

**GLOBAL WARMING AND  
EPIDEMIOLOGY OF  
CHOLERA, IS IT  
CHANGING?**

# GLOBAL WARMING AND EPIDEMIOLOGY OF CHOLERA, IS IT CHANGING?

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Malaria, Dengue, **Cholera & other diarrhoeal diseases**, Tick borne diseases, Malnutrition, Leishmaniasis, Chikangunya & other viral fever etc.

*Vibrio cholerae*  
Important points



- Gram-negative, non-spore-forming curved rod,
- Autochthonous member of diverse aquatic ecosystems
- Close association with a variety of algae and crustaceans.

*Ref: Colwell RR, Huq A. Ann N Y Acad Sci 1994; 740:44-54*

## Cont.....

- Classified, by the composition of its major surface antigen (O), into sero-groups, of which there are nearly 206.
- O1 and O139 causes cholera.
- Cholera toxin (CT) including its receptor, and the Toxin-co regulated Pilus (TCP) : virulence factor.
- Epidemiological feature: Regular seasonal appearance, Inter-annual variability, Simultaneous explosive outbreaks in several distinct foci .

*Ref: Sharma NC, Mandal PK, Dhillon R , Jain M. Indian J Med Res 2007; 125: 633-40.*

## Cont.....

- In 2005: total 131 943 cases including 2272 deaths from 52 countries.
- 30% increase compared with the number of cases reported in 2004.
- Delta region of the Ganges & Brahmaputra has been identified as cholera's 'native habitat' for centuries and source for periodic pandemic spread.

*Ref: World Health Organization, Cholera 2005. Weekly epidemiological record 2006; 81:297-308.*

# Cholera Pandemics



Seven distinct cholera pandemics have occurred since the onset of the first in 1817 in India and the seventh one in 1961 in Indonesia.

*Ref: Tauxe RV, Mintz ED, Quick RE. Emerg Infect Dis 1995; 1(4): 141–46.*

First pandemic:  
1817-23

India to South-  
east Asia,  
Central Asia,  
Middle-east  
and Russia.





**2<sup>nd</sup> : 1829-51**

Russia, Hungary, Germany,  
France, UK, USA and  
Canada.

**3<sup>rd</sup> : 1852-60**

Russia, Indonesia, China,  
Japan, Korea, Iraq and part  
of Middle-east, Iran and  
part of south Asia.

**4<sup>th</sup> : 1863-75**

Most of the Europe, part of  
Africa and Mecca.



5<sup>th</sup> Pandemic :  
1881-96

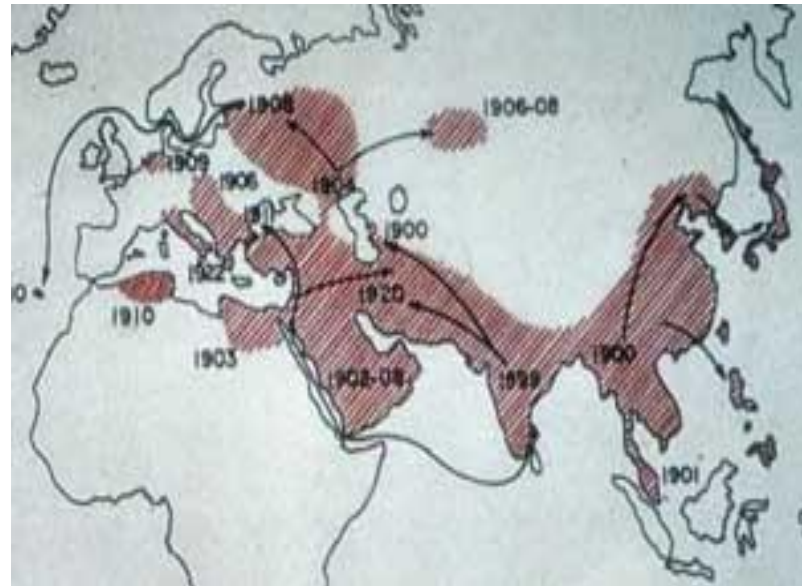
Russia and part  
of Europe  
including  
Germany, Spain,  
Persia, Japan.



6<sup>th</sup> Pandemic :  
1899-1923

Philippines and  
part of South-  
east Asia, Saudi  
Arab.

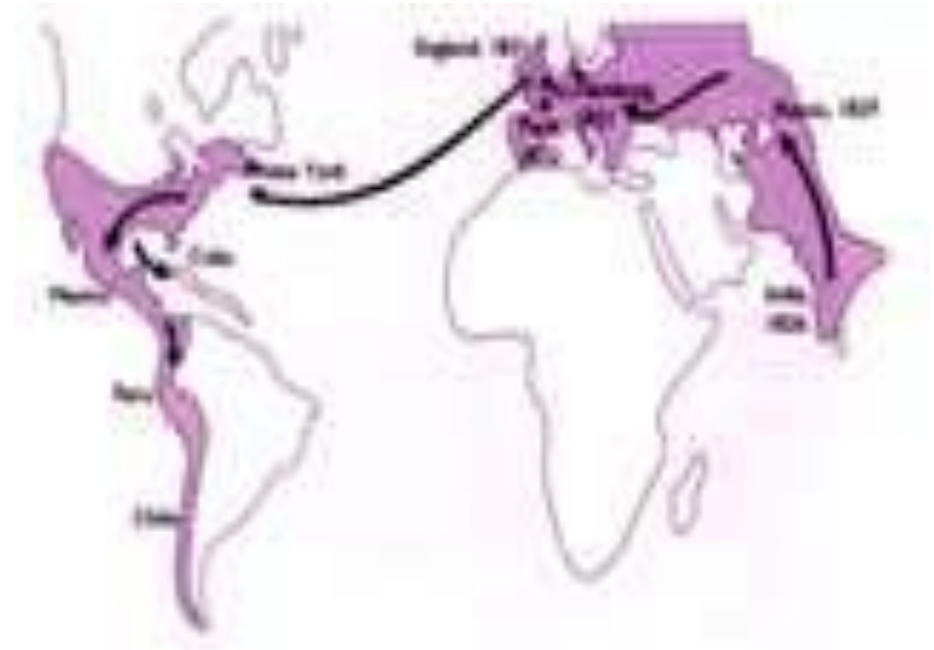
In 1907 hajj ,  
20000 people died  
of Cholera.



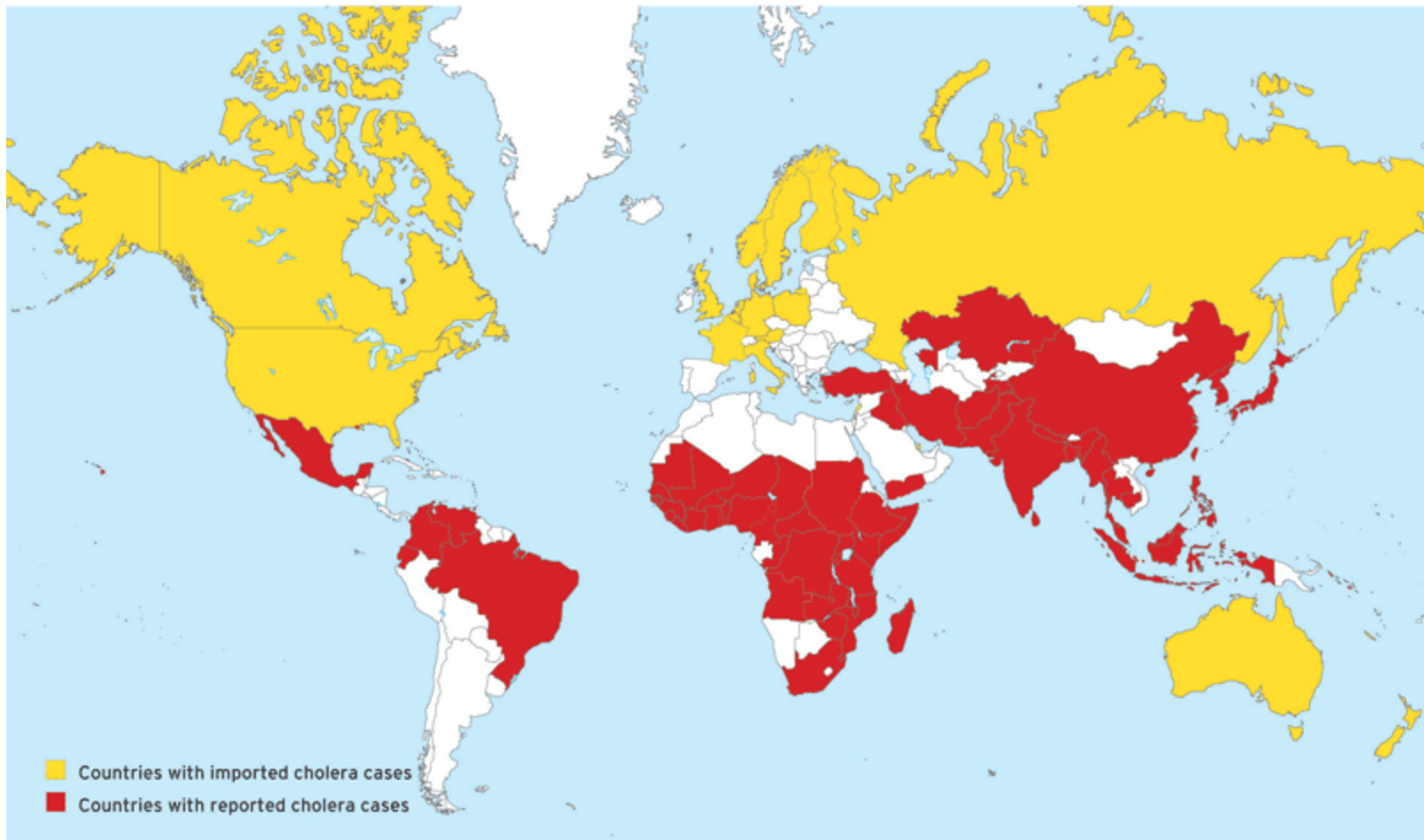
## 7<sup>th</sup> Pandemic: 1961-1991

Indonesia, Central  
Asia, Europe, Africa  
and South  
America.

In December, 1992  
Endemic attack in  
Bangladesh with a  
new strain & still  
continuing.....8<sup>th</sup>  
**Pandemic.**



# Global Epidemic Expansion



# Trend ????

- Dramatic & unexpected re-appearance: In Latin America as a continuation of seventh pandemic after a hiatus of more than a century, indicating a huge range of endemic expansion (Of the 36/28 were newly affected /16 were in Africa).
- Unprecedented appearance of completely new strain.

*Ref: Ramamurthy T, Garg S, Sharma R et,al. Lancet 1993; 341:703–4.*

## What about Strain????

- The nature of the strains causing the **First Four** pandemics is unknown.
- **Fifth and Sixth** pandemics: Classical biotype of O1 strains.
- **Seventh**: El Tor biotype.
- **Eighth** : Non-O1 strain with Sero-group O139 Bengal.

*Ref: Ramamurthy T, Garg S, Sharma R et,al. Lancet 1993; 341:703–4.*

## Cont.....

When the Latin American clone of *V. cholerae* O1 was compared with three other known global clones—the seventh pandemic clone, the Mexican Gulf coast clone, and the Australian clone—the multi-locus enzyme electrophoresis (MLEE) pattern of the Latin American clone was distinct from that of previously known clones of *V. cholerae*.

*Ref: Wachsmuth IK, Evins GM, Fields PI, et al. J Infect Dis 1993; 167:621–26.*



## Cont.....

- The transient appearance and disappearance of more than six ribotypes of classical *vibrios*, at least five ribotypes of El Tor *vibrios*, and three different ribotypes of *V. cholerae* O139 during epidemics between 1961 and 1996 in Bangladesh.
- Genetic diversity was also found among clinical and environmental isolates during and between epidemics over the past 20 years.

*Ref: Faruque SM, Ahmed KM, Siddique AK, Zaman K, Alim ARMA, Albert MJ. J Clin Microbiol 1997; 35: 2299–2306.*

*Ref: Jiang SC, Matte M, Matte G, Huq A, Colwell RR. Appl Environ Microbiol 2000; 66(1):148-53.*

- All these studies indicated that there had been a **continual emergence of new clones** of toxigenic *V. cholerae* replacing the existing clones.
- **Frequent serological switching** is another problem.

What are the factors causing this shifting?

Why the range of areas of endemism is expanding?



# Relation with Global warming

- Climatologists predict a 1.4 to 5.8°C rise in mean temperatures and 1 mm/year sea level rise over the next 100 years.
- *V.Cholerae* thrive best in 15‰ salinity, 30 °C water temperature, and pH 8.5.
- CTX and TCP : Virulence factor.

*Ref: Huq A, West PA, Small EB, Huq MI, Colwell RR. Appl Environ. Microbial 1984 ;48:420–24.*

## Cont....

- The entire CTX element constituted the genome of a filamentous bacteriophage (CTX $\phi$ ).
- CTX $\phi$  has lysogenic or self replicating element which can act under favorable environment.
- CTX $\phi$  confers increased evolutionary fitness to its host and hence to its own nucleic acids.

*Ref: Lipp EK, Huq A, Colwell RR. Clin Microbial Rev 2002; 15:757-70.*

## Cont....

- It was found that induction of CTX $\phi$  lysogens is probably controlled by precise environmental signals such as optimum temperature, sunlight, and osmotic conditions. Serological switching may also happen by Transduction which is a process by which DNA is transferred from one bacteria to another by a bacteriophage.

*Ref: Lipp EK, Huq A, Colwell1 RR. Clin Microbial Rev 2002; 15:757-70.*

Cont.....

Exposure to sunlight is another key factor in the induction of CTX prophage from the host and subsequent propagation of the phage particle which is causing the continual emergence of new strains of toxigenic *V. cholera* and their selective enrichment during cholera outbreaks.

*Ref: Faruque SM, Asadulghani, Rahman MM, Waldor MK, Sack DA. Infect Immun 2000; 68:4795-4801.*

## Cont....

- Scientists concluded that Sero-conversion from non-O1 to O1 occurred earliest (within 5 days) at a salinity of ~10‰ and temperatures near 35°C.
- Increased environmental water temperatures decrease multiplication time and fasten growth along with increase detection rate of *V.Cholera*.

*Ref: Pascual M, Chaves LF, Cash B, Rod X, Yunus M. Clim Res 2008; 36: 131–40.*



## Cont....

- Sunlight, temperature, and nutrients all influence the growth of phytoplankton and aquatic plants, which in turn raise the pH of the surrounding water that favors the growth of *V.Cholerae*.
- Availability of Chitin will increase which in addition to providing a food source for *vibrios* and enhancing survival under starvation conditions, also offers protection to *V. cholerae* at low temperatures and under acidic conditions such as the human gut.

Ref: Lipp EK, Huq A, Colwell1 RR. Clin Microbial Rev 2002; 15:757-70.

## Cont...

- Extreme events like heavy rainfall, flood and draught etc, increase sea surface height, increase pH, presence of iron and other river waste, all favors the pathogen.
- Demographic Migration: Poor sanitary conditions, Overcrowding, increase poverty, lack of proper sewage disposal system and improper water supply, all provide happy hunting ground for this organism.

# Alarming Feature

- Presence of virulence associated genes like *ctxA*, *tcpA*, *toxR* and the repetitive sequence (RS element) in environmental or non toxigenic strain (non 01 and non-0139).
- Scientists suggested that a new toxigenic strain will evolve soon from these strains in favorable condition.

*Ref: Ghosha C, Nandya RK, Dasguptaa SK, Nairb GB, Hallc RH, Ghosea  
ACMicrobial Pathogenesis 1997; 22: 199–208.*

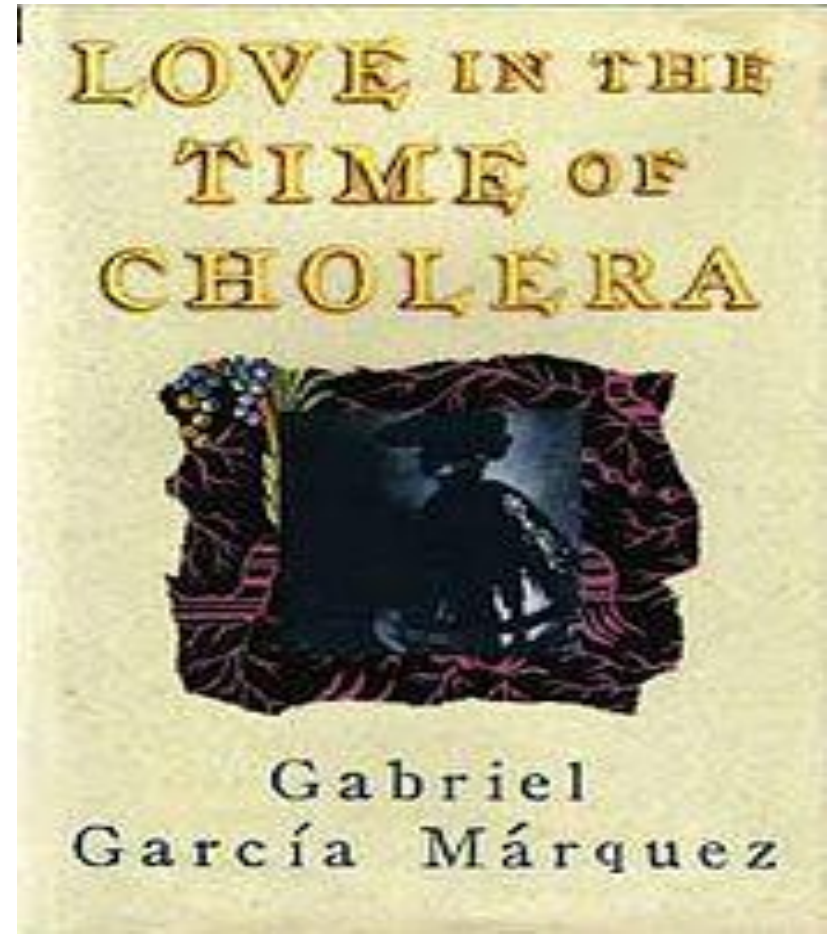
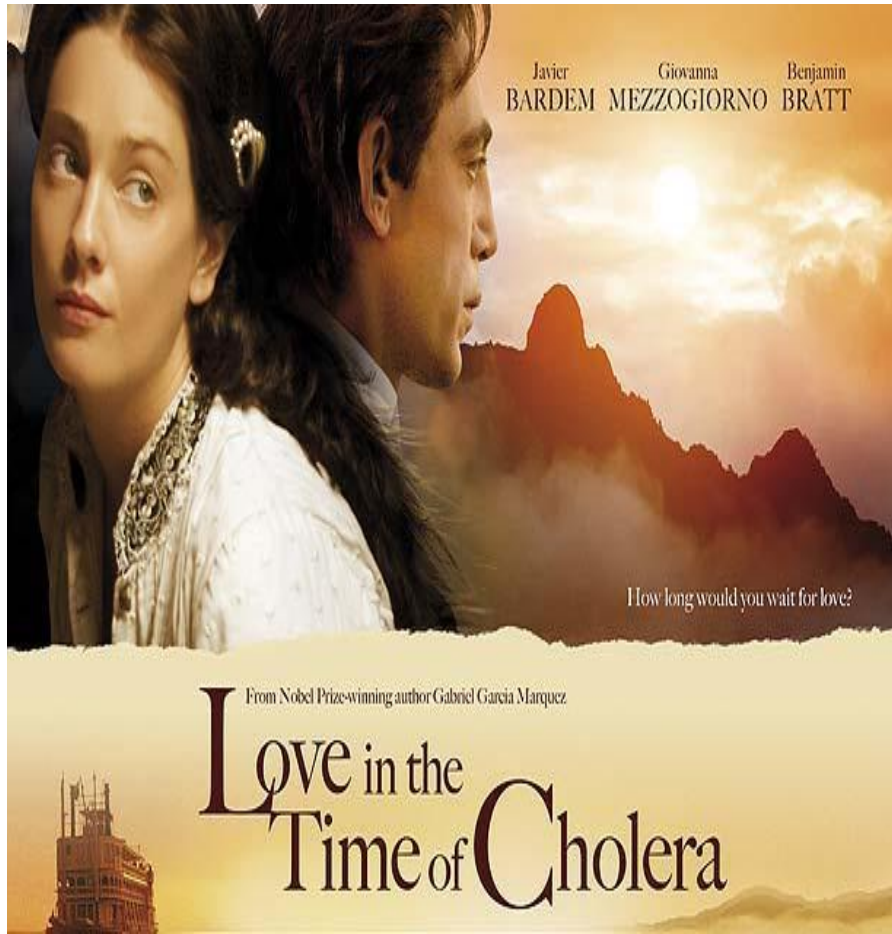
Although the doomsday scenario in the thriller film 'The Day After Tomorrow' may be far from reality, it is clear that climate is changing, challenging the health sector and the whole of human society.



# Conclusion

- With the emergence of anomalous climate no country will be spared from cholera in future.
- An interdisciplinary analysis and integrated prevention planning are mandatory.
- The development of an effective early warning system based on climate data will help us to reduce the burden of disease.

# Don't Miss It



Thanks