

Laboratory for Clinical Research on Infectious Diseases

Research Group

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Research Projects

The research activities in our department aim to investigate 1) the epidemiology, pathogenesis and prevention by vaccines of pneumonia and invasive bacterial infections. We also seek to understand 2) the pathogenesis of dengue illness and 3) the mechanism of protein secretion systems of pathogenic bacterial. In addition, our group is registered as a member of the World Health Organization (WHO)/Global Outbreak Alert & Response Network (GOARN) and will join the outbreak response team in the global effort to control emerging and re-emerging infectious diseases.

1) Epidemiology and pathogenesis of pneumonia and invasive bacterial infections and the prevention by vaccines

1. Study of pneumonia in Thailand

We have conducted a study project entitled "Surveillance of emerging respiratory infections and analysis of mechanism of secondary bacterial pneumonia in Thailand". We could investigate how virus-host-bacteria interactions promote secondary bacterial infections in pediatric patients with pneumonia. In 2009, we could also examine the clinical features of 24 cases of pandemic H1N1 influenza-associated severe community-acquired pneumonia in adults at Buddachinaraj Hospital, Phitsanulok.

2. Clinical applications of the 23-valent pneumococcal polysaccharide vaccine (PPV) and the development of new pneumococcal vaccines

a) Clinical application of 23-valent PPV

We found that the combined vaccination program of PPV and influenza vaccine (IV) reduced the incidence of acute exacerbation in patients with chronic obstructive pulmonary diseases (Vaccine, 2008). An open-label, randomized study was conducted involving 786 Japanese subjects older than 65 years of age receiving a routine IV.PPV vaccination significantly reduced the number of admissions and medical costs for all-cause pneumonia for subjects older than 75 years of age. We also started a project in 2008 that examines the effects of PPV in combination with IV on long-term-care residents. Our goal is an implementation of nationwide routine vaccination of the elderly in Japan.

b) Development of a nasal mucosal pneumococcal vaccine

Pneumococcal surface protein A (PspA) is known to elicit protective antibodies in animals. We demonstrated the effects of PspA plus TLR agonist on bacterial clearance in a mouse model of pneumococcal pneumonia (Vaccine, 2009). In addition, we also demonstrated that PspA nasal vaccine was effective in a mouse model of secondary pneumonia after influenza virus infection.

3. Research on *Streptococcus suis* infections prevalent in Thailand

Streptococcus suis, an important zoonotic pathogen, causes invasive infections such as meningitis in humans who are in close contact with infected pigs or contaminated pork-derived products. Because of a traditional custom of consuming raw pork of blood in northern Thailand, the number of human cases is rapidly increasing in this country. We demonstrated the relationships between the clinical manifestations of serotype 2 infections and the genotypic profiles of isolates, and also reported the clonal dissemination of serotype 14 in human infections, which were rare in the past periods (Figure 1). We are currently developing an epidemiological study of *S. suis* infections in Phayao Province as a project of RIMD, Osaka University (RCC-DMSc).

2) Mechanisms with which dengue virus infections lead to thrombocytopenia

Dengue illness has become a major public health concern particularly in tropical countries. From our accumulated clinical studies in the Philippines, we recently found, in an *ex vivo* setting, that patients with thrombocytopenia during acute phase secondary dengue virus infections showed increased phagocytosis of platelets

(AJTMH, 2009). Since we found that IVIG treatment did not significantly hasten the recovery from thrombocytopenia in such patients (AJTMH, 2007), this suggests that Fc γ receptor is not involved in platelet phagocytosis by macrophages. We are now currently elucidating novel mechanism of platelet phagocytosis in this disease.

3) Protein secretion systems of pathogenic bacteria

Development of bacterial infections requires many virulence factors. Most of them are proteins secreted from pathogenic bacteria, therefore, it is essential to study the mechanisms of protein secretion systems in pathogenic bacteria during infection process. In our laboratory, food-borne pathogen, *Vibrioparahaemolyticus* and a causative agent of pneumonia, *Streptococcus pneumoniae*, are used to study on their protein secretion systems and secreted virulence factors.

4) Response to emerging and re-emerging infectious diseases

The objective of GOARN is to combat the international spread of such outbreaks by ensuring that appropriate technical assistance rapidly reaches affected areas and by promoting long-term epidemic preparedness. Our group is registered as a member of GOARN. Our team will join the WHO-organized response team when there is an outbreak of infectious diseases in developing countries.

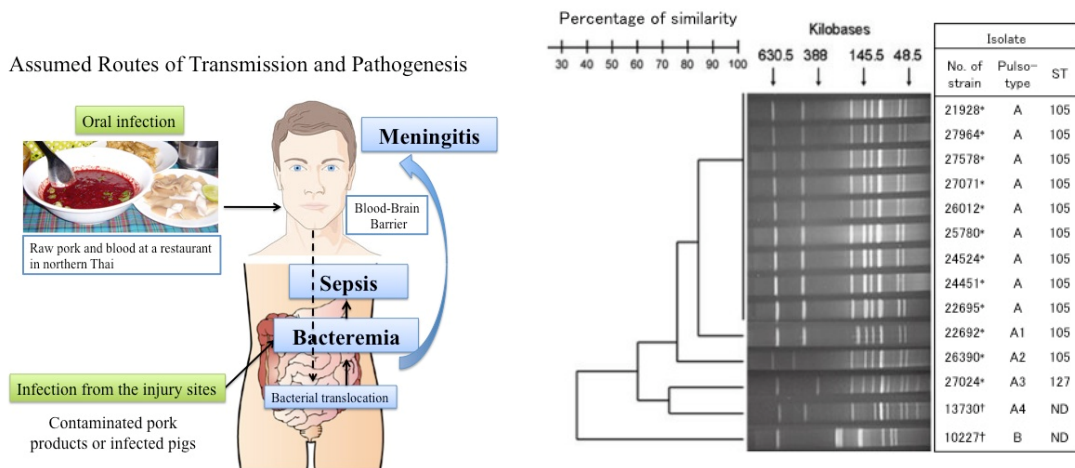


Figure 1. Assumed routes of transmission and pathogenesis of *S. suis* infection, and the clonal dissemination of serotype 14 infections in Thailand (J Med Microbiol, 2009).

Recent publications

1. Kerdsin, A., Oishi, K., Sripakdee, S., Boonkerd, N., Polwichai, P., Nakamura, S., Uchida, R., Sawanpanyalert, P., Dejsirilert, S. (2009) Clonal Dissemination of *Streptococcus suis* serotype 14 in Thailand. *J Med Microbiol* **58**:1508-1513.
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3. Akeda, Y., Okayama, K., Kimura, T., Dryselius, R., Kodama, T., Oishi, K., Iida, T., Honda, T. (2009). Identification and characterization of a type III secretion-associated chaperone in the type III secretion 1 of *Vibrioparahaemolyticus*. *FEMS Microbiol Lett.* **296**:18-25.
4. Oma, K., Zhao, J., Ezoe, H., Akeda, Y., Koyama, S., Ishii, K. J., Kataoka, K., Oishi, K. (2009). Intranasal immunization with a mixture of PspA and a Toll-like receptor agonist induces specific antibodies and enhances bacterial clearance in the airways of mice. *Vaccine* **27**:3181-3188.
5. Chen, M., Ssali, F., Mulungi, M., Awio, P., Yoshimine, H., Kuroki, R., Furumoto, A., Tanimura, S., Kityo, C., Nagatake, T., Mugenyi, P., Oishi, K. (2008) Induction of opsonophagocytic killing activity with pneumococcal conjugate vaccine in human immunodeficiency virus-infected Ugandan adults. *Vaccine*. **26**:4962-4968.
6. Furumoto, A., Ohkusa, Y., Chen, M., Kawakami, K., Masaki, H., Sueyasu, Y., Iwanaga, T., Aizawa, H., Nagatake, T., and Oishi, K. (2008). Additive effect of pneumococcal vaccine and influenza vaccine on acute exacerbation in patients with chronic lung disease. *Vaccine*. **26**:4284-4289.