A Report on the Emergence of Community-Acquired Methicillin-Resistant *Staphylococcus aureus* (CA-MRSA) in British Columbia

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Contributors

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Executive Summary

- In recent years, Community-Acquired Methicillin-Resistant S. aureus (CA-MRSA) has emerged within numerous communities in North America.

- CA-MRSA can cause clinical disease such as boils, impetigo, wound infection and invasive infection and may do so in people who have had no connection to the health care setting. Recognizable groups (e.g., IDUs) are at higher risk but CA-MRSA is effecting a large number of people without such recognizable risk factors.

- Most CA-MRSA comprise a recognizable genotype (CMRSA-10 in Canada which appears equivalent to the USA-300 strain), carry a resistance gene cassette which confers resistance to methicillin (and cloxacillin) but generally not to clindamycin and fluoroquinolones and carry other new genes which code for virulence factors.

- CA-MRSA was considered rare in BC as recently as 2000 but appears to have emerged quickly over the past 12-24 months. This is supported from observations from a number of sites. CA-MRSA isolates with the above-mentioned biological markers have been characterized from a broad distribution of communities in BC.

- More needs to be learned about modifiable risk factors, optimal therapy and the efficacy of various possible control measures in the community and health care setting.

- Physicians should be encouraged to drain staphylococcal abscesses as primary therapy and to culture drained material so as to have a better understanding of therapeutic options should antibiotics be required.

- Planned public messaging around hand-hygiene and antimicrobial stewardship may prove helpful.
Background:

In the past decade, new strains of methicillin-resistant Staphylococcus aureus (MRSA) have emerged in the community and sometimes caused aggressive infection in otherwise healthy people (1-8) This has been increasingly reported from other Canadian centres(9).

Methicillin resistance in S. aureus results from production of altered penicillin binding protein (PBP2a)(10-13) This protein is encoded by the mecA gene within the staphylococcal cassette chromosome (SCCmec). The cassette also contains regulatory genes.(11,14) There are five recognized variants of the SCCmec elements. (15,16) SCCmec types II and III are comparatively large, contain multiple determinants of resistance to non-beta-lactam antibiotics and account for most observed multi-drug resistant nosocomial MRSA. Horizontal transfer of these large SCCmec elements is thought to be less efficient than for the smaller type IV. (11,17-21)

Type IV SCCmec elements lack other resistance determinants but their smaller size may make them more efficient at horizontal transfer in the community to methicillin-susceptible S. aureus (MSSA) (16,19,20,22,23) Like MSSA, community-associated MRSA (C-MRSA) is often susceptible to clindamycin, macrolides, co-trimozole, tetracyclines and fluoroquinolones. (24).

These strains may also have unique clonal patterns by PFGE (eg USA300 and USA 400). (25) Some CA-MRSA infections remain clonally related to common nosocomial isolates, suggesting spread of MRSA from the health-care setting. Equally, some community acquired strains are now found in association with nosocomial infections (26,27).

A typical community acquired strain (MW2) has been fully sequenced and contains 19 unique genes encoding virulence factors not found in other S. aureus (28) Many strains of CA-MRSA produce Panton-Valentine leukocidin (PVL). This toxin produces tissue necrosis and leucopenia and may relate to key clinical presentations such as furunculosis and necrotizing pneumonia with a propensity to abscess formation.

While treatment of CA-MRSA can take advantage of the broader range of susceptibilities, there is a hazard in using most of the classes of drugs listed above if there is a risk that the strain is health care associated. Non-antibiotic treatment (eg I and D for abscess) may need to be encouraged. Treatment of colonization is not generally recommended.
The Situation in BC

A group recently met to address the following questions:

1. How many cases of disease are being caused by MRSA in BC?
2. How many of these are community acquired vs facility acquired/associated?
3. How can we maintain ongoing surveillance of trends in this morbidity?
4. What are the major clinical syndromes being seen?
5. Are there modifiable risk factors?
6. When will we know if we have reached a threshold at which empirical therapy for staphylococcal syndromes requiring antibiotic therapy should change?
7. What works to contain this problem in populations?
8. What do we know about the molecular characteristics of cultured S. aureus isolates in this context?
9. What is optimal therapy for CA-MRSA disease?

Various participants provided information on a number of projects which collectively provide a compelling picture of the emergence of CA-MRSA in BC.

Vancouver General Hospital
P. Doyle, S. Reynolds, G Al-Rawahi, S. Porter, W. Bowie and others.

The group is looking at MRSA cases presenting at VGH emergency going back to 2001. Ascertainment is based on wound isolates of MRSA which represent the first identification for that patient. One hundred isolates have been pulled and subjected to testing for PVL, characterization by PFGE and susceptibility testing; SCC MEC typing is pending. Health records are being reviewed but have yet to be linked.

The group is finding isolates which are CA-MRSA 10 (USA-300) beginning in 2002 with dramatic increase in 2004.

All CMRSA 10 isolates tested were PVL+ and no other strains in this ER wound study were PVL+. Most non-CMRSA 10 strains were CMRSA 6.

Canadian Hospital Epidemiology Committee Surveillance (VGH Site)
E. Bryce and Others

CHEC has been following MRSA isolates since 1994. At the VGH site, the proportion of these isolates which are community acquired has increased from 1% in 2001, through 4% in 2003 to 25-28% in 2005. A significant number of the VGH isolates from 2004 are CMRSA-10.

Point Prevalence Studies in Vancouver's Downtown Eastside
Historically, Dr. Rolando Barrios assembled information on Downtown Eastside (DTES) wound cultures in the 1996 and 1997. MRSA was not represented among S. aureus isolates from the community at that time.

During 2000, opportunistic swabbing of DTES residents (E. Bryce, P. Daly and others) yielded 27% carrying S. aureus (of which 7% was MRSA). Type 21 predominated then.

Providence Health Care and the Vancouver Coastal Health Authority are working together to determine the prevalence and associated risk factors of vancomycin-resistant enterococci (VRE) and MRSA positivity in Downtown Eastside (DTES) residents of single-room occupancy hotels, and to evaluate the relationship, if any, to ARO strains (including CMRSA) seen at St. Paul’s Hospital. Associated risk factors of study are personal hygiene, IDU, and history of hospitalizations. Data linkages to Providence Health Care medical records, as well as to existing databases of the BC Center for Excellence in HIV/AIDS drug treatment program and the Community Health Assessment and Safety Evaluation Study will supplement primary data collection and enable assessment of ARO status, history of hospitalization, and IDU use over time. This project is headed by Dr. Gayle Shimokura, with co-investigators Dr. Patty Daly, Dr. Sylvie Champagne, Dr. Marc Romney, Dr. Mark Hull, Dr. Mark Tyndall, and Dr. Chris Sherlock.

**BCCDC Typing**  
*S.H. Goh, J. Isaac-Renton and others.*

BCCDC has received isolates from Prince George, Dawson Creek, Sechelt, Penticton and Royal Jubilee (Vancouver Island). Of 160 MRSA isolates, approximately 70% are CMRSA 10. More than 95% of the CMRSA 10 strains belong to the CDN 0473 PFGE group pattern. These CMRSA 10 strains carry SCCmec IV A and are all PVL positive

**Subset of these isolates from Providence Health**  
*S. Champagne and Providence Health Care MRSA Group*

This group sent isolates to Dr. Goh in April 2005. Their sample represented 57 of the 160 isolates discussed above.

They reviewed susceptibility testing of 150 total MRSA isolates: 76 (52%) from wounds; 35 (23%) from sputum, 39 from other sites. If MRSA isolates were Clindamycin and TMP/SMX resistant, they were considered nosocomial. If susceptible to these agents, they were considered community acquired.

A subset of these MRSA (57 isolates - 77% from wounds, 59% collected in ER) were characterized for SCC mec IV gene, PVL and PFGE. Sixty-eight% of these were PVL
positive or 39 of the 57 isolates sent to Dr. Goh. All PVL + were CA-MRSA 10. Of the 39, 28 were from ER wounds, 6 from non-ER wounds, 2 from blood, 2 from nasal screens and 1 from joint fluid.

**Vancouver Island**  
*P, Kibsey and Others*

MRSA isolates are community acquired vs hospital acquired in a ratio of 2:1. Dr. Kibsey is seeing resistance to erythromycin but sensitivity to Clindamycin in isolates from IDUs.

Infections are manifesting clinically as impetigo in First Nations communities. There is no clear link in many cases to underlying health problems. Local clusters of skin and soft tissue infections from multiply susceptible MRSA are reported (to Dr. Romney from Bella Coola and Bella Bella).

**MDS**  
*S Roman*

The proportion of *S. aureus* that are MRSA seen at MDS labs doubled between 2000 and 2003. 8.9% of Mainland *S. aureus* isolates are now MRSA. 3.9% of Vancouver Island Isolates are MRSA.

MDS gets specimens from the Downtown Community Clinic; **58%** of *S. aureus* isolates from that clinic are MRSA. 30% of wound infections from that clinic are caused by MRSA.

**St. Paul’s Hospital ER Study**  
*M. Romney, G. Shimokura, M. Hall and PHC MRSA Group*

The group conducted a study of 3,000 wound specimens (Jan. 1 to June 30, 2005). 245 wounds cultured *S. aureus*. 168 of 245 *S. aureus* wound infections are caused by MRSA (70% of *S. aureus* from wounds and 5.7% of all wound infections). The group is planning chart reviews to gather more information.

**Clinical Observations**  
*W. Bowie, D. Forrest and Others*

ID Specialists have been referred several couples, both with boils and also consulted about significant clustering of boils in a residential setting.
Summary

It is clear that CA-MRSA is now being seen across BC and that there has been a marked increase in infection over the past year or so. While there are concentrations in some high risk populations, infections are occurring among members of the general public with no identified risk factors.

Here follows a review of our original questions.

1. How many cases of disease are being caused by MRSA in BC? This is not precisely quantified – but we do know it has increased in the community.

2. How many of these are community-acquired vs. facility-acquired/associated? This is not precisely quantified but we observe that a large proportion of isolates managed even by tertiary care labs are now thought to arise in the community.

3. How can we maintain ongoing surveillance of trends in this morbidity? Periodically tracking the above sources will be instructive in identifying major changes in trend.

4. What are the major clinical syndromes being seen? Boils, impetigo, wound infections.

5. Are there modifiable risk factors? Literature suggests that injection drug use and incarceration play a role as do close contact sports. Though antibacterial soaps are thought to promote selection of resistant strains, we have not measured the association.

6. When will we know if we have reached a threshold at which empirical therapy for staphylococcal syndromes requiring antibiotic therapy should change? In the general community, we have not reached such a threshold. However – physicians should be encouraged to obtain culture and sensitivity results on all major staphylococcal infections. Local scenarios (eg. The Downtown Community Clinic) may point to earlier need for consideration of alternate therapy than most settings.

7. What works to contain this problem in populations? Unknown. Hypotheses include antimicrobial stewardship, increased emphasis on handwashing with soap and water, reduced use of antibacterial soaps and well considered clinical management guidelines.

8. What do we know about the molecular characteristics of cultured S. aureus isolates in this context? We know we are seeing PVL and MEC IV cassette containing organisms in common with CA-MRSA elsewhere on the continent.
9. What is optimal therapy for CA-MRSA disease? We can’t say. Anecdotally, recurrent infection has not responded well to monotherapy. Some form of evaluation is required.

Future Actions

• Broad circulation of this report to those in public health, primary care, infectious disease, microbiology and infection control

• The BC chapter of the Association for Medical Microbiology and Infectious Disease is looking at how their surveillance of MRSA can be modified to get a better idea of the relative role of CA-MRSA

• Researchers from several sites will meet to discuss how we can answer questions about modifiable risk factors and appropriate therapy

• Communications need to be crafted. At this point, it is considered that:
  o The major need-to-know group is family physicians – and communication needs to be drafted for them to urge culture taking at the time of drainage
  o Information about this problem should be added to Health Files and campaigns. Do Bugs Need Drugs will work to spread messages about hand-washing, good hygiene around contact sports and reduced general use of bactericidal soaps.
Bibliography


