SF2H
Risque infectieux et soin

6, 7 et 8 juin 2018
XXIXe Congrès National de la Société Française d'Hygiène Hospitalière

LINKS OF INTEREST DISCLOSURE

Name of the speaker: Sara Romano-Bertrand

☑ **I have no link of interest.**

SF2H
Risque infectieux et soin

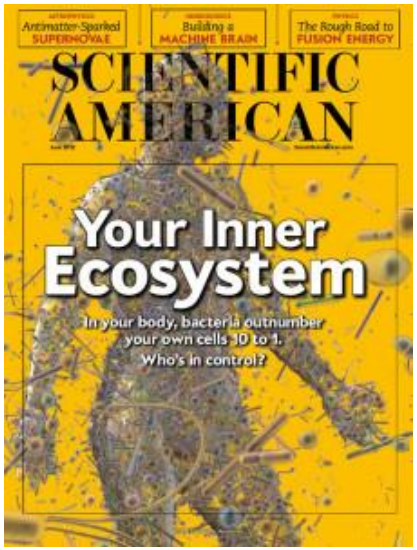
6, 7 et 8 juin 2018
XXIXe Congrès National de la Société Française d'Hygiène Hospitalière

And what about getting rid of catheter-associated urinary tract infections?

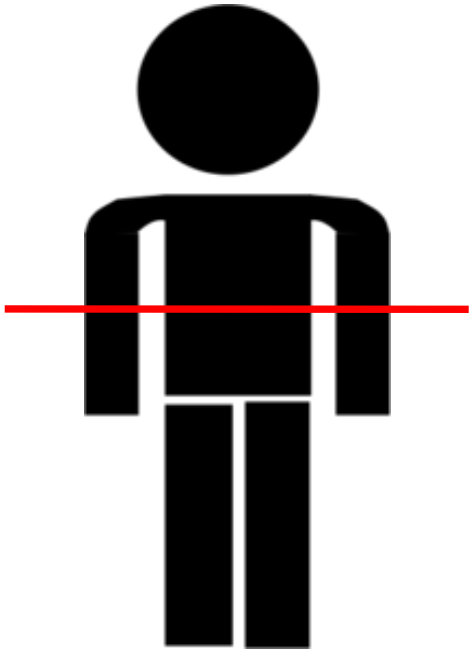
CAUTI: the valuable concept of healthcare-associated pathobiome

Dr Sara Romano-Bertrand, PharmD, PhD
Associate Professor
Microbiology, Infection Prevention and Control
University Hospital of Montpellier
Pharmacy School of Montpellier

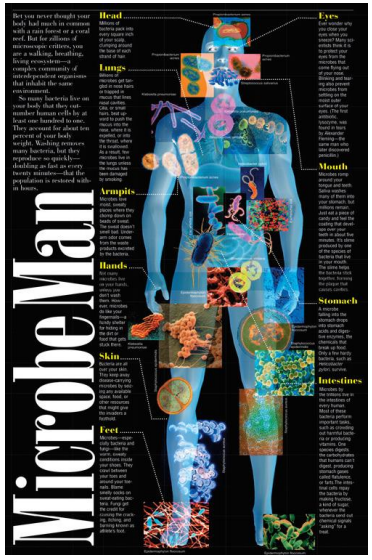
Human-associated microbiome and human body as a superorganism



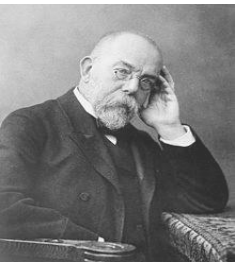
50%
human cells



50%
bacteria



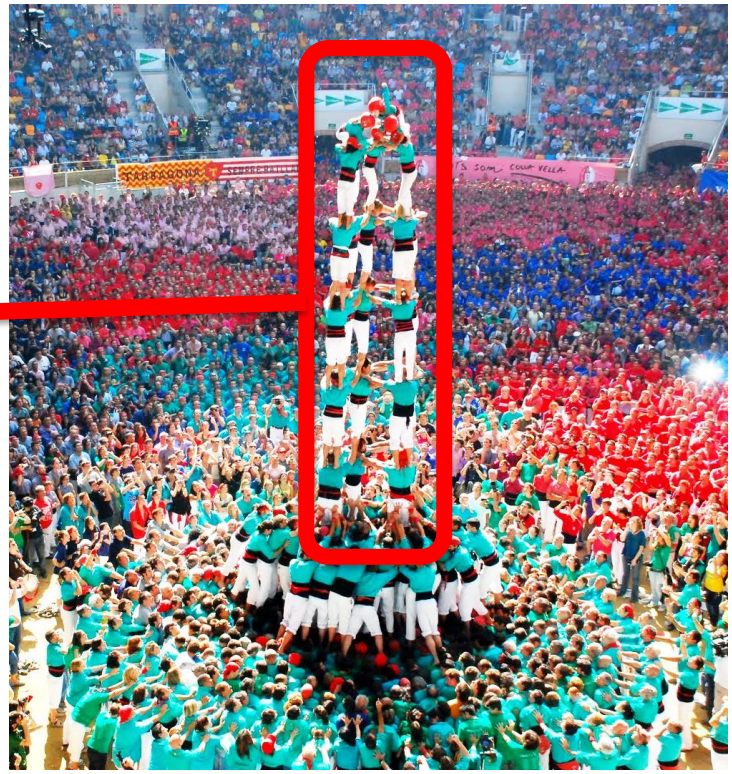
Paradigm shift in infectiology and Pathobiome Concept



Robert Koch

Classical Infectiology
1 infection = 1 bacteria

Modern Infectiology
1 infection = result of community-level phenomenon



Sergueï Winogradsky

Soil is "…a living environment, a collective entity that possessed the characteristic functions of a living organism"

⇒ Particularly true for opportunistic infections

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

Paradigm shift in infectiology and Pathobiome Concept

Vayssier-Taussat et al., *Frontiers in Microbiology, 2014*

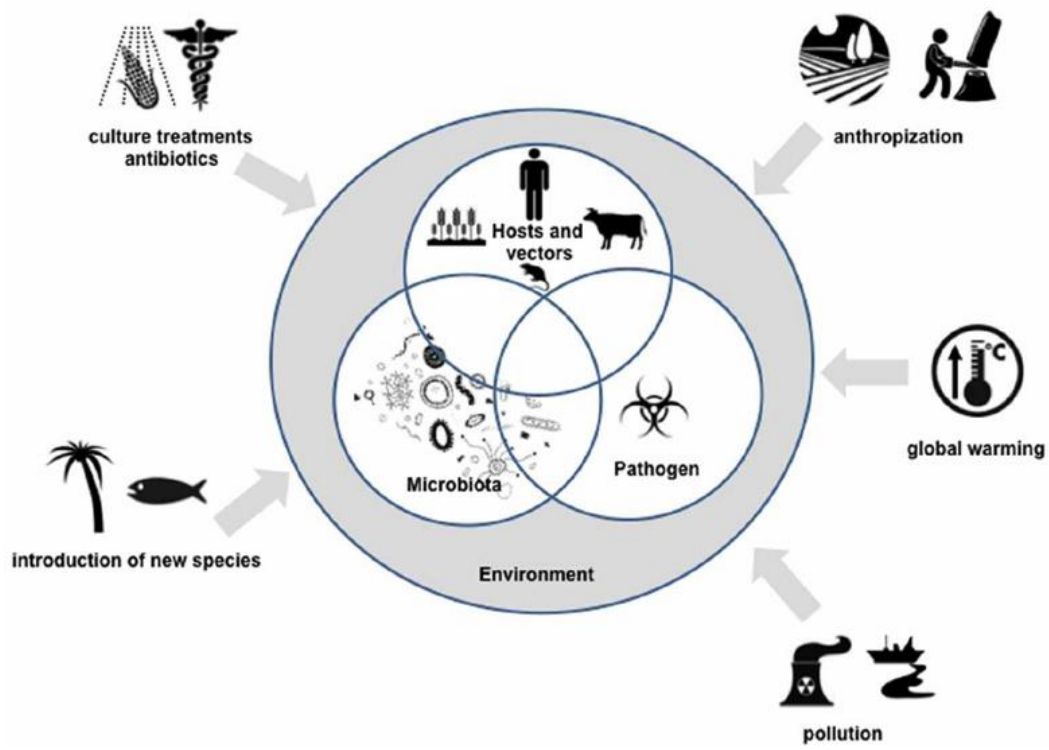


FIGURE 1 | Overview of the pathobiome concept and scientific challenges for the coming years.

Considering

the **pathogenic agent**

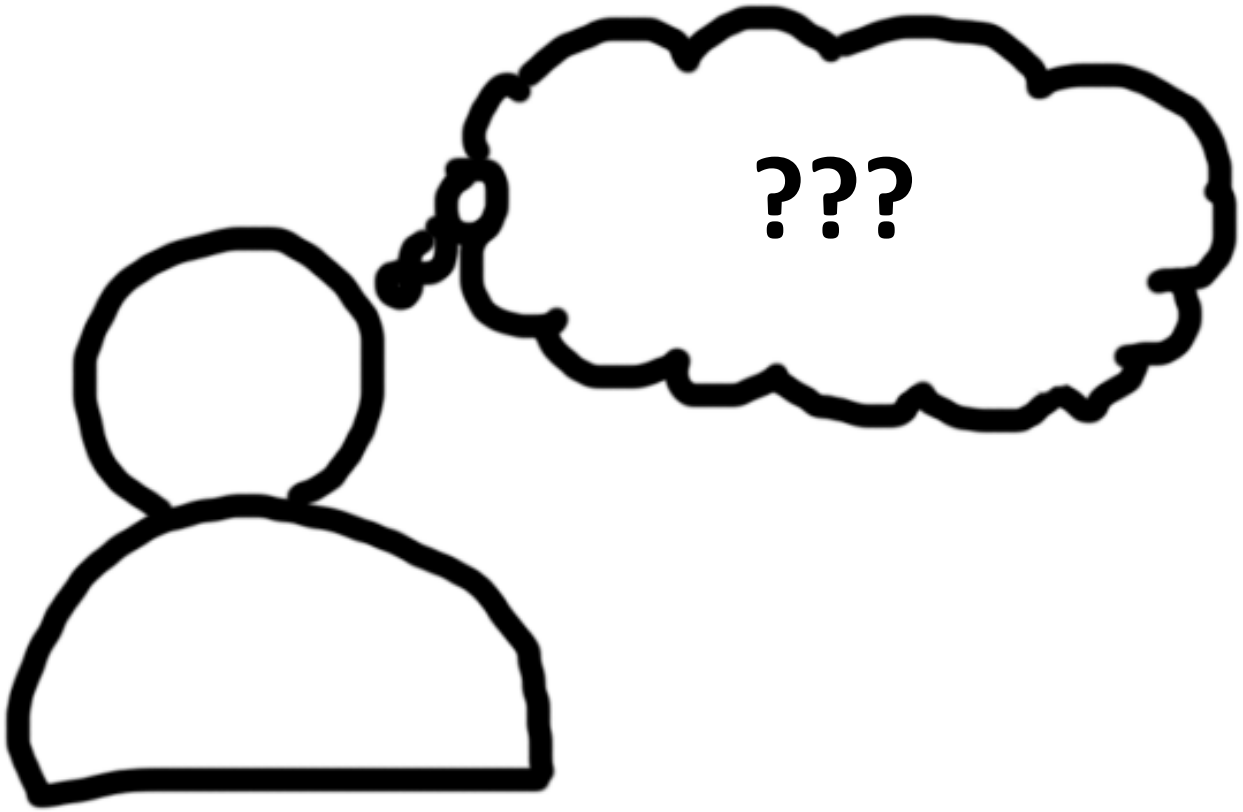
within its **host** and its **environment**

submitted to **abiotic conditions**

Interactions occurring within bacterial community influence the **pathogenesis**, **emergence**, **resistance**, **transmission**, **persistence**… of certain members of this community.

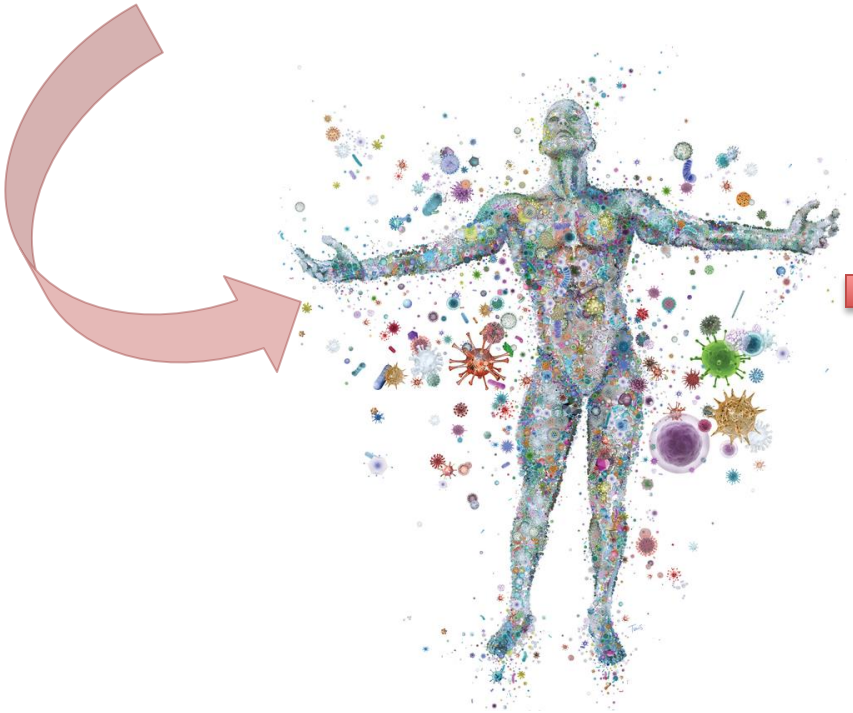
In accordance with the 'OneHealth' initiative

Why considering the Pathobiome while talking about CAUTI ?



Pathobiome & Hospital

Unusual conditions



Microbiome disruption & pathogen selection

Patients

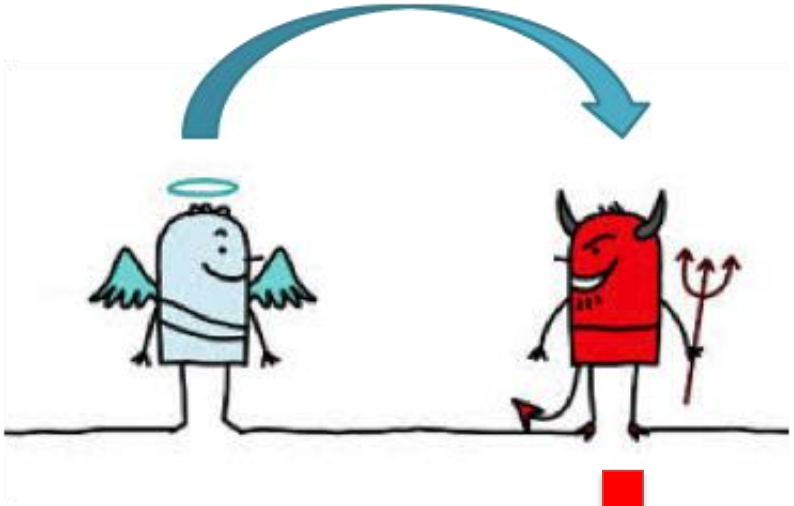
Healthcare workers

Hospital environment

Healthcare-associated pathobiome: *C. difficile* infections

Microbiota disequilibrium and/or barrier effect disruption

Gut microbiota hosting opportunistic pathogens (pathobiontes)



dysbiosis and pathobiontes selection

Infection (HAIs)

frontiers in Microbiology

REVIEW
published: 10 April 2018
doi: 10.3389/fmicb.2018.00646

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

Healthcare-associated pathobiome: *C. difficile* infections

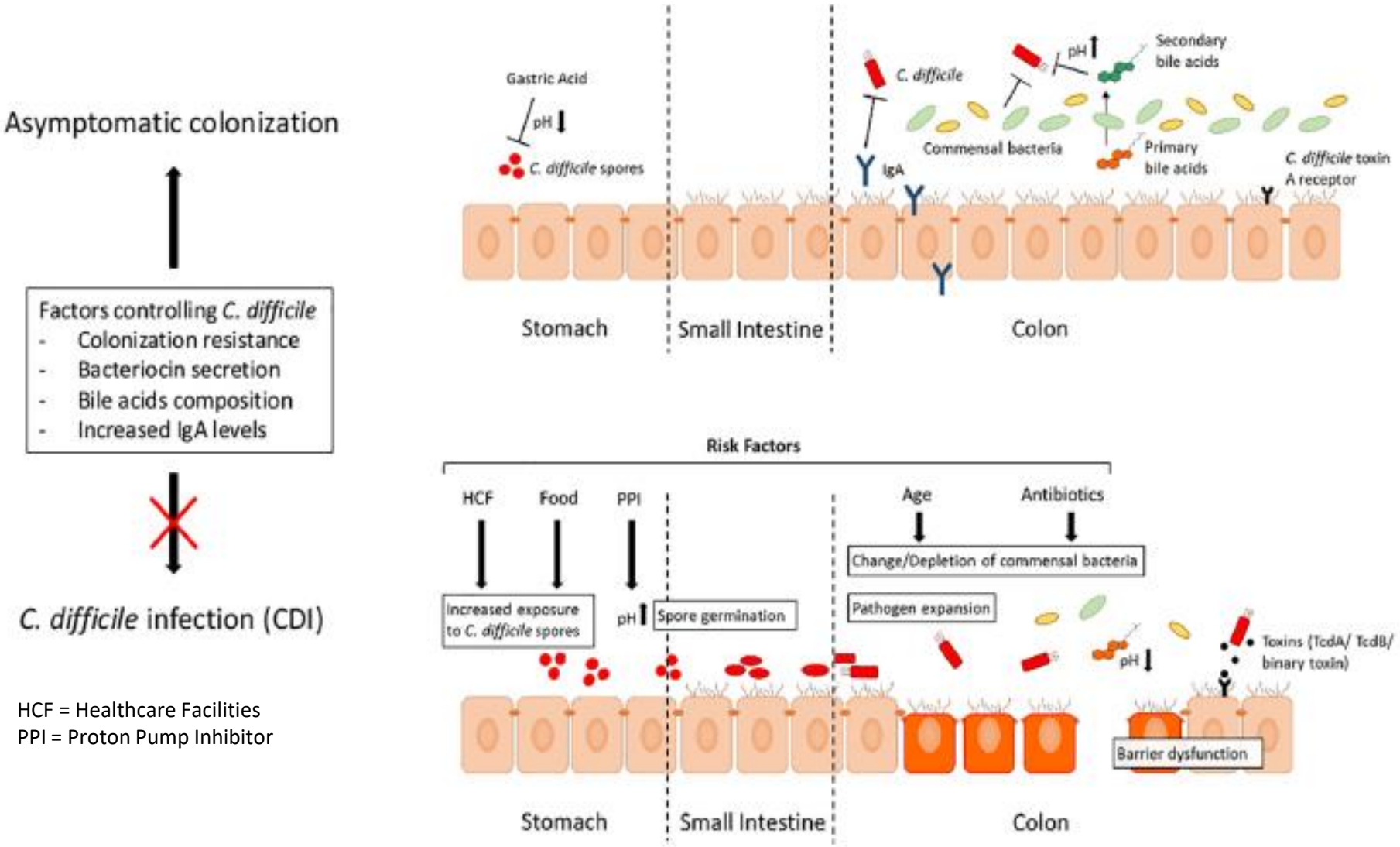


FIGURE 1 | Processes leading from asymptomatic *C. difficile* colonization to CDI.

Schäffler et al. (2018)

Healthcare-associated pathobiome: in surgery

Shock. 2016 May ; 45(5): 475–482. doi:10.1097/SHK.0000000000000534.

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

frontiers in Microbiology

PERSPECTIVE
published: 02 March 2017
doi: 10.3389/fmicb.2017.00322

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

John C. Alverdy[1] and James N. Luo[2]*

[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

Review

The gut microbiome and the mechanism of surgical infection

J. C. Alverdy[1], S. K. Hyoju[1], M. Weigerinck[2] and J. A. Gilbert[1]

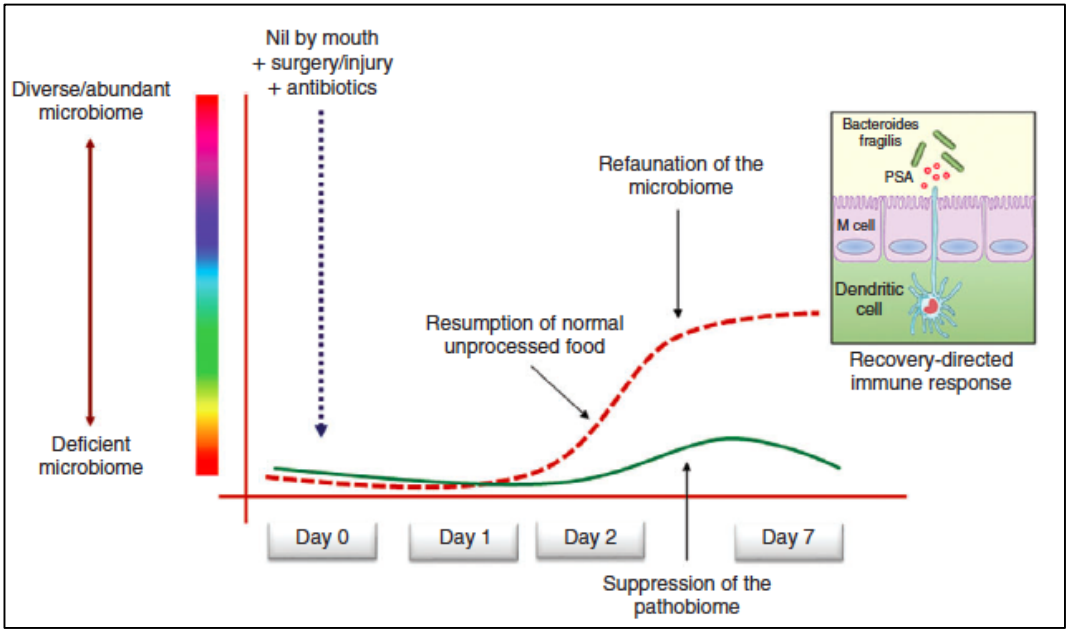
BJS 2017; **104**: e14–e23

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

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

Critical Care Medicine
February 2017 • Volume 45 • Number 2

Healthcare-associated pathobiome: in surgery



Limited surgical injury

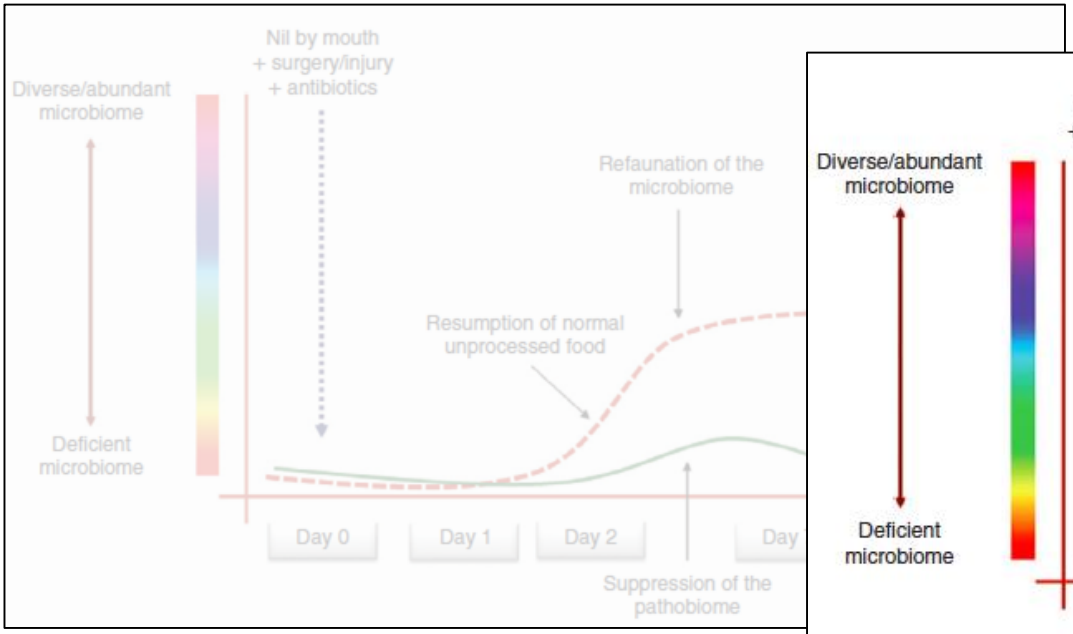
Transient pathobiome

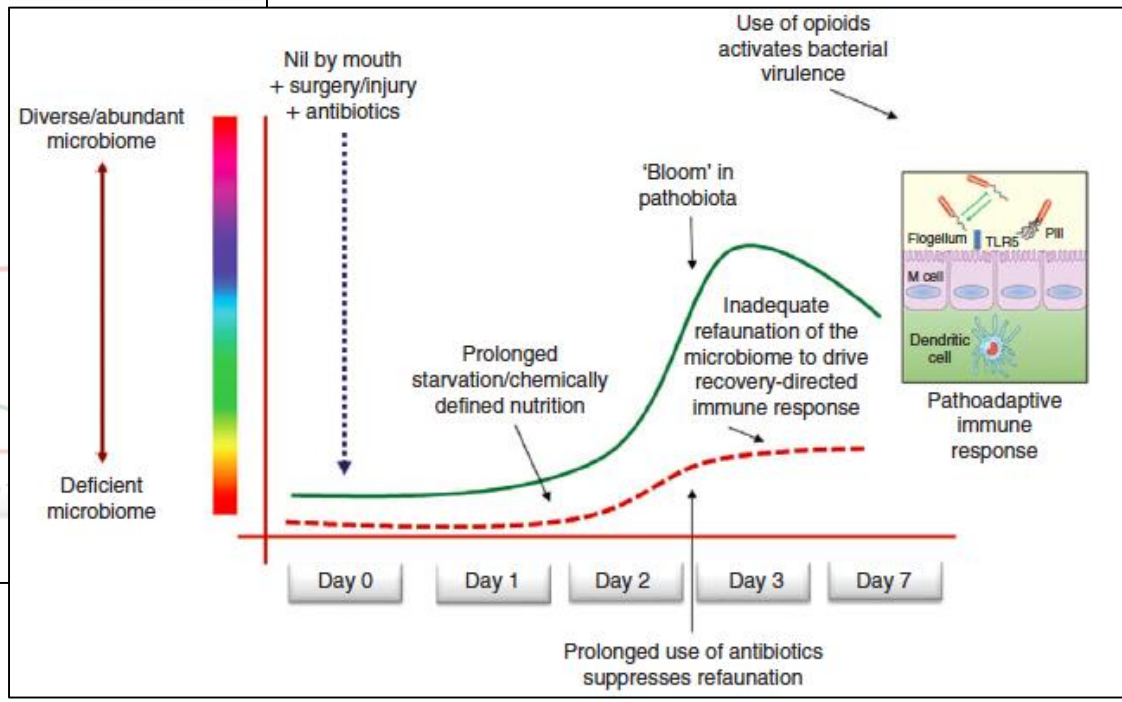
Resilience and microbiome restoration

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

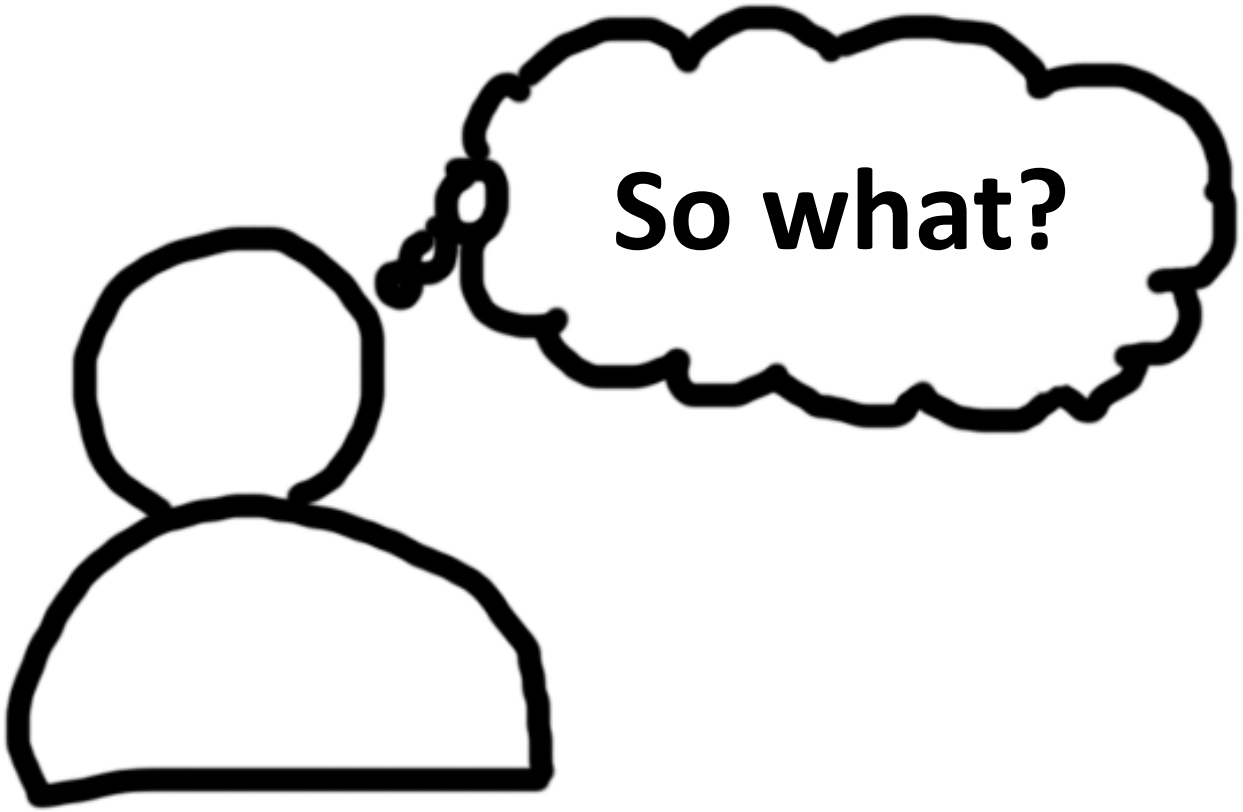
Sustained pathobiome

Pathobiontes colonization and vulnerability to infection

Figure: Host-microbiome dynamics in the gut during surgery

Alverdy et al. *BJS.* 2017

Why considering the Pathobiome while talking about CAUTI ?



1st reason: urine is not sterile!

EUROPEAN UROLOGY 68 (2015) 173–174

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Opinion

"Sterile Urine" and the Presence of Bacteria

Alan J. Wolfe [a,*], *Linda Brubaker* [b]

[a] *Department of Microbiology and Immunology, Stritch School of Medicine, Loyola University Chicago, Maywood, IL, USA;* [b] *Departments of Obstetrics and Gynecology and Urology, Stritch School of Medicine, Loyola University Chicago, Maywood, IL, USA*

The end of the long-held ''sterile urine'' paradigm?

$\Rightarrow$ the discovery of the Bladder microbiota

2nd reason: urinary microbiota in health & diseases

NATURE REVIEWS | UROLOGY

REVIEWS

The microbiome of the urinary tract —a role beyond infection

Samantha A. Whiteside, Hassan Razvi, Sumit Dave, Gregor Reid and Jeremy P. Burton

Abstract | Urologists rarely need to consider bacteria beyond their role in infectious disease. However, emerging evidence shows that the microorganisms inhabiting many sites of the body, including the urinary tract—which has long been assumed sterile in healthy individuals—might have a role in maintaining urinary health. Studies of the urinary microbiota have identified remarkable differences between healthy populations and those with urologic diseases. Microorganisms at sites distal to the kidney, bladder and urethra are likely to have a profound effect on urologic health, both positive and negative, owing to their metabolic output and other contributions. Connections between the gut microbiota and renal stone formation have already been discovered. In addition, bacteria are also used in the prevention of bladder cancer recurrence. In the future, urologists will need to consider possible influences of the microbiome in diagnosis and treatment of certain urological conditions. New insights might provide an opportunity to predict the risk of developing certain urological diseases and could enable the development of innovative therapeutic strategies.

Whiteside, S. A. *et al. Nat. Rev. Urol.* **12**, 81–90 (2015); published online 20 January 2015; doi:10.1038/nrurol.2014.361

"…the microorganisms inhabiting the urinary tract might have a role in maintaining urinary health »

Acting as a protective agent against pathogens

2nd reason: urinary microbiota in health & diseases

NATURE REVIEWS | UROLOGY

Whiteside *et al*. (2015)

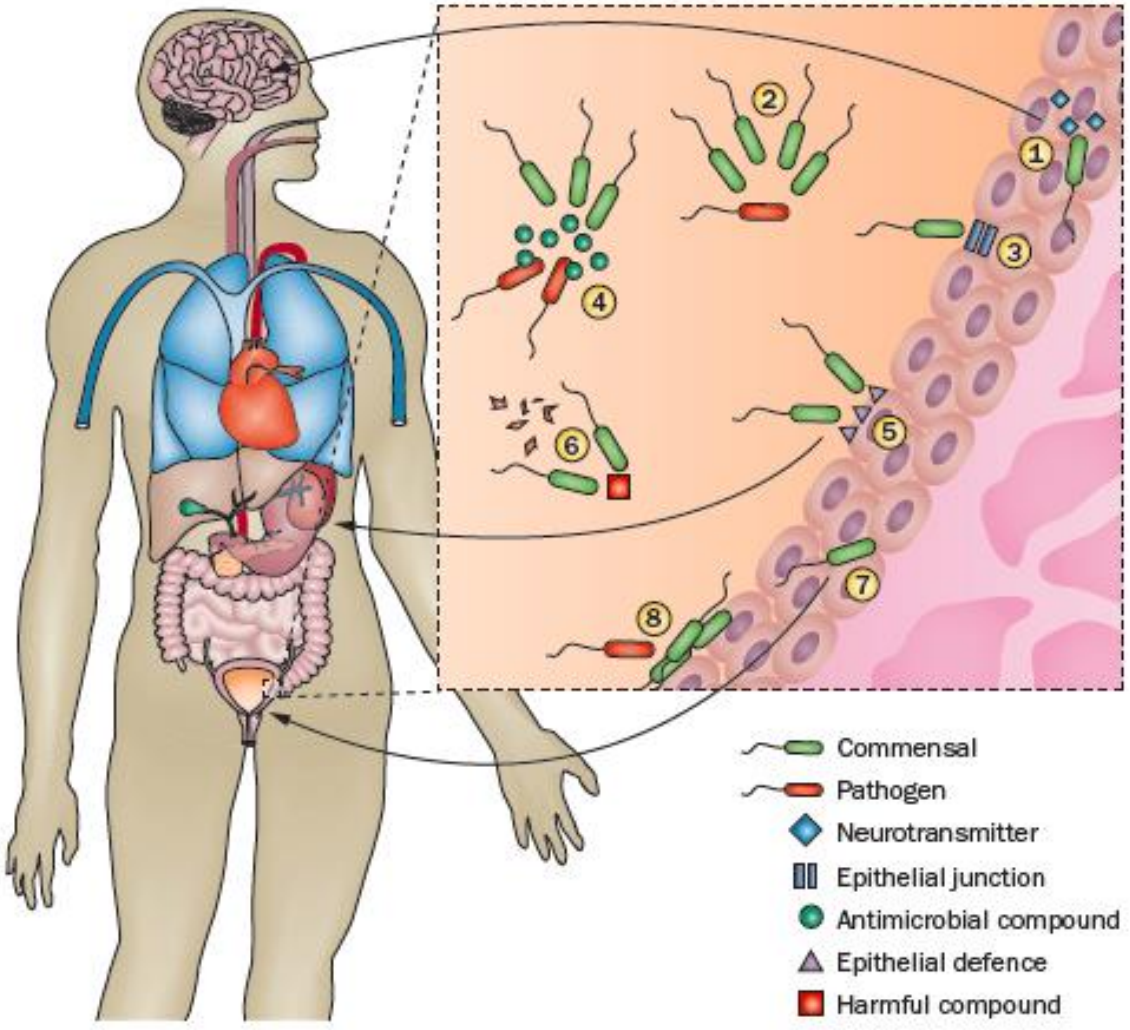


Figure 2 | Potential roles of the urinary microbiota in homeostasis of the urinary tract.

(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.

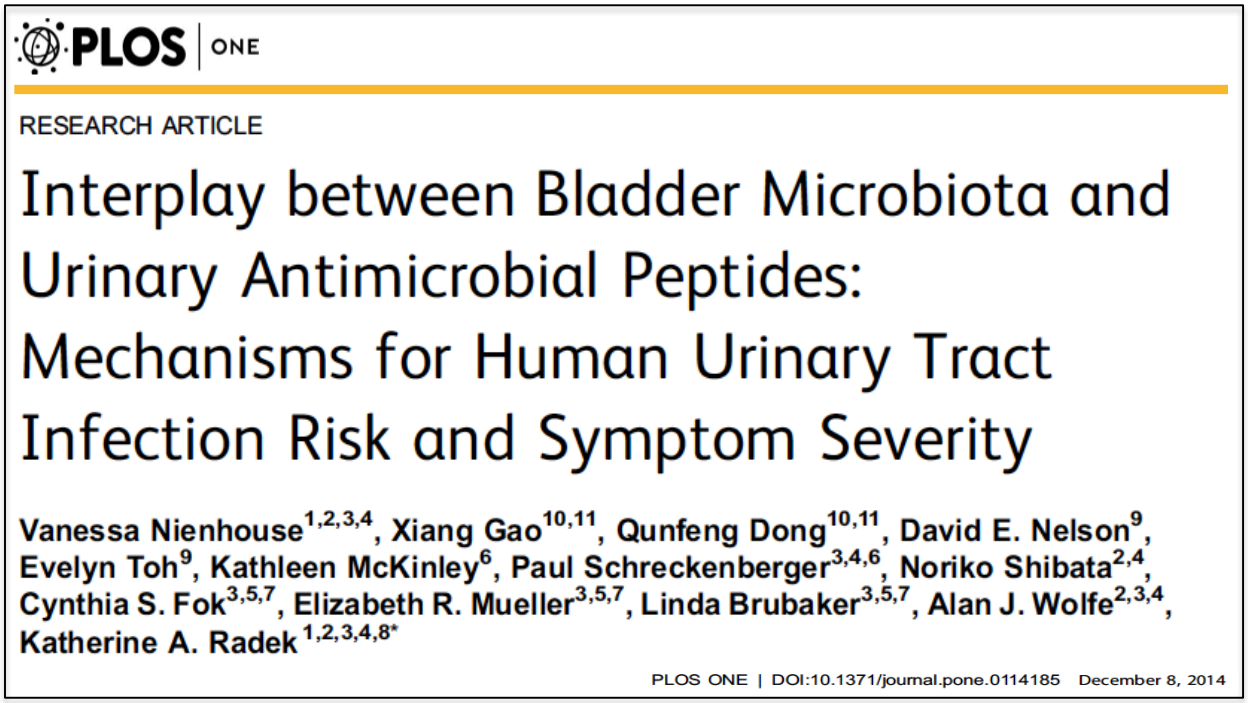
(1) Bacteria might **prime epithelial defences, including immune defences**.

(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



PLOS ONE

RESEARCH ARTICLE

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

Vanessa Nienhouse[1,2,3,4], Xiang Gao[10,11], Qunfeng Dong[10,11], David E. Nelson[9], Evelyn Toh[9], Kathleen McKinley[6], Paul Schreckenberger[3,4,6], Noriko Shibata[2,4], Cynthia S. Fok[3,5,7], Elizabeth R. Mueller[3,5,7], Linda Brubaker[3,5,7], Alan J. Wolfe[2,3,4], Katherine A. Radek[1,2,3,4,8*]

PLOS ONE | DOI:10.1371/journal.pone.0114185 December 8, 2014

Innate immune system regulation

Urinary microbiota

Antimicrobial peptides (AMP)

UTI risk
significantly correlated with specific urinary microbiota & AMP levels

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

2nd reason: urinary microbiota in health & diseases

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

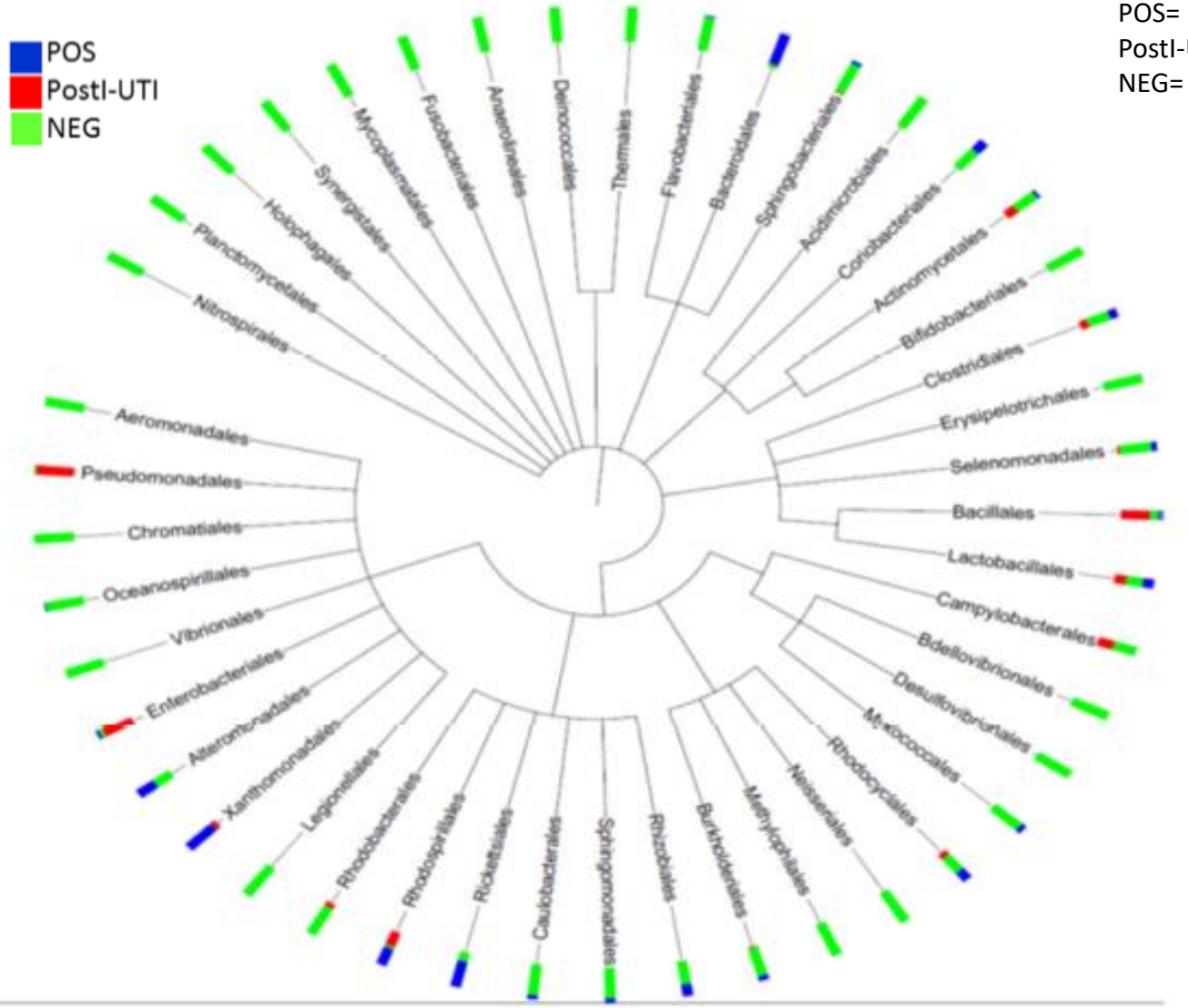


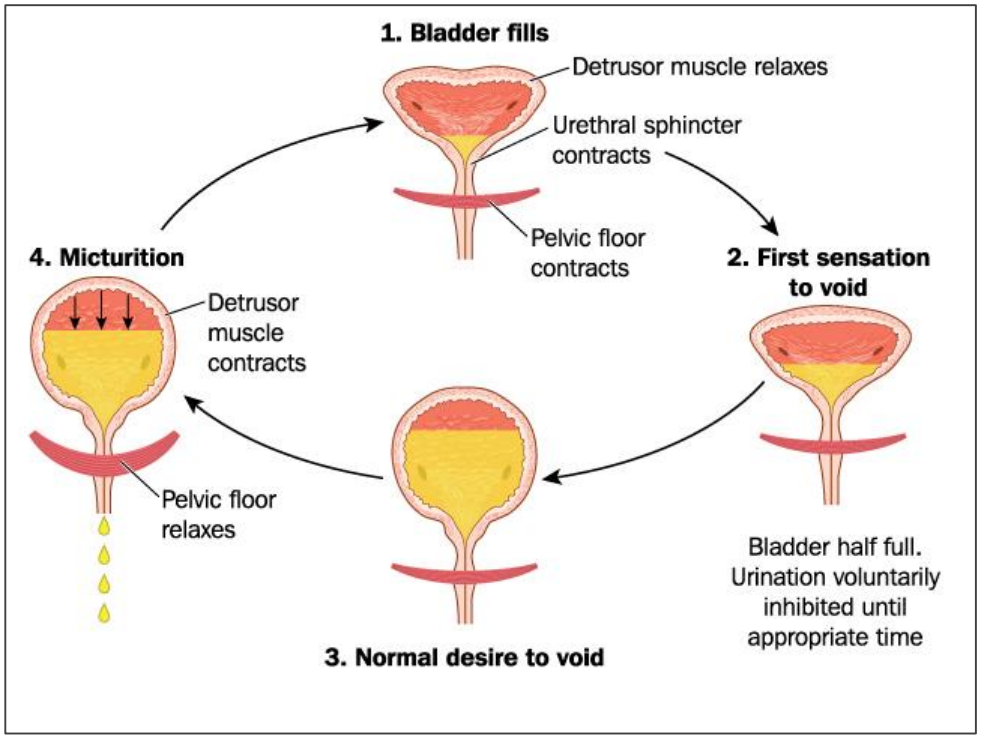
Fig. 1. Bacterial diversity correlates with the susceptibility or resistance to UTI. Phylogenetic tree comparing the bacterial diversity at the Order level within the female urinary microbiome. The bacterial diversity was compared between the three cohorts: POS (Blue), PostI-UTI (Red) and NEG (Green).

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"

Nienhouse *et al*. (2014)

3rd reason: catheter disturbs the physiology of urinary tract



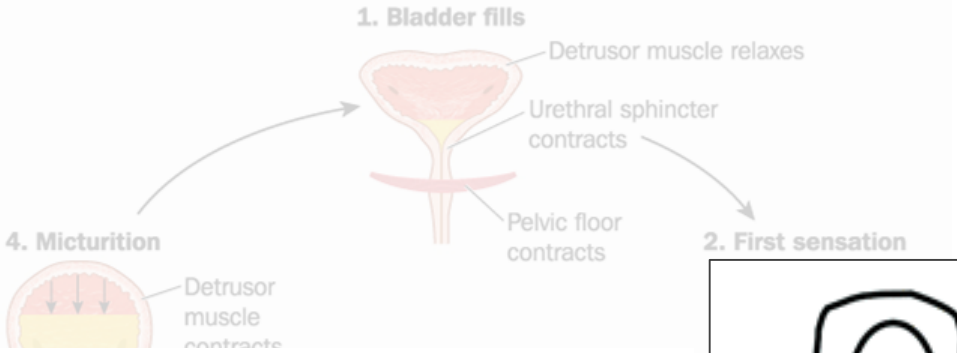
In physiologic conditions

Bacterial multiplication during bladder filling and urine stasis

but

mechanic elimination by flushing during the micturition

3rd reason: catheter disturbs the physiology of urinary tract



In physiologic conditions

Bacterial multiplication during bladder filling and urine stasis

but

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

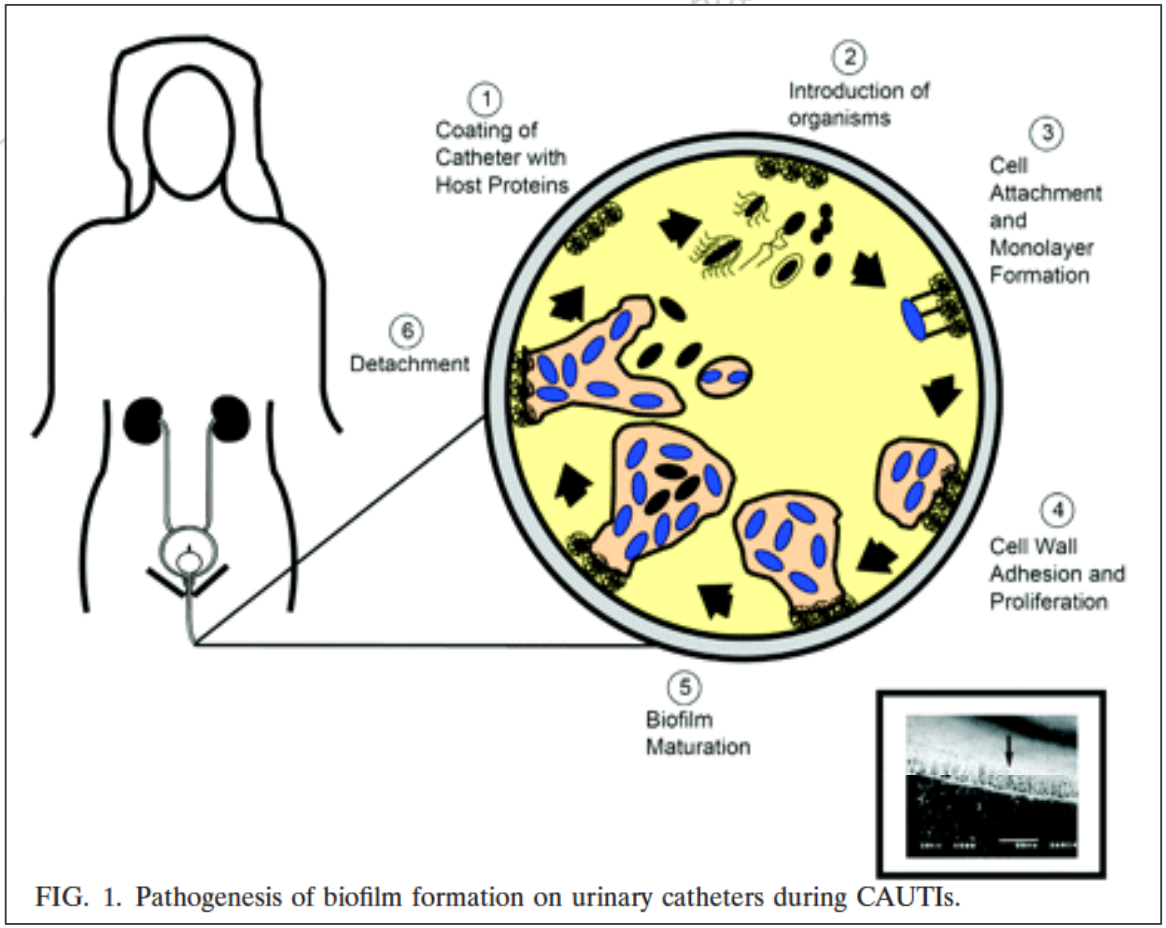


FIG. 1. Pathogenesis of biofilm formation on urinary catheters during CAUTIs.

Jacobsen *et al*. Clin Microbiol Rev (2008)

4th reason: microbial network and risk factor of CAUTI

*Mutli-Drug Resistant Organisms

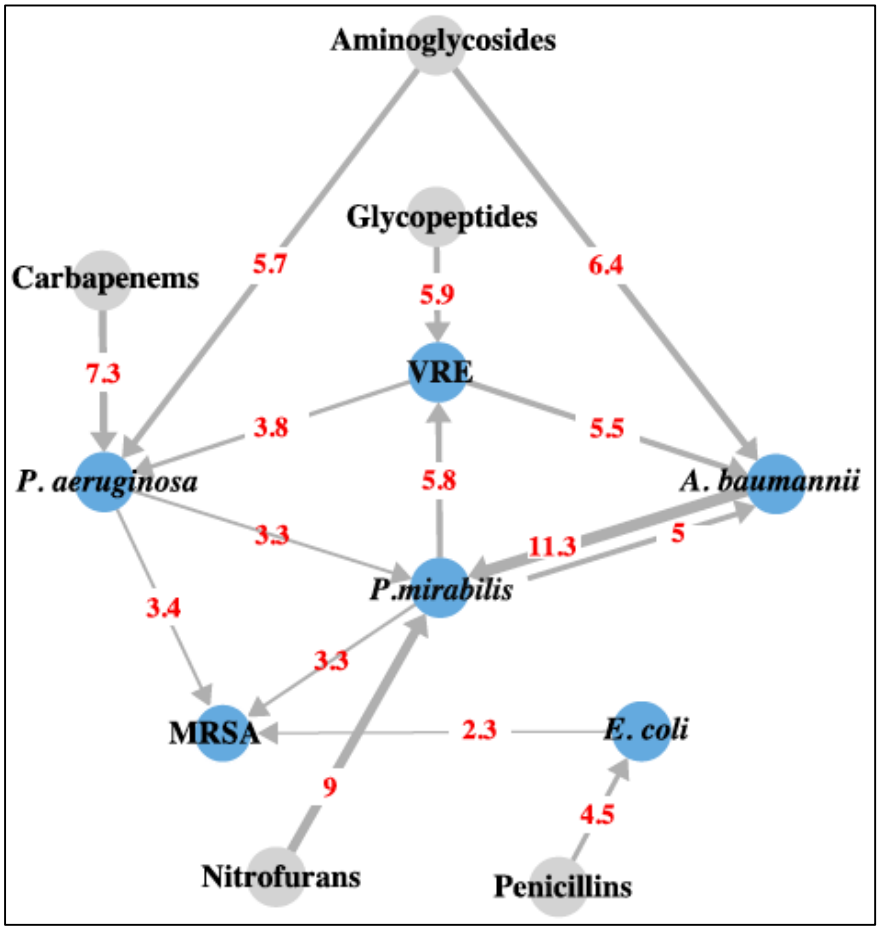


Fig2: Risk network for MDRO colonization

existing bacterial colonization ↗ risk of secondary acquisition

relationship between antibiotic exposure & MDRO* colonization

joint influence of microbial and antibiotic factors onto MDRO colonization

Wang et al. *PNAS.* 2017

4th reason: microbial network and risk factor of CAUTI

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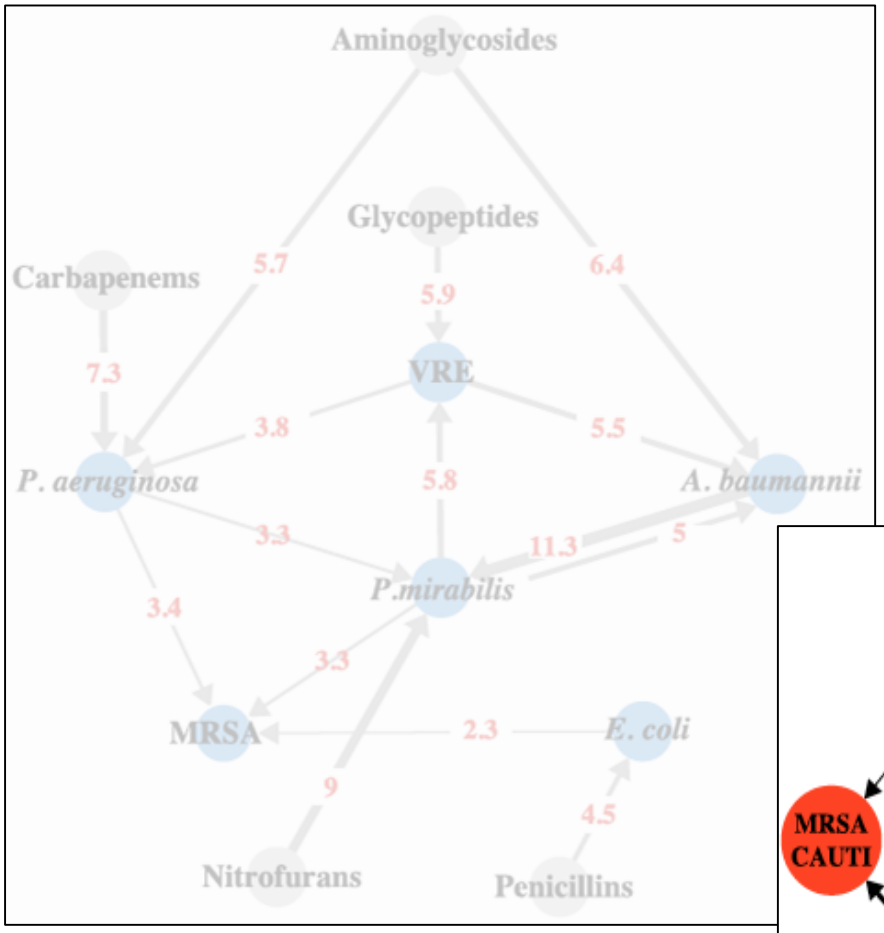


Fig2: Risk network for MDRO colonization

cocolonization associated with increased risk of CAUTI by specific bacteria

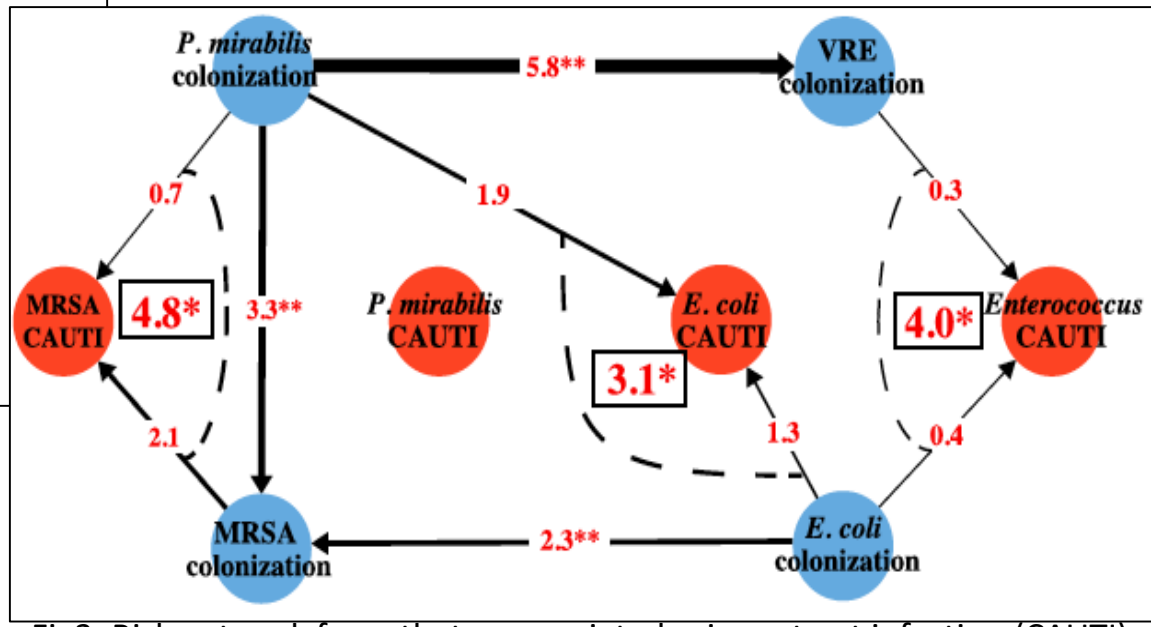


Fig3: Risk network for catheter-associated urinary tract infection (CAUTI) events

Wang et al. *PNAS.* 2017

4th reason: microbial network and risk factor of CAUTI

*Mutli-Drug Resistant Organisms

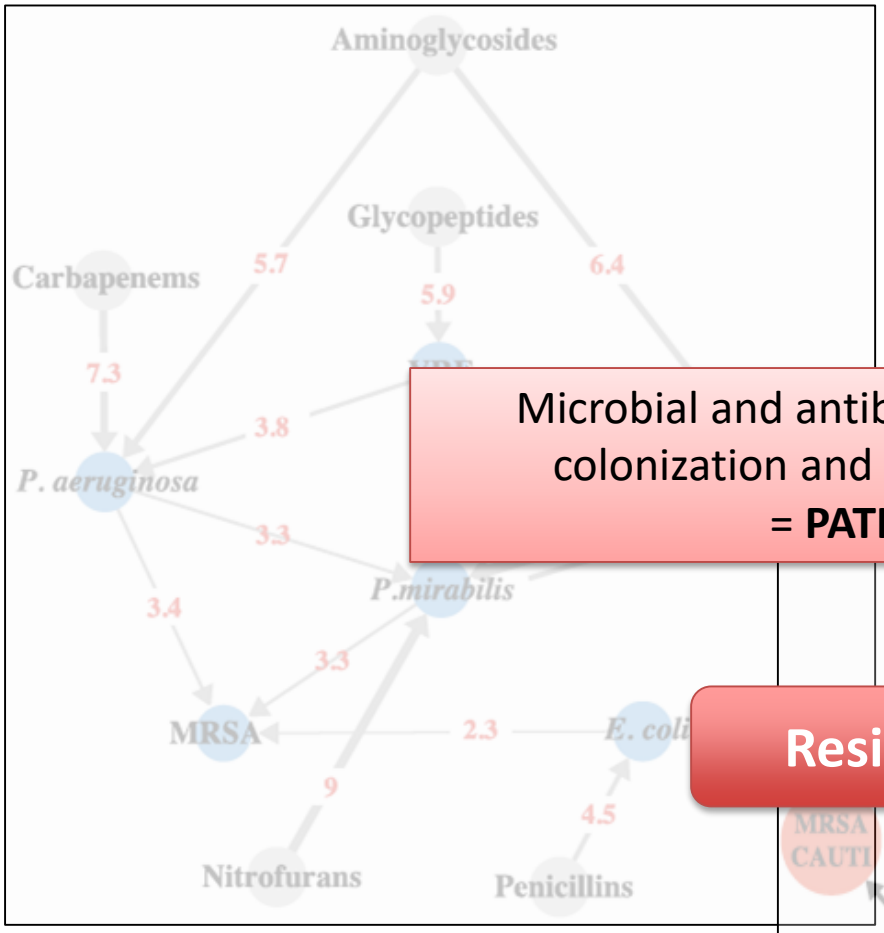
existing bacterial colonization ↗ risk of secondary acquisition

relationship between antibiotic exposure & MDRO* colonization

joint influence of microbial and antibiotic factors onto onization

Microbial and antibiotic interactions drive colonization and infection with MDRO = PATHOBIOME

Resistome



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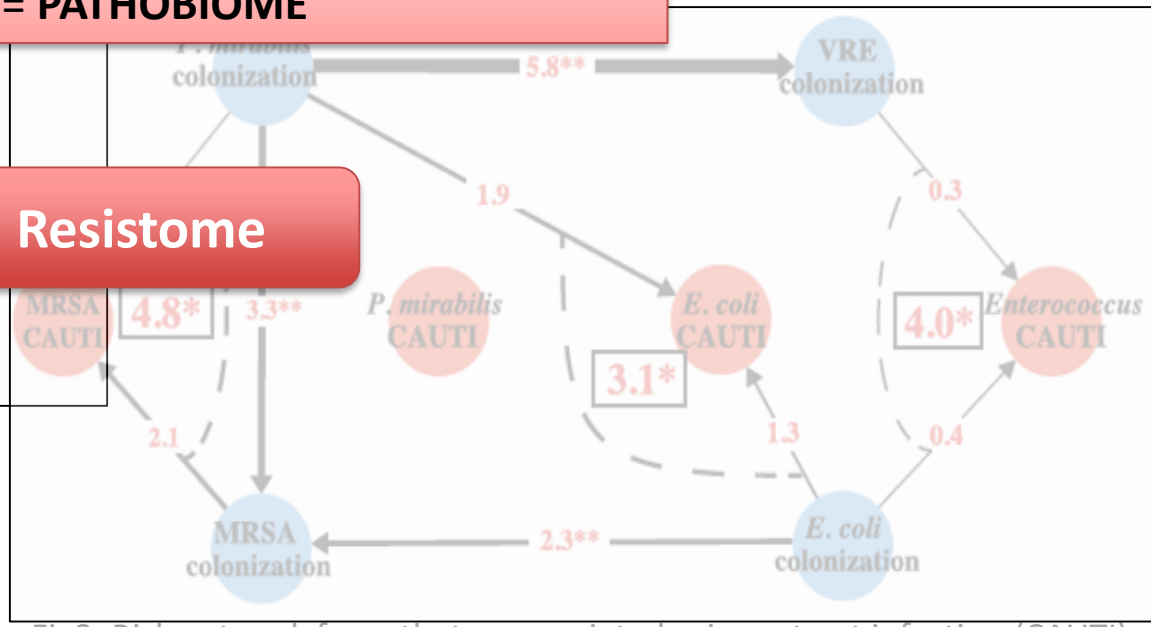

Fig3: Risk network for catheter-associated urinary tract infection (CAUTI) events

Wang et al. *PNAS.* 2017

Hospital promotes Pathobiome and 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

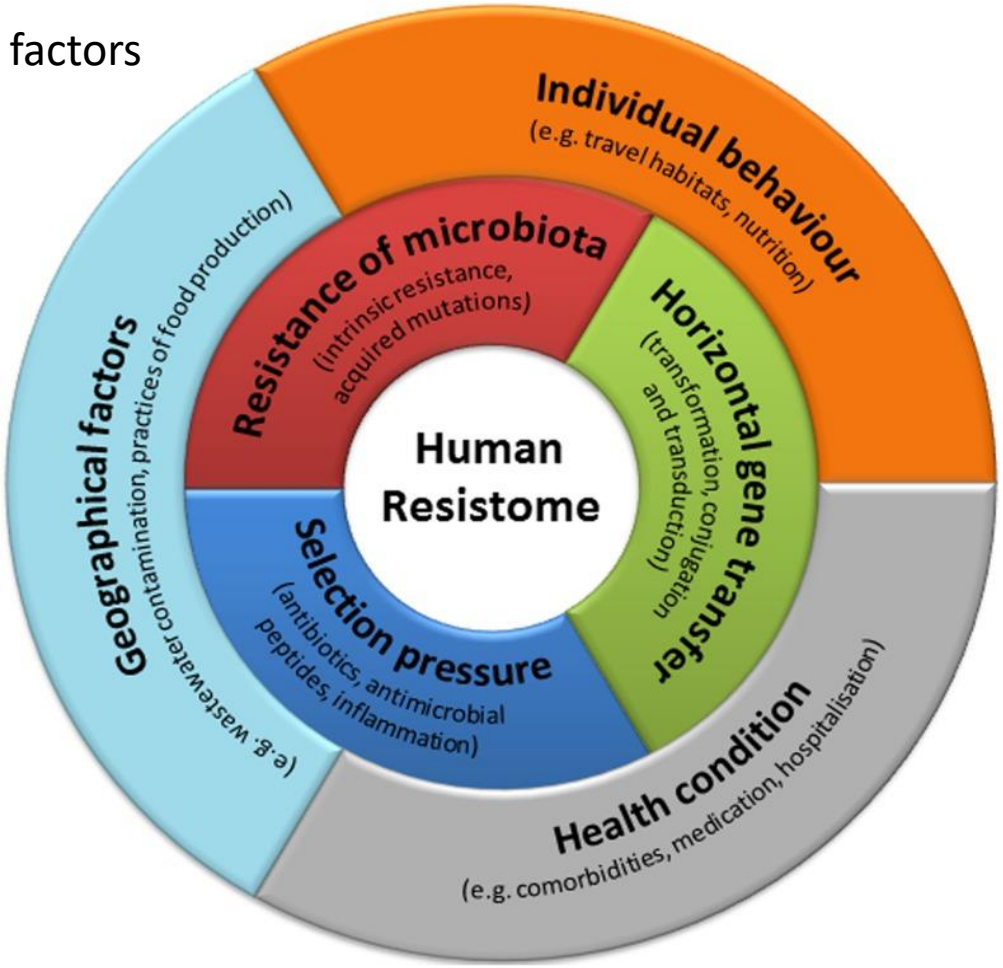

Figure: Potential factors shaping the human resistome

Willmann *J Mol Med* 2017

Hospital promotes Pathobiome and 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...

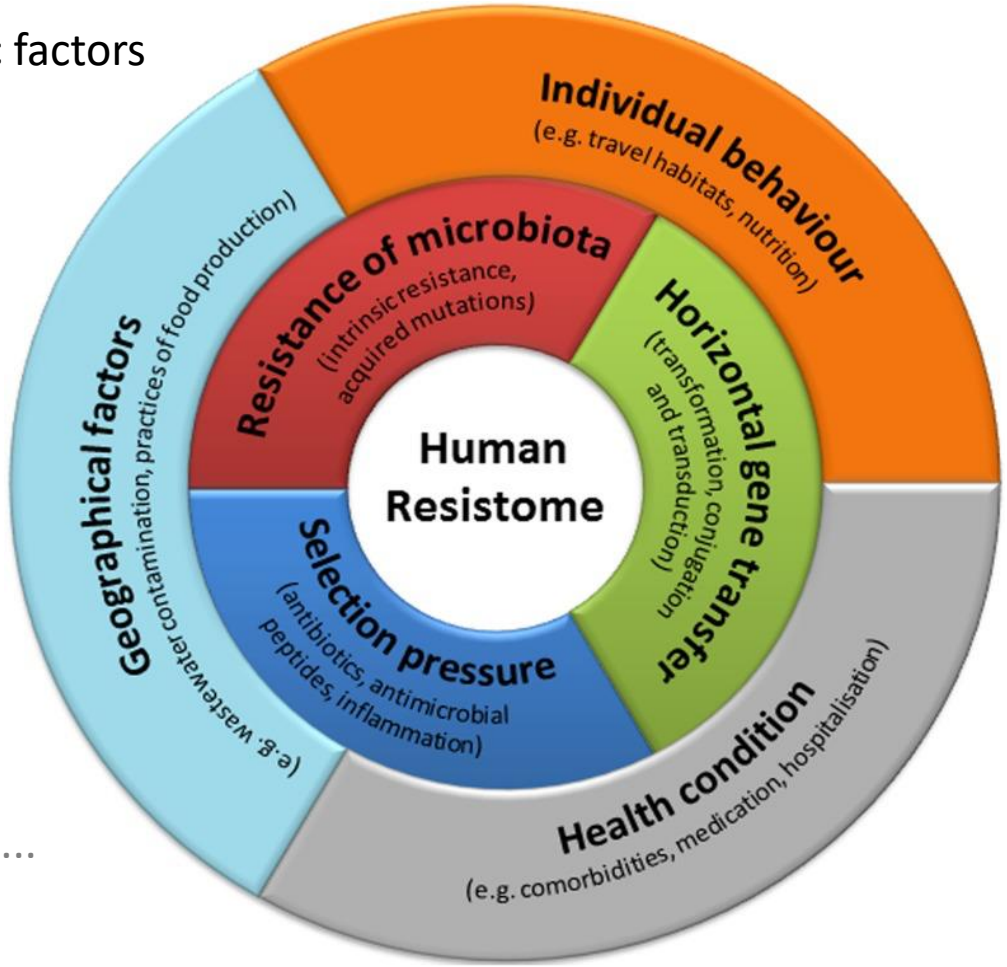

Figure: Potential factors shaping the human resistome

Willmann *J Mol Med* 2017

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 ?

Is the pathobiome concept valuable to prevent HAIs?

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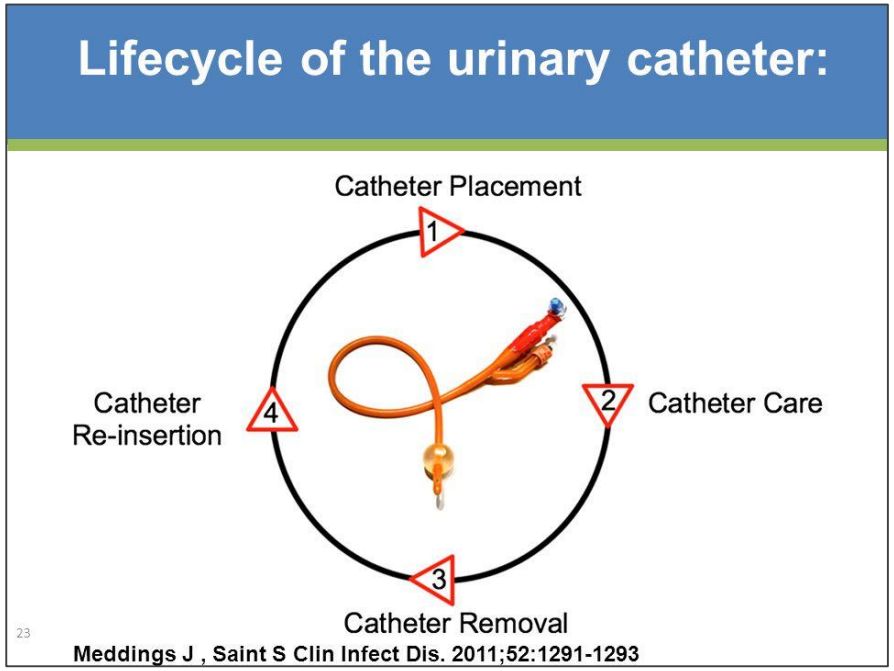

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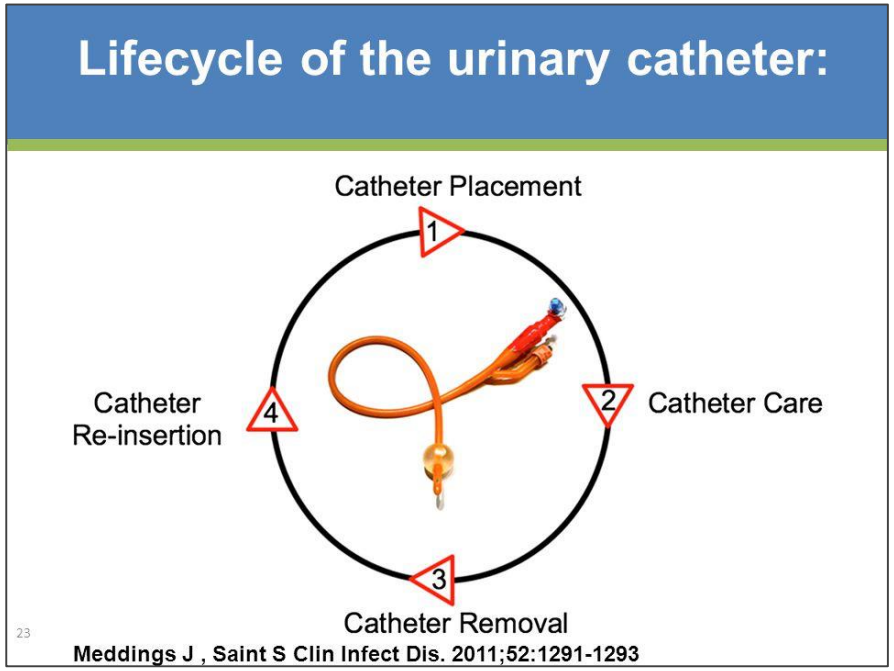

WTF?

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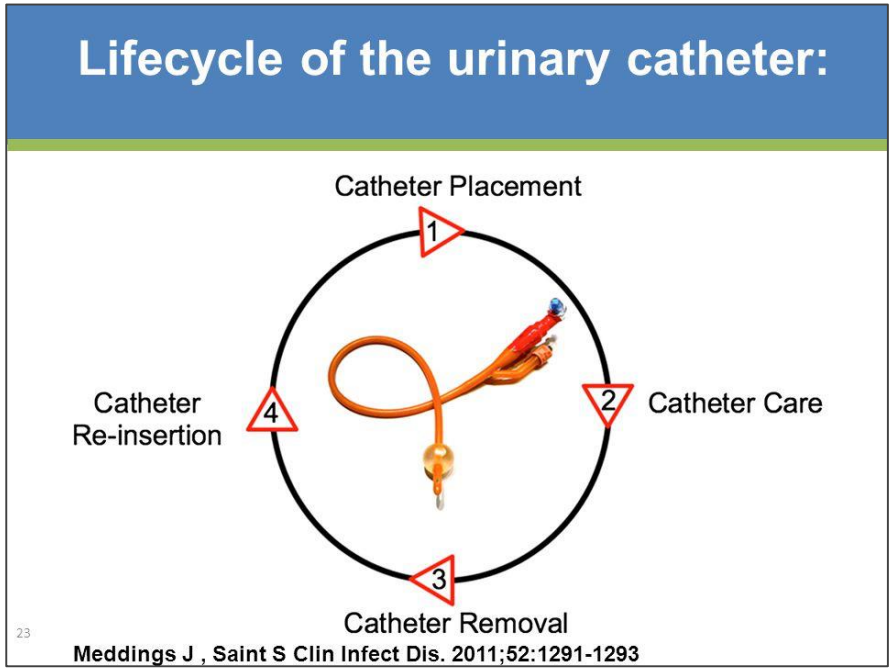

WTF?

"**W**hy **T**he **F**oley ?"

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…

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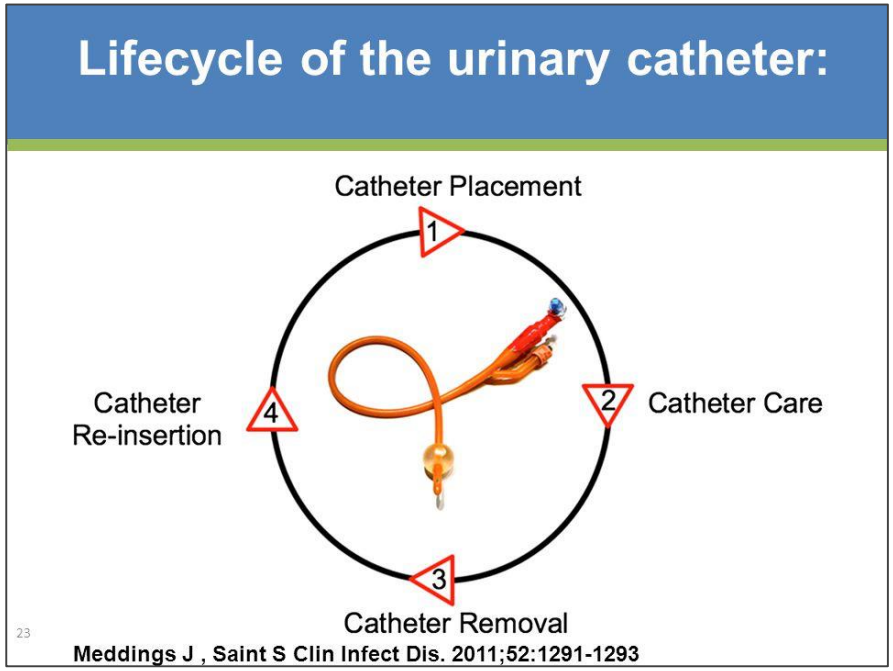

WTF?

"Why **T**he **F**oley ?"

"No answer to give?

⇒ Get the Foley out!"

SF2H
Risque infectieux et soin

6, 7 et 8 juin 2018
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Thank you for your attention!