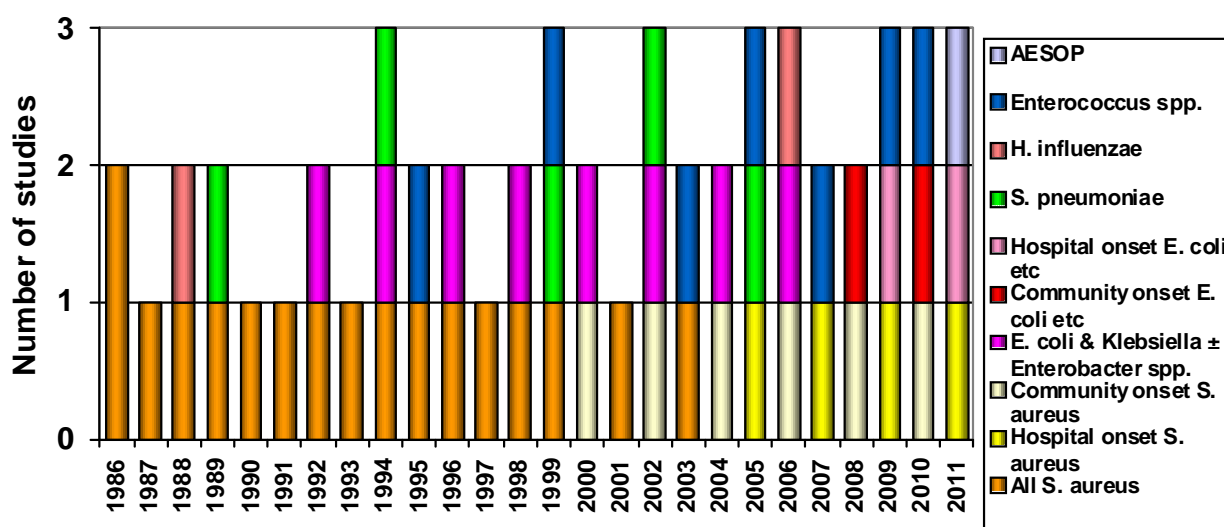


# AGAR SURVEILLANCE

## History

Agar commenced resistance surveillance studies in 1985 as the Staphylococcus Awareness Program (SAP), sponsored by Eli Lilly Australia Pty Ltd. Its focus initially was on resistance in *S. aureus*, although there were occasional surveys into other pathogens of interest such as *S. pneumoniae* and *H. influenzae*. The first survey into enteric Gram-negatives began in 1992, and focussed on *E. coli* and *Klebsiella* species. Later, *Enterobacter* species were added to the enteric Gram-negatives of interest. With the emergence on vancomycin-resistant enterococci in Australia in the mid-1990s, occasional *Enterococcus* species surveys commenced in 1995.

The SAP originally involved 14 capital city teaching hospitals around Australia. The numbers of laboratories has gradually expanded, in the last decade, private pathology laboratories have joined in order to capture data from isolates in the community. There are currently 30 member laboratories contributing to surveillance studies in AGAR.



## Surveillance Schedules

Schedule	Pathogen	Timing
<i>Biennial</i>	Hospital <i>S. aureus</i>	Odd years from 2005
	Community <i>S. aureus</i>	Even years from 2000
	<i>E.coli/ Klebsiella/ Enterobacter</i> (+ <i>Acinetobacter</i> 2006)	1992 - 2006
	Hospital <i>E.coli/ Klebsiella/ Enterobacter</i>	Odd years from 2009
	Community <i>E.coli/ Klebsiella/ Enterobacter</i>	Even years from 2008
<i>Triennial</i>	<i>S. pneumoniae</i> (last survey 2007)	
	<i>Enterococcus</i> species (all sources)	1995 - 2007
<i>Annual</i>	<i>S. aureus</i> (all sources)	1996 - 1999, 2001, 2003
	<i>Enterococcus</i> species (all sources)	2009 - 2010
<i>Occasional</i>	<i>H. influenzae</i> (last survey 2006)	
<i>Continuous</i>	Vancomycin-resistant <i>Enterococcus</i> spp. (NaVREN)	2002 onwards
	Blood culture isolates of <i>S. pneumoniae</i>	1999 - 2005
	Blood culture isolates of <i>Enterococcus</i> species	1999 - 2005
	AESOP: blood culture isolates of <i>Enterococcus</i> species with outcome and typing	2011 onwards

## Resistance Problems Addressed by AGAR Surveillance

### *Staphylococcus aureus*

#### Hospital-onset

Methicillin-resistant strains of *S. aureus* (MRSA) have been major hospital-acquired pathogens in Australia for 30 years, causing in particular post-operative wound infections prosthetic joint infections and septicaemia from intravascular lines. Multi-resistance (resistance to multiple antibiotic classes) has been a hallmark of these strains, as has their high propensity for causing cross infection. Antibiotics for treatment are restricted to last line agents such as vancomycin, as MRSA are resistant to all  $\beta$ -lactam antibiotics which would otherwise be the drugs of choice. The great majority are due to two closely related clones (called AUS-2 and AUS-3), but recently Australia has observed the introduction of a new clone from the UK into some Australian hospitals (called EMRSA-15 there), which do not harbour as many antibiotic resistances.

#### Community-onset

Community strains of MRSA first emerged in Australia in northern Western Australia more than 15 years ago. Since that time three major clones have become prominent in the community (WA-1 = ST1, SWP = ST30, and QLD = ST93) causing mostly minor skin infections, but occasionally causing serious invasive disease. Two of these three clones possess the Panton-Valentine leukocidin, which is associated with severe forms of infection in soft tissue, necrotising pneumonia and large vessel venous thrombosis. The community clones of MRSA are generally susceptible to classes of antibiotics other than  $\beta$ -lactams. Recently we have detected the arrival of USA300, a community-associated MRSA clone which has had a major impact in the United States

### **Enteric Gram-negatives**

*E. coli* and *Klebsiella* species are common causes of both hospital and community-acquired infection. Both of these species have a tendency to accumulate resistances to different antibiotic classes, especially  $\beta$ -lactams which are considered the drugs of choice. Particular problematic are strains with extended-spectrum  $\beta$ -lactamases (ESBLs), which hydrolyse third- and fourth-generation cephalosporins, used for more serious infection requiring treatment in hospital. Such strains are frequently resistant to other useful antibiotics, including aminoglycosides, fluoroquinolones and co-trimoxazole.

It is now apparent that the genes encoding ESBLs can spread to other enteric Gram-negative species, especially *Enterobacter* species which are important hospital-associated pathogens, and act as an unrecognised reservoir for these genes. For this reason, this genus will continue to be monitored. The last few years has seen the emergence of ESBLs of the CTX-M type in the community, prompting a switch to annual testing of this organism group, focussing on hospital-onset in the odd years and community-onset in the even years.

Last line antibiotics such as carbapenems are often required for treatment of infections caused by ESBL-producing strains. Hence, spread of resistance to carbapenems is feared, and outbreaks have recently occurred in at least two Australia hospitals.

### ***Enterococcus* species**

Enterococci are minor pathogens, more troublesome in hospital practice, and in complex surgical patients can cause serious infections including septicaemia. They are naturally resistant to many antibiotic classes including cephalosporins, and some species have acquired resistance to penicillins. Vancomycin-resistant strains emerged in the mid-1990s in Australia and are now endemic in some hospitals, while cause occasional outbreaks. They have one of the highest propensities for causing cross infection of all the hospital-acquired pathogens.

In 2010 it was agreed that, given the upsurge in vancomycin-resistant enterococci across the country, that we should intensify surveillance. Surveillance become focussed on blood culture isolates of *Enterococcus* species, and typing and outcome data began to be collected under the Australian Enterococcal Sepsis Outcome Program (AESOP).

**The following species are currently not focus of AGAR studies as resistance rates appear to have stabilised.**

### ***Haemophilus influenzae***

The species was previously important as a cause of invasive childhood disease, but since the introduction of the conjugate Hib vaccine into the routine childhood immunisation schedule has become a relatively rare cause of serious infection. By contrast it is a significant pathogen in the community causing otitis media, sinusitis and acute exacerbations of chronic bronchitis. Resistance to the standard treatment (amoxicillin) is common, usually through a  $\beta$ -lactamase, but more recently strains with a different mechanism of resistance have emerged which makes them resistant to cephalosporins and amoxicillin-clavulanate as well, restricting the choice for the management of community infections.

### ***Acinetobacter* species**

*Acinetobacter* species, especially *A. baumannii*, have become a significant clinical problem in intensive care units in some Australia hospitals. They cause septicaemia and ventilator-associated pneumonia in particular. *A. baumannii* and related species have a high propensity for developing multi-resistance, including to last-line agents such as the carbapenems. Sometimes they are only susceptible to potentially toxic antibiotics such as colistin.

### ***Streptococcus pneumoniae***

*S. pneumoniae* is one of the most important community-associated pathogens; causing both minor (otitis media, sinusitis, bronchitis) and serious invasive disease (septicaemia and meningitis). In the 1990s resistance to penicillin and other  $\beta$ -lactams emerged in Australia, as well as to other antibiotic classes used to treat community infections such as macrolides, tetracyclines and co-trimoxazole.  $\beta$ -lactam resistance is very problematic for the treatment of meningitis, and vancomycin must be used.