MROS OF SIGNIFICANCE

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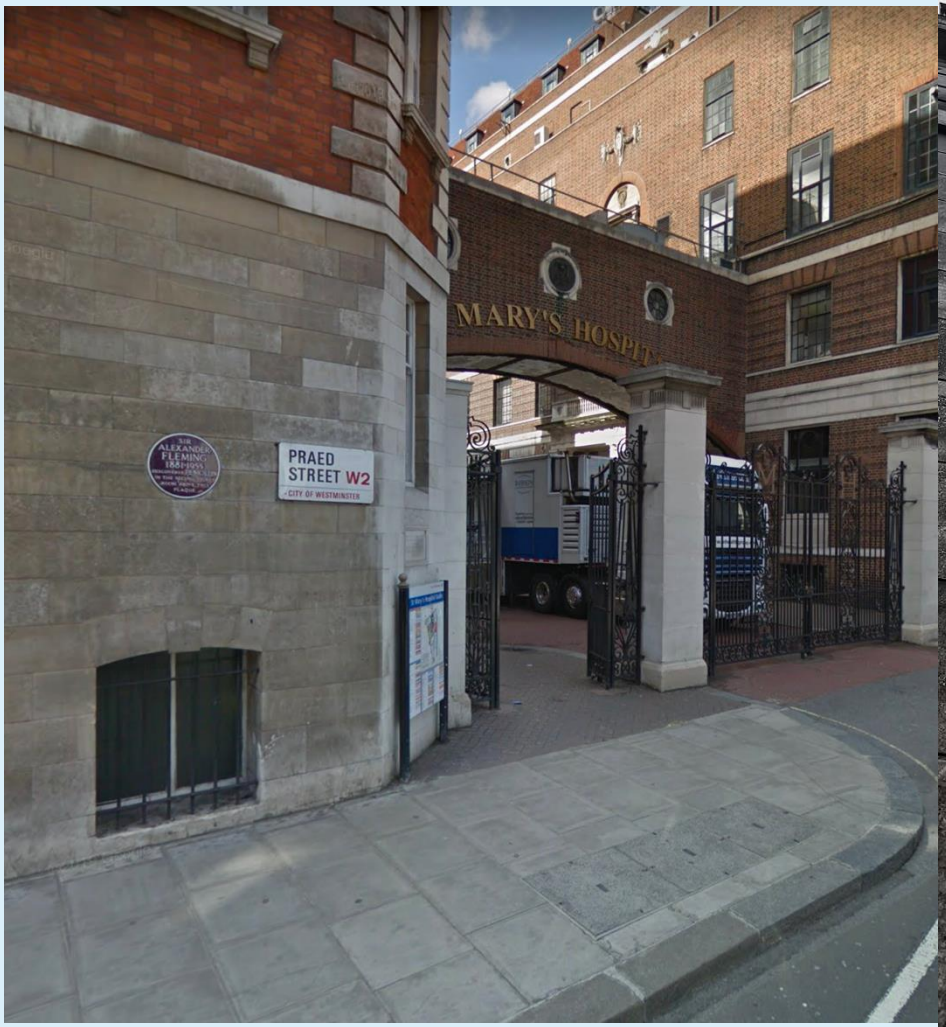
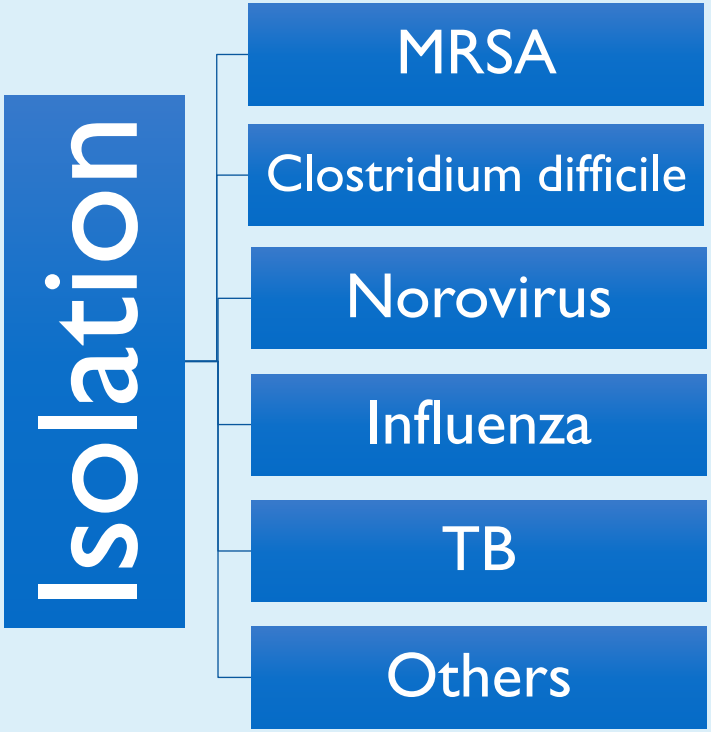
@emrsa15


MARY'S HOSPIT
PRAED
STREET W2
CITY OF WESTMINSTER

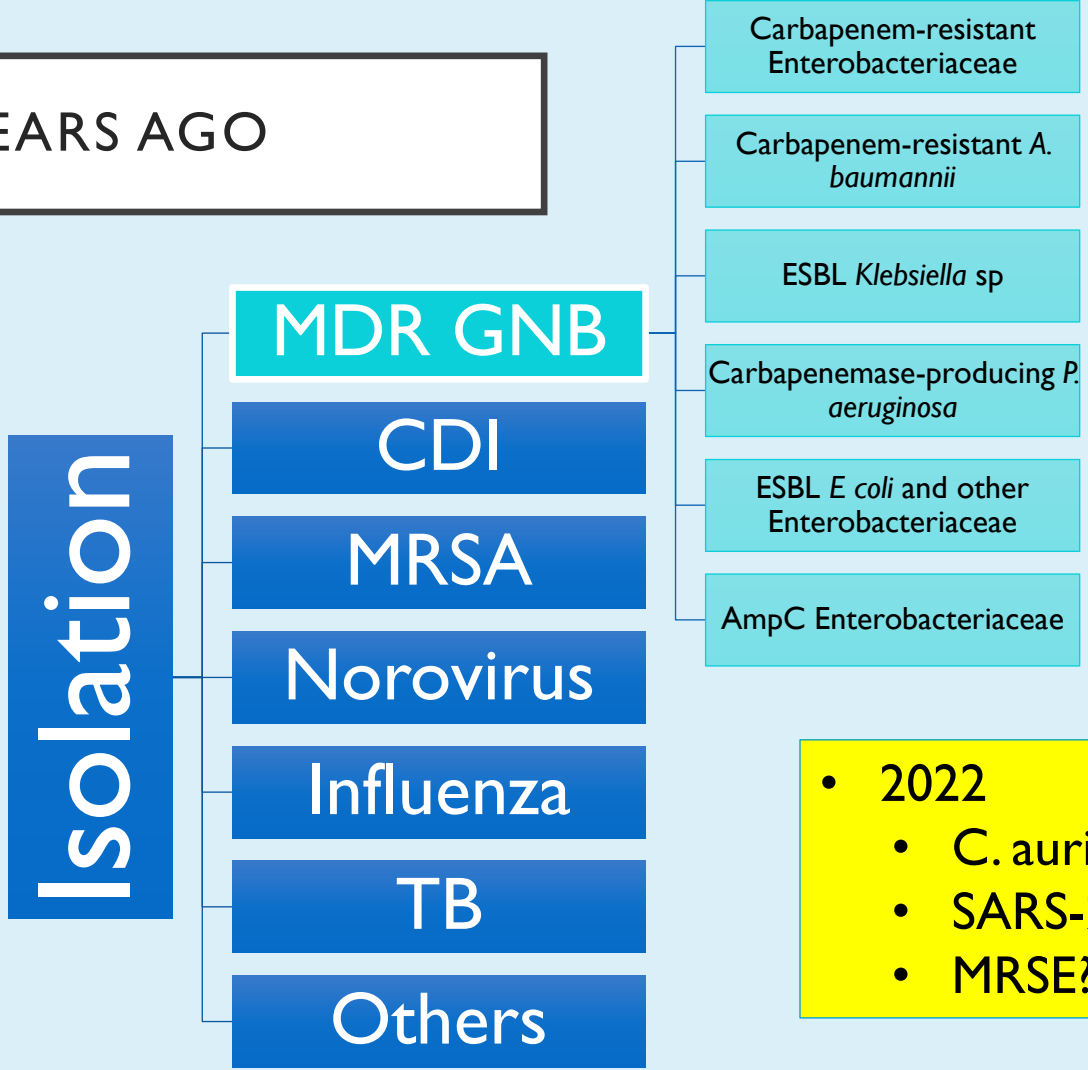

SIR
ALEXANDER
FLEMING
1881-1955
DISCOVERED PENICILLIN
IN THE SECOND STOREY
ROOM ABOVE THIS
PLAQUE

My first 15 years – Not Many MROs



GNB?

5 YEARS AGO



- 2022
  - C. auris
  - SARS-2
  - MRSE?

for ***Enterococcus faecium***

for ***Staphylococcus aureus***

for ***Klebsiella pneumoniae***

for ***Acinetobacter baumannii***

for ***Pseudomonas aeruginosa***

for ***Enterobacter*** species

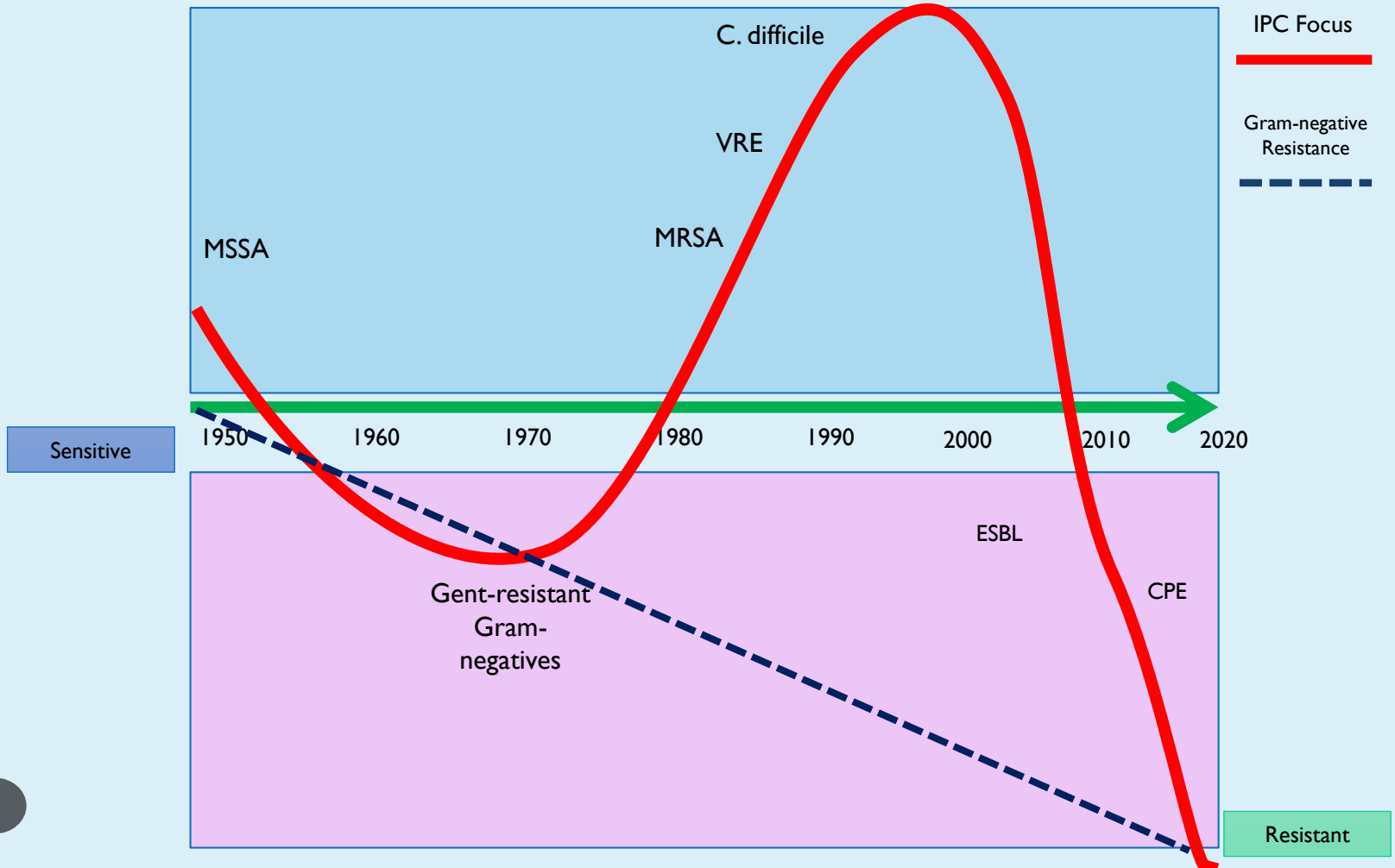
https://emerypharma.com/blog/eskape-pathogens-explained/

What can we treat?

Organism	Antibiotic effectiveness
Streptococcus pyogenes	+++++
Staphylococcus aureus	+++++
MRSA	++++
C. difficile	+++
E. coli	++++
ESBL-E. coli	++
CPE E. coli	+
Acinetobacter baumanii	++
CRE Acinetobacter baumanii	+
Colistin-resistant A. baumanii	-

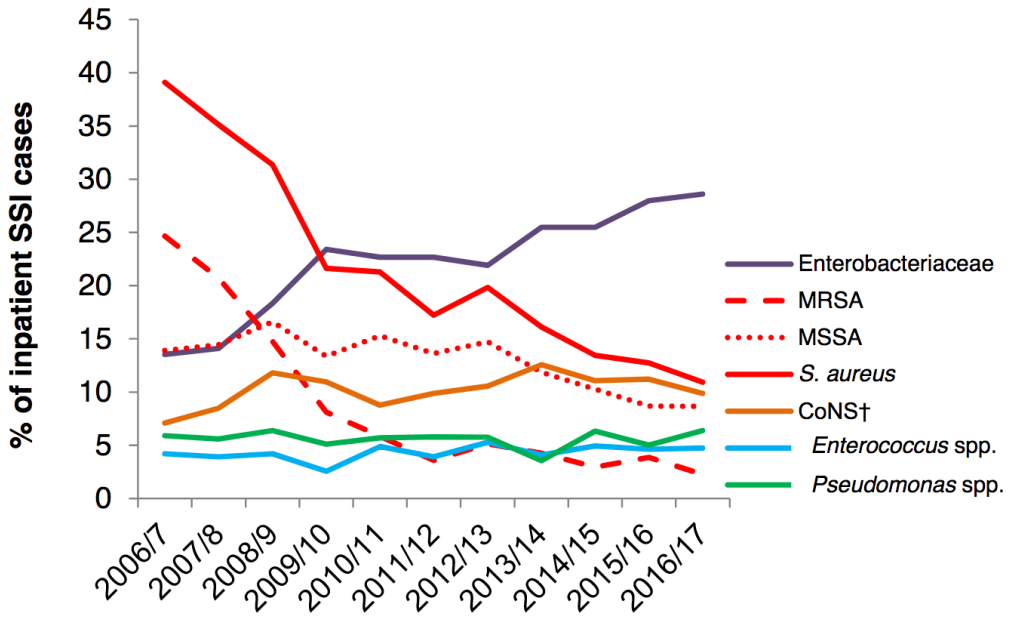
MROs- What are we talking about here?

- Basically we are talking about organisms that are more difficult to treat and that can cause significant damage
- Consider
  - Resistance to antimicrobial agents
  - Pathogenicity and virulence
  - Transmissibility
  - Persistence
- And your setting – what is the risk to those in your care?


C. difficile
VRE
MRSA
MSSA
IPC Focus
Gram-negative Resistance
Sensitive
1950
1960
1970
1980
1990
2000
2010
2020
ESBL
CPE
Gent-resistant Gram-negatives
Resistant

Recent UK Surgical Site Infection data show the direction

Figure 10: Trends in micro-organisms reported as causing inpatient SSIs, all surgical categories*, NHS hospitals, England



MROs of Significance

- Fungi
  - Candida are becoming problematic – 7% resistant to Fluconazole in the USA
    - Resistance more common in Candida auris, Candida glabrata, and Candida parapsilosis
  - C. auris is a problem organism as it is resistant, virulent, transmissible and persistent
- Gram positives
  - MRSA? Not considered to be hugely resistant by today's standards but meets all of the other criteria
  - Clostridium difficile? Cip-resistance has selecting virulent, transmissible and persistent strains like 027/NAP1
  - VRE? - Resistant but limited clinical impact unless immunocompromised. Useful canary though
  - Coagulase-negative Staphs?

We only know what we know

Mahida N. et al, J Hosp Inf (2016) 94(3) 273-5

- Non-slip socks as a 'solution' to patient falls issues
  - Socks meant to be worn continuously
  - Patient gets onto and into the bed wearing them
- Sampling revealed
  - 85% contaminated with VRE (no known cases)
  - 7% with MRSA (no known cases)

Gram negatives

- How long have we got?
  - Where you draw the line for action depends completely on your ability (and need) to do something about it
- Sources are the human gut and the environment
- Resistance has been building for years
  - Starting with ESBL
    - extended spectrum beta-lactamase producing organisms that mean that treatment with oral antibiotics will be ineffective
    - Think urinary tract infection
  - Problem: Gram-negative bacteria are very promiscuous – so resistance spreads
  - We now see resistance to our last group of 'new' antibiotics - Carbapenems

Carbapenem Resistance

- Very limited treatment options
  - Possibly colistin, however pan-resistant organisms have been increasingly reported with spread between hospitals
    - Sonnevend, A. et al Antimicrob Agents Chemother **61**(7).
    - Marais, E. et al (2004). "Interhospital transfer of pan-resistant Acinetobacter strains in Johannesburg, South Africa." Am J Infect Control **32**(5): 278-281.
- MROs also are found in the environment
  - Meir-Gruber, L. et al (2016). "Population Screening Using Sewage Reveals Pan-Resistant Bacteria in Hospital and Community Samples." PLoS One **11**(10): e0164873
    - Klebsiella pneumonia, Enterobacter spp., Escherichia coli and Citrobacter spp. were the 4 main CRE detected

Healthcare environment is contaminated

- 18% of toilet floors contaminated with ESBL Gram-negatives in a non-outbreak setting
  - Muzslay, M. et al (2017). "ESBL-producing Gram-negative organisms in the healthcare environment as a source of genetic material for resistance in human infections." J Hosp Infect **95**(1): 59-64.
- ESBL-Klebsiella pneumoniae recovered from the toilet floor, toilet seat and a bin lid in a private room three days before an occupying patient not known to be colonised at the time of sampling, presented with a urinary tract infection
  - 16% of floor samples positive from MDR Acinetobacter baumanii
  - Thom, K.A., et al (2011). Am J Infect Control **39**(9): 711-715.

Is there complacency?

- In a recent study of attitudes of Nurses in the USA, although most felt that antibiotic resistance was a global issue, they also thought that it was not an issue in their hospital
- They also thought that appropriate use of antibiotics was less likely to cause resistance
  - Merrill, K. et al (2019). "Antimicrobial stewardship: Staff nurse knowledge and attitudes." Am J Infect Control. In Press
- Similar picture with doctors
  - Zhou, J. et al (2013). "Clinicians' knowledge, attitudes, and practices regarding infections with multidrug-resistant gram-negative bacilli in intensive care units." Infect Control Hosp Epidemiol **34**(3): 274-283.
  - We must educate our colleagues

MROs in food

- Prevalence of mcr (Colistin resistance) among fresh vegetables
  - 3.6% positive overall; highest detection rate found in carrot (14.3%), pakchoi (13.3%) and green pepper (7.7%)
  - Sequenced plasmids from fresh vegetables were highly similar to those from clinical isolates and animals in various countries
    - Liu BT, et al. Colistin-Resistant mcr-Positive Enterobacteriaceae in Fresh Vegetables, an Increasing Infectious Threat in China. *Int J Antimicrob Agents*. 2019;54(1):89-94. doi:10.1016/j.ijantimicag.2019.04.013
- Also in fruit
  - Yang, F., et al (2019). Infect Drug Resist **12**: 385-389.

These infections are serious

- Outbreak in Hangzhou
  - five patients had surgery for multiple trauma and mechanical ventilation
- Mortality 100%
  - all had severe pneumonia, carbapenem-resistant K. pneumoniae infections, poor responses to antibiotic treatment and died either due to severe lung infection, multiorgan failure or septic shock
    - Gu, D. et al (2018). "A fatal outbreak of ST11 carbapenem-resistant hypervirulent Klebsiella pneumoniae in a Chinese hospital: a molecular epidemiological study." The Lancet Infectious Diseases **18**(1): 37-46.

What do we know?

- Not as much as we would like to know
- Clinical testing detects only 1 of every 9 CRE if you look harder
  - Pisney LM et al. Infect Control Hosp Epidemiol 2014;35:434–436
- study looking at possibility of predicting carriage of CRE
  - 9% of swabs positive, despite including all of the 'usual' risk factors such as recent hospitalisation, antibiotics, invasive devices, decision tree models poorly predicted CRO and CPO colonization
    - Goodman, K. et al (2019). "Predicting probability of perirectal colonization with carbapenem-resistant Enterobacteriaceae (CRE) and other carbapenem-resistant organisms (CROs) at hospital unit admission." Infect Control Hosp Epidemiol: 1-10.

Outbreaks – not so easy to detect

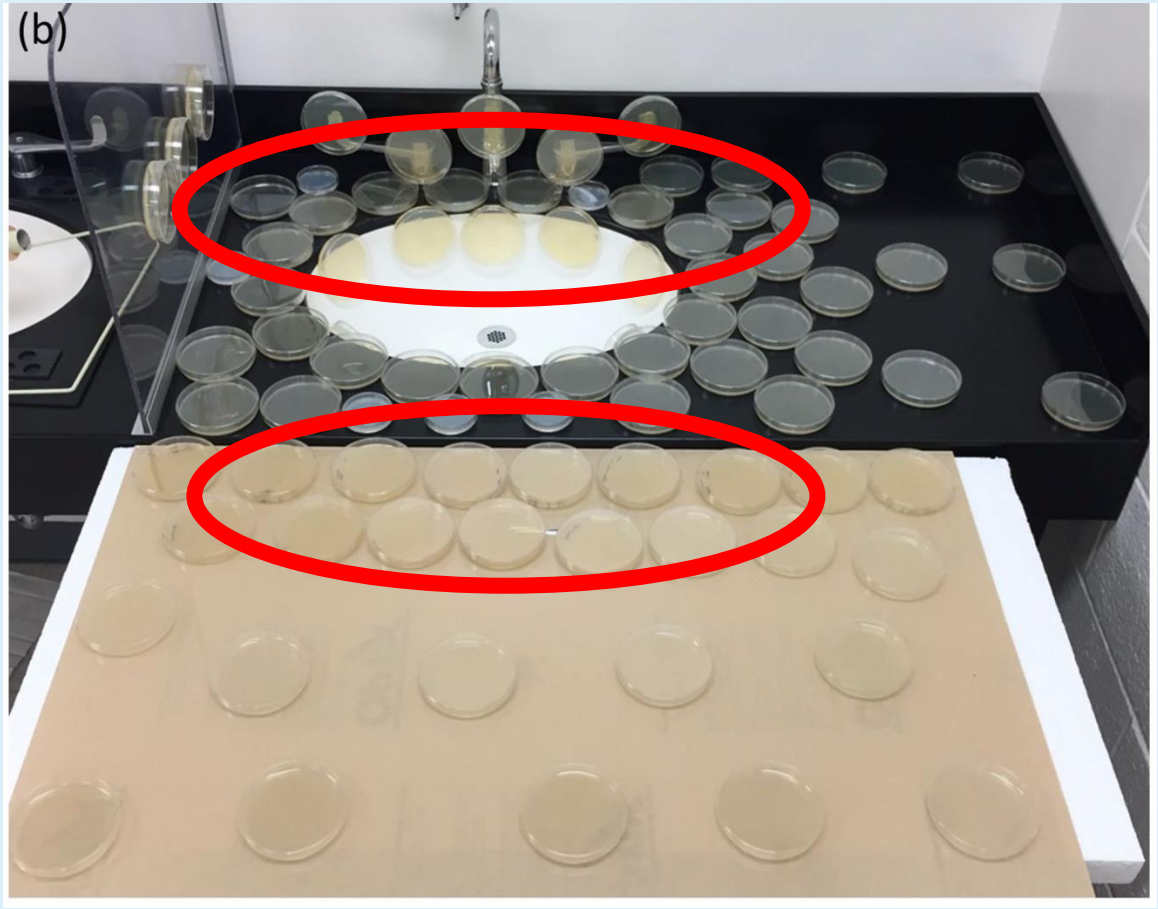
- Easy to spot
  - Clonal spread may be easy to detect – all the ‘same’ organism by antibiogram
- Not so easy
  - Plasmid transmission of a resistance gene
    - Multiple gram-negative infections but with different organisms
      - Enterobacter
      - Citrobacter
      - E. coli

How is transmission occurring?

- In a scoping review of the literature, high-quality papers demonstrated all 5 routes of transmission
  - From patient to healthcare worker hands
  - From patient to the environment
  - From healthcare worker to the patient via hands
  - From the environment to the patient
  - From the environment to the healthcare worker's hands
    - Blanco, N. et al (2019). "Transmission pathways of multidrug-resistant organisms in the hospital setting: a scoping review." Infect Control Hosp Epidemiol **40**(4): 447-456

If we do not learn from our history, we are condemned to repeat it

- The first ever lecture at the first HIS International Conference in 1980 was called ‘Pseudomonas untamed’
- Splashing of water from contaminated sinks to fomites suggested as a mode of transfer for Pseudomonas infection in a burns unit
  - Cross-contamination from patient to patient and spread by nursing personnel eliminated as major modes of transmission because hands were consistently negative
    - Edmonds, P., R. R. et al (1972). "Epidemiology of Pseudomonas aeruginosa in a burns hospital: surveillance by a combined typing system." Appl Microbiol **24**(2): 219-225



Kotay, S., et al (2017). "Spread from the Sink to the Patient: in situ Study Using Green Fluorescent Protein (GFP) Expressing-Escherichia coli to Model Bacterial Dispersion from Hand Washing Sink Trap Reservoirs." Appl Environ Microbiol 83(8)

But this was known 43 years ago

- Investigation of nosocomial infections caused by gentamicin-resistant gram-negative bacteria at a VA Hospital revealed that drains of sinks frequently harbor these organisms
  - Flournoy DJ, et al. Nosocomial infections linked to handwashing. *Hospitals (USA)*. 1979;53(15):105-107.
- Contamination by splashing of water droplets from sink basin during handwashing; faucet aerators may also be contaminated.
- Sink trap does not hinder migration of motile organisms to other sink drains
- Drain disinfection study showed that recolonization occurred within a few days after disinfection was discontinued
- Elimination of the hazard may require redesign of hospital sinks

Water as a Source of Carbapenem Resistant Organisms

Table 2. Water Reservoirs Containing Carbapenem-Resistant Organisms[a]

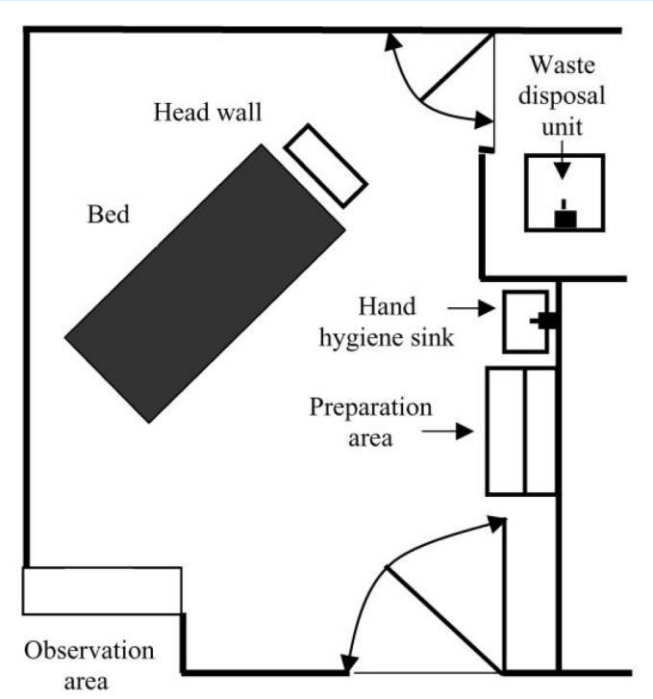
Water Reservoir	Studies, No. (N = 32)	References
Drains/drainage systems	17	Peña et al [35], Kotsanas et al [26], La Forgia et al [28], Betteridge et al [7], Leitner et al [20], Wendel et al [29], Breathnach et al [21], Leung et al [24], Snitkin et al [22], Tofteland et al [32], Vergara-López et al [33], Yomoda et al [9], Stjarne Aspelund et al [12], Odom et al [11], Knoester et al [25], Landelle et al [37], Seara et al [34]
Sink surfaces	14	Betteridge et al [7], Wendel et al [29], Knoester et al [25], Podnos et al [23], Wang et al [27], Biswal et al [8], Hong et al [30], Bukholm et al [31], Kouda et al [38], Landelle et al [37], Dewi et al [10], Kaiser et al [13], Ito et al [14], Leung et al [24]
Faucets	8	Odom et al [11], Knoester et al [25], Majumdar et al [17], Pitten et al [36], Hong et al [30], Bukholm et al [31], Alter et al [15], Leung et al [24]
Water	3	Knoester et al [25], Ambrogi et al [18], Bukholm et al [31]
Inflatable hair wash basin	2	Wendel et al [29], Knoester et al [25]
Sensor mixer taps	1	Durojaiye et al [16]
Water/tea dispenser	2	Wong et al [19], Ito et al [14]
Shower/shower equipment	3	Betteridge et al [7], Leung et al [24], Seara et al [34]
Toilet bowl/brush	2	Breathnach et al [21], Kouda et al [38]

Kizny Gordon, A. E., A. J. Mathers et al (2017) "The Hospital Water Environment as a Reservoir for Carbapenem-Resistant Organisms Causing Hospital-Acquired Infections - A Systematic Review of the Literature." Clin Infect Dis **64**(10): 1435-1444

Poor design may contribute

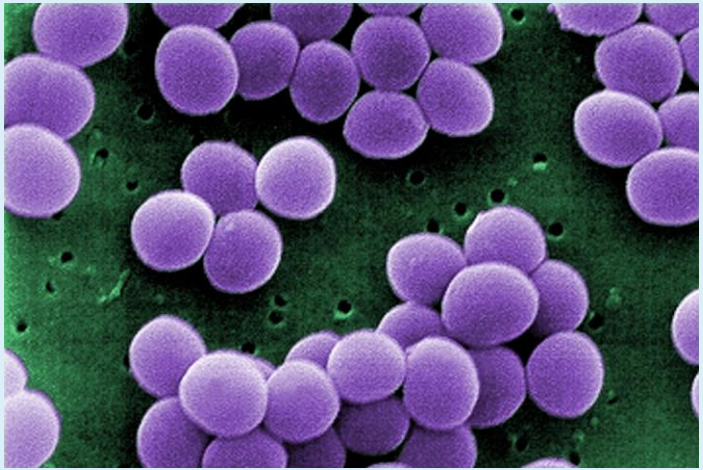
- 36 patients exposed to the intensive care unit or transplant units of a tertiary care hospital were infected with a multidrug-resistant strain of P. aeruginosa
  - 33% died with this organism directly implicated
    - Hota, S., at al (2009). "Outbreak of multidrug-resistant Pseudomonas aeruginosa colonization and infection secondary to imperfect intensive care unit room design." Infect Control Hosp Epidemiol **30**(1): 25-33
- source of outbreak was traced to hand hygiene sink drains, where biofilms containing viable organisms were found
  - Testing by use of a fluorescent marker demonstrated that when the sink was used for hand washing, drain contents splashed at least 1m from the sink, which was placed by an area used to prepare medications and equipment

We need to think about design



CoNS – who cares?

- Not often considered as pathogens, labelled as 'Contaminants'
- Often multi-resistant – very!
- Taken more seriously if
  - Blood cultures from central lines
  - Specimens from implanted devices, including joint replacements
- Not often identified to species
  - But if you look harder..



SSI from ward airborne Staphyloccocci?

- ECCMID Abstract
  - Johansson AF, et al. Airborne antibiotic-resistant Staphylococcus epidermidis in inpatient wards linked with deep surgical site infections. *31st ECCMID* Vienna (Virtual): ESCMID; 2021.
  - Investigated prevalence of MRSE in hospital air and compare with MRSE causing deep surgical site infections (SSI) or bloodstream infections (BSI
  - Airborne MRSE resistant to cefoxitin+≥3 more antimicrobials, and MRSE judged with high clinical certainty as causes of BSI or deep SSI associated with surgical implants (2015-2017) were genome sequenced
- MRSE from the air (n=133) and MRSE from sporadic BSI or deep SSI (n=27) illustrated very close relationships
  - More questions than answers (air -> nose -> SSI?)

Staphylococcus capitis

- First described in 1975
  - Kloos WE, et al. *International Journal of Systematic Bacteriology.* 1975;25(1):62-79.
- Very resistant, common flora in neonates
  - Savey A, et al. An analysis of the microbial flora of premature neonates. *J Hosp Infect.* 1992;21(4):275-289. doi:10.1016/0195-6701(92)90138-c
- Case report from 2002 (Amsterdam) – BSI in a neonate, took 3 weeks to treat
  - S. capitis with vancomycin resistance
- Looked back as 218 saved organisms 'CoNS'
  - 48 S. capitis, identical organism - suggested epidemic
    - Van Der Zwet WC, et al. Nosocomial spread of a Staphylococcus capitis strain with heteroresistance to vancomycin in a neonatal intensive care unit. *J Clin Microbiol.* 2002;40(7):2520-2525. doi:10.1128/JCM.40.7.2520-2525.2002

Staphylococcus capitis

- 2012 – evidence of clonal spread throughout French ICUs; 2013 – Australia, UK, Belgium
  - All the same clone or very closely related
- 2017 – NRCS-A clone with worldwide endemicity in NICUs
  - Australia, Belgium, Brazil, Canada, Czech Republic, Denmark, Finland, France, Germany, the Netherlands, New Zealand, Norway, South Korea, Switzerland, Taiwan, the United Kingdom, and the United States
    - Butin M, et al. Worldwide Endemicity of a Multidrug-Resistant Staphylococcus capitis Clone Involved in Neonatal Sepsis. Emerg Infect Dis. 2017;23(3):538-539. doi:10.3201/eid2303.160833

Staphylococcus capitis – why no progress?

- Biofilm formation means difficult to eradicate, after cleaning and decontamination, incubators remain positive
  - Cui B, et al. Differences between two clinical Staphylococcus capitis subspecies as revealed by biofilm, antibiotic resistance, and pulsed-field gel electrophoresis profiling. *J Clin Microbiol.* 2013;51(1):9-14. doi:10.1128/JCM.05124-11
  - Butin M, et al. Sources and reservoirs of Staphylococcus capitis NRCS-A inside a NICU. *Antimicrob Resist Infect Control.* 2019;8:157. doi:10.1186/s13756-019-0616-1
- NRCS-A clone now seen in prosthetic infections in adults
  - Tevell S, et al. Presence of the neonatal Staphylococcus capitis outbreak clone (NRCS-A) in prosthetic joint infections. *Sci Rep.* 2020;10(1):22389. doi:10.1038/s41598-020-79225-x

WE MUST ERADICATE THIS MENACE

- Xu Z, et al. Prevalence and Molecular Characterization of Methicillin-Resistant Staphylococci Recovered from Public Shared Bicycles in China. *Int J Environ Res Public Health.* 2022;19(8). doi:10.3390/ijerph19084492

- But the real question is…

Principles for dealing with these?

- Pretty much the same
- Source control
  - Segregation dependent on situation – risk assess
  - Chlorhexidine is effective in most of these
  - Rational use of PPE where appropriate
- Environmental decontamination
- Communication to other institutions when necessary is the most critical