The current literature in Infection Prevention and Control

Read for you!

By Gabriel Birgand
Epidemic of carbapenem-resistant *Klebsiella pneumoniae* in Europe is driven by nosocomial spread

- To determine the epidemiology of carbapenem-non-susceptible *K. pneumoniae* by analysing the genomes of 1,717 *K. pneumoniae* isolates from European countries
- **Carbapenemase acquisition** is the main cause of carbapenem resistance
- **Four clonal lineages**, sequence types 11, 15, 101, 258/512
- Propensity to spread in hospital environments correlates with the degree of resistance. CP-isolates have highest transmissibility
- Experienced within-hospital transmission, and interhospital spread is far more frequent within, rather than between, countries

- **21**: number of single nucleotide polymorphisms that optimizes the discrimination of hospital clusters
- ST258 isolates from the US are basal in the phylogenetic tree: lineage emerged in the US.
Estimating the association between antibiotic exposure and colonization with ESBL-GNB using machine learning methods: a multicentre, prospective cohort study

- To measure the impact of antibiotic exposure on the acquisition of colonization with ESBL-GNB accounting for individual- and group-level confounding using machine-learning methods
  - 2010-2013: 3-year multicentre, prospective, cohort study in 12 wards (six medical and six surgical) in 3 university hospitals in Italy, Serbia and Romania

- Monotherapy ranked higher than combination therapy in promoting ESBL-GNB colonization.
- Monotherapy: cephalosporins > tetracycline > macrolide > cotrimoxazole
- Ranking of cephalosporins was lower when used in combination.
- Combinations not including cephalosporins, quinolones plus carbapenems ranked highest (eighth).
- Among sequential therapies, quinolones ranked highest (tenth) when prescribed within 30 days of therapy with cephalosporins.

→ Evidence from our study suggests that antibiotic resistance is an unavoidable adverse event of antibiotic therapy.
→ New ESBL-GNB colonization is therefore a very common (>10% frequency) adverse effect of cephalosporins
The discontinuation of contact precautions for MRSA and VRE: Impact upon patient adverse events and hospital operations

- To investigate the impact of the discontinuation of contact precautions (DcCP) for endemic MRSA and VRE on patient outcomes and operations metrics in an acute care setting.

  - Outcomes: Blocked beds, occupancy and lost hospital revenue; ED admission wait times; Gown and glove expenditures; Patient satisfaction; Patient falls and nosocomial pressure ulcers; Nosocomial MRSA and VRE.

- No change in Emergency dept wait times or change in trend.
- Significant reductions in monthly expenditures on gowns (−61.0%) and gloves (−16.3%).
- Patient satisfaction remained stable.
- No significant changes in rates or trends for patient falls or pressure ulcers.
- No change in incidence rates of nosocomial MRSA (1.58 (95% CI: 0.82 to 3.04)) and VRE (1.02 (95% CI: 0.82 to 1.27)).
Epidemiology and Treatment of Multidrug-Resistant and Extensively Drug-Resistant Pseudomonas aeruginosa Infections

- Literature review of mechanisms of resistance, epidemiology, and clinical impact and current and upcoming therapeutic options
Microbiota-derived lantibiotic restores resistance against vancomycin-resistant Enterococcus

- A four-strained consortium of commensal bacteria that contains *Blautia producta* BPSCSK can reverse antibiotic-induced susceptibility to VRE infection

- BPSCSK reduces growth of VRE by secreting a lantibiotic
- In patients at high risk of VRE infection, high abundance of the lantibiotic gene is associated with reduced density of *E. faecium*.
- In germ-free mice transplanted with patient-derived faeces, resistance to VRE colonization correlates with abundance of the lantibiotic gene.

The microbiota composition determined by metagenomic sequencing of 16S rRNA genes from faecal samples collected from mice treated with CBBPSCSK or CLBP.

Lantibiotic genes are present in human microbiomes of healthy individuals and gut resident, lantibiotic-producing species inhibit VRE.
Outbreak of VRE in Interventional Radiology: Detection Through Whole Genome Sequencing-Based Surveillance

- Epidemiologic investigation to identify the route of transmission of 10 genetically highly related VRE strains

- 439 clinical VRE isolates sequenced
  - 10 (2.3%) were genetically highly related ST-1471 strains by WGS
  - Suspicion of common exposure

- 9/10 VRE patients had undergone an interventional radiology procedure (OR=17, 2-138) with intravenous contrast ≤22 days before infection (OR=39, 8-inf)

Use of nonsterile technique during invasive interventional radiology procedures was responsible for the outbreak
Faecal microbiota transplantation for eradicating carriage of multidrug-resistant organisms: a systematic review

- To assess FMT efficacy (eradication rate) for decolonizing MDROs and preventing recurrent MDR infections.

Only one RCT:
- 58.8% of patients had spontaneous decolonization at 5 to 7 months, which is a higher percentage than that estimated in earlier studies
- 22.7% of patients in the intervention vs. 17.6% in the control group received antibiotic courses after they were included in the study.

Uncontrolled trials/RCTs and cohort studies:
- Eradication rate ranged from 37.5% to 87.5%.
- 8 studies with follow-up at 6 months: eradication rates were 37.5% to 72.7%

No serious adverse events from FMT were reported.
The evolution of the use of faecal microbiota transplantation and emerging therapeutic indications

Panel 2: Summary of additional non-Clostridioides difficile infection disease states in which faecal microbiota transplantation (FMT) has been assessed as a potential therapy

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<th>Description of the problem</th>
<th>Potential future directions</th>
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<td>FMT has substantial practical drawbacks including unpalatability, the potential need for invasive administration, and a potential risk of transmission of infection. Improving the understanding of the mechanisms of action might facilitate novel targeted therapeutics that minimise these risks. The safety of using live microorganisms in a treatment like FMT remains unclear in certain patient groups—particularly, severely immunocompromised patients. The mechanism of action of FMT is not well understood, even in the context of recurrent Clostridioides difficile infection, in which the process has been used most frequently. Potential limitations in transplantability of microbiota studies between patients and humans exist because of marked differences in structure and function of gut microbiota.</td>
<td>Capsulated FMT has helped to overcome concerns of invasive administration, but not other drawbacks. Transsudonic gastrointestinal tube administration of the transplant is being explored as an alternative. Further studies defining changes in gut microbiota profile, metabolic function, and host immunological profile between pre-FMT and post-FMT microbiota transplant are needed; these could be used as a basis for mechanistic studies of the contribution of the gut microbiota to the condition. Advanced systems biology techniques (eg, shotgun sequencing of microbial proteins, metaproteomics) could be used to track individual bacterial strains between donor and recipient, and direct linkage to effect on microbiota-host interactions.</td>
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<td>The optimal means of FMT administration is poorly understood—eg, the role for anaerobic preparation and the safe length of time and temperature for storing FMT in the freezer are not clear. The preparation methods might influence the interpretability of the results from clinical trials of FMT for non-Clostridioides difficile infection indications—eg, does a negative primary outcome reflect purely a suboptimal means of FMT preparation and administration, or is the result negative because of a true absence of efficacy?</td>
<td>Future translational research is needed to explore the specific influences of such variables upon microbial and metabolic profiles of FMT. Further investigation into the effect of FMT preparation upon clinical outcomes in randomised trials (eg, use of anaerobic preparation) is also needed.</td>
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<td>Donor screening is laborious and expensive and even minor perturbations in health (eg, short course of oral antibiotics) can result in at least a temporary exclusion of donors from the donor pool. A small but appreciable number of unsuccessful FMT courses for recurrent Clostridium difficile infection, with a lack of clarity as to whether this relates to donor or recipient factors. Donor selection relies on relatively crude risk factor and laboratory screening based on expert consensus opinion. Additionally, there is no consensus definition of a healthy microbiota, which might biologically guide matching of donor and recipient.</td>
<td>Development of stool banks and the so-called hub and spoke FMT services, in which a central centre prepares the fixatives and provides the FMT material to an entire region, streamlines the process of maintaining a donor pool. Additionally, further mechanistic investigation of the potential contribution of the gut microbiota to various disease states might improve donor-recipient matching.</td>
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<td>Novel clinical applications of FMT mean only limited long-term follow-up clinical data exist. There are theoretical concerns that FMT could transmit gut microbiota traits from the donor to the recipient, including those associated with potential increased future risk of disease (eg, type 2 diabetes). FMT trials are increasingly including conditions prominent in children and young people (eg inflammatory bowel disease).</td>
<td>FMT registry data (eg, American Gastroenterological Association Fecal Microbiota Transplant National Registry [NCT03325055]) will allow early recognition of potential concerns. Most FMT regulatory bodies and guidelines recommend long-term storage of donor semen and stool for so-called look back exercises in case of future concerns.</td>
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Autistic spectrum disorders

In one open-label trial, 18 children (aged 7-16 years) with autistic spectrum disorders and moderate-to-severe gastrointestinal problems were treated with 2 weeks of vancomycin, a bowel purge, and then 7-8 weeks of FMT. Either high dose oral or rectal FMT was used as the initial administration method, followed by daily, low dose oral FMT for the remainder of the study. Gastrointestinal tract symptoms scores and autistic spectrum disorders behaviour scores had both significantly improved by the end of FMT administration in these patients, and these improved scores were still maintained at week 18 after commencement of the study (ie, at least ten weeks after FMT administration). A follow-up study at two years post-FMT demonstrated maintained clinical improvements, particularly in gastrointestinal symptoms.
**Clostridioides difficile:** diagnosis and treatments

### Summary
- **C difficile epidemiology**
- **C difficile diagnosis**
  - Indications of C difficile testing—implementation of stool rejection criteria
  - Reference methods
  - Other methods: Enzyme immunoassays for toxins, Glutamate dehydrogenase assay, Nucleic acid amplification tests, Value of free toxin versus presence of toxigenic culture
  - Recommended algorithm
  - New methods—biomarkers
- **Treatment**
  - Antibiotics: Fidaxomicin, Teicoplanin, Tigecycline
  - Fecal microbiota transplantation: Efficacy, New indications in C difficile infection, Mechanism of action, Donor selection
  - Emerging treatments: Ridinilazole, Ursodeoxycholic acid, Other drugs
  - Bacteriophage: Non-toxigenic strains
- **Prevention**: Rifaximin, Probiotics, Microbiota based drugs, Antibodies and vaccines
- **International guidelines—a critical view**
N95 Respirators vs Medical Masks for Preventing Influenza Among Health Care Personnel: A Randomized Clinical Trial

**QUESTION** Is the use of N95 respirators or medical masks more effective in preventing influenza infection among outpatient health care personnel (HCP) in close contact with patients with suspected respiratory illness?

**CONCLUSION** This cluster randomized clinical trial found that as worn by HCP, N95 respirators were no more effective than medical masks as measured by the rate of laboratory-confirmed influenza events.

**POPULATION**
- 2369 Women
- 493 Men
- HCP in settings with a high prevalence of acute respiratory illness
- Mean age: 43 years

**INTervention**
- 5180 HCP-seasons randomized

**Primary Outcome**
- Incidence of laboratory-confirmed influenza over 4 years during peak viral respiratory illness season (5180 total HCP-seasons analyzed)

**FINDINGS**
- **N95 respirators**
  - 2512 HCP-seasons
  - 107 influenza infection events in 2512 HCP-seasons
  - Incidence 8.2% (95% CI, 5.5% to 11.1%)

- **Medical masks**
  - 2668 HCP-seasons
  - 193 influenza infection events in 2668 HCP-seasons
  - Incidence 7.2% (95% CI, 5.5% to 8.7%)

Difference in influenza rates was not significant: **1.0%** (95% CI, -0.5% to 2.5%)
Prospective, Real-time Metagenomic Sequencing During Norovirus Outbreak Reveals Discrete Transmission Clusters

- Real-time metagenomic sequencing during an ongoing norovirus outbreak associated with a retrospective cohort study.

- 10 chronologically overlapping, hospital-acquired norovirus cases partitioned into 3 discrete transmission clusters.

- Close genetic relationships between hospital-acquired and some community-acquired cases.

- Chronic viral shedding by an immunocompromised, hospital-acquired case patient.

The number of single-nucleotide variant differences between cluster members is shown on the bottom of each panel.
Sources of Airborne Norovirus in Hospital Outbreaks

- To investigate associations between symptoms of gastroenteritis and the presence of airborne norovirus, and to investigate the size of norovirus-carrying particles.
  - Air sampling was repeatedly performed close to 26 patients with norovirus infections

Norovirus RNA found in 21 (24%) of 86 air samples:
- during outbreaks, or before a succeeding outbreak
- associated with a shorter time period since the last vomiting episode

Airborne transmission can be an important transmission route
Time-Series Analysis of Health Care–Associated Infections in a New Hospital With All Private Rooms

- To examine whether single-patient rooms are associated with decreased rates of common MDRO transmissions and HAI
  - Time-series analysis analysis the move to a hospital with 100% single-patient rooms, with individual toilets and showers and easy access to sinks for hand washing.

Notable and sustained decrease in the rates of new MRSA and VRE colonization and VRE infection, but not of CDI or MRSA infection
To investigate routine use of mechanical and oral antibiotic bowel preparation in patients undergoing colon resection in a prospective randomised context

• Multicentre, parallel, single-blinded trial, patients undergoing colon resection were randomly assigned (1:1) to either

1. Mechanical and oral antibiotic bowel preparation: n=209 patients
2. No bowel prep: n=208 patients

Mechanical and oral antibiotic bowel preparation does not reduce SSIs or the overall morbidity of colon surgery compared with No Bowel Preparation
Chlorhexidine-alcohol versus iodine-alcohol for surgical site skin preparation in elective arthroplasty (ACAISA) study: cluster randomised controlled trial

- To compare the incidence of superficial wound complications and SSIs in patients undergoing elective hip or knee arthroplasty receiving skin preparation with either
  - 0.5% tinted chlorhexidine gluconate (w/v) in 70% ethanol (v/v) (Orion Laboratories Pty Ltd) (‘chlorhexidineealcohol’)
  - 1% iodine (w/v) in 70% ethanol (v/v) (Orion Laboratories Pty Ltd) (‘iodineealcohol’)
- Design: cluster randomized, controlled, single-centre, assessor-blinded, superiority trial

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Conclusion: No difference was observed for superficial wound complications, iodine/alcohol was superior to Chlorhexidine/alcohol as a surgical site skin preparation for the prevention of SSIs when used for hip and knee arthroplasty.
Thank you

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