Estimating the global burden of typhoid fever

John A Crump, MB, ChB, DTM&H
Foodborne and Diarrheal Diseases Branch
Centers for Disease Control and Prevention

Overview

- Existing typhoid fever burden estimates
- Methodology for typhoid fever burden
  - Incidence
  - Mortality
  - New estimate
- Limitations
- Future directions

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Estimates of global typhoid burden

- 1984
  - Dr Dhiman Barua, WHO
  - PAHO meeting
  - Reviews of Infectious Diseases, 1986
- 1986
  - United States Institute of Medicine
  - Committee on Issues and Priorities for New Vaccine Development
- 1996
  - World Health Report
  - 16 million illnesses
  - 600,000 deaths (3.8% mortality)

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Limitations of existing estimate

- Methods not outlined in detail
- Limited source data
- Do not adjust for age distribution
  - Incidence
  - Mortality
- Exclude China

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Changes since 1984

- Growth of global population
- Changes in sanitary conditions
- Improved surveillance
- Initiation of population-based typhoid incidence studies
- Publication vaccine studies from new regions
- Improved understanding of age distribution of typhoid fever
- Formalization of methods for assessment of disease burden

Incidence: sources

- Literature search (Medline)
- National typhoid surveillance data

Incidence: results

- Literature search
  - 859 articles
  - 250 articles selected
  - 22 reliable, population-based
- National surveillance data
  - Developed countries

Incidence: data sources

Reliable national surveillance data

Limited national surveillance data

Incidence study

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Incidence: global population

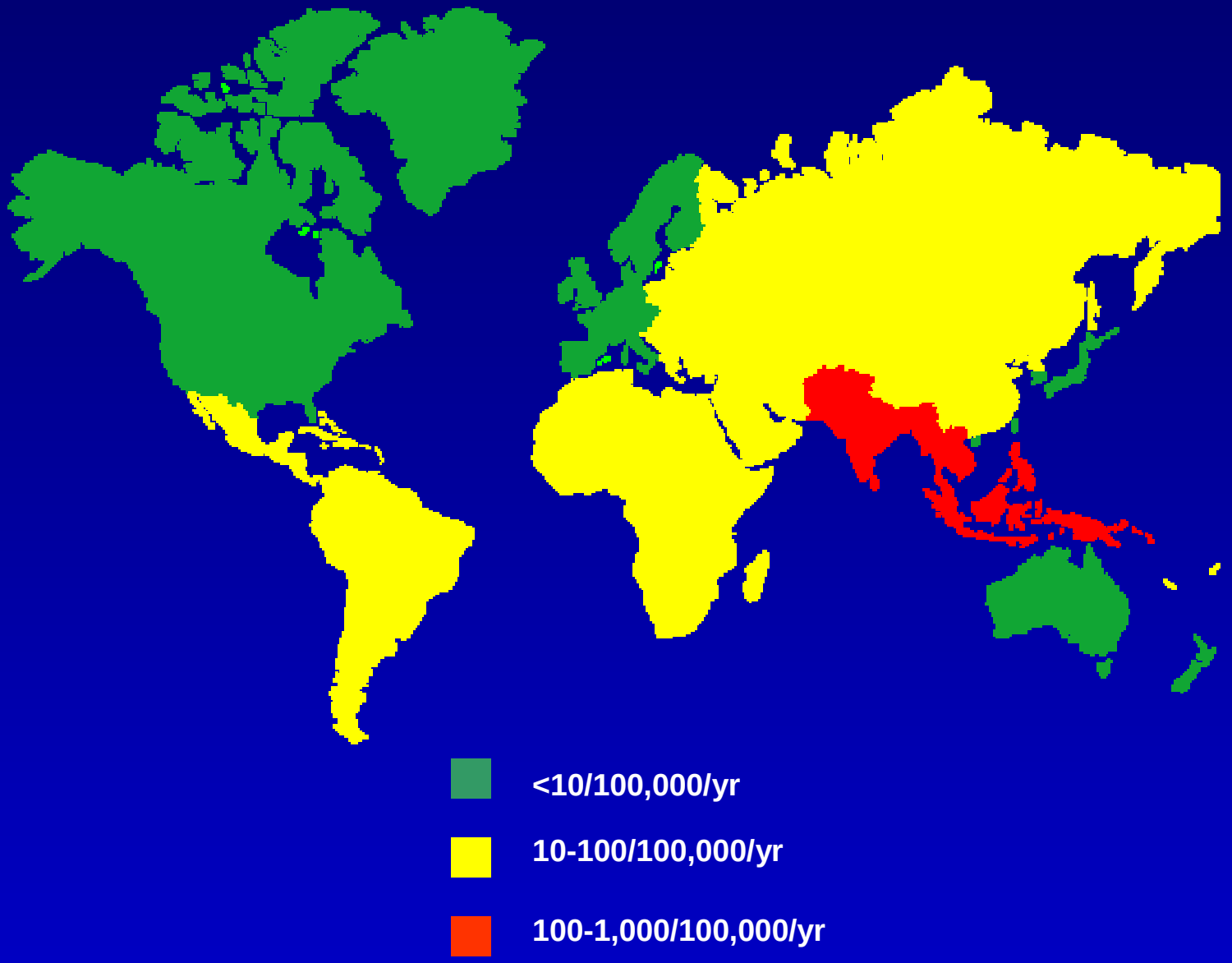
- United Nations Sex and Age of the World's Population
  - 2000 medium fertility variant estimate
- Standard age strata
- United Nations regions

The United Nations classification of major areas and regions

Area	Region
Africa	Eastern Africa
	Middle Africa
	Northern Africa
	Southern Africa
	Western Africa
Asia	Eastern Asia
	South-central Asia
	South-eastern Asia
	Western Asia
Europe	Eastern Europe
	Northern Europe
	Southern Europe
	Western Europe
Latin America/Caribbean	Caribbean
	Central America
	South America
Northern America	Northern America
Oceania	Australia/New Zealand
	Melanesia
	Micronesia
	Polynesia

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

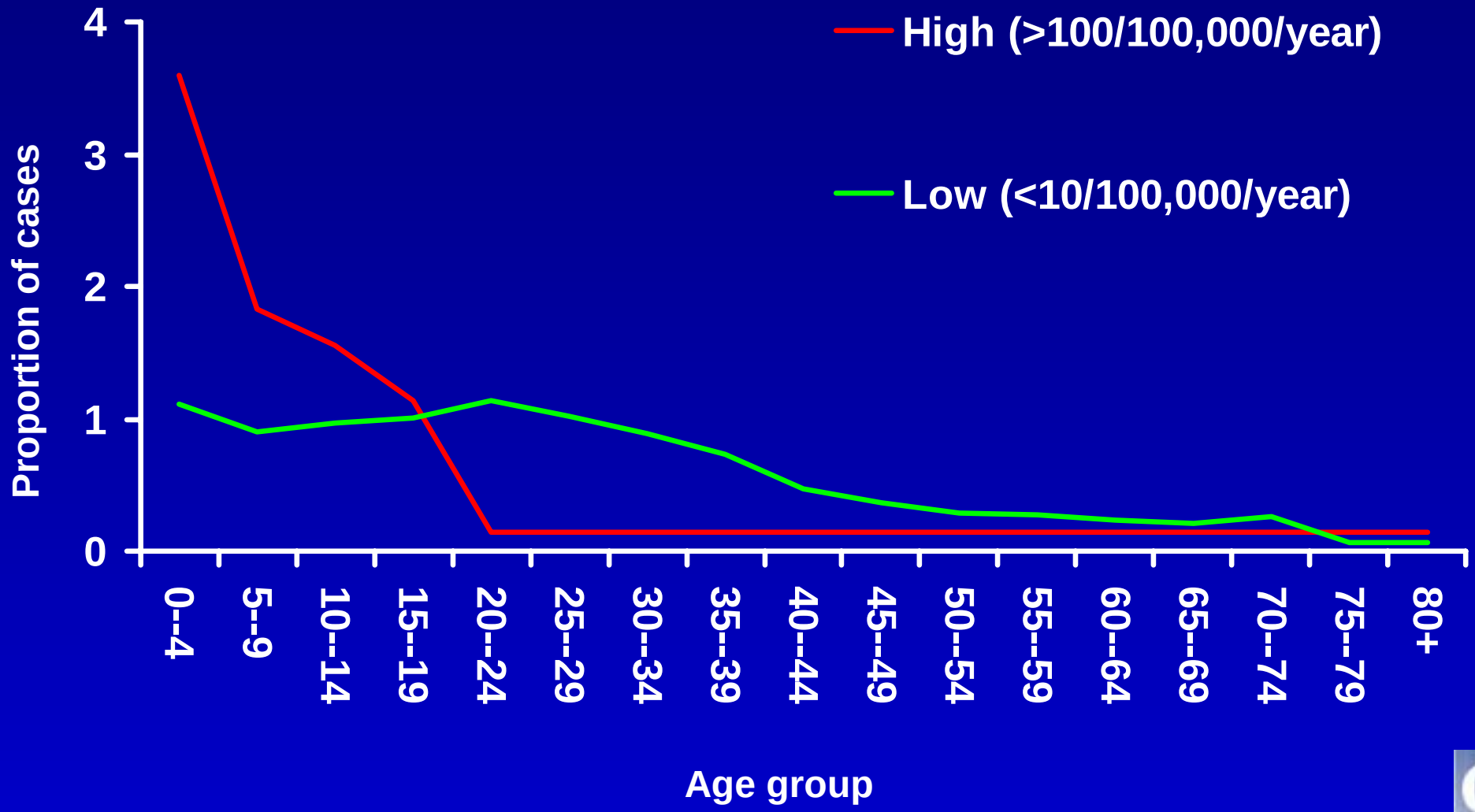
Typhoid fever incidence by region



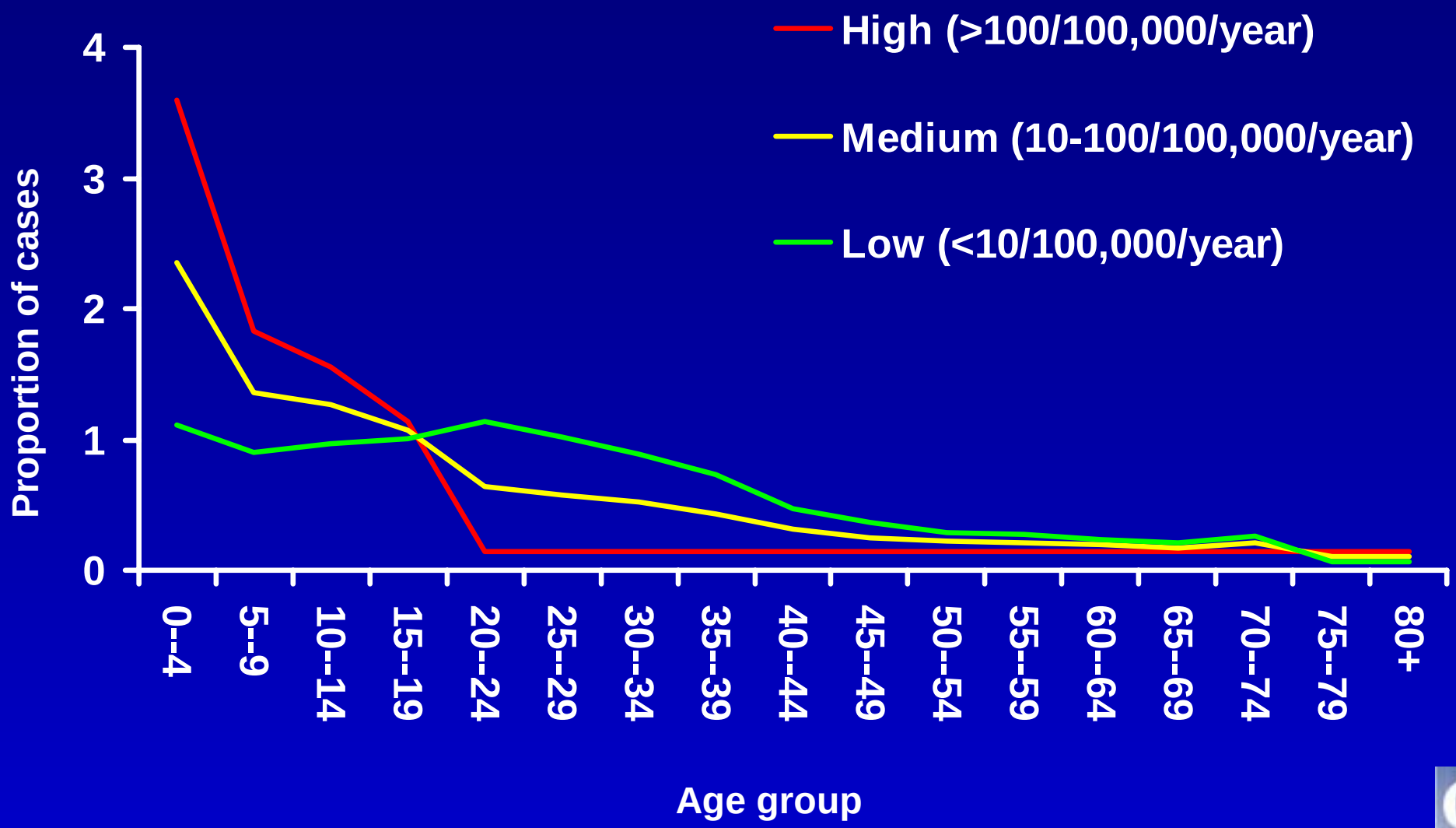
Incidence: extrapolating data

- **Extrapolate**
  - **One age group to others**
- **Age distribution of typhoid fever**
  - **Three incidence levels**
  - **Limited range of population-based typhoid incidence studies with data by age group**

Age incidence profiles



Age incidence profiles



Incidence: calculation

- Global population divided into regions and age strata
- All data sources considered for each region
- Most conservative rates selected
- Incidence for each age stratum calculated from age distribution curves

Example:

Northern Africa region

Age strata	Population	Source data incidence	Extrapolated incidence	Total cases by age stratum
0-4	21,995,000		83	18,255
5-9	20,613,000	48	48	9,894
10-14	20,258,000		44	8,914
15-19	19,285,000		38	7,328
20-24	16,926,000		23	3,893
25-29	14,236,000		20	2,847
30-34	12,562,000		18	2,261
35-39	10,892,000		15	1,634
40-44	9,490,000		11	1,044
45-49	7,823,000		9	704
50-54	5,807,000		8	465
55-59	4,255,000		7	298
60-64	3,746,000		7	262
65-69	2,990,000		6	179
70-74	2,160,000		7	151
75-79	1,211,000		4	48
80+	788,000		4	32
Total				58,210

Incidence: estimate

- 11 million (10,825,486) illnesses/year

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Mortality

- Lack population-based data
- Published studies
  - Hospital-based
  - Overestimate
- Infants and children
  - Mild illness

Mortality

- Highest incidence
  - Children <5 years
  - South-central and south-east Asia
- Conservative mortality 1%

Global typhoid burden

- 11 million (10,825,486) illnesses/year
- 110,000 (108,254) deaths/year
- South-central and south-eastern Asia

Limitations

- Few data points to extrapolate from
- Vaccine studies
  - High incidence areas
- Adjustments
  - Blood culture sensitivity
  - Antibiotic therapy
  - Mild illness

Future directions

- Standard method
- Sentinel surveillance tool
  - Incidence
  - Mortality
- Widely applied
- Integrated with disease burden estimates for other febrile illnesses

Acknowledgements

Centers for Disease Control and Prevention, Atlanta

Foodborne and Diarrheal Diseases Branch

Eric D. Mintz, MD, MPH

Stephen P. Luby, MD

Robert V. Tauxe, MD, MPH

Paul S. Mead, MD, MPH

Biostatistics and Informatics Branch

R. Michael Hoekstra, PhD

World Health Organization, Geneva

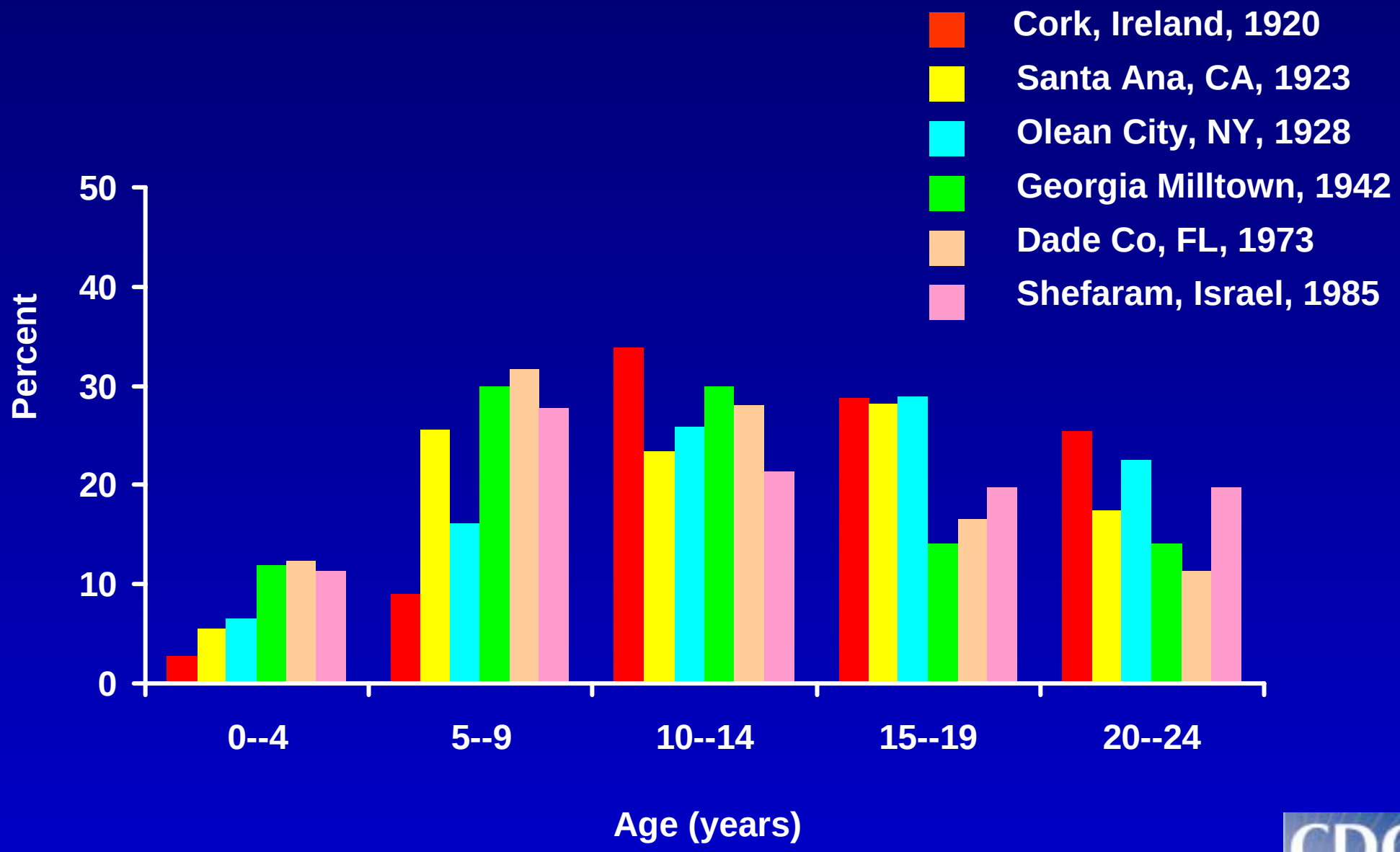
Global Programme on Evidence for Health Policy

Claudia Stein, MD, MSc

Department of Communicable Disease Surveillance and Response

Claire-Lise Chaignat, MD

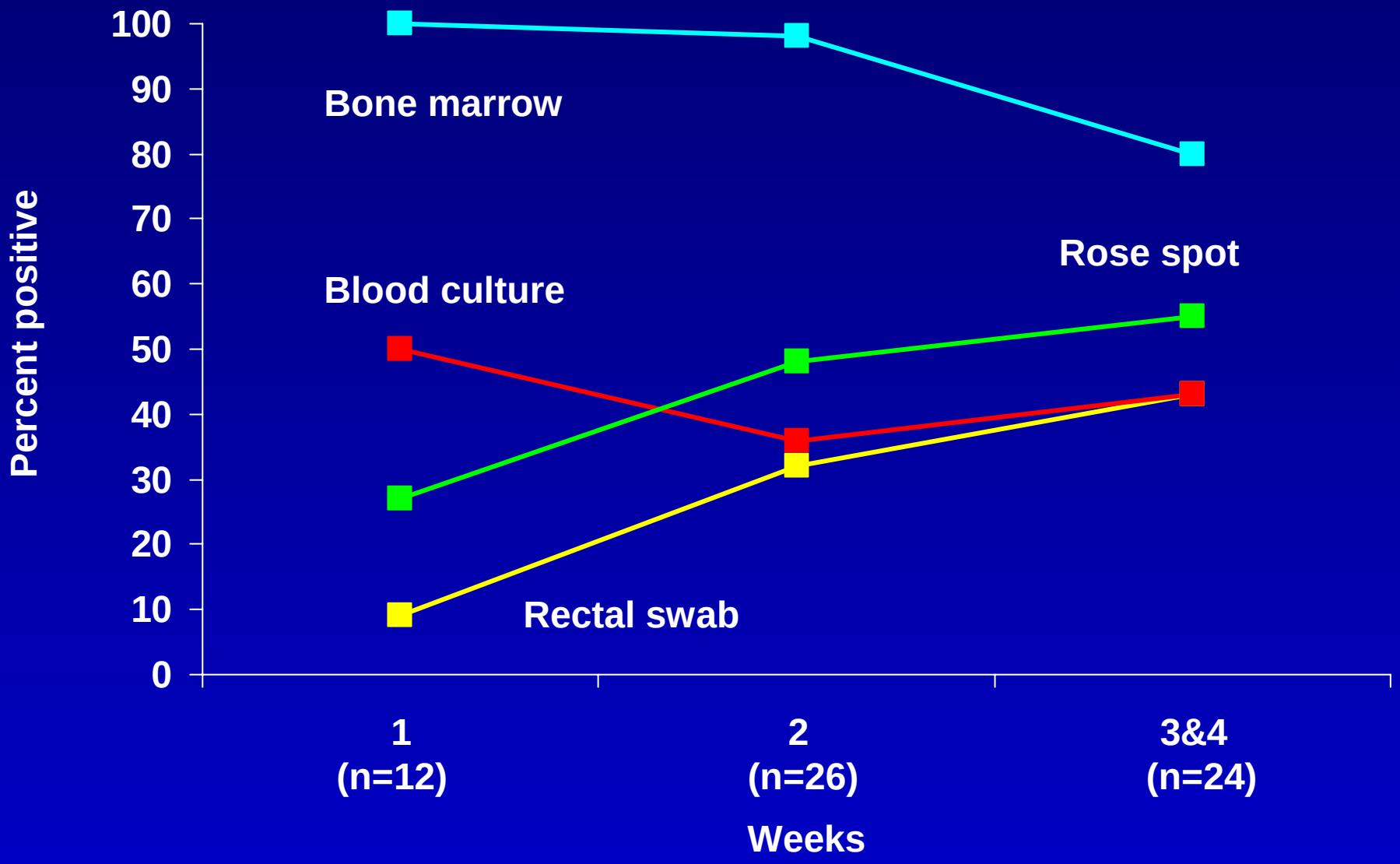
Age incidence of waterborne typhoid outbreaks



Mahle WT, Levine MM. Pediatr Infect Dis J 1993;12:627-31

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Culture methods for typhoid fever



From: Gilman RH et al. Lancet 1975; 1: 1211-3

Serologic tests for typhoid fever

- **Widal test**
  - **O and H antigens**
  - **Limited use even when paired sera collected**

- **Better rapid diagnostic tests**
  - **Antibody and antigen detection**
  - **Need to be inexpensive, practical, sensitive, specific**
  - **Countries with endemic typhoid fever**

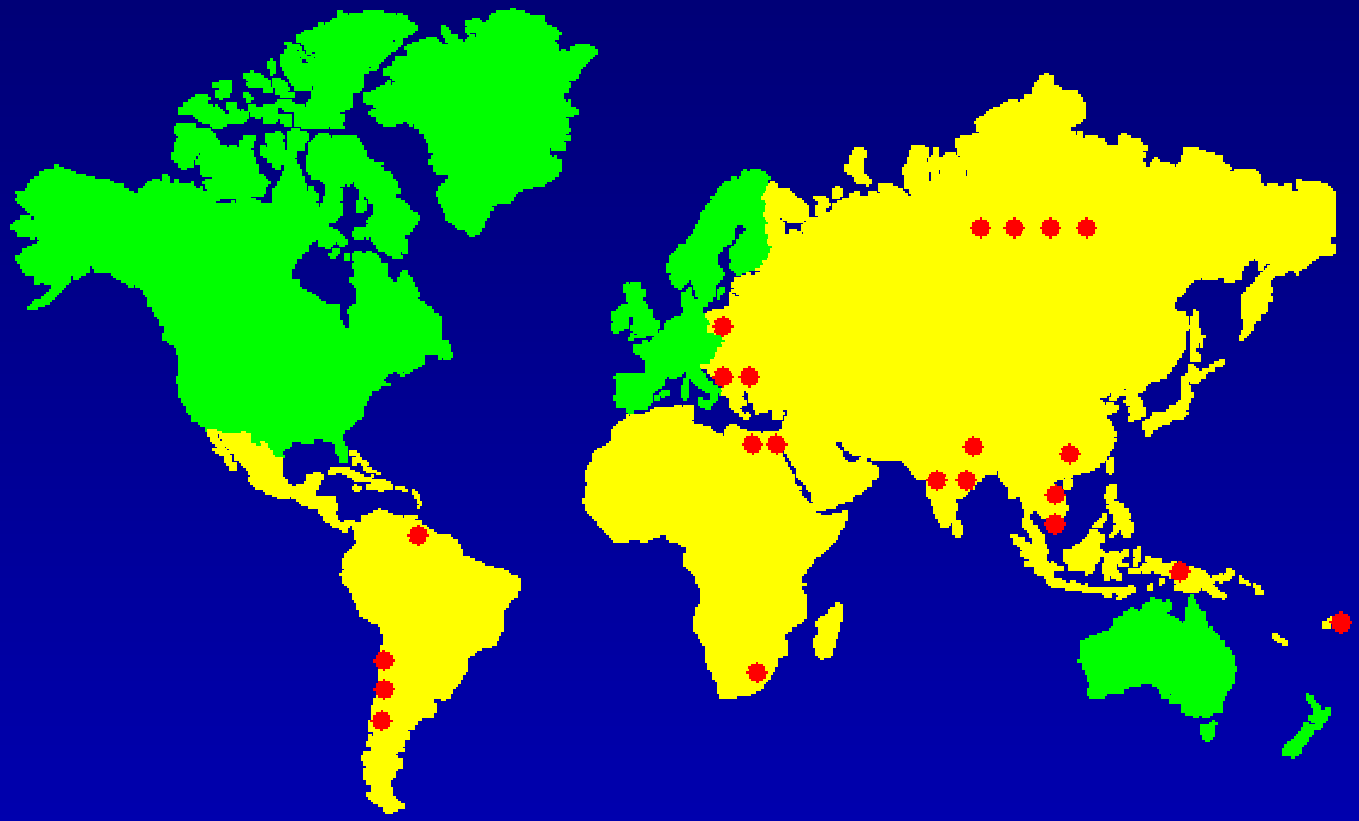
Global burden of *Shigella*

- CDC and WHO
- Kotloff KL et al. Bull WHO 1999;77:651-666
- Global population stratified
  - Age
  - Developed and industrialized
- Published studies of diarrhea incidence for each stratum
- Published studies of etiology of diarrhea for each stratum
- Calculated global burden

Shigella method is not appropriate for typhoid

- Syndrome of undifferentiated fever, not diarrhea
- Little data exist on fever incidence
- Even fewer data on the etiology of fever in developing countries
- Another approach is needed

Incidence: data sources



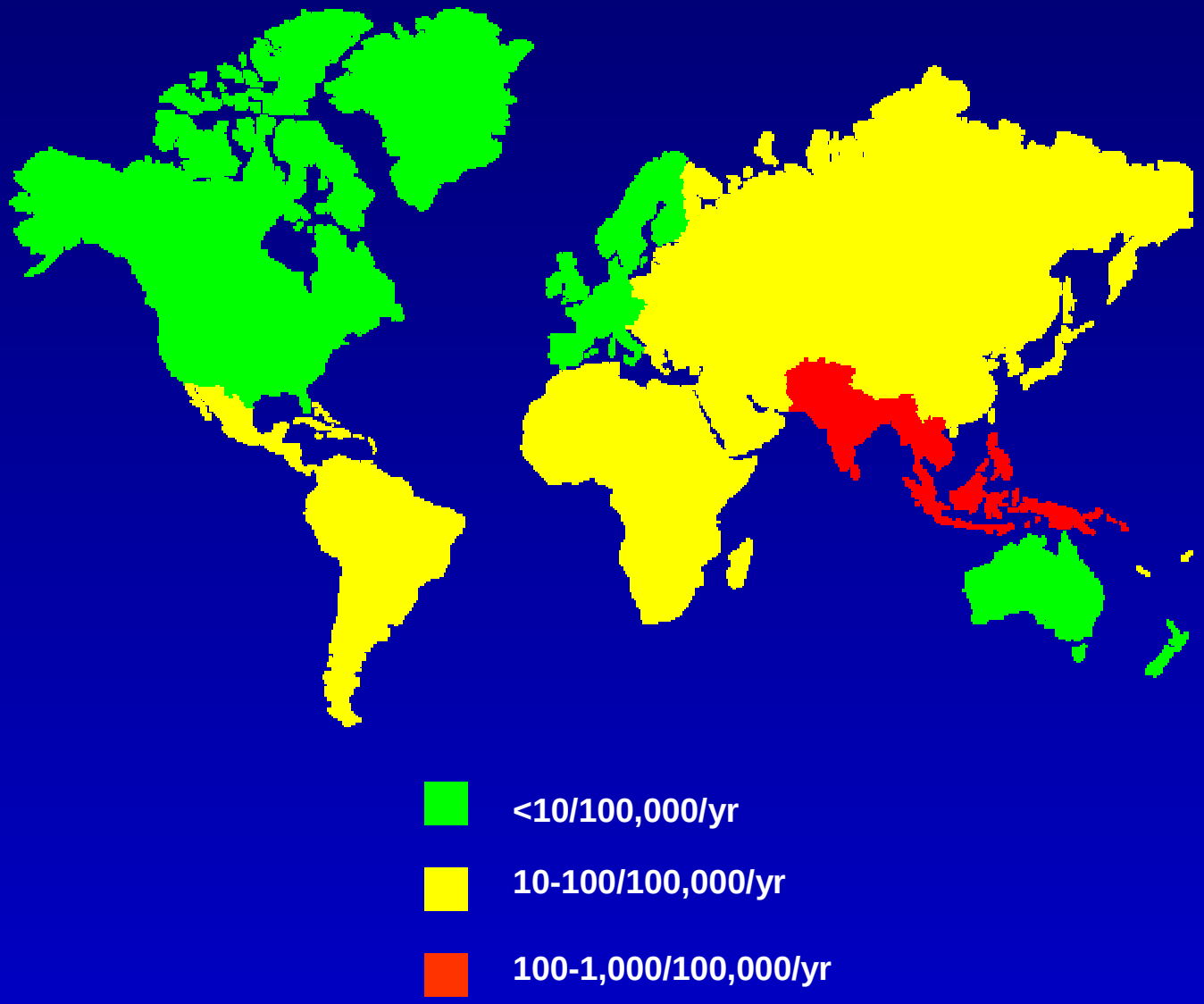
Reliable national surveillance data

Limited national surveillance data

Incidence study

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Typhoid fever incidence by region



Rationale for estimating global burden

Evaluation of policies for health improvement requires detailed, reliable assessment of the epidemiologic conditions and the burden of disease

Murray CJL, Lopez AD. Global burden of disease

Incidence: extrapolating data

- **Extrapolate**
  - **One country in a region to others**