variant typing by molecular or monoclonal antibody characterization. Categorical variables were summarized as frequency (%), and continuous variables were summarized as median (interquartile range [IQR]). We compared bat- and dog-acquired cases using chi-square or Fisher's exact tests for categorical variables, and Mann Whitney U tests for continuous variables. Of 120 cases, 38 (32%) were dog-acquired and 54 (45%) were bat-acquired. Survivors and cases acquired from aerosolized viral exposure or tissue/organ transplantation were excluded. The median incubation times for dog- and bat-acquired rabies were 63 (IQR 42.75, 108) and 52.5 (IQR 27.25, 92.5) days, respectively (p=0.074). The median durations of illness for dog- and bat-acquired rabies were 17 (IQR 11.75, 23) and 14 (9.25,18.5) days, respectively (p=0.201). There was no difference in patients with bat- and dogacquired rabies in terms of the presence of fever, prodromal malaise, encephalopathy, sore throat, cranial nerve abnormalities, hemiparesis or seizures. Clinical manifestations that were more common in bat- than dog-acquired rabies included a local prodrome of sensory or motor symptoms (p=0.026), hemisensory abnormalities (p=0.042), tremor (p=0.003), and myoclonus (p=0.009). Neither tremor nor myoclonus was observed in patients with dog-acquired rabies. Aerophobia and facial or pharyngeal spasms were more common in dog- than bat-acquired rabies (p=0.007 and p=0.029, respectively). Hydrophobia was more common in dog-acquired rabies (p=0.054). There was no difference between dog- and bat-acquired rabies in terms of results of diagnostic investigations such as skin biopsy, salivary analysis or the detection of antibodies in serum and cerebrospinal fluid (CSF). The CSF protein was higher for bat rabies (79; IQR 52, 109 mg/dL) than dog rabies (31; IQR 26, 48, mg/dL,; p=0.012). In summary, bat-acquired rabies is associated with more local symptoms, tremor, and myoclonus, whereas dog-acquired rabies has more hydrophobia, aerophobia, and pharyngeal or facial spasms. We speculate that these clinical differences may reflect differences in the route of viral entry of the rabies virus variants into the nervous system because fundamental differences in the neuropathology or viral distribution have not been identified. Bat rabies virus variants may also have greater effects on the blood-CSF barrier by affecting endothelial cell permeability through unknown mechanisms.

CO.07
IMMUNE RESPONSES IN HUMAN CNS DURING RABIES VIRUS INDUCED ENCEPHALITIS

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Understanding the mechanisms of rabies virus clearance from the CNS will be a significant step towards the treatment of clinical rabies. Although a few animal studies have provided insight about immune responses in the CNS during rabies encephalitis, data about the same are very scarce for humans. In our study, formalin-fixed, paraffinembedded, central nervous system (CNS) tissues from patients who succumbed to rabies following infection with RABV variants common to the tricolored bat (*Perimyotis subflavus*) in the United States, canine RABV present in Haiti, and canine RABV from Afghanistan, as well as tissues from a patient who recovered from clinical laboratory confirmed rabies following cat bite in Colombia, but succumbed as a result of secondary medical intervention, were subjected to comparative immunohistological evaluations identifying particular immune cell populations associated with rabies encephalitis. A non-encephalitic brain from an influenza patient was used as a negative control. Populations of B-cells (CD20), T-cells (CD3), and macrophages (CD68), as well as the presence of rabies virus antigens were compared using a semi-quantitative scale. In addition, gene expression analyses, using the Human Antiviral Response RT^2 Profiler™ PCR Array, focusing on the expression of 84 key genes involved in the innate antiviral immune response, were performed. No rabies virus antigens were detected in the brain tissue of the patient who survived clinical rabies or in the control brain. T-cells and macrophages were abundant in the parenchyma in all rabies patients, but B-cells were detected only in the perivascular tissue of the putative rabies survivor, and rabies patients infected with canine RABVs. Few T- and B- cells, and only local microglia cells, were detected in the influenza patient. Differences in the expression of multiple genes associated with innate immunity, as well as inflammatory responses, were identified, suggesting the importance of their role in rabies encephalitis and viral clearance from CNS tissue.

CO.08
FIRST *MYOTIS LUCIFUGUS* RABIES VIRUS VARIANT DETECTED IN A HUMAN

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A 63 year old male from Barnstable County, MA was evaluated at Massachusetts tertiary care facility for possible stroke and encephalitis. Although the patient's first symptoms were joint stiffness, within 2 days the patient was exhibiting signs of hydrophobia, and acute progressive encephalitis. Serum, CSF, nuchal (skin) biopsy, and saliva samples from the patient were sent to CDC for rabies diagnostic testing. No rabies virus IgG or IgM antibodies were detected in serum and CSF by the indirect fluorescent antibody (IFA) test, and no viral neutralizing antibodies were detected in the serum or CSF samples by the rapid fluorescent focus inhibition test (RFFIT). Rabies virus antigen was detected in nuchal biopsy samples using direct fluorescent antibody (DFA) test. Nested (and heminested) RT-PCR amplicons were produced from skin and saliva using multiple rabies virus nucleoprotein gene primers sets. Sequence analysis of the entire nucleoprotein gene and comparisons with samples in the CDC database and Genbank indicated that the rabies virus variant was associated with *Myotis sp* bats. Further analysis of phylogenetic trees (1000) by Neighbor Joining, Maximum Parsimony and Maximum Likelihood indicated the variant was most parsimonious with the common "little brown bat" *Myotis lucifugus*. Postmortem brain tissues were positive for rabies virus antigen by the direct fluorescent antibody test. Antigenic typing with monoclonal antibodies to the rabies virus nucleoprotein was consistent with the previous results of a bat rabies variant, but lacked the resolution of genetic typing methods. Sequence analysis of the RT-PCR amplicons from the complete nucleoprotein gene were consistent with the previous findings of the variant seen in *M. lucifugus*. Although *M. lucifugus* is common in the US and frequently has had known encounters with humans and animals, this is the first documented case of this rabies virus variant in a human. In contrast to this unique finding, the rabies virus variant associated with a solitary bat with rare known human or animal encounters *Lasionycteris noctivagans (silver-haired bat)* has been responsible for most human rabies cases in the USA over the last 2 decades.