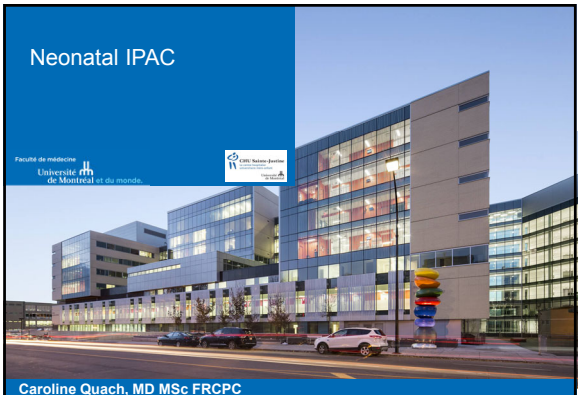
Neonatal IPAC



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

Faculté de médecine
Université de Montréal et du monde.

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.

Faculté de médecine
Université de Montréal et du monde.

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[a]

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

[a]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.

Faculté de médecine Université de Montréal et du monde.

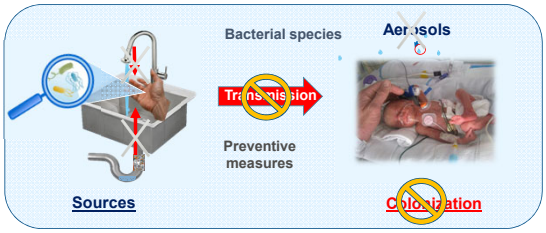
Impact of HAIs in NICU

- 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.

Faculté de médecine Université de Montréal et du monde.

Source of infection



E. Bédard, 2019

Faculté de médecine Université de Montréal et du monde.

Outbreaks in NICU

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

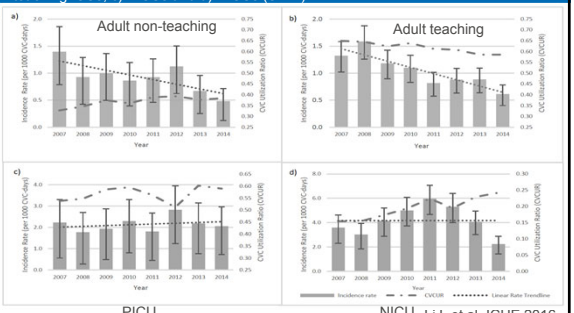
Bacterial (cum. outbreaks) (no. of individual outbreaks)	Fungal (no. of individual outbreaks)
Gram-positive [9]	*Candida albicans* (1)
Enterococcus faecium (1)	*Candida parapsilosis* (2)
Staphylococcus aureus (7)	
Staphylococcus epidermidis (1)	**Viral (no. of individual outbreaks)**
	Human rhinovirus 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

Faculté de médecine Université de Montréal et du monde.

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

Faculté de médecine Université de Montréal et du monde.

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

Faculté de médecine Université de Montréal et du monde.

Preventing CLABSI

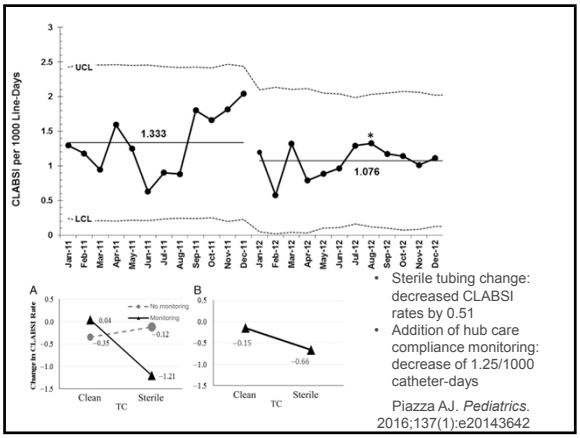
NICU staffing – CLABSI

- 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



- 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.

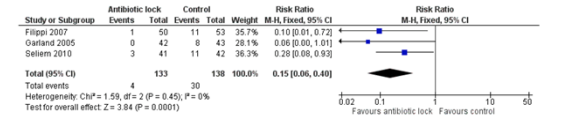
Faculté de médecine Université de Montréal et du monde.

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.

Faculté de médecine Université de Montréal et du monde.

Locks in pediatrics

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

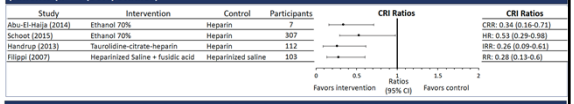
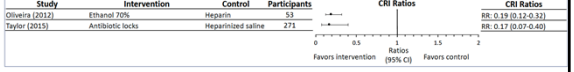


Figure 4. Effect measure of catheter-related infections comparing locks in review articles on pediatric patients (n = 2 (100%) studies)



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

Iachimov D et al. AMMI Canada 2019

Faculté de médecine Université de Montréal et du monde.

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)

Faculté de médecine Université de Montréal et du monde.

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

té de médecine Université de Montréal et du monde.

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)

Faculté de médecine Université de Montréal et du monde.

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

Faculté de médecine Université de Montréal et du monde.

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

Faculté de médecine Université de Montréal et du monde.

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

Faculté de médecine Université de Montréal et du monde.

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.

Faculté de médecine Université de Montréal et du monde.

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

Faculté de médecine Université de Montréal et du monde.

CA-UTI

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

Faculté de médecine Université de Montréal et du monde.

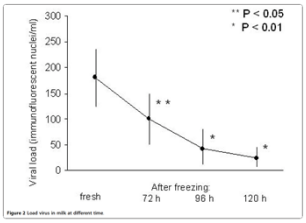
Breast milk – Administration error

- 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

de Montréal et du monde.

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

Faculté de médecine Université de Montréal et du monde.

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

Faculté de médecine Université de Montréal et du monde.

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

Faculté de médecine Université de Montréal et du monde.

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

Faculté de médecine Université de Montréal et du monde.

- 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

Faculté de médecine Université de Montréal et du monde.

More references

- *The PIDS Handbook of Pediatric Infection Prevention and Control* - Editors: Kristina A. Bryant, MD et Judith A. Guzman-Cottrill, DO; Oxford Press, 2019.
  - 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&