RABIES VIRUS

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RABIES VIRUS

Family **: Rhadboviridae**

Genus **: Lyssavirus**

80 members

A. Classic rabies virus

1.Street virus (Mammals & bats)

2. Fixed virus (Laboratory adapted)

B. Rabies related viruses.

1. Mokola virus

2. Lagos bat virus

3. European bat virus

Morphology:

- 75 x 180 nm.
- Bullet shaped.
- Enveloped.
- Knob like spikes 9 nm long project from envelope (Glycoprotein- G).
- Nucleocapsid helical with 30 – 35 coils.

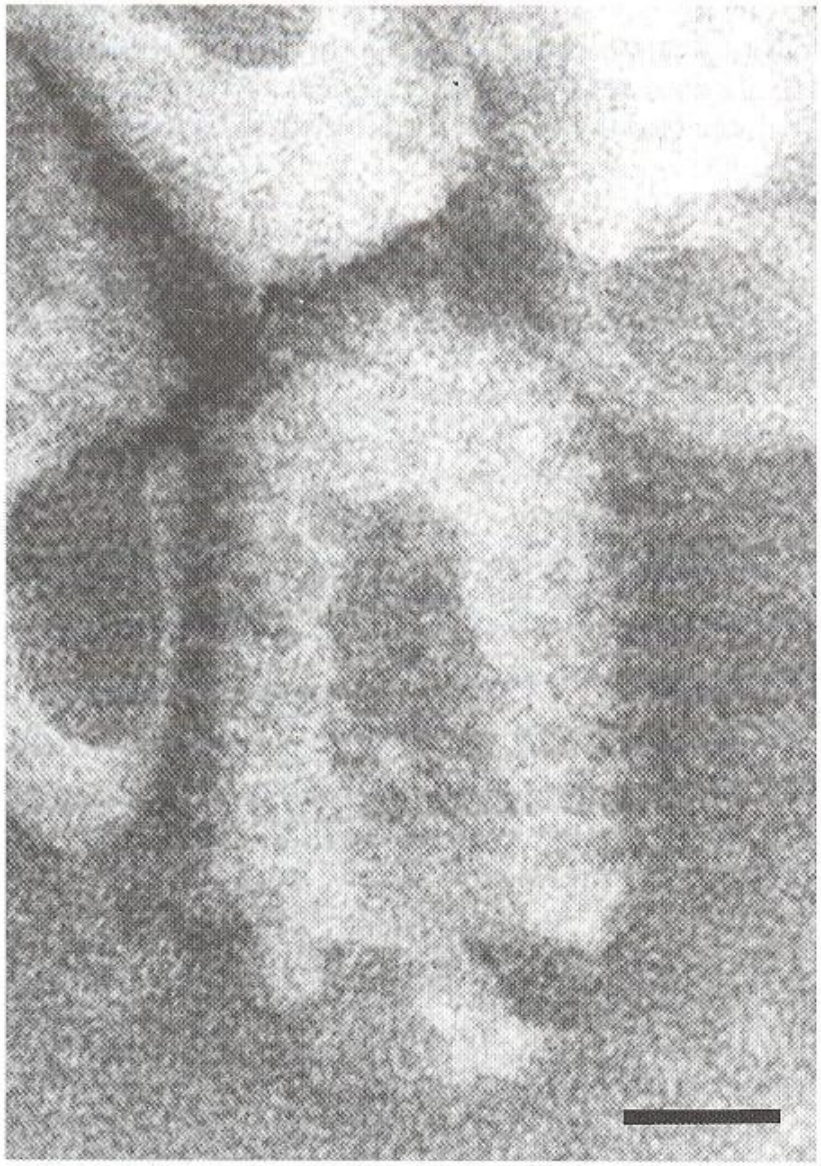
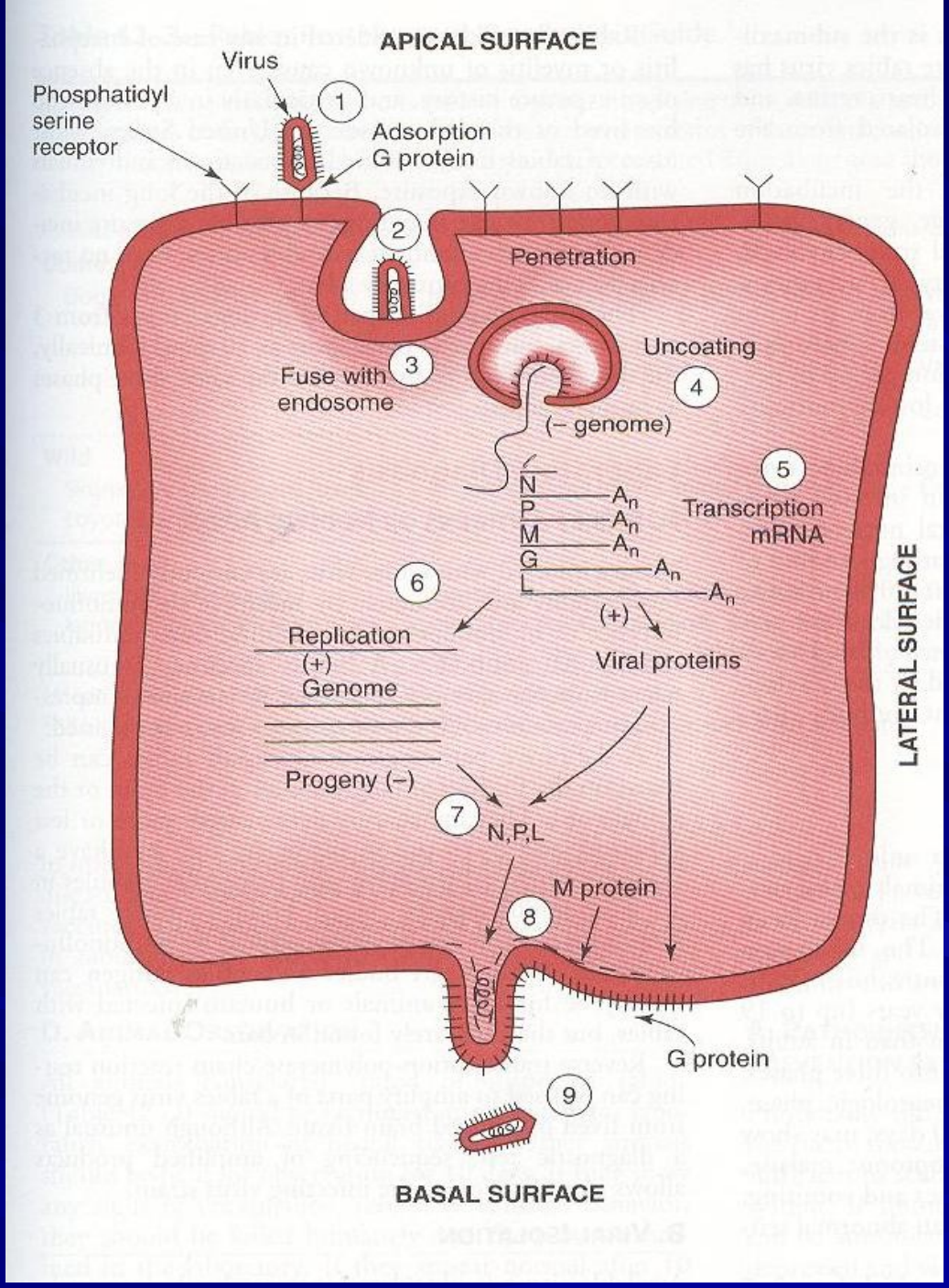


Fig. 58.2 Rabies virus particle. Bar, 30 nm. (By courtesy of Dr Joan Crick, Animal Virus Research Institute, Pirbright, UK.)

- **Genome single stranded, negative sense RNA, Non infectious.**
- **Viral RNA dependent RNA polymerase present**

Transcription occurs in host cell cytoplasm.


APICAL SURFACE
Virus
Phosphatidyl serine receptor
1
Adsorption G protein
2
Penetration
Uncoating
3
Fuse with endosome
4
(– genome)
5
N
P
M
G
L
An
Transcription mRNA
6
Replication
(+)
Genome
Progeny (–)
(+)
Viral proteins
7
N,P,L
M protein
8
G protein
9
LATERAL SURFACE
BASAL SURFACE

Genome codes for 5 proteins.

1) Glycoprotein (G)

2) Nucleocapsid (N)

3) Polymerase (L)

4) Matrix (M)

5) Nucleocapsid small (NS)

1. Glycoprotein (G)

- Structural component of surface spikes – produces neutralizing antibodies.

2. Nucleocapsid (N) – Group specific common to all Lyssa viruses.

- Associated with RNA to form ribonucleoprotein (RNP)

3. Polymerase (L) viral RNA replication & transcription.

4. Matrix (M) lies between core and envelope, packages RNA & proteins.

5. Nucleocapsid small protein (NS) associated with nucleocapsid, acts as polymerase.

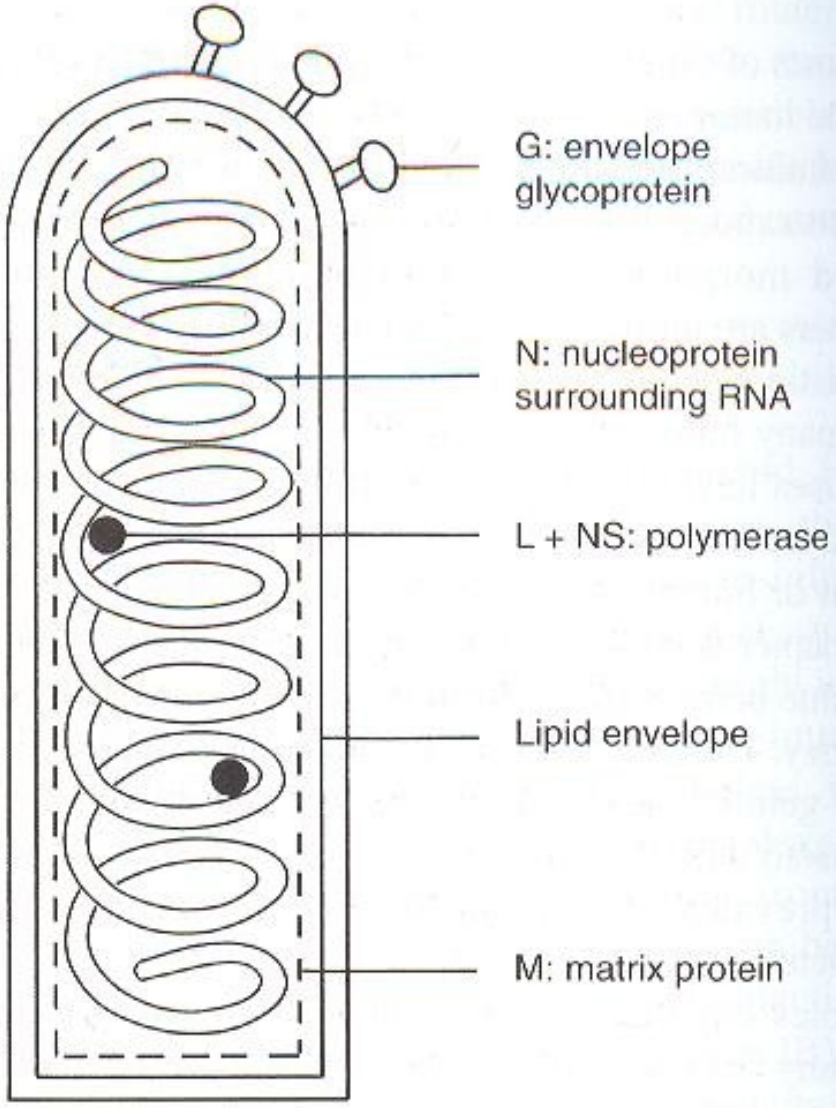


Fig. 58.3 Diagram of rabies virus.

Physiology:

- Killed rapidly by exposure to
- Sunlight / UV radiation.
- By Heat ($60^{o}C$ x 35 sec).

- Ether & other lipid solvents.

- Hypochlorite.

- Stable for many years when frozen at – $70^{o}C$.

PATHOGENESIS:

- **Single serotype, strains differ among viruses from different animals & localities.**

- **Highly neurotropic virus.**

- **After inoculation (bite wound) attaches to cell membrane (muscle cells) by binding of glycoprotein spikes to cell membrane receptors.**

- **Endocytosis.**

- **Incubation period follows.**

- **Virus replicates & increases in number.**

- **Enters peripheral nerves.**

(Unmyelinated motor & sensory axon terminals) through neuromuscular junctions via acetylcholine receptors.

- **Travels through retrograde axonal flow at 12 – 24 mm per day.**
- **Reaches spinal cord**
- **Multiplies within neurons of spinal ganglia (sensory).**
- **Disseminates rapidly in CNS. (200 – 400mm /day).**

- Produces rapidly progressive encephalitis.
- Inflammatory response is minimal.
- Spreads centrifugally again along peripheral nerves/ autonomic nerves.
- No viremia.

Reaches

- Salivary glands
- Oral mucosa.
- Conjunctiva
- Cornea.

- **Kidneys**
- **Skin**
- **lungs.**
- **Mammary gland.**
- **Adrenals**
- **Pancreas.**
- **Myocardium**

PATHOLOGY:

- Encephalitis
- Death of neurons & Demyelination.
- Hyperemia & pyknosis.
- Irreversible functional damage.
- Perivascular cuffing with lymphocytes & plasma cells.

Negri bodies

Specific cytoplasmic inclusions
in 70 – 80% of cases

- Sharply defined round / oval.
- 7 - 10µm, eosinophilic mass having basophilic spots/granules.
- In Hippocampus, Purkinje cells of cerebellum & spinal ganglia.

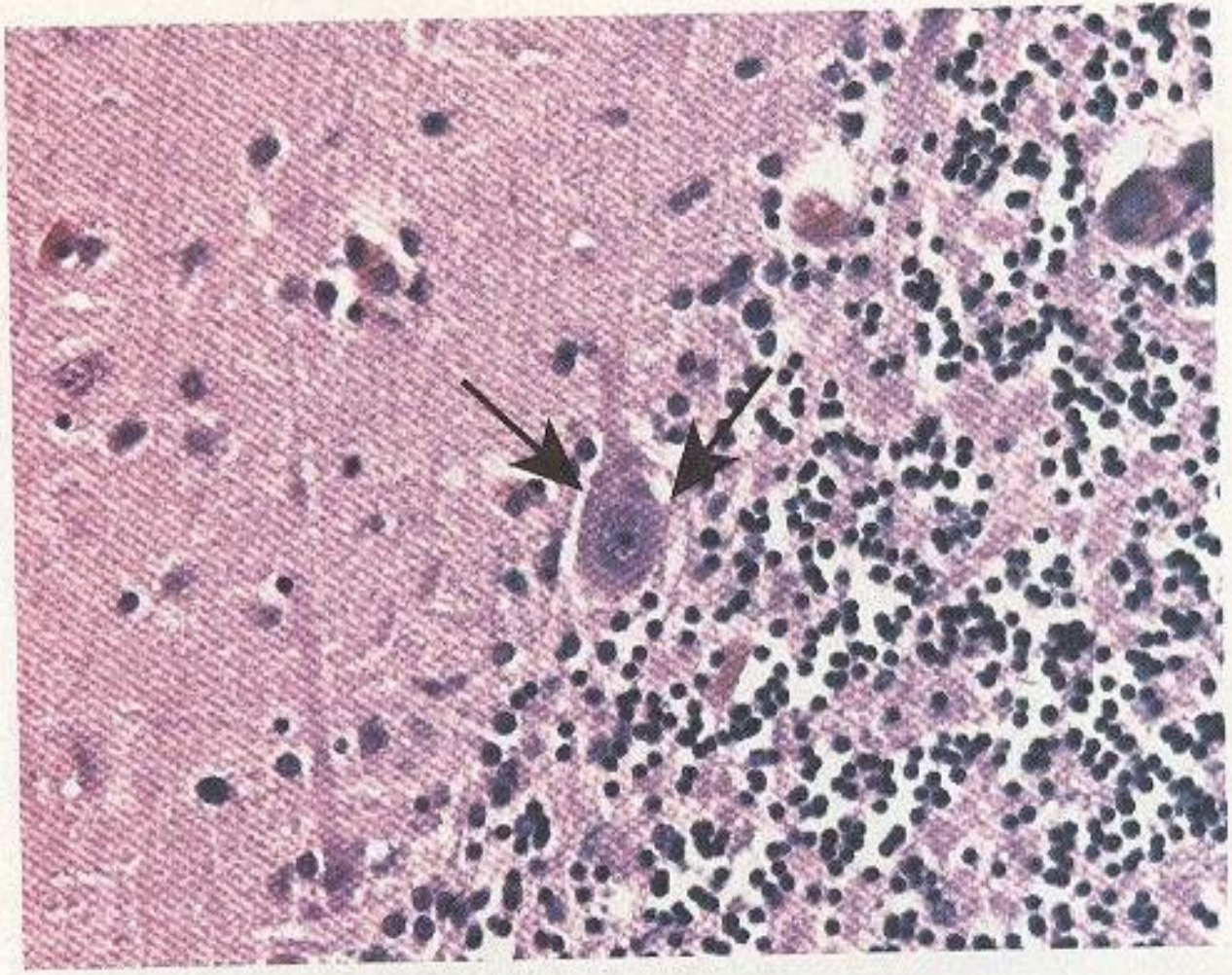


FIGURE 28–25 The diagnostic histologic finding in rabies is the eosinophilic Negri body, as seen here in a Purkinje cell *(arrows)*.

Clinical Features:

Incubation period extremely variable one week to a year or more (1 – 3 months).

a) Prodrome (2 – 10 days).
b) Acute neurological phase.
c) Coma.

a.Prodrome:

- Early & non-specific
- Malaise, fatigue & headache
- Anorexia, fever & chills
- Cough & sore throat
- Nausea, vomiting & diarrhoea.

- Wound site has
- Pain
- Tingling
- Numbness
- Hyperaesthesia
- Paraesthesia

b.Acute Neurologic Phase:

1) Furious.
2) Paralytic

1. **Furious:**

Hyperactivity, disorientation, hallucination & abnormal behavior.

Agitation, thrashing, running & biting, alternating with periods of calmness.

More than 50% have hydrophobia.

Spasm of pharynx, larynx & diaphragm leading to choking.

Due to sensory stimuli or spontaneous.

1.72 'Furious rabies' in a 14-year-old Nigerian boy. Inspiratory spasms occur spontaneously or are induced by attempts to swallow. This may lead to fear of water (hydrophobia).

2.) Paralytic:

- Occurs in 20% of cases
- No hyperactivity
- Paralysis maximum in bitten extremity, diffuse or symmetrical.
- Disorientation & stupor.

1.73 Flaccid paralysis in rabies follows the 'furious' stage and is often accompanied, as in this Thai boy, by autonomic disorders including hypersalivation.

c. Coma:

- Sets within 10 days
- Lasts for days,
- Respiratory arrest.
- Death.

Diagnosis:

Clinical

History of animal bite

No tests available before onset of clinical disease.

Laboratory tests confirm the diagnosis.

ANTEMORTEM

- Identification of rabies antigens by
- Direct Immunofluorescence of
- Salivary
- Corneal or conjunctival smears
- Skin biopsy

Post – mortem:

1. Impression smears of cut surface of

- Salivary glands
- Brain stem
- Hippocampus
- Cerebellum.
- For Negri bodies

2. Histological examination of

Fixed brain tissue by immunofluorescence. or staining by

- Seller
- Giemsa
- Mann

3. Detection of specific antibodies from serum or CSF by

Flouresence antibody technique (FAT)

ELISA

CF.

4. PCR in fixed / unfixed brain tissue.

5. Virus isolation from saliva & CSF

From Salivary gland or brain tissue extract by

a. Intra cerebral inoculation of mice

b. Cell culture technique in hamster or mouse cell line.

PROPHYLAXIS:

a) Post – exposure
b) Pre – exposure

a. Post – exposure:

Cleaning of wound with detergents.

Vaccination with Human Diploid Cell vaccine (HDCV) on day 0,3,7,14 & 28

And Human Rabies immunoglobulin (HIRG) (20 IU / Kg body wt)

Active & passive immunization

b. PRE – EXPOSURE:

High risk persons like

Veterinarians

Lab workers

Wildlife workers

Travelers to endemic areas

HDCV (0, 7 & 28 days)

THE END