

MDRO's (e.g. MRSA, ESBL, VRE)

Understanding population based MDRO occurrence and approaches to prevent transmission

We develop most infections (non viral, non foodborne) from our own normal microbial microbiome (i.e. endogenous infections) when we have a compromised site and/or are immunocompromised

e.g. *Staphylococcus aureus* skin infections (whether MSSA or MRSA), *E. coli* UTI, etc.

500 People



If three of these 500 people above developed a *Staph aureus* skin infection they would have 'caught it from themselves'. About 30-50% of the population carry *Staphylococcus aureus* routinely at any one time (some are transient carriers, some permanent carriers) as part of their normal microbial flora.

3 of 500 people with a *Staph aureus* skin infection



Community sourced swabs routinely received from infected patients via GP's throughout NZ show that MRSA is found and so present routinely in between 5% of all *Staph aureus* isolates in the South Island, and 12% in the Auckland region.

i.e. **MRSA is already endemic in the population.**

We also know that carriers of any MDRO including MRSA and ESBL, spontaneously lose that resistant carriage to that resistant organism 90% of the time in 1 – 12 months without any microbial intervention treatment.

i.e. the MDRO is transient for carriers who do not take antimicrobials to re select for it.

We know that the reason we have any MRSA, ESBL or VRE in the community is because of our combined cumulative total ongoing appropriate and inappropriate use of antibiotics i.e. we have bred this resistance by the combined tonnage of antibiotics used – thus the importance of effective Antibiotic Stewardship Programmes.

We know that because each one of us has 10 times as many bacteria (perhaps 90 trillion each) as tissue cells (? 10 trillion) we cannot but help share our microbial microbiome with others (touch, shedding skin cells, door handles, etc).

Excellent Standard Precautions (e.g. hand hygiene) for all by all, plus Transmission based precautions (e.g. Contact and Droplet/cough) as indicated, **slow down our microbial sharing but cannot stop it.**

i.e. **'Your Bugs are My Bugs'**

25 carriers of MRSA without infection in 500 people in the community (i.e. 5%)



Similar to bloodborne viruses (e.g. hepatitis B, C and HIV), the majority of people who have an infection and/or are a carrier of one of these viruses do not know they harbour the virus.

The MOH estimate 100,000 people in NZ are HBV carriers and 50,000 are HCV carriers. That is approximately one in 45 and 90 people respectively in the population. Because we do NOT know the majority of carriers, we do not isolate the known positive patients or handle their blood/body fluids differently but treat **all blood and body fluids as though they may be potentially infectious.** To do differently would be foolish.

Similarly with MDRO's.

All people, healthcare workers, patients and residents must be thought of as transient carriers of an MDRO, because they/we not uncommonly will be. Especially healthcare workers sharing treated patients more resistant microbiomes.

Standard Precautions (especially hand hygiene) by all people for all people/patients, in addition to good Antimicrobial Stewardship, is the most effective way to reduce creating and spreading MDRO's

We know that there are many other microbial resistances routinely endemic in the community also. e.g. in a regional South Island hospital study in January 2014 the first 100 routine adult admissions were screened for MDRO's, **six were ESBL positive**, one was VRE positive. **Only one had a known risk factor**.

And these are only when we look for resistance in known likely potential pathogens (e.g. *Staphylococcus aureus*, *E. coli*, *Klebsiella*, *Enterococcus spp*). **We do not routinely look for any antibiotic resistance in most of our normal bacterial microbiome** e.g. anaerobes, *Staph. epidermidis*, etc. We know that bacteria routinely share genetic resistance mechanism ability amongst themselves, other species and other genera (e.g. plasmid transfer).

Because of selective antibiotic pressure we **know most antibacterial resistance is where antibiotics are used the most in defined areas** e.g. hospitals, long term care facilities (LTCF, rest homes). In an acute hospital approximately 30% of patients will be on antibiotics, and about 30% of residents in a LTCF will have antibiotics per year. **So it is likely each healthcare worker will be a transient carrier of a number of MDRO's several times each 5-10 years**, and that **in addition** to the normal community transient resistant carriage rates where they live, even if they were MDRO/MRSA negative screen when they started work at any given health facility.

The vast majority of antibiotic resistance is carried harmlessly at the time by people (healthcare workers, patients, residents and the public) who are totally unaware of it and in good health without any infection

5% MRSA + 5% ESBL carriers



From time to time a few of 500 people will 'catch an infection from themselves' e.g. infected cut, wound, ulcer. If a swab of an infection or a screen swab is taken and it happens that an MDRO is isolated, should they be isolated and treated differently?

Or would that create a larger false sense of security by believing we can relax our Standard Precautions on others, including ourselves, because we/they are not known MDRO carriers??

3 of 500 people with an infection who had a swab taken, one was found to have MRSA, should they be specially isolated?? What would be the increased risks of doing this??



MRSA Decolonisation

Although decolonisation (e.g. nasal mupirocin plus chlorhexidine body washes) may seem intuitively a good idea, the well controlled trials supporting its efficacy and indications for proceeding with it are limited, with few exceptions (e.g. some preop procedures).

When MRSA decolonisation is performed we must realise that **anybody with a known MRSA (or other MDRO) is only a symptom or indicator, not a cause, of a much larger issue in the community and healthcare facility at large.**

And there are significant toxicity and allergic issues with decolonisation.

In addition the associated stigmatisation of the affected individual and their family should not be underestimated.

We should also ask ourselves, why would we use antimicrobial agents to attempt to remove an organism that is only present in the community due to our high use of antimicrobials in the first place, and which will spontaneously clear when colonised 9 times out of 10 within 1 – 12 months without any antimicrobial intervention?

In addition there is increasing evidence that microbial contact with not only antibiotics but also biocides/disinfectants has the effect of driving up antibiotic resistance.

e.g. Increasing MIC numbers (minimum inhibitory concentration) shows increasing bacterial antibiotic resistance post biocide/disinfectant contact for different durations (highlighted or bold) below:

Chlorhexidine promoting Antibiotic Resistance Journal of Antimicrobial Chemotherapy (2008) 61, 524– 532 :

| | Hours Drying with Chlorhexidine | AMP | CTX | VAN | GEN | CIP | CEF | TET | OXA |
|--|---------------------------------|-------|-----|-------|------|-------|-------|-------|-------|
| MRSA (EMRSA 16) | control (no exposure) | >128 | 8 | 1 | 0.5 | 1 | 8 | 2 | 4 |
| | 2 | >128 | 8 | 1 | 0.5 | 2 | 8 | 2 | 8 |
| | 24 | >128 | 8 | 1 | 0.5 | 2 | 4 | 2 | 4 |
| | 48 | >128 | 16 | 128 | 2 | 2 | 64 | 2 | 128 |
| | | | | | | | | | |
| MSSA (susceptible <i>Staph. aureus</i>) | control (no exposure) | 0.06 | 1 | 1 | 0.25 | 0.25 | 4 | 0.5 | 0.12 |
| | 2 | 0.06 | 1 | 1 | 0.5 | 0.25 | 1 | 0.25 | 0.12 |
| | 24 | 0.002 | 1 | 0.002 | 0.25 | 0.002 | 0.002 | 0.002 | 0.002 |
| | 48 | 128 | 32 | >128 | 2 | 2 | 64 | 1 | 128 |
| | | | | | | | | | |

AMP ampicillin, CTX cefotaxime, VAN vancomycin, GEN Gentamicin, CIP ciprofloxacin, CEF cefuroxime
TET tetracycline, OXA oxacillin

Disinfectants promoting Antibiotic Resistance Journal of Antimicrobial Chemotherapy 7 May 2015 :

Table 1. Antimicrobial susceptibility of representative mutants selected after biocide exposure

| Strain | Selective biocide | Sub-culture ^a | MIC (mg/L) ^b | | | | | |
|--|-------------------|----------------------------|-------------------------|--------|--------|-----|-----|-------|
| | | | NAL | CIP | CHL | TET | KAN | TRI |
| SL1344 (<i>Salmonella typhimurium</i>) | none | 8 | 2 | <0.015 | 1 | 0.5 | 4 | 0.06 |
| AQ1 | AQAS | quaternary ammonium | 5 | 32 | 0.015 | 2 | 0.5 | 8 |
| AQ2 | AQAS | " | 6 | 32 | 0.06 | 64 | 4 | 4 |
| AQ4 | AQAS | " | 8 | 32 | 0.06 | 64 | 8 | 4 |
| AQ5 | AQAS | " | 8 | 16 | 0.03 | 32 | 4 | 4 |
| SK1 | Superkill | aldehydes and quat | 2 | 32 | 0.12 | 64 | 8 | 2 |
| SK3 | Superkill | ammonium mixture | 5 | 32 | 0.12 | 64 | 8 | 4 |
| SK4 | Superkill | " | 6 | 16 | 0.06 | 16 | 4 | 4 |
| SK7 | Superkill | " | 7 | 4 | <0.015 | 4 | 1 | 4 |
| T2 | Trigene | halogenated tertiary amine | 2 | 512 | 0.25 | 1 | 0.5 | 4 |
| T3 | Trigene | " | 3 | 512 | 0.25 | 1 | 0.5 | 4 |
| T6 | Trigene | " | 4 | 512 | 0.25 | 1 | 0.5 | 4 |
| T9 | Trigene | " | 5 | 512 | 0.25 | 1 | 0.5 | 4 |
| V2 | Virkon | oxidative compound blend | 2 | 512 | 0.25 | 4 | 2 | 4 |
| V4 | Virkon | " | 4 | 8 | <0.015 | 4 | 2 | 4 |
| V6 | Virkon | " | 6 | 512 | 0.25 | 4 | 2 | 4 |
| V8 | Virkon | " | 8 | 16 | <0.015 | 8 | 2 | 2 |
| Site-directed mutants and complements | | | | | | | | |
| SL1344- <i>rpoA</i> | NA | NA | 32 | 0.015 | 2 | 0.5 | 8 | 0.015 |
| SL1344- <i>zur</i> | NA | NA | 2 | <0.015 | 1 | 0.5 | 4 | 0.06 |
| T2-pBAD- <i>zur</i> | NA | NA | 512 | 0.25 | 1 | 0.5 | 4 | >1024 |
| AQ1-pBAD- <i>rpoA</i> | NA | NA | 2 | <0.015 | 1 | 0.5 | 4 | 0.06 |
| AQ2-pBAD- <i>rpoA</i> | NA | NA | 32 | 0.06 | 64 | 4 | 4 | 0.5 |

NAL, nalidixic acid; CIP, ciprofloxacin; CHL, chloramphenicol; TET, tetracycline; KAN, kanamycin; TRI, triclosan; NA, not applicable.

^aNumber of biocide exposures after which each strain was recovered.

^bValues in bold indicate MICs ≥ 8 -fold higher compared with SL1344.

The large randomised controlled study summarised below on over 6,000 rest home residents in over 100 rest homes shows not only **no benefit to extensive MRSA decolonisation attempts (including pharyngeal chlorhexidine disinfection) but also that the MRSA carriage was transient to individuals regardless of intervention or not** i.e. decolonisation appeared to clear a number, but the Control group **showed most would have cleared anyway without any intervention and added antimicrobial pressure**, so there was no benefit to decolonisation but increased potential harm (resistance, toxicity/allergies, stigmatisation). The large non intervention Control group allowed this effect to be seen :

'Search-and-destroy' strategy versus standard precautions for control of methicillin-resistant Staphylococcus aureus (MRSA) in nursing homes (NH) a randomized controlled study

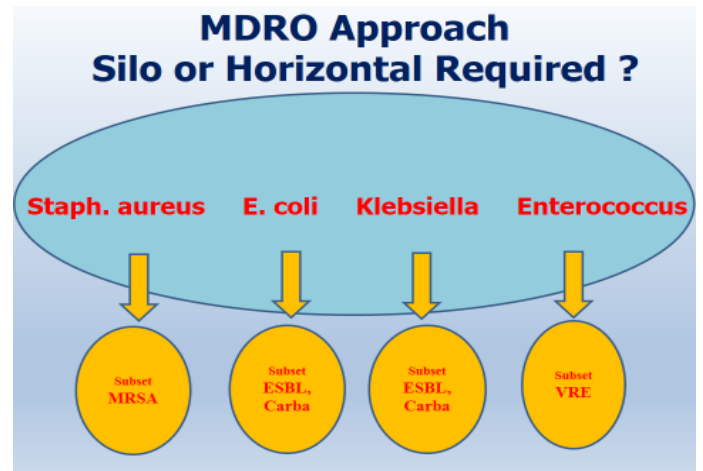
C. Bellini*, C. Petignat, E. Masserey, C. Büla, B. Burnand, D. Blanc, G. Zanetti (Lausanne, CH)
April 27, 2013, 14:30 - 14:42

Objectives: Prevalence of MRSA carriage increased from 4.5% in 2003 to 12% in 2008 among NH residents in Canton Vaud, Switzerland. As MRSA control strategy has not been clearly defined in this setting, **the aim of our study was to compare the one-year impact of standard precautions either alone (control) or with universal screening followed by decolonization of carriers (intervention) on the prevalence of MRSA carriage at NH level.**

Methods: All 157 NH of canton Vaud were invited to participate to this randomized controlled study. In all participating NH, Standard Precautions were enforced and residents underwent MRSA screening at study entry and 12 months thereafter, except if they had documented ongoing MRSA infection or bacteriuria, or stage IV skin ulcers. In the intervention group, residents admitted during the 12 study months were also screened, and all MRSA carriers underwent a 5-day topical decolonization (nasal mupirocine and chlorhexidine disinfection of skin and pharynx) combined with environmental disinfection. Decolonization was repeated once in case of failure.

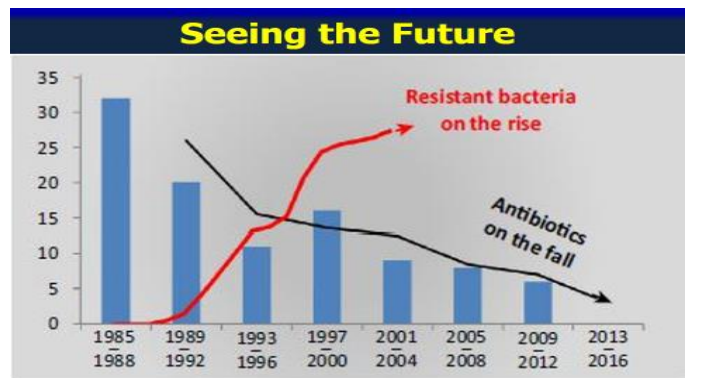
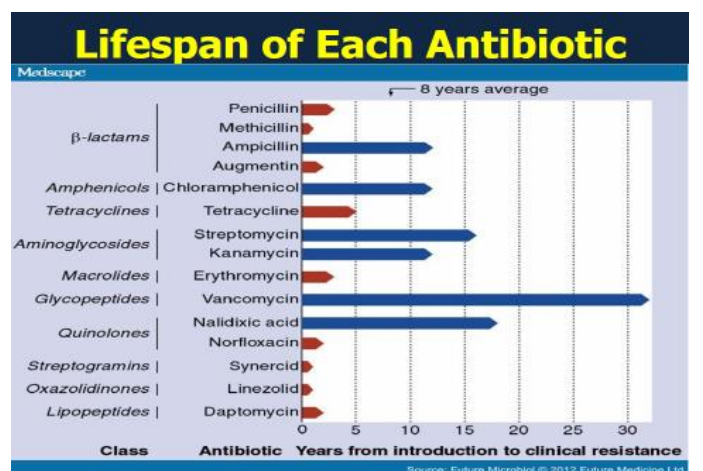
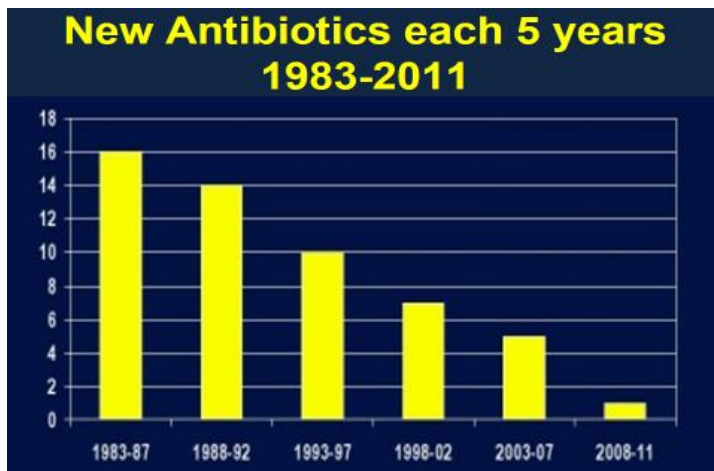
Results: **104/157 NH (67%) were included and randomly allocated to control (51%) or intervention (49%).** Characteristics of NH (size, proportion of single rooms, healthcare workers/resident ratio), and of residents (age, gender, diabetes, ulcers, medicals devices, performance score, previous admission in acute care hospital, previous antibiotic therapy) were similar in both groups. **A total of 6,036 residents were screened at baseline**, which represented 86% (range: 27-100%) of the NH population in the control group and 87% (20-100%) in the intervention group. 60% of carriers in the intervention group were successfully decolonized, and 47% remained negative at study end. Mean MRSA prevalence at baseline was 8.9% in both groups (range 0- 44%). After 12 months, it significantly declines to 6.6% in the control group and to 5.8% in the intervention group (difference: -0.8%, $p=0.3$). The impact of the intervention did not reach significance in multivariate analysis, even if restricted to NH with screening rates > 95% (-2.5%, $p=0.33$).

Conclusion: Topical MRSA decolonization was successful in 60% of NH residents. Nevertheless, **universal screening followed by decolonization of carriers had no significant additional impact in reducing prevalence of MRSA carriage rate at one year compared to Standards Precautions alone.**



Time is running out

Every time antibiotics are used creates opportunities for resistance to develop



Standard Precautions (especially hand hygiene) by all people for all people/patients, in addition to good Antimicrobial Stewardship, is the most effective way to reduce creating and spreading MDRO's