



Global Invasive Bacterial Vaccine Preventable Diseases (IB-VPD) Information and Surveillance Bulletin

Reporting Period: January through December 2010
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The World Health Organization (WHO) produces a global invasive bacterial vaccine preventable diseases (IB-VPD) surveillance bulletin twice a year to share information and data with partners at national, regional, and global levels. This bulletin presents surveillance data for January through December of 2010, as reported by Member States participating in the WHO-coordinated network for IB-VPD sentinel surveillance that targets children under 5 years of age hospitalized with suspected meningitis and/or pneumonia-sepsis.



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

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Spotlight on Efforts to Improve IB-VPD Surveillance Data Quality

Launch of the Global IB-VPD Global Laboratory External Quality Assessment Programme during 2011

The IB-VPD epidemiology and laboratory technical experts who attended the September 2010 Global IB-VPD and Rotavirus Surveillance Meeting recommended that WHO launch a laboratory External Quality Assessment (EQA) programme that targeted all laboratories that are participating in the network. Through the EQA programme, participating sentinel hospital laboratories, National Reference Laboratories (NLRs) and Regional Reference Laboratories (RRLs) receive simulated cerebrospinal fluid (CSF) and slides which contain the vaccine preventable disease pathogens that the laboratory then seeks to identify correctly. The results of the EQA programme are thus critical in determining which

laboratories require additional support to improve diagnostic capacity.



EQA process. Photo courtesy of NICD

During 2010, WHO partnered with the National Institute for Communicable Diseases in South Africa to expand the existing Microbiology EQA programme that has been conducted in the African Region since 2002. The global EQA was launched during 2011 in stages with Regional Reference Laboratories (RRLs) participating in the first round held in February 2011, and subsequently expanded to National Laboratories and hospital sentinel sites in June of the same year. During 2012, WHO will support an annual EQA programme for all participating laboratories.

Strengthening the laboratory network via clearly defining the roles and responsibilities of the Regional Reference Laboratories

RRLs are a critical component of the IB-VPD surveillance network as they provide direct support to the sentinel site laboratories. In order to maximize the impact of RRL support, the IB-VPD surveillance network agreed in December 2010 on the roles and responsibilities of the RRLs which include:

1. Monitor the Implementation of Quality Assurance/Quality control (QA/QC) System:

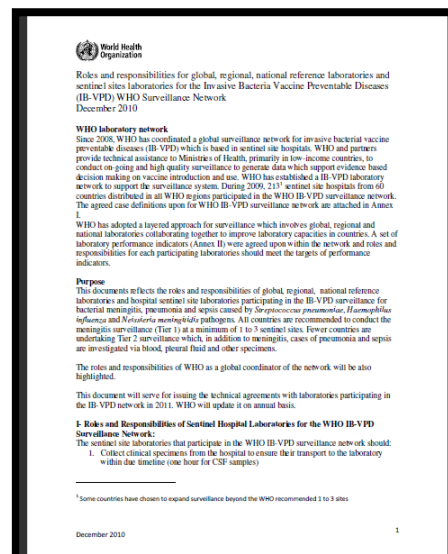
- Actively participate in the EQA programme
- Provide duplicate testing for selected IB-VPD isolates and specimens from the national laboratories and sentinel hospital laboratories
- Perform serotyping/serogrouping from routine clinical surveillance specimens (e.g. blood, CSF, pleural fluid cultures)
- Report serotype/serogroup distribution and antimicrobial resistance data to the MOH, WHO country office and WHO Regional Office

2. Provide technical support to improve capacities of national and sentinel hospital laboratories in the regional network

- Conduct on-site visits to monitor the hospital sentinel sites using the WHO IB-VPD laboratory questionnaire with a reports including recommendations to improve the laboratory capacities provided within two weeks of the visit
- Provide standard operating procedures and resource persons for laboratory training on WHO recommended methodology for laboratory diagnosis of IB-VPD.
- Provide expert guidance, standard training modules and essential reagents for IBVPD training to allow bacteriologist trainees to reach a high proficiency in applying standardized WHO methods for IB-VPD species detection, isolation, and serotyping (if appropriate)

3. Provide technical advice to the WHO IB-VPD surveillance program.

- Provide expert contributions at meetings of the laboratory network.
- Provide coordination/communication with WHO regional laboratory coordinators
- Provide advice on an *ad hoc* basis to the WHO



WHO document describing the agreed roles and responsibilities of the IB-VPD Regional Reference Laboratories, December 2010

Summary of January through December 2010 IB-VPD Surveillance Data

Note: Data in this bulletin comes from a nascent IB-VPD surveillance network where quality assurance systems are only now being established. Thus, care needs to be taken in interpreting the data and drawing conclusions. The wide variation in data from different countries reported in this bulletin may represent variation in surveillance quality, and laboratory testing methods used, rather than true epidemiological differences.

The global IB-VPD surveillance network collects data related to the detection of 3 vaccine-preventable organisms: *Haemophilus influenzae* (Hi), *Streptococcus pneumoniae* (Spn) and *Neisseria meningitidis* (Nm). Furthermore, the global IB-VPD sentinel surveillance utilizes a 3-tiered approach:

- Tier 1 surveillance targets children under-five with suspected meningitis;
- Tier 2 surveillance also targets children under-five with pneumonia and/or sepsis;
- Tier 3 surveillance seeks to determine incidence rates of IB-VPD, through surveillance in a defined catchment population.

The current network, consisting mainly of Tier 1 sentinel sites, provides information that will be useful to monitor trends in disease occurrence and to estimate vaccine effectiveness using a case-control approach, once high-quality data are obtained. However, information from Tier 1 sites should be bridged with data from Tier 2 and Tier 3 surveillance sites as well as from special studies in order to provide a comprehensive understanding of disease epidemiology.

This Bulletin presents IB-VPD surveillance data for January through December 2010. Summarized below are the main findings:

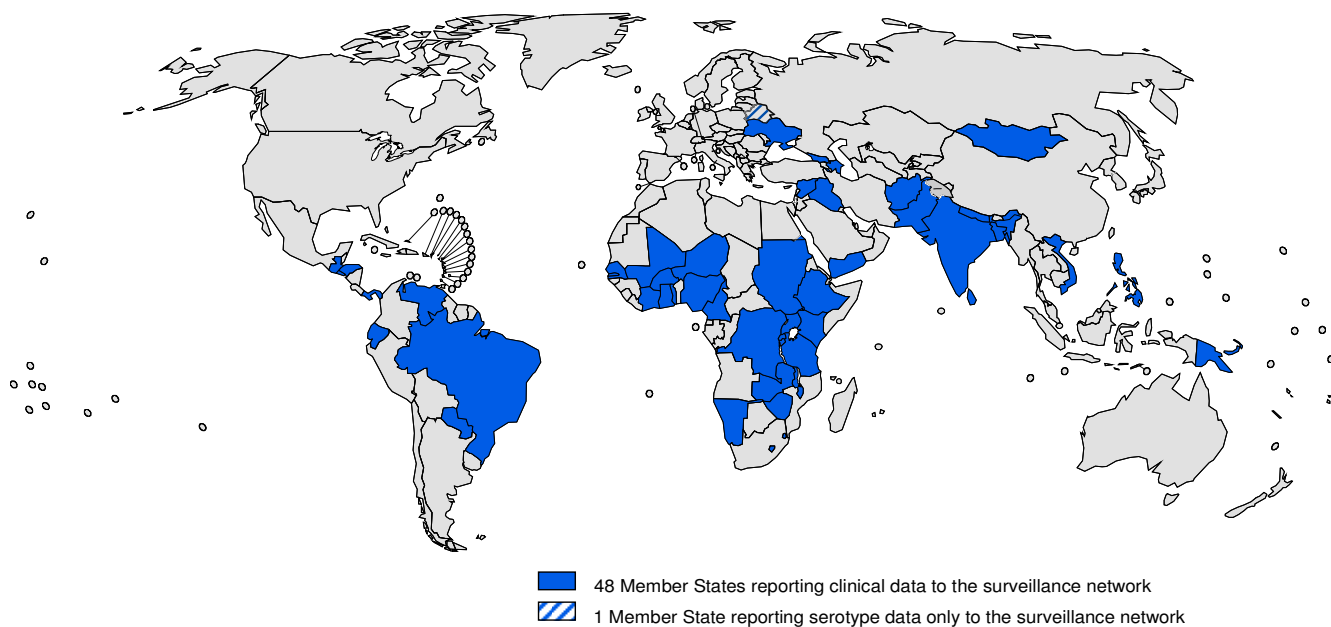
- 49 Member States reported IB-VPD surveillance data to WHO
 - 36 of 49 (73%) reporting countries were GAVI Phase II eligible countries
 - 48 Member States reported clinical data and 1 Member State (Belarus) reported serotype data only
- Among children with probable bacterial meningitis:
 - Any one of the vaccine preventable organisms was detected in 37% of children with probable bacterial meningitis, globally, in 2010 as compared to only 9% of children with probable bacterial meningitis in 2009.
 - Spn, Hi and Nm were not detected in any of the tested specimens in 7 of 48 (15%) reporting countries (6 were from the African Region), pointing to the need to strengthen surveillance practices in these countries.
 - Eight (8) countries identified ≥ 20 Spn organisms: Bangladesh, Brazil, the Gambia, Ghana, Nigeria, Senegal, Togo, and Viet Nam. The scientific community is currently debating the minimum number of isolates that may be required to determine impact and for making assessments about serotype distribution. For assessing serotype replacement, Tier 3 surveillance will be required, with adequate numbers of isolates for proper interpretation. WHO is in the process of developing criteria for the type and quality of surveillance required to assess serotype replacement.

Annex: January through December 2010 IB-VPD Surveillance Data

The Global IB-VPD Surveillance Network

During 2010, 49 Member States participated in the IB-VPD surveillance network, and reported data to WHO. Of these, 48 (98%) provided data on the cases while Belarus provided genotype only data (Figure 1).

Figure 1: WHO Member States reporting to the global surveillance network for IB VPD –2010.



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.
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Source: Data collected from WHO Regions and partners. Date of slide: 05 September 2011

Overall, 47% of reporting countries were based in the WHO African Region (AFR), (Table 1.) Among the 49 countries, there were 121 hospital sentinel sites, of which the WHO Eastern Mediterranean Region had the largest percentage (26%). GAVI eligible countries, who were provided funding support for surveillance, accounted for 73% of countries that reported to the WHO global surveillance network.

Table 1. Characteristics of WHO IB-VPD Surveillance Network by WHO Region, January to December 2010.

WHO Region*	Total number and % of countries reporting	Number of GAVI-eligible countries reporting	% of all countries reporting who are GAVI-eligible	Total number and % of sentinel sites reporting
AFR	23 (47%)	21	91%	30 (25%)
AMR	8 (16%)	1	13%	25 (21%)
EMR	6 (12%)	4	67%	32 (26%)
EUR	4 (8%)	3	75%	5 (4%)
SEAR	4 (8%)	4	100%	8 (7%)
WPR	4 (8%)	3	75%	21 (17%)
Total	49	36	73%	121

*The following countries participated in the global surveillance network for IB VPD in 2010: Burkina Faso, Burundi, Cameroon, Côte d'Ivoire, Democratic Republic of the Congo (the), Ethiopia, Gambia (the), Ghana, Kenya, Lesotho, Malawi, Mali, Namibia, Niger (the), Nigeria, Rwanda, Senegal, Swaziland, Togo, Uganda, United Republic of Tanzania (the), Zambia and Zimbabwe in the African Region (AFR); Brazil, Ecuador, El Salvador, Guatemala, Honduras, Panama, Paraguay and Venezuela (Bolivarian Republic of) in the Region of the Americas (AMR); Afghanistan, Iraq, Pakistan, Sudan (the), Syrian Arab Republic (the) and Yemen in the Eastern Mediterranean Region (EMR); Azerbaijan, Georgia and Ukraine in the European Region (EUR); Bangladesh, India, Nepal and Sri Lanka in the South-East Asian Region (SEAR); Mongolia, Papua New Guinea, Philippines (the) and Viet Nam in the Western Pacific Region (WPR).

Belarus from the European Region (EUR) reported serotype data only

WHO has adopted a tiered approach to IB-VPD 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. Fewer sites with the required technical capacity undertake Tier 2 surveillance where, in addition to meningitis, cases of pneumonia and sepsis are investigated using blood culture. Tier 3 surveillance includes meningitis, pneumonia and sepsis in a well characterized catchment population that allows estimation of disease incidence. Tier 3 is proposed in one site in each WHO region or sub-region. Among the 48 countries reporting data to WHO, 100% reported Tier 1 data, 16 (33%) reported Tier 2 data, and 1 (2%) country, Mongolia, collected population-based data (Table 2). Tier 2 and 3 surveillance are ongoing in some AFR countries, with efforts under way to capture data from these sites in the WHO surveillance network.

Table 2. Number of countries reporting IB-VPD data by surveillance tier and WHO Region, 2010.

WHO Region	Type of IB VPD surveillance		
	Tier 1	Tier 2	Tier 3
	Meningitis	+Pneumonia and/or Sepsis	+Population-based
AFR	23	0	0
AMR	8	7	0
EMR	6	4	0
EUR	3	0	0
SEAR	4	4	0
WPR	4	1	1
Total	48	16	1

Tier 1: Burkina Faso, Burundi, Cameroon, Côte d'Ivoire, Democratic Republic of the Congo (the), Ethiopia, Gambia (the), Ghana, Kenya, Lesotho, Malawi, Mali, Namibia, Niger (the), Nigeria, Rwanda, Senegal, Swaziland, Togo, Uganda, United Republic of Tanzania (the), Zambia and Zimbabwe from AFR; Brazil, Ecuador, El Salvador, Guatemala, Honduras, Panama, Paraguay and Venezuela (Bolivarian Republic of) from AMR; Afghanistan, Iraq, Pakistan, Sudan (the), Syrian Arab Republic (the) and Yemen from EMR; Azerbaijan, Georgia and Ukraine from EUR; Bangladesh, India, Nepal and Sri Lanka from SEAR; Mongolia, Papua New Guinea, Philippines (the) and Viet Nam from WPR; **Tier 2:** Ecuador, El Salvador, Guatemala, Honduras, Panama, Paraguay and the Bolivarian Republic of Venezuela from AMR; Afghanistan, Pakistan, Syrian Arab Republic and Yemen from EMR; Bangladesh, India, Nepal and Sri Lanka from SEAR; Mongolia from WPR; **Tier 3:** Mongolia from WPR;

Tier 1 - Meningitis Surveillance

During 2010, 30,457 children <5 years of age hospitalized with suspected meningitis¹ were enrolled in the WHO IB-VPD surveillance network (Table 3). This represented a 16% increase in reported suspect meningitis cases as compared to 2009.

Table 3: Number (No.) of children <5 years of age with suspected meningitis and percent of suspected meningitis that had a lumbar puncture performed, by WHO region, 2010

WHO Region	Suspected meningitis			% Suspected meningitis with a LP performed
	No.	% of Total	Range (by country)	
AFR	9,262	30	21-1,458	99
AMR*	11,805	39	38-10,514	91
EMR	3,746	12	54-1,444	82
EUR	244	1	50-115	98
SEAR	4,328	14	153-3,325	59
WPR	1,072	4	23-651	98
TOTAL	30,457	100	21-10,514	88

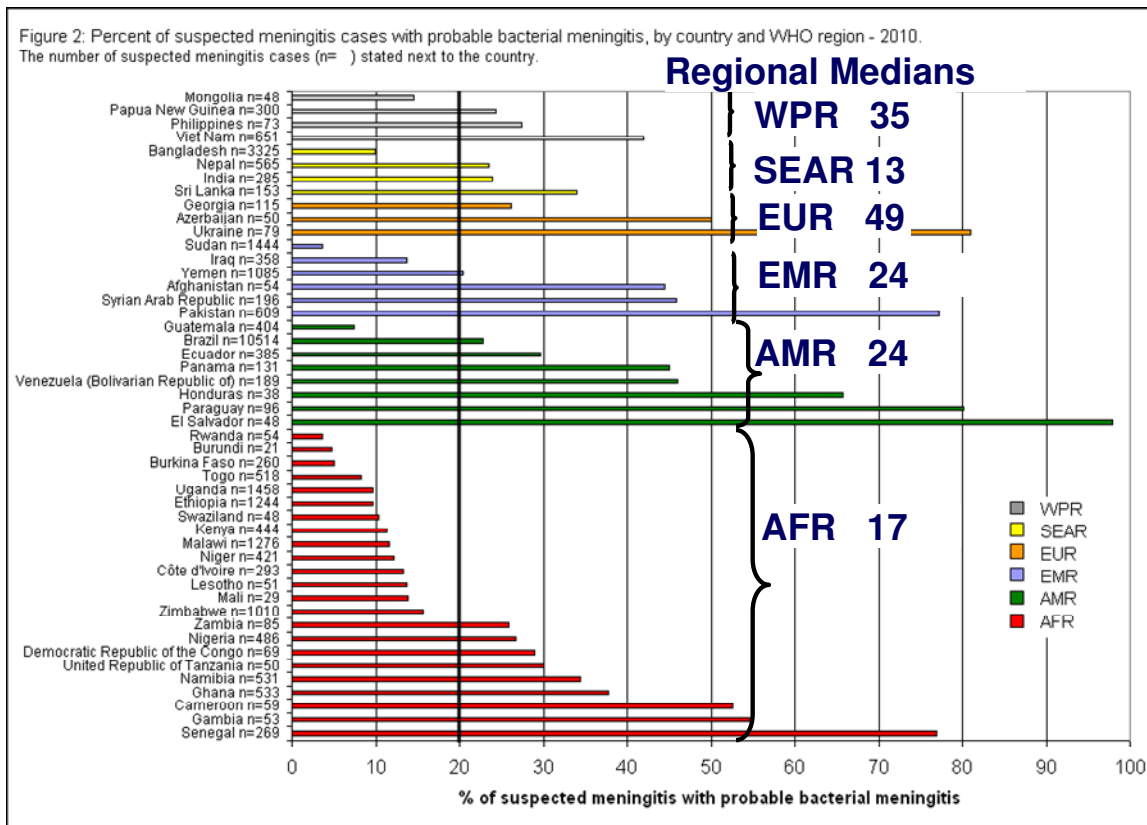
*Brazil accounts for 89% of the suspected meningitis cases in the Americas, with 10,514 cases reported.

Among children with suspected meningitis, the percent with probable bacterial meningitis² varied widely between countries, ranging from 4% in the Sudan and Rwanda to 98% in El Salvador (Figure 2). Three countries reported probable meningitis constituting 80% or more of suspected meningitis: El Salvador (98%), Paraguay (80%), and Ukraine (81%).

¹ Any child 0-59 months of age admitted to a sentinel hospital with sudden onset of fever (>38.5°C axillary) and one of the following signs: neck stiffness, altered consciousness with no other alternative diagnosis or other meningeal sign OR 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.

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).

The global IB-VPD surveillance network currently has a target of $\geq 20\%$ of probable bacterial meningitis cases detected among enrolled suspected meningitis cases. In 2010, four regions met this: AMR (24%), EMR (24%), EUR (49%) and WPR (35%). The regional medians of the percent of probable bacterial meningitis cases detected among suspected meningitis cases within AFR and SEAR were 17% and 13%, respectively. However, as shown in Figure 2, there were wide variations between reporting sites, indicating differences in clinical practice and thresholds for performing lumbar punctures.



Tier 1 - Aetiologic agents of probable bacterial meningitis

The WHO IB-VPD surveillance system only gathers pathogen information as related to detection of one of the three vaccine preventable organisms, *Haemophilus influenzae* (HI), *Streptococcus pneumoniae* (Spn), or *Neisseria meningitidis* (Nm). Data must be cautiously interpreted, as sites varied in the use of antigen detection or polymerase chain reaction (PCR) for etiologic diagnosis with some sites using them for one or more of the three pathogens and other sites using only conventional culture.

With these caveats, there may have been some improvement in the Tier 1 surveillance data from 2009 to 2010. For example, any one of the vaccine preventable organisms was detected in 37% of children with probable bacterial meningitis, globally, in 2010 as compared to 9% of children with probable bacterial meningitis in 2009. During both years, there was a wide variation among countries in the percent of probable bacterial meningitis identified with any one of these pathogens, ranging from 0% to 91% during 2010 (Figure 4). As compared to pathogen detection in 2009 among probable bacterial meningitis cases, there appeared to be a larger percentage of pathogens detected during 2010 in some countries.

Figure 4: Percent of probable bacterial meningitis caused by *Streptococcus pneumoniae* (Spn), *Haemophilus influenzae* (Hi) and *Neisseria meningitidis* (Nm), by country and WHO region, 2010. No. of probable bacterial meningitis (n =) stated next to country.

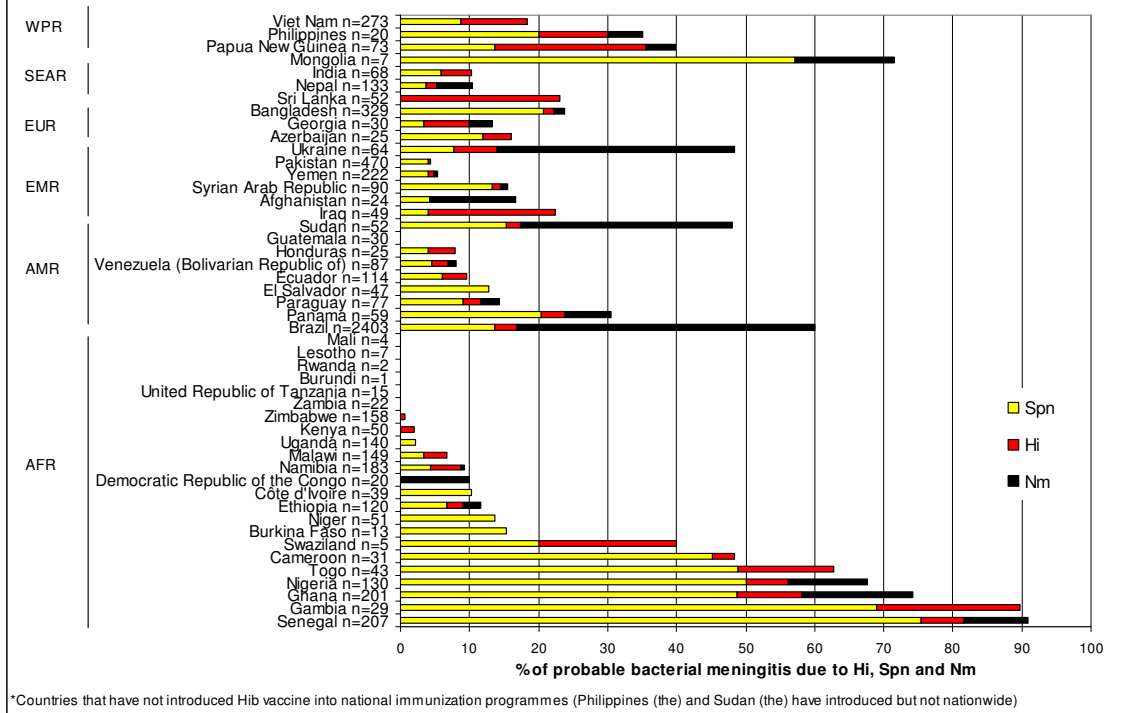
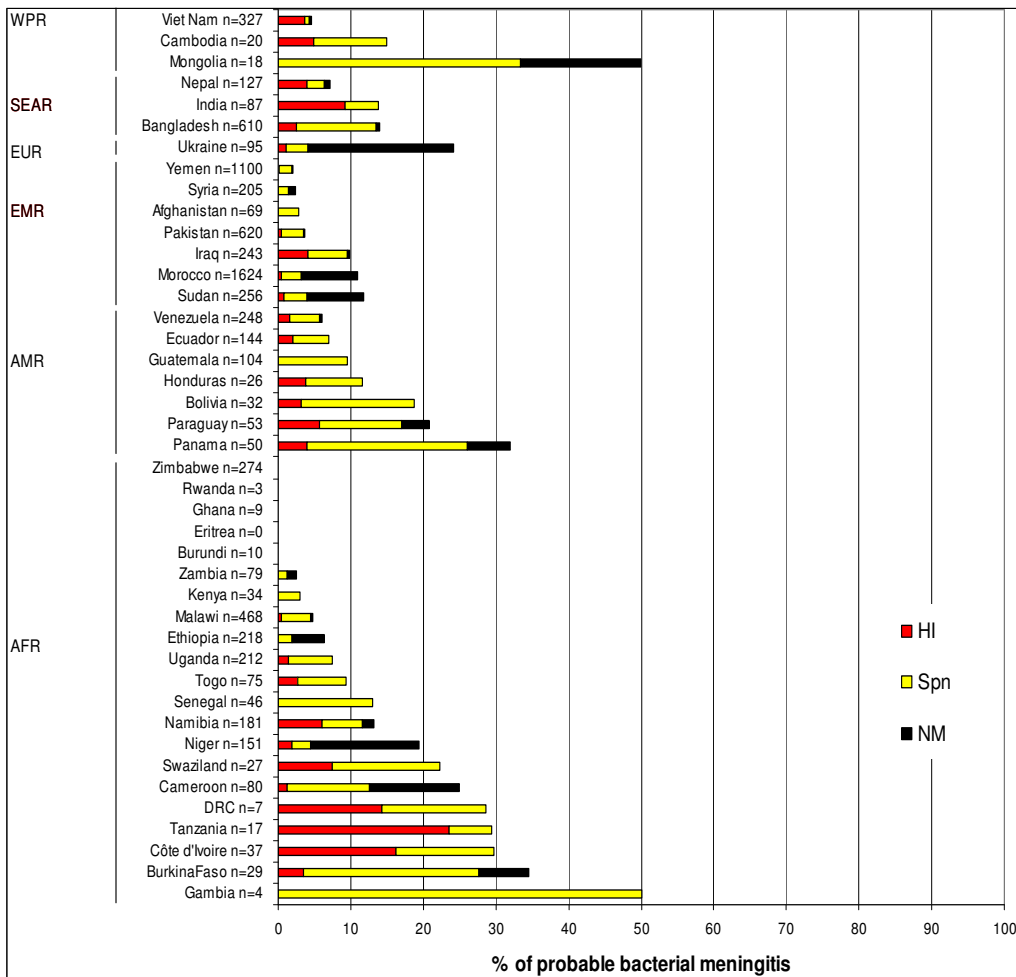


Figure 4b. Percent of probable bacterial meningitis caused by *Haemophilus influenzae* (HI), *Streptococcus pneumoniae* (Spn), and *Neisseria meningitidis* (NM), by country and WHO Region, 2009.



Tier 2 - Pneumonia and/or Sepsis Surveillance

During 2010, Tier 2 data was reported by 16 countries in 4 WHO Regions with over 28,000 children < 5 years of age hospitalized with pneumonia³ and enrolled in the WHO IB-VPD surveillance network (Table 4). Overall, 1.3% of the 15,454 blood cultures obtained were found to contain a VPD, consistent with expected results of 1-4% positive blood cultures.

Table 4: Number of children <5 years of age with pneumonia and sepsis enrolled in the WHO IB-VPD surveillance network, by WHO region, 2010

WHO Region	No. of countries reporting	Pneumonia			Sepsis		
		No. of children	% of Total	Range (by country)	No. of children	% of Total	Range (by country)
AMR	7	10,670	38	404-3,181	NS	NS	NS
EMR	4	2,026	7	10-1,652	325	82	7-201
SEAR	4	12,290	44	458-9,636	ND	ND	ND
WPR	1	3,212	11	--	70	18	--
TOTAL	16	28,198	100	10-9,636	395	100	7-201

NS: No Surveillance

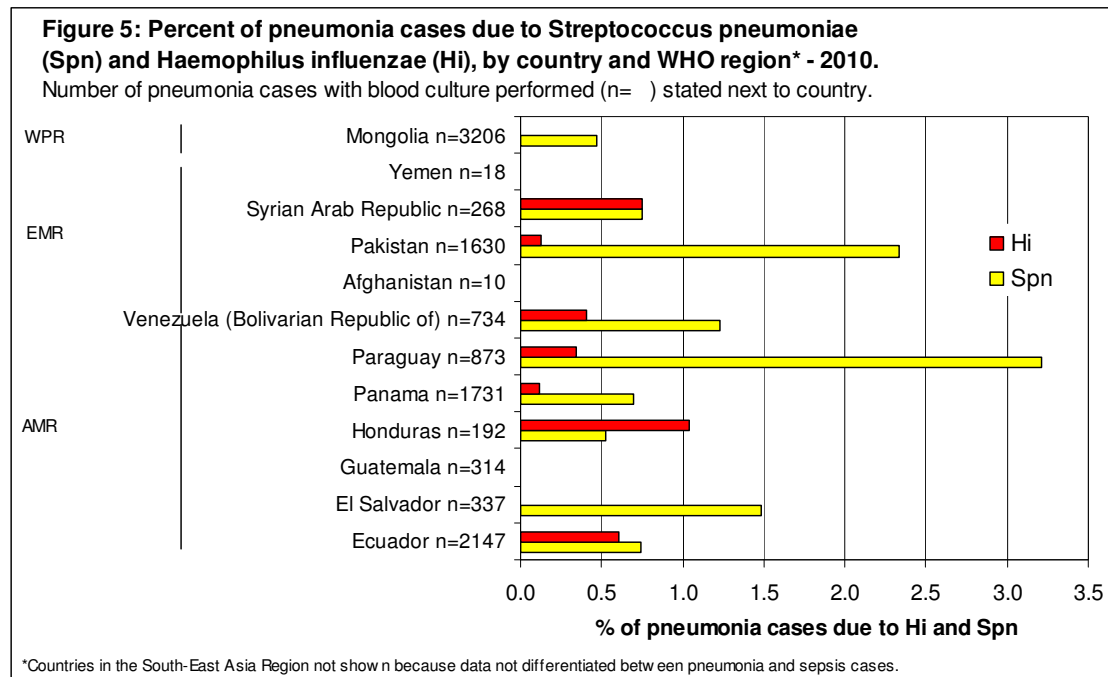
ND: No Data

Note: WPR only reported data from Mongolia

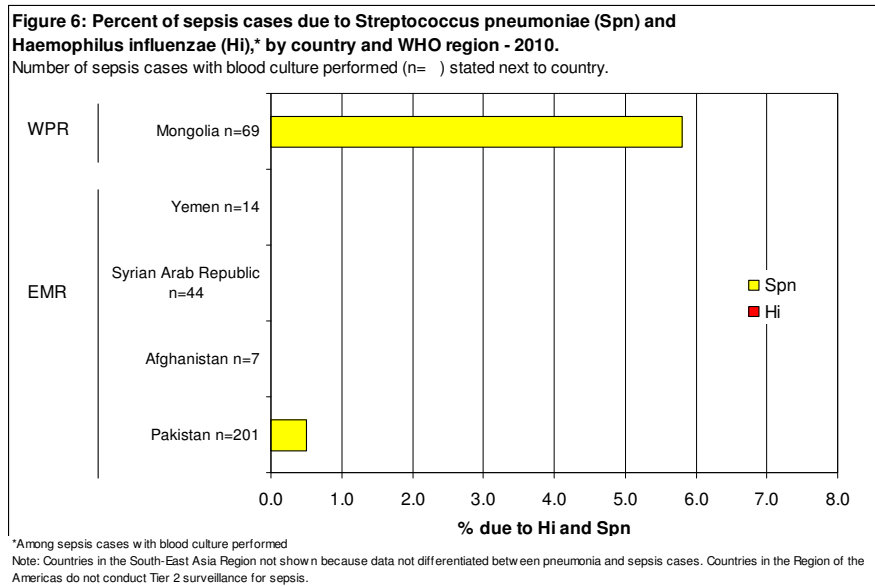
Table 5: Blood culture results for the children <5 years of age with pneumonia enrolled in the WHO IB-VPD surveillance network, 2010

Number of pneumonia cases	28,198
Number (%) with blood culture performed	15,454 (55%)
Number (%) of blood cultures with a bacterial pathogen identified	931 (6%)
Of those:	
● Number (%) due to HI	37 (4%)
● Number (%) due to Spn	162 (17%)
Overall: positive blood cultures (37+162) / 15,454(1.3%

Figures 5 and 6 present the percent of pneumonia and sepsis cases, due to Spn and HI.



³ Any child <5 years of age hospitalized with signs and symptoms of pneumonia as defined by the clinician. IB-VPD Surveillance data reporting period: January - December 2010



Serotype Data

During 2010, serotype data was reported by 5 WHO Regions as compared to 2 Regions in 2009. The number of countries with serotype data increased to 28 during 2010 from 8 in 2009. Table 5 presents the distribution of serotypes among the 639 meningitis cases with this information reported during 2010.

Table 6: Distribution in number (no.) and percentage (%) of *Streptococcus pneumoniae* (Spn) serotypes among cases of meningitis, by WHO region, 2010

Serotype	AFR n=394		AMR n=189		EMR n=14		EUR n=27		SEAR n=15	
	No.	%	No.	%	No.	%	No.	%	No.	%
4	15	4%	4	2%	1	7%	2	7%	0	0%
6B	2	1%	25	13%	0	0%	0	0%	0	0%
9V	2	1%	3	2%	0	0%	0	0%	1	7%
14	18	5%	44	23%	2	14%	2	7%	0	0%
18C	13	3%	14	7%	0	0%	0	0%	0	0%
19F	7	2%	8	4%	0	0%	0	0%	1	7%
23F	10	3%	15	8%	0	0%	1	4%	2	13%
1	80	20%	3	2%	2	14%	0	0%	0	0%
5	37	9%	3	2%	0	0%	0	0%	2	13%
7F	10	3%	5	3%	0	0%	0	0%	1	7%
3	2	1%	5	3%	0	0%	1	4%	0	0%
6A	11	3%	11	6%	0	0%	2	7%	0	0%
19A	1	0%	10	5%	2	14%	0	0%	0	0%
2	0	0%	0	0%	1	7%	0	0%	2	13%
8	0	0%	0	0%	0	0%	0	0%	1	7%
9A	0	0%	0	0%	0	0%	0	0%	0	0%
9N	0	0%	0	0%	0	0%	0	0%	0	0%
10A	0	0%	3	2%	0	0%	0	0%	0	0%
11A	1	0%	2	1%	0	0%	0	0%	0	0%
12A	0	0%	0	0%	0	0%	0	0%	1	7%
12F	2	1%	3	2%	0	0%	0	0%	2	13%
15B	0	0%	1	1%	0	0%	0	0%	0	0%
17F	2	1%	1	1%	0	0%	0	0%	0	0%
20	0	0%	1	1%	0	0%	1	4%	0	0%
22F	0	0%	1	1%	0	0%	0	0%	0	0%
33F	0	0%	0	0%	0	0%	0	0%	0	0%
45	0	0%	0	0%	0	0%	0	0%	0	0%
Others	181	46%	26	14%	0	0%	1	4%	2	13%
NT	0	0%	1	0%	6	43%	17	63%	0	0%
Total	394		189		14		27		15	

pcv 13	208	150	7	8	7
pcv10	194	124	5	5	7
pcv 7	67	113	3	5	4

AFR includes Benin, Côte d'Ivoire, Gambia (the), Ghana, Kenya, Niger, Nigeria, Senegal, Togo, Uganda, United Republic of Tanzania

AMR includes Brazil, El Salvador, Ecuador, Honduras, Paraguay, The Bolivarian Republic of Venezuela, Panama

EMR includes Afghanistan, Pakistan, Syria

EUR includes Belarus, Ukraine, Azerbaijan

SEAR includes India, Nepal, Sri Lanka, Bangladesh

NT= not typed

Comments

Tier 1/meningitis data included data from 48 countries and >30,000 children <5 years of age with suspected meningitis. There were substantial variations in the proportion of suspected meningitis cases with probable bacterial meningitis, ranging from 4% in Rwanda and The Sudan to 98% in El Salvador. This raises the possibility of differences in clinical practices that influence whether a lumbar puncture is performed or laboratory investigations undertaken. The considerable variation in the proportion of cases caused by the different pathogens 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 make comparisons and interpretations difficult. Tier 1 IB-VPD surveillance data has continued to vary considerably by country and WHO region during 2010. While some variability may represent true epidemiological differences and be a result of Hib vaccine use, it is likely that differences in surveillance practices, quality of specimen handling and laboratory processes may account for much of the observed differences.

Tier 2/pneumonia-sepsis data was reported by 16 countries in 6 WHO Regions and >28,000 children with pneumonia were enrolled. *Haemophilus influenzae* was only isolated in about 6% of pneumonia cases. *Streptococcus pneumoniae* was isolated in about 20% of pneumonia cases and about 6% of sepsis case. Overall, Spn or HI were identified in 1.3% of blood cultures, falling within the expected rate of positive blood cultures among children <5 years of age with pneumonia of 1-4%.

Serotype data was available for 5 WHO regions and 24 countries total. Though it is important to mention that the number of countries reporting serotype data has increased greatly since 2009, regions reported relatively small numbers of isolates (all regions n<60, except for AMR), and so this data must be interpreted with caution.

Next Steps to Improve Quality

WHO, Global/Regional Reference Laboratories and other partners discussed the data during the September 2011 Global Rotavirus and Invasive Bacterial Vaccine Preventable Diseases Surveillance Meeting held in Geneva and agreed to:

- Further ensuring Ministry of Health ownership including engagement of a surveillance management team of clinician, laboratory expert, and data manager;
- Increased on-site monitoring and supportive supervision of activities; and
- Improving laboratory processes by recommending rapid diagnostic testing, polymerase chain reaction (PCR) testing via RRLs, and additional laboratory training and support for all practices including Gram stain and culture.

Acknowledgements

WHO gratefully acknowledges the dedicated efforts of the numerous individuals and organizations involved with compiling this surveillance information, including Ministries of Health, sentinel hospitals, as well as the network of global, regional and national reference laboratories.

WHO IB-VPD Surveillance Websites

http://www.who.int/immunization_monitoring/diseases/meningitis_surveillance/en/index.html

<http://www.who.int/nuvi/surveillance/en/>

