

## Pilot study with a murine model to further dissect the pathogenesis of Japanese encephalitis.

Ricci, E and Galbraith, SE and Kipar, A (2015)

**Introduction:** Japanese encephalitis virus (JEV) is a neurotropic flavivirus transmitted by *Culex* spp. mosquitoes and responsible for life-threatening encephalitides in man and animals in east and south Asia. To fully reveal the pathogenesis of Japanese encephalitis (JE) in man, reproducible and comparable animal models are needed. Here we describe the neuropathological findings of a pilot study to assess the validity of a mouse model using intraperitoneal infection.

**Materials and Methods:** Six 10-month-old female C57BL/6 mice were inoculated intraperitoneally with a single dose of JEV (JEV P3 strain); a further four received PBS (controls). Animals were killed after 10 days, when clinical signs developed. Brains were fixed in formalin and embedded in paraffin wax. A detailed histopathological examination was performed and immunohistology for the demonstration of viral antigen, astrocytes (GFAP), microglia (Iba1), iNOS and apoptotic cells (cleaved caspase-3) undertaken.

**Results:** Infected animals exhibited severe non-suppurative encephalitis, affecting the cerebrum and thalamus and characterized by lymphocyte-rich perivascular cuffs and vigorous microglial and astrocyte proliferation/activation. Viral antigen was detected in both intact and cleaved caspase-3 positive apoptotic neurons. Iba1-positive microglial cells exhibited strong iNOS co-expression.