

Rift Valley Fever - 2. Aetiology and Pathogenesis



- ≡ Objective and themes

- ≡ Classification of the virus

- ≡ Morphology

- ≡ Morphology, Viral stability to temperature and chemicals

- ≡ Pathogenesis

- ≡ Summary

Objective and themes

Objective and themes



Start ▶

Classification of the virus



The **viral** agent of the **RVF** is a ***Phlebovirus***, which belongs to the ***Phenuiviridae*** family (formerly *Bunyaviridae*), order *Bunyavirales*.

Besides the ***Phlebovirus***, there are a further **14 genera** in the ***Phenuiviridae*** family and **58 viruses** belong to the ***Phlebovirus*** genus:

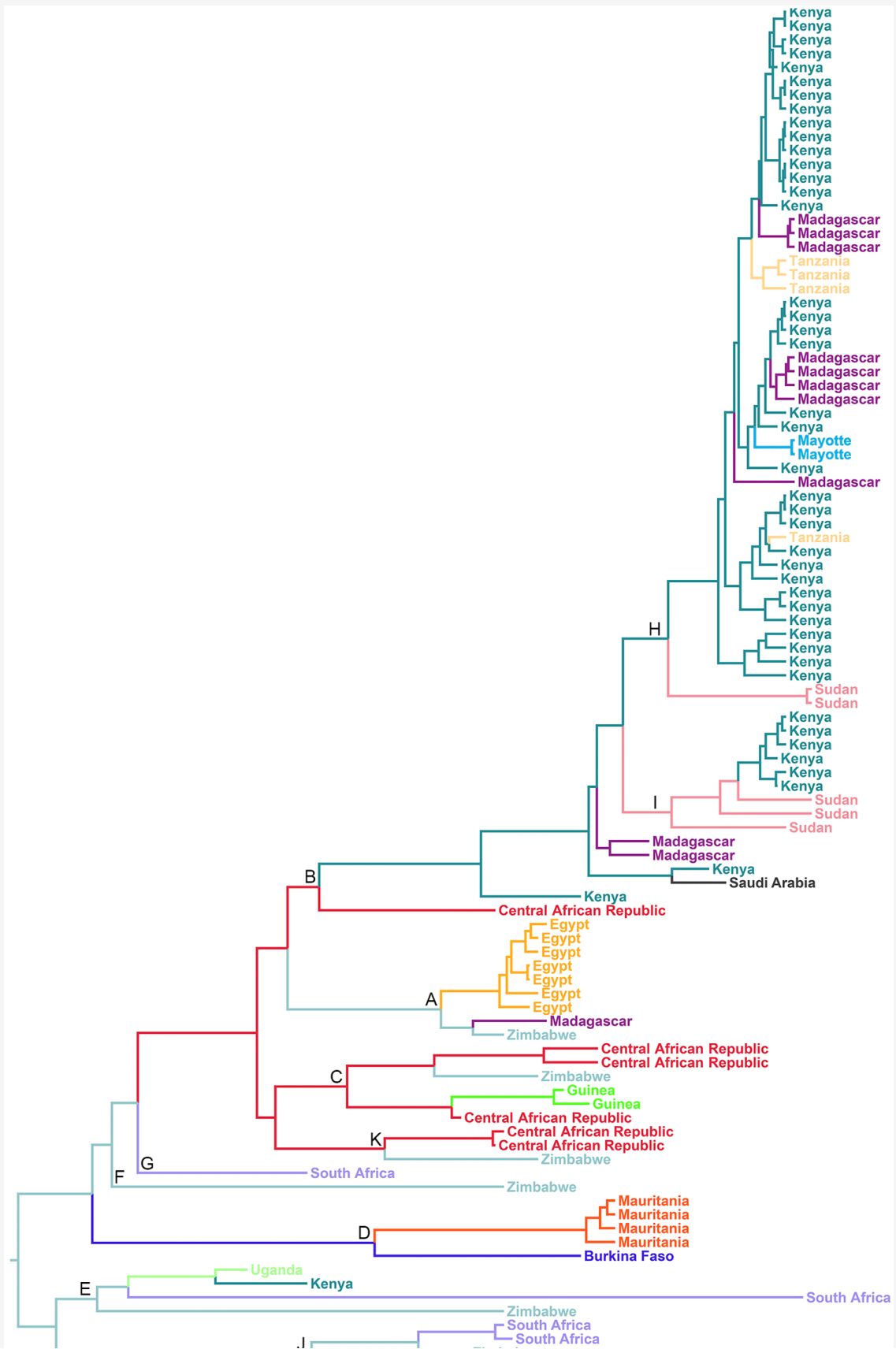
RVFV isolates can be separated into **eleven distinct genetic lineages** (A to K) but strains with diverse geographic origins can be found in each lineage indicating a broad dispersal of RVFV genotypes across

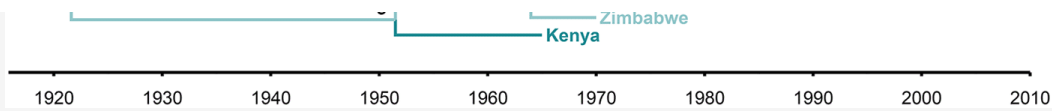
Africa (Bird et al. 2007, Samy et al. 2017).

The dynamic and evolution of RVFV is still not fully understood. Recent studies attempted to explain its history using **phylogenetic analysis**.

Although the **RVF** virus shows genetic mixing abilities (in vectors and in cell cultures) it is **relatively stable*** from an **antigen** standpoint.

i *Several studies on isolates from different geographic areas found a variation of less than 5% in the sequence of segment M nucleotides, which translates to less than a 2.5% variation in the amino acid sequence of the coded proteins.





Source: Samy AM, Peterson AT, Hall M (2017)

Phylogeography of Rift Valley Fever Virus in Africa and the Arabian Peninsula. PLoS Negl Trop Dis 11(1): e0005226. [doi:10.1371/journal.pntd.0005226](https://doi.org/10.1371/journal.pntd.0005226)

Maximum Clade Credibility tree based on all sequences of the medium minigenomic segment (M) of RVFV isolates in the study.

NCBI accession number, country, and date of sampling are presented at the tree tips. Tree branches are colored and labelled alphabetically by lineage (A to K). Lineage nomenclature is from *Bird et al., 2007**. The red triangle identifies the clade containing isolates from both Saudi Arabia and Africa. Clades with posterior probability >0.9 are labelled with red circles.

i **Bird et al., 2007*. Bird BH, Khristova ML, Rollin PE, Ksiazek TG, Nichol ST (2007). Complete genome analysis of 33 ecologically and biologically diverse Rift Valley Fever virus strains reveals widespread virus movement and low genetic diversity due to recent common ancestry. J Virol.81:2805–2816.



Morphology

The RVF virus is an enveloped RNA virus consisting of three segments: L (large), M (medium) and S (small), each of which is contained in a separate nucleocapsid within the virion.

It has a **lipid envelope** of cellular origin with two types of **glycoprotein spikes** on its surface.

The RVF virus is sensitive to lipid solvents (ether and chloroform) and is inactivated by acid conditions and by common disinfectants:

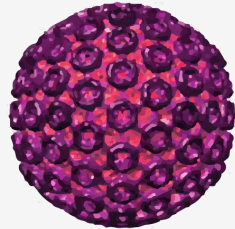
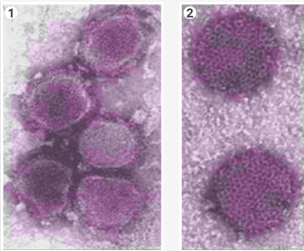
- formol;
- β -propiolactone;
- sodium deoxycholate;
- formalin (even at low concentrations);
- sodium or calcium hypochlorite (residual chlorine must be more than 5,000 ppm).

The virus is resistant in alkaline environments but **inactivated at pH <6.8**.

Viraemic blood preserved in **oxalate-carbol-glycerine** remains infectious for **8 years** even if stored in different refrigeration conditions.

For more information on the morphology of **RVF**
(Ikegami T., 2012)

[CLICK HERE](#)



(1) Negative-stain transmission electron micrograph (TEM) showing pleomorphic RVFV MP-12 particles. (2) Negative-stain TEM micrograph showing spherical RVFV MP-12 particles with a distinct surface structure composed of morphological units with a central cavity. Scale bar: 100 nm.

Surface-shaded representation of RVFV MP-12.

At which of the following pH ranges is the RVF stable?

- pH 3 to pH 6.8
- pH 6.8 to pH 8



pH 8 to pH 10

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Morphology, Viral stability to temperature and chemicals

The virus can multiply in several **cell lines**:

- lamb and calf renal cells;
- lamb and calf testicular cells;
- VERO (African Green Monkey Kidney);
- BHK21 (Baby Hamster Kidney);
- AP61 (*Aedes pseudoscutellaris*);
- CER (Chicken embryo related).

The **cytopathic effect** (CPE) manifests **24-48 hours** after inoculation and spreads to the entire cell monolayer in **3-5 days**.

Viral **replication** entails the following phases:

Phase 1

Attachment to cell and penetration by endocytosis

Phase 2

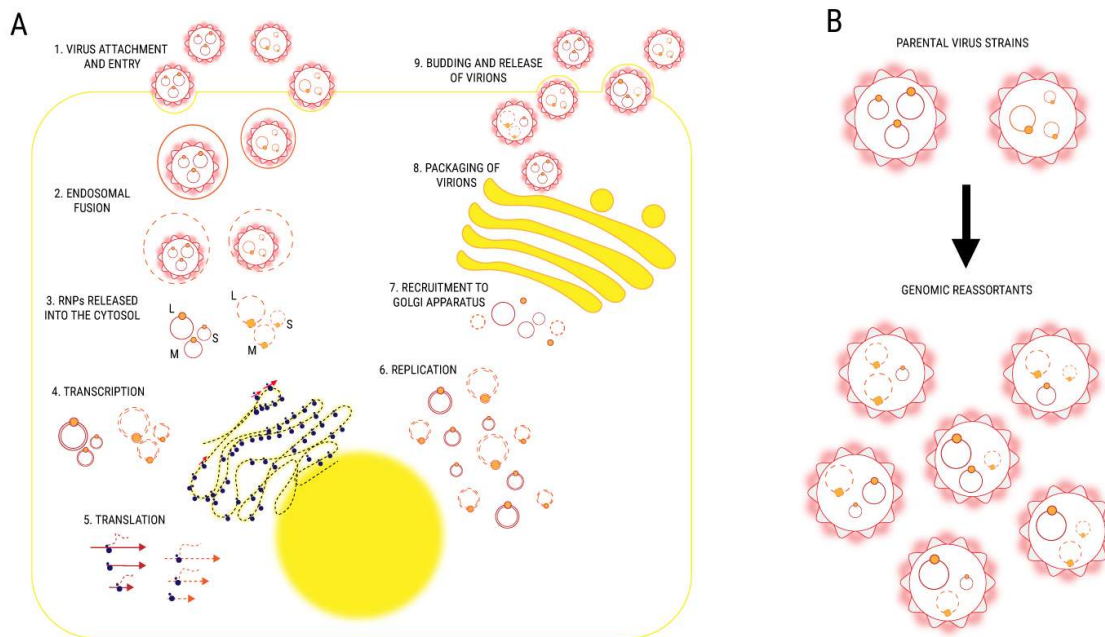
Replication in the cytoplasm

Phase 3

Accumulation of virions in the reticulum of the Golgi apparatus where they give rise to cytoplasmic vesicles

Phase 4

Migration of vesicles towards the plasma membrane, into which they fuse, thus enabling the virus to exit



Molecular aspects of Rift Valley fever virus and the emergence of reassortants.



Pathogenesis

Once the **RVFV** has penetrated the host organism, it is transported by the lymphocytes to the liver and adrenal glands. The liver is primary target organ and **replication** takes place in the **hepatocytes** and the **adrenal cortical zone cells**.

Next, the virus spreads to the spleen and the renal glomeruli and tubules.

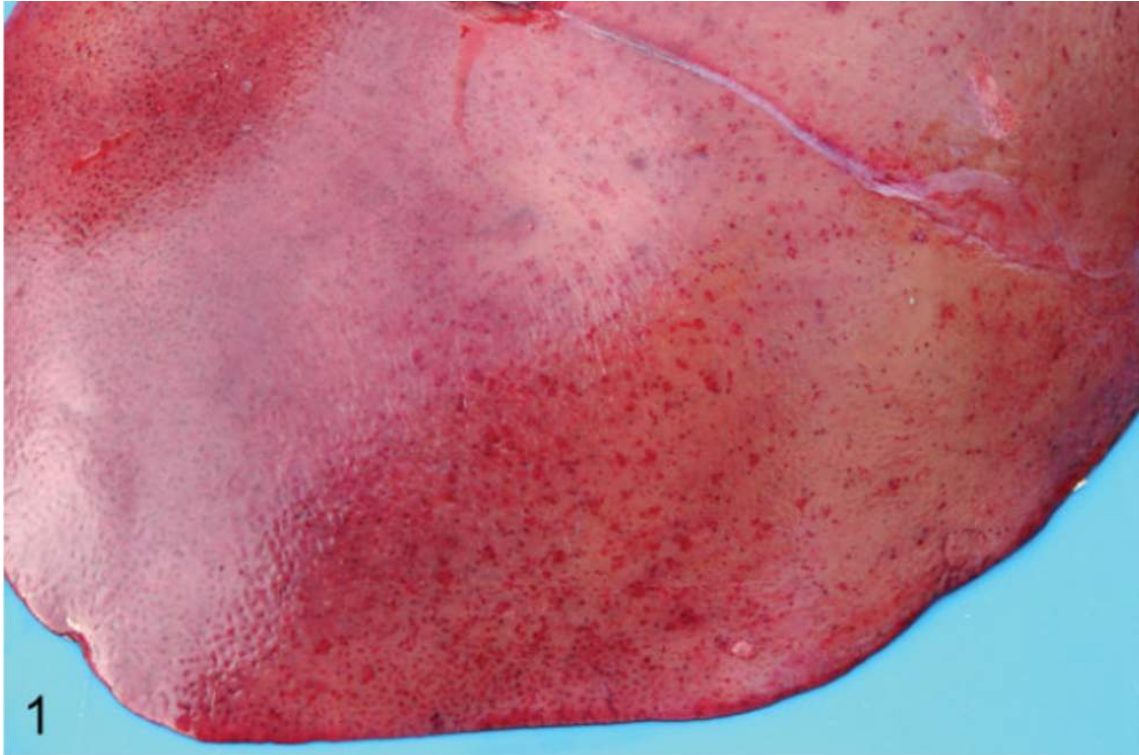
The **liver** is strongly affected and its functions are drastically altered.

Prothrombin synthesis becomes difficult and its rate drops dramatically, leading to impaired coagulation and consequent haemorrhaging.

The virus replicates in the placenta.

Fig. 1

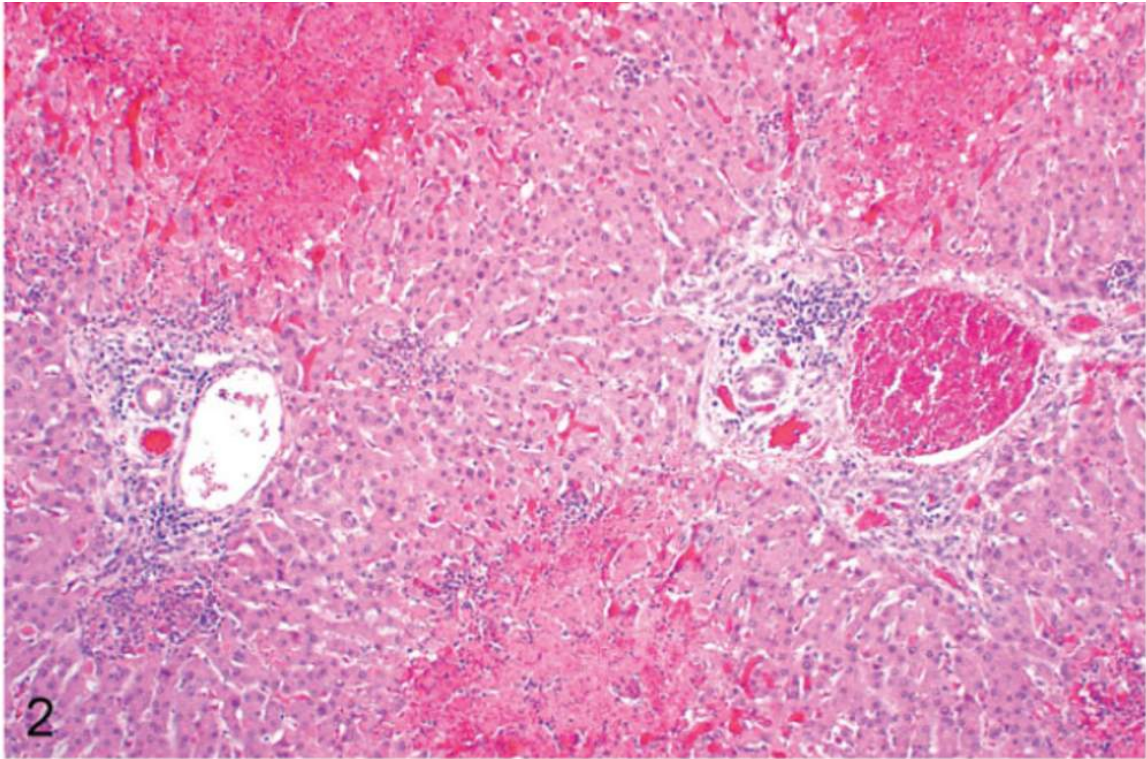
Rift Valley fever virus (RVFV), liver, sheep.



Multifocal to coalescing hemorrhage and necrosis.

Fig. 2

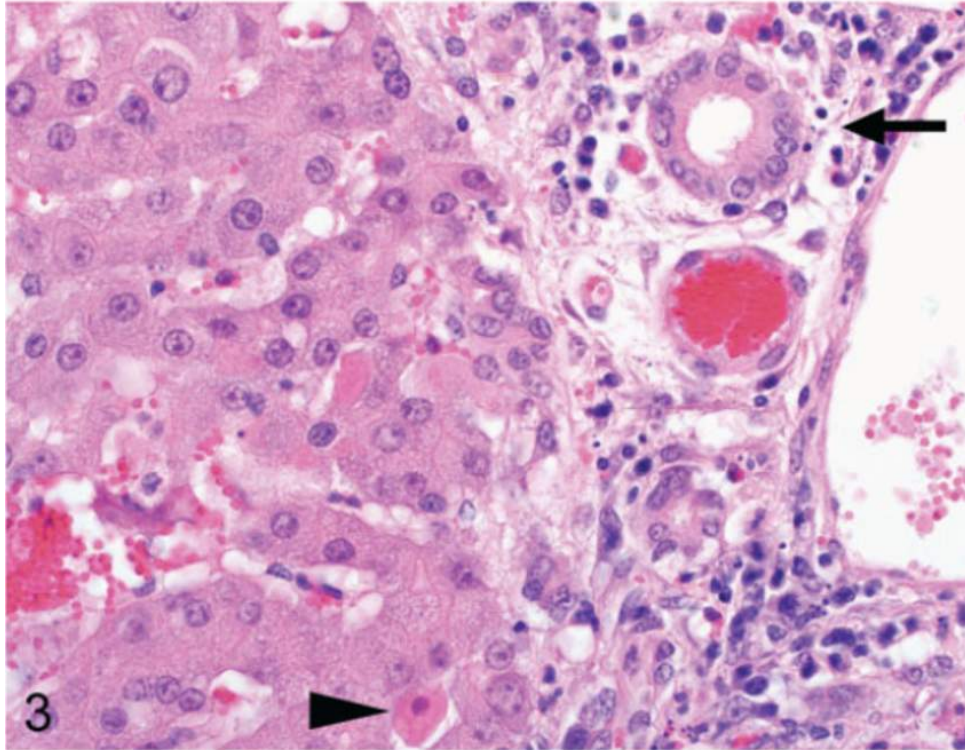
Rift Valley fever virus (RVFV), liver, sheep.



Multifocal random hepatocellular hemorrhage and necrosis. Hematoxylin and eosin (HE).

Fig. 3

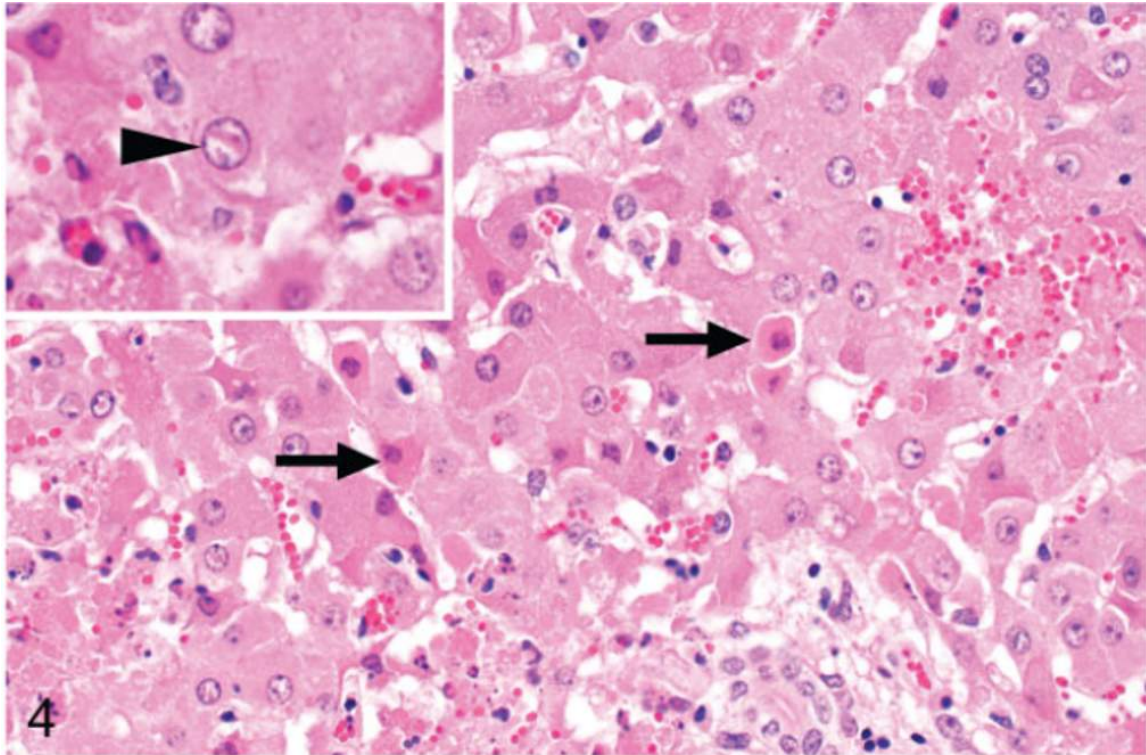
Rift Valley fever virus (RVFV), liver, sheep.



Mild edema and mononuclear cell inflammation with karyorrhexis (arrow) in the portal area. Early apoptotic body (arrowhead) also referred to as a Councilman body. HE.

Fig. 4

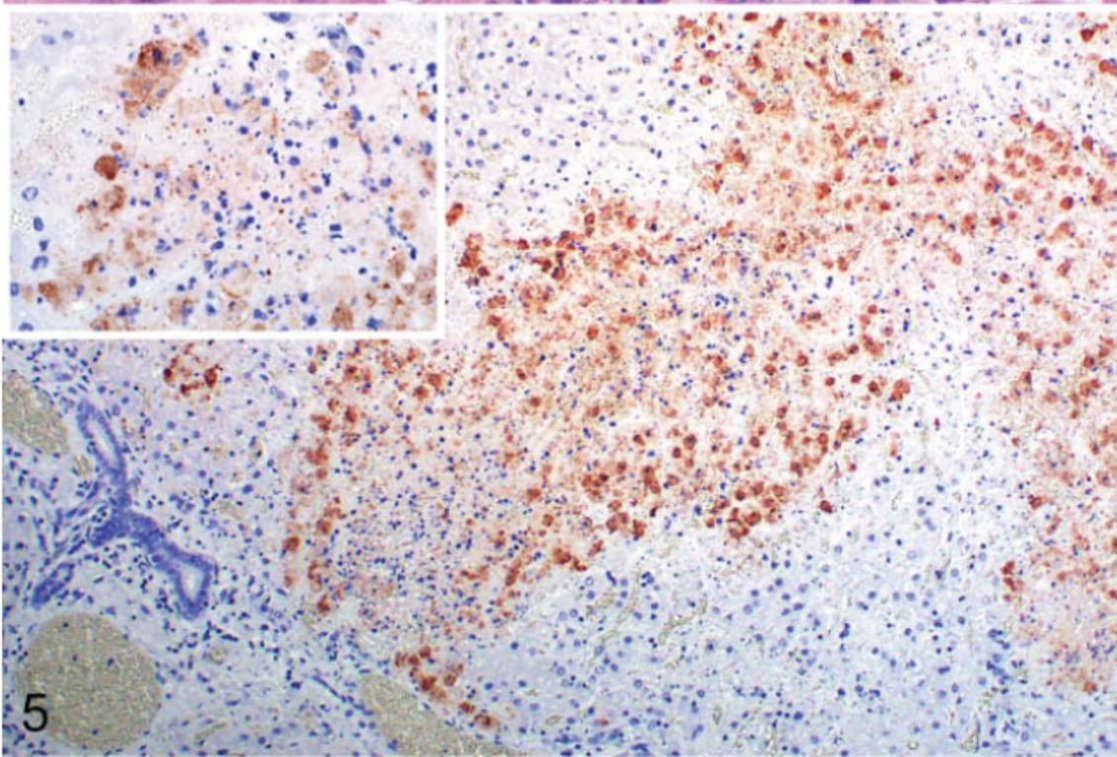
Rift Valley fever virus (RVFV), liver, sheep.



Early apoptotic bodies (arrows) characterized by shrinkage of affected cells with acidophilic cytoplasm and pyknosis. Inset: Rod-shaped acidophilic intranuclear inclusion in the nucleus of a hepatocyte (arrowhead). HE.

Fig. 5

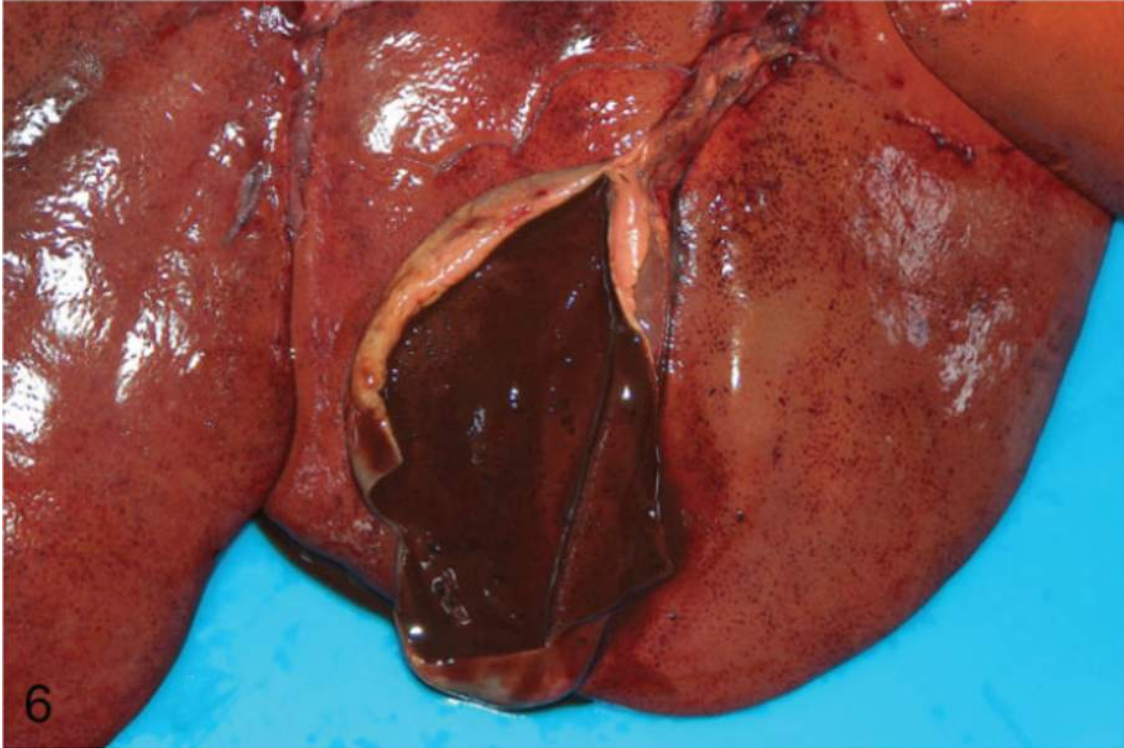
Rift Valley fever virus (RVFV), liver, sheep.



RVFV antigen in areas of hepatocellular death. Inset: Fine granular labeling in the cytoplasm of injured hepatocytes and cytoplasmic fragments. Immunohistochemistry for RVFV.

Fig. 6

Rift Valley fever virus (RVFV), liver, sheep.



Hemorrhage in the wall of the gall bladder.

Source

Fig. 1 to 6. Odendaal L. et al.,2019. Lesions and Cellular Tropism of Natural Rift Valley Fever Virus Infection in Adult Sheep. *Veterinary Pathology* 2019, Vol. 56(1) 61-77.

Which organ is the primary target of the RVFV?

- Liver
- Brain
- Spleen
- Lungs
- Adrenal glands

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Summary

**Summary
of the concepts
presented**



Start 