Candida auris outbreak in a UK intensive care unit driven by multiuse patient monitoring equipment

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Candida auris

- First identified in the literature 2009 - retrospective review found earliest known strain of *C. auris* dates to 1996 in South Korea
- Genetic analysis - simultaneous emergence of separate clades in different geographical locations: South Asia, South Africa, South America and East Asia
- Emerging pathogen associated with nosocomial outbreaks on five continents, mainly in high-dependency settings
- Requires specialized laboratory methods for identification – frequently misidentified in commercial tests (*C. haemulonii / S. cerevisiae*)
- Variable antifungal susceptibility, and development of resistance on treatment observed
- High mortality rates reported in the literature – up to 50% for those with invasive infection.
- Infection prevention and control guidance currently based on extrapolation from MRSA and CRE.
Oxford *C. auris* experience

• Alerted to ‘emerging pathogen’ status and potential for outbreaks by Public Health England July 2016

• Look-back exercise identified four *C. auris* colonised patients and five with invasive infection between Feb 2015 and Oct 2016. 8/9 had been on the neurological intensive care unit (NICU)

• Further cases identified mid-October 2016. Introduction of a patient and environmental screening programme.

• Typing data – all strains ‘South African’
Neuro-ICU setting

• Regional neuro-surgical unit
• 16 beds, 13 open-plan and 3 side-rooms
• 650 admissions/year
Infection, Prevention and Control Measures

• Regular staff meetings (formal outbreak meetings and informal ‘brain-storming’)
• Three times weekly screening on NICU and in step-down areas
• Isolation or cohorting of all positive patients. Long sleeved gowns
• Enhanced clean whole unit daily (Acticlor plus 2000ppm) floors and level surfaces.
• Terminal cleans for all vacated bedspaces
• General ‘decluttering’ of the unit
• Restricted traffic
• Removal of fans and forced air convection blankets
• Reduction of bedside stocks of equipment, single use items in the immediate patient environment discarded on discharge
• Single use equipment where possible e.g. blood pressure cuffs
• Environmental screening and whole genome sequencing in collaboration with PHE and local NIHR Health Protection Research Unit
• Introduction of Micafungin prophylaxis (single dose) for device related surgical procedures in colonised patients
• Addition of *C. auris* alert to patient transfer form
• Discharge advice on isolation and screening for receiving wards
Patient screening

- Screened on admission and weekly, all sites
- Modified to three times weekly, axilla/groin
- Cultures identified using MALDI-TOF
C. auris screening results in 60 cases with ≥1 screen.

Defining colonisation as 3 negative screens, median (IQR) duration of carriage was 58 (29-82) days.
Environmental screening

152 samples obtained
Nov ‘16, Feb, April and Sept ‘17

Concentrating on high touch points and multi-use equipment

Methods:
• Swabs
• Sponges
• Passive and active air sampling
• Contact plates
• Sink waste water samples
Positive environmental sites for *Candida auris*

- *C. auris* rarely detected in the general environment or air

- **November 2016** – 36 samples
  - 1/13 pulse oximeters
  - 1/16 settle plates

- **February 2017** – 25 samples
  - Nil positive

- **April 2017** – 55 samples
  - 1 temperature probe
  - 1 hoist

- **May 2017** – 10 samples
  - 4/10 temperature probes

- **September 2017** – 26 samples
  - Nil positive
Skin surface temperature probes (axillary)

Used routinely in ventilated patients for continuous temperature monitoring
Weekly Candida auris new acquisition rate on the NITU

Majority of probes removed

All probes removed
Case-control study to determine risk factors for infection

• IORD (Infections in Oxford Research Database)
• Cases (N=66)
  – any patient with new C. auris colonisation/infection post admission to NICU
• Controls (N=361)
  – any patient never C. auris colonised/infected admitted to NICU
• Statistical methods
  – Independent predictors for C. auris colonisation/infection were identified using multivariable logistic regression.
  – Survival compared using Cox regression
• Independent predictors of C. auris colonisation/infection:
  – Controlling for length of NICU stay, patient physiology and biomarkers

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<thead>
<tr>
<th></th>
<th>Controls (N=361)</th>
<th>Cases (N=66)</th>
<th>Univariate</th>
<th>Multivariate</th>
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<tbody>
<tr>
<td></td>
<td>n / median</td>
<td>n / median % / IQR</td>
<td>Odds ratio</td>
<td>p value</td>
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<tr>
<td>Axillary temperature monitoring</td>
<td>122</td>
<td>34%</td>
<td>57</td>
<td>86%</td>
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<tr>
<td></td>
<td>n / median</td>
<td>n / median % / IQR</td>
<td>Odds ratio</td>
<td>95% Confidence interval</td>
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<tr>
<td>Any antifungal (fluconazole)</td>
<td>3</td>
<td>1%</td>
<td>3</td>
<td>5%</td>
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Mortality

• Survival from first-positive (cases) and last-negative screen (controls) was compared using Cox regression adjusting for age, sex, and admission diagnosis.

• 14/58(24%) cases identified after the start of screening died compared with 67/341(20%) controls surviving the day of their last screen

• NO evidence that *C. auris* acquisition was associated with increased mortality (hazard ratio 1.21, 95%CI 0.64-2.29, p=0.55).
Sequence analysis

- 72 patient samples from 37 patients
- 6 environmental isolates
- WGS undertaken using Illumina MiSeq
- Reads mapped to an out-break specific reference generated by long-read sequencing of one isolate on the Oxford Nanopore MinION
- Sequence comparison performed using single nucleotides polymorphisms, maximum likelihood and Bayesian time-scaled phylogenies
- Isolates formed a single genetic cluster from the South African clade
Whole genome sequencing of isolates

- First and last isolates
- Isolates from different sites at the same time
- Suggests introduction in 2013/14
- Rate of C. auris evolution: 5.75 mutations/genome/year

Time-scaled Bayesian phylogeny of 104 unique outbreak sequences obtained from 78 isolate pools.
Current position

- 73 cases of infection/colonisation with Candida auris
- 70 cases have had in-patient stay on NITU
- All strains typed are ‘South African’ clone
- 3 with CNS device related infection and 1 pin-site infection (all in 2015)
- 5 candidaemias
- Invasive infection rate - 8/73 cases (11%)
- 2/61 since IPC precautions put in place (3%)
- No attributable mortality
Summary of the Oxford Experience

We’ve been able to describe several aspects of *C. auris* epidemiology - including risk factors for acquisition, duration of carriage, effect on patient outcomes, and its molecular epidemiology.

We are also able to describe control of the outbreak - although not a complete elimination of *C. auris*

Environmental survival appears to be key to *C. auris* persistence and transmission in health care settings

Our findings reinforce the need to carefully investigate multi-use patient equipment in any unexplained healthcare-associated outbreak
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