From the labo to the ICU: Surveillance cultures in daily ICU practice

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Question 1:
What is the current practice of surveillance cultures at your ICU?

- No surveillance cultures are taken
- Surveillance cultures are only taken when outbreak of MDR
- Surveillance cultures are taken upon admission only
- Surveillance cultures are taken upon admission and then once weekly during ICU stay
- Surveillance cultures are taken upon admission and then twice or more weekly during ICU stay

Question 2:

Do you use surveillance cultures for infection control purposes at your ICU (what practice fits best with the situation at your ICU)?

- We use *diagnostic cultures only* as a guidance for patient cohortation/barrier precautions
- We use *diagnostic cultures* as daily guidance, and use *surveillance cultures* in case of MDR outbreak
- We use *regular surveillance cultures* as a guidance for barrier precautions/ patient cohortation
- We use *surveillance cultures on admission only* as a guidance fo barrier precautions/patient cohortation

Question 3:

Do you use surveillance cultures for guidance of empirical therapy at your ICU? (what practice fits best with the situation at your ICU)?

- We use *regular surveillance cultures* as a strategy for guidance of empirical therapy
- We use *surveillance cultures* for infection control purposes; when available, surveillance cultures are used to modify empirical therapy
- We use *surveillance cultures* for infection control purposes: surveillance cultures are not taken into account for choice of empirical therapy
- We do not use regular surveillance cultures

Microbiological surveillance

- Surveillance
  - Definition: monitoring of behaviour, activities or other changing information of individuals/organism/system
- Microbial surveillance
  - Definition: continual, systematic collection, analysis and interpretation of microbiologica data
  - Aim: planning, implementation and evaluation of infection control practices and/or treatment strategies

Microbial surveillance

- Level:
  - Geographic:
    - Data: infection burden, trends in resistance, emergence and spread of new resistance mechanisms
    - Aim: guidance of healthcare policy, alerts, development and adaptation of (supra)national guidelines

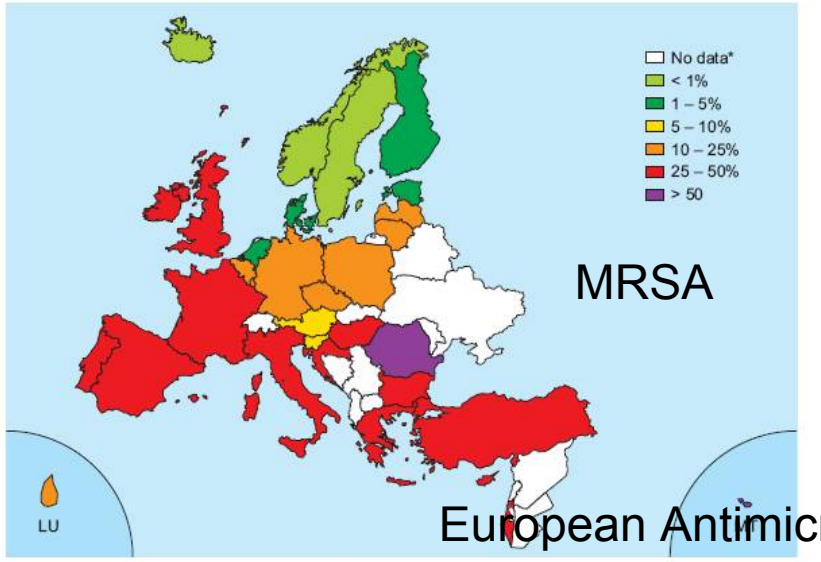
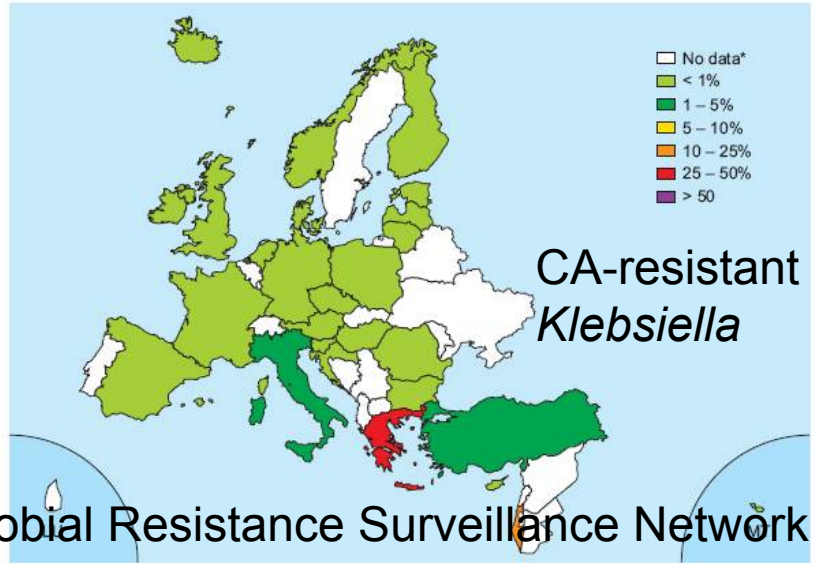


Figure 5.8. *Staphylococcus aureus*: proportion of invasive isolates resistant to oxacillin (MRSA) in 2006.
* These countries did not report any data or reported less than 10 isolates.



European Antimicrobial Resistance Surveillance Network

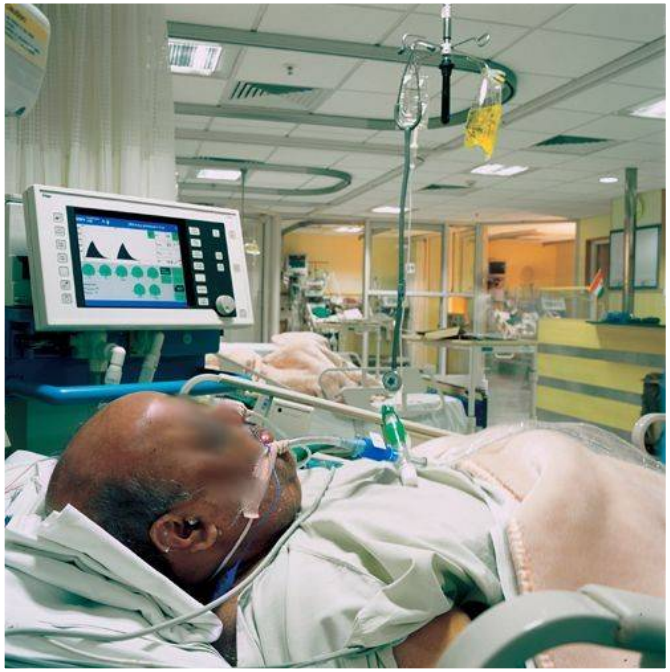
Figure 5.26. *Klebsiella pneumoniae*: proportion of invasive isolates resistant to carbapenems in 2006.
* These countries did not report any data or reported less than 10 isolates.

Microbial surveillance

- Level:
  - Institutional
    - Data: infection rates (benchmark), local trends in resistance, import and spread of new resistance mechanisms
    - Aim: Guidance and evaluation of infection control strategies, detection of outbreaks, development and adaptation of local formulary

Microbial surveillance

- Level:
  - Patient
    - Data: colonization status, infection status (MDR strain)
    - Aim: Guidance of barrier precautions, guidance of (empirical) antibiotic therapy



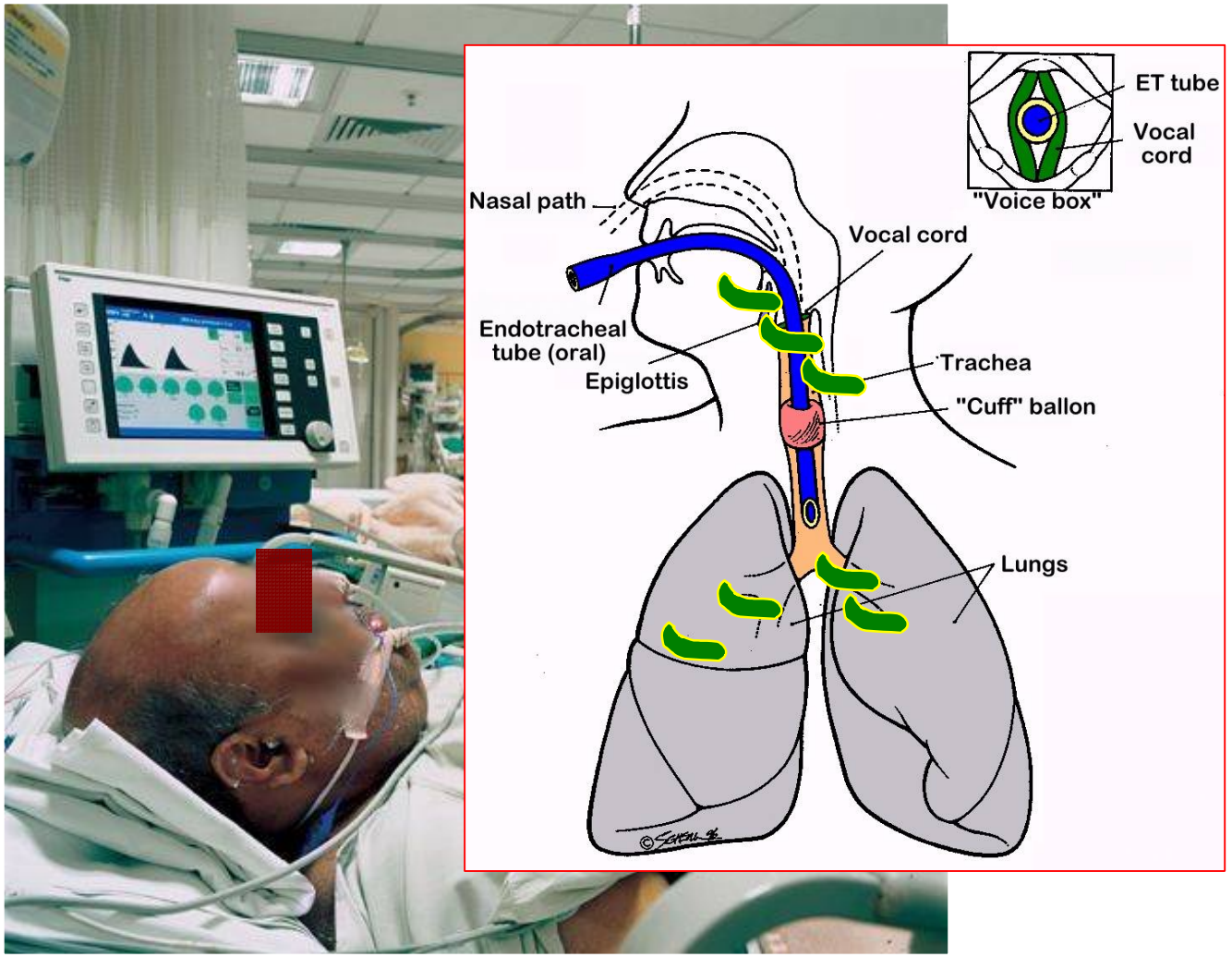
Microbiological cultures for surveillance

- Diagnostic cultures:
  - Sampled upon clinical suspicion of infection
  - Targeted at focus of infection, ‘deep sites’, avoidance of ‘contaminated’ sites
  - Aimed to document infection (probability and site) and to modify empirical antibiotic therapy
- Surveillance cultures:
  - Sampled upon regular basis, regardless of clinical suspicion of infection
  - Targeted at preferentially colonized sites, ‘superficial sites’
  - Aimed to document colonization for infection control practice and/or for anticipation of possible infection

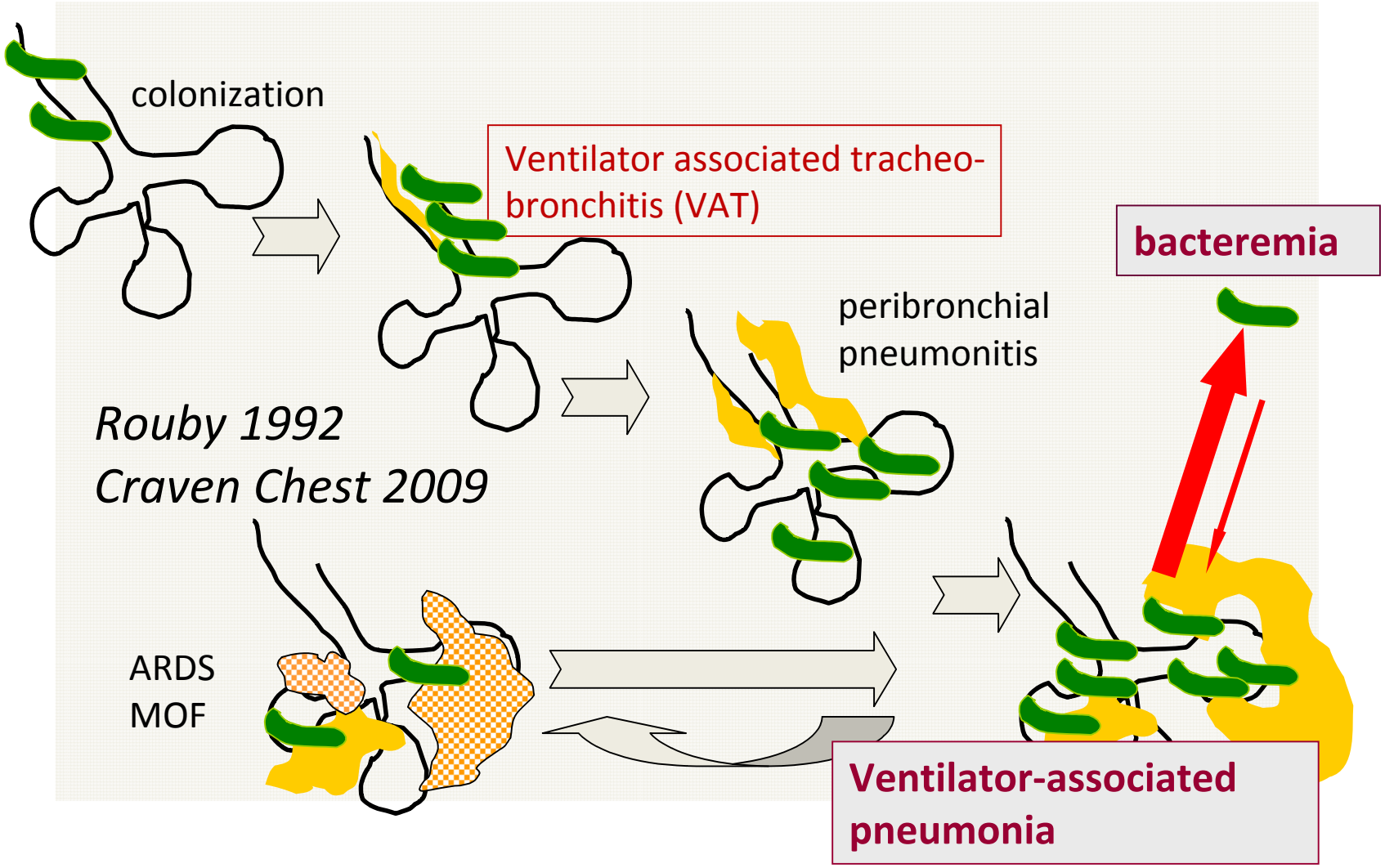
Ill patients get colonized by pathogens…

- Valenti et al.: Factors predisposing to oropharyngeal colonization with Gram-negative bacilli in aged. N Engl J Med 298 1978
  - 407 patients >65y, none received AB
  - Oropharyngeal colonization Gram-negative pathogens in 9% outpatients vs. 60% hospitalized patients
  - More colonization if urinary incontinence, deterioration general status, dependency, bed-ridden

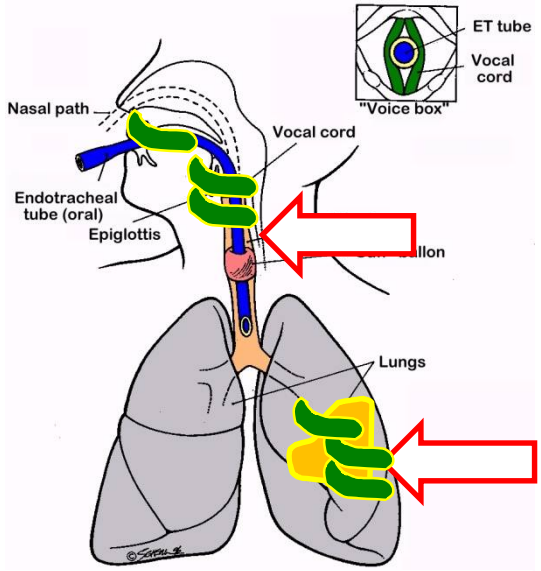
Colonization precedes nosocomial infection (VAP)



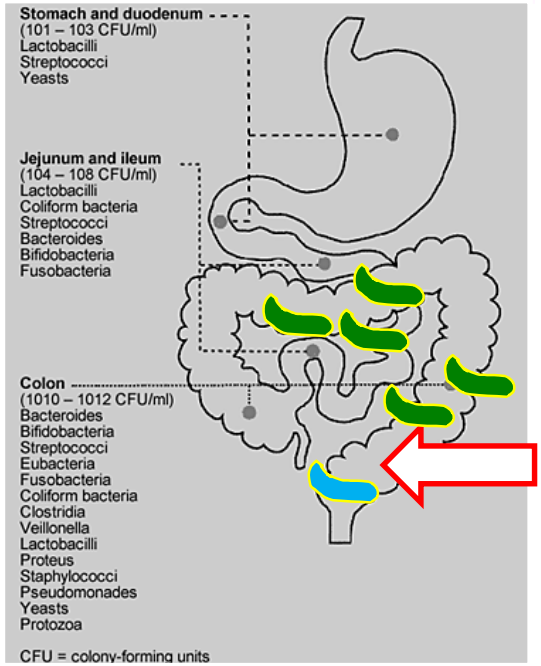
Colonization precedes nosocomial infection (VAP)



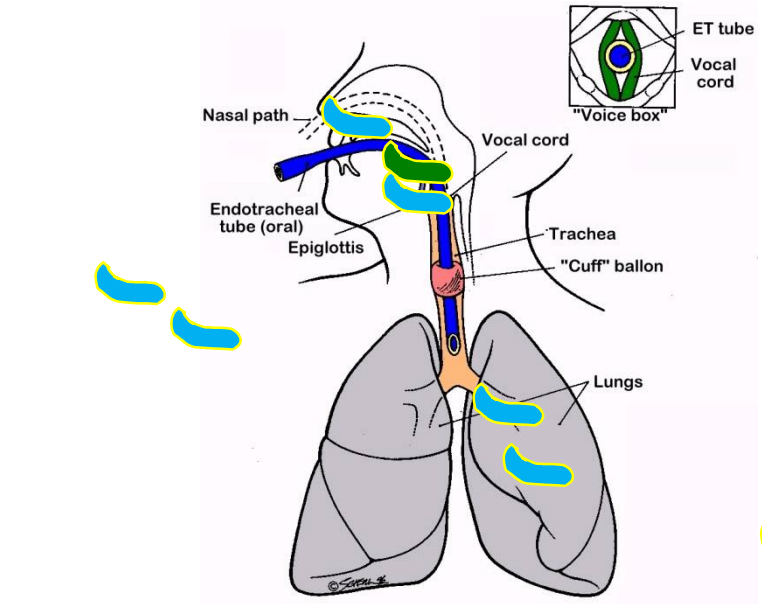
Selection of antibiotic resistant pathogens in ‘colonization’ site

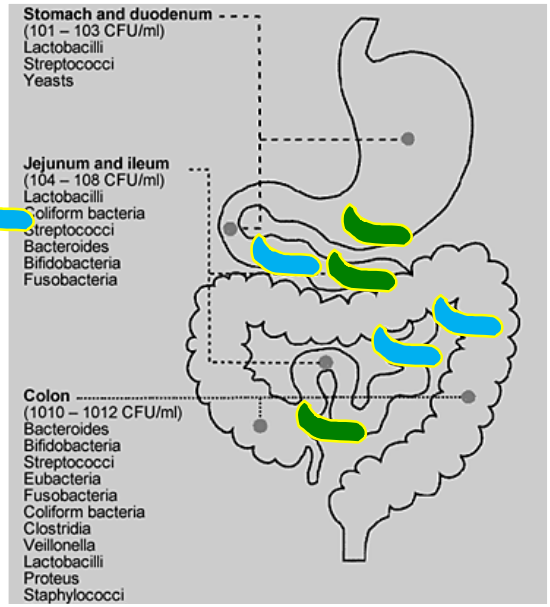


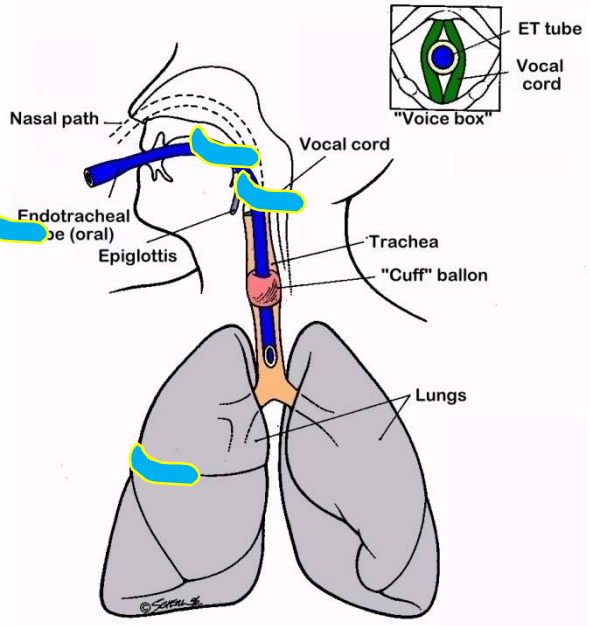
Antibiotic therapy



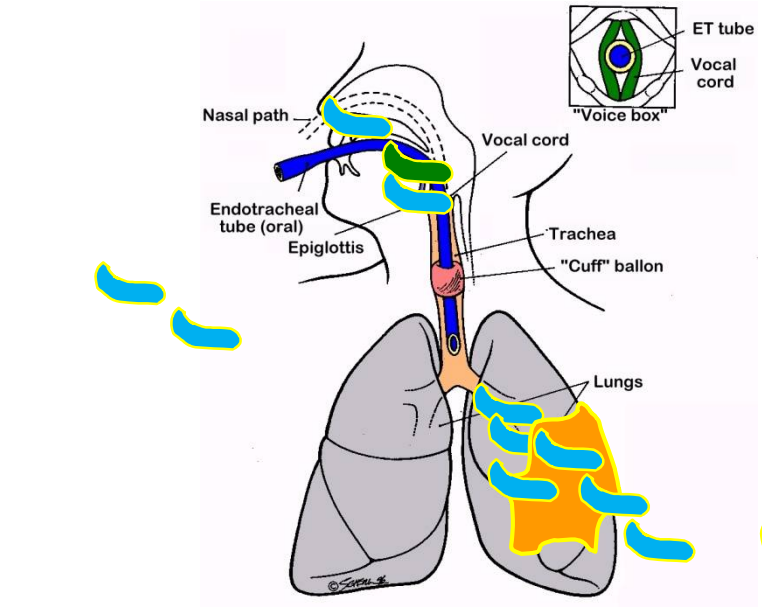
Spread of antibiotic resistant pathogen from one colonization site to another

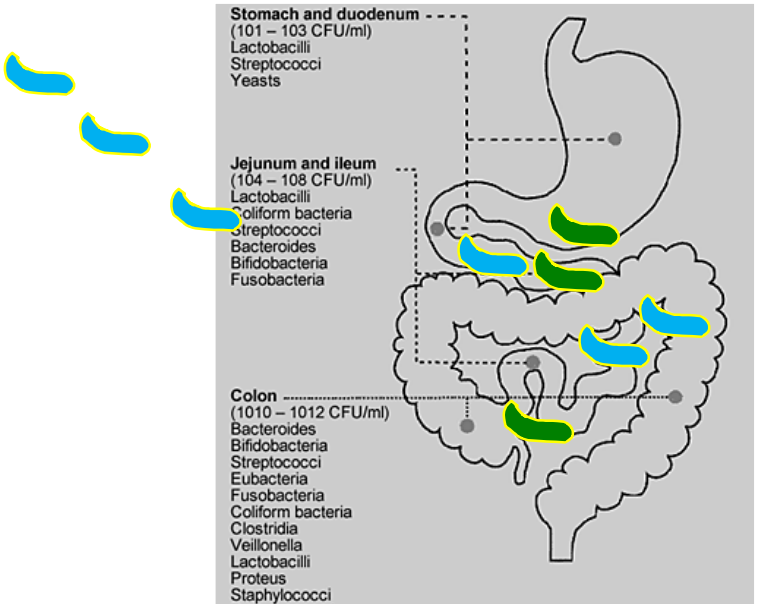


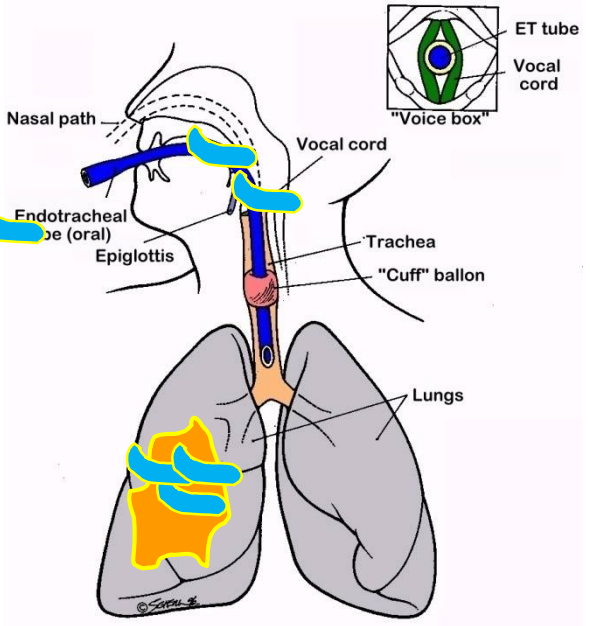




From colonization to infection…

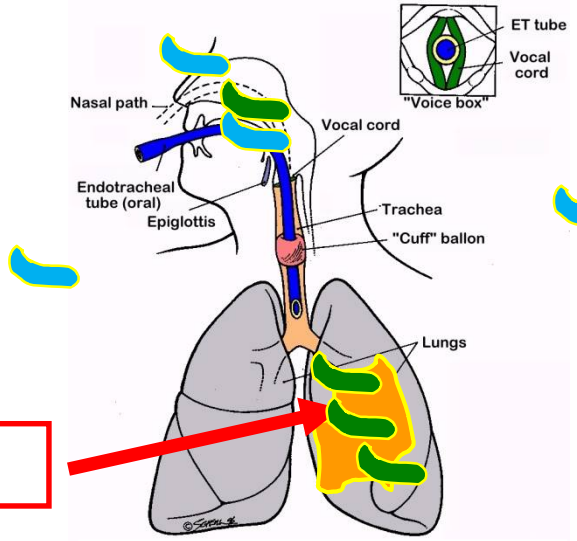


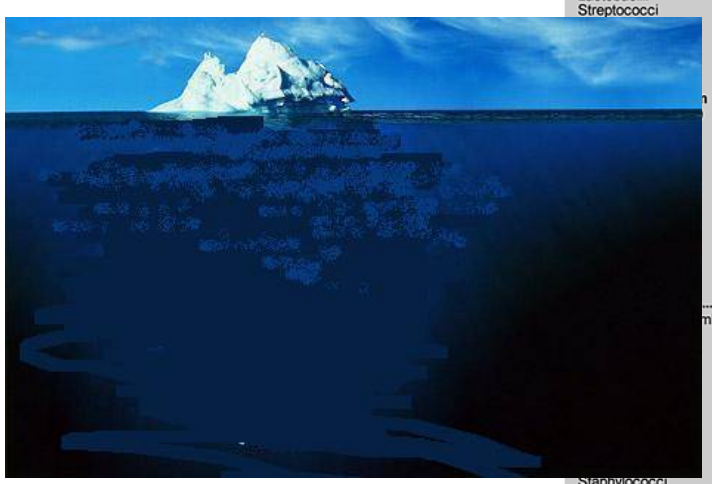


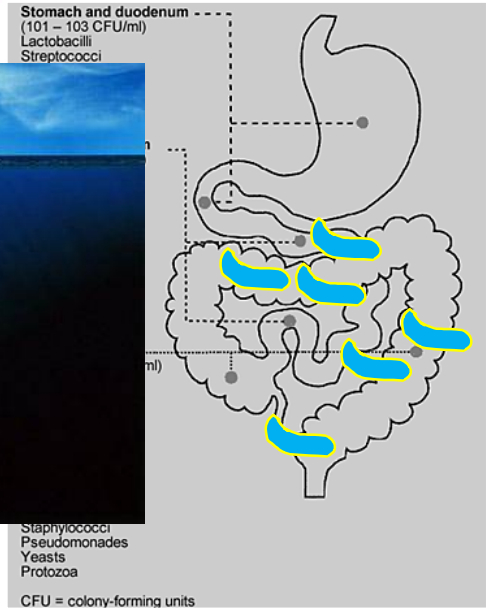


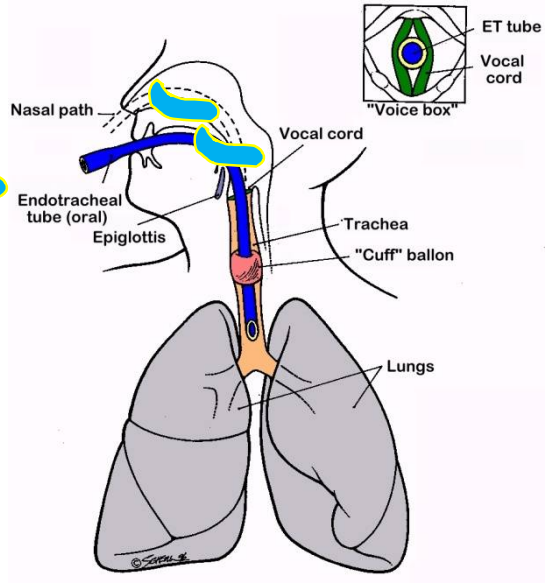
Diagnostic cultures versus surveillance cultures

Diagnostic cultures





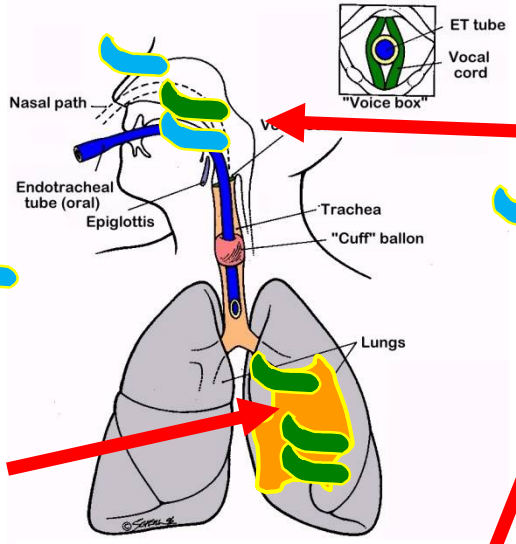


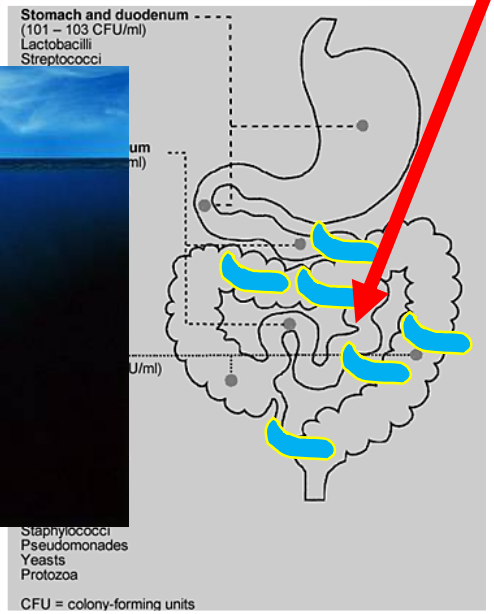


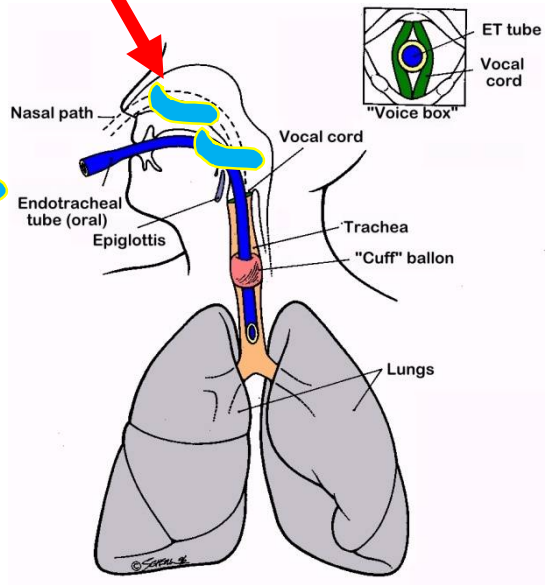
Diagnostic cultures versus surveillance cultures

Surveillance cultures

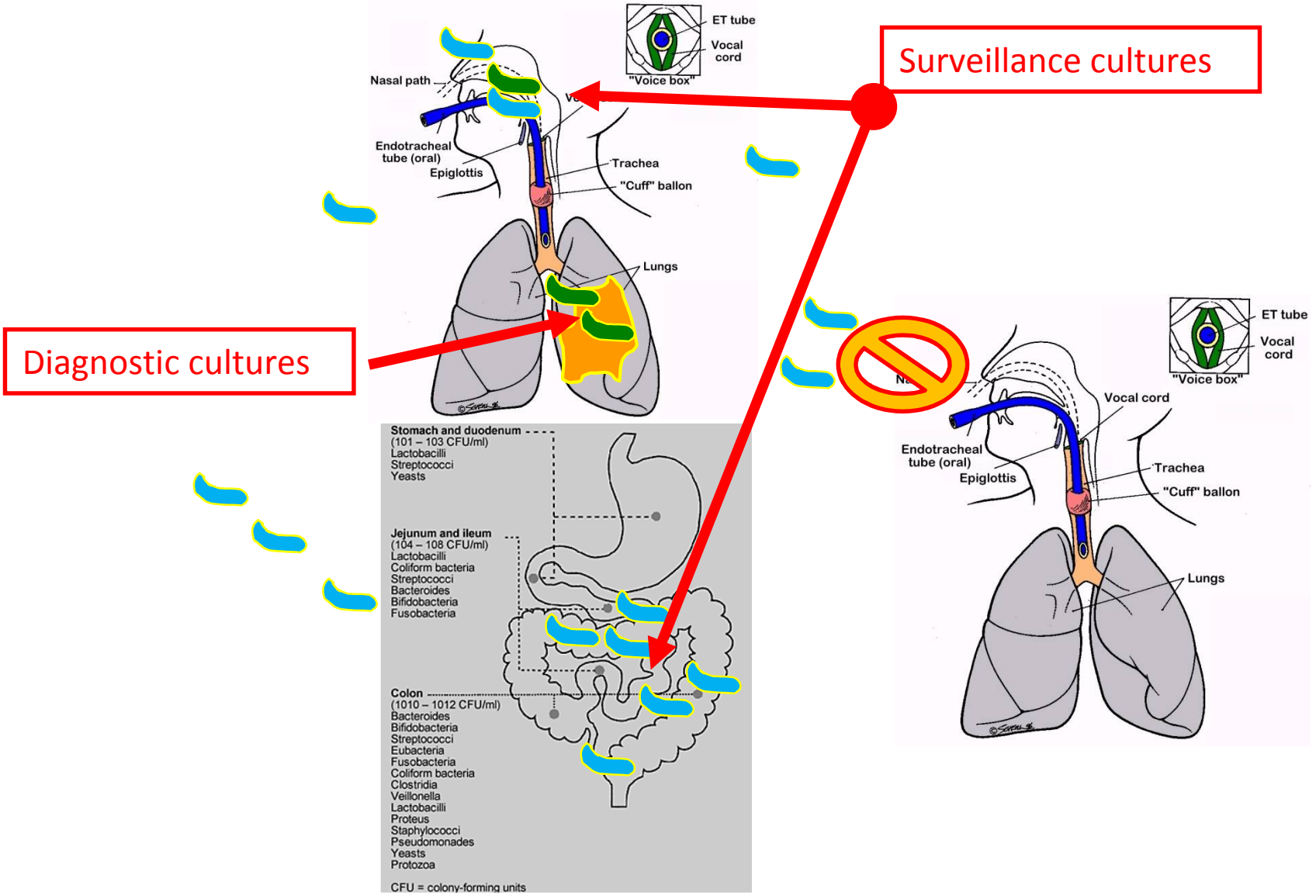
Diagnostic cultures



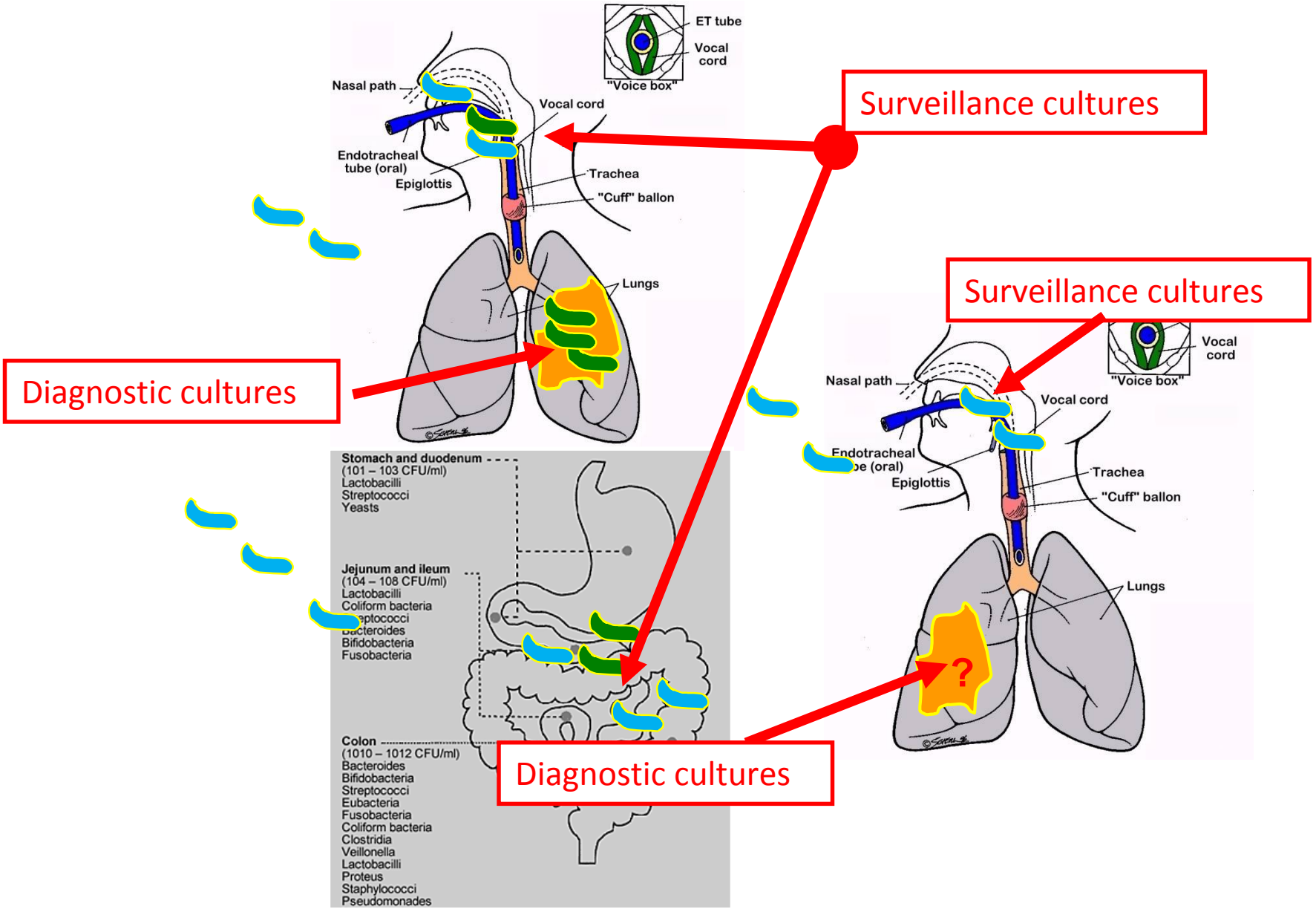




Limiting spread of antibiotic resistant pathogen by early detection of ‘carriers’?



Prediction of nosocomial infection by antibiotic resistant pathogen?



Are surveillance cultures helpful in limiting spread of MDR pathogens?

National Park Service: Statue of Liberty National Monument

Surveillance cultures to limit spread of MDR pathogens

- During outbreaks:

Journal of Hospital Infection (2002) **50**: 110–114
doi:10.1053/jhin.2001.1127, available online at http://www.idealibrary.com on IDEAL®

Carbapenem-resistant Acinetobacter and role of curtains in an outbreak in intensive care units

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**Department of Microbiology, Queen Elizabeth Hospital, †Department of Pharmaceutical & Biological Sciences, Aston University, and ‡Department of Anaesthetics and Intensive Care, Queen Elizabeth Hospital, Birmingham, UK*

Summary: Multiple-antibiotic-resistant *Acinetobacter baumanii*, including meropenem resistance, was first isolated from a patient in the general intensive care unit of a tertiary-referral university teaching hospital in Birmingham in December 1998. Similar strains were subsequently isolated from 12 other patients, including those on another intensive care unit within the hospital. The outbreak followed an increase in the use of meropenem in both the units. Environmental screening revealed the presence of the multiple-resistant *Acinetobacter* species on fomite surfaces in the intensive care unit and bed linen. The major source appeared to be the curtains surrounding patients' beds. Typing by pulsed field gel electrophoresis demonstrated that the patients' isolates and those from the environment were indistinguishable. Rigorous infection control measures including increased frequency of cleaning of the environment with hypochlorite (1000 ppm) and twice-weekly changing of curtains were implemented, along with restriction of meropenem use in the units. Isolation of the multiple-resistant *Acinetobacter* spp. subsequently diminished and it was not detected over a follow-up period of 18 months. To our knowledge, this is the first reported outbreak of carbapenem-resistant *Acinetobacter* spp. from the UK. This outbreak also highlights environmental sources, particularly dry fabrics such as curtains, as an important reservoir for dissemination of acinetobacters.

Keywords: Acinetobacter; intensive care units; meropenem resistance.

  - surveillance cultures essential component of multifaceted strategy…

Control of a multi-hospital outbreak of KPC-producing *Klebsiella pneumoniae* type 2 in France, September to October 2009

A Carbonne (anne.carbonne@sap.aphp.fr)[1], J M Thiolet[2], S Fournier[3], N Fortineau[4], J C Séguier[6], H Sénéchal[7], M P Tavolacci[8], B Coignard[2], P Astagneau[1,9], V Jarlier[3,9,10]

- During outbreaks:
- surveillance cultures essential component of multifaceted strategy…

An outbreak of *Klebsiella pneumoniae* carbapenemase (KPC)-producing *Klebsiella pneumoniae* type 2 was detected in September 2009 in two hospitals in a suburb south of Paris, France. In total, 13 KPC-producing *K. pneumoniae* type 2 cases (four with infections and nine with digestive-tract colonisations) were identified, including a source case transferred from a Greek hospital. Of the 13 cases, seven were secondary cases associated with use of a contaminated duodenoscope used to examine the source case (attack rate: 41%) and five were secondary cases associated with patient-to-patient transmission in hospital. All isolated strains from the 13 patients: (i) exhibited resistance to all antibiotics except gentamicin and colistin, (ii) were more resistant to ertapenem (minimum inhibitory concentration (MIC) always greater than 4 mg/L) than to imipenem (MIC: 1–8 mg/L, depending on the isolate), (iii) carried the bla_{KPC-2} and bla_{SHV12} genes and (iv) had an indistinguishable pulsed-field gel electrophoresis (PFGE) pattern. These cases occurred in three hospitals: some were transferred to four other hospitals. Extended infection control measures implemented in the seven hospitals included: (i) limiting transfer of cases and contact patients to other wards, (ii) cohorting separately cases and contact patients, (iii) reinforcing hand hygiene and contact precautions and (iv) systematic screening of contact patients. Overall, 341 contact patients were screened. A year after the outbreak, no additional case has been identified in these seven hospitals. This outbreak emphasises the importance of rapid identification and notification of emerging highly resistant *K. pneumoniae* strains in order to implement reinforced control measures.

Surveillance cultures to limit spread of MDR pathogens

- CDC 2008 (Management of multidrug-resistant pathogens in healthcare settings):

'V.b;: Intensified interventions to prevent MDR transmission'

► "Develop and implement protocols to obtain **active surveillance cultures (ASC)** for targeted MDROs from patients in populations at risk "

– V.B.5.b.i. Obtain ASC from areas of skin breakdown and draining wounds. In addition, include the following sites according to target MDROs:

– V.B.5.b.i.1. For MRSA: Sampling the anterior nares is usually sufficient; throat, endotracheal tube aspirate, percutaneous gastrostomy sites, and perirectal or perineal cultures may be added to increase the yield. Swabs from several sites may be placed in the same selective broth tube prior to transport.(117, 383, 384) Category IB

– V.B.5.b.i.2. For VRE: Stool, rectal, or perirectal samples should be collected.(154, 193, 217, 242) Category IB

– V.B.5.b.i.3. For MDR-GNB: Endotracheal tube aspirates or sputum should be cultured if a respiratory tract reservoir is suspected, (e.g., Acinetobacter spp., Burkholderia spp.).(385, 386) Category IB.

Surveillance cultures to limit spread of MDR pathogens

- Outside outbreak periods: ?
  - prerequisites
    - Endemicity: not too rare, not too common…
    - ‘threat’, priority: search and destroy…
    - Horizontal spread
    - Low rate of infection to carrier: tip of the iceberg…
    - Preferential colonization sites missed by clinical cultures: e.g. nares, perineum

Surveillance cultures to limit spread of MDR pathogens outside outbreak

- Prerequisites: MRSA
  - Endemicity: +
  - Threat, priority: +
  - Horizontal Spread: +
  - Low rate of infection to carrier: +
    - MRSA nasal carriage at ICU admission: PPV MRSA infection of 11% (Kollef Crit Care Med 2010)
  - Carrier sites missed by clinical cultures: +
    - Routine admission screening for MRSA reveals a much larger reservoir than clinical cultures alone (Lucet 2003, Eveillard M 2005, Huang 2007)

Journal of Antimicrobial Chemotherapy (2008) **62**, 1422–1429
doi:10.1093/jac/dkn373
Advance Access publication 1 September 2008

JAC

Impact of routine surgical ward and intensive care unit admission surveillance cultures on hospital-wide nosocomial methicillin-resistant *Staphylococcus aureus* infections in a university hospital: an interrupted time-series analysis

Iris F. Chaberny[1]*, Frank Schwab[2], Stefan Ziesing[1], Sebastian Suerbaum[1] and Petra Gastmeier[1]

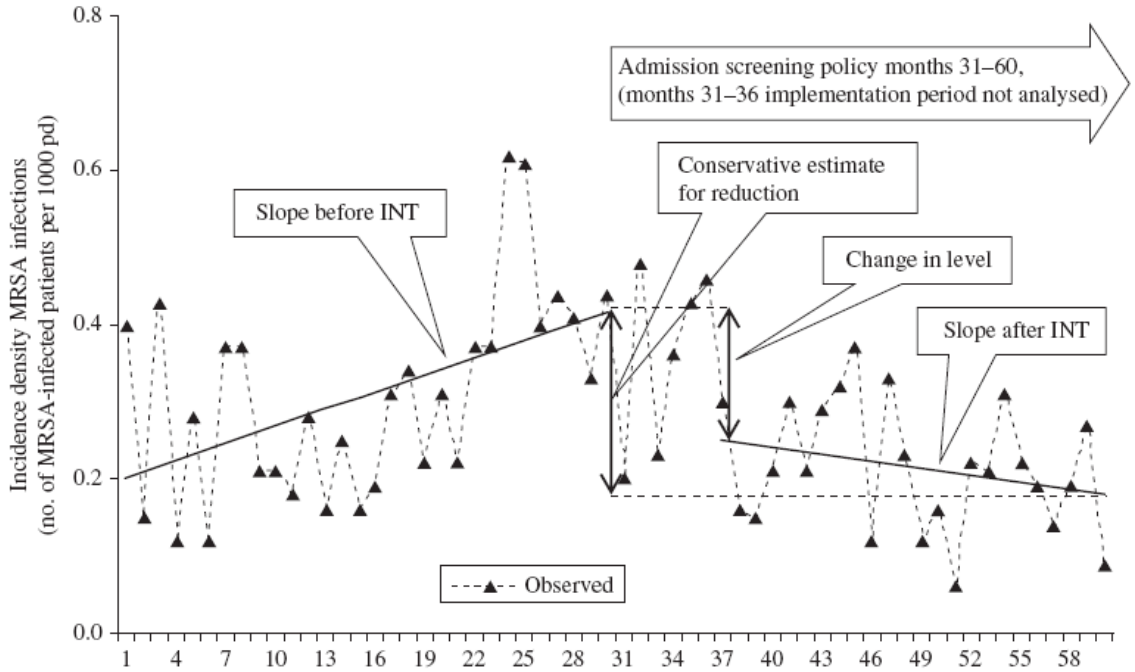


Figure 2. Changes in the hospital-wide incidence density of MRSA-infected patients/1000 pd 30 months before and 24 months after the intervention (INT = implementation admission screening for MRSA, 6 month implementation period). All parameters in the full segmented regression model are significant, the slope (month-to-month change) before intervention is 0.007 MRSA-infected patients/1000 pd, the change in level is −0.163 MRSA-infected patients/1000 pd and the change in slope after intervention is −0.010 MRSA-infected patients/1000 pd (when compared with the slope before implementation of admission screening). This means that the slope after the 6 month implementation period is −0.003 MRSA-infected patients/1000 pd.

Chaberny J Antimicrob Chemother 2008

Annals of Internal Medicine | ARTICLE

Universal Surveillance for Methicillin-Resistant *Staphylococcus aureus* in 3 Affiliated Hospitals

Ari Robicsek, MD; Jennifer L. Beaumont, MS; Suzanne M. Paule, BS; Donna M. Hacek, BS; Richard B. Thomson Jr., PhD; Karen L. Kaul, MD, PhD; Peggy King, RN, MBA; and Lance R. Peterson, MD

Table 2. Prevalence Density of Hospital-Associated Methicillin-Resistant *Staphylococcus aureus* and Methicillin-Susceptible *Staphylococcus aureus* Infections in 3 Periods*

Criteria	No Active Surveillance	Intensive Care Unit Surveillance	*P* Value†	Universal Surveillance	*P* Value†
Total patient-days	172 876	150 418	–	275 862	–
Prevalence density‡ of MRSA infection (95% CI)					
Bloodstream	1.45 (0.94 to 2.13)	1.26 (0.76 to 1.97)	–	0.44 (0.22 to 0.76)	–
Respiratory	2.89 (2.15 to 3.81)	2.93 (2.13 to 3.93)	–	1.05 (0.70 to 1.51)	–
Urinary tract	1.74 (1.17 to 2.48)	1.20 (0.71 to 1.89)	–	0.76 (0.47 to 1.16)	–
Surgical site	2.83 (2.10 to 3.75)	2.06 (1.40 to 2.93)	–	1.63 (1.19 to 2.18)	–
Bacteremia					
MRSA	2.14 (1.51 to 2.95)	1.99 (1.35 to 2.85)	–	1.09 (0.73 to 1.55)	–
MSSA	2.14 (1.51 to 2.95)	1.93 (1.29 to 2.77)	–	1.60 (1.16 to 2.14)	–
Total	8.91 (7.56 to 10.43)	7.45 (6.13 to 8.96)	–	3.88 (3.18 to 4.69)	–
Absolute change in prevalence density from baseline (95% CI), %					
Bloodstream	–	−0.18 (−0.99 to 0.62)	0.66	−1.01 (−1.63 to −0.39)	<0.001
Respiratory	–	0.03 (−1.15 to 1.21)	0.96	−1.84 (−2.79 to −0.90)	<0.001
Urinary tract	–	−0.54 (−1.37 to 0.29)	0.21	−0.97 (−1.62 to −0.33)	0.004
Surgical site	–	−0.77 (−1.85 to 0.30)	0.165	−1.20 (−2.07 to −0.34)	0.008
Bacteremia					
MRSA	–	−0.15 (−1.14 to 0.85)	0.77	−1.05 (−1.87 to −0.24)	0.006
MSSA	–	−0.21 (−1.20 to 0.77)	0.77	−0.55 (−1.39 to 0.30)	0.30
Total	–	−1.46 (−3.43 to 0.51)	0.149	−5.03 (−6.59 to −3.47)	<0.001

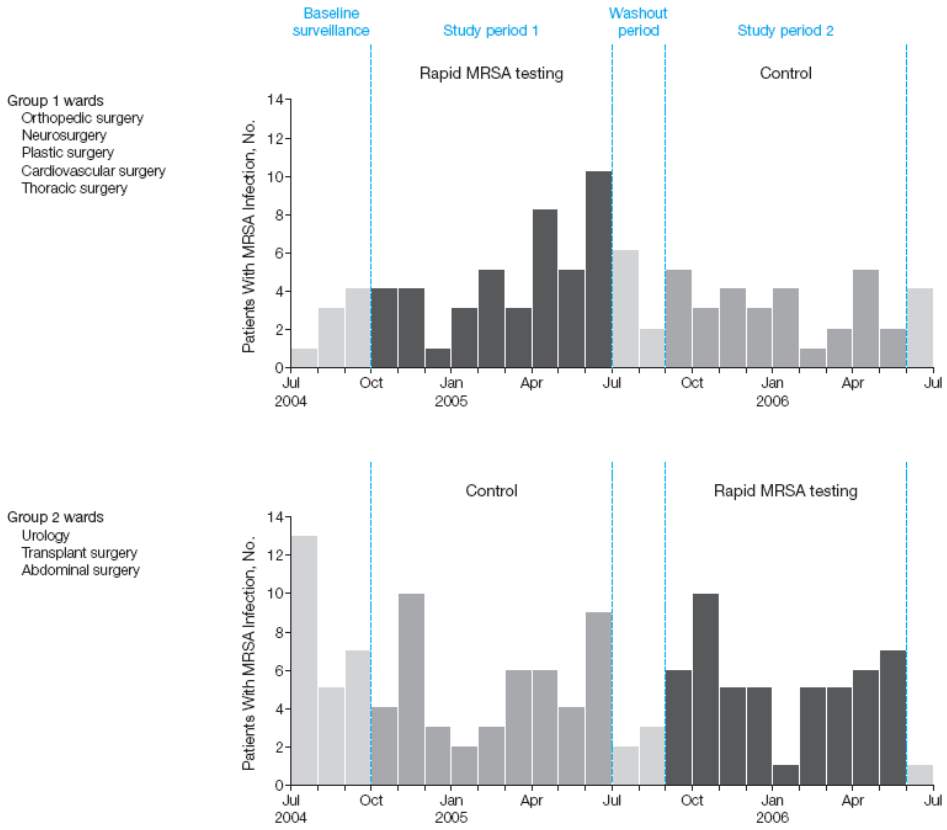
hours after admission and ≤30 days after discharge. MRSA = methicillin-resistant *Staphylococcus aureus;*

Surveillance with clinical cultures only would have identified 18% of patient MRSA days

Robicsek Ann Intern Med 2008

Universal Screening for Methicillin-Resistant *Staphylococcus aureus* at Hospital Admission and Nosocomial Infection in Surgical Patients

Figure 1. Incidence of MRSA Infections



Data are incident cases of any type of nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infection, stratified by period and intervention group. The total number of admissions in the control periods was 10 910 and in the intervention periods was 10 844.

Harbarth JAMA 2008

Surveillance cultures to limit spread of MDR pathogens:MRSA

- Cookson et al. Int J Antimicrob Ag (European consensus conference) 2011
  - In environment where MRSA is endemic, universal or targeted screening of patients to detect colonization is essential pillar of any MRSA control program
  - Depending on incidence – resources
    - Universal or targeted screening?
    - Decolonizing carriers?
    - Screening of staff?

Surveillance cultures to limit spread of MRSA: who to screen?

Table 1
Risk factors for colonisation with meticillin-resistant *Staphylococcus aureus* (MRSA) at hospital admission.

HCA-MRSA infection	CA-MRSA infection
• Previously colonised or infected, or their close contacts	• Previously colonised or infected, or their close contacts
• Previous therapy with quinolones, cephalosporins or carbapenems	• Previous antibiotic therapy with quinolones or macrolides
• Previous hospitalisation (especially in a hospital known to have high incidence of MRSA), surgery or healthcare contact	• Underlying chronic illness
• Previous MRSA colonisation or infection	• Livestock/animal workers, including veterinary staff
• Dialysis	**Without risk factors**
• Indwelling bladder or vascular device at home	*Groups with a higher incidence*:
• Underlying chronic illness	Athletes
• i.v. Drug abuse	Military personnel
• Residency in LTCFs or NHs, i.v. therapy, or specialised nursing at home	Male having sex with male
• Open wounds (pressure sores, varicose ulcers)	Prison inmates
• International or interhospital transfers from high-risk location	i.v. Drug users
	Homeless persons
	Native Americans
	Pacific Islanders
	Children in day-care programmes
	Recent travel to an endemic area such as North America

HCA-MRSA, healthcare-associated MRSA; CA-MRSA, community-acquired/associated MRSA; i.v. intravenous; LTCF, long-term-care facility; NH, nursing home.

Cookson Int J Antimicrob Ag 2010

Surveillance cultures to limit spread of MDR pathogens:MRSA

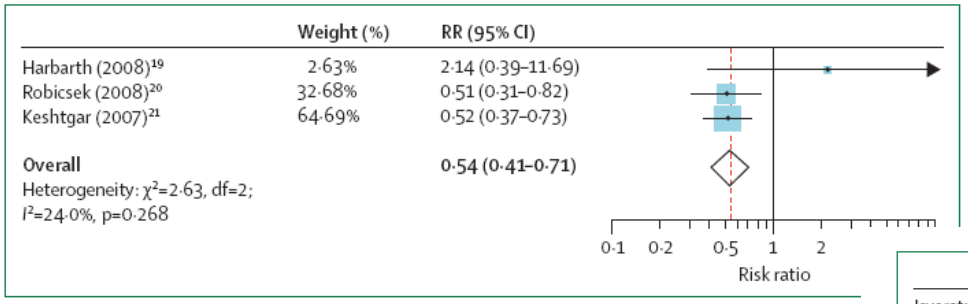


Figure 3: **Effect of rapid molecular tests for meticillin-resistant *Staphylococcus aureus* (MRSA) at ho admission on the incidence of MRSA bloodstream infections per 1000 patient-days**
Comparison is between units in which screening was done by molecular tests and units in which screeni done at all. Risk ratios (RR) and their 95% CIs are shown (fixed effects). Dotted line indicates combined indicate point estimates and the size of the square indicates the weight of each study in the meta-analy

◄Rapid molecular tests vs. no test

Rapid molecular test vs. surveillance culture alone ►

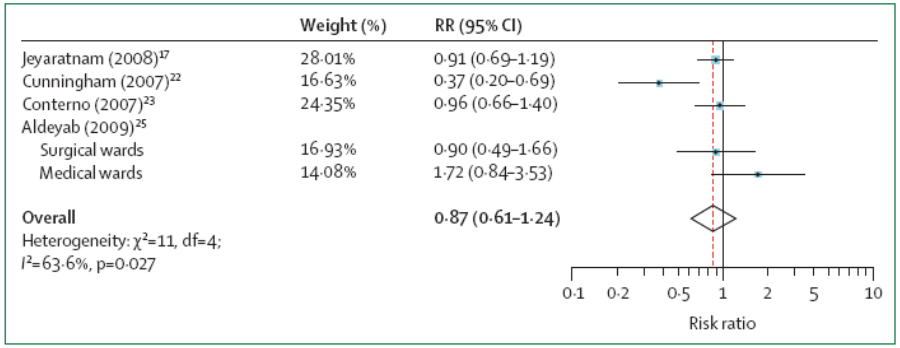


Figure 2: **Effect of rapid molecular tests for meticillin-resistant *Staphylococcus aureus* (MRSA) at hospital admission on MRSA acquisition rate per 1000 patient-days**
Comparison is between units in which screening was done by molecular tests and units in which screening was done by culture alone. Risk ratios (RR) and their 95% CIs are shown (random effects). Dotted line indicates combined RR. Squares indicate point estimates and the size of the square indicates the weight of the each study in the meta-analysis.

Taconelli Lancet Infect Dis 2009

Surveillance cultures to limit spread of MDR pathogens outside outbreak

- Prerequisites: ESBL
  - Endemicity: +
  - Threat, priority: +
  - Horizontal Spread: ?
    - ►Epidemiology of nosocomial ESBL-infection
      - Patient-to-patient transmission is important factor in acquisition of ESBL Enterobacteriaceae (Harris 2007, Lautenbach 2001) – no (Gardam 2002) or few (Gobel 2005, Harris 2007) clinical ESBL infections result from patient-to-patient transmission
      - Antibiotic use is the main risk factor for ESBL infection or colonization (Lautenbach 2001, Hyle 2007, Harris 2007)

Surveillance cultures to limit spread of MDR pathogens outside outbreak

- Prerequisites: ESBL
  - Low rate of infection to carrier: +
  - Carrier sites missed by clinical cultures: +
    - ►Rectal surveillance cultures increase the number of detected ESBL-carriers, ESBL-carriage occurs outside high risk settings, overall ESBL-prevalence increased >4fold in 5 years (Reddy 2007)
    - ►Optimal screening strategy?
      - Anatomical site: perineal vs. rectal vs. stool
      - Screening strategy: ceftazidime disc vs. cefotaxime disk vs. cefpodoxime vs. combination of disks)

Surveillance cultures for infection-control purposes outside outbreak periods: Gram-negative MDR pathogens: ESBL

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Letters to the Editor

Screening to select patients carrying extended-spectrum β-lactamase-producing *Enterobacteriaceae* for isolation in Flemish intensive care units: a Swiss cheese strategy?

Madam,

The increasing prevalence of clinical isolates of *Enterobacteri-*

NJ, USA) with a 30 μg ceftazidime disc (Becton Dickinson Sensi-disc, NJ, USA). Identification and antibiogram of all Gram-negative organisms growing within the 18 mm zone were performed. Clinical and Laboratory Standards Institute guidelines were followed for confirmation of ESBL production.[8] This screening practice was introduced in our laboratory in the 1990s to detect multidrug-resistant TEM-24 positive *Enterobacter aerogenes*.

The response rate to the electronic questionnaire was 70% (23/33). Only three out of 23 (13%) hospitals screened the gastrointestinal tract. Of those three hospitals, one hospital screened for

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R. Cartuyvels[a,b]
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I.C. Gyssens[c,d,e]
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1 Questionnaire: 23/33 ICU's; only 3 screened GI tract, perineal (2) vs. rectal (1)

Surveillance cultures for infection-control purposes outside outbreak periods: Gram-negative MDR pathogens: ESBL

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The increasing prevalence of clinical isolates of *En*

Table I
Distribution of positive anatomical screening sites of intensive care unit patients carrying ESBL-GNB during their admission in 2009 in the Virga Jesse Hospital

Screening	No. of ESBL-GNB carriers/ total no. of carriers
Positive anatomical screening site	
Perineum only	16/45
Throat only	1/45
Urine only	3/45
Respiratory tract only	3/45
Perineum and urine	4/45
Perineum and throat	1/45
Perineum and respiratory tract	1/45
Perineum, respiratory tract and urine	2/45
Perineum, throat and respiratory tract	6/45
Perineum, throat, respiratory tract and urine	6/45
Clinical isolates	Wound 1/45; blood 1/45
Carriers of ESBL-GNB in:	
Perineum	80% (36/45)
Urine	33% (15/45)
Respiratory tract	40% (18/45)
Throat	31% (14/45)

ESBL, extended-spectrum β-lactamase; GNB, Gram-negative bacilli.

2 Only 3 out of 5 patients with ESBL bacteremia had positive surveillance cultures…

Emerging problem:

Carbapenem resistance…

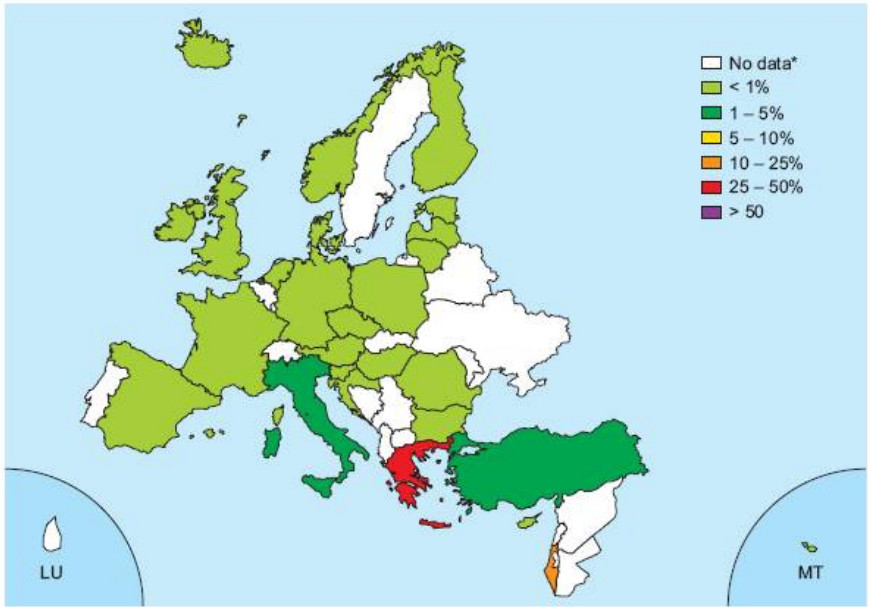


Figure 5.26. *Klebsiella pneumoniae*: proportion of invasive isolates resistant to carbapenems in 2006.
* These countries did not report any data or reported less than 10 isolates.

BRIEF REPORT

Detection and Spread of *Escherichia coli* Possessing the Plasmid-Borne Carbapenemase KPC-2 in Brooklyn, New York

Simona Bratu,[1] Steven Brooks,[2] Sibte Burney,[2] Sandeep Kochar,[1] Jyoti Gupta,[3] David Landman,[1] and John Quale[1]
[1]State University of New York Downstate Medical Center, [2]Kingsbrook Jewish Medical Center, and [3]Brookdale University Medical Center, Brooklyn, New York

A carbapenem-resistant isolate of *Escherichia coli* was iden-
coding *Klebsiella*
2). A subsequent
ooklyn, New York,
7 isolates (from 3
sessing KPC-2 is
nods for detection

f urinary tract in-
sociated with neo-
ion. Production of
is become increas-
ae and *E.coli*. The
e System reported
ites obtained from
th the number of
01, representing a
the treatment of
ducing gram-neg-
coli isolates is rare;

2 (KPC-2), was detected in *E. coli* isolates from France [5] and Israel [6]. The closely related enzyme KPC-3 was reported in a single patient in the United States [7]. In this report, a carbapenem-resistant clinical isolate of *E. coli* obtained in Brooklyn, New York, was found to possess the plasmid-borne bla_{KPC-2} gene. A subsequent surveillance study was conducted to assess the spread of KPC-positive *E. coli* isolates in the region.

Methods. Isoelectric focusing was performed using crude cellular extracts, as described elsewhere [8]. Transformation experiments were performed using *E. coli* DH5-α according to standard methods [9]. Electroporation was carried out using *E. coli* ElectroMax DH10B (Invitrogen). The transformant, *E. coli* DH10B801, was selected on Luria Bertani agar plates containing streptomycin (120 μg/mL) and ertapenem (0.8 μg/mL). Broth mating experiments were performed in Luria Bertani broth using cephalosporin- and carbapenem-susceptible clinical isolates of *E. coli*, *K. pneumoniae*, *Proteus mirabilis*, *Citrobacter koseri*, *Serratia marcescens*, and *Pseudomonas aeruginosa* according to standard procedures [10]; transconjugants were screened for by growth on MacConkey agar containing meropenem (2–16 μg/mL).

Table 1. Antimicrobial susceptibility patterns of *Escherichia coli* EC801, *E. coli* DH10B, and *E. coli* DH10B801.

	MIC, μg/mL		
Antibiotic	*E. coli* EC801[a]	*E. coli* DH10B	*E. coli* DH10B801[b]
Imipenem	32	0.5	32
Meropenem	16	0.06	32
Ertapenem	32	0.008	32
Ceftriaxone	>32	1	>32

Surveillance cultures to limit spread of carbapenemase-producing Enterobacteriaceae

- Calfee et al. Infect Control Hosp Epidem 2008
  - Mount Sinai Hospital, New York, 2005-2007
  - Screening upon ICU admission, once weekly in half of ICU's
  - Perineal swab, McConkey agar with ertapenem disk (+ imipenem E-test as confirmation)
  - 2% of 11.236 patients colonized with carbapenem-resistant *Klebsiella pneumoniae*, in 37%-53% first detected by surveillance culture, 3x more detection if weekly screening
  - Prevention of 1.396 unprotected patient and staff exposure days…

Surveillance cultures to limit spread of MDR pathogens: conclusions

- Outbreaks: yes
- MRSA: probably yes, screening may be more important than screening method
- ESBL Enterobacteriaceae:
  - More evidence needed
  - Site?
  - Technique?
  - In whom?

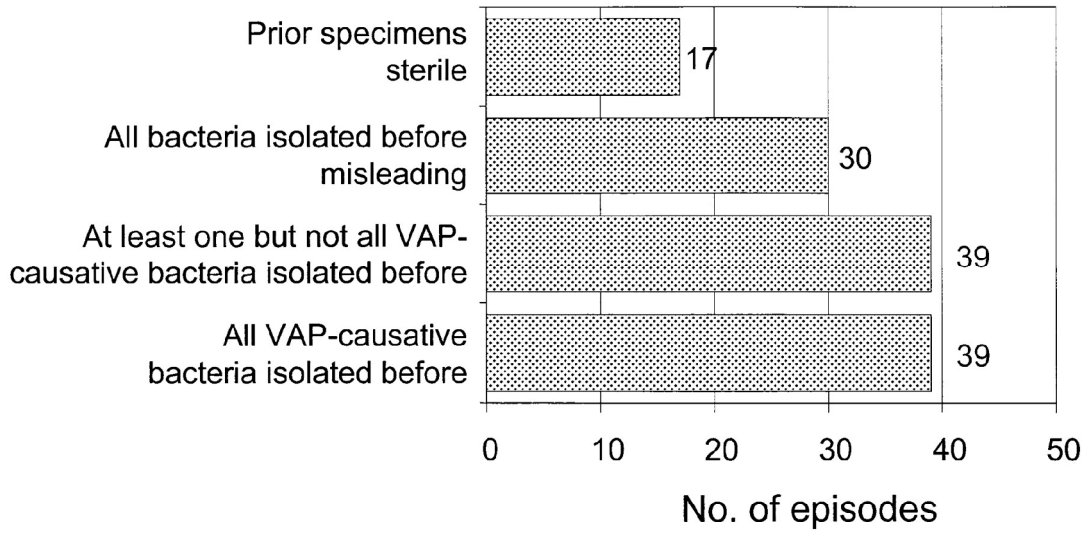
Are surveillance cultures helpful in guiding empirical antibiotic therapy?

Colonization precedes VAP

- Delclaux et al. Am J Respir Crit Care Med 1996
  - 50 patients with ARDS
  - Repetitive sampling of lower airways (plugged telescoped catheter) and quantitative cultures, BAL if suspected VAP
  - 16 of 24 (66%) VAP episodes preceded by colonization by same pathogen (2-6d), only 2 of 18 episodes of colonization not followed by VAP

Surveillance cultures as a guide to empirical therapy: earlier reports disappointing

- Hayon et al. AJRCCM 2001
  - 125 episodes of microbiologically confirmed VAP, 220 pathogens
  - 5576 prior microbiological specimens, 732 surveillance cultures



Surveillance cultures as a guide to empirical therapy: earlier reports

- Hayon et al. Am J Respir Crit Care 2002

For each VAP episode, all microbiologic specimen results available in the patient's chart on the day of fiberoptic bronchoscopy were prospectively reviewed and recorded. During the study period, all patients admitted to the ICU were screened with nasal and rectal swabs within 24 h of admission and weekly thereafter to identify *S. aureus* and *A. baumannii* carriages. Urine samples were systematically cultured at admission, every Monday, and when urinary tract infection was clinically suspected. Central venous catheters, arterial catheters, and Swan and Ganz catheters were systematically cultured at removal. For postoperative cardiac surgery patients with acute bacterial mediastinitis, mediastinal drainage fluids were cultured three times a week until removal of drainage tubes. All other microbiologic specimens, for example, blood cultures, and other miscellaneous specimen cultures were obtained based on clinical suspicion of infection. No bronchopulmonary samples (BAL, PSB, and tracheal aspirates) were obtained at predetermined times, but only when they were considered clinically justified by the team of physicians in charge of the patients. However, our general policy is to maintain a very high index of clinical suspicion in all patients who are mechanically ventilated in our ICU, in order not to miss any episode of VAP. This is why a large number of pulmonary specimens were obtained from ventilated patients during the study period. Microorganism susceptibilities were determined using the criteria established by the "Comité National de l'Antibiothérapie," the official French committee responsible for this classification.

- No systematic surveillance, use of clinical cultures
- Better correlation VAP culture and preceding culture in patients with >15d MV (49%) and if specimen available <72h (56%) before VAP onset

Surveillance cultures as a guide to empirical therapy: earlier reports disappointing

- Bouza Crit Care Med 2003
  - 356 cardiac surgery patients, 28 episodes of VAP
  - 1626 surveillance samples (4.5 samples per patient)
  - 1 VAP pathogen predicted by surveillance culture,
  - However
    - Low rate of SC: following extubation, after 3d, once weekly if prolonged MV: median interval SC-VAP 4.3d (2-7d)
    - Low incidence of VAP caused by ‘nosocomial pathogens’ (10 episodes)

Better prediction of more intensive surveillance protocols?

- Surveillance cultures at the ICU of Ghent University Hospital
  - Aims
    - Primary aim (1980s): containing outbreak of ESBL *Klebsiella pneumoniae* by early detection of colonization by ESBL producing strains
    - 'Exaptation' (1990s-2008): incorporated in antibiotic strategy as 'upfront' microbiological information
  - Protocol
    - Frequency
      - Upon admission (prior hospitalization, referral from other hospital/ICU/nursing home): oral/nasal, urinary, rectal swab
      - During ICU stay
        - » All patients: oral and faecal 1x/week, urinary 3x/week
        - » Intubated patients: oral and faecal 1x/week, urinary 3x/week + endotracheal aspirate 3x/week
    - Pathogens: MDR pathogens in oral/nasal/faecal cultures, all pathogens in endotracheal aspirate and urinary culture
    - Techniques: Semiquantitative culture in endotracheal aspirate and urinary culture, qualitative in oral/nasal/faecal

Better prediction of more intensive surveillance protocols?

- Blot et al. Infect Control Hosp Epidem 2005
  - Retrospective evaluation of 157 episodes of bacteremia caused by MDR pathogens

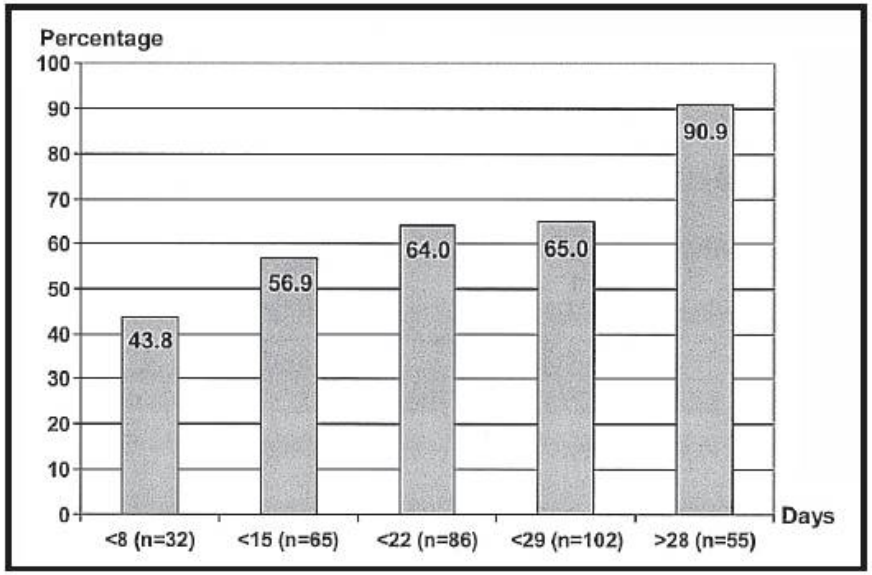


FIGURE 1. Rates of colonization preceding bacteremia caused by antibiotic-resistant gram-negative bacteria according to length of stay in the intensive care unit before onset of the bacteremia.

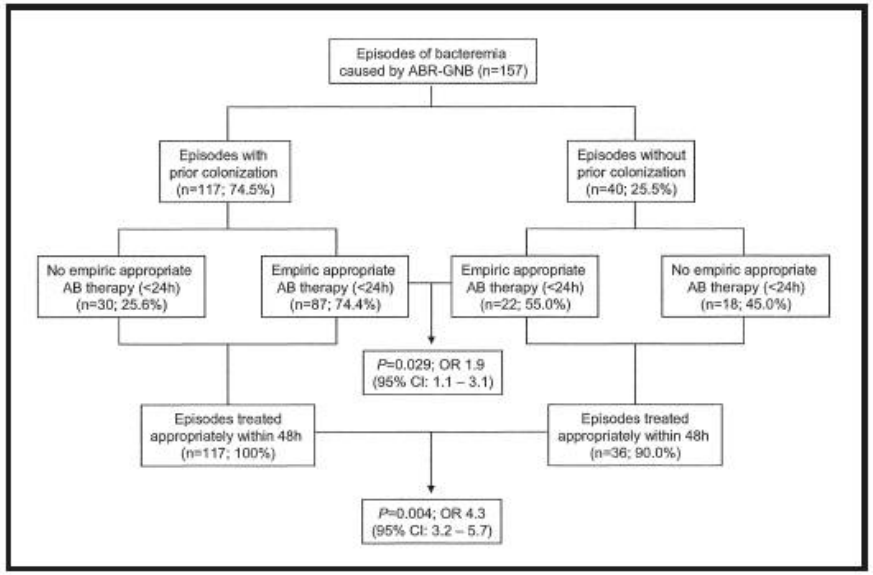


FIGURE 2. Rates of appropriate empiric antibiotic (AB) therapy for episodes of bacteremia caused by antibiotic-resistant gram-negative bacteria (ABR-GNB) with or without prior colonization. OR = odds ratio; CI = confidence interval.

Better prediction of more intensive surveillance protocols?

- Depuydt et al. Intensive Care Med 2007
  - Prospective evaluation of 199 episodes of microbiologically confirmed VAP (2004-2006), MDR involved in 86 (43%)

Table 2 Prevalence of multidrug antibiotic-resistant (*MDR*) pathogens, availability of surveillance cultures (*SC*) and prediction of MDR pathogens by SC according to risk category for MDR VAP

	Early onset ($n=79$) No prior antibiotics ($n=28$)	Prior antibiotics ($n=51$)	Late onset ($n=120$)[a]	p[a]
MDR cause	4 (15%)	15 (29%)	67 (56%)	<0.001
SC available at diagnosis of VAP	1 (4%)	36 (71%)	114 (95%)	<0.001
MDR predicted by tracheal SC	1 (25%)	6 (40%)	50 (75%)	0.023
MDR predicted by any SC	1 (25%)	8 (53%)	58 (85%)	0.36
False MDR prediction by tracheal SC	0	0	6 (5%)	0.29
False MDR prediction by any SC	0	3 (8%)	11 (10%)	0.36

[a] 118 patients received prior antibiotic therapy
[b] Pearson's χ^2 comparison between more than two groups

Better prediction of more intensive surveillance protocols?

- Depuydt et al. Intensive Care Med 2007

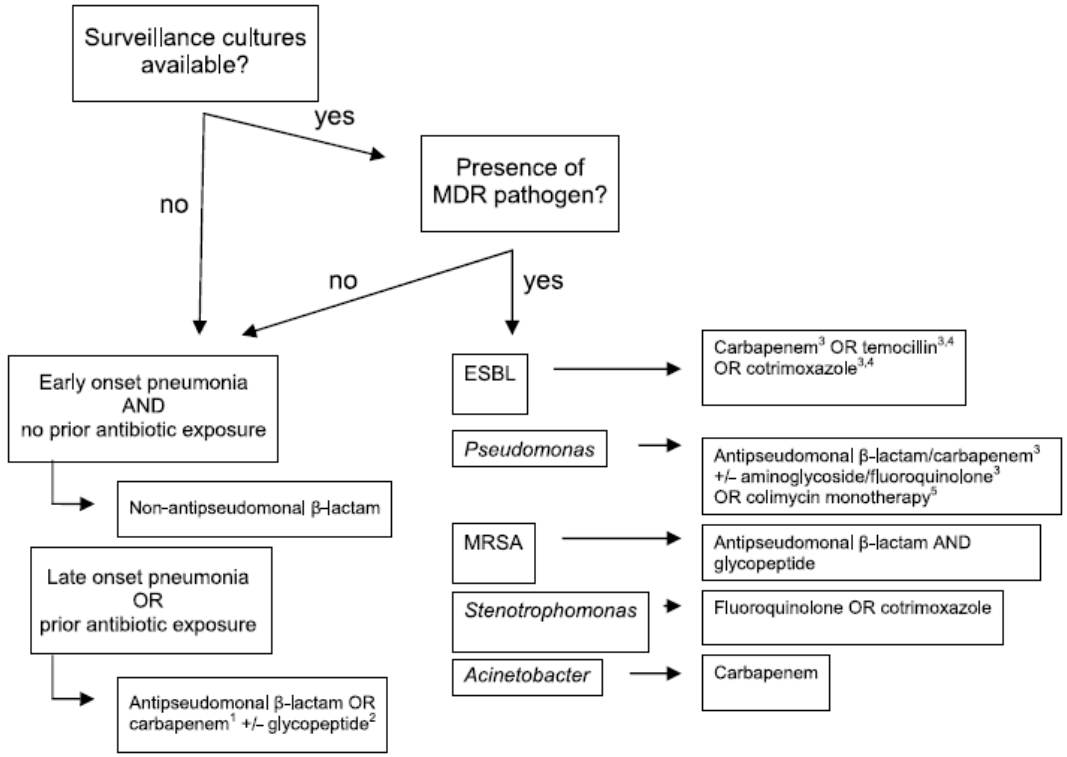


Fig. 1 Surveillance-guided prescription and empirical prescription (in the absence of surveillance cultures (*SC*) or with negative SC). [1] If previous exposure to antipseudomonal β-lactam; [2] if Gram-positive cocci on Gram-staining and (other) MRSA-colonized patient at the ICU unit; [3] if documented susceptibility on SC; [4] in the absence of septic shock; [5] if *P. aeruginosa* resistant to both β-lactam and carbapenem

Better prediction of more intensive surveillance protocols?

Table 3 Appropriate coverage rates and components of actual antibiotic prescription (overall episodes and in subgroups with and without multidrug resistant, *MDR*, pathogens) in comparison with three hypothetical, empirical schemes[a]. Antibiotic components are expressed as sum of defined daily dose (*DDD*) of antibiotic classes (*naPBl*, non-antipseudomonal β-lactam antibiotic; *aPBl*, antipseudomonal β-lactam antibiotic; *Fq*, fluoroquinolone; *Ag*, aminoglycoside; *Gly*, glycopeptide; *Ca*, carbapenem; *DDD*, daily defined dose; *MDR*, multidrug resistant; *VAP*, ventilator-associated pneumonia)

	Observed	Hypothetical Carbapenem scheme	β-lactam/ fluoroquinolone scheme	β-lactam/ aminoglycoside scheme
Overall episodes ($n=199$)				
Appropriate coverage				
24 h	86%	88%	76%[a]	80%
48 h	93%	88%	76%[a]	80%[b]
Antibiotic DDD for the first 48 h				
naPBl	101	55	55	55
aPBl/Ca	201	342	342	342
Fq	55	342	240	0
Ag	8	0	0	240
Gly	44	342	240	240
Other[c]	45	0	0	0
Episodes with MDR ($n=86$)				
Appropriate coverage				
24 h	77%	81%	56%[a]	68%[b]
48 h	89%	81%	56%[a]	68%[b]
Antibiotic DDD for the first 48 h				
naPBl	25	8	8	8
aPBl/Ca	95	164	164	164
Fq	26	164	134	0
Ag	4	0	0	134
Gly	37	164	134	134
Other[c]	32	0	0	0
Episodes without MDR ($n=113$)				
Appropriate coverage				
24 h	92%	92%	89%	89%
48 h	96%	92%	89%	89%
Antibiotic DDD for the first 48 h				
naPBl	76	47	47	47
aPBl/Ca	106	178	178	178
Fq	29	178	106	0
Ag	4	0	0	106
Gly	7	178	106	106
Other[3]	13	0	0	0

[a] Appropriate antibiotic coverage of the β-lactam-fluoroquinolone scheme was significantly lower than that of actual prescription both at 24 h and 48 h ($p<0.05$) in the overall group and in the subgroup with MDR VAP

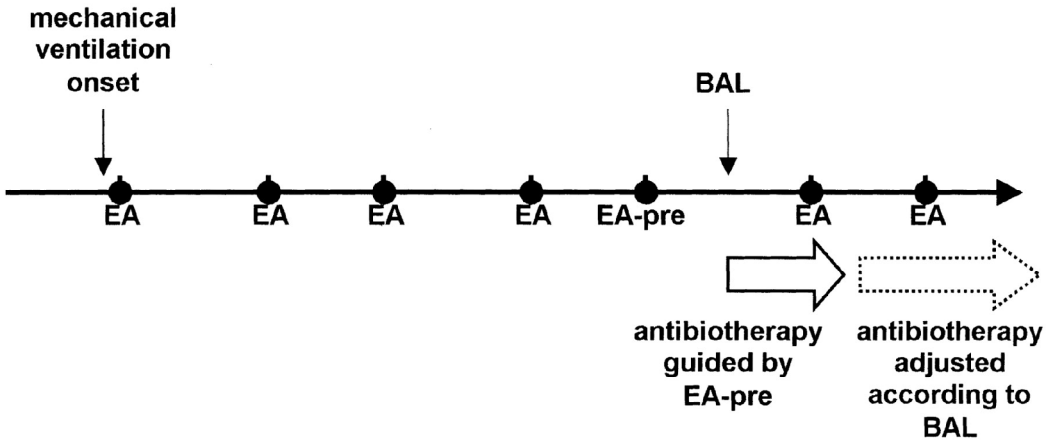
[b] Appropriate antibiotic coverage of β-lactam-aminoglycoside scheme at 48 h was significantly lower than that of actual prescription at 48 h ($p<0.05$) in the overall group and in the subgroup with MDR VAP; at 24 h this difference showed a trend to significance in the subgroup with MDR VAP ($p=0.06$)

[c] Other antibiotics include trimethoprim-sulfamethoxazole and colimycin

Depuydt et al Intensive Care Med 2007

Surveillance cultures as a guide to empirical therapy: more recent reports

- Michel Chest 2005
  - Prospective study in 229 patients ventilated >48h, 41 episodes of VAP
  - SC (ETA) 2x weekly



Surveillance cultures as a guide to empirical therapy: more recent reports

Concordance between pathogens recorded from BAL and SC (ETA)

	Positive BAL culture	
EA-pre	MV≤5d (n=11)	MV>5d (n=29)
Identical	9 (82)	25 (86)
Differing	2 (18)	4 (14)

Michel Chest 2005

Surveillance cultures as a guide to empirical therapy: more recent reports

Table 5—*Antibiotics Received by the 41 Patients With a VAP and Antibiotics That Would Have Been Prescribed According to the Classifications of Trouillet et al[25] and the ATS[24]***

Antibiotics	EA Strategy, No.	Trouillet et al[25] Strategy, No.	ATS Classification, No.
Imipenem + AG + vancomycin	0	11	0
Imipenem + AG	10	0	0
Antipseudomonal cephalosporin + AG	2	20	33
Antipseudomonal peni + AG	5	0	0
Nonpseudomonal cephalosporin + AG	5	0	0
Nonpseudomonal cephalosporin	0	10	8
β-lactam/β-lactamase inhibitor + AG	1	0	0
β-lactam/β-lactamase inhibitor	3	0	0
Vancomycin	1	0	0
Clavulanic acid + amoxicillin	11	0	0
No antibiotics	2	0	0
Not evaluable	1	0	0

*AG = aminoglycoside.

Adequate antibiotics 95% 83% (p=0.15) 68% (p=0.005)

Michel Chest 2005

Surveillance cultures as a guide to empirical therapy: more recent reports

- Malacarne Infect Control Hosp Epidem 2007
  - 20 episodes of *Acinetobacter baumannii* VAP
  - 18 predicted by SC (sensitivity 90%, NPV 96%)

- Boots Respirology 2008
  - 58 episodes of VAP in 50 patients
  - SC 3x/week by blinded mini-BAL
  - 85% concordant pathogens VAP vs. SC 2d earlier, antimicrobial susceptibility stable for up to 4d
  - No benefit of quantification

Surveillance cultures as a guide to empirical therapy: more recent reports

- Jung Intensive Care Med 2006
  - 113 episodes of VAP
  - Routine 1x weekly SC (ETA)
  - SC-guided AB adequate in 85%, compared to 73% (ATS guidelines) and 81% (Trouillet guidelines)

- Bagnulo Crit Care 2007 (abstract)
  - 118 episodes of VAP
  - Routine 2x weekly SC (ETA)
  - 63% full concordance SC-BAL,14% partial concordance SC-BAL, 80% full concordance SC-BAL if MDR pathogen

Predictive value of systematic surveillance cultures on microbial etiology of VAP

Study	# cases with VAP	Sampling frequency Sampling type	Microbial etiology of VAP preceded by detected colonization
Johanson 1972	26	/24-48h (5-7d) oropharyngeal	84% prior colonization
Delclaux 1997	24	/48-72h protected LRT	66% true positive 8% false positive
Ewig 1999	19	/24h (≤ 4d) /72h (>4d) nasal, orophar, trach	75%-88% prior colonization
Cardenoso 1999	25	/24h orophar, trach	88% prior colonization
Bertrand 2001	184	/7d nose, rect,trach	56% prior colonization (*P.aeruginosa*)
Hayon 2002	125	/7d orophar, rect, trach?	33% true positive >50% false positive
Bouza 2003	28	/7d orophar, rect, trach	<5% true positive
Rello 2003	18	48h before tracheotomy	69% true positive <25% false positive
Depuydt 2006	112	/7d orophar, rect, ur /48-72h trach	70-88% true prediction 15-46% false prediction
Michel 2006	41	/72h tracheal	83% true prediction 5% false prediction
Berdal 2007	179	/48-72h orophar, trach	95% (simultaneous orophar-trach) 27% false positive
Bagnulo 2007	118	/72h trach	60% (80% MDR) true positive 11% false positive
Depuydt 2007	199	/7d orophar, rect, ur /48-72h trach	69-82% true prediction 4-9% false prediction
Malacarne 2007	20	/72h	90% (*Acinetobacter baumannii*)

Surveillance cultures as a guide to empirical therapy: conclusions

- SC may predict 70-90% of (MDR) pathogens in ICU-acquired infection (>VAP, bacteremia) provided that a regular sampling scheme (≥2 weekly) is applied

- Diagnostic culture results still mandatory

- Guidance of empirical therapy by SC may allow high rates of early appropriate antibiotic therapy (≥ current 'best practice' (guidelines)) with less antibiotics

Thank you