

# Invasive *Staphylococcus aureus* infections

## AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien  
vid Göteborgs universitet kommer att offentligen försvaras i  
föreläsningssalen, Infektionskliniken, Sahlgrenska  
Universitetssjukhuset/Östra

**Fredagen 18 december 2009 kl. 13.00**

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Avhandlingen baseras på följande delarbeten:

- I. Jacobsson G, Dashti S, Wahlberg T, Andersson, R.  
The epidemiology of and risk factors for invasive *Staphylococcus aureus* infections in western Sweden.  
Scand J Infect Dis 2007;39(1):6-13.
- II. Jacobsson G, Gustafsson E, Andersson R.  
Outcome for invasive *Staphylococcus aureus* infections.  
Eur J Clin Microbiol Infect Dis 2008;27(9):839-848.
- III. Jacobsson G, Colque-Navarro P, Gustafsson E, Andersson R, Möllby R.  
Antibody responses in patients with invasive *Staphylococcus aureus* infections.  
Submitted 2009.
- IV. Colque-Navarro P, Jacobsson G, Andersson R, Flock JI, Möllby R.  
Antibody levels against eleven *Staphylococcus aureus* antigens in a healthy population.  
In manuscript.



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# Abstract

*Staphylococcus aureus* is a leading cause of septicaemia-related death.

The aims of this thesis were to describe the epidemiology of invasive *Staphylococcus aureus* infections (ISA), the clinical course, and serological response in ISA in a prospective, population-based study. The antibody response was compared with the serological findings in healthy individuals.

During two years 170 episodes of ISA were registered, with an incidence of 33.9 cases/100,000/year. Haemodialysis (relative risk 291) and peritoneal dialysis (relative risk 204) patients were at the highest risk. Soft tissue infections, bacteraemia without focus, infections of intravenous lines, and joint/bone infections were the most common diagnoses. The spectrum of signs and symptoms was wide, with nearly a quarter of the patients being afebrile.

The mortality rate was 19.1% (28-day mortality), with an annual population mortality of 5.9/100,000. Patients with complicated bacteraemia (32% of all episodes) had a mortality rate of 32%, and patients with severe sepsis (30% of all episodes) 54%. Patients with bacteraemia without focus, patients with respiratory infections, and patients with endovascular infections had the highest mortality figures.

Only severe sepsis and low systolic blood pressure were independent factors for mortality in a multivariable regression model. We found a relapse rate of 9.3%, and a rate of remaining symptoms after the antibiotic treatment had ended of 34%. Sequelae were seen among 60% of the patients with arthritis.

The frequency of different *agr*, accessory gene regulator, groups within the bacterium, was not correlated to the disease presentation.

The antibody response in ISA showed a great variability. Patients with a fatal outcome produced lower amounts of antibodies to all antigens, and significantly to four antigens (teichoic acid, lipase, enterotoxin A, and scalded skin syndrome toxin). The same trend was noted for patients with a complicated course of infection.

Healthy carriers of *S. aureus* in the nares had higher levels of antibodies to all eleven tested antigens, and significantly to five (teichoic acid, lipase, enterotoxin A, toxic shock toxin-1, and extracellular adherence protein) than non-carriers. Ages over 65y showed only slightly lower levels.

*Keywords:* *Staphylococcus aureus*, epidemiology, risk factors, clinical presentation, mortality, recurrence, sequelae, *agr*, serology, colonization.