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Of goats and humans; the societal costs of the Dutch Q fever saga

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Background: In the Netherlands, more than 4.000 human Q-fever cases and 19 deaths were notified between 2007 and 2010 during an unprecedented outbreak, implicating dairy goats as the main source. Veterinary control measures were taken reluctantly as economic damage was feared. Measures were introduced late, gradually increased and culminated in the culling of approximately 60.000 goats, 3 years after the outbreak began. Following acute Q fever 40% of working Dutch patients reported long-term (>1 month) sick-leave. One to two years after initial infection 40% of patients reported persisting physical symptoms and 60% a severely affected health status. Furthermore their general Quality of life (QoL) was affected in 44.9% of casus and 43.5% suffered from persisting fatigue. Growing numbers of Dutch patients are reported to develop late complications; Q fever fatigue syndrome or chronic Q fever, with implicit high costs to society. We estimated the societal cost of the outbreak by combining data from veterinary and human health sector sources.

Methods: Our cost data are based on real cost data on QoL, sick leave, health care use, complaints from patients notified in 2007 and 2008 and data from reports on the economic consequences of Q fever. Cost data were modelled and projected based on Q fever information from literature and Dutch data.

Results: The estimated projected societal costs of the Q fever outbreak amount to approximately 250-600 million Euros. Human costs account for 85%, are spread out over a decade and delayed. The largest costs are due to loss of QoL followed by productivity loss. Veterinary costs vary between 6% and 15% (depending on costs included) are much smaller but immediate.

Conclusion: Q-fever poses a serious persisting long-term burden on patients and society. The real impact of a zoonosis outbreak only becomes apparent when combining human health, societal and animal costs. Veterinary cost are immediate and therefore more apparent although proportionally small. Because of a slow trickle down effect human cost and societal implications tend to be underestimated. Finding the balance between economic veterinary interests and human health remains a challenge when dealing with future outbreaks of zoonotic diseases.

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Carriage of *Corynebacterium sp.* among contacts diphtheria in a low resource area in Indonesia (interim report)

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Background: In 2011, outbreak of diphtheria had occurred in East Java Province, Indonesia. Little is known about factors associated with the outbreak. Carriage of *Corynebacterium diphtheria* might play a role to the epidemiology of diphtheria. This study aimed to investigate the risk factors related to *Corynebacterium diphtheria* carriage among contacts diphtheria.

Methods: Screening of contacts diphtheria was conducted during February to November 2011 in 5 sub districts in Malang city, Indonesia. Throat swabs were taken from contacts diphtheria in 2 playgroups, 10 kindergartens, 10 elementary schools, 5 high schools, and 5 primary health cares. The swabs were inoculated to PAI culture medium and incubated at 37°C overnight. Metachromatic staining (Neisser method) was carried out to the colony to identify *Corynebacterium sp.* Demographic data including gender, age, address, and screening location were collected.

Results: We screened 1739 contacts diphtheria in this study. 469/1739 (27%) were *Corynebacterium sp.* positive. Logistic regression analysis showed that patients at the age of 19 and above and kindergarten screening location were associated with the carriage of *Corynebacterium sp.* ($p < 0.01$ and $p < 0.05$, respectively).

Conclusion: Contacts diphtheria in Malang city was at risk to be carriage of *Corynebacterium sp.*

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Monkeypox detection in maculopapular lesions in two young Pygmies in the Central African Republic

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Background: In June 2010, two Pygmy boys living in a settlement in the deep forest area of the southern Central African Republic (CAR) were found to have diffuse maculopapular lesions associated with pustules and crusts after eating a wild rodent.

Methods: High density resequencing microarray (RMA) developed at the Pasteur Institute was used with success to the detection of a large panel of pathogens such as *Monkeypox virus* directly from a child skin sample, respiratory and influenza viruses, rhabdovirus, arboviruses including Dengue, Chikungunya and West Nile viruses. In this study the RMA were used for the identification various types

of infectious diseases responsible for the presence of maculopapular lesions in the two young pygmies from RCA.

Results: Laboratory investigations were performed on samples of sera, scabs and on a biopsy from the brain of a young mouse after inoculation with ground scab samples. Monkeypox virus (MPV) was detected by qPCR. After sequencing of A-type inclusion gene (ATI), the phylogenetic tree indicated that the strain was identical with the Zaire strain circulating in central Africa. The strain was also found to be identical to a strain associated with a small outbreak occurring in 2001 in a Bantu family few days after eating a dead monkey and living in a village at the border of the CAR and Zaire, 480 km from the cases reported here. DNAs extracted from the brain of two different young mice inoculated with samples from the two outbreaks were amplified and hybridized on RMA. This allowed us to detect two sequences of haemagglutinin and DNA polymerase DNA-dependent genes of the monkeypox genome in both tested samples. Call rates values of 91 and 94% respectively for the haemagglutinin and the DNA dependent DNA polymerase genes were obtained for the 2001 and 2010 samples. Sequence analysis allowed to confirm the viral genotype (Zaire clade).

Conclusion: We describe the occurrence of two small typical outbreaks of MPV occurring at a 10-year of interval in different populations (Pygmies and Bantus) living in the southern CAR and demonstrate that they were due to the same monkeypox strain, belonging to the Zaire genotype.

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Clinical profile of scrub typhus

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Background: Scrub typhus is an acute febrile illness which presents mainly as multiorgan dysfunction. It is caused by *Orientia tsutsugamushi*.

It is found in India but there is less data available. Here we studied the clinical presentation, complications, treatment and outcome of scrub typhus in a tertiary care hospital in south India.

Methods: A prospective observational study of scrub typhus positive patients admitted in kasturba hospital, Manipal during a period of 1 and half yrs meeting the following inclusion criteria was done: acute febrile illness with IgM scrub ELISA positive or Weil Felix > = 1:160 titre or presence of eschar. Malaria, dengue, enteric fever and leptospira positive patients were excluded. Detailed history, Clinical examination, laboratory parameters, Weil Felix test and IgM ELISA were done on all patients.

Results: A total of 300 cases were included in the study. 210 patients (70%) were in the age group 40 to 50yrs, majority were males who were agriculturist. Primary symptoms at the time of presentation were fever < 1 week in 258(86%) with myalgia and headache in 270(90%) with predominant signs being lymphadenopathy in 225(75%) and hepatosplenomegaly in 201(67%) 162(54%) had eschar and rash was seen in 90(30%). Most common site of eschar was axilla and groin. Complications were renal fail-

ure in 57 (19%), ARDS in 87(29%), thrombocytopenia in 204(68%) hepatitis in 135(45%) meningoencephalitis in 36(12%), myocarditis in 21(7%). Rare complications being focal neurological deficit in 6 (2%). Interesting observation was high ALP with mild elevations in AST/ALT. 269 patients were treated with doxycycline, and majority showed defervescence of fever within 48 hrs after starting doxycycline. Mortality was 3% (9 patients).

Conclusion: Sporadic cases occurred throughout the year with escalation noticed in rainy season, the months of July to November. Majority were males. Fever with myalgia and lymphadenopathy was common. Eschar was pathognomonic. Thrombocytopenia, hepatitis, Acute respiratory distress syndrome and Multiorgan dysfunction were the most common complications. Majority showed improvement with doxycycline. Early diagnosis and treatment had favourable outcomes with very low mortality.

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Surveillance of DENV in a city from São Paulo from 2006 to 2011: the emergence of DENV-3 and DENV-4 and the reemergence of DENV-2 and DENV-1

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Background: Dengue belongs to the *Flavivirus* genus and is the most common arboviral infection worldwide. It is caused by four antigenically different serotypes (DENV 1-4). Dengue infection may be asymptomatic and lead to undifferentiated fever, dengue fever or evolve to dengue hemorrhagic fever or dengue shock syndrome. São José do Rio Preto, located at northwestern portion of São Paulo State, has been presenting autochthonous transmission of DENV since 1990. In our study we describe the emergence of DENV-3 and DENV-4 and the reemergence of DENV-2 and DENV-1 in São José do Rio Preto/SP – Brazil in a period of five years.

Methods: Blood samples of patients that were NS1 positive or presenting dengue like symptoms were tested by a Multiplex-RT-PCR with *Flavivirus* generic primers based on non-structural protein (NS5), followed by Nested assays with species-specific primers for the identification of DENV serotypes.

Results: We analyzed 1519 blood samples in five years: 612 in 2006, 94 in 2007, 313 in 2008, 10 in 2009, 65 samples in 2010 and 425 samples in 2011. The major dengue serotype circulating during the 2006 and 2007 epidemics was DENV-3, which is an indication of its recent introduction in the city. Among the DENV positive patients in 2008, 90 were infected by DENV-2, suggesting the reemergence of this serotype, which has been circulating in São José do Rio Preto since 1998. DENV-1 was detected in two patients in 2008, in four patients in 2009 and in the majority of patients in 2010 and 2011.

Conclusion: DENV-1, DENV-2 and DENV-3 are co-circulating in the city and these data suggest a dynamical circulation with a continuous emergence and reemergence of serotypes. The recent introduction of DENV-4 is extremely alarming. When a new serotype is introduced in one site, it is going to find a susceptible