4th Arab Symposium for Antimicrobial agents
Tunis, Tunisia, 17-20 April 2006

Epidemiology of Bacterial Meningitis in the WHO Eastern Mediterranean Region

Dr E.Mohsni, MO, VPI, WHO EMRO

VPI,WHO/EMRO

Outline

- Epidemiology
  - at the global level
  - In the E.M. Region
- WHO Eastern Mediterranean Regional Network for bacterial Meningitis Surveillance

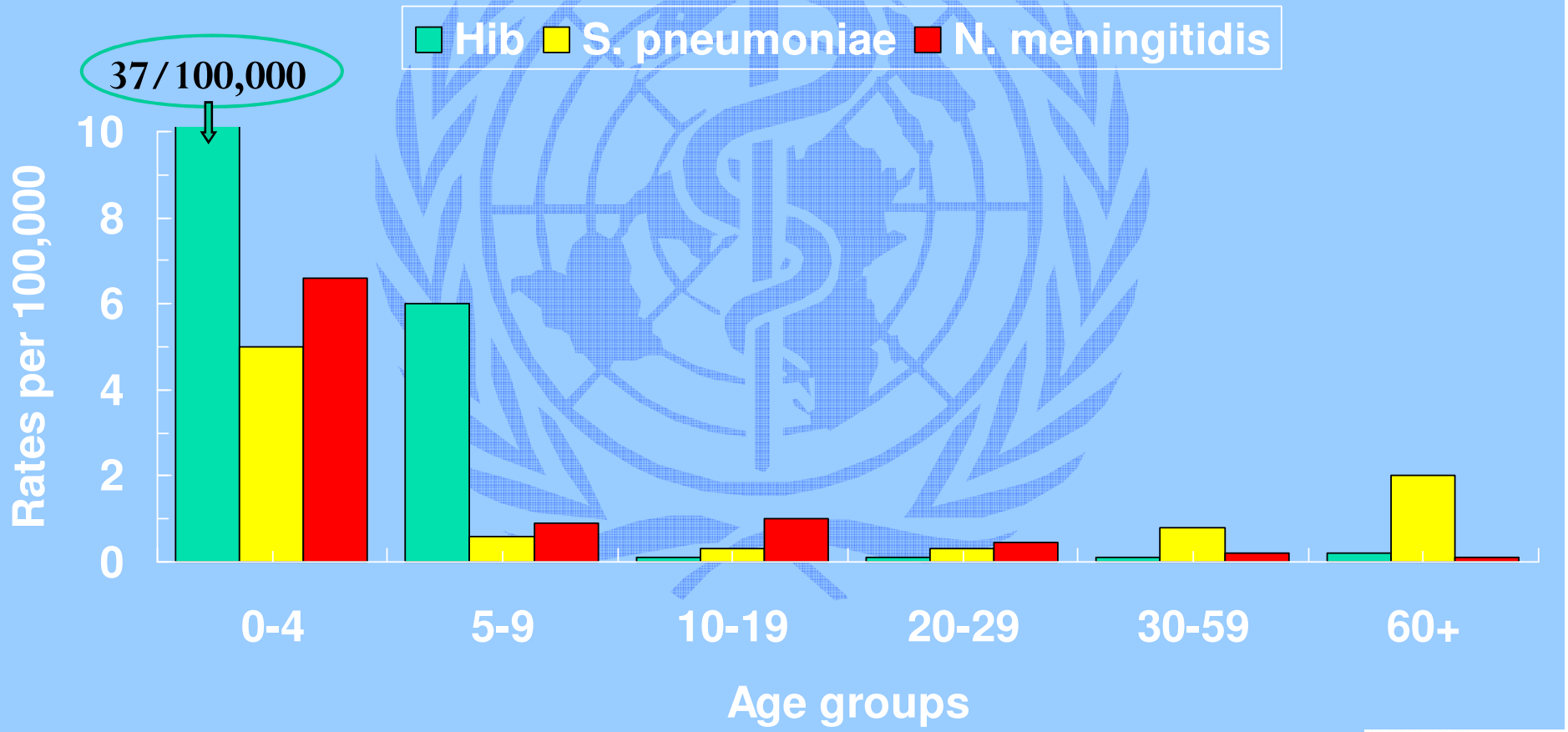
Bacterial Meningitis

- Bacterial infection affecting the brain and the spinal cord
- *3 main Pathogens:*
  - *Hib*
  - *Streptoc.Pneumoniae*
  - *Neisseria meningitidis* (serogroups: A, B, C, W135, X, Y, Z, 29E..) ➔ Epidemics
- *Etiology varies by age group and region of the world*

Burden of meningitis

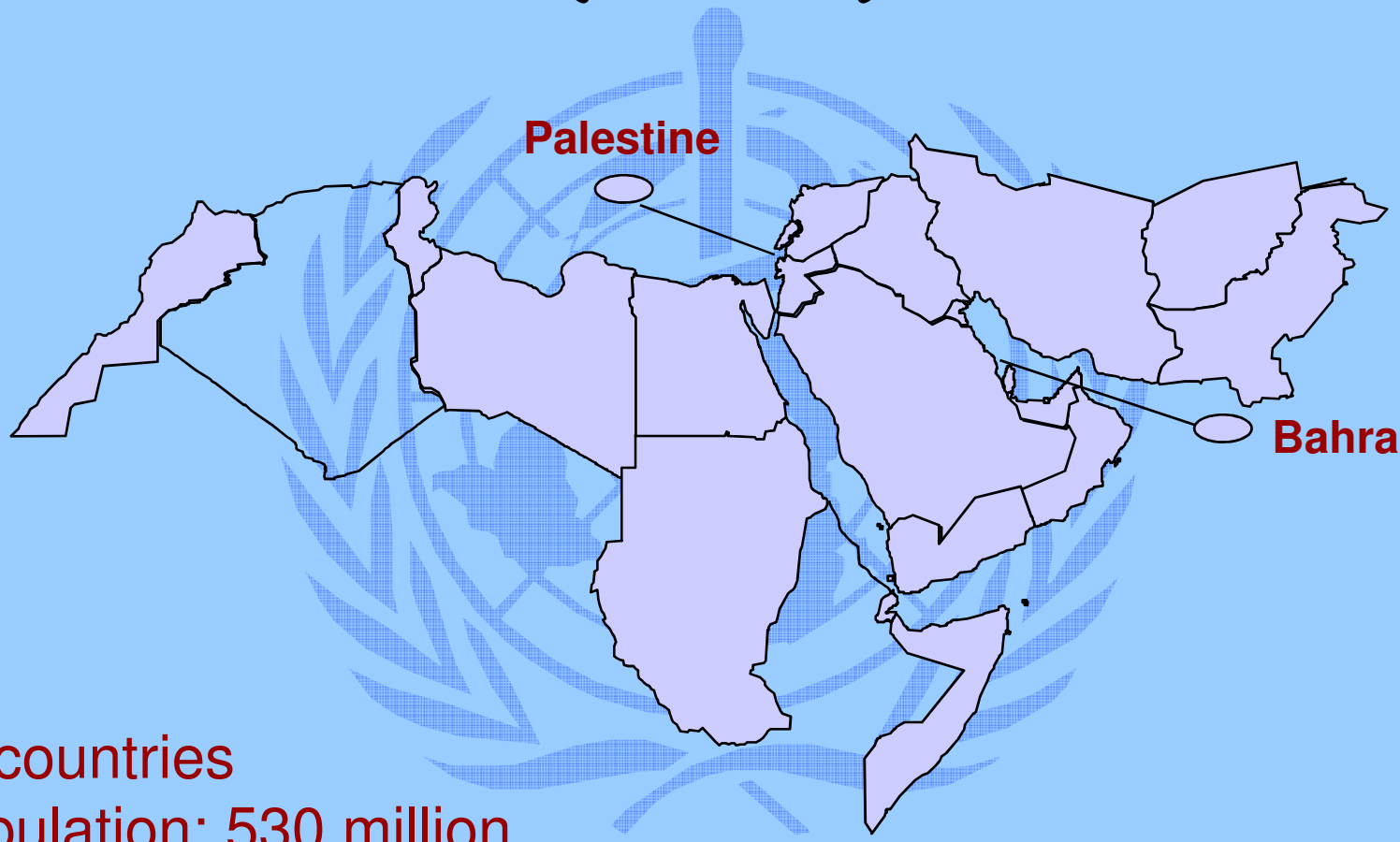
- Without epidemics:
  - 1 million cases per year
  - 173,000 deaths
  - Case fatality rates vary with age and the causative agent
    - 3 to 19% in developed countries
    - Much higher (37 to 60%) in developing countries
  - High proportion (up to 50%) of survivors are left with disability
  - 6,192,000 DALYs
- During epidemics (African Meningitis Belt)
  ➔ Burden is much higher

Global Burden of Bacterial Meningitis



VPI,WHO/EMRO

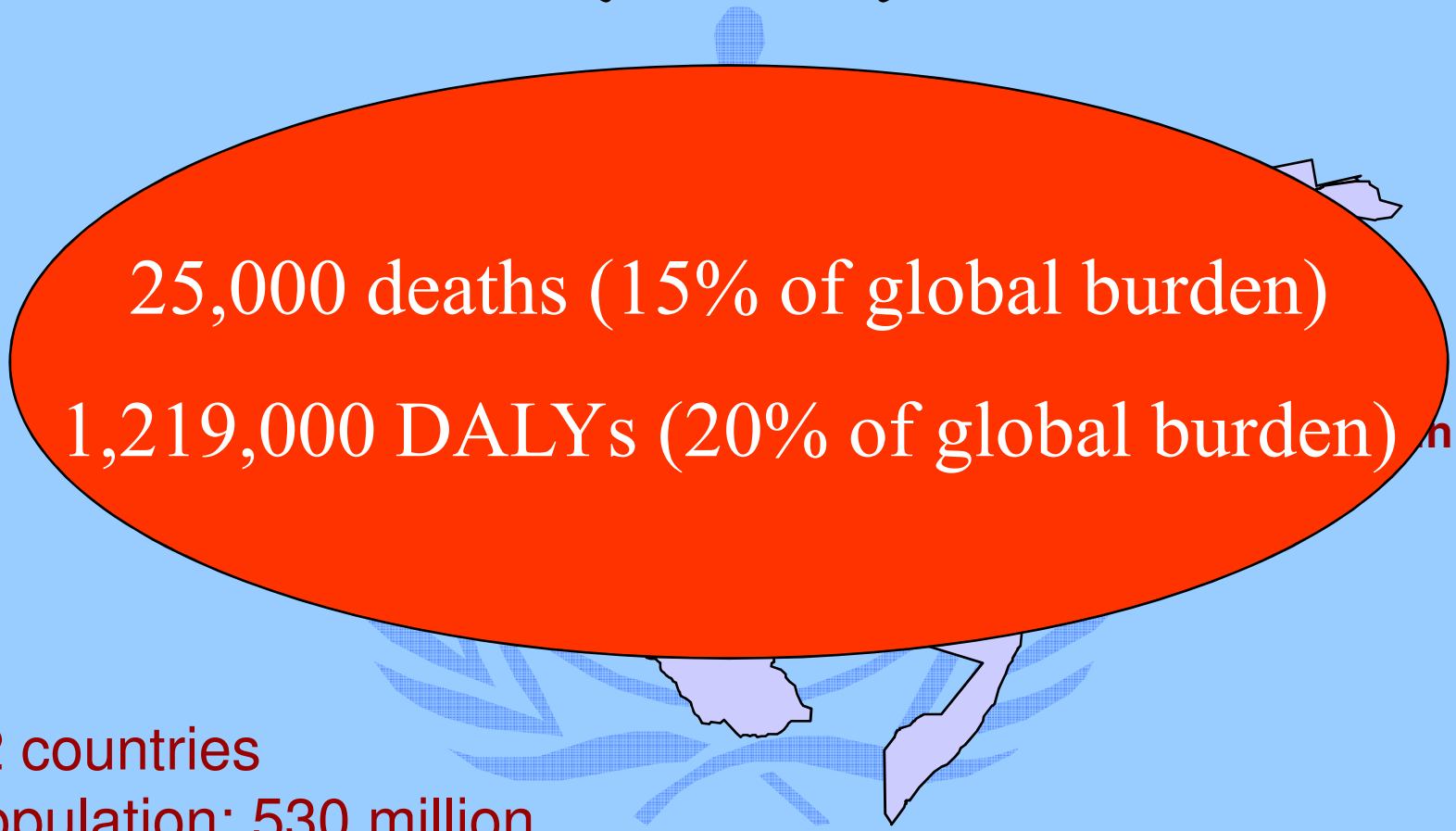
WHO Eastern Mediterranean Region (EMRO)



22 countries
Population: 530 million
Birth cohort: >15 million

VPI,WHO/EMRO

WHO Eastern Mediterranean Region (EMRO)



22 countries
Population: 530 million
Birth cohort: >15 million

VPI,WHO/EMRO

Studies on the etiology of bacterial meningitis among children in selected EMR countries

Study (Year)	Ages (years)	Total Cases	Cause of Disease No. of cases (%)			
			H. influenzae	*S. pneum.*	*N. mening.*	Other
Kuwait ('81-87)	0-12	110	49 (45%)	23 (21%)	14 (13%))	24 (21%)
KSA ('82-'90)	0.1-10	55	26 (47%)	19 (35%)	2 (4%)	8 (15%)
Libya ('94)	0.1- 10	60	26 (43%)	20 (33%)	0	14 (24%)
Jordan ('95)	0.1-12	121	39 (32%)	18 (15%)	40 (33%)	24 (20%)
Egypt ('98-01)	0-5	228	89 (39%)	68 (30%)	30 (13%)	41 (18%)

Source: Published data

VPI,WHO/EMRO

1. Meningococcal meningitis

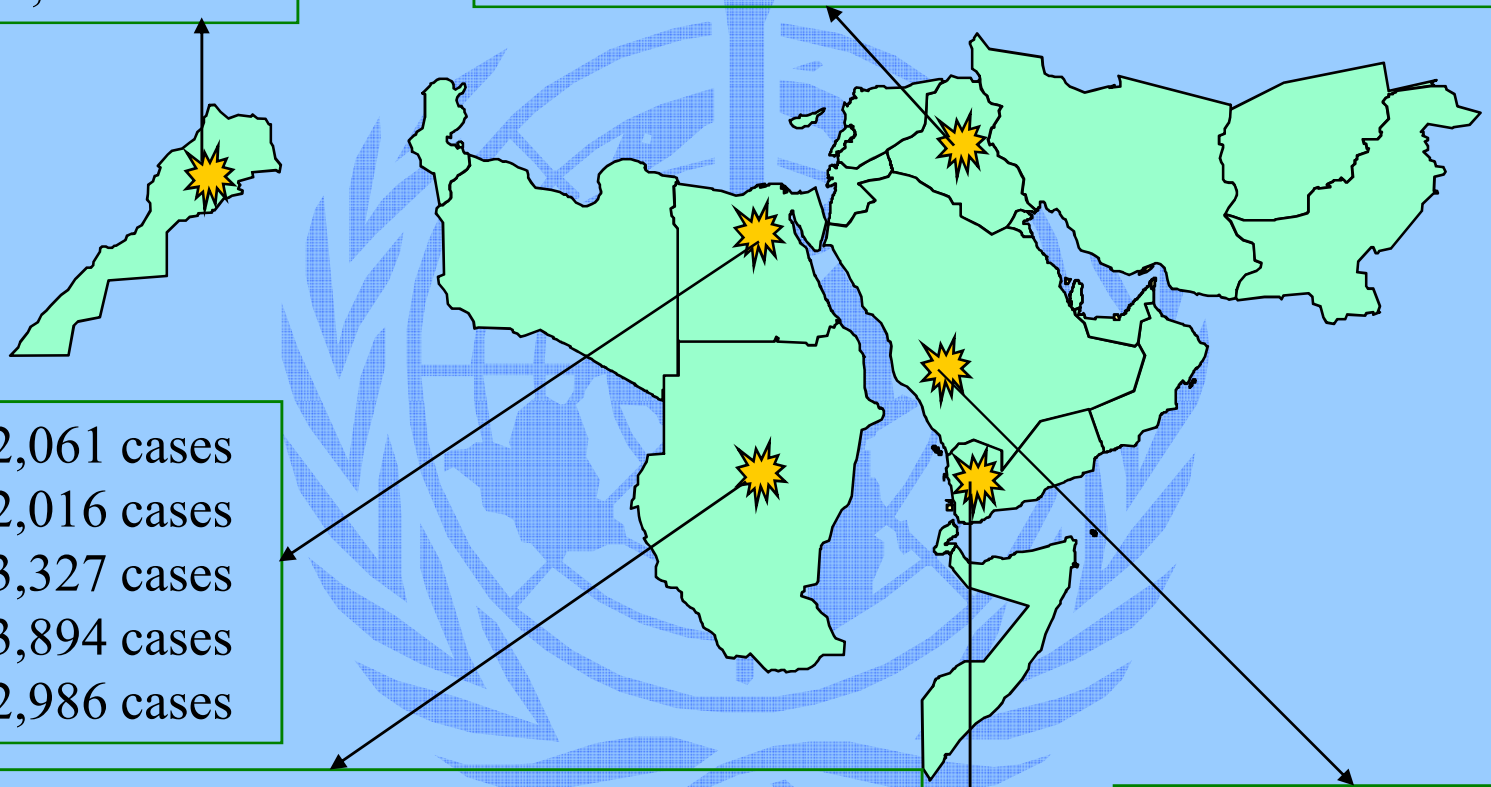
- *Neisseria meningitidis:* serogroups: A, B, C, W135, X, Y, Z, 29-E…
  - **Africa: 80% of the burden (meningitis belt)**
    - 18 countries (250 million people)
    - 700 000 cases in the past 10 years
    - 10-50 % lethality
    - 10-20 % of survivors suffer permanent sequels

VPI,WHO/EMRO

Major outbreaks of MCD in the EMR 1976-2002

1988: 1,348 cases
1989: 1,802 cases

1991: 5,792 cases, 1992: 4,534 cases; 1993: 3,923 cases, 1994: 3,427 cases; 1995: 3,138 cases



1982: 2,061 cases
1983: 2,016 cases
1988: 3,327 cases
1989: 3,894 cases
1990: 2,986 cases

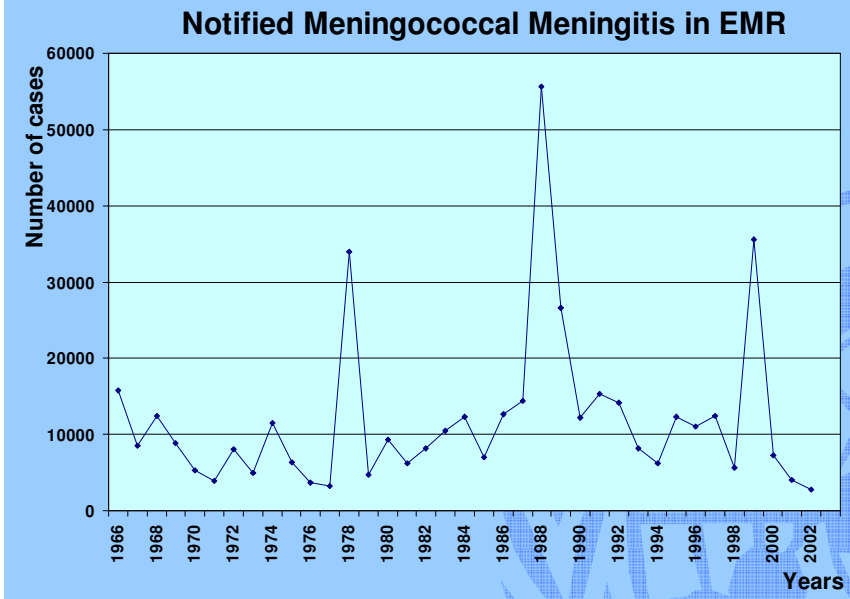
1950-51: 72,000 cases & 9,972 deaths
1978: 29,170 cases
1988: 32,016 cases
1989: 7,051 cases
1999: 33,313 cases , 2,400 deaths (CFR 7.2%)

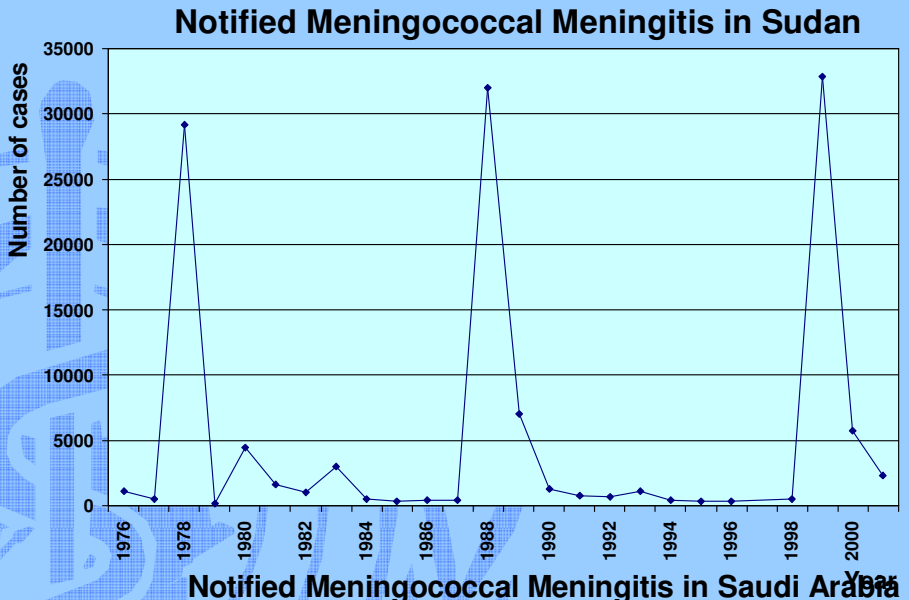
1987: 1,841 cases

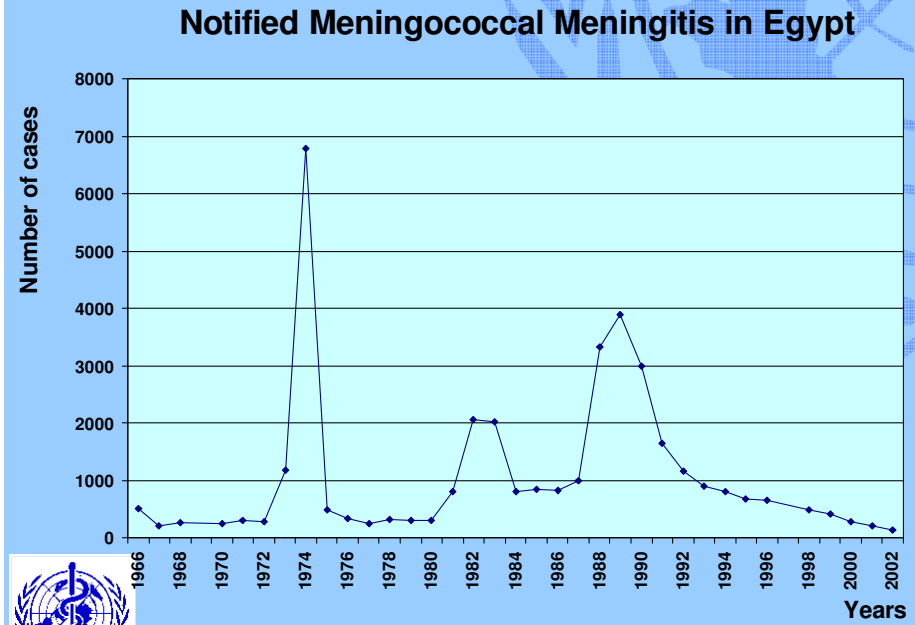
1988: 8,211 cases
1989: 4,264 cases

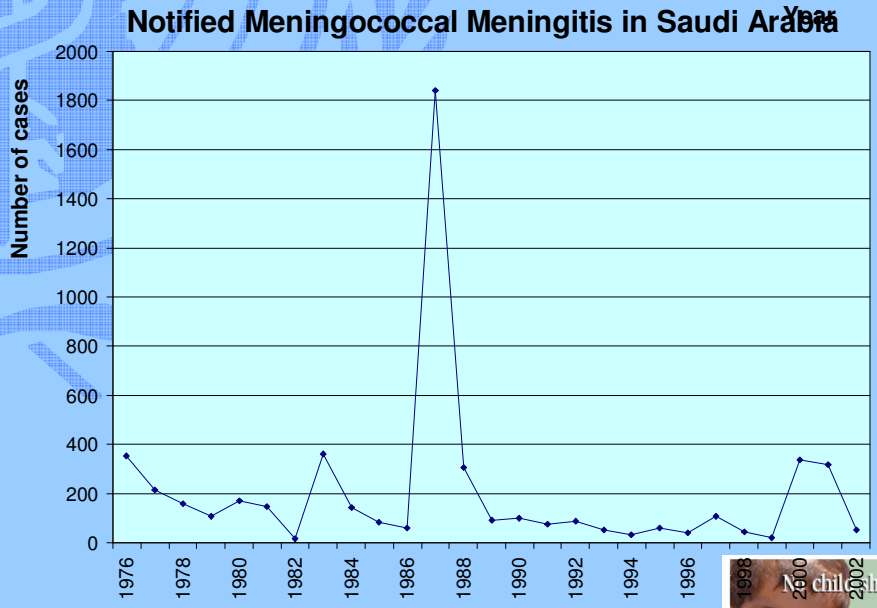
VPI,WHO/EMRO

Meningococcal meningitis in the EMR









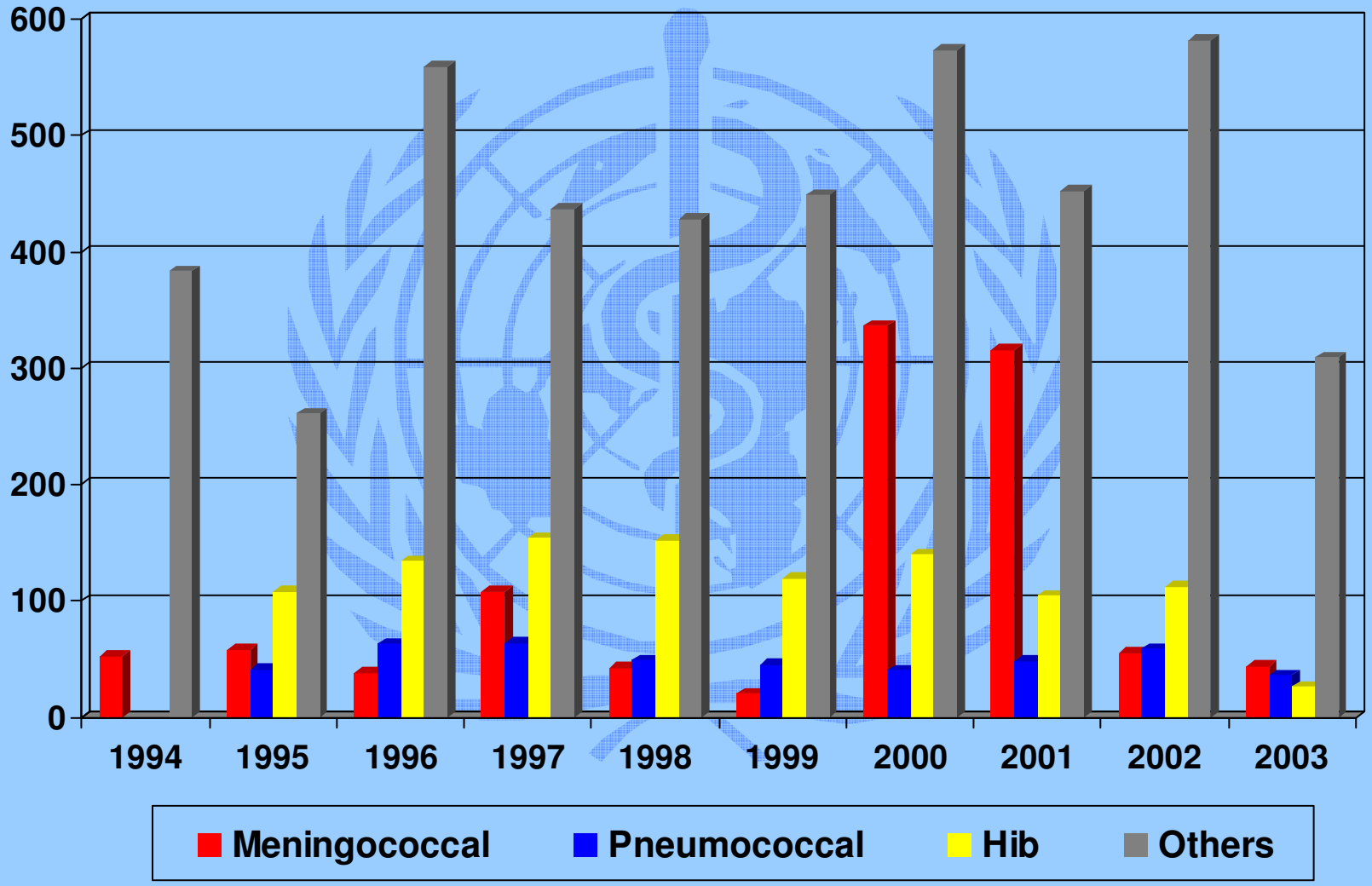
VPI,WHO/EMRO

W135: an emerging threat

- **Up till yr 2000, epidemics were mainly caused by serogroup A**
  (B & C → sporadic cases & localized outbreaks)

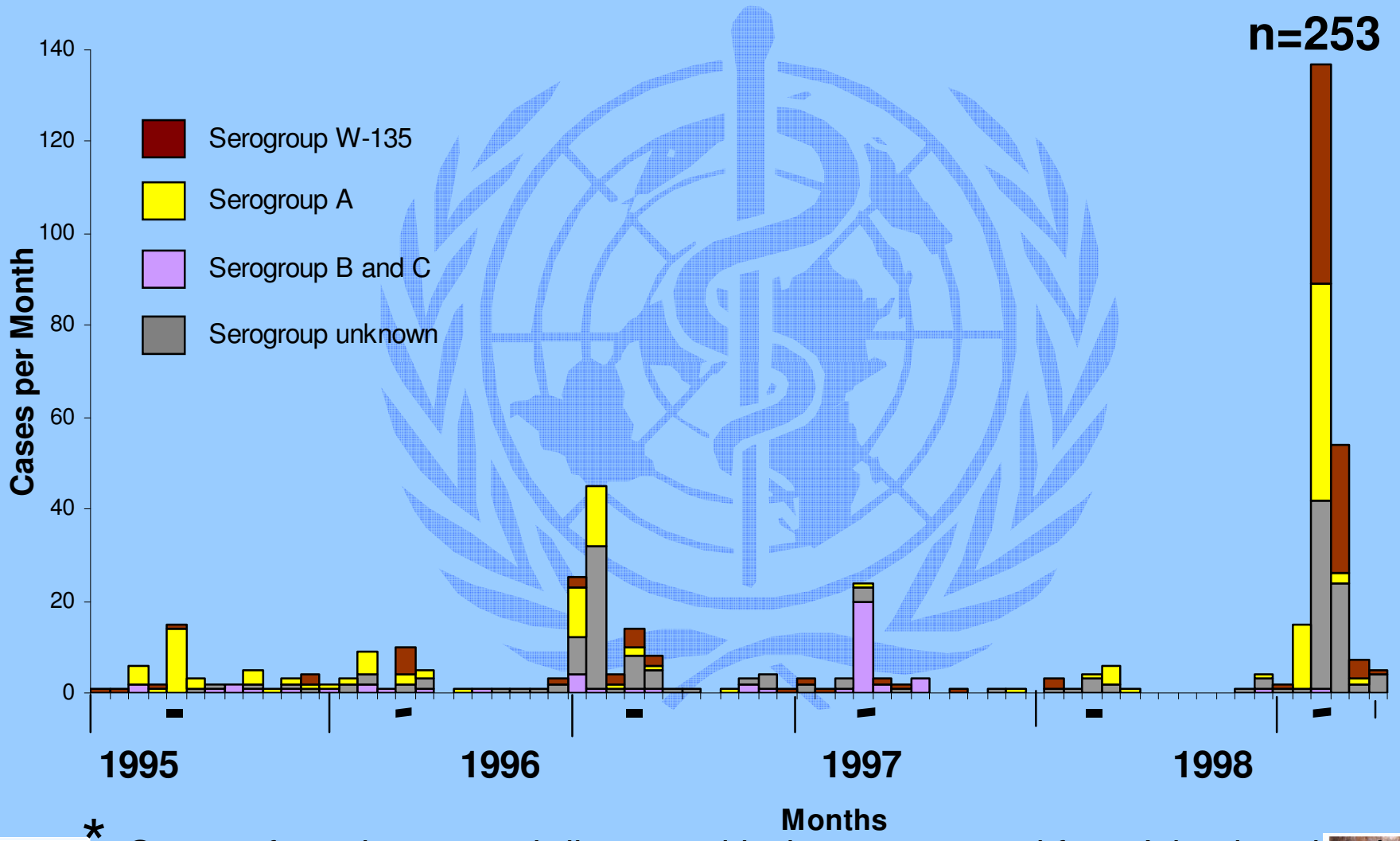
- **Emergence of W135 as an epidemic sero-group:**
  - 2000-2001: epidemics in Saudi Arabia during Hajj
  - 2000-2001: world-wide epidemic after Hajj
  - 2002: W135 epidemic affected Burkina Faso (14,000 cases – 1,500 deaths)
  - 2003: Mixed epidemics A-W135 confirm spread of W135 in the meningitis belt
  - 2005: mixed localized A-W135 outbreak in Darfur, Sudan
  - 2006:
    - localized W135 outbreak in Darfur, Sudan
    - Sero-group A epidemic in southern Sudan

Reported Meningitis Cases, KSA, 1994 - 2003



VPI,WHO/EMRO

Meningococcal disease in Saudi Arabia, 1995–2000 (Lingappa et al. EIDJ 2003)



* Cases of meningococcal disease with dates converted from Islamic calendar months. The period of the Hajj pilgrimage for each year is underscored.

Meningococcal Vaccines

- Polysaccharide vaccines
  - AC, ACW135, ACYW135
  - Poorly immunogenic in infants
  - Only short term protection for children below 4 years
  - NOT recommended for routine vaccination
  - Mass vaccination is the only way to control epidemics

- Conjugate vaccines:
  - Conjugate vaccine for C only is available
  - Conjugate vaccine against Group A is expected 08-09
  - Several combinations of conjugate vaccines are being developed

Properties of meningococcal vaccines

	Polysaccharide vaccines	*Conjugate vaccines*
Immunogenicity		
5 yr olds-adults	**High**	**High**
Young children	**Poor**	**High**
Response to Booster	**Poor**	**High**
Quality of Antibody in Children		
Avidity	**Low**	**High**
Bactericidal activity	**Low**	**High**
Induction of memory	**+/-**	**Yes**
Effect on Colonization	**+/-**	**Yes**

The Meningitis Vaccine Project

- Created in June 2001 by a $US 70 million grant from the Bill & Melinda Gates Foundation as a 10 year partnership between WHO and PATH

- Eliminate epidemic meningitis as a public health problem in Sub-Saharan Africa through the development, testing, licensure, and widespread use of *conjugate* meningococcal vaccines.

Guiding Principles

- The project is about public health impact and not simply making vaccines available
- Decisions about candidate vaccines linked to introduction strategies and likely financial constraints
- African public health officials to be closely involved with MVP

Discussions with African Public Health Officials & WHO/AFRO, Fall 01-Spring 02

- Cost of vaccine was the most important limiting factor to the introduction of new vaccines
- Meningitis belt countries are the poorest in the world
- Success of MVP (widespread use of a conjugate meningococcal vaccine in mass campaigns) would not be possible unless vaccines were priced less than than $US 0.50 per dose

VPI,WHO/EMRO

Choice of Men A Conjugate Vaccine

Extensive discussions throughout the Fall of 01 and a decision was made to pursue the development of a monovalent A vaccine because:

- Great proportion of meningococcal isolates from Africa still Group A
- Advantage of simplicity, low risk, and solid public health impact
- Low price-sustainability of the program

Use of the Monovalent A Conjugate Vaccine

- Used as a single dose in mass vaccination campaigns throughout the meningitis belt for persons between 1 and 29 years of age (target population about 250 million in 18 countries)
- EPI antigen in under ones (2 doses; 14 weeks with DTP3 and at 9 months with measles)

Men A Conjugate Vaccine Development

- Could not reach agreement with major vaccine manufacturers; negotiations ended in March 02
- Consortium of manufacturers has been created
  - Amsterdam company to produce A PS
  - Public laboratory in US to develop conjugation method
  - Indian company to produce vaccine

– ***Available by 1009-2010***
– ***Target price of 40 cents per dose***

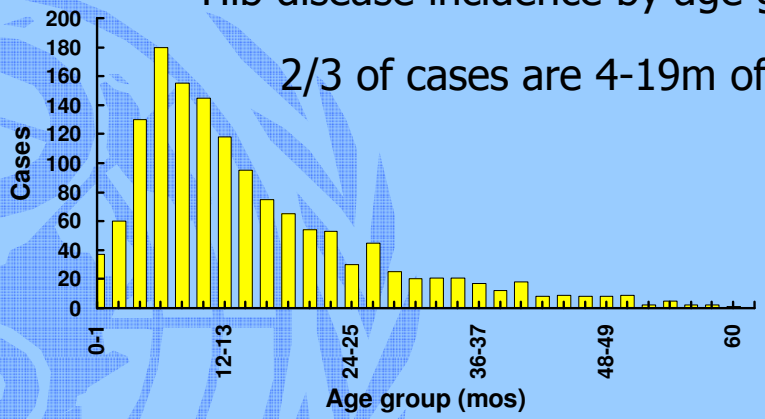
VPI,WHO/EMRO

2. Hib Disease

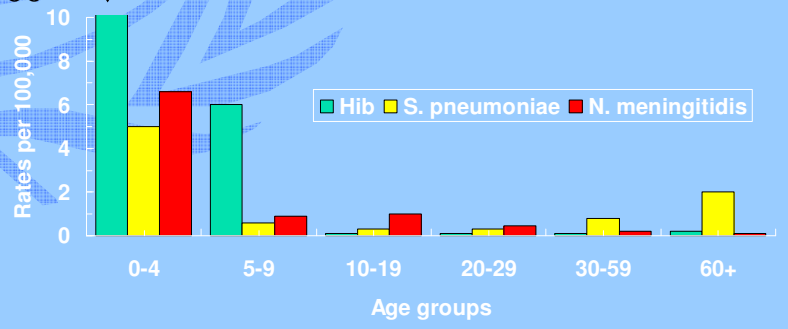
- Global burden:
  - in children less than five years of age
    - Hib is the most common cause of bacterial meningitis
    - Hib is the second most common cause of serious bacterial pneumonia
    - 400,000-500,000 deaths/year estimated in children less than five years of age

Hib disease incidence by age group

2/3 of cases are 4-19m of age

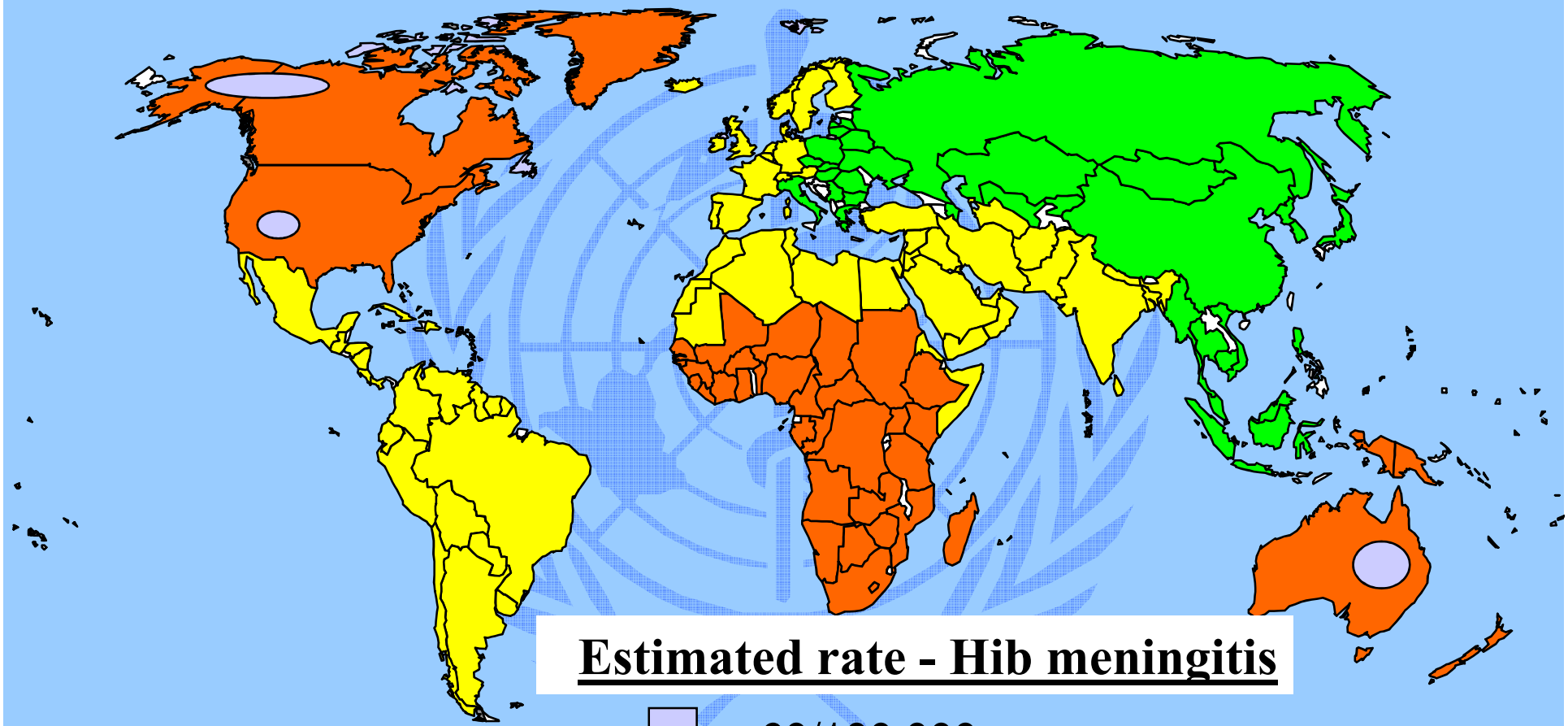


37/100,000



VPI,WHO/EMRO

Hib meningitis burden

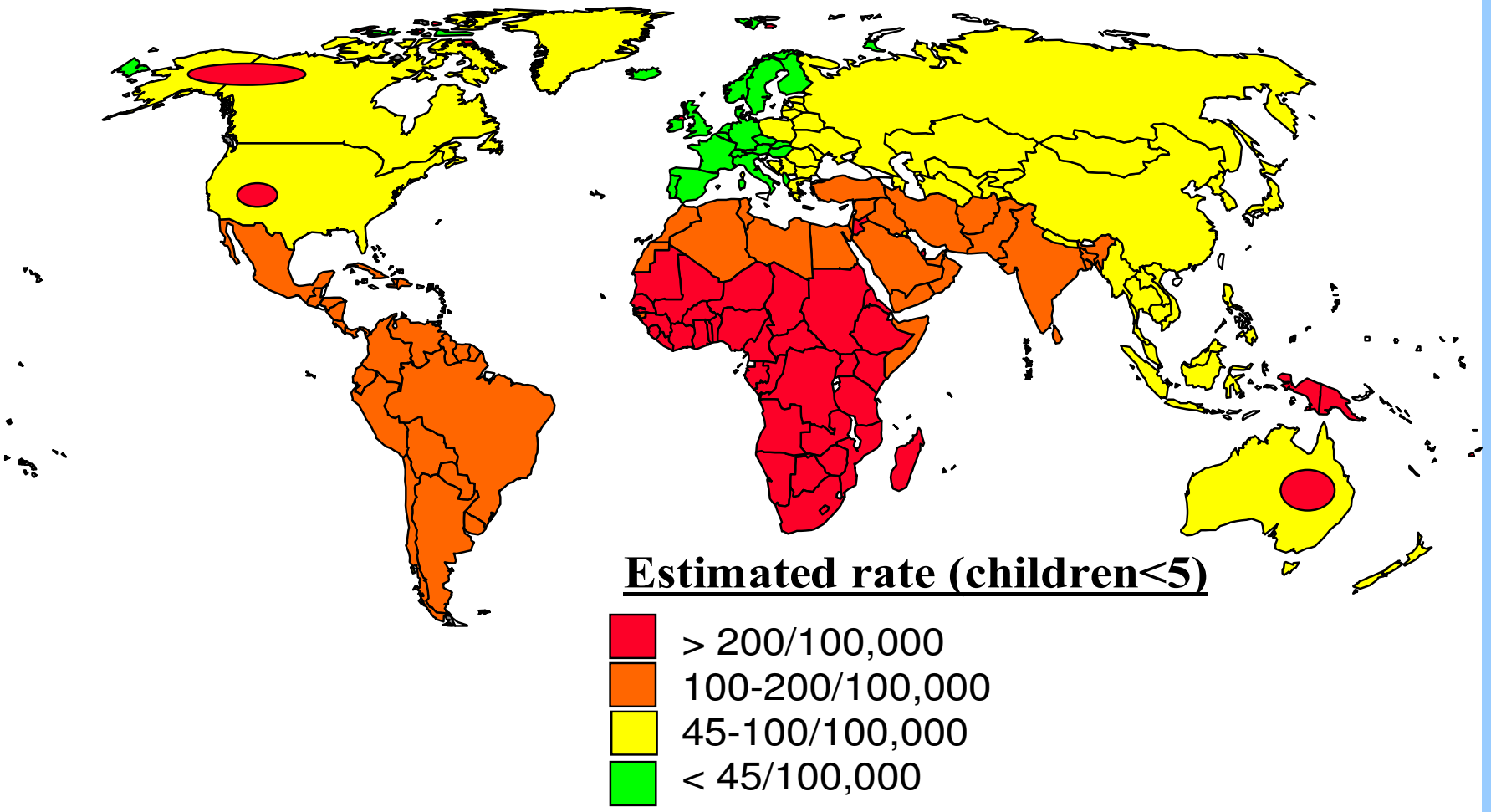


Estimated rate - Hib meningitis

- > 60/100,000
- 30-60/100,000
- 15-29/100,000
- 5-15/100,000

VPI,WHO/EMRO

Hib meningitis and pneumonia burden



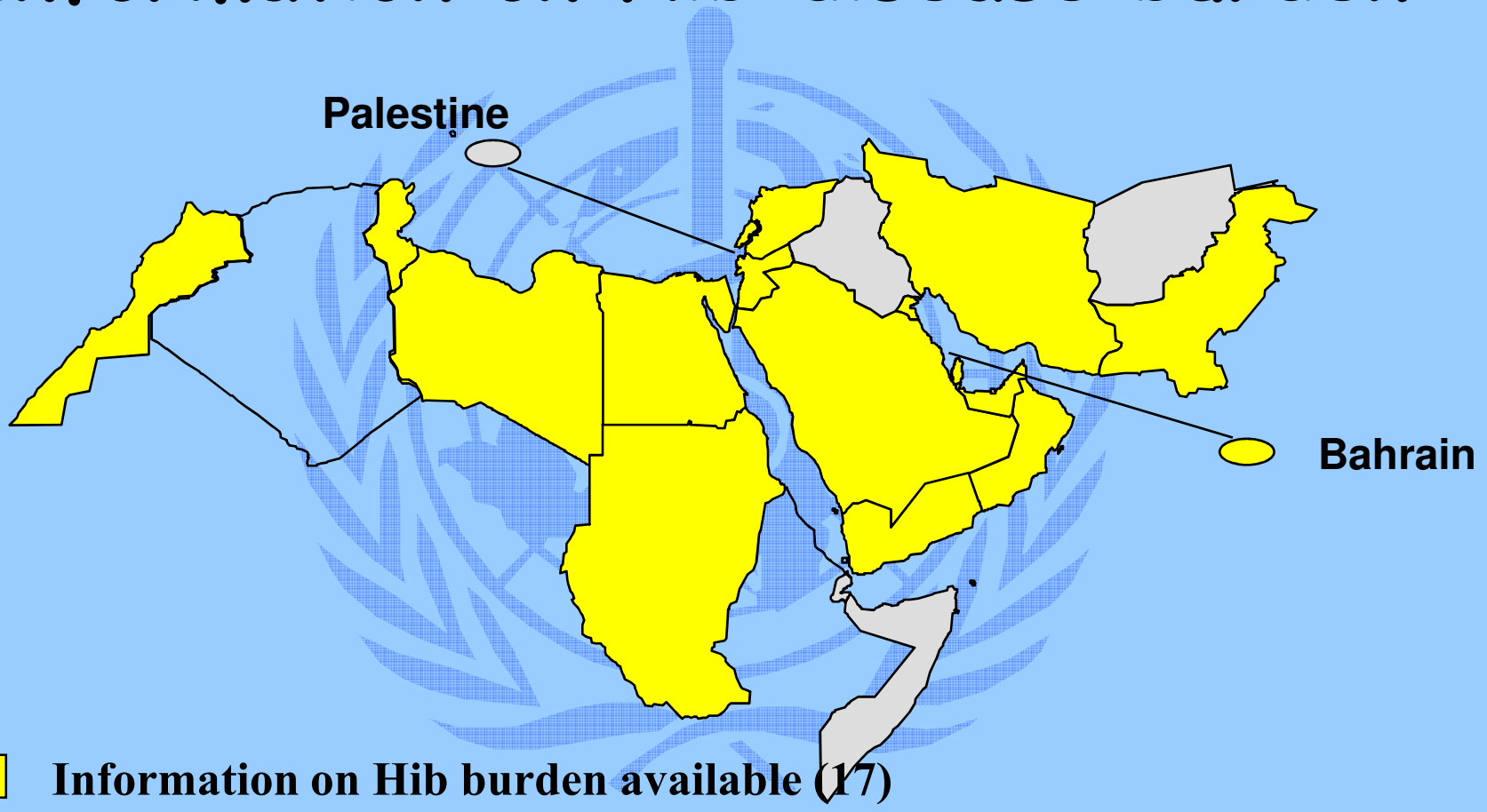
Hib disease in the EMR

- Total Hib disease cases:

  estimated 90,000-120,000 Hib cases/year
- Hib meningitis
  - cases:
    - Incidence: up to 58/100000 <5 children
    - estimated 16 000 cases/year, (>12% of the global cases)
  - Deaths:

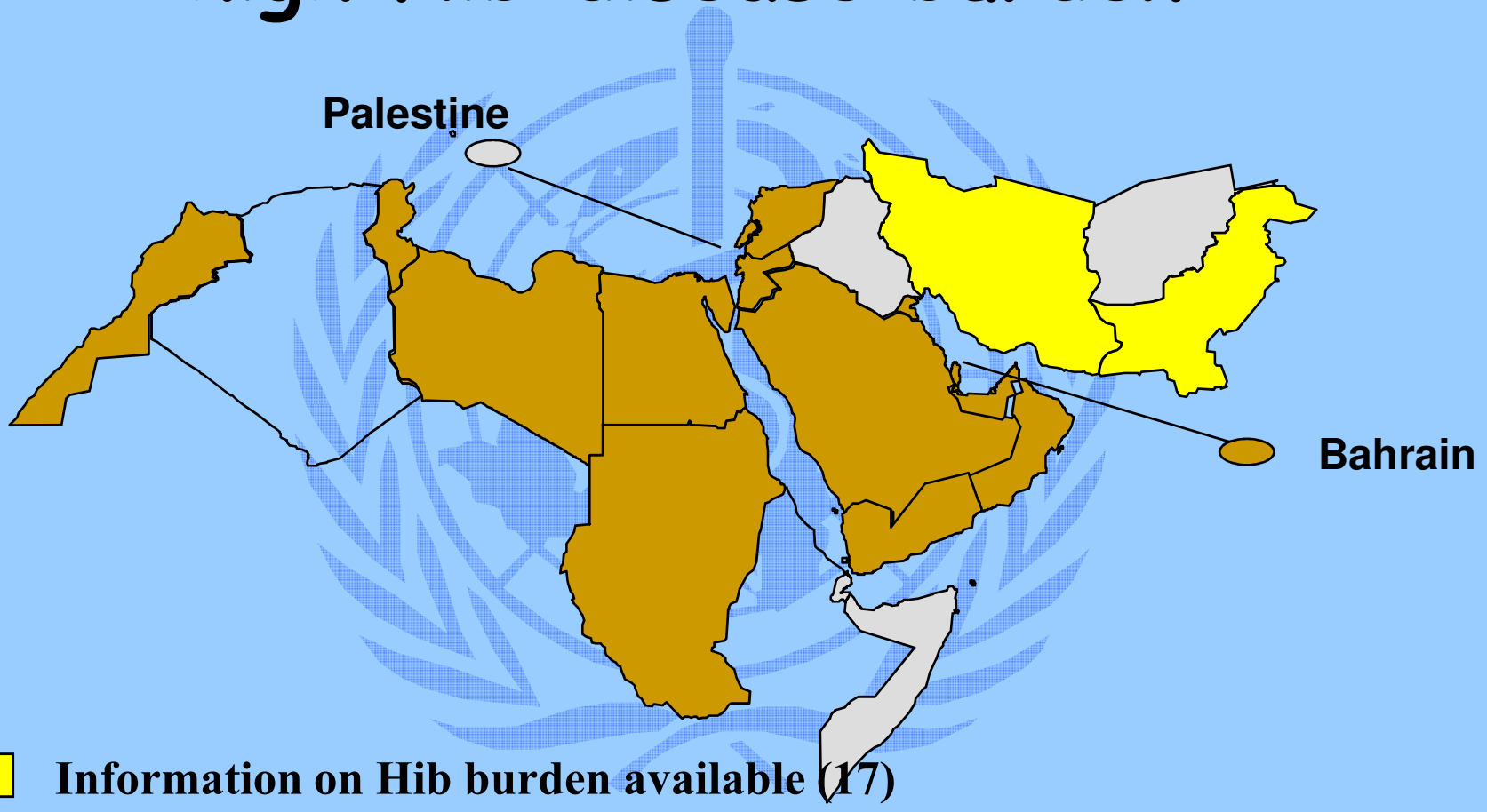
    Estimated >6 500/year

Countries with available information on Hib disease burden



VPI,WHO/EMRO

Countries with "demonstrated" high Hib disease burden

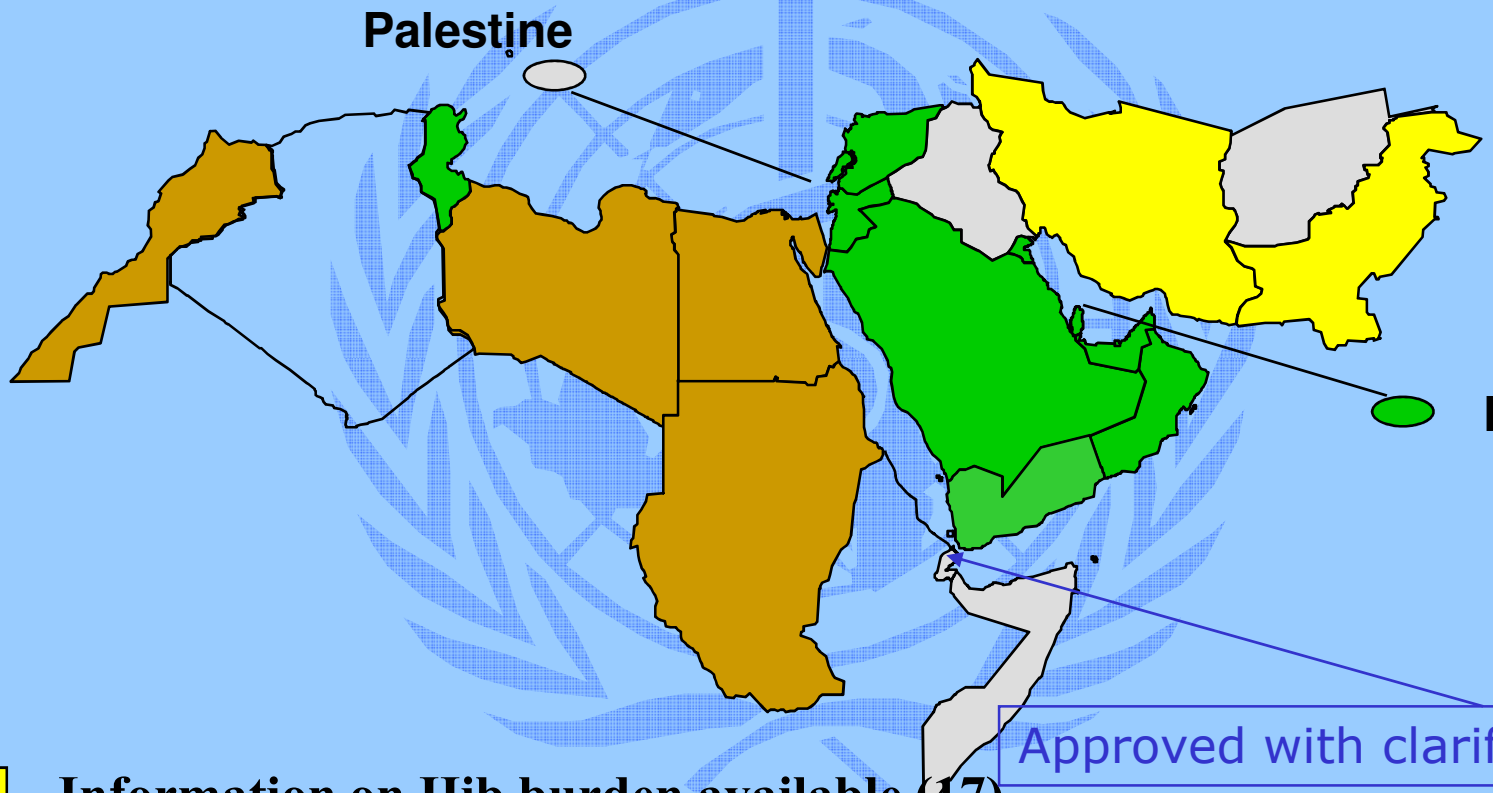


Information on Hib burden available (17)

Moderate to High disease burden (15)

VPI,WHO/EMRO

Countries with Hib vaccine introduced into routine EPI



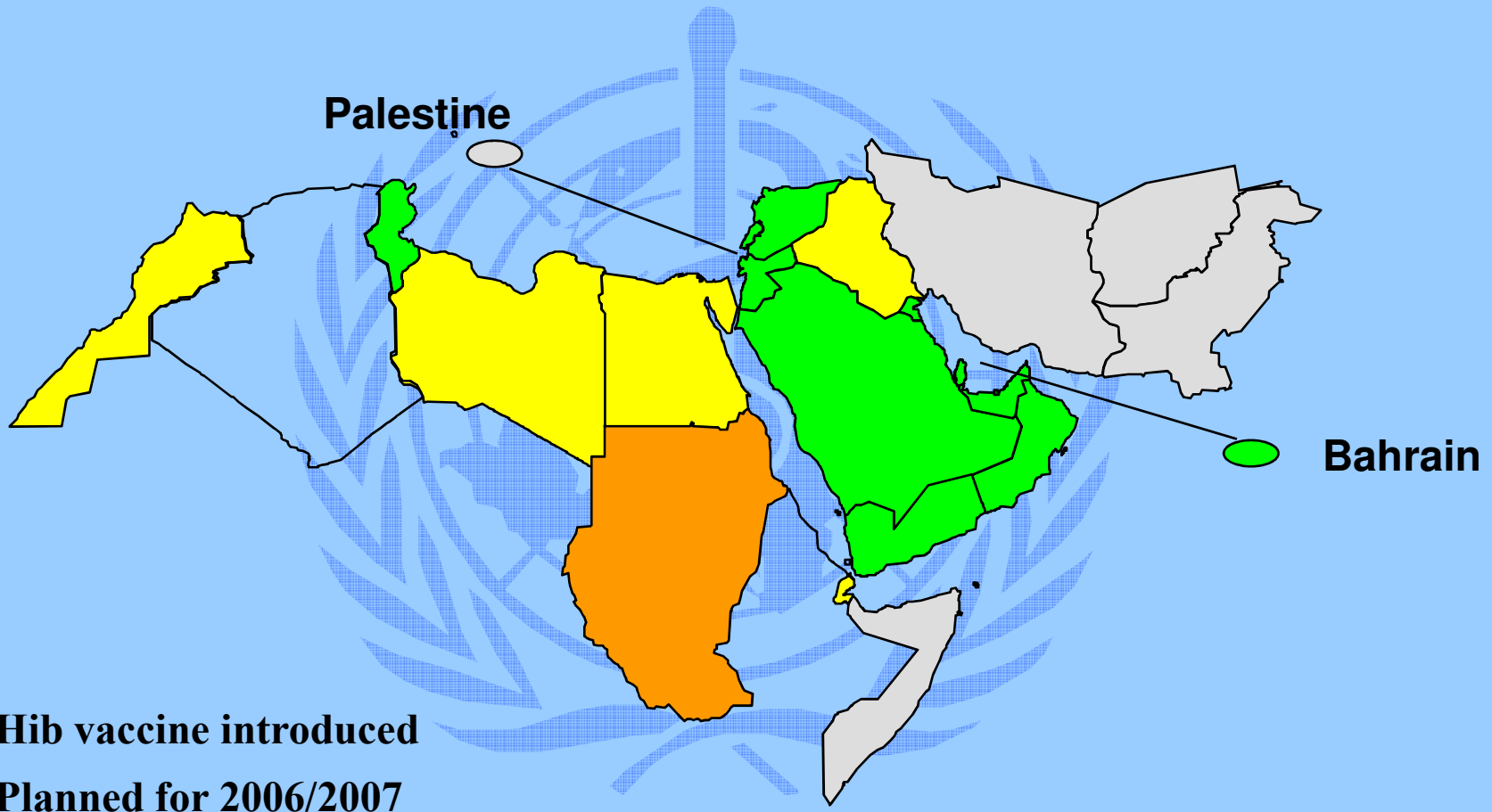
Information on Hib burden available (17)

Moderate to High disease burden (15)

Hib vaccine introduced (11)

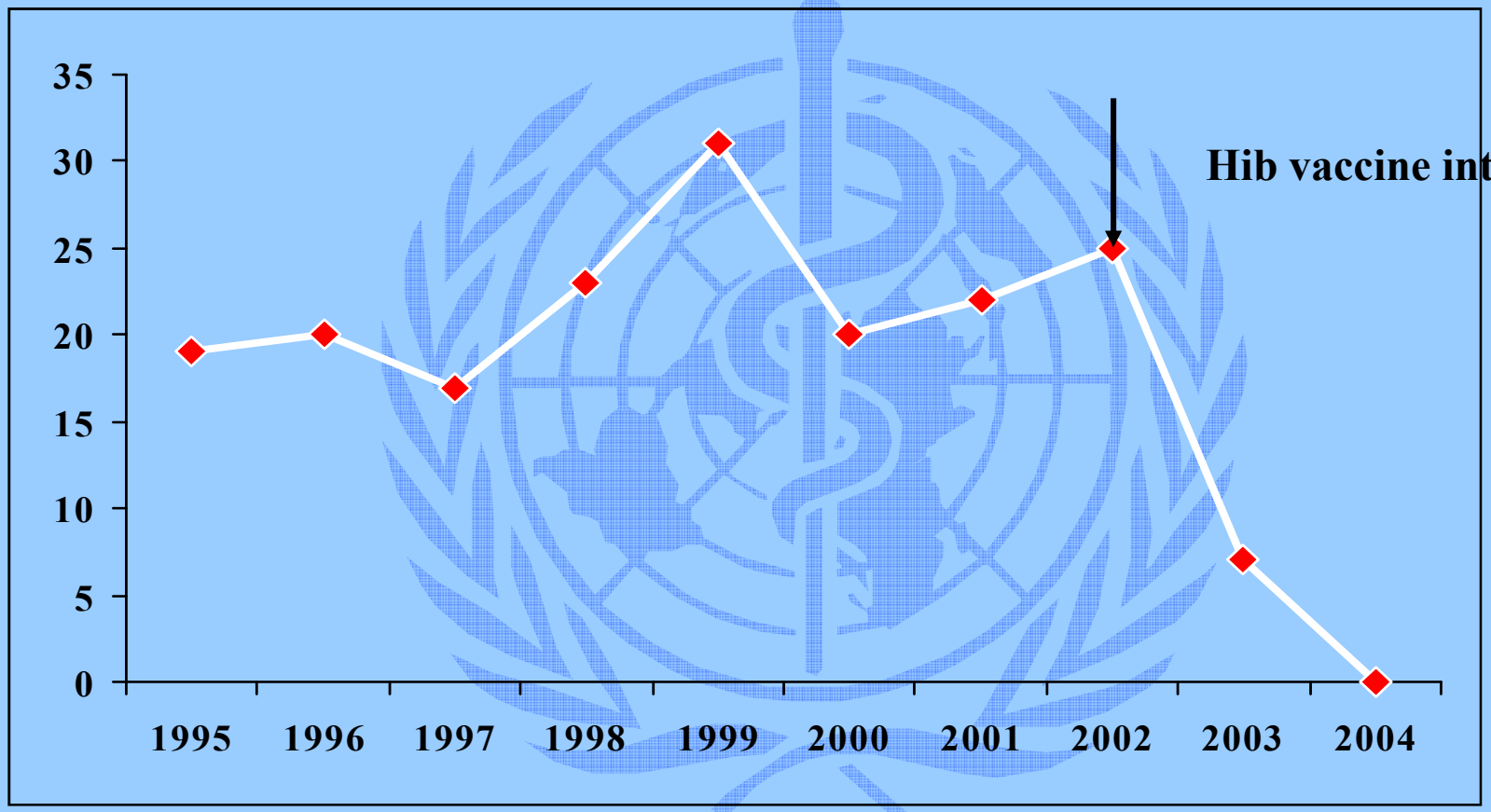
VPI,WHO/EMRO

Hib vaccine in the EMR, as of March 2006



VPI,WHO/EMRO

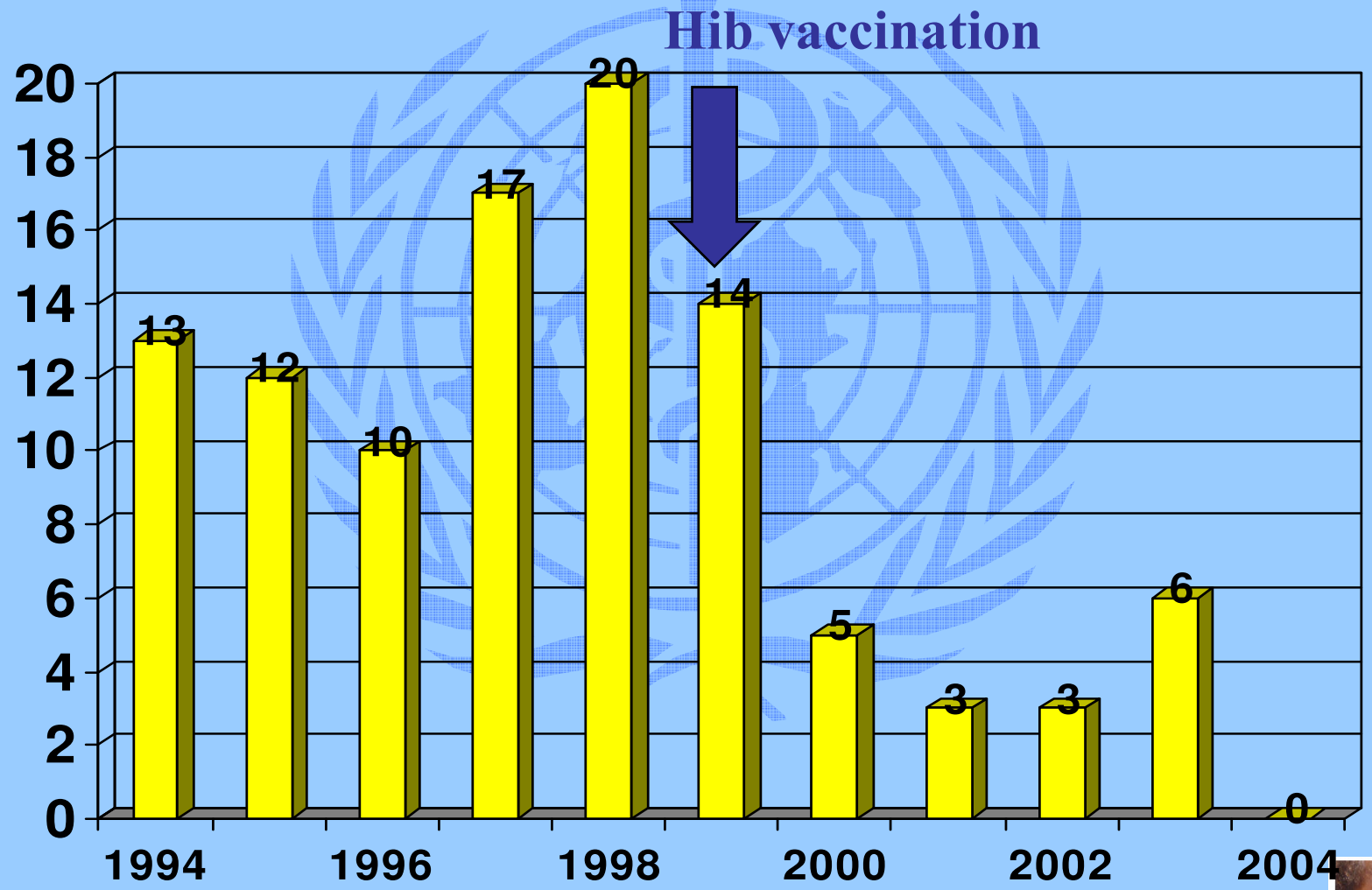
Hib Meningitis among children <5 y in Oman



Source, EPI programmes

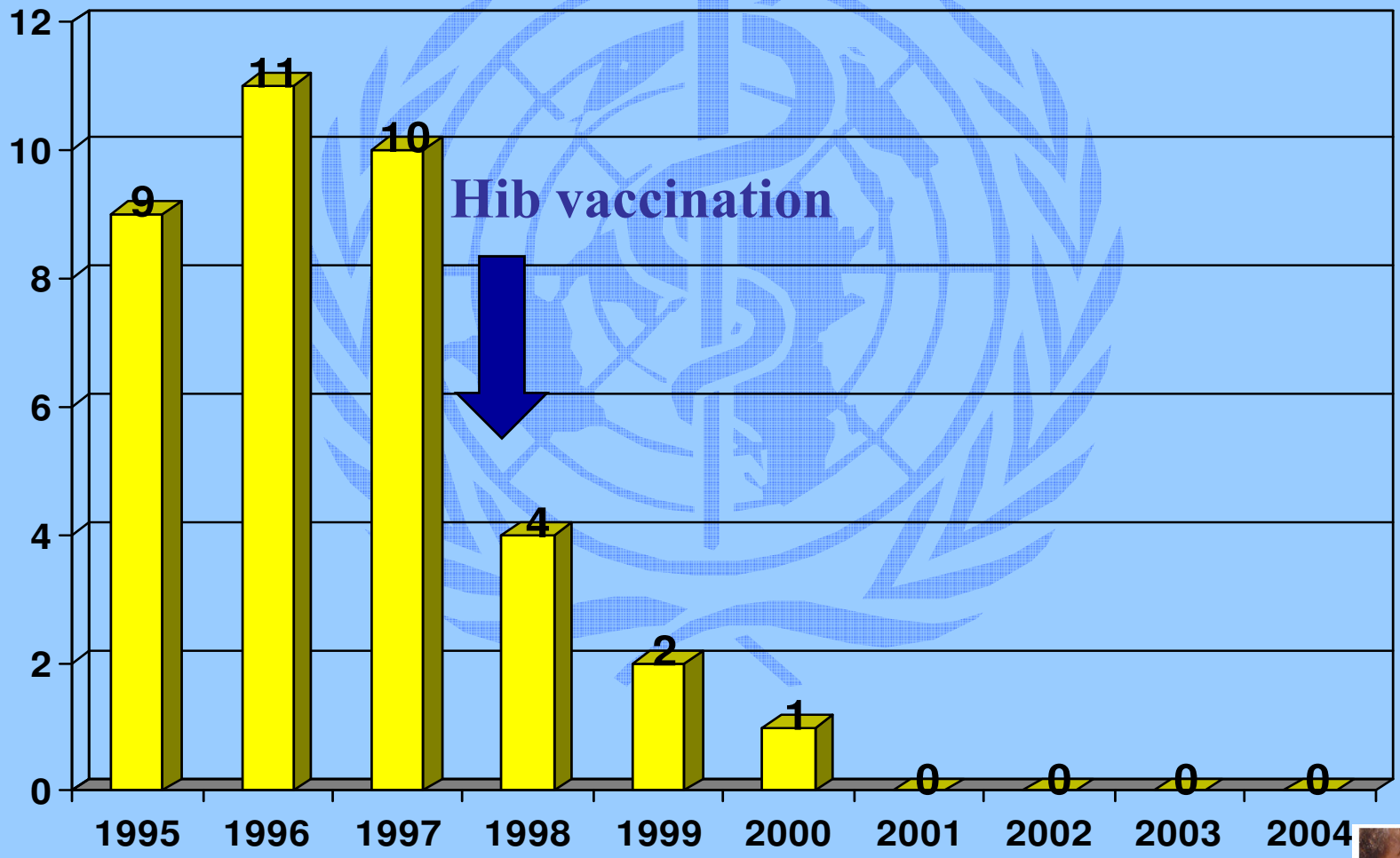
VPI,WHO/EMRO

Hib meningitis cases < 5 years, UAE



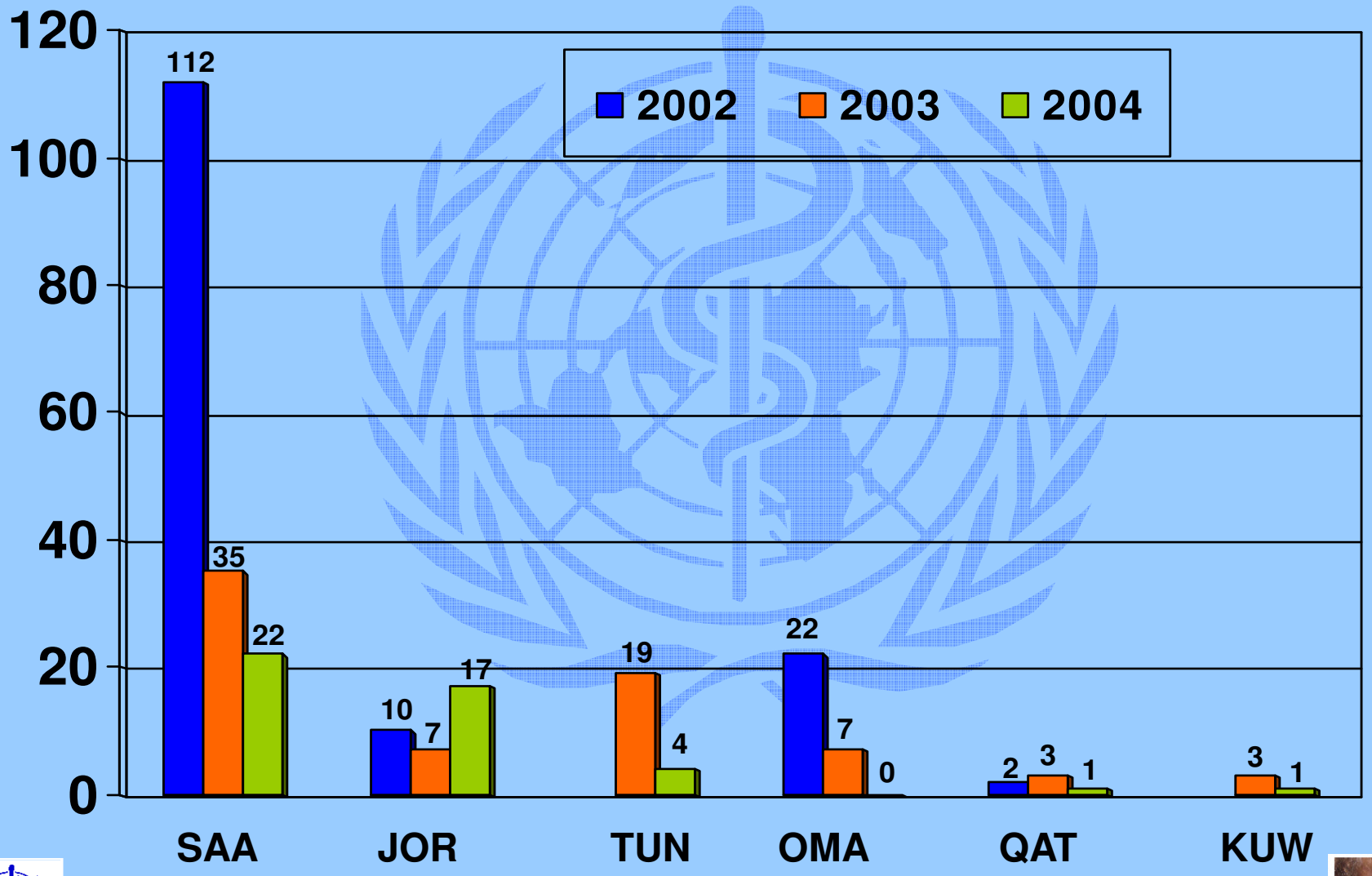
VPI,WHO/EMRO

Hib meningitis cases < 5 years Bahrain



VPI,WHO/EMRO

Hib meningitis cases < 5 years



VPI,WHO/EMRO

3. Pneumococcal diseases in the EMR

- Pneumococcal Pneumonia
  - 146,000 deaths (Pneumo-ADIP estimate)
- Pneumococcal meningitis
  - 15-35% of the total bacterial meningitis cases with higher mortality and disabling sequels (published data)

The pneumococcus as a cause of acute bacterial meningitis in EMR

Country	Ref, year	Age	% due to the Pneumococcus
Egypt:	Sentinel surveillance 98-02, NAMRU-3	≤ 5 years >5 years All age	32 40 37
Iran:	population-based study, Shiraz, 2001-03	2 ms-12 years 2-12 months 13-48months 48 ms-12 years	34.3 18.8 23.5 51.6
Jordan	Daoud, 1995	0.2-12	15
Lebanon	2004	All ages	34.4
Libya	(Rao, 98)	0.1-10	26

Source: Published data

The pneumococcus as a cause of acute bacterial meningitis in EMR (cont'd)

Country	Ref, year	Age	% due to the Pneumoc
Kuwait	Zaki,90	All ages	20.9
Oman	2004	All ages	50.0
Qatar	2003	All ages	30.3
Pakistan	khan, 98	0-15	**67.1**
SAA	Almuneef,, King Fahd hosp, 01	0-15	31
Sudan	Khartoum 2004	All ages	15.3
Tunisia:	population based study, 4 gov. 00-02	< 5 years	13

Source: Published data

Antimicrobial resistance of pneumococci

Country	Antibiotic, % intermediate to high resistance			
	Penicillin	Chloramp	Cotrimx	Ceftria
Egypt, Alkholy 03, (all infections) NAMRU-3, 98-2002 (meningitis)	 37 50	 21	 	 16 0
Iran, Oskoui 03 (all infections) Zamanzad, 03 (meningitis)	 68 50	 22 13	 52 	 25
Libya (98), meningitis	18			
Kuwait, Ahmed, 99 (ARI)	53.8			
Morocco, Benbachir 01 (all infections)	9.2	2	14.8	

Source: Published data

Antimicrobial resistance of pneumococci (cont'd)

Country	AB, % intermediate to high resistance			
	Penicillin	Chloramp	Cotrimx	Ceftria
Oman, Elhag, 97 (all infections)	38			
Pakistan, Rajper 97, (meningitis)	34	22	35	
SAA, AlAqeel, 2002 (bacteremia)	51			7
Yemen, Alzubiery 01, (meningitis)	33.3	33.3		16.7
Tunisia, Ben Redjeb 2005, (1999-2003)	33-51%	7-12%	30-40%	7-12%

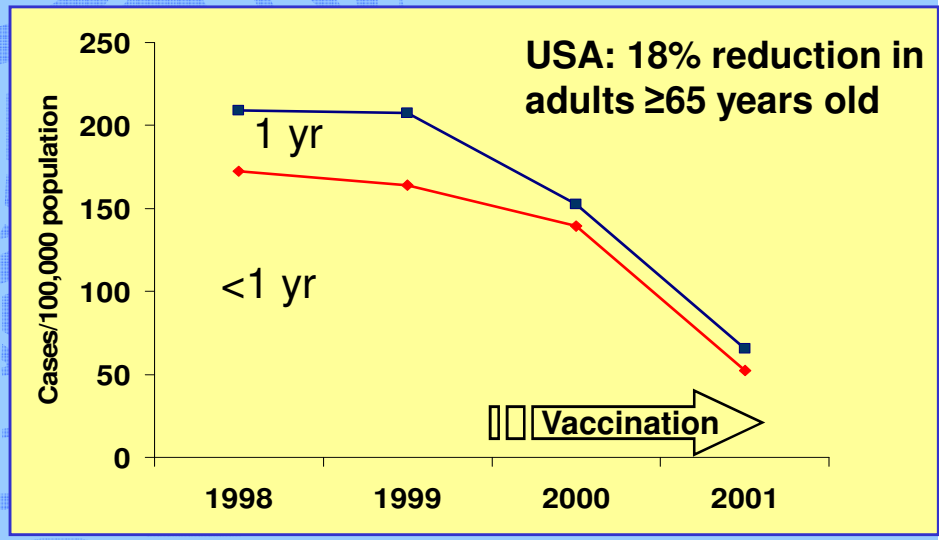
Source: Published data

Pneumococcal vaccines

- Pneumococcal polysaccharide vaccine: 23 valent

Pneumococcal conjugate vaccines:

- suitable for EPI
- 7 Valent available, covers around 80% of disease serotypes in US
- 10 valent: coming soon



Pneumococcal vaccines

- Circulating Serotypes in different countries*:
  - Egypt: 49% and 69 % of the circulating serotypes are vaccine serotypes (7valent and 10-valent respectively)
  - Tunisia: 62% (7valent)
  - Saudi Arabia: 63% (7valent) and 78% (10-valent)
  - Qatar: 54% (7 valent) and 56% (10valent)

Culture is a must to identify the circulating serotypes and, hence, suitability of the vaccine

*Source: Data presented to intercountry pneumococcal surveillance workshop, December 2004 and monitoring and evaluation workshop, Tunis March 05

Eastern Mediterranean Lab-Based Bacterial Meningitis Surveillance Network

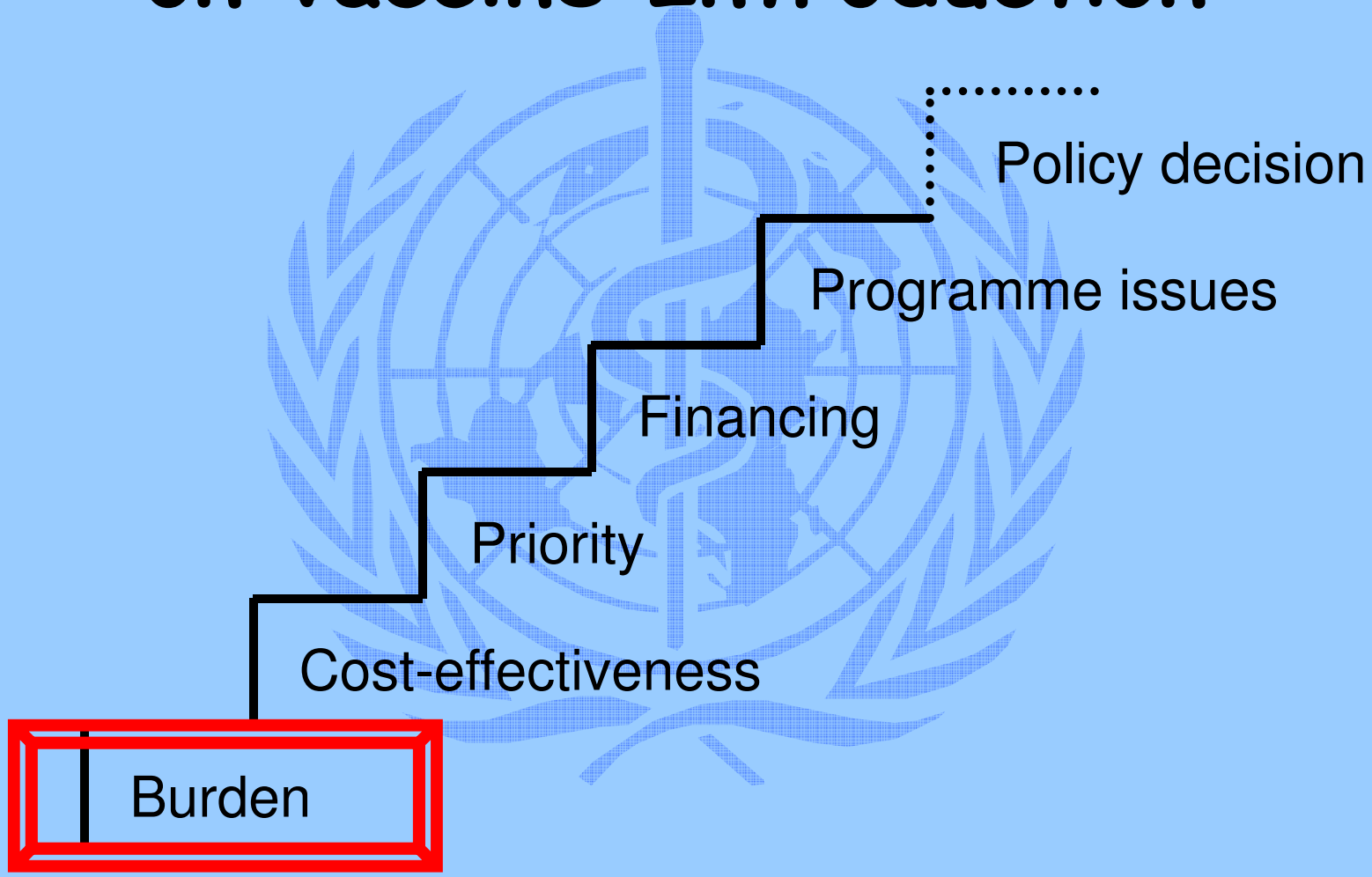
BMS-Net

Introduction of new vaccines:
How much we care about

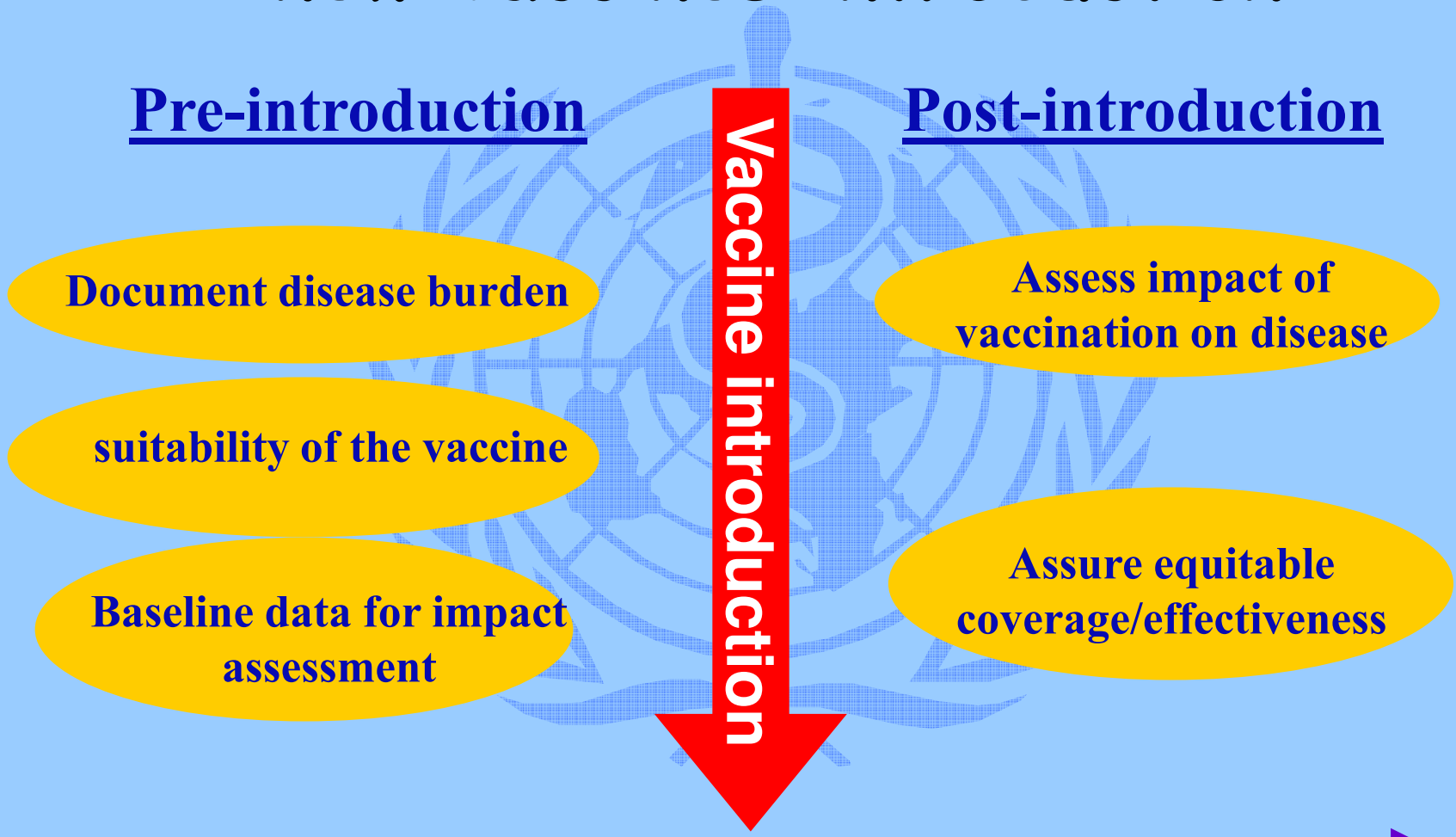
Vision of WHO/EMRO

ensure providing safe vaccine for every childhood vaccine preventable diseases to every child in the Region

Tools for Decision Making on vaccine Introduction



The importance of surveillance in new vaccines introduction



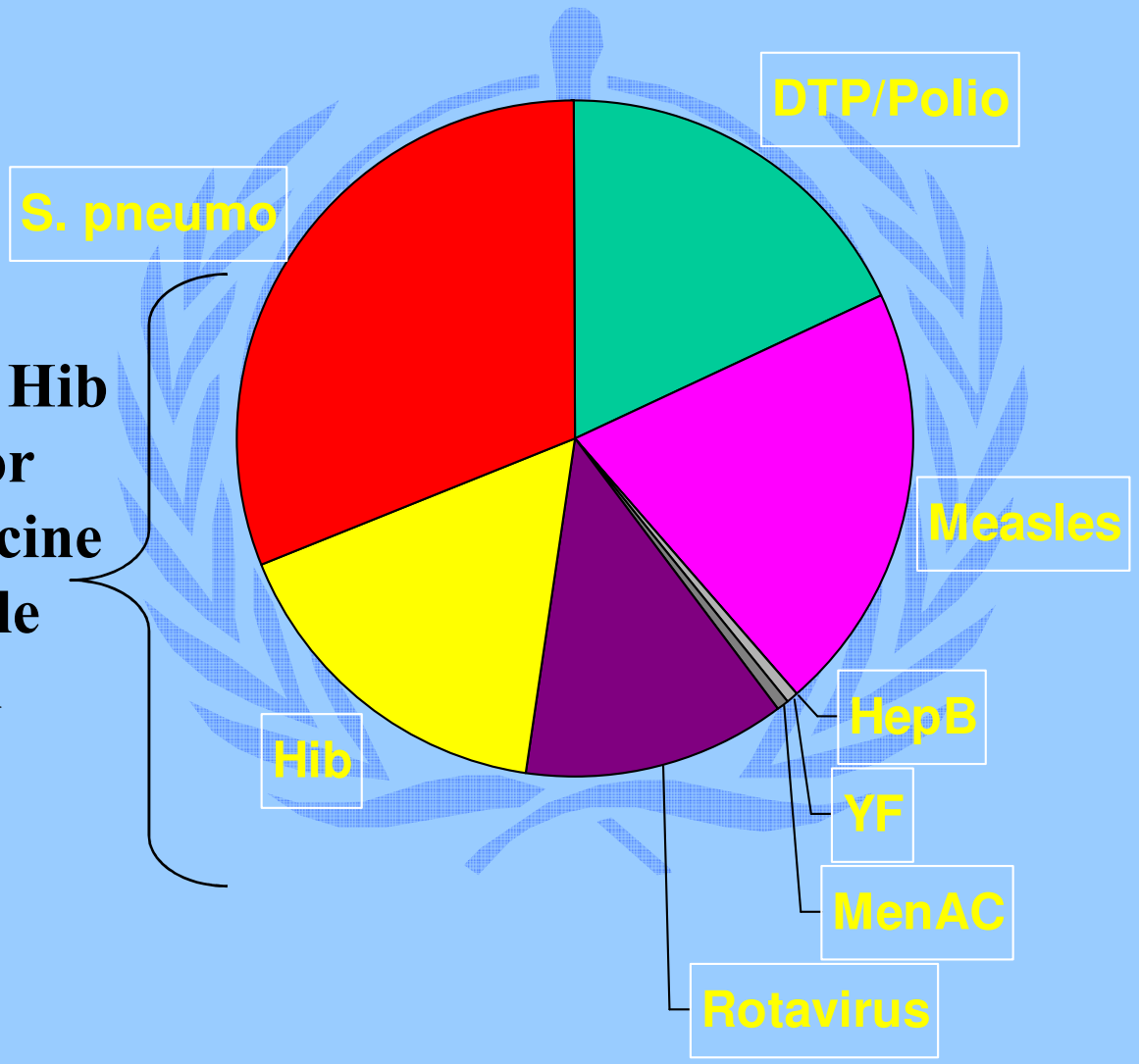
VPI,WHO/EMRO

Bacterial meningitis surveillance network in the EMR: Why Nm, Sp and Hib:

- Meningitis caused by Hib, N. meningitides, s. pneumoniae: 80% of bacterial meningitis in the region
- Hib and S. Pneumoniae are the leading cause of pneumonia among children
- Burden of Meningitis caused by Hib and pneumococci is an indicator of pneumonia caused by them
- Effective preventable measures are available/in the pipelines (new vaccines)
- Data are needed to guide introduction of new vaccines

WHO estimates 2.7M childhood deaths from vaccine preventable illnesses.

Pneumo and Hib account for ~50% of vaccine preventable deaths in children



VPI,WHO/EMRO

BMS-Net

Objectives of lab-based BMS

- Generate quality data in order to:
  - document burden and trends of bacterial meningitis caused by Hib, Pneumococcus and meningococcus
  - support evidence-based decision making for prevention and control strategies specially introduction of new vaccines
  - guide clinical management of cases
  - study antibiotic susceptibility/resistance pattern
  - monitor and evaluate prevention and control measures specially vaccination programmes
- Build surveillance capacity for long term use

Why a regional surveillance network:

- Provides common protocols/methods and standards: ensures standardized, comparable data
- Share expertise and experience: Creates group of regional experts
- Foundation for training and infrastructure building
- Share/reduce costs of some components
- Mobilize resources and builds platform for international collaborations
- Elevates visibility of disease and results of surveillance among regional and global community

BMS-Net

EMRO perspective:

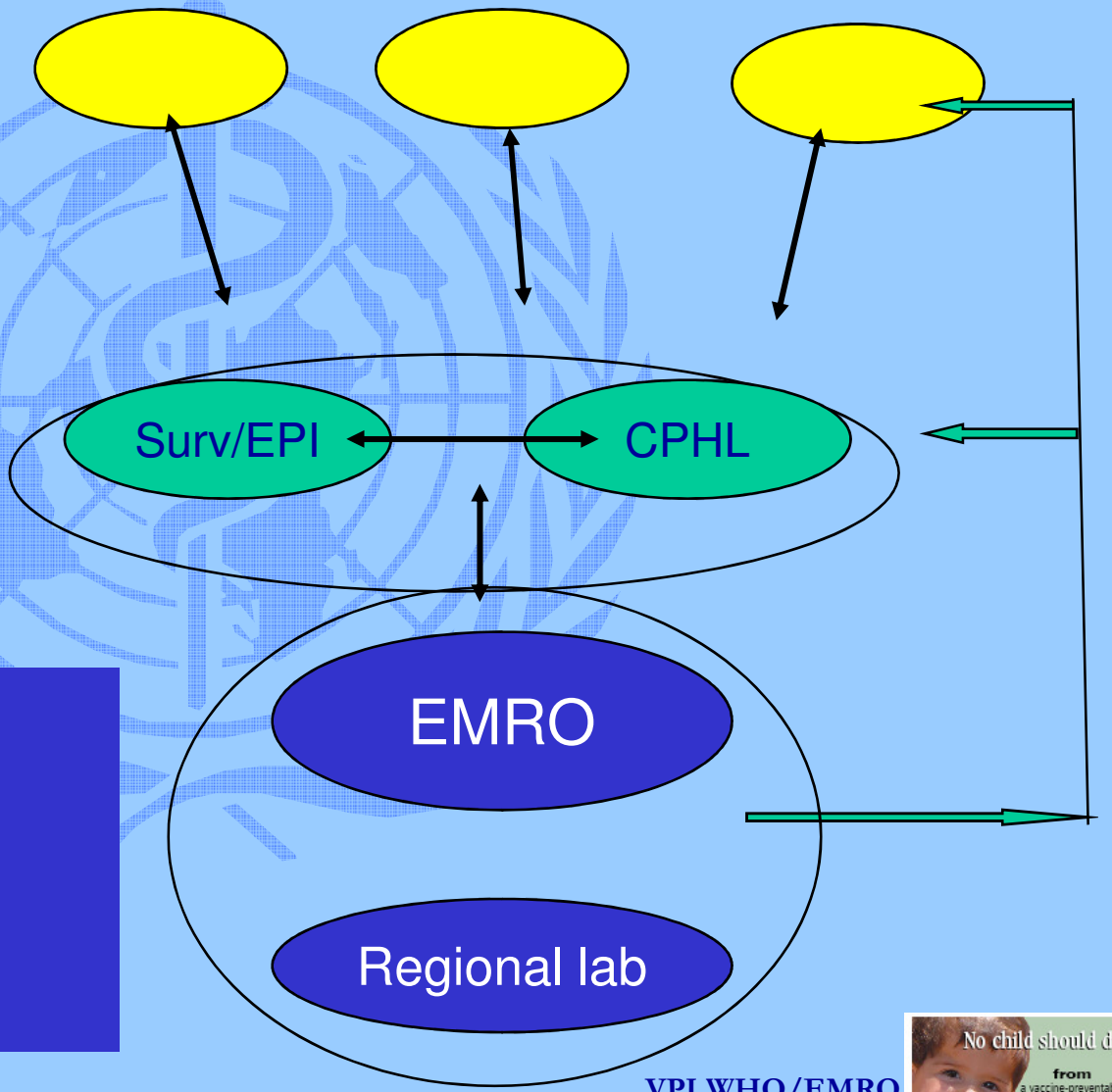
- A Country programme:
  - »ownership of MoH
- Building on/strengthening ongoing activities
- Emphasis on culture for confirmation:
  - »Identifying circulating strains and suitability of the available vaccines
  - »Studying AST (Anti-Microbial Sensitivity testing)

BMS Net: coordination

Sentinel sites-
hospital coordinator

Central level (MOH)
coordination/support, Data
management, QC

Standards,
Technical support
Resource mobilization
QA/QC
Strain characterization
Follow-up visits



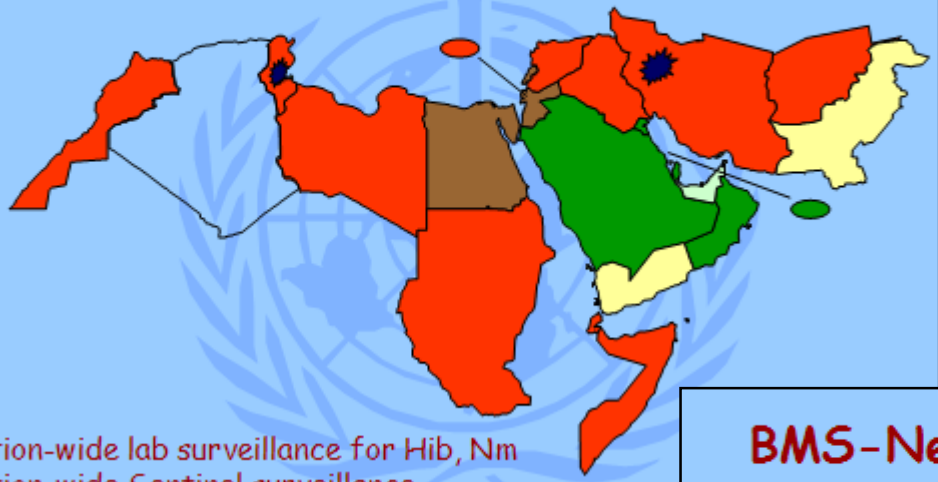
BMS-Net

Current situation (April 2006)

- Nation-wide lab surveillance
- Nation-wide Sentinel surveillance
- Sentinel surveillance in some regions
- Population-based surveillance
- Syndromic surveillance
- No surveillance

VPI,WHO/EMRO

BMS-Net
Situation, January 2004

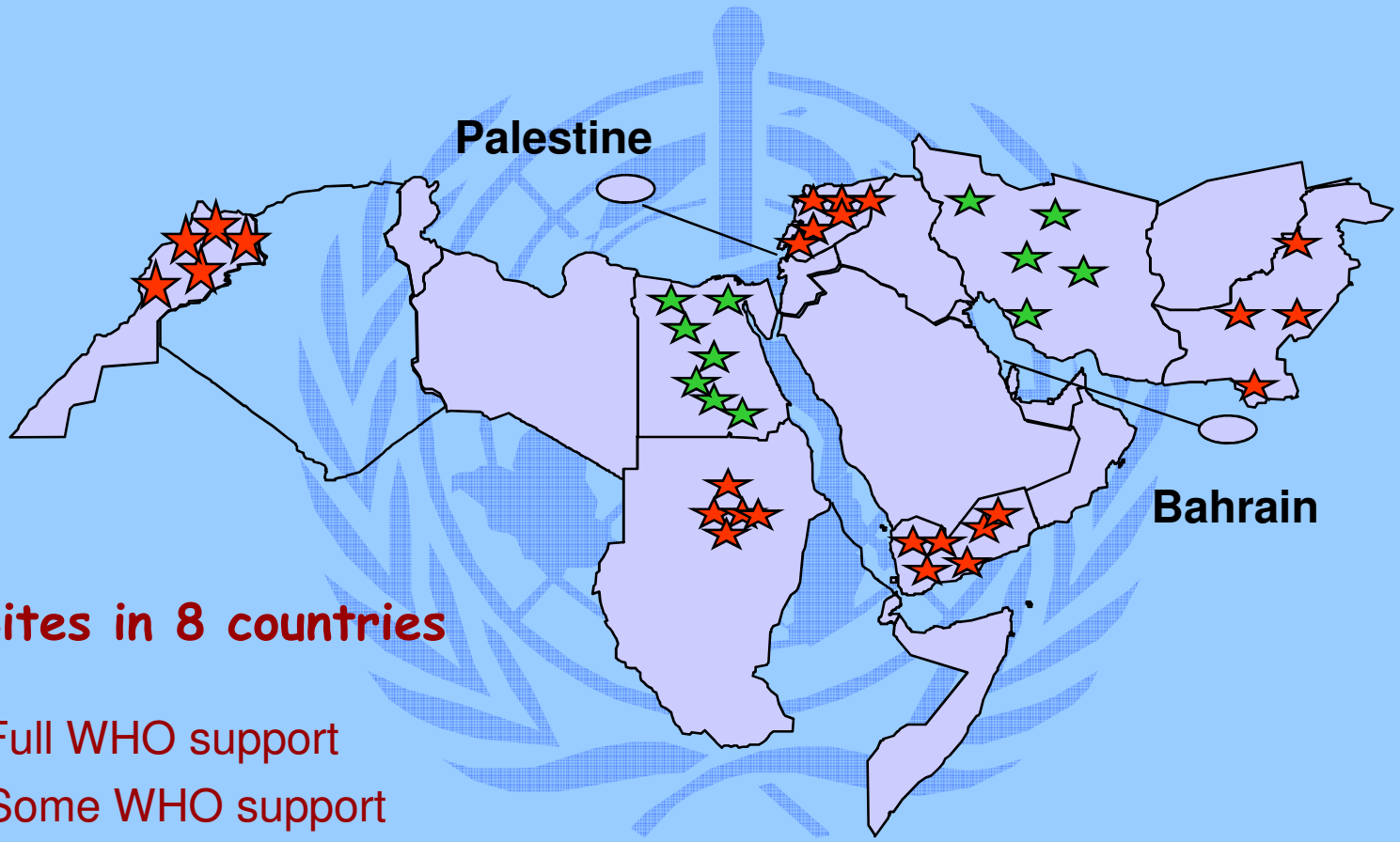


- Nation-wide lab surveillance for Hib, Nm
- Nation-wide Sentinel surveillance
- Syndromic surveillance, Nm confirmation
- Population-based surveillance, Hib only
- None

BMS-Net
Current situation (April 2006)

- Nation-wide lab surveillance
- Nation-wide Sentinel surveillance
- Sentinel surveillance in some regions
- Population-based surveillance
- Syndromic surveillance
- No surveillance

BMS: Sentinel/pop-based sites supported by WHO, March 06



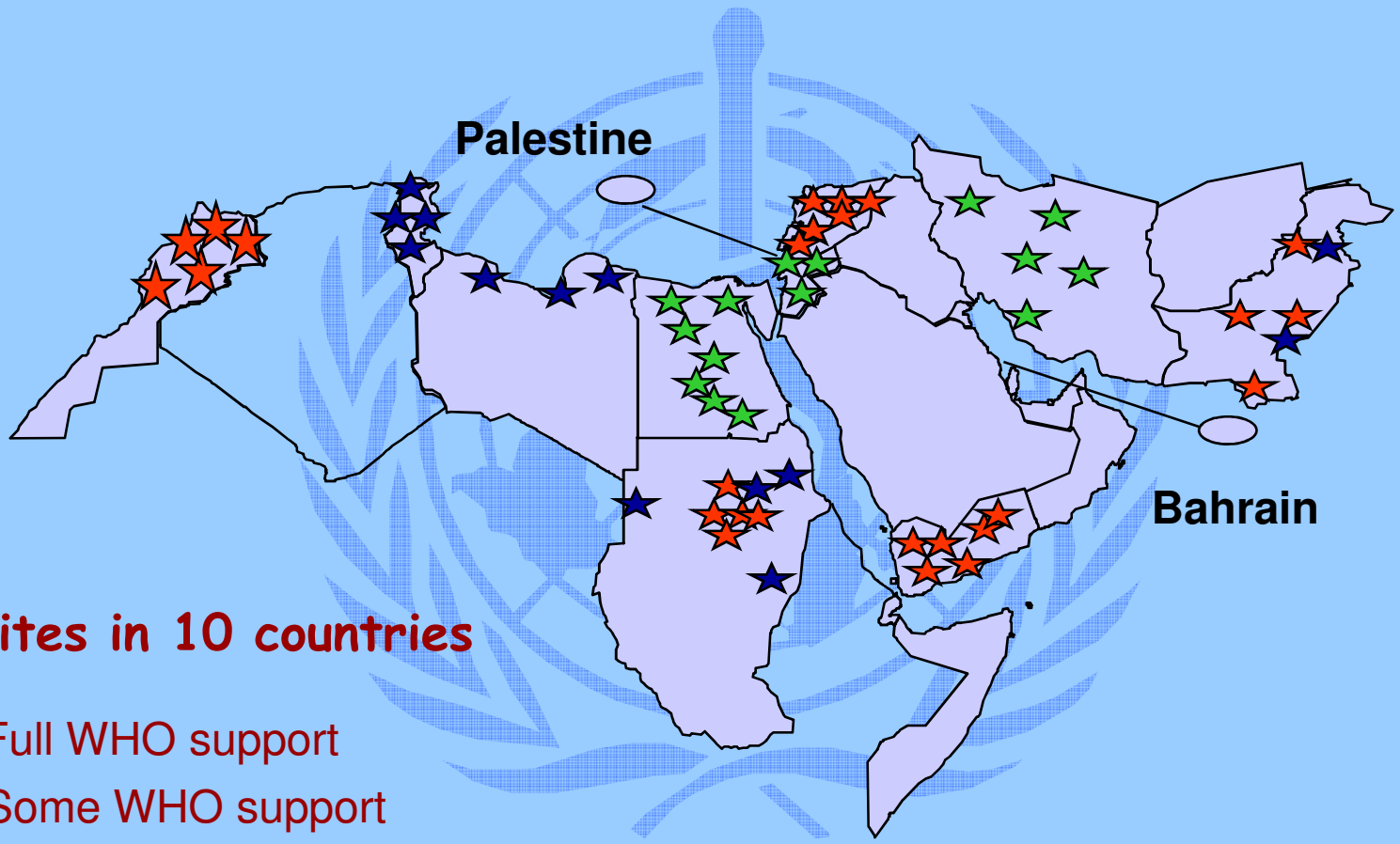
38 Sites in 8 countries

★ Full WHO support

★ Some WHO support

VPI,WHO/EMRO

BMS: additional sites: planned May 06



51 Sites in 10 countries

- Full WHO support
- Some WHO support
- Additional sites 06

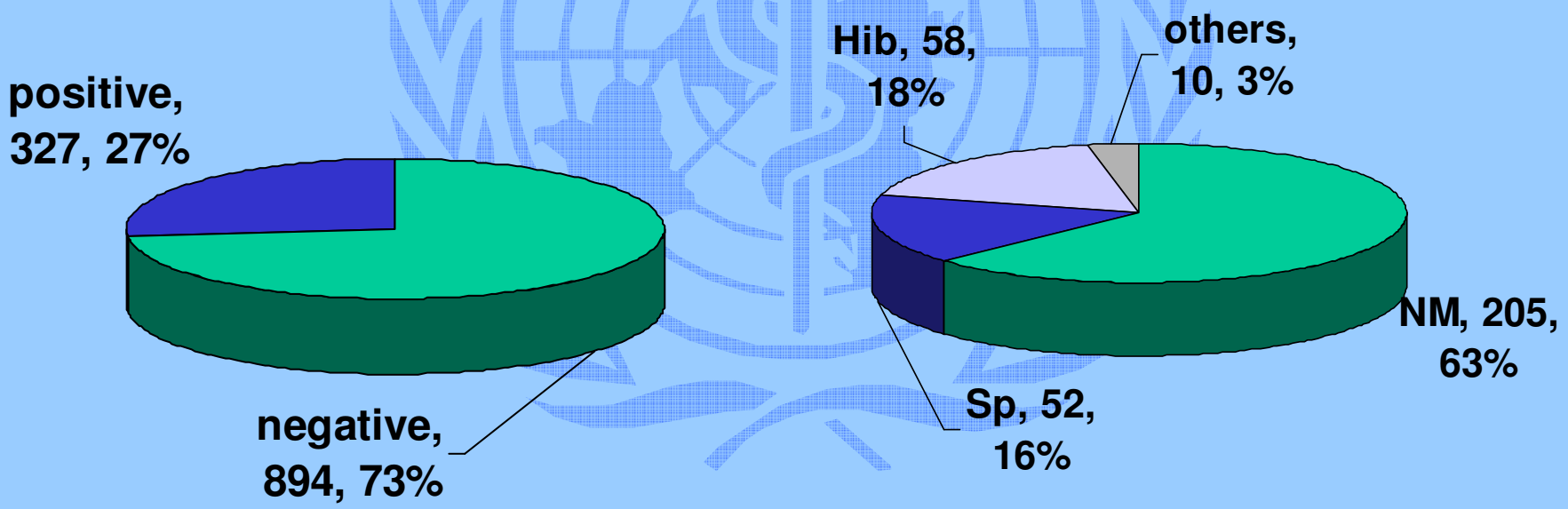
VPI,WHO/EMRO

Bacterial meningitis surveillance, all ages, National system, Morocco 2005

Total suspect. meningitis:1579

prob. bact meningitis 1221

Culture+latex

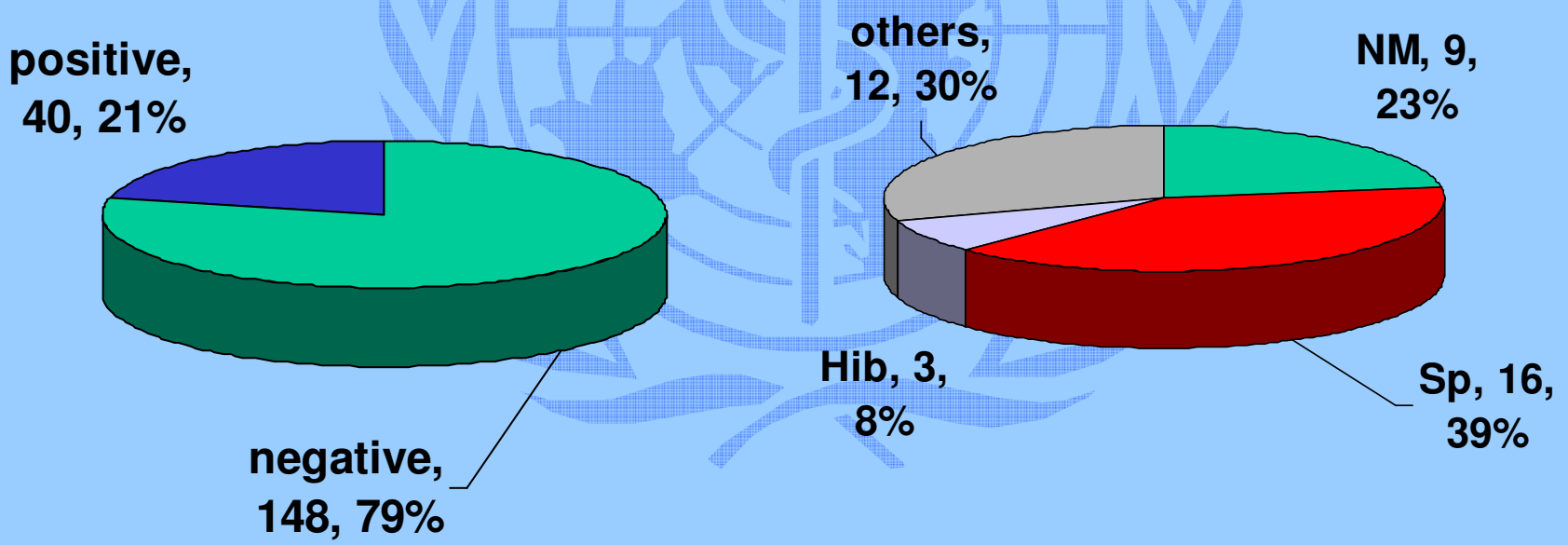


VPI,WHO/EMRO

Bacterial meningitis surveillance, All ages, Lebanon, 2005

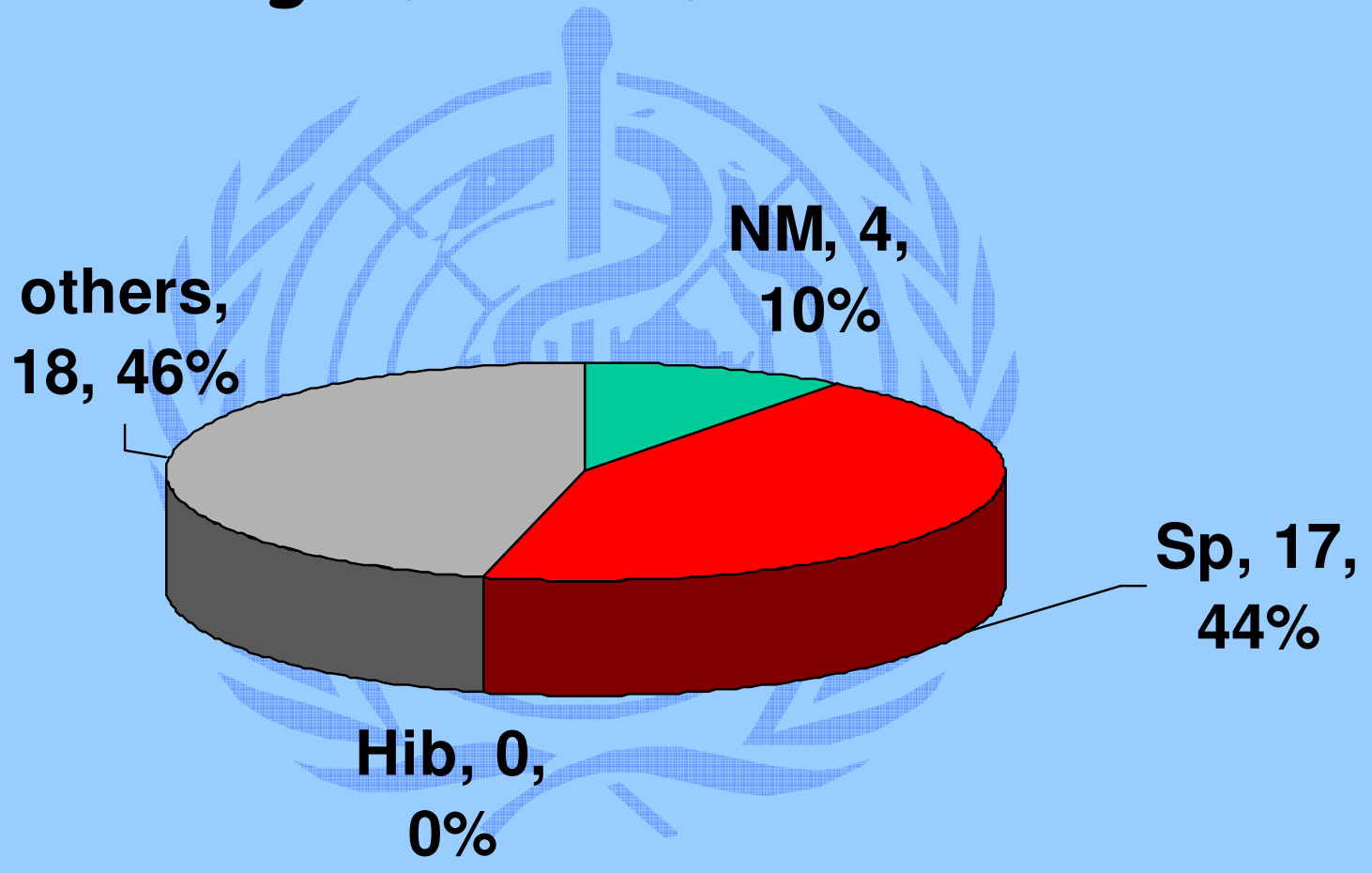
Total CSF tested: 188

Culture + latex

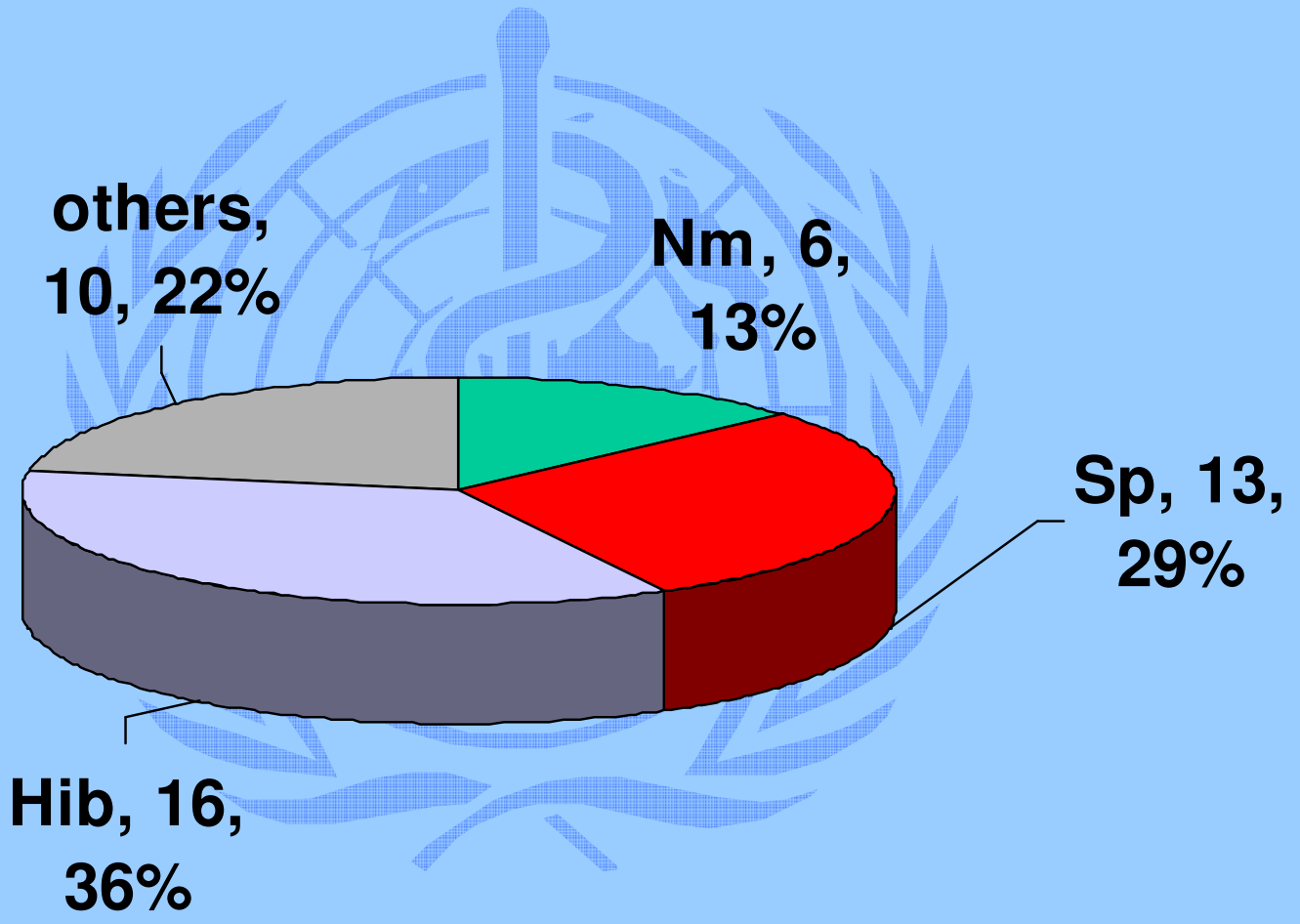


VPI,WHO/EMRO

Bacterial meningitis surveillance, All ages, Oman, 2004



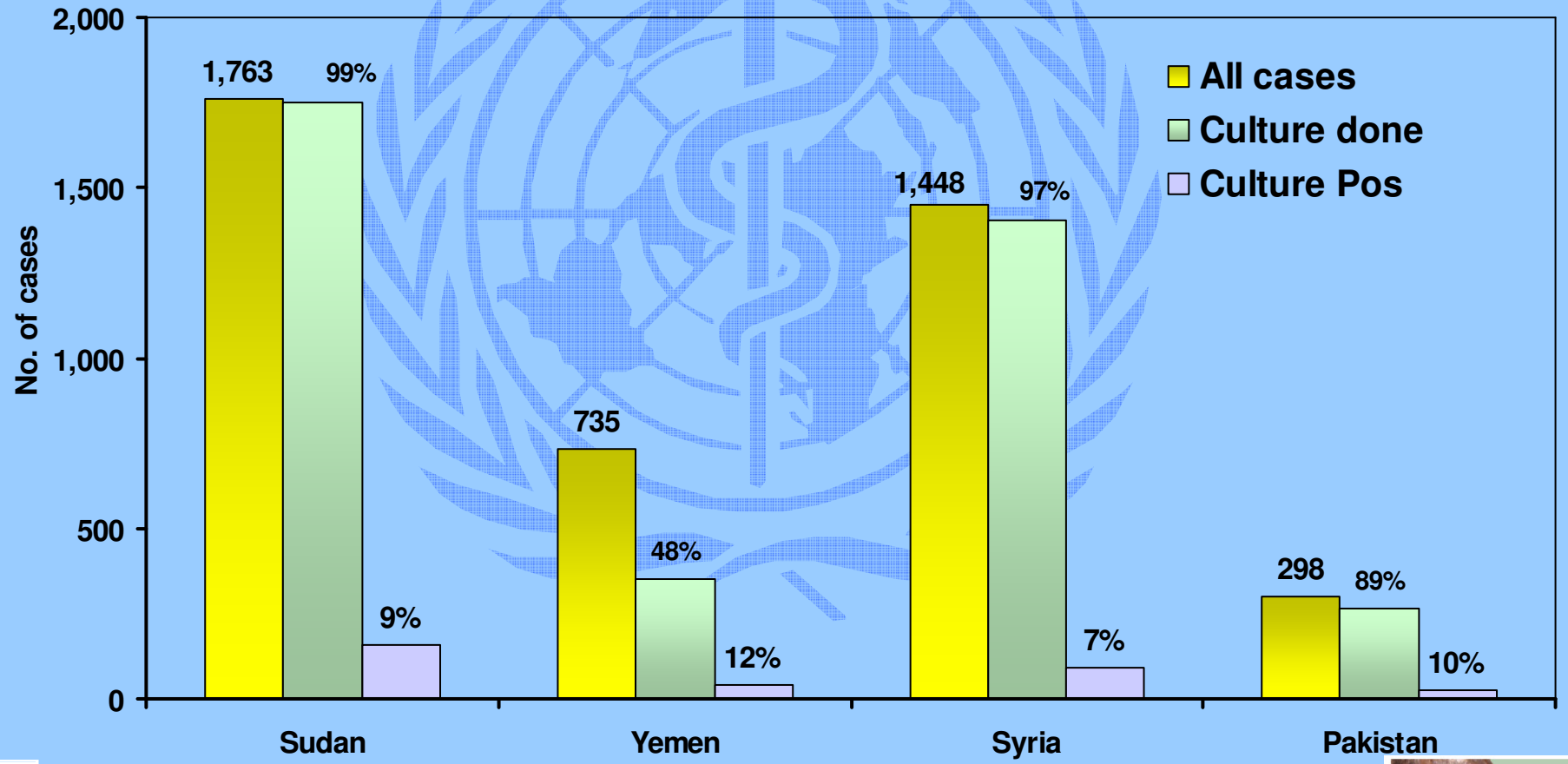
Bacterial meningitis surveillance, Iran Pop-based sites, 2ms-15yrs, 2004-2005



VPI,WHO/EMRO

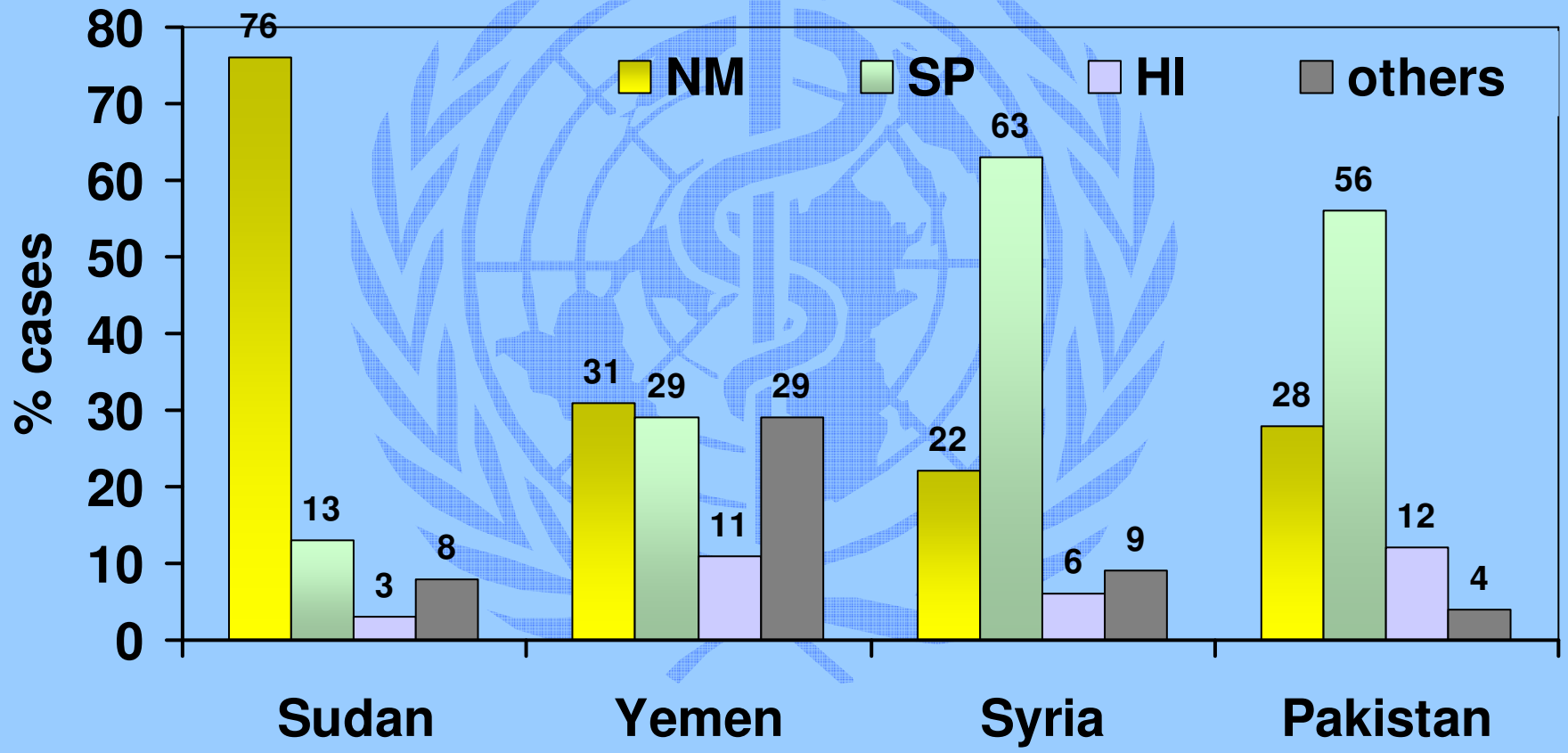
Sentinel surveillance in Sudan, Pakistan, Syria and Yemen (full WHO support)

Start date: Sudan: Jan04, Yemen: Aug 04, Syria: Feb 05, Pak: May 05



VPI,WHO/EMRO

Bacteria Isolated from CSF cultures, all ages >1 ms
Sudan, Yemen, Syria, Pakistan (Culture results)

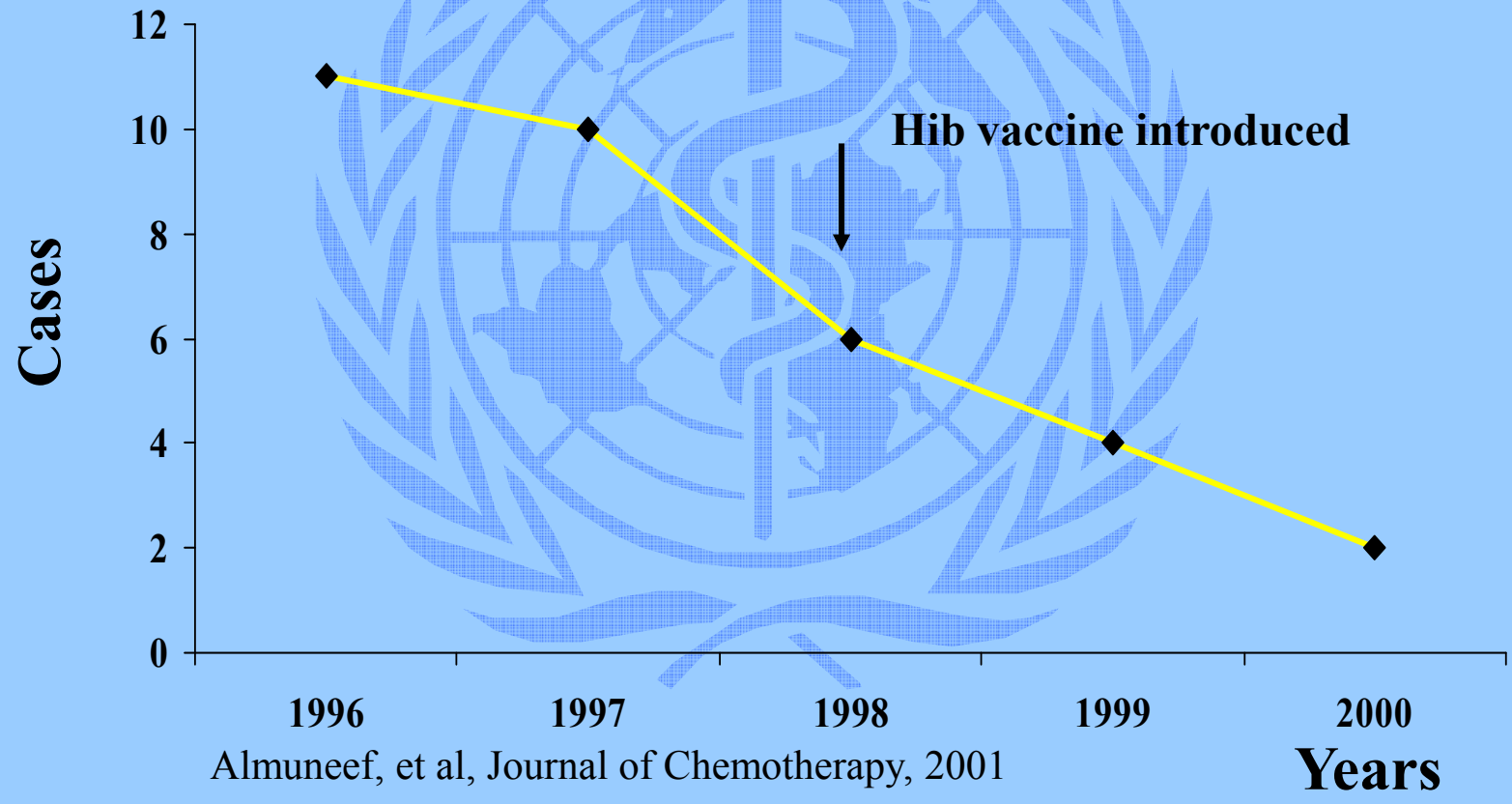


VPI,WHO/EMRO

THANK YOU

VPI,WHO/EMRO

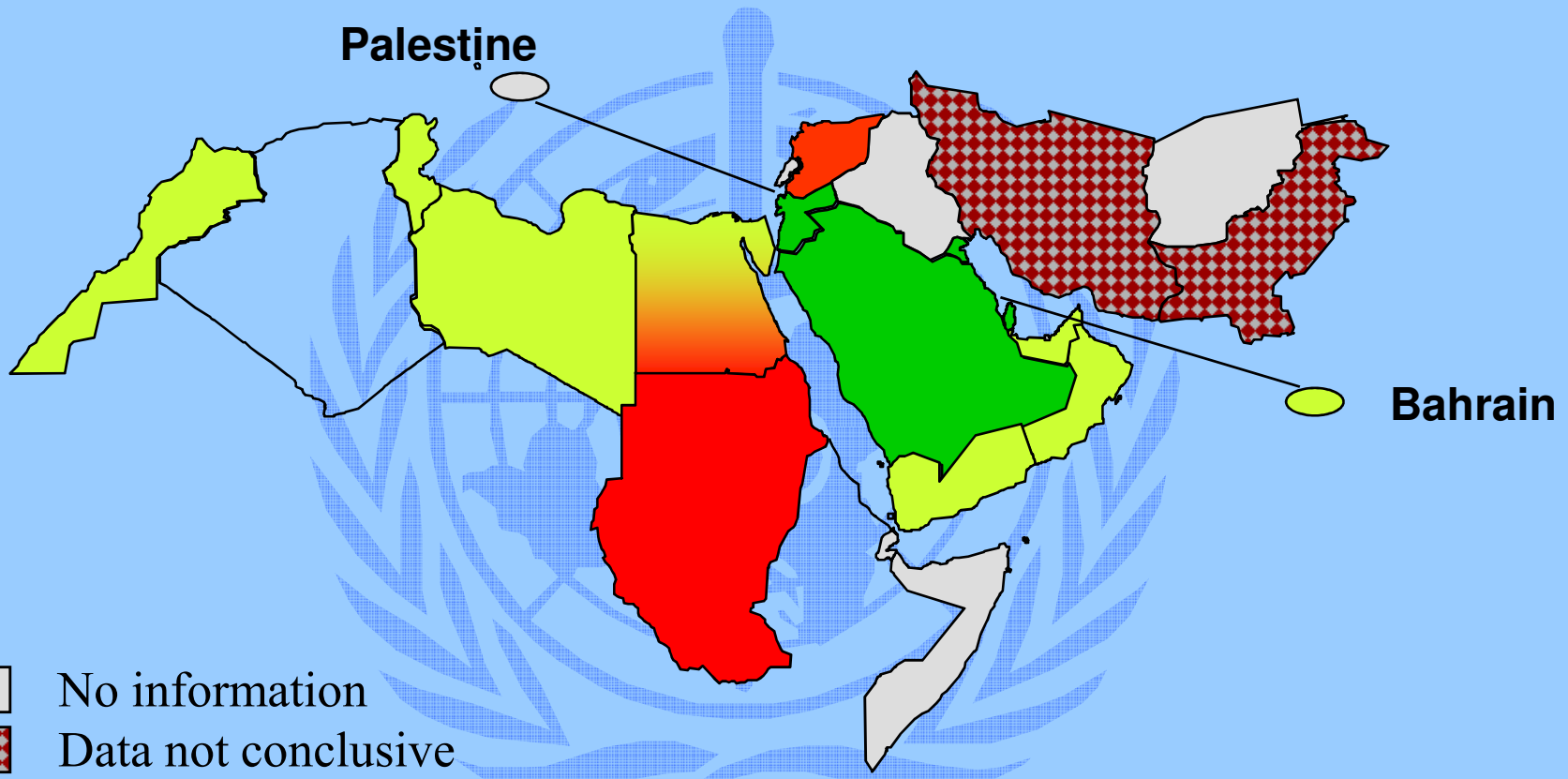
Hib Meningitis in children <5 years: King Fahad National Guard Hospital, Saudi Arabia



Almuneef, et al, Journal of Chemotherapy, 2001

VPI,WHO/EMRO

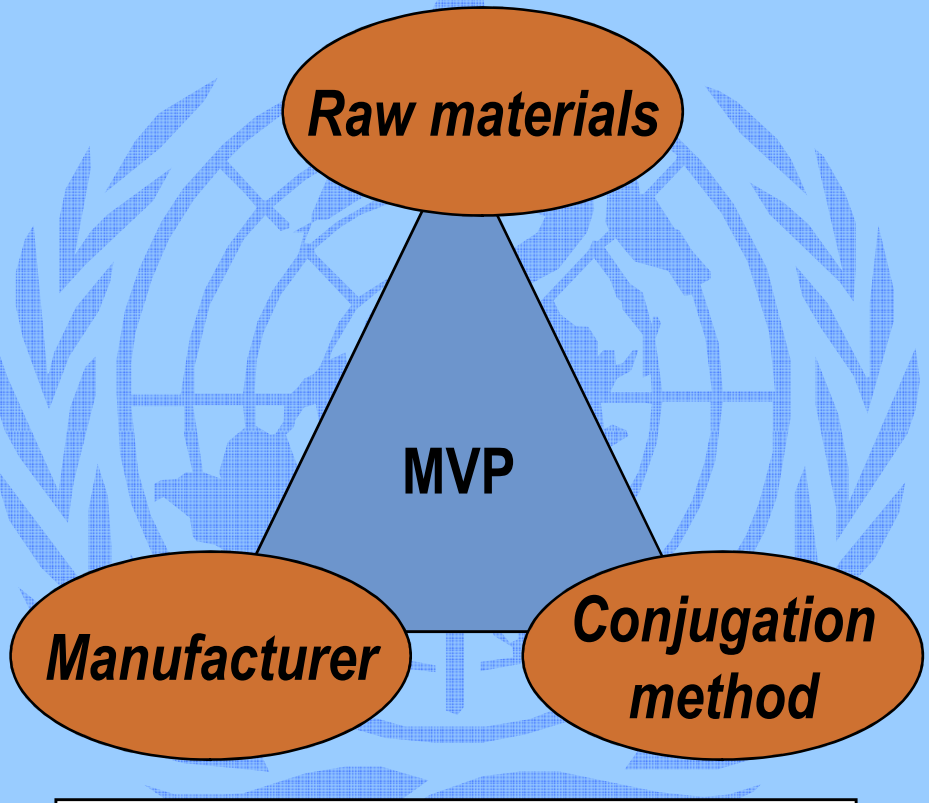
Estimated Hib meningitis incidences before Hib vaccine introduction in EMR



- No information
- Data not conclusive
- High incidence (> 40‰ <5years children)
- Moderate incidence (20-40‰ <5years children
- Low incidence (10-20‰ <5years children)

VPI,WHO/EMRO

MVP Men A Vaccine Development Model



Target price $US 0.40/dose