DIRECT BACTERIAL ENTRY INTO THE BRAIN: BURKHOLDERIA PSUEDOMALLEI AND THE OLFACTORY NERVE

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Melioidosis is a potentially fatal disease endemic to northern Australia which is caused by the bacteria *Burkholderia pseudomallei*. In the Northern Territory in 2009/2010, the disease had an incidence of 50-100/100,000*. There is a mortality rate of around 14%. **Purpose:** It is unclear how the bacteria penetrate the brain and cause the neurological form of the disease. One potential route is via the olfactory and trigeminal nerves of the nasal cavity. **Methods:** We inoculated mice with *B. pseudomallei* for 24-48 hrs (n=6 animals at each timepoint) and analysed them for localisation of the bacteria within the nasal cavity. **Results:** Two levels of infection occurred. In widespread major infection, the olfactory epithelium rapidly responded by degradation and an immune response which limited the penetration of bacteria in the mucosal layer. In contrast, in low level minor infection, very small numbers of bacteria penetrated the olfactory mucosa without causing degradation of the epithelium or an obvious immune response. In both levels of infection, the bacteria penetrated and colonised the olfactory and trigeminal nerves and migrated directly into the olfactory bulb within central nervous system. Importantly, we have previously determined that the cells of the immune system, macrophages, are largely excluded from olfactory nerve bundles. We instead propose that the olfactory glia are the primary cells responsible for the phagocytosis of bacteria within the olfactory nerve and act to limit the spread of infection. **Conclusion:** These results demonstrate that *B. pseudomallei* enters the CNS via the olfactory and trigeminal nerves within 24 hr after inoculation.

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