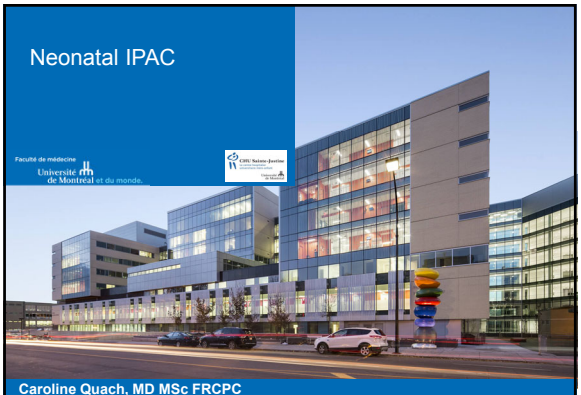
# Neonatal IPAC



**Caroline Quach, MD MSc FRCPC**
Professor – Dept. Microbiology, Infectiology and Immunology
CHU Sainte-Justine/Université de Montréal

26-MAY-2019

## Disclosures

- I have received a research grant from SAGE for a project on CLABSI risk factors in the NICU (ended in 2015)

## Objectives

- Outline the infection prevention challenges that are unique to the neonatal intensive care unit

## What is unique about a neonate?

- **Microbiota**: sum of all microbial life living in and on the human body and depends on what/who we have encountered.
- In utero: sterile/ near-sterile environment
- Fine balance between:
  - Preventing HAI
  - Modifying unique microbiota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## When normal is OR/NICU?

- Newborns born by c-section and cared for in our NICU/nursery:
  - Microbiota from hospital, HCP and other babies…
- Almost 20 years ago, the AAP said:

> "Each neonate should be approached as though he or she harbored colonies of unique flora that should not be transmitted to any other neonate"

AAP, American College of Obstetricians and Gynecologists. Infection control. In: Hauth JC, Merenstein GB, eds. Guidelines for Perinatal Care, 4th edn. Elk Grove Village: AAP, 1997:251-77.

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## Impact of environment

- Microorganisms found on NICU surfaces before being found in infants' gut
- Reservoir: NG tubes, incubators and sinks
- Other high touch areas:
  - Cell phones

Table 1. Bacterial growth frequency on cell phone, before-gel hand and after-gel hand cultures*

| Bacterial growth | Cell phone | Before-gel hand | After-gel hand |
|---|---|---|---|
| | n = 50 | n = 50 | n = 50 |
| Any growth | 50 (100%) | 48 (96%) | 37 (74%) |
| *Gram-positive cocci* | | | |
| *Enterococcus faecalis* | 1 (2%) | 2 (4%) | 3 (6%) |
| *Micrococcus* spp. | 27 (54%) | 2 (4%) | 0 |
| *Staphylococcus* spp. (coagulase negative) | 48 (96%) | 41 (82%) | 30 (60%) |
| *Staphylococcus aureus* | 4 (8%) | 6 (12%) | 3 (6%) |
| *Staphylococcus aureus* (Methicillin-resistant) | 1 (2%) | 1 (2%) | 0 |
| *Streptococcus* spp. (α-hemolytic) | 2 (4%) | 1 (2%) | 0 |
| *Streptococcus viridans* | 0 | 1 (2%) | 0 |
| *Gram-positive rods* | | | |
| *Bacillus* spp. | 18 (36%) | 7 (14%) | 8 (16%) |
| *Diphtheroid* spp. | 10 (20%) | 20 (40%) | 7 (14%) |
| *Gram-negative rods* | | | |
| *Acinetobacter* spp. | 1 (2%) | 2 (4%) | 1 (2%) |
| *Enterobacter* spp. | 1 (2%) | 1 (2%) | 1 (2%) |
| *Klebsiella* spp. | 1 (2%) | 2 (4%) | 1 (2%) |
| *Moraxella* spp. | 2 (4%) | 0 | 0 |
| *Pantoea* spp. | 0 | 3 (6%) | 0 |
| Unspecified Gram-negative rods | 1 (2%) | 0 | 3 (6%) |
| *Other* | | | |
| Yeast (unspecified) | 1 (2%) | 0 | 0 |

*Most cultures grew multiple organisms; therefore, absolute number of pathogens is higher than the sample number (n = 50).

Beckstrom AC. *J Perinatol* 2013; 33: 960-3
Brooks B, *Microbiome*. 2014;2:1.

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## Impact of HAIs in NICU

- Two-fold increase in death
- BSI associated mortality:
  - CoNS infections: 1.8%
  - Non-resistant GNR: 10.5%
  - MDR GNR: 28.6%
- CoNS sepsis: 5.6x increase in CP at 18-24 mo.

Goldmann DA. *J Infect Dis.* 1983;147:635-41; Blanchard AC. *Clin Perinatol.* 2015; 42:119-132; Tsai MH. *Pediatrics.* 2014;133:e322-9; Shah DK. *J Pediatr.* 2008;153:170-5, 5 e1; Schlapbach LJ. *Pediatrics.* 2011;128:e348-57.

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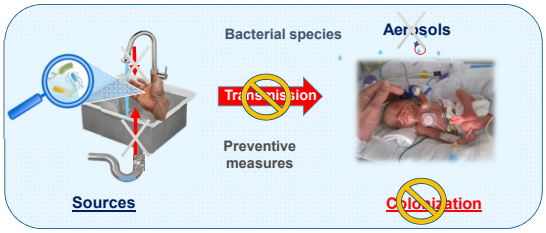
## Source of infection




E. Bédard, 2019

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## Outbreaks in NICU

**Table 1.** Pathogens responsible for neonatal ICU outbreaks reported in the literature, 2015–2017

| Bacterial (cum. outbreaks) (no. of individual outbreaks) | Fungal (no. of individual outbreaks) |
|---|---|
| Gram-positive [9] | *Candida albicans* (1) |
| *Enterococcus faecium* (1) | *Candida parapsilosis* (2) |
| *Staphylococcus aureus* (7) | |
| *Staphylococcus epidermidis* (1) | **Viral (no. of individual outbreaks)** |
| | Human rhinovirus C (1) |
| Gram-negative [21] | Parainfluenza-3 (1) |
| *Acinetobacter baumannii* (1) | Respiratory syncytial virus (3) |
| *Burkholderia cepacia* (3) | |
| *Escherichia coli* (3) | **Parasite (no. of individual outbreaks)** |
| *Enterobacter ludwigii* (1) | *Cimex hemipterus* (1) |
| *Klebsiella pneumoniae* (7) | |
| *Pseudomonas aeruginosa* (1) | |
| *Serratia marcescens* (5) | |

- 33%: source of outbreak not identified
- 54%: GNR

Johnson J. *Curr Op Infect Dis* 2017

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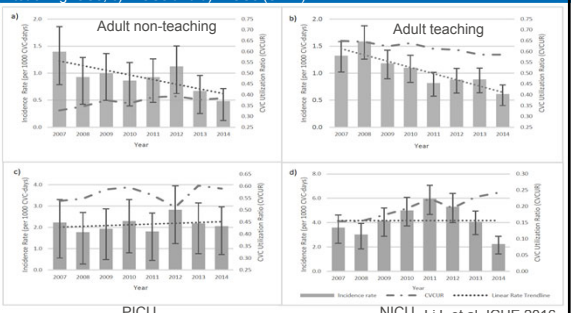
Incidence Rate (CLABSI cases / 1000 CVC-days) and central venous catheter utilization Ratios (CVCURs) by year for a) Adult nonteaching ICUs, b) Adult teaching ICUs, c) PICUs and d) NICUs (SPIN)




PICU NICU Li L et al. ICHE 2016

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Central line–associated BSI rate*

| Birth-weight category | No. of locations† | No. of CLABSIs | Central line days | Pooled mean |
|---|---|---|---|---|
| ≤750 g | 389 (345) | 403 | 191,246 | 2.1 |
| 751–1,000 g | 411 (354) | 210 | 156,909 | 1.3 |
| 1,001–1,500 g | 429 (385) | 136 | 173,835 | 0.8 |
| 1,501–2,500 g | 433 (349) | 91 | 161,626 | 0.6 |
| >2,500 g | 432 (334) | 134 | 182,144 | 0.7 |

Dudeck M. AJIC 2015

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# Preventing CLABSI

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## NICU staffing – CLABSI

- Guidelines: 3-4:1 (lower acuity) to 1:1 (higher acuity)

| Variables | OR | 95%CI |
|---|---|---|
| <95% planned staffing | 1.47 | 1.11, 1.95 |
| BW: 500-749g | 3.17 | 1.85, 5.45 |
| 750-999g | 2.28 | 1.47, 3.53 |
| 1000-1249g | 1.36 | 0.86, 2.14 |

- NEO-KISS

Leistner R. *Antimicrob Resist Infect Contr* 2013; 2: 11

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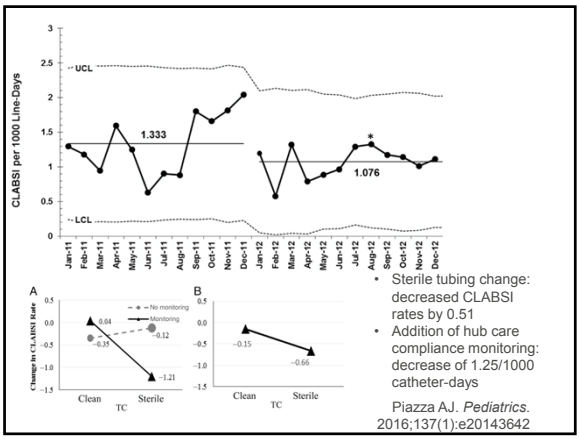


- Sterile tubing change: decreased CLABSI rates by 0.51
- Addition of hub care compliance monitoring: decrease of 1.25/1000 catheter-days

Piazza AJ. *Pediatrics.* 2016;137(1):e20143642

## Dressing/skin cleansing

- CHG/alcohol vs. polyurethane /povidone-iodine
  - Sepsis without a source: RR 1.06 (95%CI 0.75, 1.52)
  - CLABSI: RR 1.18 (95%CI 0.53, 2.65)
  - Catheter colonization: RR 0.62 (95%CI 0.45, 0.86)
  - Contact dermatitis: RR 43.06 (95%CI 2.61, 710.44)

Lai NM. *Cochrane Database Syst Rev.* 2016; CD011082.

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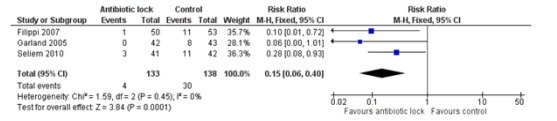
## Antimicrobial locks

NO data on development of resistance

- Confirmed CLABSI: RR 0.15 (95%CI 0.06, 0.4)
- Suspected CLABSI: RR 0.65 (95%CI 0.22, 1.92)
- All CLABSI: RR 0.25 (95%CI 0.12, 0.49)
- Mortality: RR 0.12 (0.01, 2.13)

**Figure 4. Forest plot of comparison: 1 Antibiotic lock versus no antibiotic lock, outcome: 1.1 Confirmed catheter-related infections.**




Taylor JE. *Cochrane Database Syst Rev. 2015;* CD010336.

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## Locks in pediatrics

**Figure 3. Effect measure of catheter-related infections rates comparing locks in clinical studies on pediatric patients (n = 4 (50%) studies)**

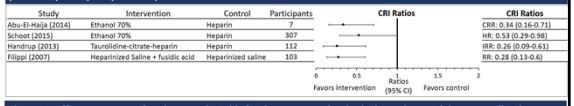
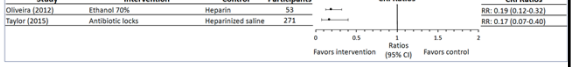



**Figure 4. Effect measure of catheter-related infections comparing locks in review articles on pediatric patients (n = 2 (100%) studies)**




- Taurolidine-citrate locks seem most effective for CLABSI prevention… need to add heparin

Iachimov D et al. AMMI Canada 2019

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## Other interventions

- CHG sponges:
  - Reduces CLABSI rates in adult population (1.3 to 0.4/1000 catheter-days)
  - Not shown to be better than best practices in PICU
  - No data in NICU – 46% of NICUs were using in 2012 (US>Canada)
  - NHS recommends – if used – to limit to > 27 weeks and at least 7 days
- Antimicrobial impregnated CVC:
  - Silver-zeolite impregnated UVL: RR 0.11 (95% CI 0.01, 0.87) but only one study
- Ethanol lock: no data in neonatal population
- Desinfectant caps: no data in neonatal population
  - Risk of backward leakage and absorption

Balain M. Cochrane Syst Rev 2015 (9)

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## Other etiology?

TABLE 1. Baseline Characteristics of Neonatal CLABSI Cases and Their Controls[a]

| | Cases (n = 120), No. (%) | Controls (n = 293), No. (%) |
|---|---|---|
| Male sex | 76 (63) | 150 (51) |
| Mean gestational age | 30.7 wk | 29.8 wk |
| CVC dwell time at T0 (matching) (IQR) | 10 (7–16) | 9 (7–14) |
| Singleton pregnancy | 89 (74) | 225 (77) |
| Spontaneous vaginal delivery | 51 (42.5) | 123 (42) |
| Concomitant pathologies[b] | | |
| Apneas + bradycardias | 41 (34) | 118 (40) |
| Respiratory distress syndrome | 34 (28) | 76 (26) |
| Patent ductus arteriosus | 30 (25) | 72 (25) |
| Intraventricular hemorrhage[c] | 9 (7.5) | 35 (12) |
| Necrotizing enterocolitis[c] | 14 (12) | 26 (9) |
| Intra-abdominal pathology[d] | 35 (29) | 33 (11) |
| Ostomies[e] | 11(9) | 24 (8) |
| ≥1 surgery[f] | 46 (39) | 87 (30) |
| ≥1 abdominal surgery[e] | 28/46 (61) | 40/87 (46) |

Dahan M. *Infect Control Hosp Epidemiol* 2016; 37: 1446-52

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TABLE 2. Matched Univariate and Multivariate Analyses of Risk Factors for CLABSI in Neonates

| | Case (n = 120), No. (%) | Control (n = 293), No. (%) | Univariate OR (95% CI) | Multivariate OR (95% CI) |
|---|---|---|---|---|
| Male sex | 76 (63) | 150(51) | 1.7 (1.05–2.63) | 1.76 (0.98–3.16) |
| Intra-abdominal pathology[a] | 35/120 (29) | 33/293 (11) | 3.39 (1.81–6.36) | 5.9 (2.50–14.05) |
| Surgeries | | | | |
| Any surgery[b] | 46/120 (39) | 87/293 (30) | 1.28 (0.69–2.37) | … |
| Any abdominal[b] | 28/46 (61) | 40/87 (46) | 1.54 (0.83–2.89) | … |
| Abdominal surgery[a] | 7/120 (6) | 6/293 (2) | 3.49 (1.12–10.90) | … |
| Other Invasive devices[a] | 65/120 (54) | 168/293 (57) | 0.76 (0.46–1.26) | … |
| >1 CVC at T0 | 4/120 (3) | 23/293 (8) | 0.42 (0.14–1.27) | … |
| Arterial lines[b] | 17/120 (14) | 54/293 (18) | 0.66 (0.34–1.30) | … |
| ≥3 heel punctures[c] | 31/102 (30) | 23/247 (9) | 4.01 (1.93–8.33) | 5.36 (2.37–12.15) |

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## BSI in the presence of same pathogen BSI in past 30 days

| Pathogen | GEE adjusted OR | (95% CI) |
|---|---|---|
| *S. aureus* | 3.58 | (2.29, 5.63) |
| *Enterobacter spp* | 3.99 | (2.07, 7.7) |
| *E. coli* | 2.75 | (1.19, 6.35) |
| *Serratia spp.* | 39.17 | (14.04, 108.24) |
| *P. aeruginosa* | 24.68 | (3.76, 162.15) |

- Reported ratios – sterile site infections: colonizations: 1:6 (*Serratia)* vs. 1:27 (*Klebsiella*)
- Attack rates: 20% for *Pseudomonas* and 50% for *Serratia* during outbreaks

Reichnert F. *Pediatr* 2016; e2 0152860

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**Table 1** Overview of surveillance and infection control measures before and during the *S. marcescens* cluster of colonisation

Surveillance and routine infection control measures *before* the detection of the *S. marcescens* cluster of colonisation

1. Pharyngeal and rectal swab on admission from each patient from the delivery room or other hospital
2. Once weekly screening of all patients by pharyngeal and rectal swabbing
3. Barrier precautions (coat and gloves) until colonisation status is known
4. Performance of hand hygiene measures according to WHO's "Five moments"
5. Communication of findings between physician and microbiologists immediately after the first detection of pathological findings
6. All microbiological findings accessible to all departments involved via a joint electronic database

Additionally, measures of surveillance and routine infection control *during* the detection of the *S. marcescens* cluster of colonisation

7. Implementation of weekly meetings of a task force comprising of neonatologists, ID physicians, microbiologist, infection control practitioners and a member of the local health authority
8. Strictly barrier precaution of colonised patients
9. Increase in the patient to health care worker ratio (from 5:1 to 3:1)
10. Cohorting of colonised patients and assignment of separated staff for colonised patients
11. Re-training in hand hygiene procedures for staff and parents
12. Information on outbreak and possible transmission routes provided to staff and parents
13. Implementation of single-use breast milk pump sets
14. Increase in disinfectant concentration (see text for details)

Dawczynski K. *Infection* 2016: DOI 10.1007/s15010-016-0922-y

## Do we need **more** screening?

- Allows for earlier detection of colonization and potential source for outbreak
- No evaluation of cost-effectiveness
- Vertical approach to IPAC vs. baseline infection control practices

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## VAP

- Definition difficult to implement; surveillance complex
- New definition being evaluated (VAE) from CDC:
  - VAC: ≥ 2 days PEEP or $FiO_2$ stable or improving followed by increase in PEEP ≥ 3cm $H_2O$ or 20% increase in $FiO_2$ x ≥ 2 days
  - IVAC: Infection-related VAC: systemic evidence of infection with antibiotics x ≥ 4 days
  - Possible VAP: IVAC + Gram+ (purulent) on sputum
  - Probable VAP: IVAC + Gram+ + culture for pathogen or respiratory virus

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## VAP (Pedatric adaptation)

- VAC: ≥ 2 days MAP or $FiO_2$ stable or improving followed by increase in MAP ≥ 4 or 25% in $FiO_2$ x ≥ 2 days
  - Correlated with mortality, longer LOS and ventilation in PICU/NICU
- IVAC: Infection-related VAC: systemic evidence of infection with antibiotics x ≥ 4 days
- Possible VAP: IVAC + Gram+ (purulent) on sputum
- Probable VAP: IVAC + Gram+ + culture for pathogen or respiratory virus

Corcoros NM. *Crit Care Med*. 2016;44(1):14-22.

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## VAP prevention

- Clear recommendations:
  - Avoid intubation and decrease duration of intubation
  - Regular oral care
  - Minimize breaks in ventilator circuit
  - Only change circuit if soiled
- No systematic review of impact of in-line suctioning on VAP – however, was shown to decrease hypoxia and decrease risk of change in heart rate

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## CA-UTI

- Incidence low in NICU – urinary catheter use is low
- No prevention guidelines

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## Breast milk – Administration error

- Handle as blood/body fluid exposure with disclosure – test mothers, not babies
- Risk evaluation based on:
  - Age of newborn at time or exposure
  - Gestational age at delivery
  - Potential effect of transmission
  - Health/infectious status of donor mother and « recipient » mother.
- 

| Viral agents | Contraindication to breastfeeding |
|---|---|
| HIV | YES |
| HBV | NO |
| HCV | NO unless cracked/bleeding nipples |
| CMV | NO |
| HTLV-I/II | YES |

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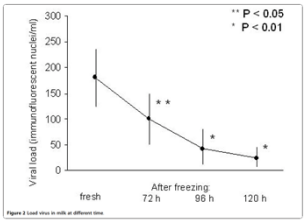
## CMV load in milk




- Risk of CMV transmission to preterm infants
- 40 of 57 seropositive mothers (70.2%) had virus reactivation with milk excretion in first 6 weeks postpartum
- **CMV transmission in extremely preterm infants**:
  - Freeze-thaw: 3/37 (8%)
  - Controls: 2/33 (6%)
  - Whole milk: 0/22
  - Pasteurized: 0/62
  - Freeze-thaw: 27/301 (8%)

Chiavarini et al. J Pediatr 2011, 37:6
Omarsdottir et al. PIDJ 2015; 34: 482-9
Soo Yoo et al. Yonsei Med J 2015; 56: 998

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## Breast milk

- Mother's own milk
- Donor breast milk
  - Volunteers screened for viral agents and syphilis
  - Milk: Holder pasteurization (62$^0$C for 30 minutes)
  - Batches screened before release
- Expressed BM: in glass or food-grade plastic containers with tight-fitting lids or plastic bags designed for human milk storage
  - Container should be labeled with infant's full name, medical record number, date/time expression
- Storage:
  - Freshly expressed: 4$^0$C up to 96h or frozen up to 3 months
  - Thawed BM: refrigerated and used in 24h

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## Breast milk

- Milk technicians to assist with storage, labelling, handing and dispensing of expressed human BM
- Cost-effective over time, improve quality, enhance family satisfaction
- ** Yearly competence training

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Thermo

## Conclusions

- HAIs in the NICU differ from everywhere else. Children are not small adults, neonates are not just small children
- Infants should be considered as having their unique microbiota that should not be shared with others
- HAI impacts long-term development
- Balance between impact on microbiota and preventive measures

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- Need to study changes in microbiota/clinical outcomes (short and long term)
- Need to refine surveillance definitions to be specific to NICU conditions for indicators to reflect reality
- Infection control program in the NICU needs to be multi-pronged and multidisciplinary – improved practice, helpful technology and stewardship, regardless of etiology
- But to improve, need to be able to measure

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## More references

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  - Chapter 3: **Device-Related Infections in the NICU** (Quach C)
  - Chapter 7: **Breast Milk Handling and Misadministration** (Fisher D)
- Johnson J, **Quach C***. Outbreaks in the Neonatal Intensive Care Unit: A Review of the Literature. *Current Opinion in Infectious Diseases,* 2017

https://global.oup.com/academic/product/handbook-of-pediatric-infection-prevention-and-control-9780190697174?cc=ca&lang=en&