Name of the speaker: Sara Romano-Bertrand

☑️ I have no link of interest.
And what about getting rid of catheter-associated urinary tract infections?

CAUTI: the valuable concept of healthcare-associated pathobiome

Dr Sara Romano-Bertrand, PharmD, PhD
Associate Professor
Microbiology, Infection Prevention and Control
University Hospital of Montpellier
Pharmacy School of Montpellier
Human-associated microbiome and human body as a superorganism

50% human cells

50% bacteria
Paradigm shift in infectiology and Pathobiome Concept

Classical Infectiology
1 infection = 1 bacteria

Modern Infectiology
1 infection = result of community-level phenomenon

⇒ Particularly true for opportunistic infections

(Seredberg & McCray 2001; Grice & Segre 2011; Human Microbiome Project Consortium 2012; Boutin et al. 2013; Stecher et al. 2013)

Soil is “...a living environment, a collective entity that possessed the characteristic functions of a living organism”
Interactions occurring within bacterial community influence the **pathogenesis, emergence, resistance, transmission, persistence**... of certain members of this community.

**In accordance with the ‘OneHealth’ initiative**

[www.sf2h.net](http://www.sf2h.net)
Why considering the Pathobiome while talking about CAUTI ?
Unusual conditions

Microbiome disruption & pathogen selection

Patients

Healthcare workers

Hospital environment

www.sf2h.net

Human Microbiome Illustration © Charis Tsevis.
Healthcare-associated pathobiome: *C. difficile* infections

Microbiota disequilibrium and/or barrier effect disruption

Gut microbiota hosting opportunistic pathogens (pathobiontes)

**Clostridium difficile** – From Colonization to Infection

*Holger Schäffler*¹ and *Anne Breitrück*²,³*

¹ Division of Gastroenterology, Department of Medicine II, University of Rostock, Rostock, Germany, ² Extracorporeal Immunomodulation Unit, Fraunhofer Institute for Cell Therapy and Immunology, Rostock, Germany, ³ Institute of Medical Microbiology, Virology and Hygiene, University of Rostock, Rostock, Germany

Infection (HAIs)

dysbiosis and pathobiontes selection
Healthcare-associated pathobiome: *C. difficile* infections

Schäffler et al. (2018)

HCF = Healthcare Facilities
PPI = Proton Pump Inhibitor
Healthcare-associated pathobiome: in surgery

The shift of an intestinal “microbiome” to a “pathobiome” governs the course and outcome of sepsis following surgical injury

Monika A. Krezalek, MD, Jennifer DeFazio, MD, Olga Zaborina, PhD, Alexander Zaborin, PhD, and John C. Alverdy, MD FACS
Center for Surgical Infection Research and Therapeutics Pritzker School of Medicine, University of Chicago, Department of Surgery, 5841 S. Maryland, Chicago, Illinois 60637

The Influence of Host Stress on the Mechanism of Infection: Lost Microbiomes, Emergent Pathobiomes, and the Role of Interkingdom Signaling

John C. Alverdy¹ and James N. Luo²
¹ Sarah and Harold Lincoln Thompson Professor of Surgery, Pritzker School of Medicine, The University of Chicago, Chicago, IL, USA. ² Pritzker School of Medicine, The University of Chicago, Chicago, IL, USA

The gut microbiome and the mechanism of surgical infection

J. C. Alverdy¹, S. K. Hyoju¹, M. Weigerinck² and J. A. Gilbert¹

Collapse of the Microbiome, Emergence of the Pathobiome, and the Immunopathology of Sepsis

John C. Alverdy, MD, FACS, Monika A. Krezalek, MD

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Healthcare-associated pathobiome: in surgery

Figure: Host-microbiome dynamics in the gut during surgery

Alverdy et al. BJS. 2017
Healthcare-associated pathobiome: in surgery

Limited surgical injury

Transient pathobiome

Resilience and microbiome restoration

Severe surgical injury & prolonged pressures

Sustained pathobiome

Pathobiontes colonization and vulnerability to infection

Figure: Host-microbiome dynamics in the gut during surgery

Alverdy et al. BJS. 2017

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Why considering the Pathobiome while talking about CAUTI?

So what?
The end of the long-held “sterile urine” paradigm?

⇒ the discovery of the Bladder microbiota
“...the microorganisms inhabiting the urinary tract might have a role in maintaining urinary health »

Acting as a protective agent against pathogens

www.sf2h.net
2nd reason: urinary microbiota in health & diseases

Whiteside et al. (2015)

(1) Bacteria might produce neurotransmitters that interact with the nervous system.

(2) Commensal bacteria might **outcompete pathogens for common resources**.

(3) Bacteria might have a role in the regulation and maintenance of **epithelial junctions**.

(4) Commensals might produce **antimicrobial compounds** that kill pathogens.

(1) Bacteria might **prime epithelial defences**, including immune defences.

(2) Commensal bacteria might **degrade harmful compounds**.

(3) Bacteria might be necessary for **proper development of the urinary tract**, including the uroepithelium, immune system and peripheral nervous system within the bladder and surrounding tissues.

(4) Commensals might create a **barrier**, blocking pathogen access to the uroepithelium.
**2nd reason: urinary microbiota in health & diseases**

Interplay between Bladder Microbiota and Urinary Antimicrobial Peptides: Mechanisms for Human Urinary Tract Infection Risk and Symptom Severity

Vanessa Nienhouse¹,²,³,⁴, Xiang Gao⁵,⁶, Qunfeng Dong⁵,⁶,⁷, David E. Nelson⁸, Evelyn Toh⁹, Kathleen McKinley⁹, Paul Schreckenberger³,⁴,⁶, Noriko Shibata²,⁴, Cynthia S. Fok³,⁶,⁷, Elizabeth R. Mueller³,⁵,⁷, Linda Brubaker³,⁵,⁷, Alan J. Wolfe²,³,⁴, Katherine A. Radek¹,²,³,⁴,⁸

AMP hydrophobicity and protease activity in urine ↑ in case of UTI and correlated positively with both UTI risk and pelvic floor symptoms

Interdependency between the urinary microbiota, AMP responses and symptoms

UTI risk significantly correlated with specific urinary microbiota & AMP levels

Innate immune system regulation

Urinary microbiota

Antimicrobial peptides (AMP)
**2nd reason: urinary microbiota in health & diseases**

Urinary microbiota diversity correlated to risk of UTI

“Some members of the urinary microbiota could contribute to lower urinary tract infections, while others could be protective”

POS= Positive Urine Culture
PostI-UTI= Post-Intervention UTI
NEG= Negative Urine Culture

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Nienhouse et al. (2014)

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Fig. 1. Bacterial diversity correlates with the susceptibility or resistance to UTI. Phylogenetic tree comparing the bacterial diversity at the Order level within the female urinary microbiome. The bacterial diversity was compared between the three cohorts: POS (Blue), PostI-UTI (Red) and NEG (Green).
3rd reason: catheter disturbs the physiology of urinary tract

In physiologic conditions

Bacterial multiplication during bladder filling and urine stasis

*but*

mechanic elimination by flushing during the micturition
In physiologic conditions, bacterial multiplication during bladder filling and urine stasis is followed by mechanistic elimination by flushing during micturition. 

**3rd reason:** catheter disturbs the physiology of urinary tract

When the catheter is placed...

1. Catheter surfaces are coated with proteins
2. Microorganisms are introduced
3. Colonizing
4. Proliferating
5. Forming a biofilm
6. That maturate

⇒ Catheter-colonization in few hours
⇒ CAUTI

4th reason: microbial network and risk factor of CAUTI

*Multi-Drug Resistant Organisms

existing bacterial colonization → risk of secondary acquisition

relationship between antibiotic exposure & MDRO* colonization

joint influence of microbial and antibiotic factors onto MDRO colonization

Fig2: Risk network for MDRO colonization
4\textsuperscript{th} reason: microbial network and risk factor of CAUTI

existing bacterial colonization \( \rightarrow \) risk of secondary acquisition

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*Mutli-Drug Resistant Organisms

cocolonization associated with increased risk of CAUTI by specific bacteria

Fig 2: Risk network for MDRO colonization

Fig 3: Risk network for catheter-associated urinary tract infection (CAUTI) events

Wang et al. *PNAS.* 2017
Microbial and antibiotic interactions drive colonization and infection with MDRO = PATHOBIOME

Fig 2: Risk network for MDRO colonization
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Fig 3: Risk network for catheter-associated urinary tract infection (CAUTI) events

Wang et al. PNAS. 2017
Resistome = reservoir for antimicrobial resistance genes in the human microbial ecosystem

- open and dynamic entity
- shaped by several extrinsic and intrinsic factors
- massive interactions

Figure: Potential factors shaping the human resistome
Resistome = reservoir for antimicrobial resistance genes in the human microbial ecosystem

- open and dynamic entity
- shaped by several extrinsic and intrinsic factors
- massive interactions

Considering resistome and factors acting upon it as a whole

emergence of MDRO and change commensal/mutualistic bacteria to pathogens

Ex: *E. coli* pathotypes
Carbapenem-producing Enterobacteria...

**Figure: Potential factors shaping the human resistome**
Is the pathobiome concept valuable to prevent HAIs?

Proofs of concept

*Clostridium difficile* and faecal transplant resistome and MDRO post-surgical sepsis, CAUTI, ventilator-associated pneumonia...

Preserving microbiota balance = preserving patients’ safety?
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**Lifecycle of the urinary catheter:**

1. Catheter Placement
2. Catheter Care
3. Catheter Removal
4. Catheter Re-insertion

*Meddings J, Saint S Clin Infect Dis. 2011;52:1291-1293*
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WTF?
“Why The Foley?”

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**Lifecycle of the urinary catheter:**

WTF?
“*Why The Foley?*”

“No answer to give?
⇒ *Get the Foley out!*

Thank you for your attention!