EMERGING INFECTIONS AND ISSUES

- INFECTIONS:
  - AVIAN FLU
  - SARS
  - DHF
  - XDR-TB

ISSUES:

- ANTIBIOTIC RESISTANCE
- STOCKPILING OF DRUGS/VACCINES
- NEW APPROACHES TO THERAPY
- GENETIC SUSCEPTIBILITY

"The global future of mankind will probably unfold as episodes of a suspense thriller that could be entitled, *"Our Wits Versus Their Genes."*

- Joshua Lederberg

EMERGING INFECTIONS IN PEDIATRICS: PHILIPPINE EXPERIENCE

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MANILA

EMERGING DISEASES: DEFINITIONS

- Has increased in the past 20 years
- Comprise at least 12 % of infections

- Types are:

  -newly identified organism or a new strain

  eg. SARS, AIDS

  -change due to evolution

  eg. Influenza H1N1

-Known infection identified in a new location

eg. Japanese B encephalitis

- New infection in an area undergoing ecologic transformation

eg. Lyme disease

-Pre-existing disease re-emerging as drug-resistant

eg. MDRTB

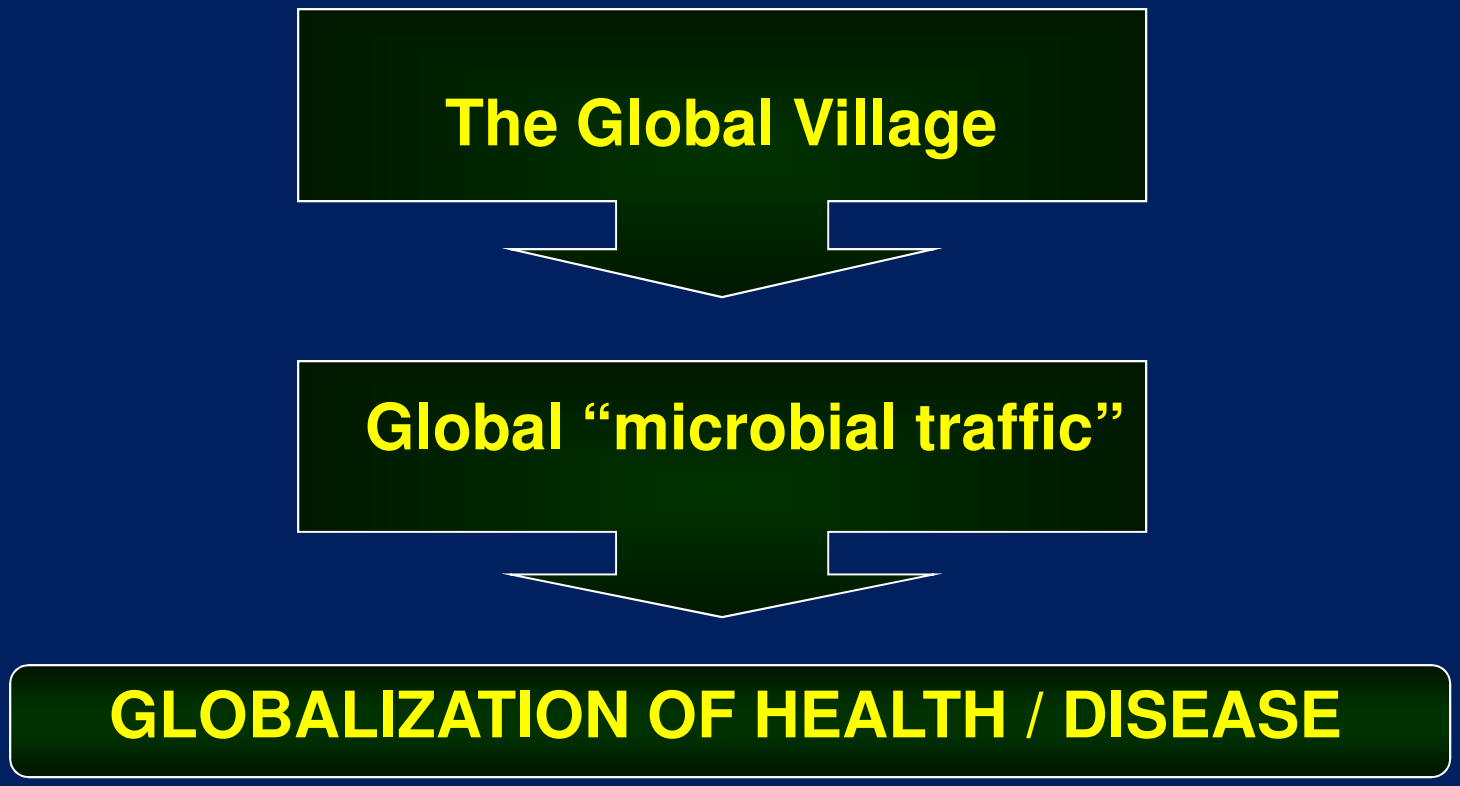
MECHANISMS OF EMERGENCE AND RE-EMERGENCE

- Microbial adaption; e.g. genetic drift and genetic shift in Influenza A
- Changing human susceptibility; e.g. mass immunocompromisation with HIV/AIDS
- Climate and weather; e.g. diseases with zoonotic vectors such as Dengue (transmitted by mosquitoes) are moving further from the tropics as the climate warms

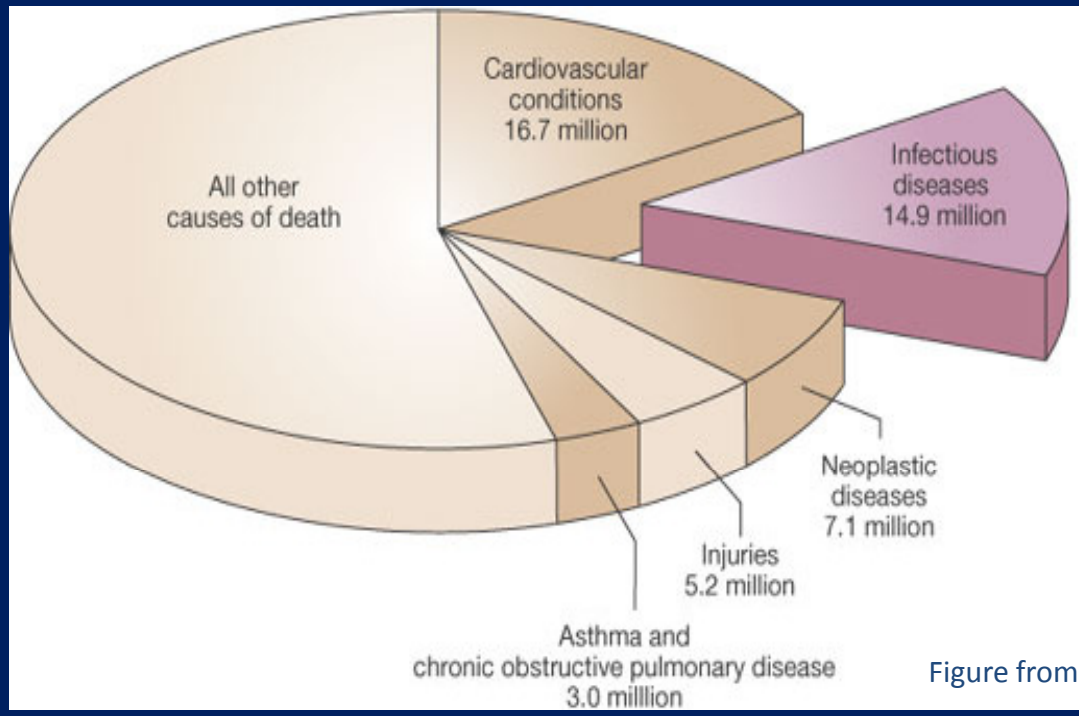
- Change in human demographics and trade; e.g. rapid travel enabled SARS to rapidly propagate around the globe
- Economic development; e.g. use of antibiotics to increase meat yield of farmed cows leads to antibiotic resistance
- Breakdown of public health; e.g. the current situation with Measles

- Poverty and social inequality; e.g. tuberculosis is primarily a problem in low-income areas
- War and famine
- Bioterrorism; e.g. 2001 Anthrax attacks
- Dam and irrigation system construction; e.g. malaria and other mosquito borne diseases

THE GLOBAL CHALLENGE



Global Burden of Infectious Diseases



Infectious diseases	Annual deaths (million)
Respiratory infections	3.96
HIV/AIDS	2.77
Diarrhoeal diseases	1.80
Tuberculosis	1.56
Vaccine-preventable childhood diseases	1.12
Malaria	1.27
STDs (other than HIV)	0.18
Meningitis	0.17
Hepatitis B and C	0.16
Tropical parasitic diseases	0.13
Dengue	0.02
Other infectious diseases	1.76

Figure from Morrens et al, Nature Vol 430 July 2004

Leading cause of death worldwide: About 15 million (>25%) of 57 million worldwide are the direct result of infectious diseases

-WHO Report 2004

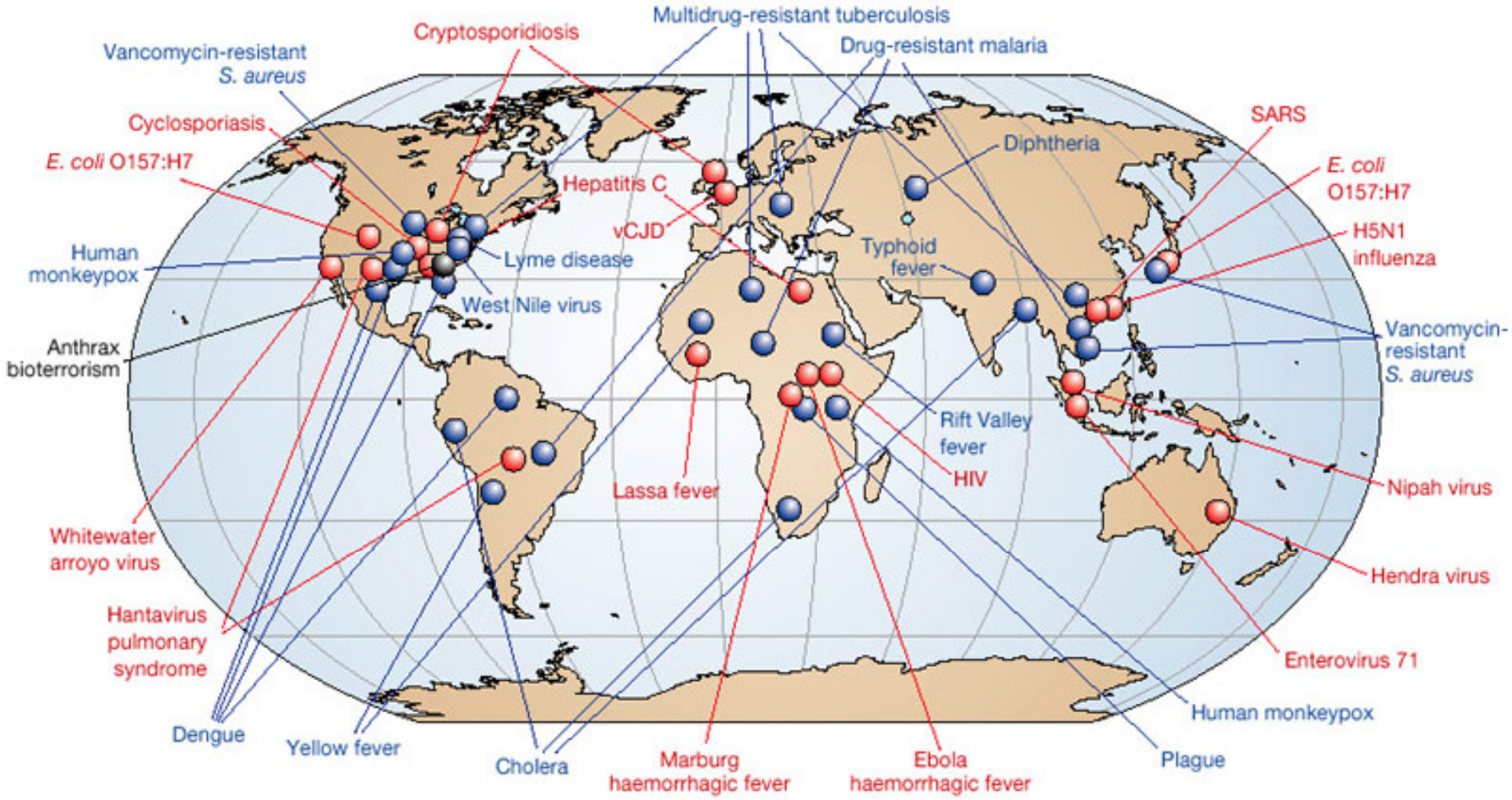


Figure from Morrens et al, Nature Vol 430 July 2004

Global examples of emerging and re-emerging infectious diseases. Red represents newly emerging diseases; Blue, re-emerging diseases; Black, a 'deliberately emerging' disease

THE PHILIPPINE SITUATION

… THE VIRUSES

….THE BACTERIA

…. THE PARASITES

AND OTHERS…

Japanese B Encephalitis

SENTINEL SURVEILLANCE ON ETIOLOGY OF MENINGITIS ENCEPHALITIS AND MENINGO-ENCEPHALITIS IN THE PHILIPPINES

A TECHNICAL PROGRESS REPORT SEPTEMBER TO DECEMBER 2010

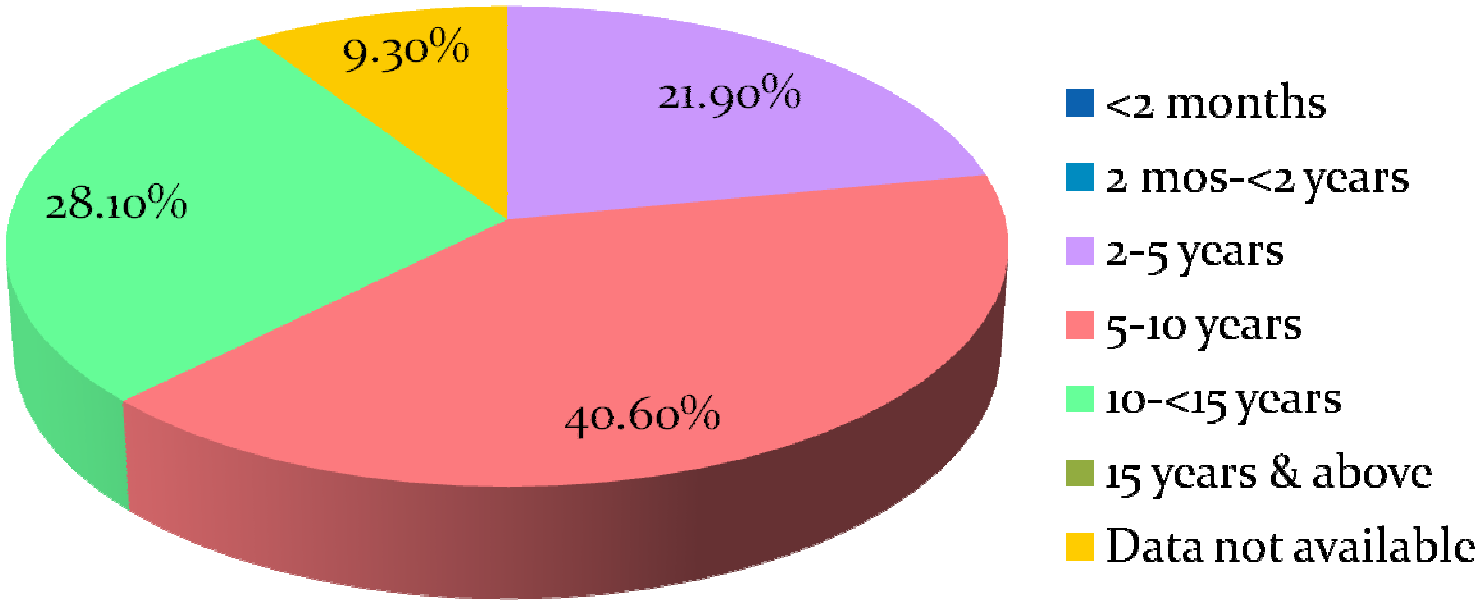
ESPINO, FE et al...

Research Institute of Tropical Medicine

Distribution of Japanese B Encephalitis by age group (January to December 2010)- From sentinel hospitals during a 22 month period

Age Group in Years	Total Number of specimens	Japanese Encephalitis (%)
Neonate-< 2 months	31	0
2 months-<2 years	41	0
2-5 years	18	7 (38.9)
5-10 years	30	13 (43.3)
10-<15 years	28	9 (32.1)
15 years and above	3	0
Data not Available	16	3 (18.8)
Total	167	32 (19.2)

Distribution of Japanese B Encephalitis by Age Group (January to December 2010)- From sentinel hospitals during a 22-month period

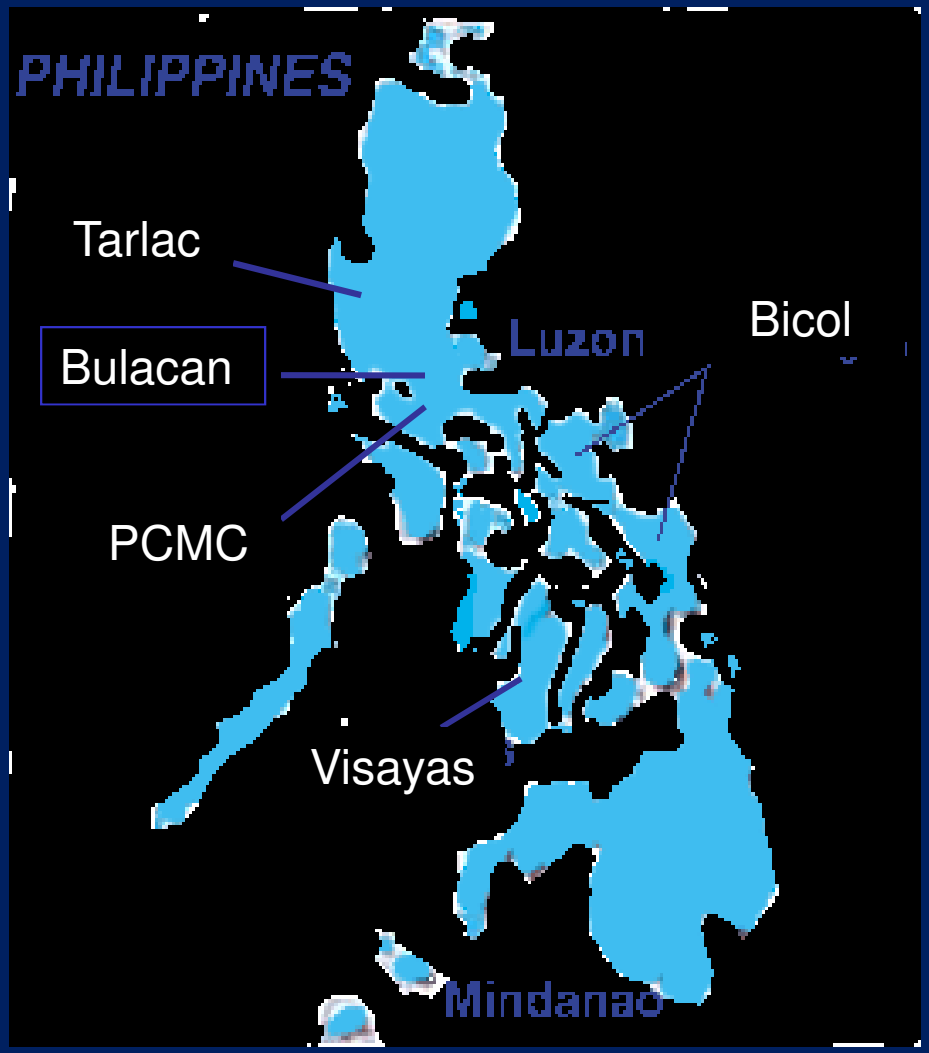


Frequency of Japanese B Encephalitis cases by Hospital (January to December 2010)

Results	BuMC (%) n=49	BiMC (%) n=37	WVMC (%) n=50	TPH (%) n=30	PCMC (%) n=1	Total (%) n=167
JE Positive	6 (12.2%)	14 (37.8%)	5 (10%)	7 (23.3%)	0	32 (19.2%)

[1] Bulacan Medical Center
[2] Bicol Medical Center
[3] Western Visayas Medical Center
[4] Tarlac Provincial Hospital
[5] Philippine Children's Medical Center

Distribution of Sentinel Hospitals for Japanese Encephalitis



Japanese Encephalitis in the Philippines

1991

1. **Dagupan City (Luzon) reported *4 deaths from encephalitis***

   13 hospitalized cases identified as encephalitis

   → **5 deaths confirmed (45% fatality rate)**

   → **5 from different barangays discharged & improved at time of investigation**

Japanese Encephalitis in the Philippines

2. ***Pigcawayan at North Cotabato***

Review of Records Jun-July 1991 at Cotabato Regional Hospital

- **40 CNS infections identified**

  → 8 JE cases suspected from Pigcawayan (confirmation not reported)

Japanese Encephalitis in the Philippines

Characteristic neurologic features for JEV

- **Abulia with masked facies**
- **Variable changes in mentation**
- **Relative absence of cranial nerve involvement**
- **Lack of gross sensory deficit**
- **Asymmetric and irregular distribution of motor and tone abnormality**

Japanese Encephalitis in the Philippines

Among Clinically Diagnosed Dengue Cases in 1999

- **6% (46/770) were positive for JE**
- **0.8% (6/770) had co-infections of Chikungunya & JE**

Japanese Encephalitis in the Philippines

Among Clinically Diagnosed Dengue Cases in 1999

- **6% (46/770) were positive for JE**
- **0.8% (6/770) had co-infections of Chikungunya & JE**

Japanese Encephalitis in the Philippines

NOTIFIABLE DISEASES, 2001	No.	Rate/100,000 pop
Encephalitis / Meningitis	207	0.3
Meningococcemia	57	0.1
Dengue	23,235	29.8
Diarrhea	845,526	1085.0

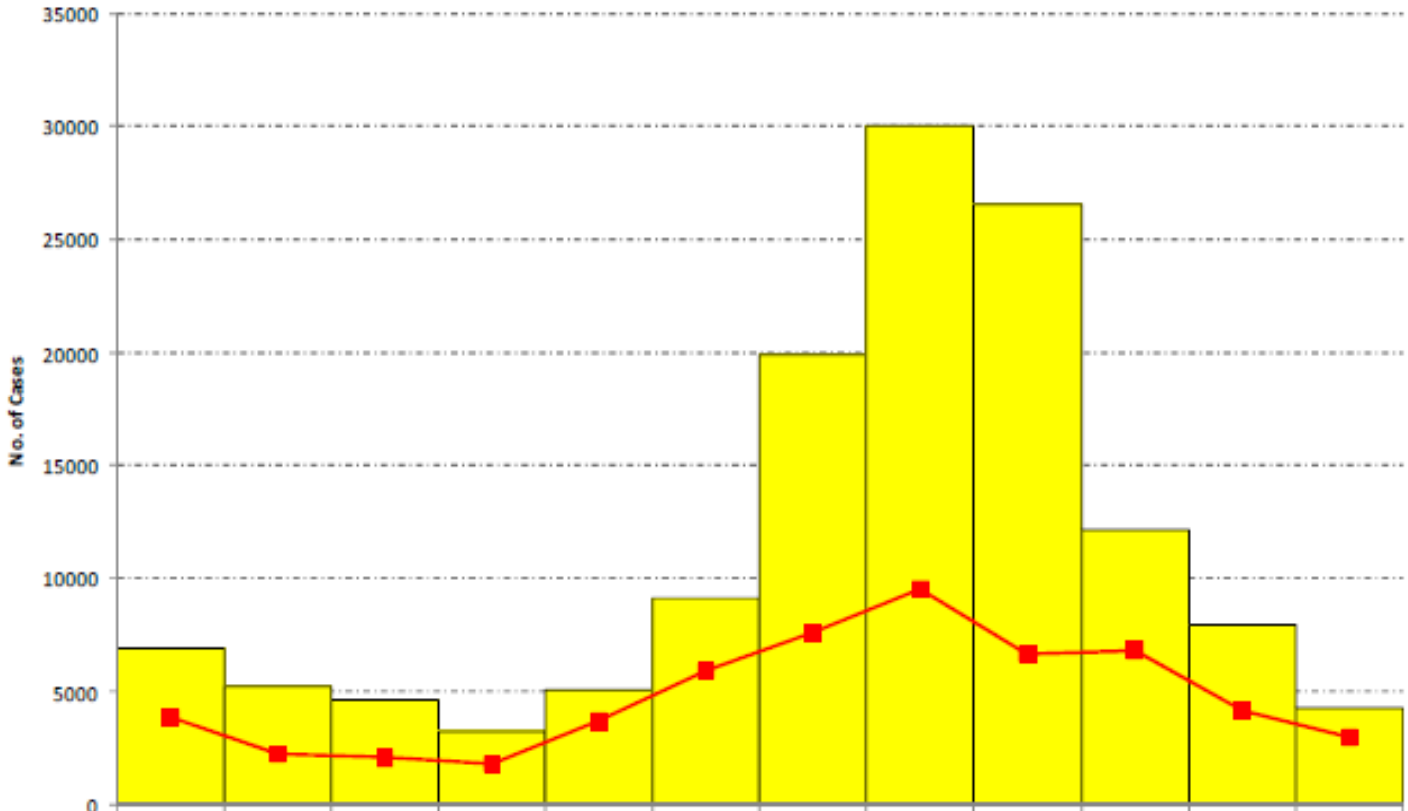
Japanese Encephalitis in the Philippines

NOTIFIABLE DISEASES, 2008	No.	Rate/100,000 pop
Encephalitis / Meningitis	788	0.9
Meningococcemia	17	0.0
Dengue	13,014	14.5
Diarrhea	434,445	485.4

DENGUE

- Number of cases nationwide from January to Dec 2010 → 135,355
  - 134.84% higher compared to the same period last year (57,636)
- Patients' ages ranged between less than 1 month - 95 years old
  - 78% belong to the 1-20 years age group
  - More deaths recorded in those below one year and in the 1-10 years age groups
  - Males comprised 52%

Fig. 2 DENGUE Cases by Month, Philippines, 2010 vs 2009



	J	F	M	A	M	J	J	A	S	O	N	D
2010	6956	5216	4697	3292	5082	9146	19990	30009	26589	12144	7955	4279
2009	3881	2260	2100	1840	3720	5928	7616	9532	6689	6867	4191	3012

DENGUE

- Total of 793 deaths recorded for the period → case fatality rate of 0.59% which decreased by 40% from 2009
- Reported cases with highest CFR are in region IX and ARMM
- Lowest CFR was found in CAR

MENINGOCOCCAL DISEASE

Region	Meningococcal Disease +			
	MW 1 - 51 (Jan. 1 - Dec. 25)		MW 52 Dec. 26 - Dec. 31)	
	Cases	Deaths	Cases	Deaths
1	2	2	0	0
2	1	1	0	0
3	7	1	0	0
4A	15	2	0	0
4B	3	0	0	0
5	3	1	0	0
6	9	5	0	0
7	2	0	0	0
8	4	0	0	0
9	6	0	0	0
10	1	0	0	0
11	3	0	0	0
12	9	2	0	0
ARMM	1	0	0	0
CAR	3	1	0	0
CARAGA	5	0	0	0
NCR	28	6	0	0
Subtotal	102	21	0	0
Total	102		21	
	Cases		Deaths	

HIV- AIDS

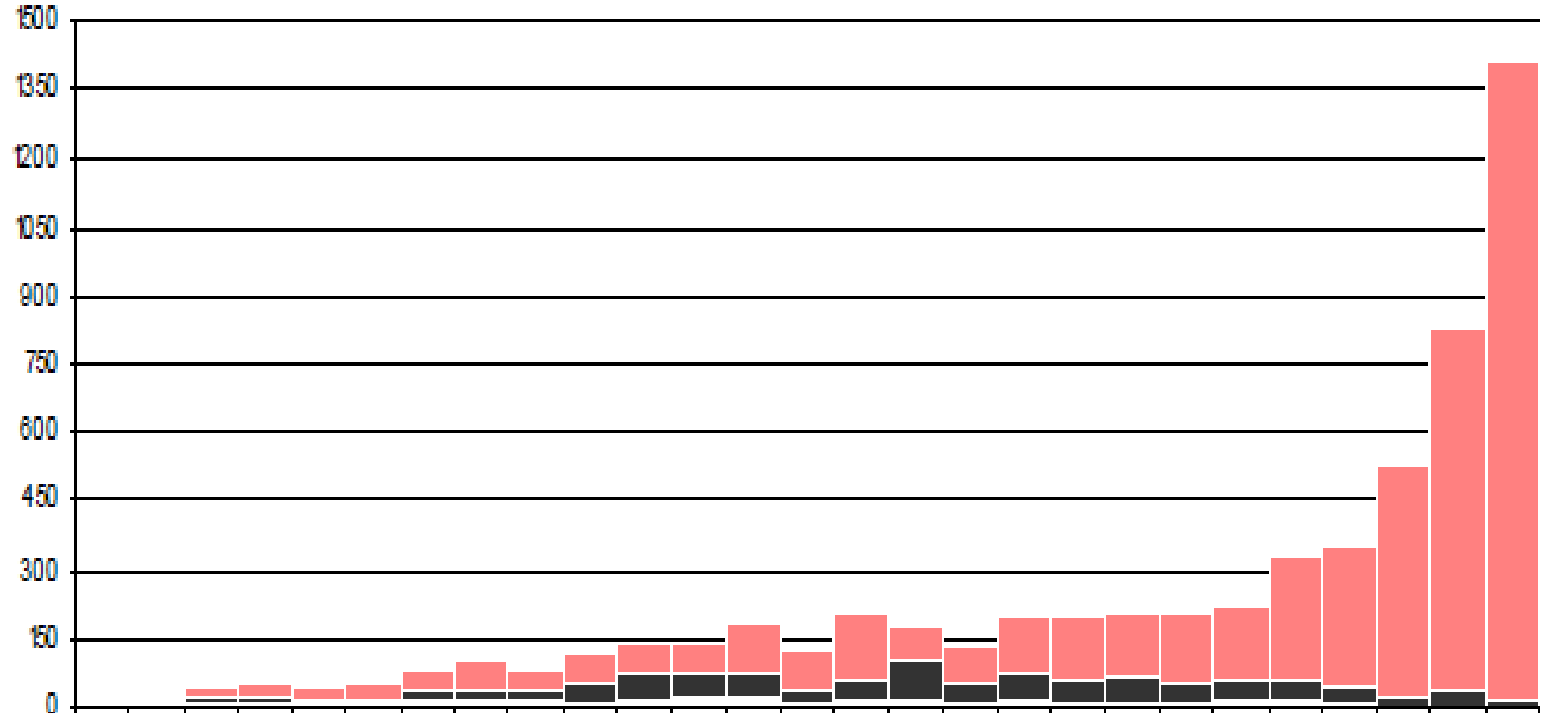
Table 1. Quick Facts 1

Demographic Data	Nov 2010	Jan-Nov 2010	Cumulative Data: 1984–2010
Total Reported Cases	112	1,417	5,841
Asymptomatic Cases	110	1,400	4,987
AIDS Cases	2	17	854
Males	103	1,300	4,532*
Females	9	117	1,298*
Youth 15-24yo	31	430	1,154
Children <15yo	0	3	55
Reported Deaths due to AIDS	0	2	323

**Note: No data available on sex for eleven (11) cases.*

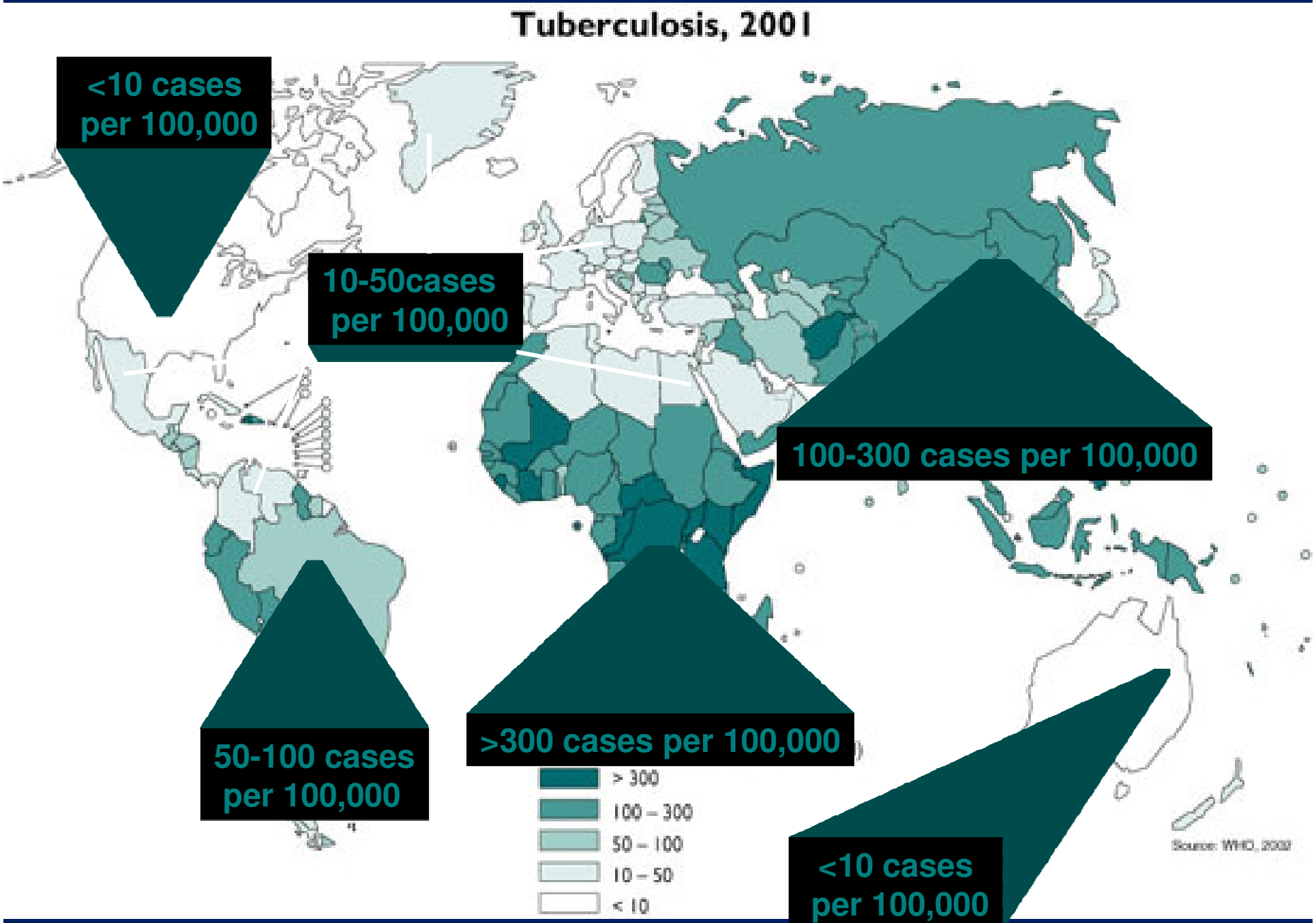
HIV- AIDS

Figure 3. Number of HIV/AIDS Cases Reported in the Philippines by Year, Jan 1984 to November 2010 (N=5,841)



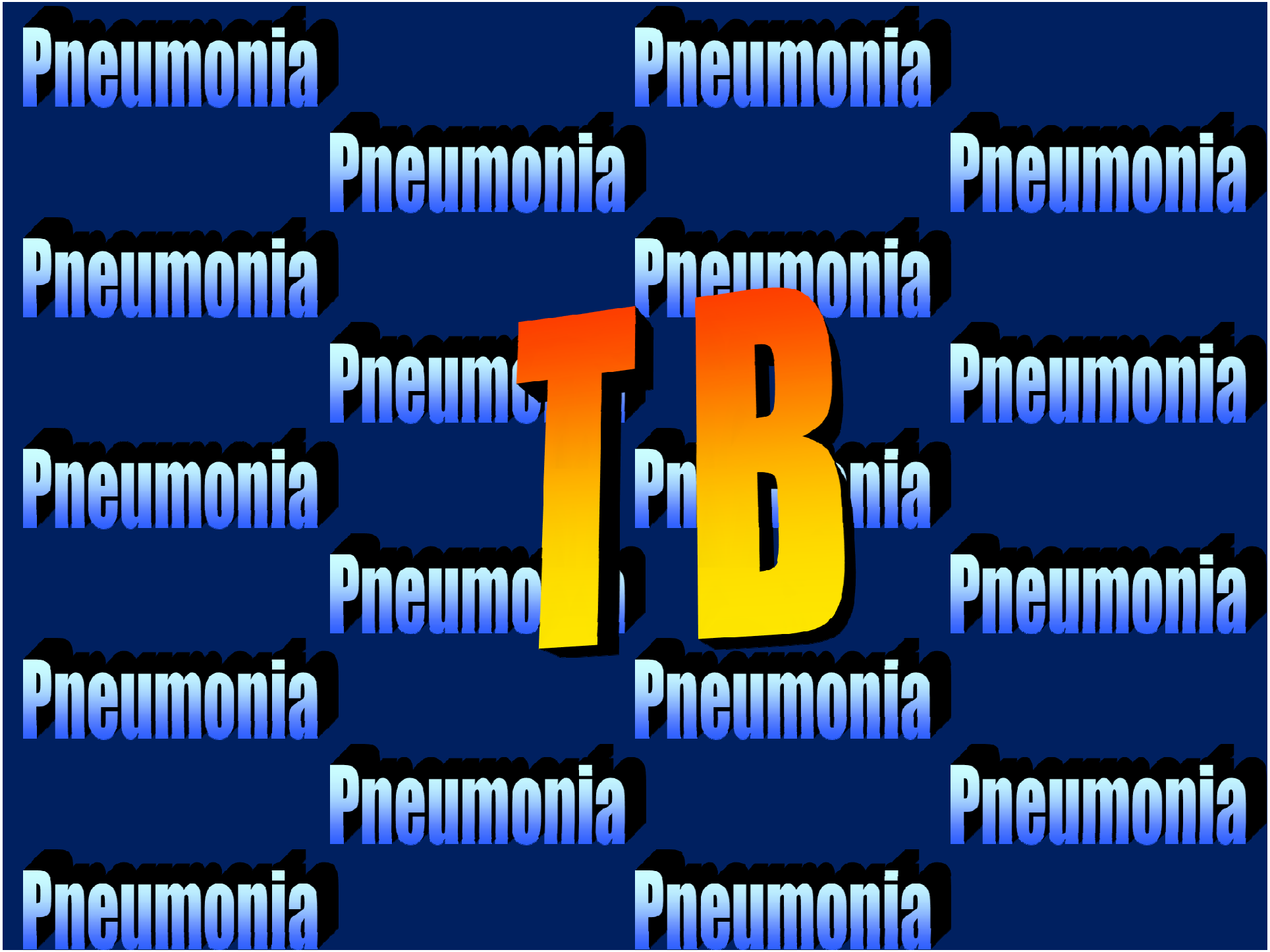
	'84	'85	'86	'87	'88	'89	'90	'91	'92	'93	'94	'95	'96	'97	'98	'99	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10
TOTAL	2	10	29	38	32	39	66	85	72	102	118	116	154	117	189	158	123	174	184	193	189	210	309	342	528	835	1417
Asymptomatic	0	6	18	26	21	29	48	68	51	64	61	65	104	94	144	80	83	118	140	139	161	171	273	312	506	806	1400
AIDS	2	4	11	13	11	10	18	17	21	38	57	51	50	23	45	78	40	56	44	54	38	39	36	30	22	29	17
Death	2	4	10	12	9	8	15	13	13	11	19	24	27	10	16	17	9	20	11	11	8	16	18	10	*7	1	2

*Five initially asymptomatic cases reported in 2008, died due AIDS that same year.


Tuberculosis, 2001
<10 cases per 100,000
10-50cases per 100,000
100-300 cases per 100,000
50-100 cases per 100,000
>300 cases per 100,000
<10 cases per 100,000
> 300
100 – 300
50 – 100
10 – 50
< 10
Source: WHO, 2002

Estimated TB incidence and mortality, 2002 (WHO)

WHO REGIONS	Number of cases (thousands)		Cases per 100,000 population		Deaths from TB (including TB deaths in people infected with HIV)	
	All Forms (%)	Smear-positive	All forms	Smear-positive	Number (thousands)	Per 100 000 population
Africa	2354 (26)	1000	350	149	556	83
The Americas	370 (4)	165	43	19	53	6
Eastern Mediterranean	622 (7)	279	124	55	143	28
Europe	472 (5)	211	54	24	73	8
South-East Asia	2890 (33)	1294	182	81	625	39
Western Pacific	2090 (24)	939	122	55	373	22
Global	8797 (100)	3887	141	63	1823	29


Pneumonia
TB

TB

HIV-infected areas

HIV-uninfected areas

High impact on countries with HIV infections due to considerable overlap between clinical pictures caused by TB and HIV-related lung disease

TB  HIV

HIV status often "unknown" in children suspected with TB

Thus:

- important to do HIV testing for more appropriate treatment and prophylaxis


MDR-TB
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Multidrug-Resistant (MDR) TB

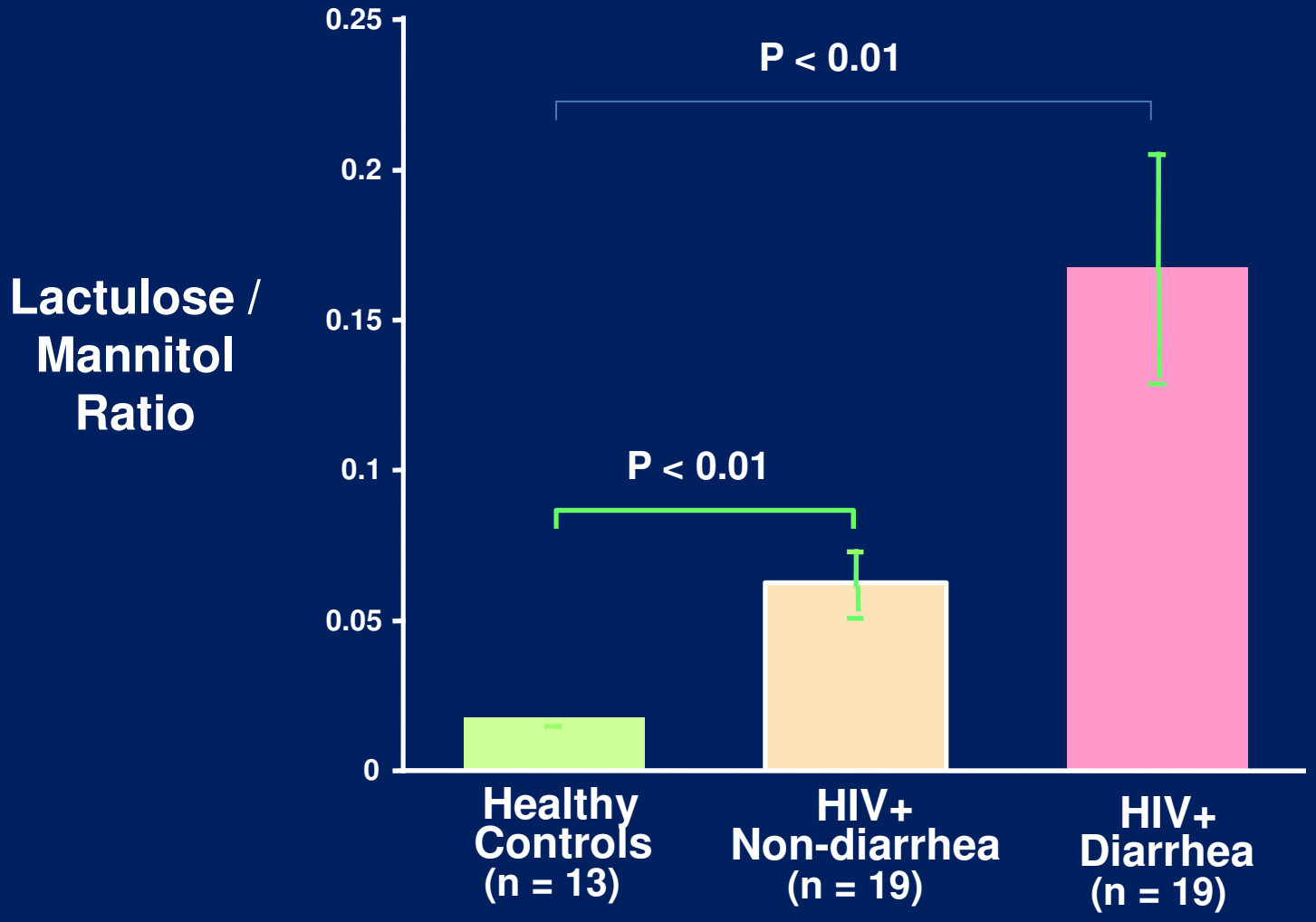
- MDR-TB is as infectious as drug susceptible TB
- Diagnosis is confused by lack of culture and susceptibility testing
- Suspected if:
  - an adult index case has MDR-TB
  - child is a treatment failure despite compliant therapy
  - the adult index case has unknown susceptible testing and with treatment failure or a retreatment case

NEGLECTED FOOD-BORNE DISEASES

Prevalence

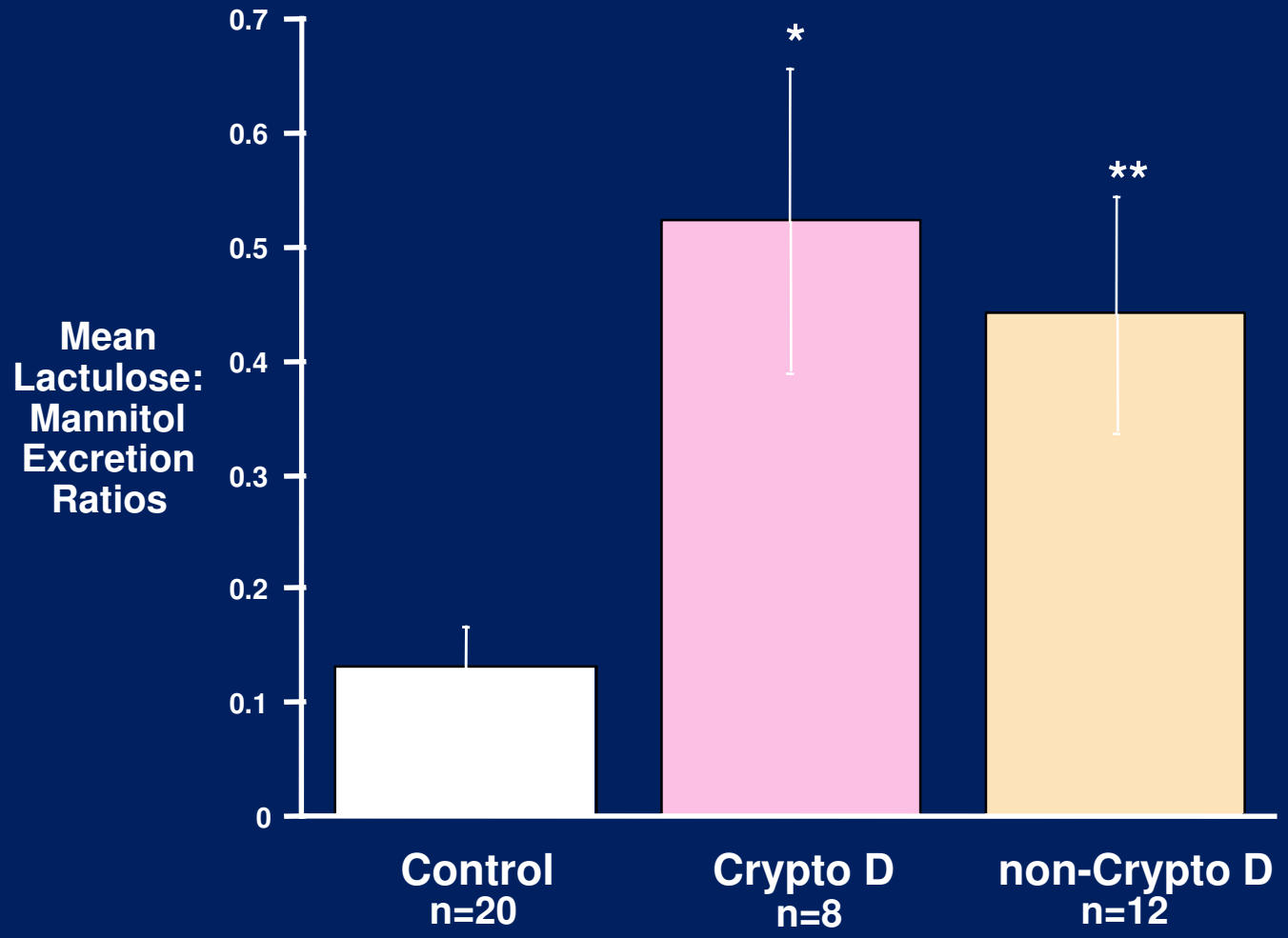
Philippines	Rate		Bangladesh	
Cryptosporidium	8.9%	Menorca M, et al. SEAJTM 1994 By EIA	8.4%	Haque, R et al. AJTMH 2003
	2.5%	Paje-Villar E, et al. Ann Trop Med Parasitol 1994 By Microscopy		
G. lamblia	0.6%	Adkins HJ, et al., JCM 1987, Method (?)	11%	Haque, R et al. AJTMH 2003
E. histolytica	0.1%	Adkins HJ, et al., JCM 1987, Method (?)	8%	Haque, R et al. AJTMH 2003

Disruption of intestinal barrier function in HIV-infected patients with and without diarrhea in Fortaleza, Brazil



Lima et al. AJGastro. 92:1861, 1997

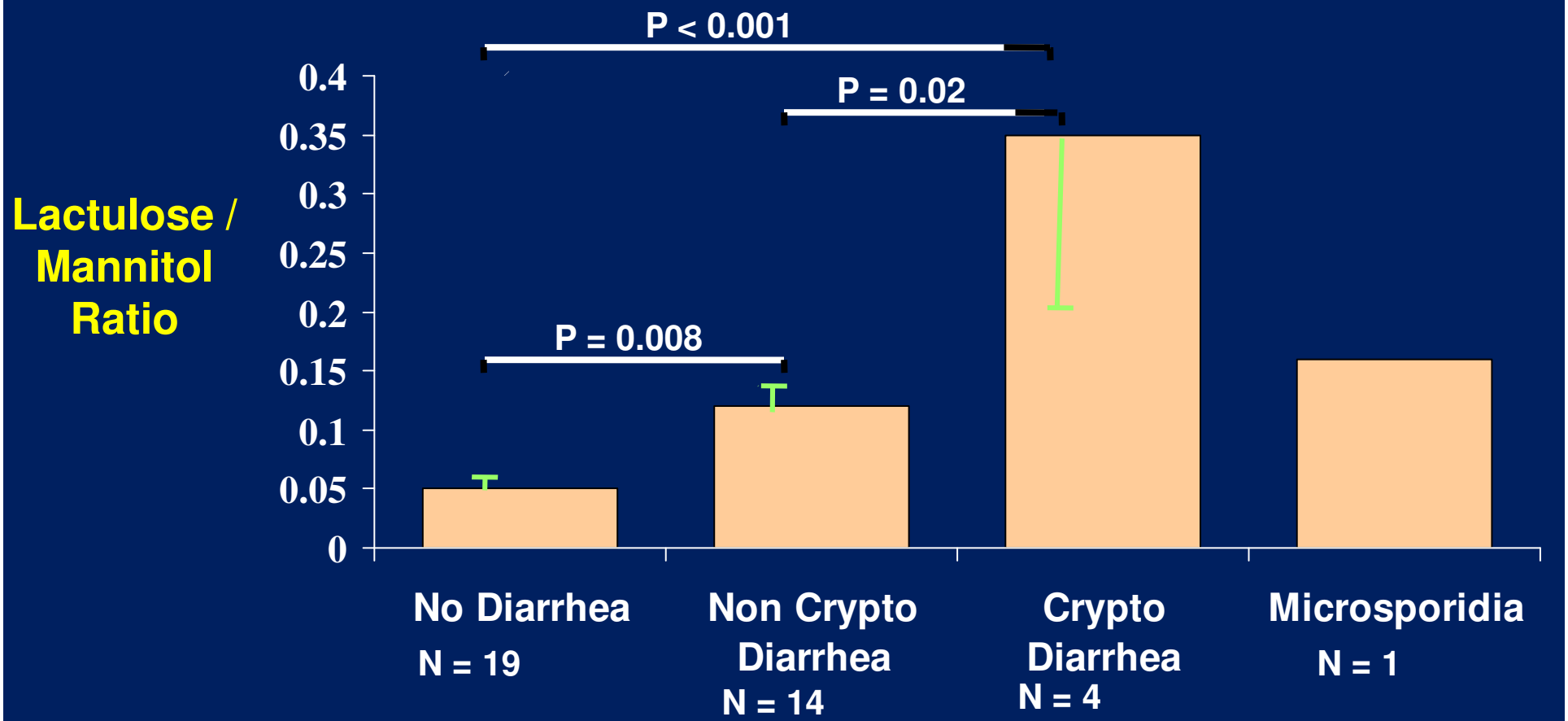
Disruption of Intestinal Barrier Function in Children with Cryptosporidial and non-Cryptosporidial Diarrhea in Fortaleza, Brazil



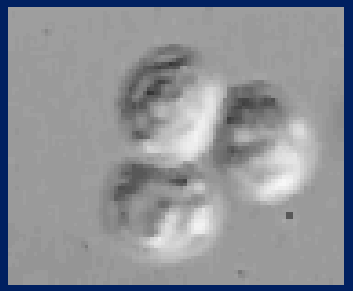
[vs controls: *p=0.001; **p<0.01]

Guerrant, Lima, Barboza, et al Adv Exp Med Biol 473:103-11, 1999.
Barboza et al BrasJ Med Biol Res 32:1499-1504, 1999.

Intestinal Barrier Disruption in HIV-infected patients with cryptosporidial, non-cryptosporidial, and microsporidial diarrhea



Lima et al. Am J Gastro. 92:1861, 1997.



Cryptosporidiosis

- Causal Agent
  - Many species of Cryptosporidium exist that infect humans and a wide range of animals
  - C. parvum and C. hominis (formerly known as C. parvum anthroponotic genotype or genotype 1) are the most prevalent species causing disease in humans

Clinical Features

- Wide range of manifestation
  - Asymptomatic to severe life-threatening illness
  - Watery diarrhea is the most frequent symptoms
  - Dehydration, weight loss, abdominal pain
  - Fever
  - Nausea
  - Vomiting

Cyclosporiasis

- Recently identified as a unicellular coccidian parasite
- Causal agent: *Cyclospora cayetanensis*
- Designation given in 1994 to Peruvian isolates of human-associated Cyclospora
- Appears that all human cases are caused by this species

Clinical Features

- Incubation period: 1 week
- Symptomatic infections
  - Watery diarrhea, which can be severe
  - Anorexia
  - Weight loss
  - Abdominal pain
  - Nausea and vomiting
- Untreated infections typically lasts for 10-12 weeks and may follow a relapsing course

Laboratory Diagnosis

Specimen processing

- Fixed in 10% formalin
  - Direct microscopy
  - Concentration procedure
  - Preparation of stained smears
- Fixed in 2.5% potassium dichromate
  - For sporulation assay and molecular diagnosis
- Frozen without fixation
  - For molecular diagnosis

Microsporidiosis

- Causal agents
  - **14 microsporidian species**
    - **Enterocytozoon bieneusi**
    - **Encephalitozoon intestinalis**
    - **Encephalitozoon hellem**
    - **Encephalitozoon cuniculi**
    - **Pleistophora sp.**
    - **Trachipleistophora hominis**
    - **T. anthropophtera**
    - **Nosema ocularum**
    - **N. algerae**
    - **Vittaforma corneae**
    - **Microsporidium ceylonensis**
    - **M. africanum**
    - **Brachiola vesicularum**
    - **B. connori**
- **Increasingly recognized as opportunistic infectious agent worldwide**

Clinical Features

- Represents an important and rapidly emerging opportunistic disease
- Occurring mainly, but not exclusively, in severely immunocompromised patients with AIDS
- Cases of microsporidiosis in immunocompromised persons not infected with HIV as well as in immunocompetent persons also have been reported

Laboratory Diagnosis

- Light Microscopy
  - Chromotrope 2R method
- Transmission electron Microscopy
- Immunofluorescence Assay
- Molecular Methods

THE CHALLENGE FOR EMERGING DISEASES

- Need for Surveillance and Accurate Reporting
- Appropriate Laboratory procedures for Identification
- Networking
- Rapid Response In Outbreak Situations
- Control Measures in Place

REMAINING CHALLENGES AND ISSUES

- VECTOR CONTROL
  - MALARIA
  - JAP B ENCEPHALITIS
  - DENGUE
- MASS DRUG ADMINISTRATION
  - SCHISTOSOMIASIS
  - FILARIASIS
  - OTHER NEGLECTED DISEASES

InterAcademy Network for Emerging Infections (IANEI)

- UP MANILA- NIH AND NAST ENDEAVORS TO ESTABLISH A NETWORK FOR EMERGING INFECTIONS IN THE PHILIPPINES AND ASIA.

The IANEI aims to achieve the following objectives

1. **To facilitate communication between academies of medicine and medical sciences on issues related to emerging infections**

2. **To develop and maintain a database of researches and programmes on the emerging infections**

Objectives
IANEI

3. To provide evidence-based recommendations for health policy development for the control of emerging infections

4. To encourage collaboration between academies of medicine and medical sciences on researches and programmes on the control of emerging infections

5. To mobilize support for researches that would provide new knowledge crucial to increasing the effectiveness of control programmes for emerging infections

"If history is our guide, we can assume that the battle between the intellect and will of the human species and the extraordinary adaptability of microbes will be never-ending. To successfully fight our microbial foes, we must continue to vigorously pursue research on the basic mechanisms that underlie microbial pathogenesis and develop novel strategies to outwit these ingenious opponents. The past 10 years have been challenging but no more so than will be the future."

- Steven A Fauci, EID 2005