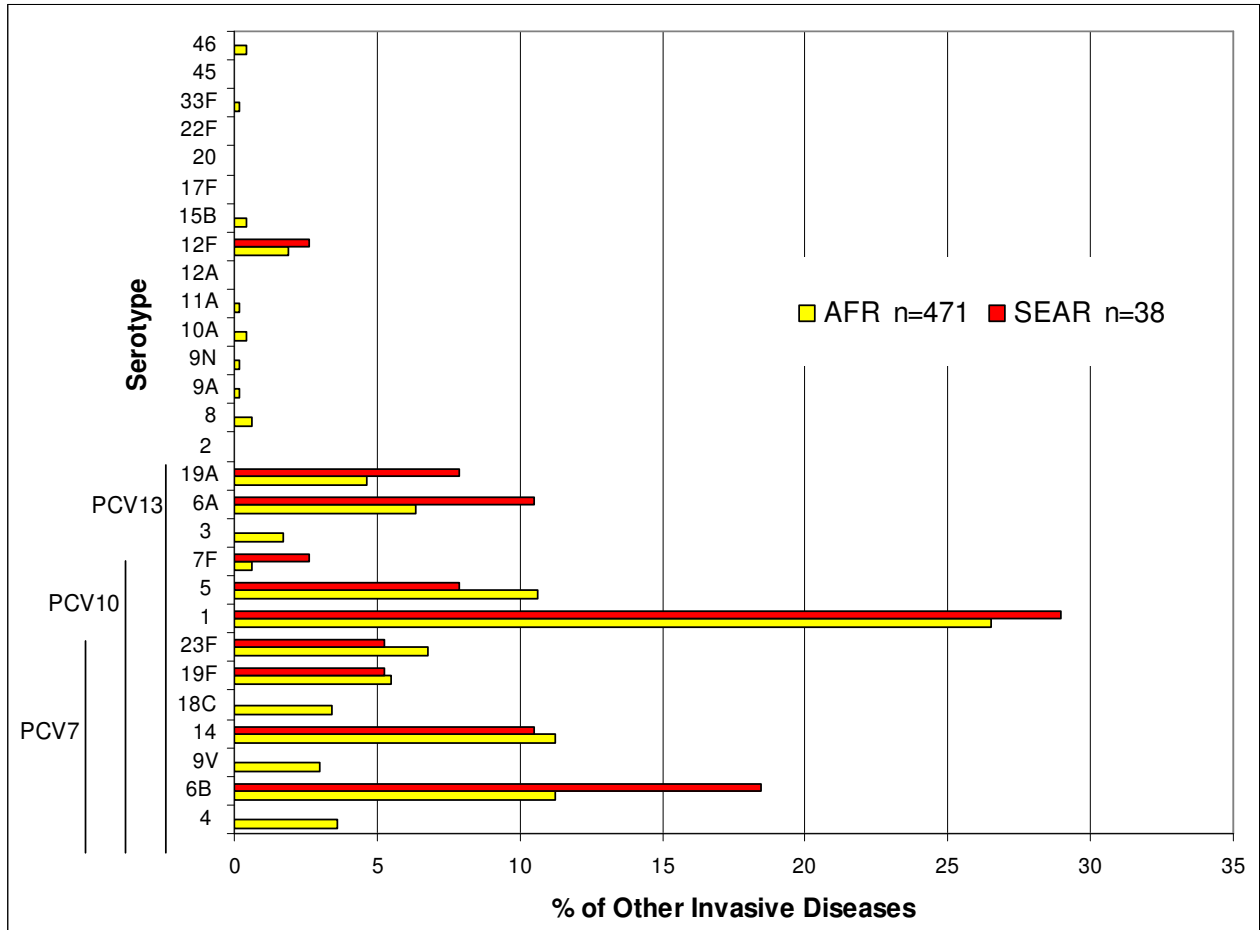
Among cases of meningitis caused by *Streptococcus pneumoniae*, the percent of isolates with serotypes included in the PCV-7, 10, and 13 vaccines were 48%, 80%, and 91%, respectively in AFR, and 44%, 69%, and 75%, respectively in SEAR reporting countries (Figure 5).

Figure 5. Percent distribution of *Streptococcus pneumoniae* (Spn) serotypes among cases of meningitis due to Spn, 2009. Serotypes are grouped according to those included in the PCV-7, 10 and 13 vaccines. Total number of isolates (n=) shown next to each region.



Among cases of other invasive diseases caused by *Streptococcus pneumoniae*, the percent of isolates with serotypes included in the PCV-7, 10, and 13 vaccines were 45%, 83%, and 95%, respectively in AFR, and 39%, 79%, and 97%, respectively in SEAR reporting countries (Figure 6).

Figure 6. Percent distribution of *Streptococcus pneumoniae* (Spn) serotypes among cases of other invasive diseases due to Spn, 2009. Serotypes are grouped according to those included in the PCV-7, 10 and 13 vaccines. Total number of isolates (n=) shown next to each region.



Comments

VP-IBD surveillance data varied considerably by country and WHO region. While some of the differences may represent true epidemiological differences and a result of Hib vaccine use, it is very likely that differences in surveillance practices, quality of specimen handling and laboratory processes may have accounted for much of the observed differences. WHO will continue working to improve the consistency of surveillance procedures and the quality of the data. At a recent meeting in Geneva, a decision was made to promote stricter adherence to case definitions and procedures, as well as to use standardized case report forms. These actions would help to ensure uniformity of data reporting and to collect epidemiologic information that would facilitate proper interpretation of the observed results.

Tier 1/meningitis data included >25,000 children <5 years of age with suspected meningitis, a 15% increase over 2008. There was substantial variation in the proportion of suspected meningitis cases with probable bacterial meningitis, ranging from 0% in Eritrea to 92% in Ukraine. This raises the possibility of differences in clinical practices that influence whether a lumbar puncture is performed or laboratory investigations undertaken. There was considerable variation in the proportion of cases caused by the different pathogens, some of which could be related to the variable use of non-culture diagnostics (i.e. antigen detection and PCR) for one or more pathogens. These factors and variations in the quality of the laboratory procedures may have influenced the observed results, making comparisons and interpretations difficult.

Within AFR, comparison could be made between countries that had introduced Hib vaccine within time spans of <1 year, 1-4 years and ≥ 5 years ago. AFR countries that introduced vaccine for >1 year reported substantially fewer probable *Haemophilus influenzae* bacterial meningitis cases than countries that had introduced vaccine <1 year ago (1% versus 14%). In none of the countries where Hib vaccine was in use for >2 years was *Haemophilus influenzae* the predominant pathogen. The highest CFR among case-children with suspected meningitis was found in WPR (10%), with AMR and EUR both at 6%.

Tier 2/pneumonia-sepsis data was reported by 17 countries in 4 WHO Regions and >17,000 children with pneumonia were enrolled. The pathogens of interest, namely *Haemophilus influenzae* and *Streptococcus Pneumoniae*, were isolated in less than 1% of enrolled cases. The proportion of pneumonia cases in those enrolled varied considerably between regions, suggesting variability in clinical practices between regions. Ministries of Health and WHO are working to further standardize Tier 2 data and reporting from both Tier 2 and Tier 3/population based sites.

Serotype data was available for 4 AFR and 4 SEAR countries. The proportions of serotypes in PCV-7, PCV-10 and PCV-10 causing meningitis and other invasive disease were similar to previously reported data, though the data from SEAR countries were based on relatively few isolates and needs to be interpreted with caution.

Spotlight on Global Laboratory Network

A strong laboratory network is essential in ensuring a high-quality VP-IBD surveillance network as the laboratory will ultimately determine whether disease is due to *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis* or another organism. During 2008 and 2009, the VP-IBD laboratory network has developed to include:

Table 7. Global and Regional VP-IBD Laboratories of the WHO Coordinated Global Surveillance Network, 2010

Type of VP-IBD Laboratory	Institution Name and Location
Global Reference	Centers for Disease Control and Prevention, USA
Reference for African Region	<ul style="list-style-type: none"> • National Institute of Communicable Disease, Johannesburg, South Africa • Medical Research Council Laboratories, Banjul, The Gambia • Medical Research Institute, Nairobi, Kenya
Reference for the Region of the Americas	<ul style="list-style-type: none"> • Instituto Adolfo Lutz, Sao Sao Paulo, Brazil • Instituto Nacional de Salud, Bogotá, Columbia
Reference for the Eastern Mediterranean Region	Center for Public Health, Cairo, Egypt
Reference for the European Region	Moscow Gabrichevsky Institute, Russia
Reference for the Southeast Asia Region	<ul style="list-style-type: none"> • Christian Medical College, Vellore, India • Dhaka Shishu hospital laboratory, Bangladesh (partial role)
Reference for the Western Pacific Region	<ul style="list-style-type: none"> • Korea Centers for Disease Control and Prevention, Seoul, South Korea • University of Melbourne, Australia

Efforts are currently under way to define the following: specific roles and responsibilities of global, regional, national and hospital sentinel site labs, a standardized checklist for assessing a lab, performance indicators for assessing the quality of a lab and external quality assurance procedures. These issues were discussed in-depth by WHO and the global and regional reference laboratories during the 22-24 September 2010, Global Vaccine Preventable Invasive Bacterial Diseases and Rotavirus Surveillance meeting in Geneva. At this meeting, it was also decided to rationalize the use of non-culture techniques such as antigen detection and PCR to improve yield and to facilitate comparison between surveillance sites.

Acknowledgements

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