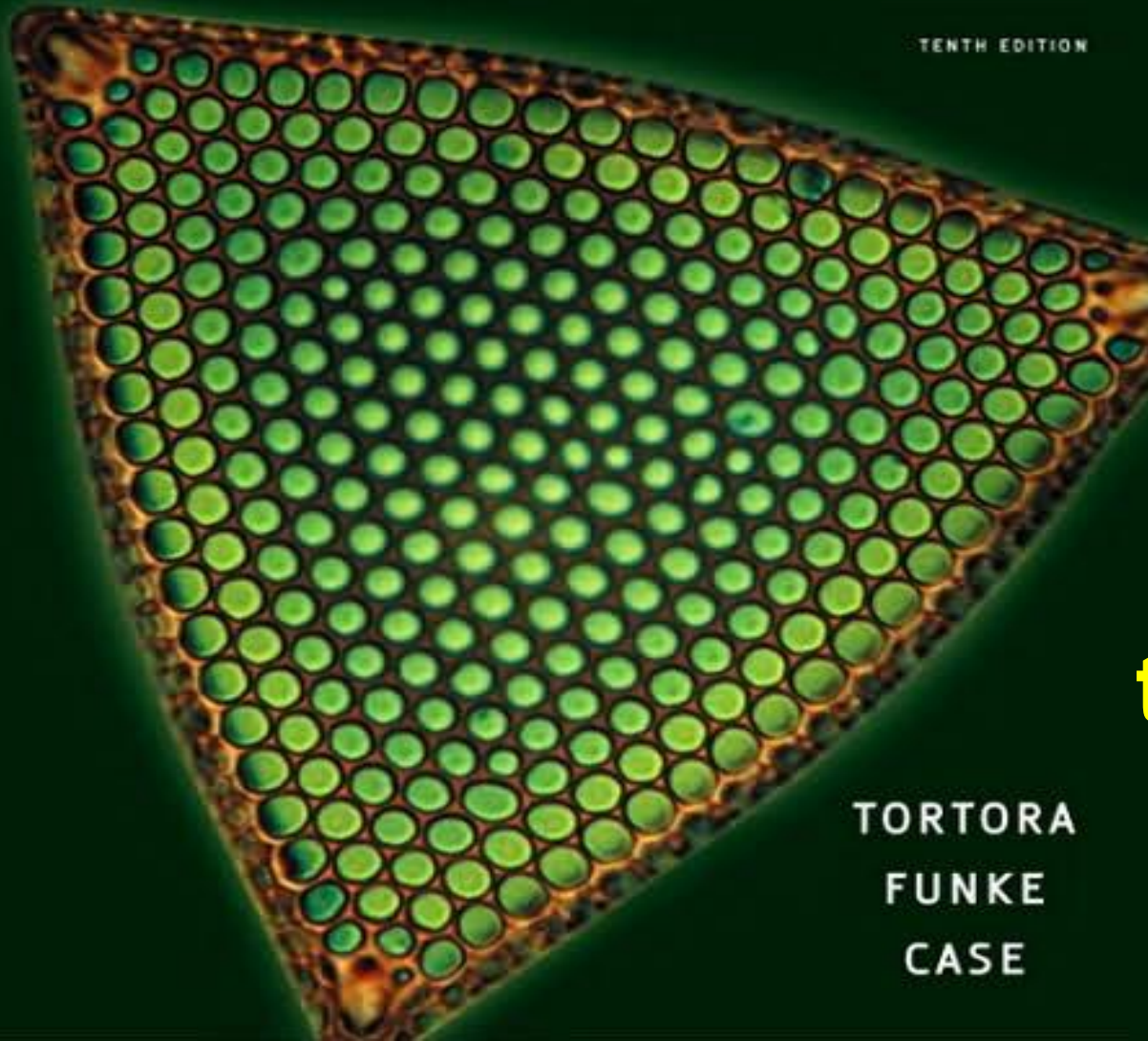


# MICROBIOLOGY

AN INTRODUCTION

TENTH EDITION



TORTORA  
FUNKE  
CASE

## Ch 22

## Microbial Diseases of the Nervous System

# Student Learning Outcomes

Review anatomy of CNS, PNS, meninges, BBB

Differentiate meningitis from encephalitis including diagnosis and treatment.

Discuss mode of transmission, etiology, disease symptoms, treatment, and preventive measures of

- Bacterial meningitis caused by *H. influenzae*, *S. pneumoniae*, *N. meningitidis*, and *L. monocytogenes*
- Tetanus
- Botulism
- Leprosy
- Rabies
- Arboviral encephalitis,
- Cryptococcosis.
- African trypanosomiasis
- Prion diseases

Compare and contrast the Salk and Sabin vaccines

# Anatomy and Physiology Review

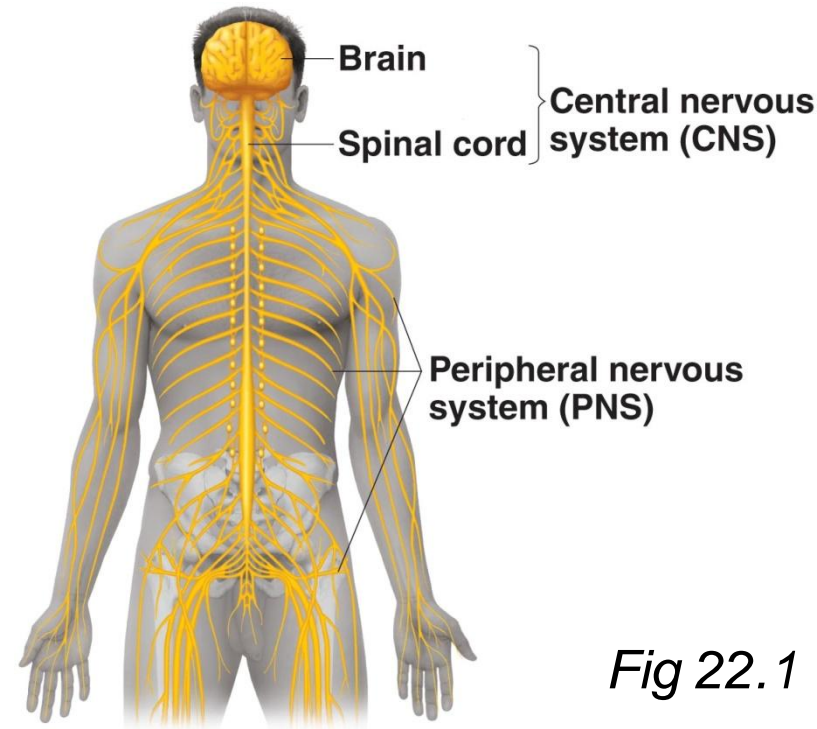
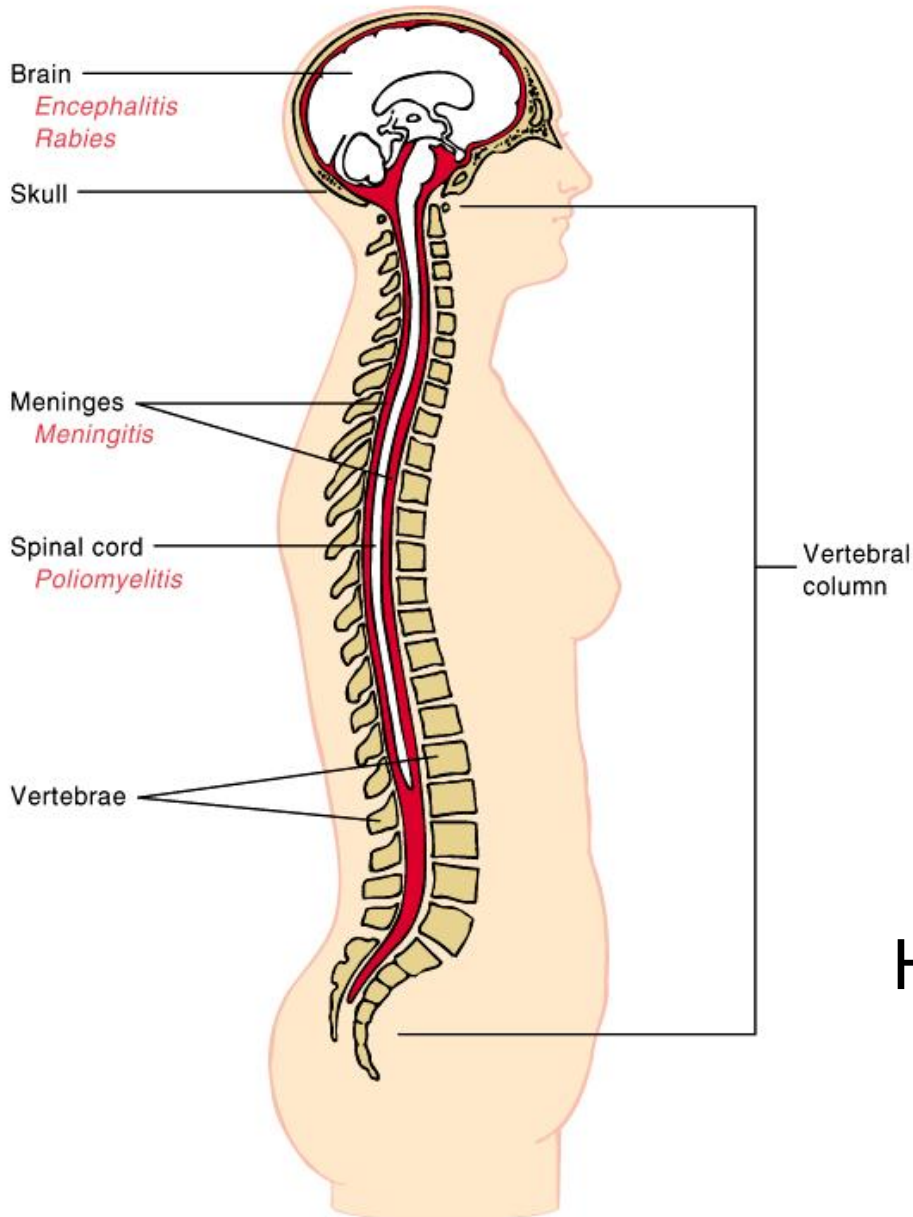


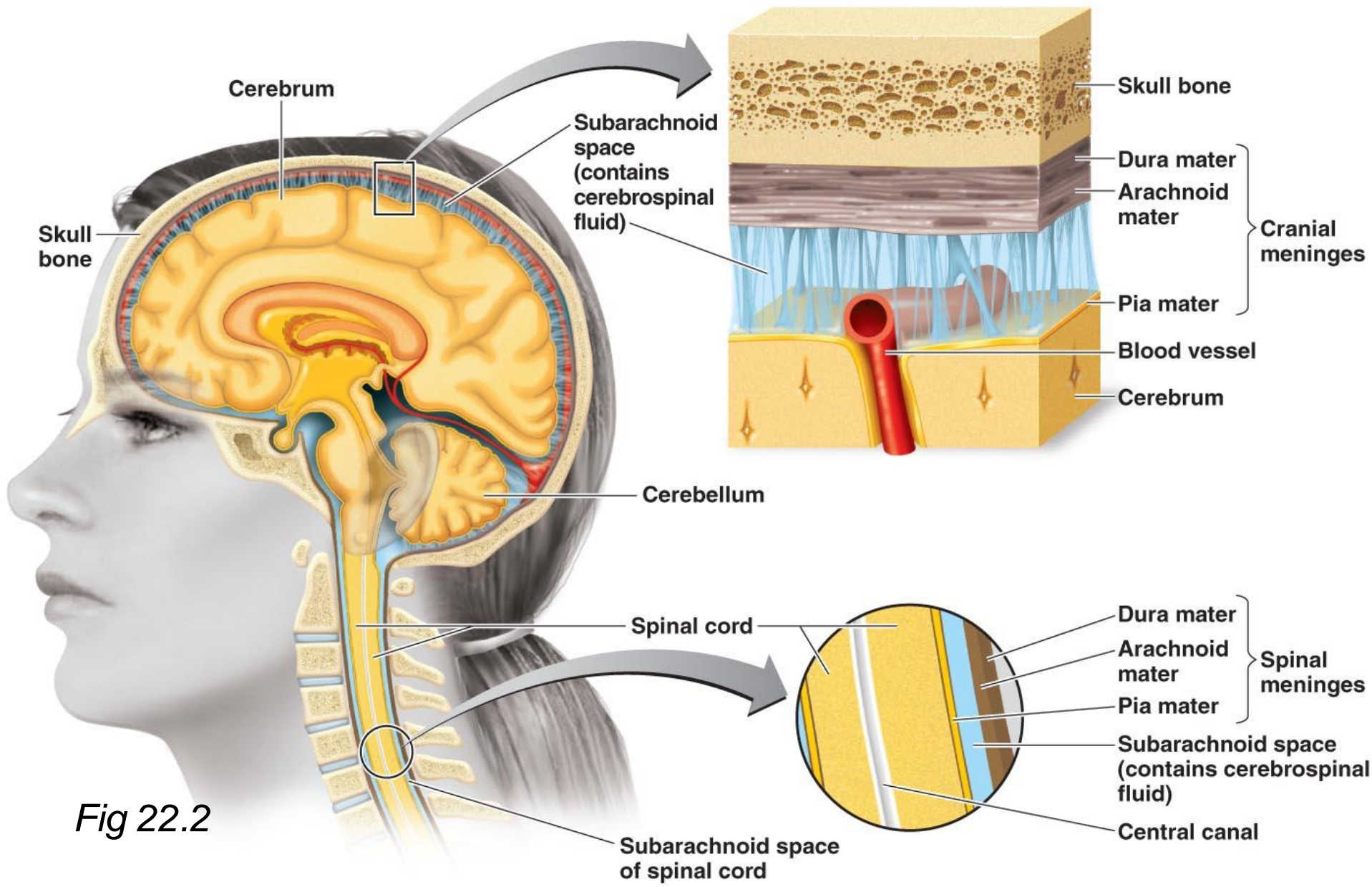
Fig 22.1

How do microbes enter the CNS ?

Fig 22.2



# The Meninges and Cerebrospinal Fluid



# Bacterial Diseases of the CNS

Bacteria can grow in CSF in subarachnoid space.

The BBB prevents passage of some materials (such as antimicrobial drugs) into CNS.

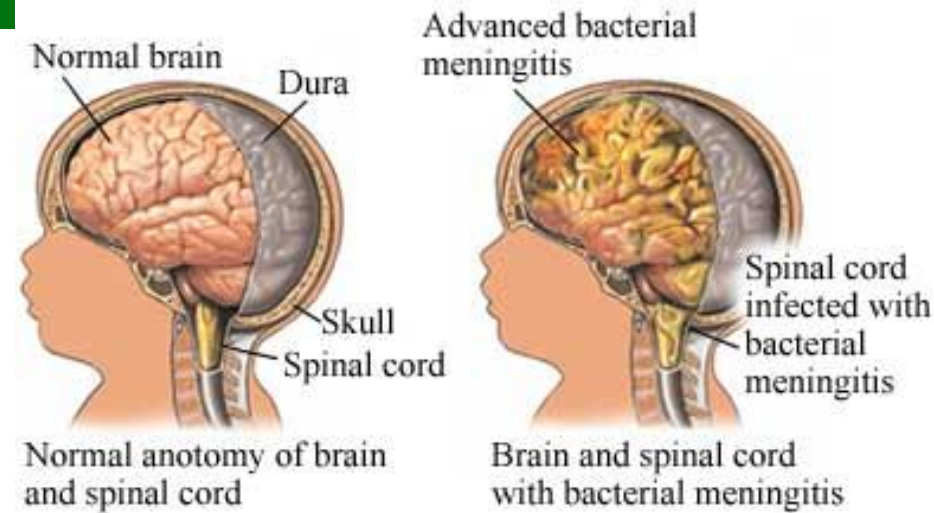
Meningitis vs. encephalitis

Meningitis can be caused by viruses, bacteria, fungi, and protozoa.

**BACTERIAL MENINGITIS:** Much more serious than viral. Can cause severe disease resulting in brain damage and death.

# Bacterial Meningitis

- The three major causes:
  - *Haemophilus influenzae*
  - *Neisseria meningitidis*
  - *S. pneumoniae*
- Nearly 50 species of opportunistic bacteria can cause meningitis (*L. monocytogenes*, *S. pyogenes*, *S. aureus*)
- Symptoms: Fever, headache, stiff neck, followed by nausea and vomiting ⇒ may progress to convulsions, coma, shock, and death
- Diagnosis by Gram stain or latex agglutination of CSF
- Cephalosporins before identification of pathogen!



# Epidemiology of Bacterial Meningitis

Not very contagious → spreads by **direct close contact** with discharges from nose/throat of infected person.

*Vaccines:*

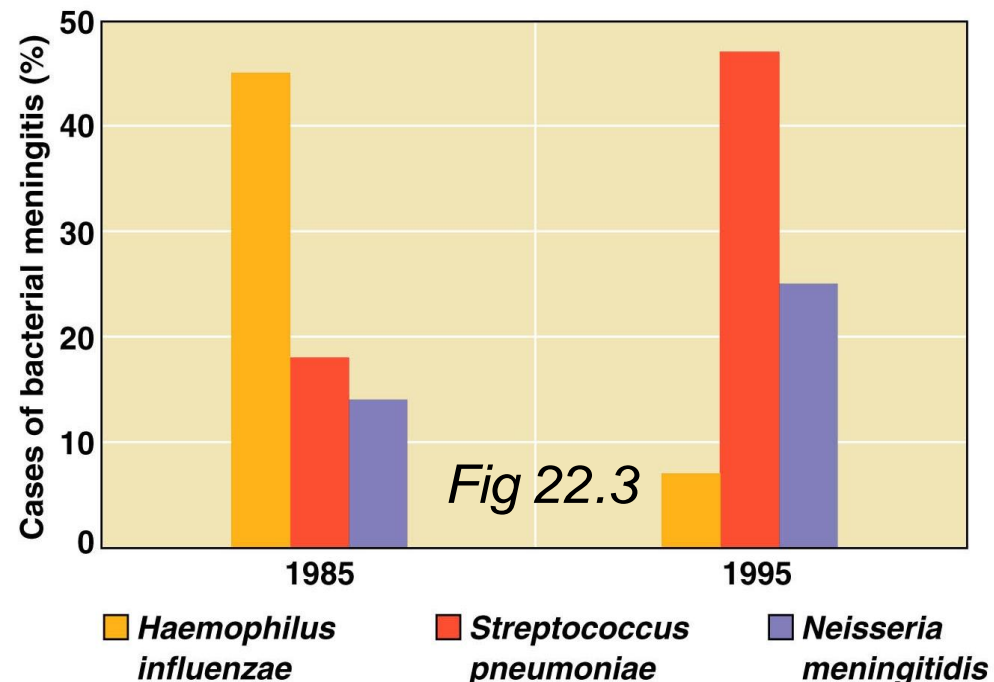
1988: **Hib**

2000: **PCV7**

(Prennar®) new for use in children < 2 y old.

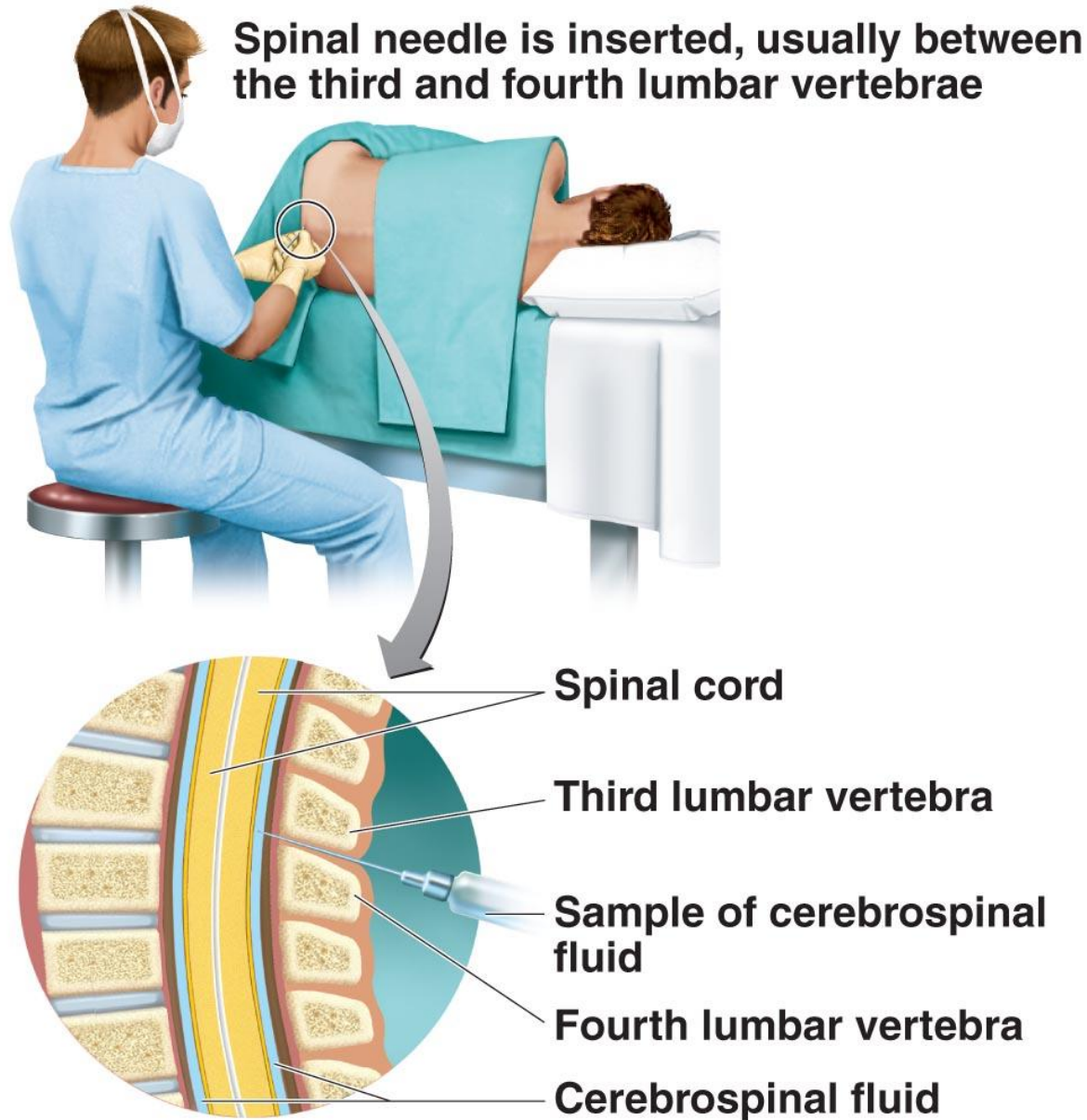
2005: **MCV4**

(MenactraT®) vaccine of choice for 11 to 55 y old (old vaccine since 1982)





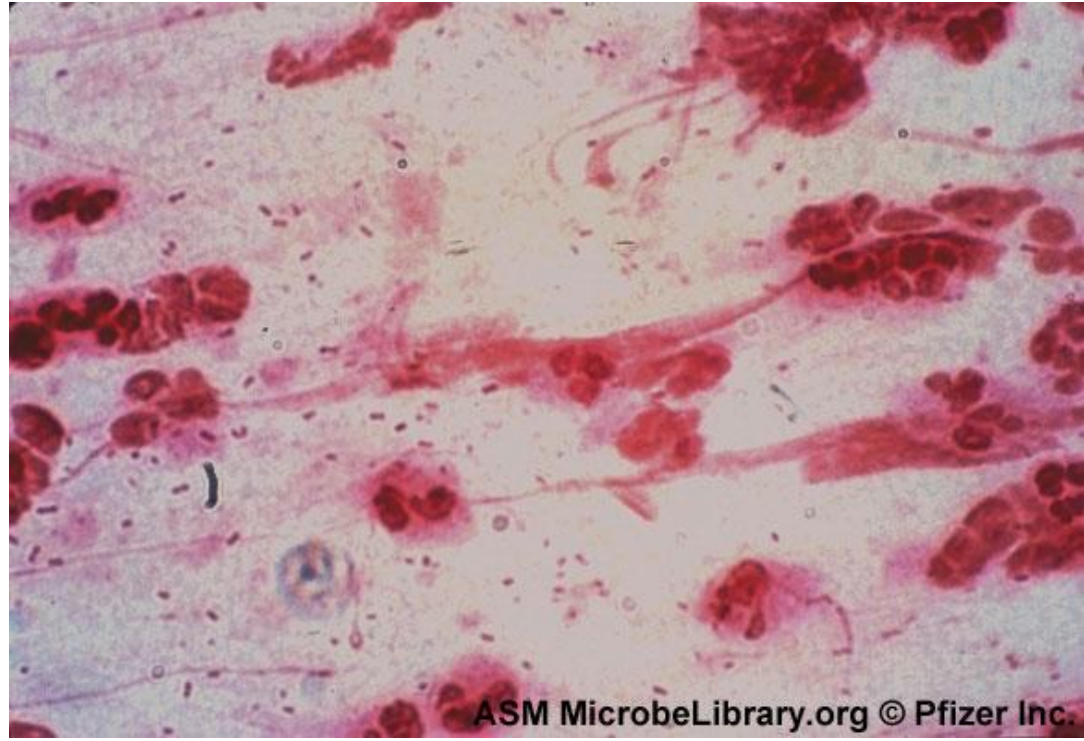
# Spinal Tap (Lumbar Puncture)





# *Haemophilus influenzae* Meningitis (Hib)

- Gram-negative, pleomorphic coccobacilli, capsule
- Common part of normal throat microbiota



- Fastidious → needs factors in blood (genus name!). Species name is misnomer.
- Mostly in children under age 4 (especially around 6 month of age. Why?)
- Also causes pneumonia, otitis media, epiglottitis

# ***Neisseria* Meningitis: Meningococcal Meningitis**

Gram-neg cocci,  
capsule

~ 10% of people are  
healthy naso-  
pharyngeal carriers

Begins as throat  
infection, typical rash → death may occur within a  
few hours of onset.

Continuing threat in day-care centers and schools.

Mostly in children < 2 y of age.

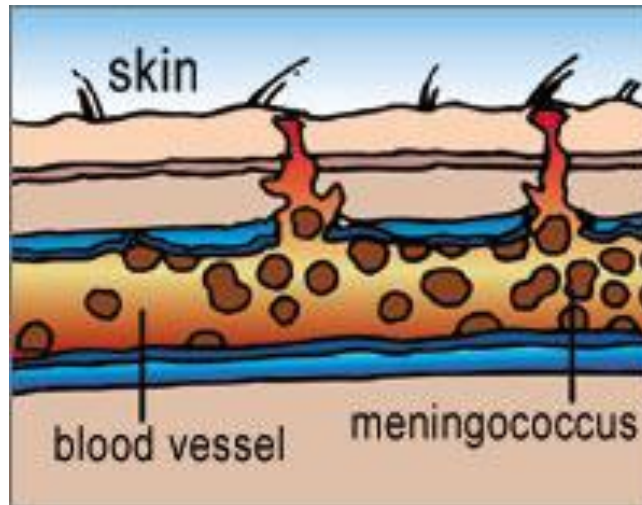
Sporadic outbreaks among young adults.

Vaccination recommended for college students



# Meningococcal Rash

About **half** the children or adults with meningococcal meningitis have rash that does not fade



Exotoxins  
damage blood  
vessel walls →  
blood leaks into  
skin

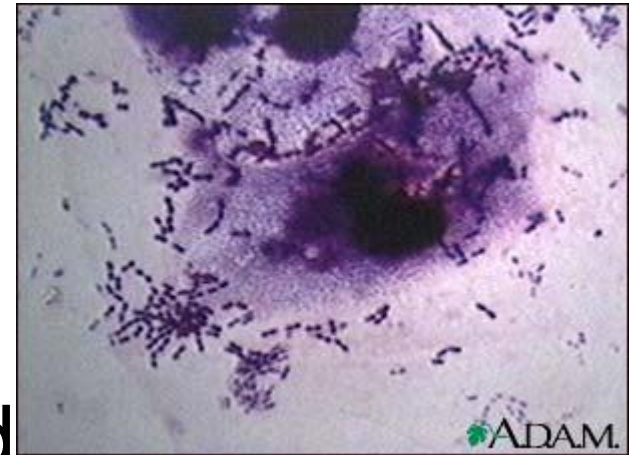


Glass test, or pressure test –  
septicaemic rash usually does not  
fade under pressure. (Not 100%  
reliable.)



# Pneumococcal Meningitis – *S. pneumoniae*

- Gram-positive diplococci
- Typically associated with pneumonia, but may cause pneumococcal meningitis and pneumococcal septicemia.
- 70% of people are healthy nasopharyngeal carriers
- Most common in children (1 month to 4 years)
- Mortality: 30% in children, 80% in elderly

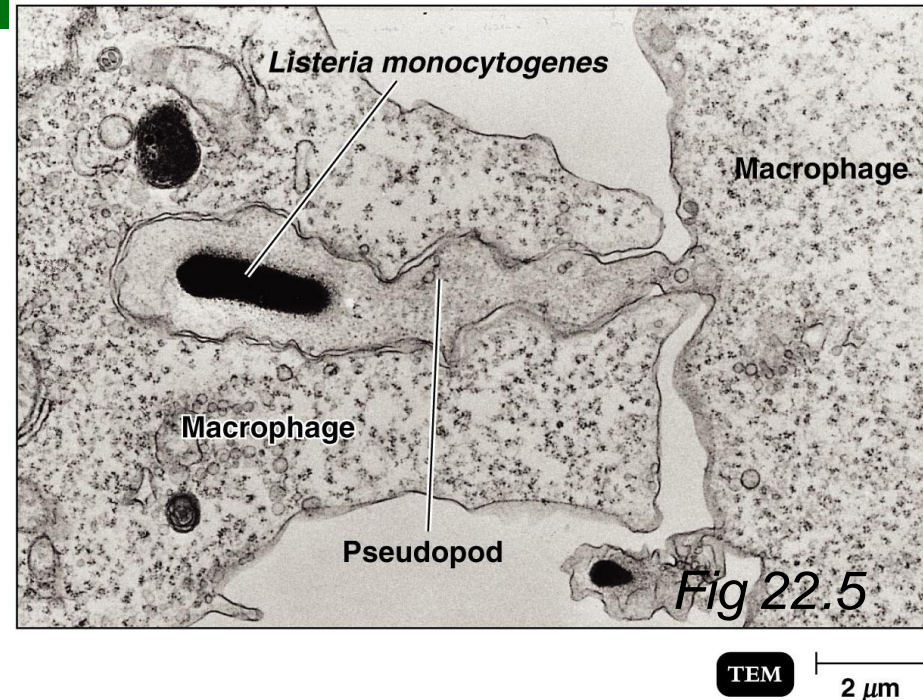




# Listeriosis

- *Listeria monocytogenes*

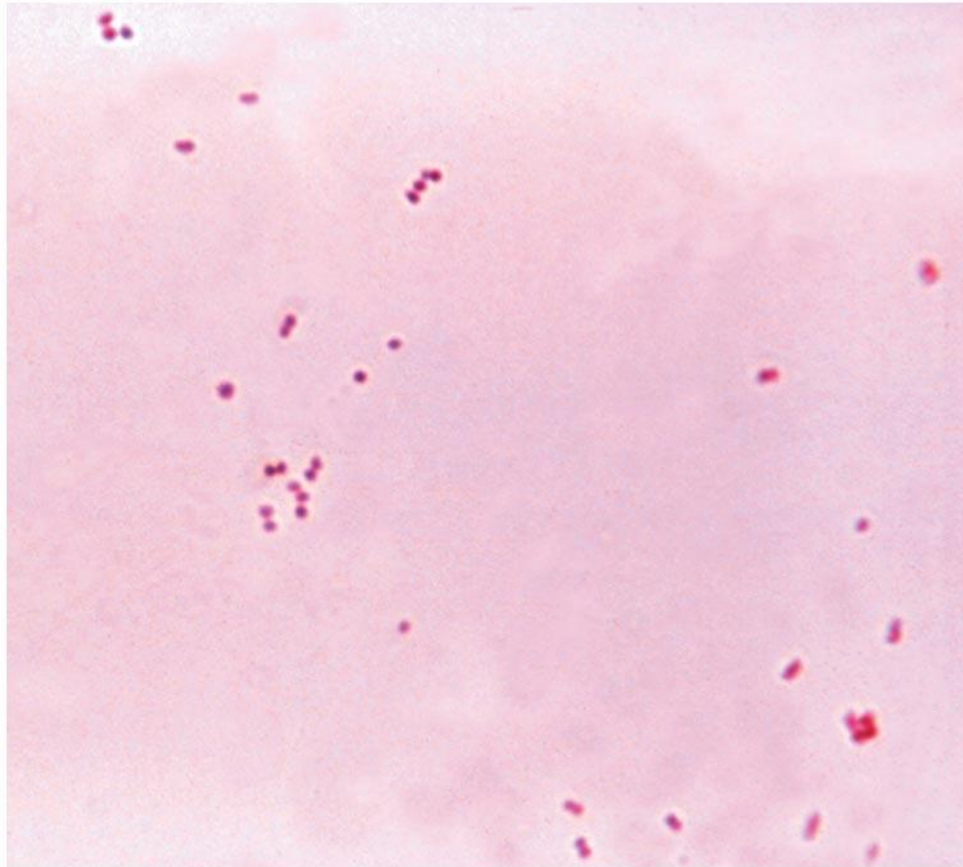
- Gram-positive
- Reproduce in phagocytes.



- Acquired by ingestion of contaminated food - psychrophil!
- May be asymptomatic in healthy adults.
- Causes meningitis in newborns, immunosuppressed, pregnant women, and cancer patients.
- Can cross placenta and cause spontaneous abortion and stillbirth

# Diseases in Focus:

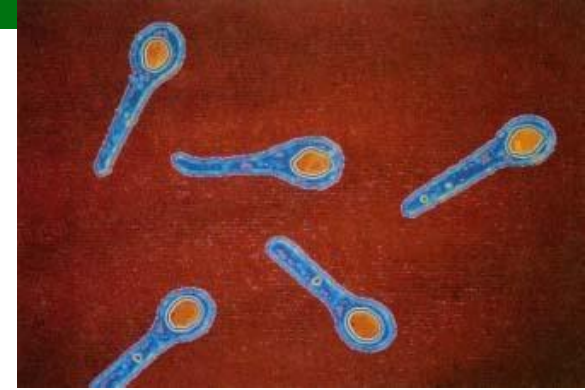
## Meningitis and Encephalitis



LM 6  $\mu$ m

- A worker in a day-care center in eastern North Dakota became ill with fever, rash, headache, and abdominal pain. The patient had a precipitous clinical decline and died on the first day of hospitalization. Diagnosis was confirmed by Gram staining of cerebrospinal fluid.
- Can you identify infections that could cause these symptoms?

# Tetanus (Lockjaw)

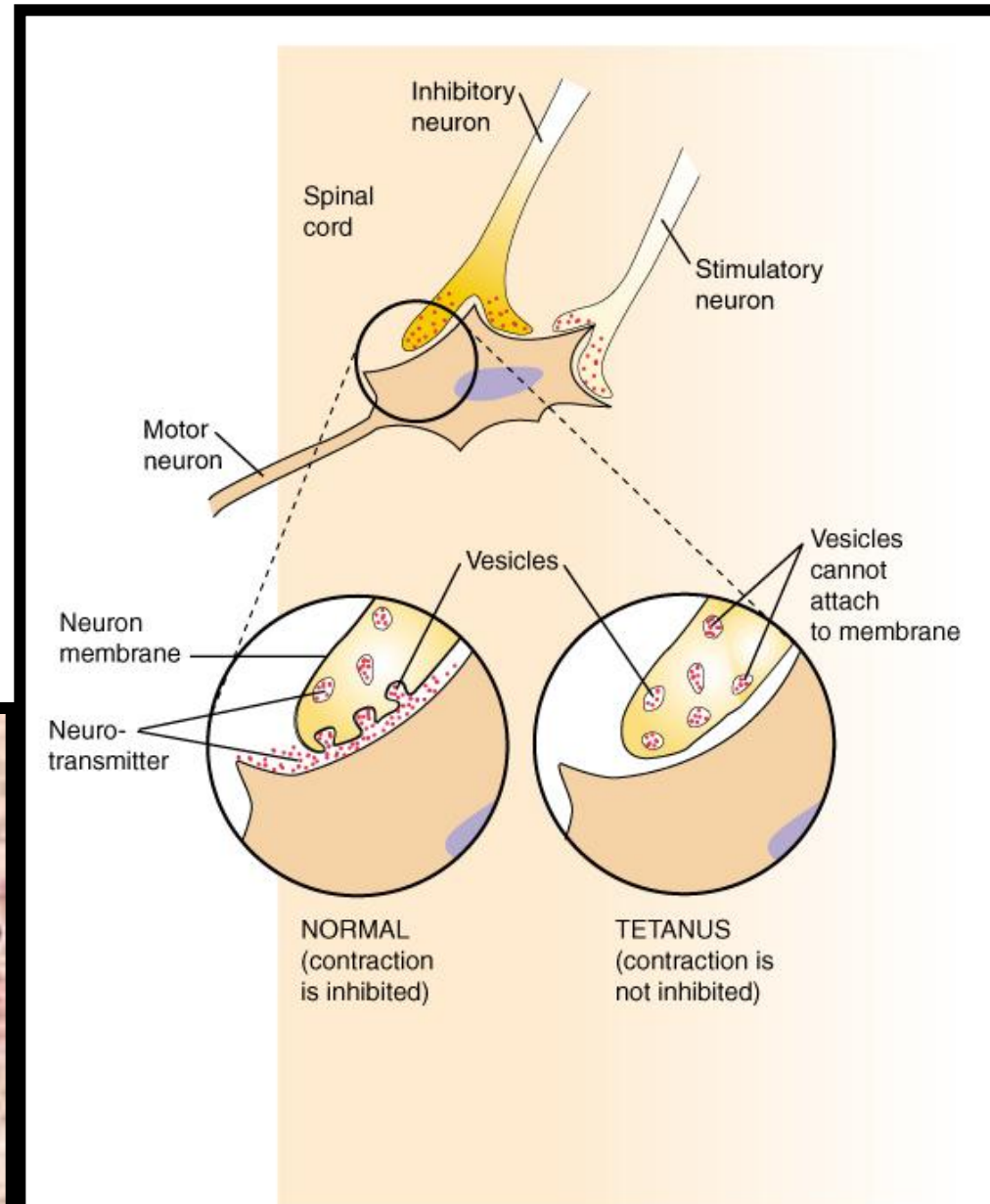


- *Clostridium tetani*
- Gram-positive, endospore-forming, obligate anaerobe
- Grows in deep wounds.
- Tetanospasmin (exotoxin / neurotoxin) released from dead cells blocks relaxation pathway in muscles. [Tetanospasmin action.](#)
- Prevention by vaccination with tetanus toxoid (DTaP) and booster (dT).
- Treatment with tetanus immune globulin.

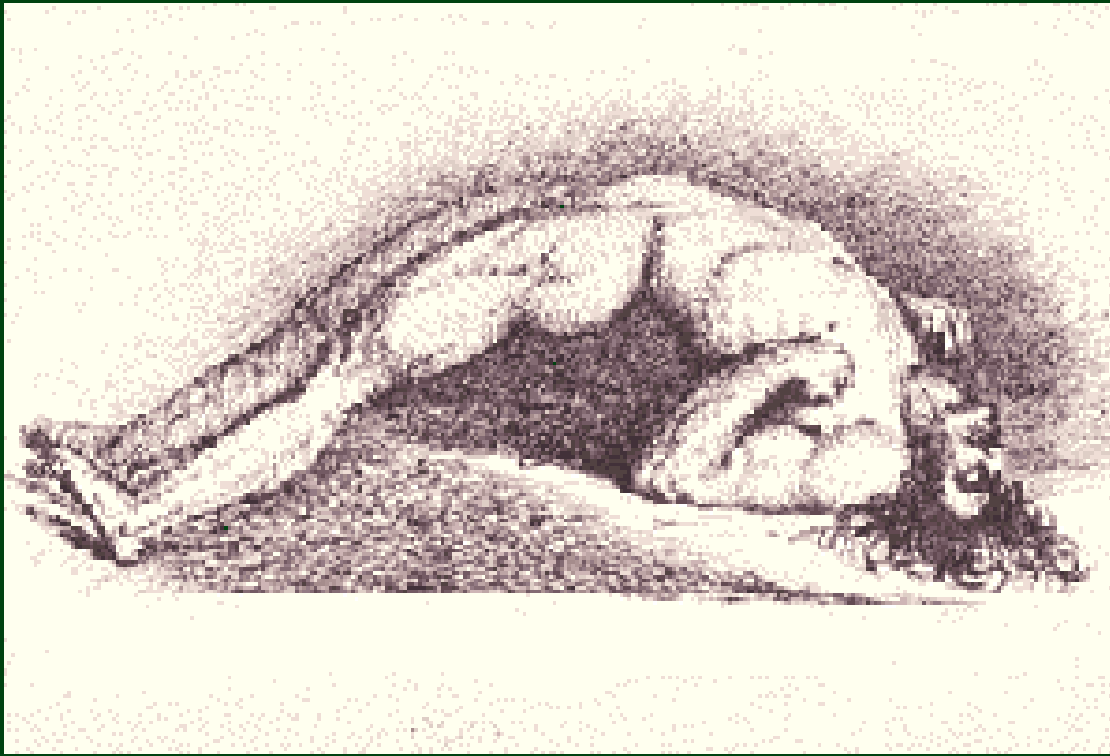
# Tetanus Action

**Blockage of inhibitory NT release in CNS (glycine and GABA – gamma-aminobutyric acid)**

**Result ?**





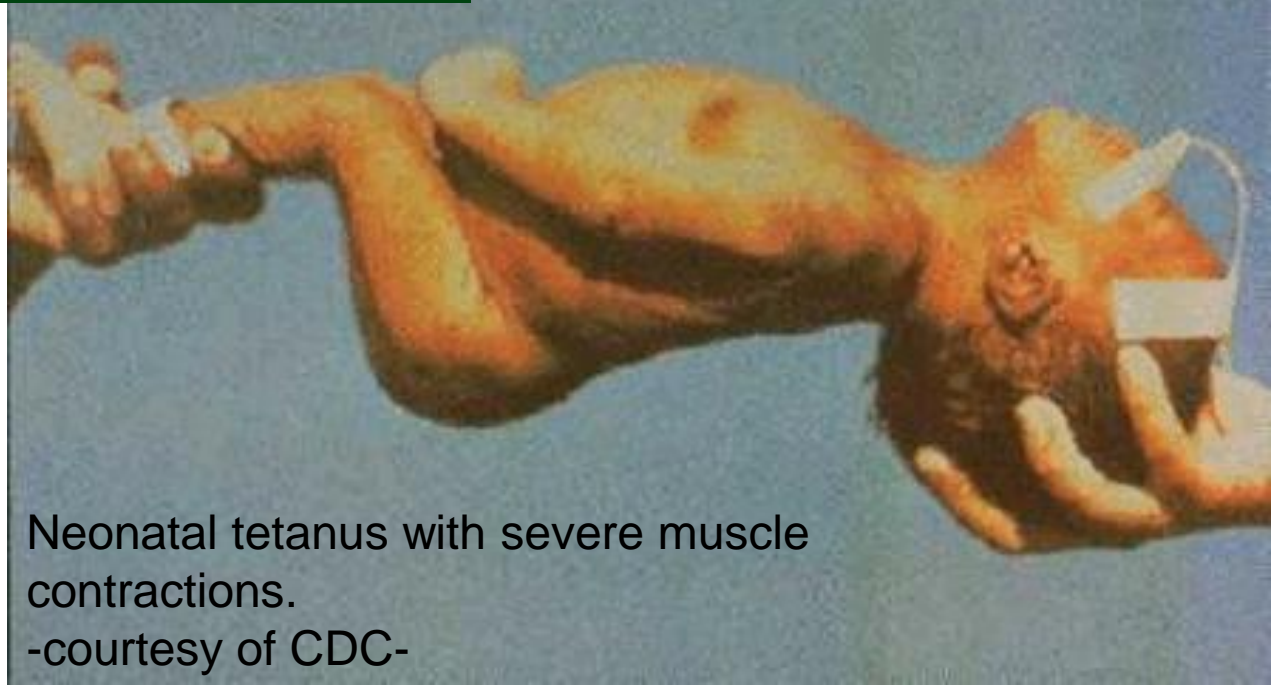


Why characteristic backward arc?

Characteristic condition:  
**Opisthotonos**

*90% fatality rate*

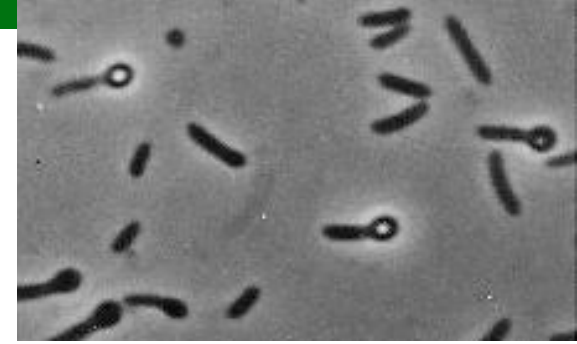
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Neonatal tetanus with severe muscle contractions.

-courtesy of CDC-

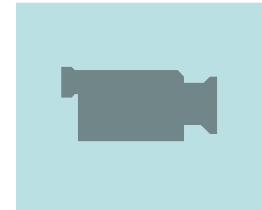
# Botulism



- *Clostridium botulinum*
- Gram-positive, endospore-forming, obligate anaerobe, ubiquitous in soil and H<sub>2</sub>O
- Intoxication (ingestion of botulinum toxin): 7 different Neurotoxins (exotoxins, A, B and E cause most human illness)
- Type A
  - 60-70% fatality
  - Found in CA, WA, CO, OR, NM.
- Type B
  - 25% fatality
  - Europe and eastern United States
- Type E
  - Found in marine and lake sediments

# Botulinum Toxin: Most Potent Toxin on Earth

- **Mechanism of action:** Irreversible inhibition of ACh release from motor neuron  
→ \_\_\_\_\_
- Treatment: ?
- Prevention
  - Proper canning
  - Nitrites prevent endospore germination in sausages



# 3 Forms of Botulism

1. **Foodborne botulism:** Intoxication not infection! Endospores survive improper canning procedures.
2. **Wound botulism:** ~ symptoms as above, start ~ 4 days after wound infection
3. **Infant botulism:** due to ingestion of endospores  $\Rightarrow$  *C. botulinum* growing in intestines.

In animals: limberneck





# Botulinum Toxin: Killer and Healer

**Botox<sup>®</sup>** (Botulinum toxin type A)

Medical uses: blepharospasms,  
strabismus, torticollis . . . . . etc.

Under investigation: migraine  
headaches, hyperhidrosis

Cosmetic purposes



# Spastic torticollis: neck in a twisted or bent position



Blepharospasm is a focal dystonia characterized by increased blinking and involuntary closing of the eyes.

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# Leprosy or Hansen's Disease



- *Mycobacterium leprae* (acid-fast rod)
- Grows best at 30° C  $\Rightarrow$  cooler body regions (peripheral nerves and skin cells)
- Transmission requires prolonged contact with an infected person. Mostly via nasal secretions of lepromatous leprosy patients

Incubation time: Months to 10 years

*Two forms depending on immune response*

1. **Tuberculoid** (neural) form: Loss of sensation in skin areas; positive lepromin test
2. **Lepromatous** (progressive) form: in case of cell mediated IS failure) Disfiguring nodules over body; negative lepromin test





Tuberculoid leprosy in a 24-year-old Samoan woman with seven-month history of expanding plaque on cheek. Note the thickened accessory nerve coursing over the sternomastoid muscle.



Patient with active, neglected nodulolobular leprosy. With treatment, all nodules could be reversed.

©WHO/TDR/McDougall



Azadegan Clinic,  
Teheran: The foot of  
a woman that has  
been grossly  
disfigured through  
leprosy infection. ©  
World Health  
Organization/TDR/C  
rump



Deformity due to nerve damage with its consequent ulcers and  
resorption of bone. Such deformities can be worsened by careless  
use of the hands. © WHO/TDR

# Viral Diseases of the Nervous System

## **VIRAL MENINGITIS:**

Usually mild. Clears up within a week or two without specific treatment. Also called aseptic meningitis.

**Poliomyelitis**

**Rabies**

**Viral meningitis**

**Viral encephalitis**



# Poliomyelitis – Infantile Paralysis

Poliovirus (Enteroviruses of picornaviridae)

Transmitted by ingestion. 3 strains of polio virus (1,2,3)

90% of cases asymptomatic

Initial symptoms: Sore throat and nausea

Viremia may occur; if persistent, virus can enter the CNS; Selective destruction of motor neurons and paralysis occurs in <1% of cases.

Prevention: vaccination (enhanced IPV)

Post-polio syndrome 30 y later: Crippling deterioration of originally affected muscles due to aging process of “replacement neurons”.

# Worldwide Annual Incidence of Poliomyelitis

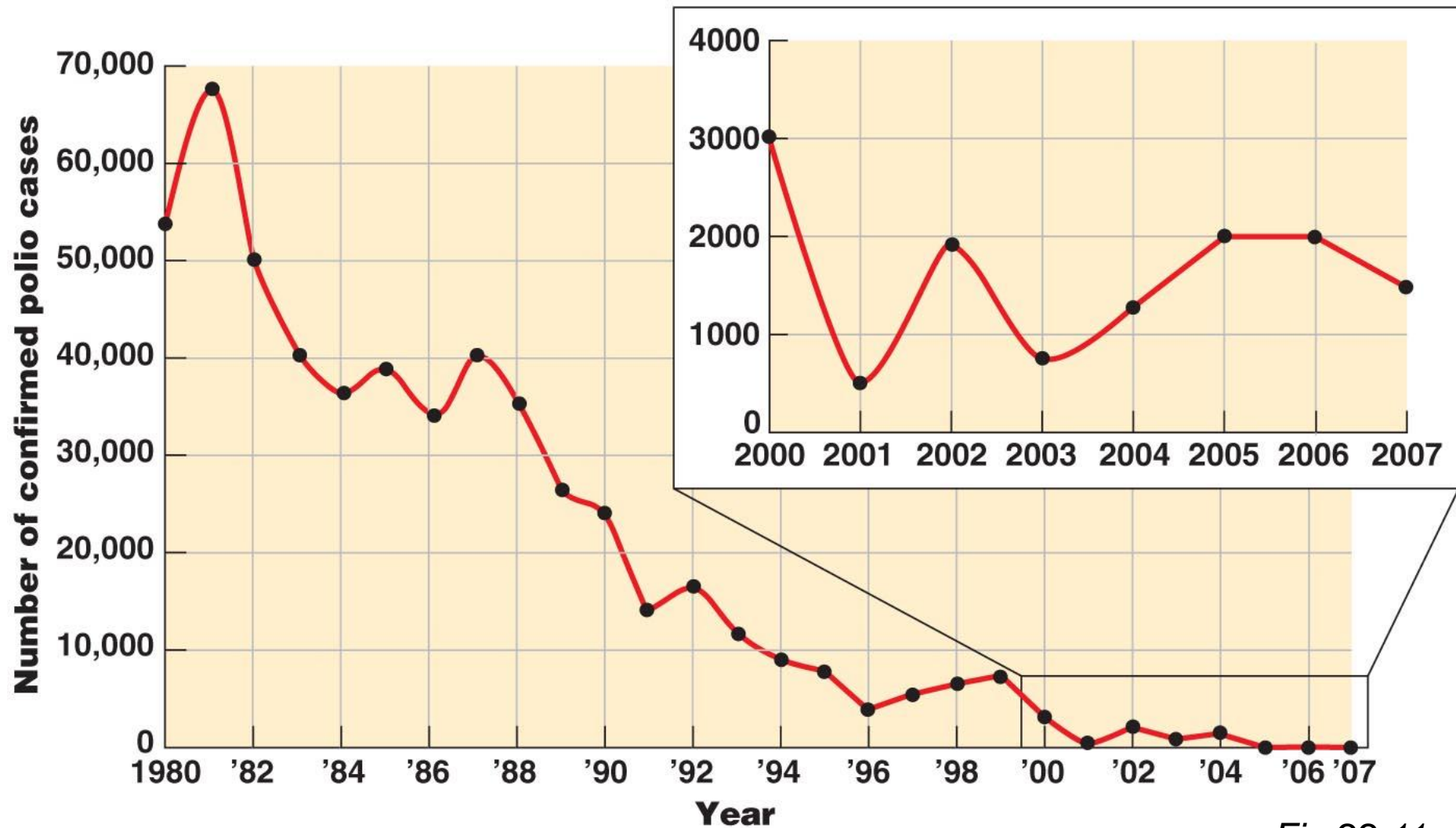


Fig 22.11

# Prevention and Treatment

FDR, *President* from  
1932 to 1945



- 1955: Salk vaccine (Inactivated – IPV)
- 1961: Sabine vaccine (Live, attenuated, oral – OPV). *Advantages ?*
- OPV has caused all the polio cases in the US between 1980 and 1999
- 2000: CDC recommends new IPV (E\_IPV) for routine immunization

# Rabies Virus (of *Rhabdoviridae*)

- **Zoonosis** – Transmission from saliva of rabid animal
- Virus multiplies in skeletal muscles, then retrograde axonal transport to CNS (encephalitis), then back out to periphery (salivary glands etc.)
- Initial symptoms may include muscle spasms of the mouth and pharynx and hydrophobia.
- **Furious rabies:** Animals restless then highly excitable.
- **Paralytic rabies:** Animals unaware of surroundings.





# Pathology of Rabies Infection

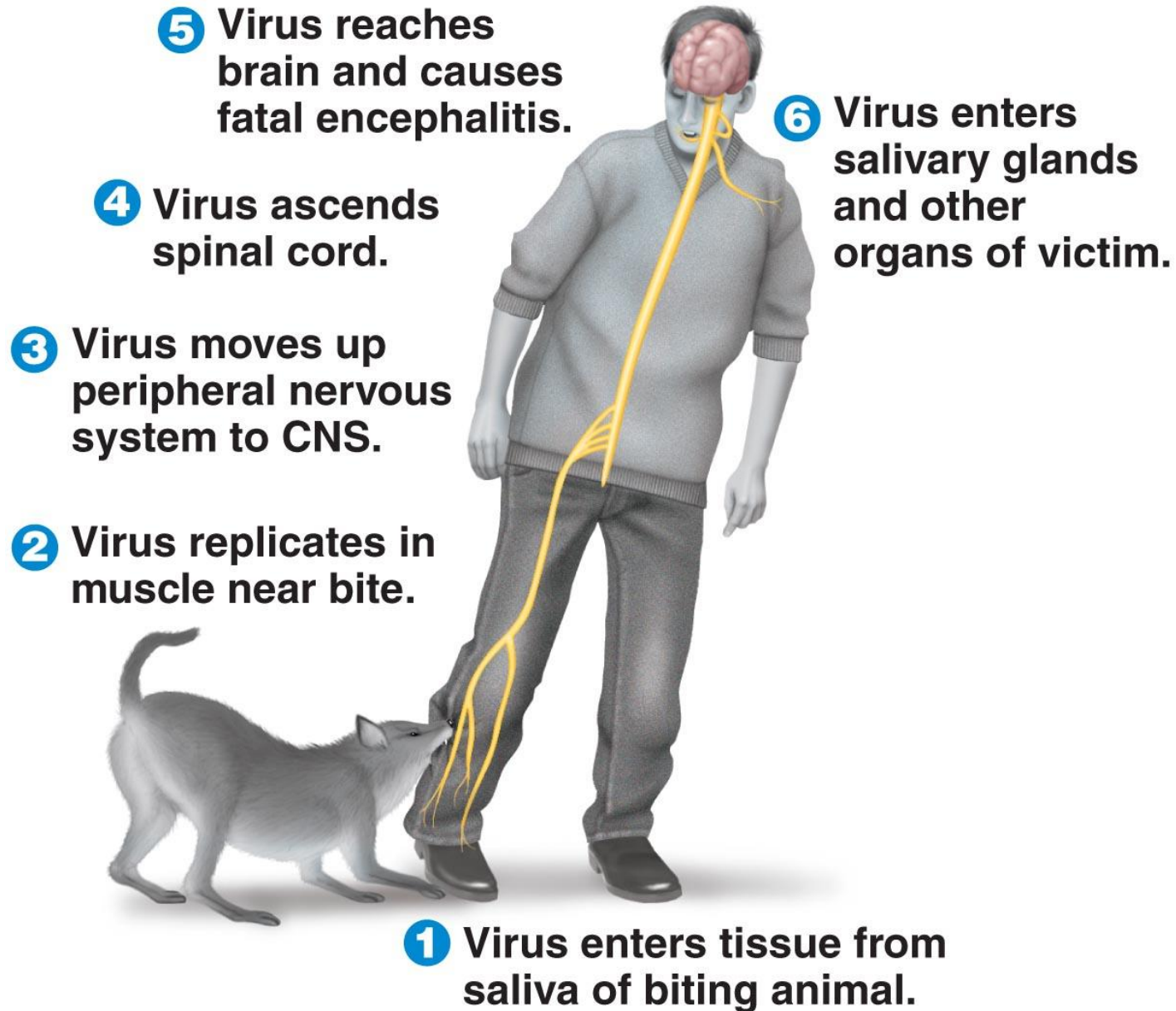


Fig 22.12

# Treatment and Prevention

- Highly fatal – only handful of people survived
- **Preexposure prophylaxis:** Human diploid cells vaccine (HDCV) applied *i.m.*
- **Postexposure prophylaxis (PEP):**
  - Vaccine (HDCV, applied *i.m.* on days 0, 3, 7, 14, and 28)
  - Human rabies immune globulin (RIG)
- Rodents and rabbits seldom get rabies. Dogs, cats, cattle, skunks, raccoons, bats, etc. do ⇒ Vaccination of pets! If necessary vaccination of wild populations

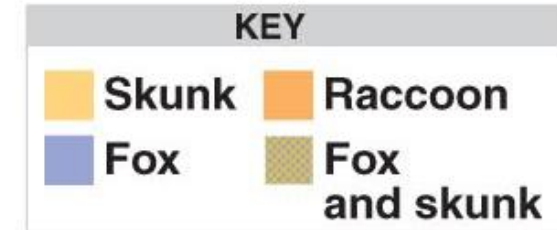
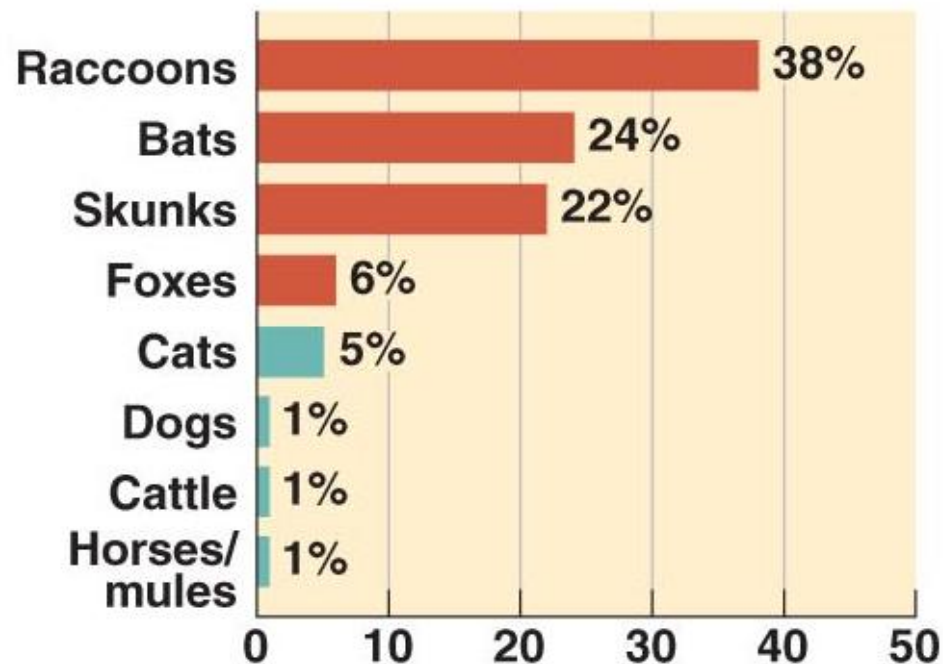
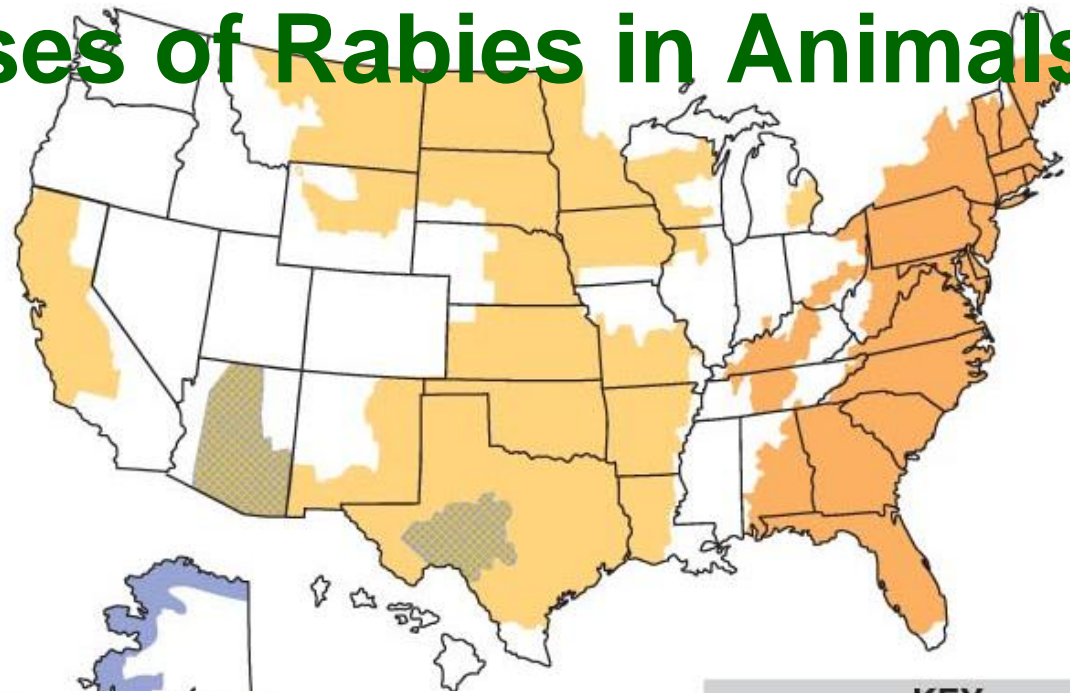
genetically engineered,  
vaccinia-rabies  
glycoprotein (V-RG) virus  
has proven to be orally  
effective in raccoons.

ORV



# Reported Cases of Rabies in Animals

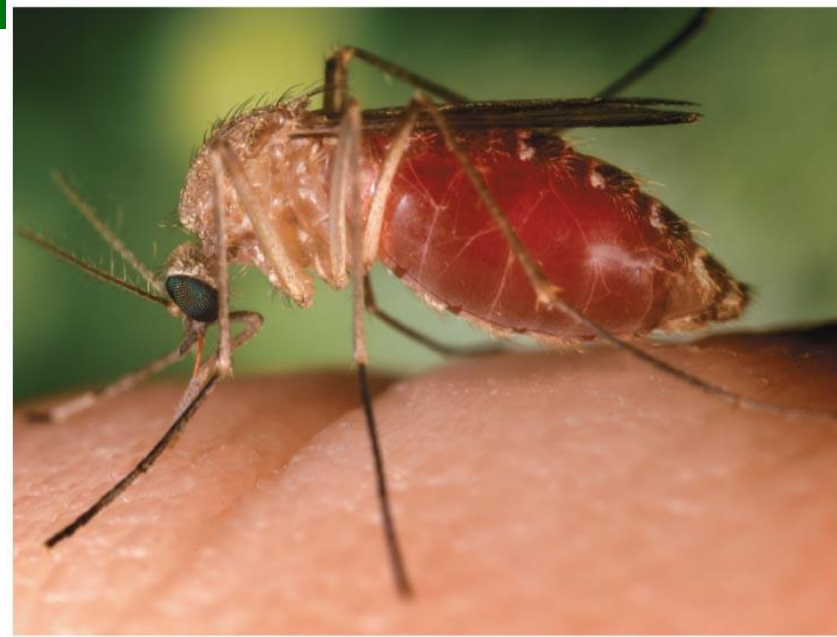
Fig 22.13










# Arboviral Encephalitis

- Arboviruses are arthropod-borne viruses that belong to several families.
- Prevention by mosquito control.
- Horses and humans affected.
- Incidence of arboviral encephalitis ↑ in summer, when mosquitoes are most numerous.
- Sentinel animals, *e.g.*: caged chickens
- Diagnosis based on serological tests.
- Symptoms from subclinical to coma and death



# Notifiable Arboviral Encephalitis Infections

Encephalitis	Reservoir	Mosquito vector	U.S. distribution
Western equine	Birds, horses	<i>Culex</i>	
Eastern equine	Birds, horses	<i>Aedes</i> , <i>Culiseta</i>	
St. Louis	Birds	<i>Culex</i>	
California	Small mammals	<i>Aedes</i>	
West Nile	Birds, mammals	<i>Culex</i> , <i>Aedes</i>	

# Diseases in Focus:

## Types of Arboviral Encephalitis (*p. 628*)



- An 8-year-old girl in rural Wisconsin has chills, headache, and fever and reports having been bitten by mosquitoes.
- Which type of encephalitis is most likely?

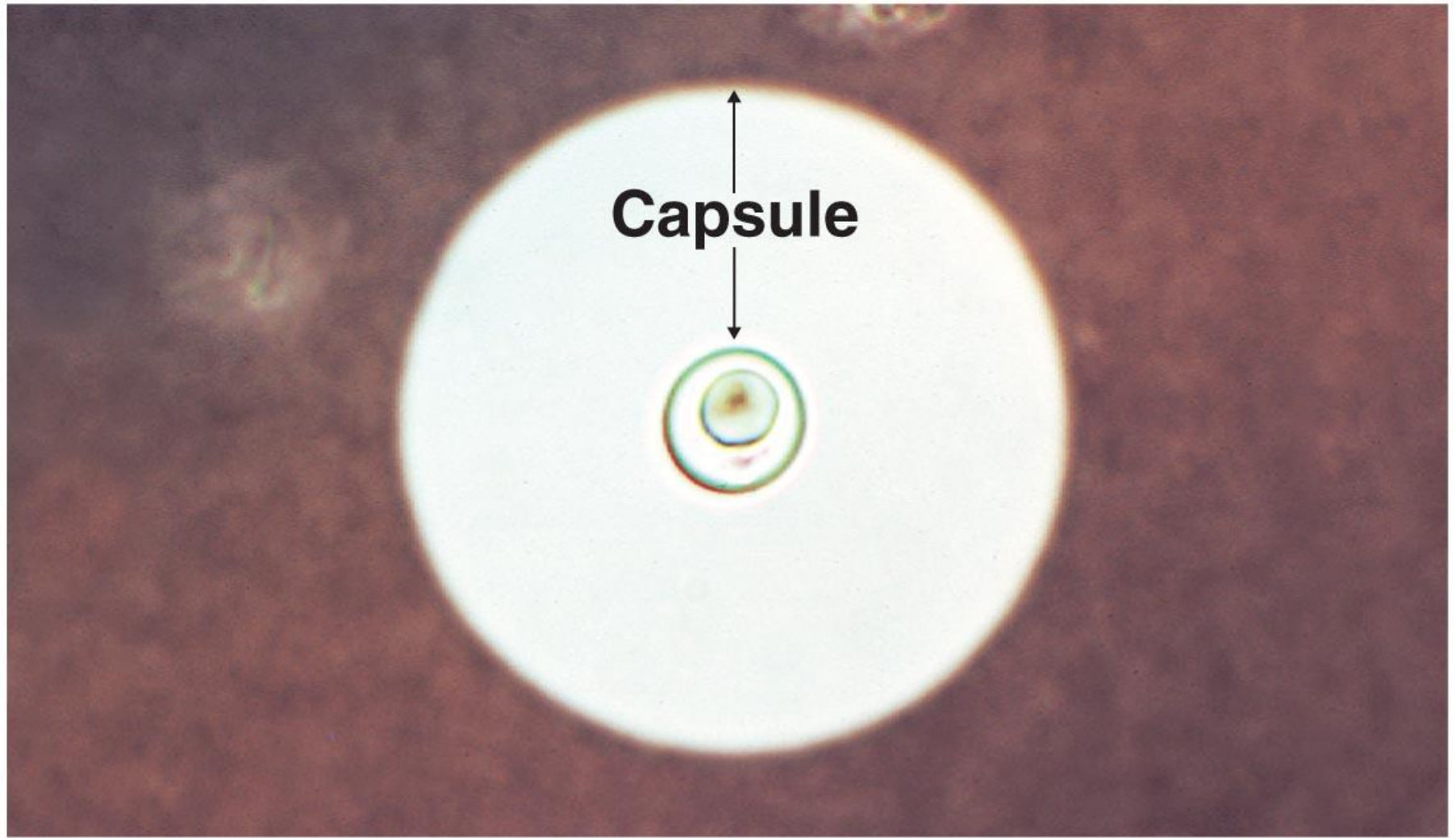
# Fungal Disease of Nervous System

## *Cryptococcus neoformans* Meningitis

- Also called **cryptococcosis**
- Soil fungus associated with pigeon and chicken (aerosolization of dried up contaminated droppings)
- Transmitted by the respiratory route; spreads through blood to the CNS
- Mortality up to 30% – Primarily affects AIDS patients (~ .4%)
- Diagnosis: Serology to detect cryptococcal antigens in serum or CSF
- Treatment: Amphotericin B and fluconazole



# *Cryptococcus neoformans*



LM

5  $\mu$ m

# Protozoan Disease of Nervous System

## African Trypanosomiasis (Sleeping Sickness)

Caused by *Trypanosoma brucei*; vector: tsetse fly (day-biting)

- *T.b. gambiense* infection is chronic (2 to 4 years).
- *T.b. rhodesiense* infection is more acute (few months).

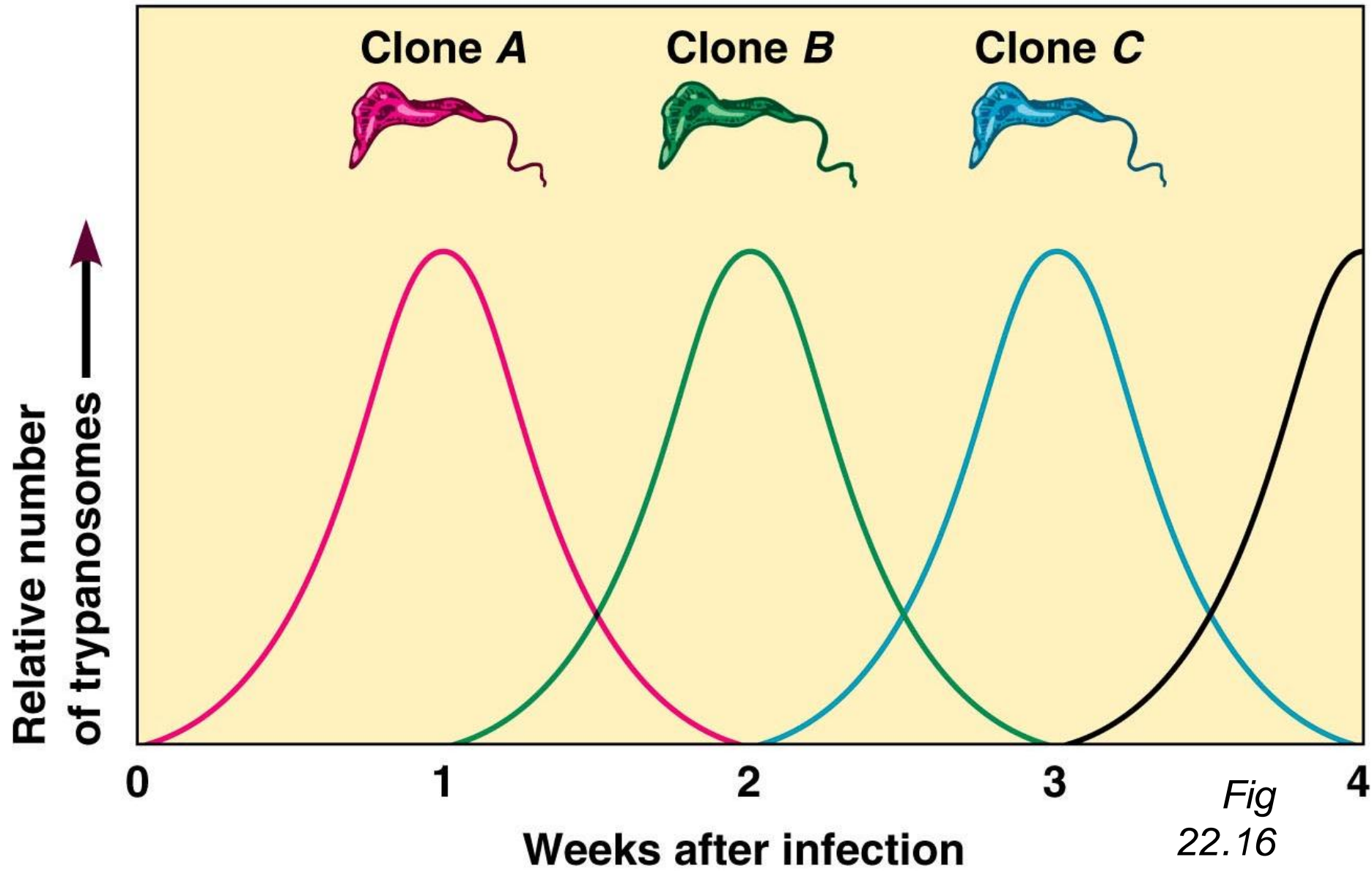
Symptoms: chancre - intermittent fever – CNS invasion.  
Without treatment: death



Treatment: **Eflornithine**  
blocks an enzyme  
necessary for the parasite

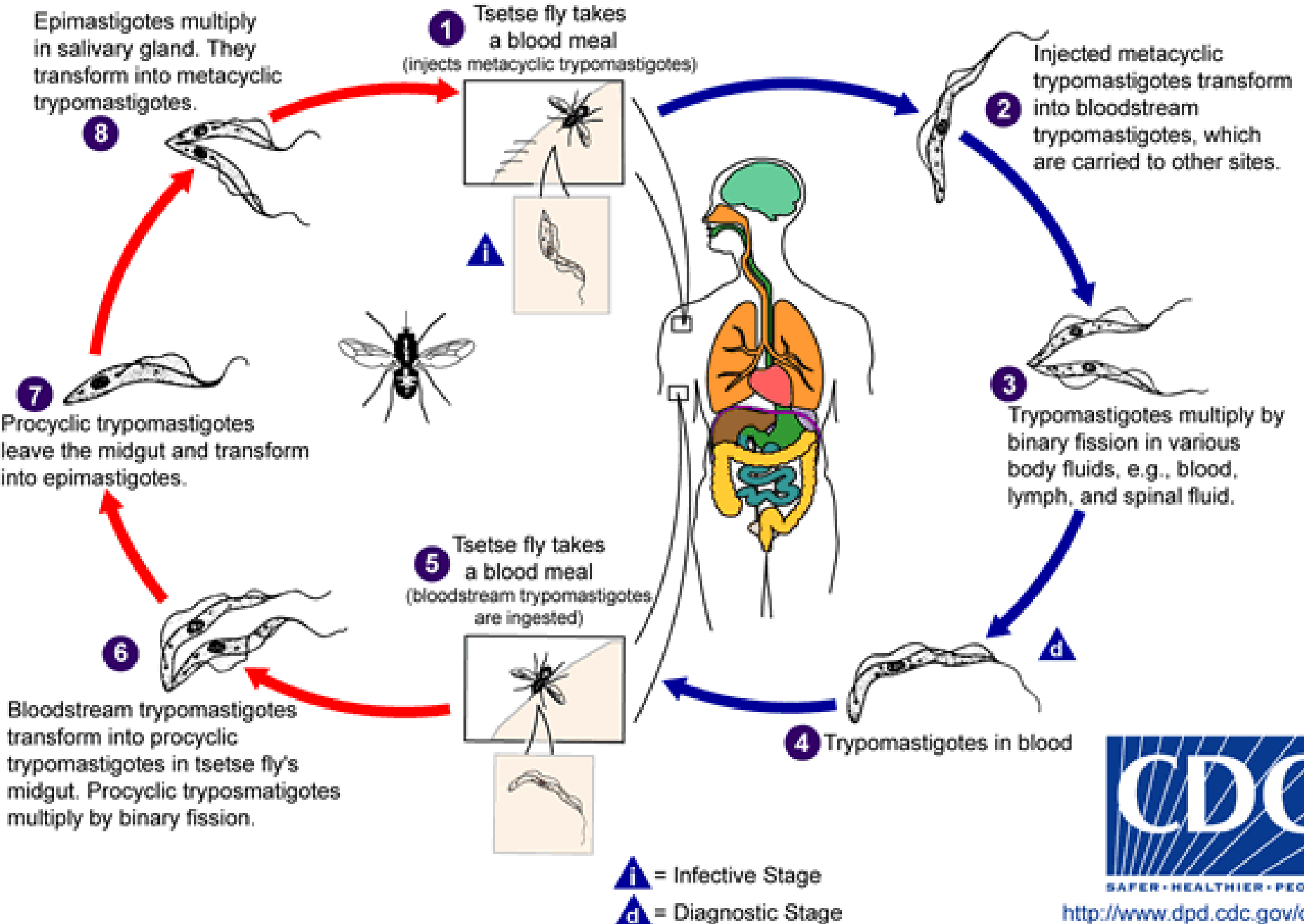


**Antigenic variation** allows for persistent evasion of the immune system  $\Rightarrow$  Cyclic parasitemia (7-10 days)



## Tsetse fly Stages

## Human Stages





# **Nervous System Diseases Caused by Prions**

## **Transmissible Spongiform Encephalopathies**

Prions convert normal proteins into abnormal proteins

Post mortem sponge-like appearance of brain tissue

large vacuoles in cortex and cerebellum due to loss of neurons

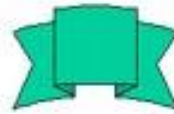
Chronic and fatal

Transmitted by ingestion or transplant or inherited.

- Typical diseases
  - Sheep scrapie
  - Creutzfeldt-Jakob disease
  - Kuru
  - Bovine spongiform encephalopathy

# Prions

## PRION PROTEIN (PrP)



**PrP**

**alpha-helical  
protease sensitive**

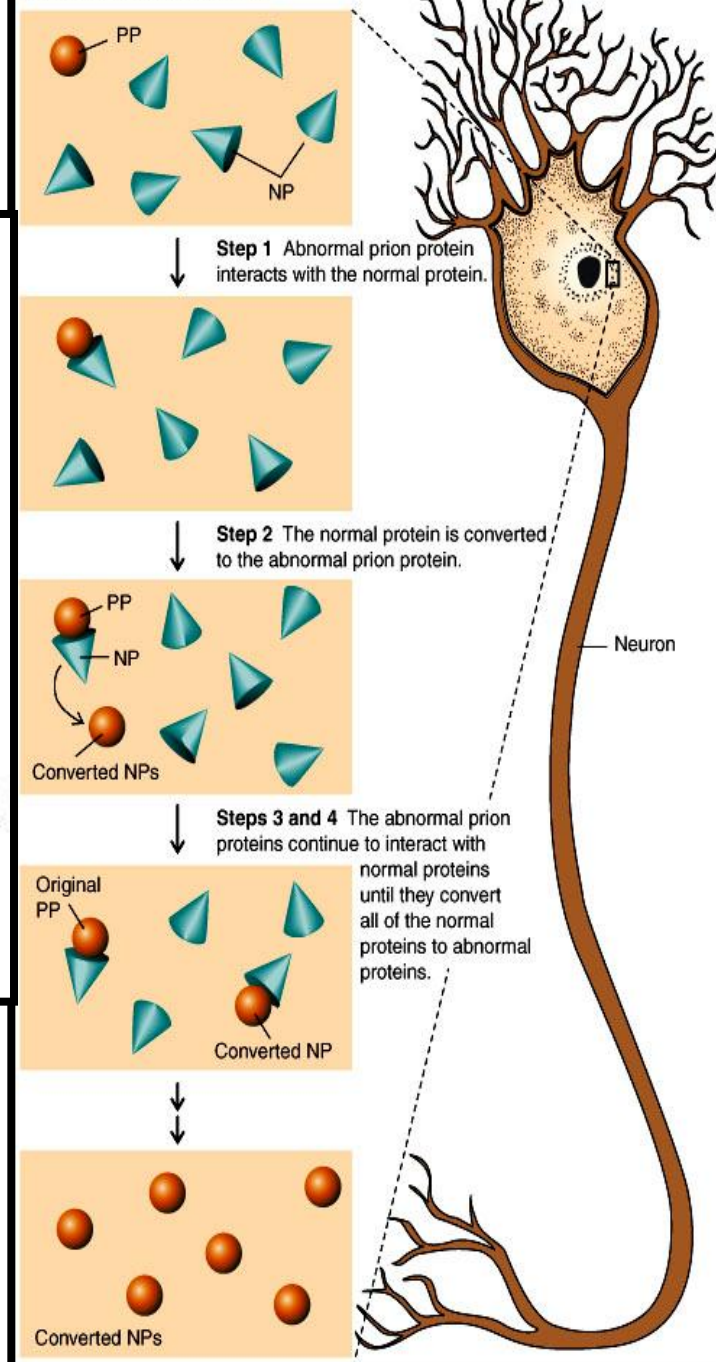
Helical - Happy

**PrP<sup>RES</sup> or PrP<sup>SC</sup>**

**beta-pleated sheet  
protease resistant**

Beta-pleated sheet - Bad

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Both normal protein (NP) and abnormal prion protein (PP) are present.



# How can a protein be infectious?

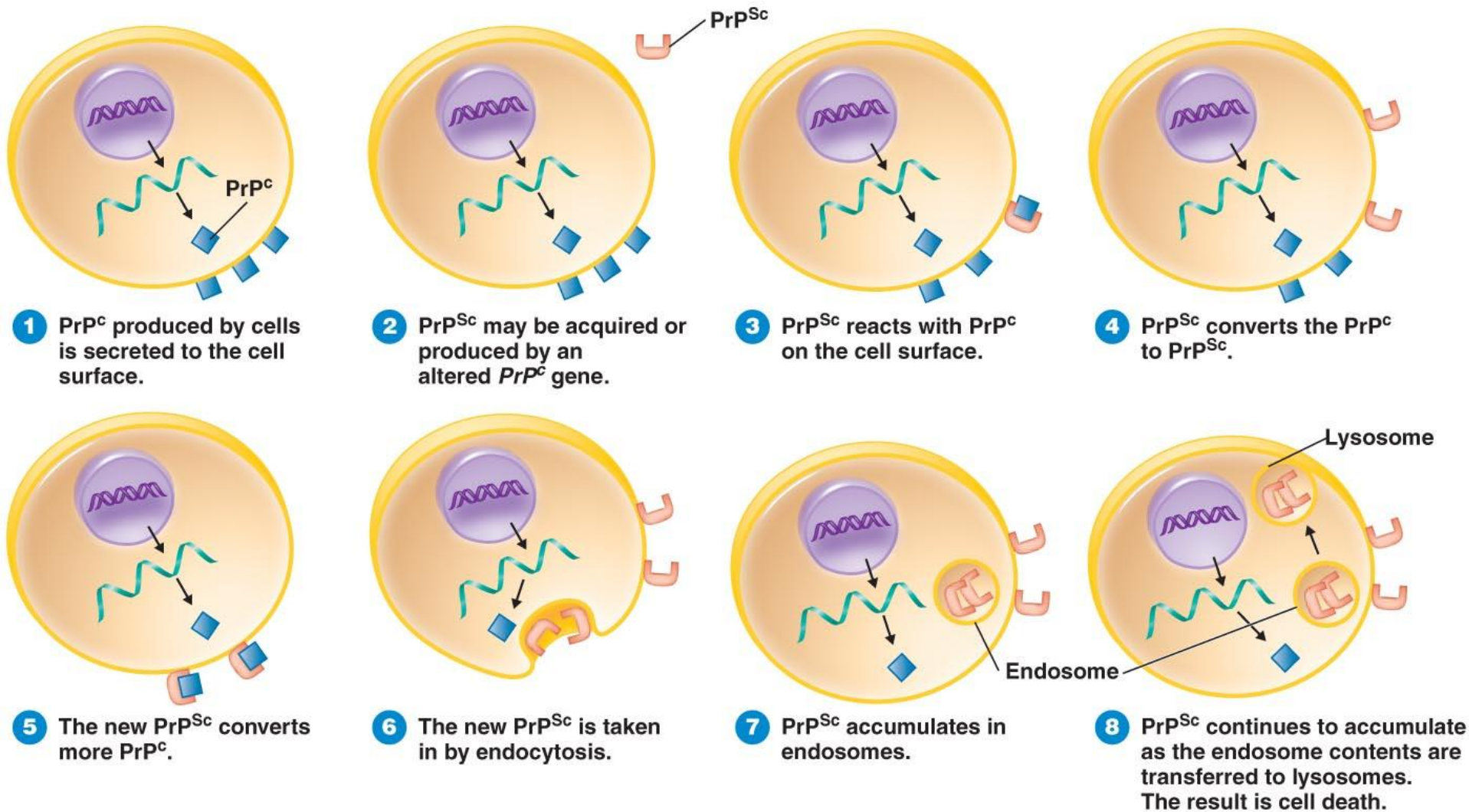
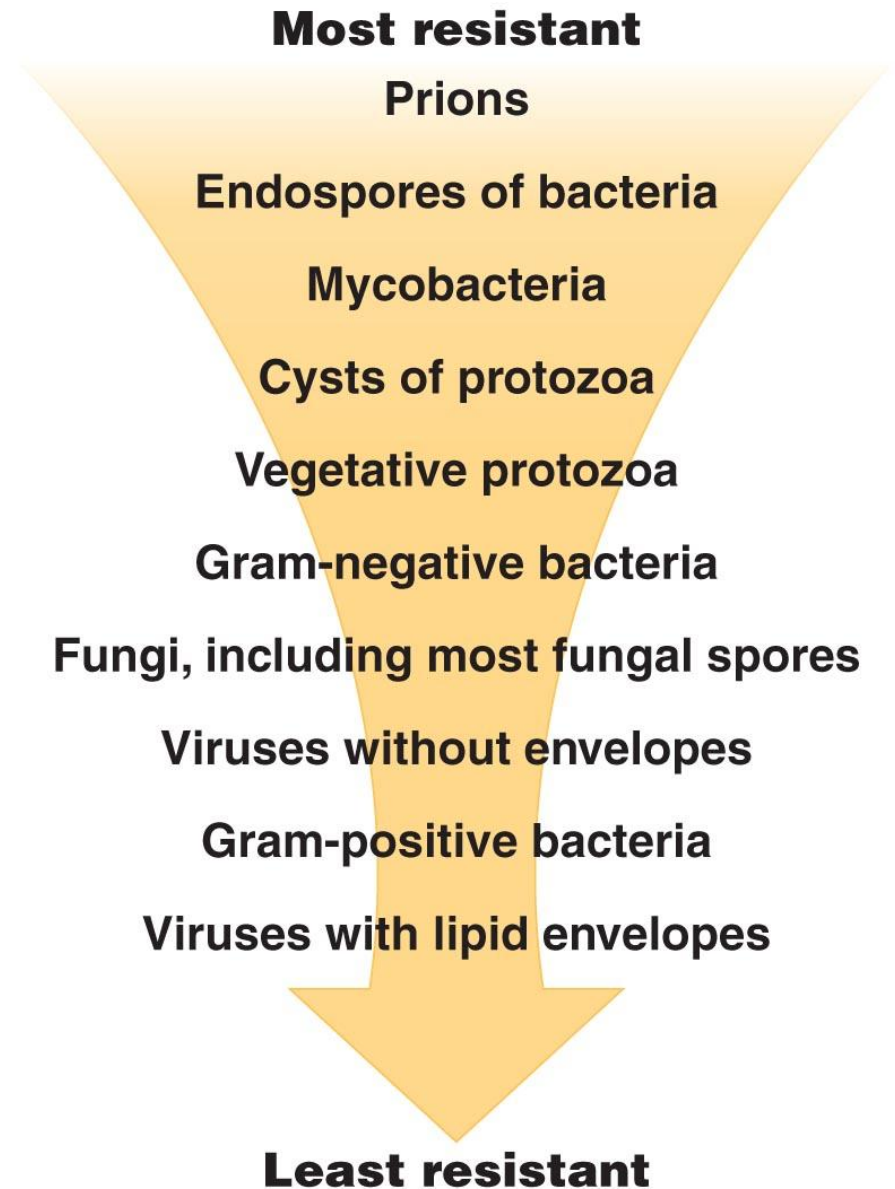


Fig 13.22 / Fig 22.18

# Preventing Prion Diseases

Fig 7.11

- Surgical instruments sterilized by
  - NaOH
  - + extended autoclaving at 134° C



The End