Attachment 2:4:(a):13

Abstract #86

Rickettsial Infections and their Clinical Presentations in the Western Province of Sri Lanka: A Hospital Based Study

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Introduction: Rickettsial infections are re-emerging in Sri Lanka. A study of the geographical distribution of rickettsial infections, their clinical manifestations, and their complications would facilitate early diagnosis.
Methods: Thirty-one patients who fell into case definition of rickettsial infections from the Western Province of Sri Lanka were studied for rickettsial species, clinical manifestations, and complications. Indirect fluorescent antibody assays (IFA) were carried out using antigens of *Rickettsia conorii*, *Rickettsia typhi*, and *Orientia tsutsugamushi*. Confirmed and presumptive cases, those with past exposure and serological cross reactivity were defined according to standard CDC serological criteria.
Results: Of 31 patients with possible rickettsioses, 29 (94%) fell into the categories of confirmed, presumptive, or exposed cases of acute rickettsial infections [scrub typhus(ST) in19 (66%), spotted fever group(SFG) in 8 (28%)]. Early acute infection or past exposure was 2 (7%), cross reactivity of antigens or past exposure to one or more species was 9 (31%). Seventeen out of 19 (89%) patients with ST had eschars. Nine out of 29 (32%) patients had a discrete erythematous papular rash; 7 caused by SFG, 2 by ST. Severe complications were pneumonitis 8 (28%), myocarditis 5 (17%), deafness 5 (17%) and tinnitus 4 (14%). The mean duration for illness before onset of complications was 12.1 (SD:0.9) days. All patients except one had good clinical recovery with doxycycline, chloramphenicol, or with a combination.
Conclusion: In a region representing the low country wet zone of Sri Lanka, the main rickettsial infection seems to be *Orientia tsutsugamushi*. Delay in diagnosis may result in complications. All species responded well to current treatment.

Abstract #87

Coxiella burnetii Nine Mile Phase II Infection of Wild Type and SCID Mice as Models of Pulmonary Q Fever

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Q fever, caused by *C. burnetii,* is a zoonotic infection that presents as an acute, self limiting pneumonia in humans. Infection is commonly acquired via inhalation Previous studies with Nine Mile phase II (NMII) *Coxiella* have focused mainly on intraperitoneal infections and it was concluded that this variant does not cause significant disease in either immunocompetent or immunocompromised mice. However, we demonstrate here that intratracheal inoculation of phase II into immunocompetent mice results in a lung infection that persists for weeks and inoculating immunocompromised SCID mice caused a lethal infection.
SCID and BALB/c mice were infected with doses of *C. burnetii* between $10^5 - 10^9$ genome copies via intratracheal inoculation. Bacteria replicated in the lungs and spleens of both mouse strains. Splenomegaly was marked in the SCID mice by day 25 p.i. and, by day 32, regardless of the initial dose, spleens were all enlarged. SCID mice also exhibited ruffled fur and huddling. Wild type mice exhibited transient symptoms early in infection. By 32 days p.i. SCID mice were moribund and were euthanized. The accumulation of $CD4^+$ and $CD8^+$ T cells peaked in the wild type mice between 16 and 25 days. This accumulation corresponded to clearing of bacteria from the lungs of wild type mice. *Coxiella* persisted in the lungs of wild type mice receiving a high dose of bacteria for at least 78 days post infection.
We have demonstrated that NMII, delivered by an intratracheal route, can be used as a model of acute pulmonary Q fever in mice and causes a lethal infection in immunocompromised mice. NMII can replicate in the lungs of both immunodeficient and wild type mice and persist for over 9 weeks in the lung suggesting that the infection may not be completely cleared in an immunocompetent host.