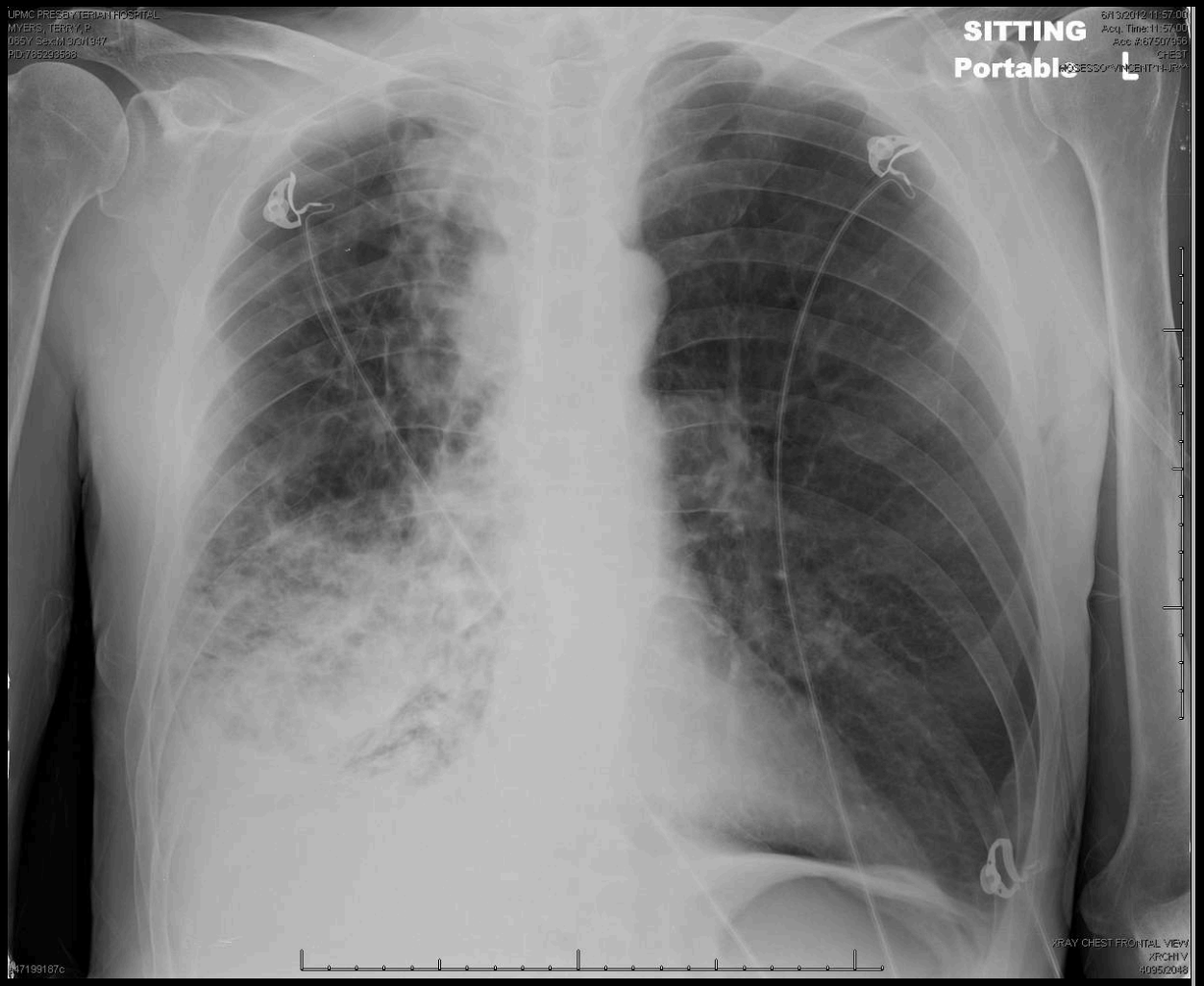
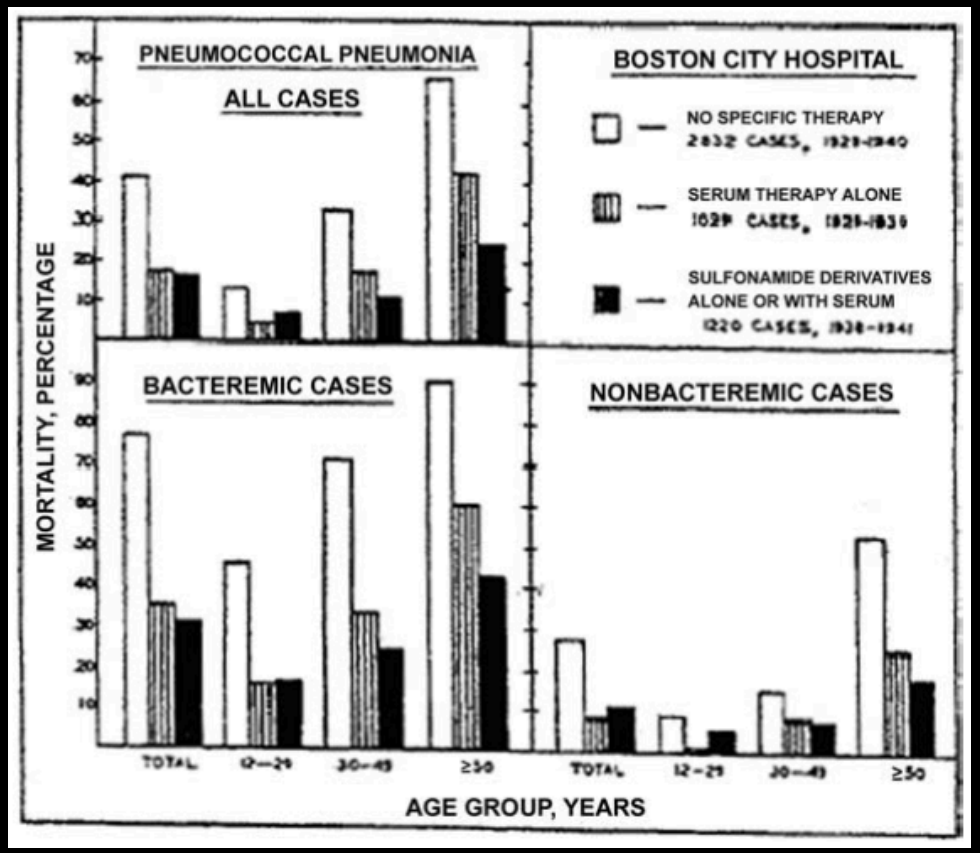
Community Acquired Pneumonia



Anna Zemke, MD. PhD.
February 2017

Captain of the Men of Death



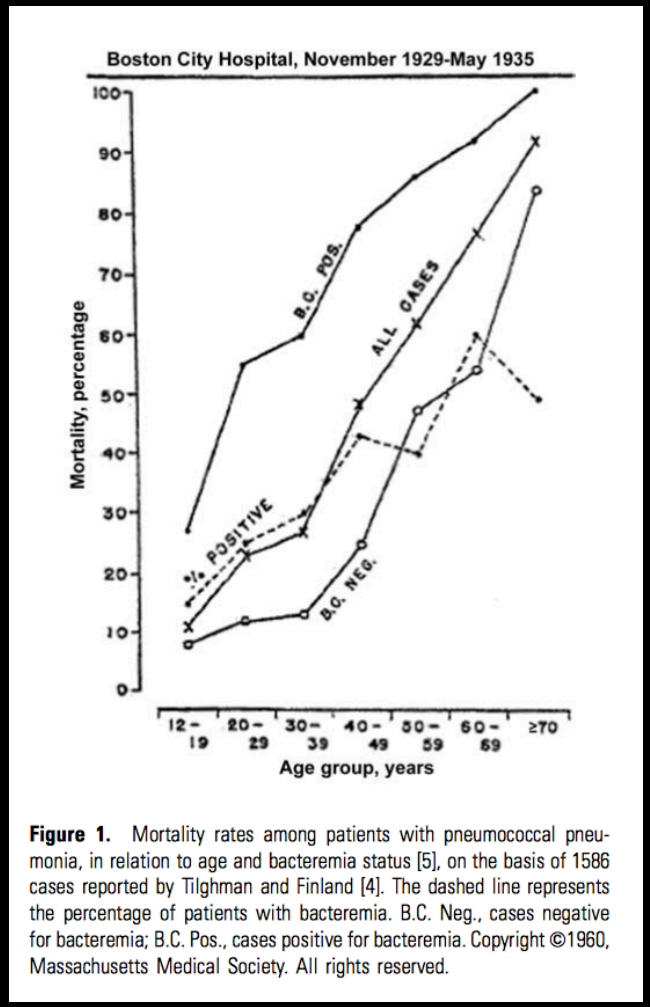


Figure 1. Mortality rates among patients with pneumococcal pneumonia, in relation to age and bacteremia status [5], on the basis of 1586 cases reported by Tilghman and Finland [4]. The dashed line represents the percentage of patients with bacteremia. B.C. Neg., cases negative for bacteremia; B.C. Pos., cases positive for bacteremia. Copyright ©1960, Massachusetts Medical Society. All rights reserved.

Historical and Regulatory Perspectives on the Treatment Effect of Antibacterial Drugs for Community-Acquired Pneumonia M. Singer, S. Nambiar, T. Valappil, K. Higgins, and S. Gitterman

Objectives

Review of ATS/IDSA guidelines on CAP (2007)

Interim developments:
H1N1 flu outbreak
development of RVP swabs
discovery of human metapneumovirus
changes in antimicrobial susceptiblity
removal of Xigris from the market
Anna Zemke got an iphone

Case 1

65 y/o man with COPD on 3lpm home oxygen. Last admitted 14 months ago. No recent antibiotics. Not on home steroids. Still smoking.

Presents with cough, increased oxygen requirement and leukocytosis (WBC 18).

Where would you admit this patient?

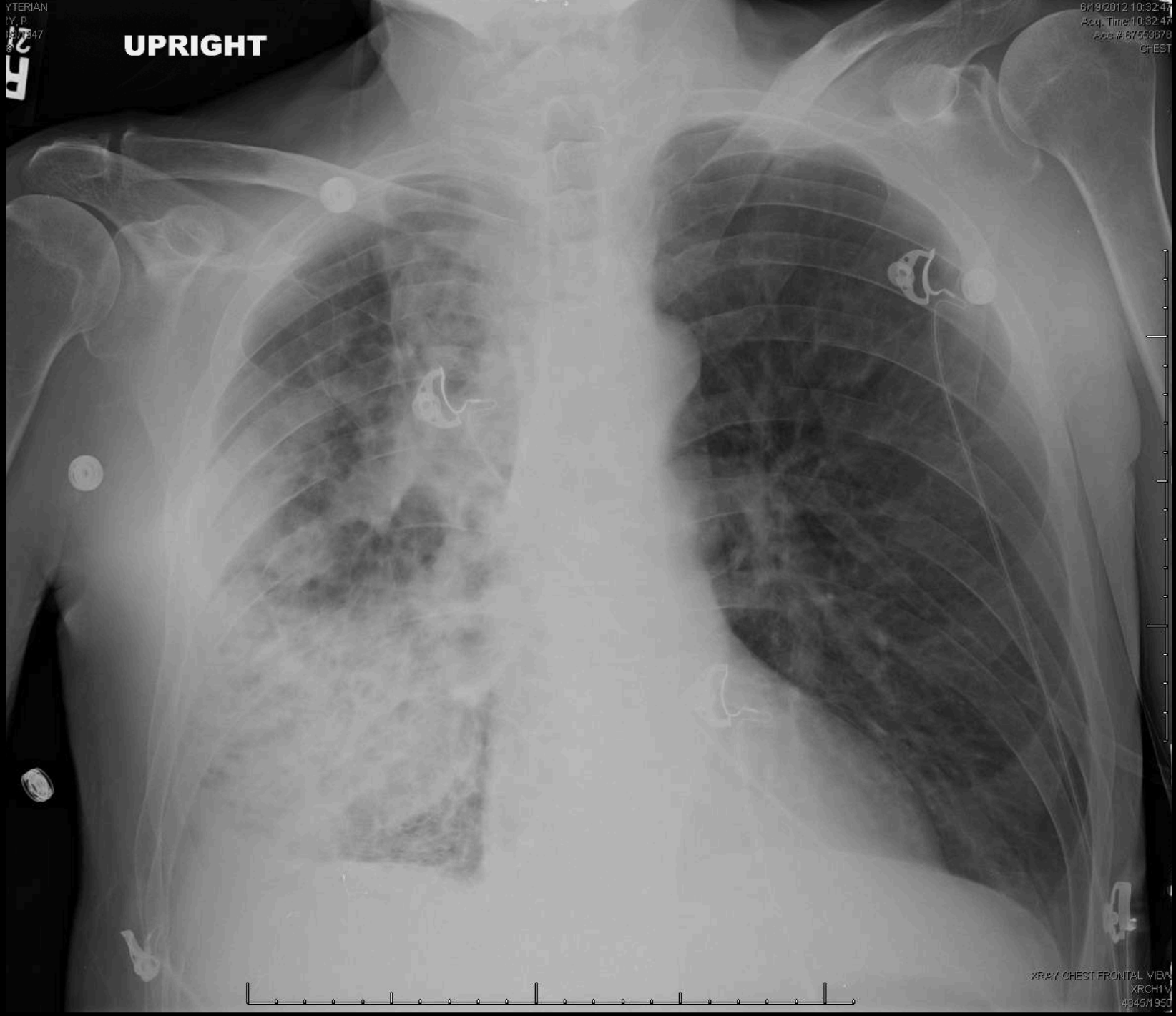
RR28, now on 6lpm oxygen, mental status normal, BUN 36, WBC 18, Plts 150, Temp 38.5, normotensive.

ICU admission decision

Major criteria: pressors, ventilator (strong rec, level II evidence)

OR

Three minor criteria: RR>30, P/F ratio <250, multilobar infiltrate, confusion, BUN>20, WBC <4K, Plt <100K, hypothermia, hypotension requiring aggressive fluids resuscitation (ATS definition of "Severe CAP").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What diagnostic testing is indicated?

Blood cultures and sputum samples should be obtained.

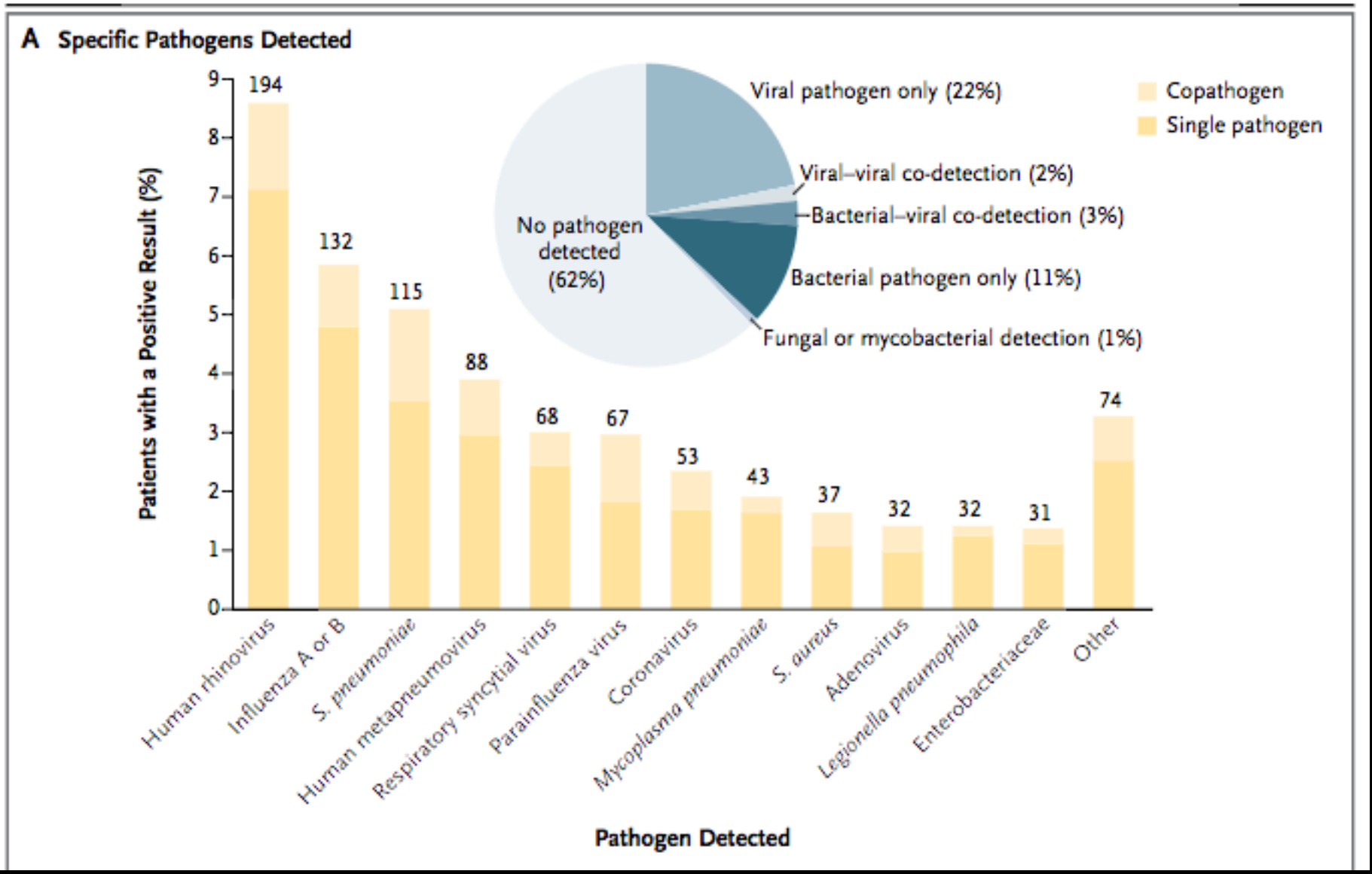
ICU admission is an indication for *Legionella* and Pneumoccal UAT

Pleural effusion is an indication for *Legionella* and Pneumococcal UAT

If intubated, obtain an endotracheal aspirate

Thoracentesis if pleural effusion >5cm

Top 5 guess for etiology?



CAP etiology

- EPIC study (CDC). Chicago and Nashville 2010-2012.
- Enrolled patients admitted with pneumonia. 21% patients required ICU admission and 2% died (older people, people on vent and who died quickly were less likely to be enrolled).

Etiology – part 2

Study in the elderly (>75 y/o) from 1996-1999 admitted to ICU in Buffalo NY. 53% with pathogens detected. Davies *AJRCCM* 2001.

S. pneumo (19%)

Legionella (9%)

S. aureus (7%)

H. influenza (7%)

Treatment Recommendations

Empiric treatment: potent antipneumonoccal b-lactam and macrolide (cover *S. pneumoniae* and *Legionella sp.)*

Does not necessarily apply to post-influenza pneumonia (increased risk for S. aureus), people with severe structural lung disease or the immunosuppressed.

Would you treat with steroids?

Many small-medium sized studies. Metanalysis (Siemieniuk, 2015).

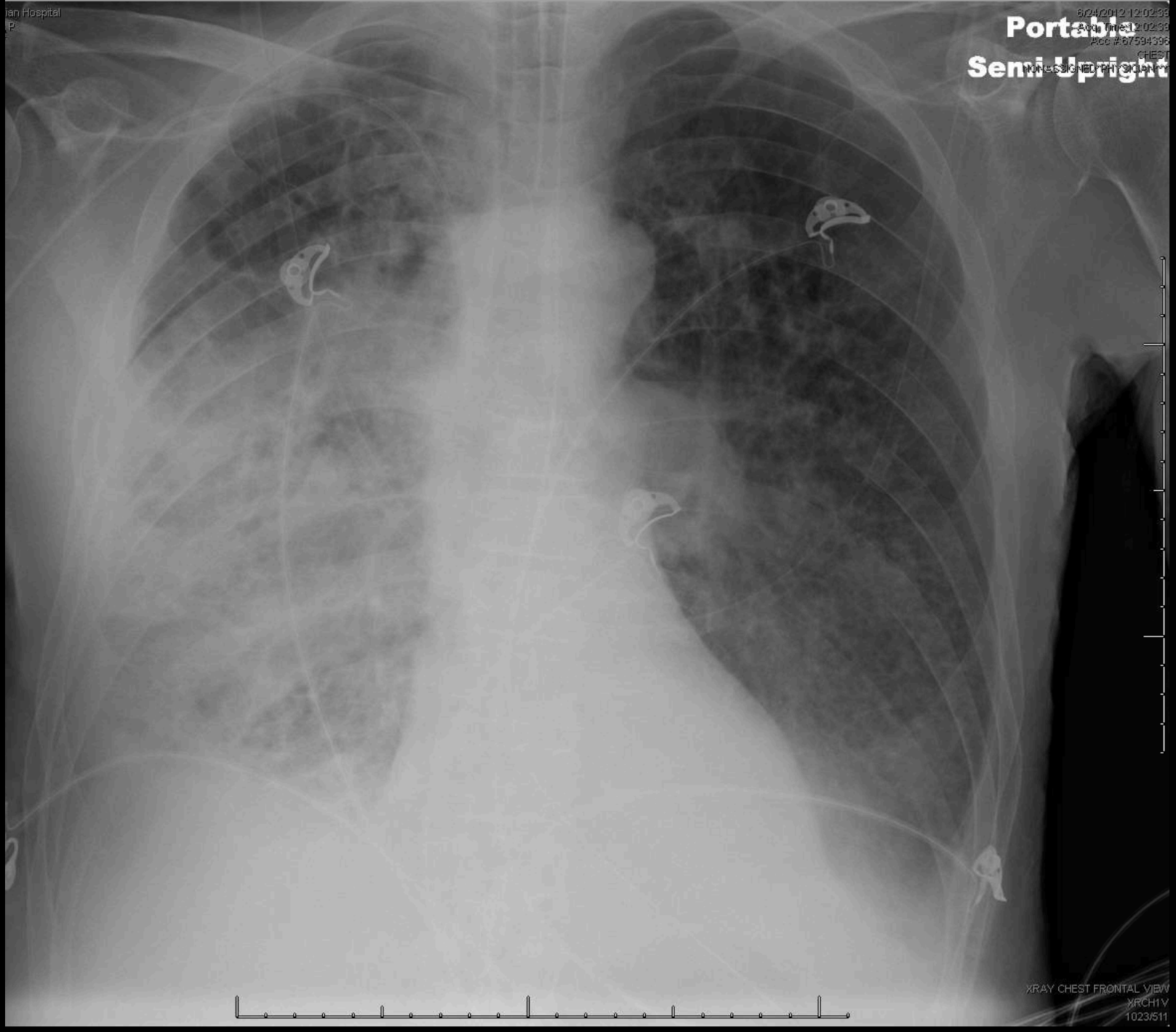
-- no effect on all-cause mortality, possible mortality benefit in those with severe CAP.

-- reduces the need for mechanical ventilation (RR, 0.45)

-- reduced risk of ARDS (RR, 0.24. ARR 5%, NNT 20)

-- time to clinical stability (1 days less).

-- 4% of subjects with hyperglycemia requiring treatment.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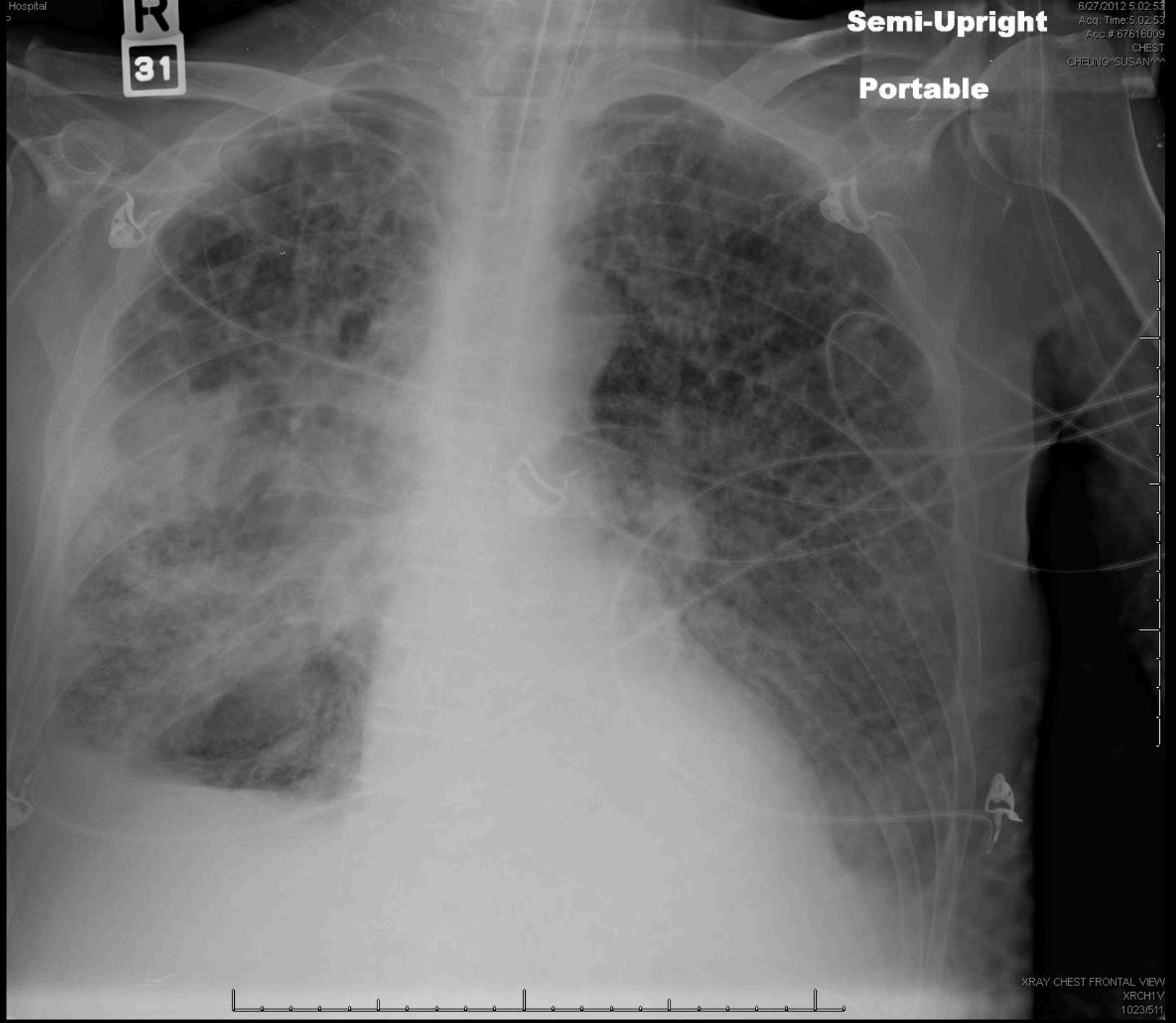
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Objective 2

IDSA/ATS HAP/VAP Guidelines (2016)

0/44 have strong quality evidence

7/44 have moderate quality evidence

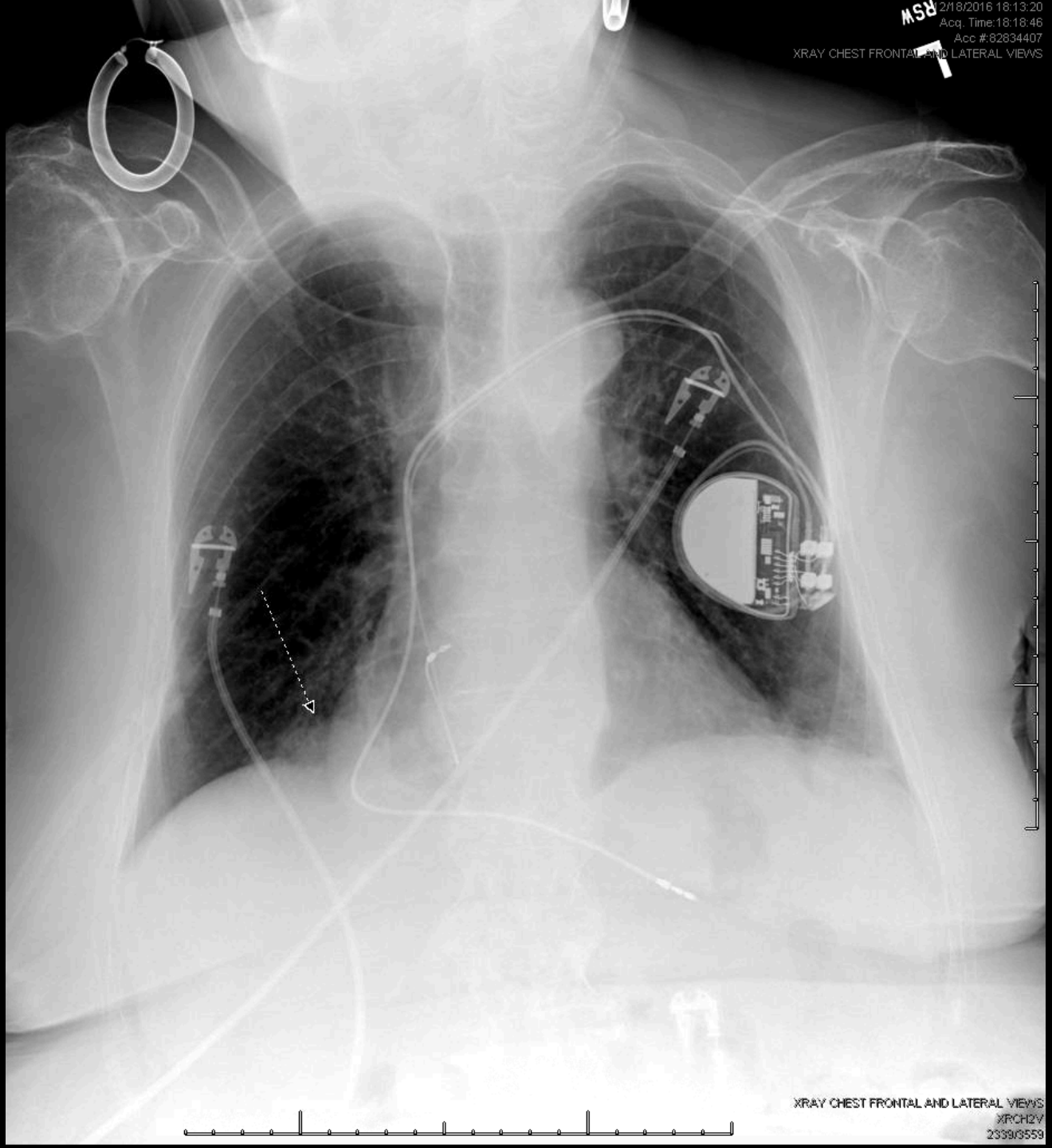
keep subtracting….

Case 2:

75 y/o female SNF resident with ischemic cardiomyopathy, pacer placement, DM, gout, cognitive impairment. Admitted to hospital after a fall, atrial fibrillation.

Develops fever, cough and infiltrate on day 3.

Gets worse. Condition C. Intubated. Now yours.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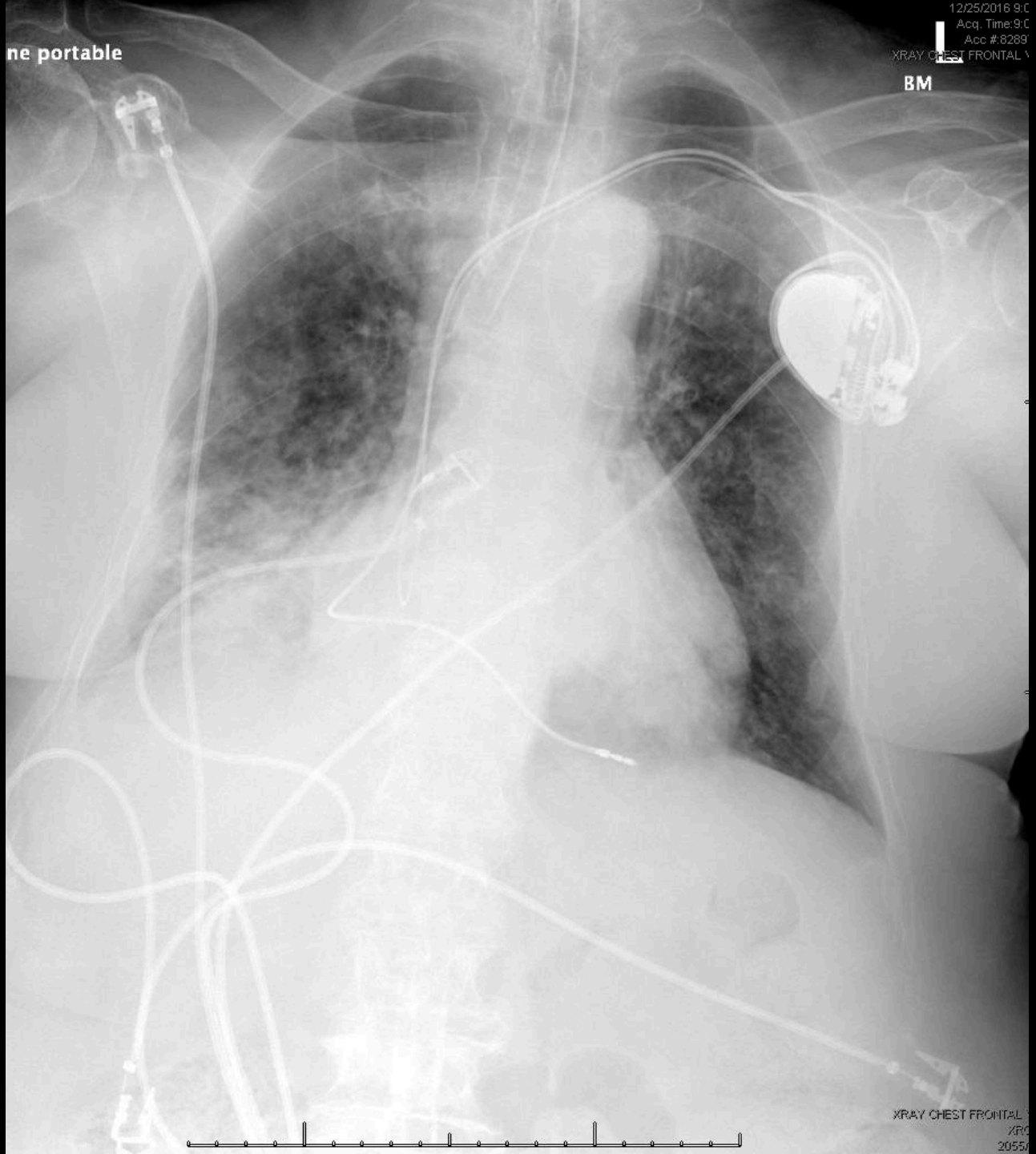
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Bronchoscope?

Should patients with suspected VAP be treated based on results of invasive sampling with quantitative culture

OR

noninvasive sampling with semiquantitative culture?

Recommend noninvasive sampling over bronchoscopy.

Weak rec, low qual evidence

Should procalcitonin, CRP or CPIS be used to decide whether or not to start antibiotics?

No!

One of only two strong recommendations with moderate evidence in the entire guideline.

None of these tests have adequate sensitivity or specificity to improve decision making regarding addition of antibiotics.

Etiology?

One day survey of hospitals in 2010:

16% *S. aureus*
13% *P. aeruginosa*
12% *Klebsiella sp.*
6.4% Strep sp.
5.5% S. maltophilia
3.6% A. baumannii

NEJM 2014, Magill et al

Should you use your local antibiogram?

Really!!! How can anyone say no to this?

Antibiotic Selection I

You start pip-tazo. Does she need MRSA coverage as well?

Percent Susceptible
January-December, 2015

Percent Susceptible
Gram Positive Organisms

Organism	# Tested	PEN	OX	VAN	ER	CLN	LZD	DOX	DAP	AMS	CRO	SXT
S. aureus	517		45	100	33	81	100	92	100	45		98

OR

2. >10-20% isolates on your unit are MRSA

January-December, 2015

Percent Susceptible

Gram Positive Organisms

Organism	# Tested	PEN	OX	VAN	ER	CLN	LZD	DOX	DAP	AMS	CRO	SXT	LVX	NFD
S. aureus	517		45	100	33	81	100	92	100	45		98		
Coag. neg. Staph	104		37	100	26	58	100	87	99	37		64		
S. pneumoniae	12	58/100*		100	58			83			83/100'	100	100	
		*meningitis/non meningitis									*meningitis/non meningitis			
E . Faecium	43			28			98	18	79	16			3	37
E. faecalis	189	99		96			97	17	99				58	100

Gram Negative Organisms

		AMS	CXM	CRO	CFTZ	CFP	PIP/TZ	AZTR	GM	TO	SXT	CIP	IPM	MERP	NFD
E. coli	803	61	93	98	99	99	97	97	91	88	76	75	100	100	97
P. aeruginosa	202				84	85	88	76	75	98	0	79	78	90	0
E. cloacae	43	3	3	71	68	87	84	71	97	97	82	79	92	98	32
Citrobacter freundii	37	0	0	73	69	91	91	76	97	97	85	70	92	97	100
Kleb. pneumoniae	246	84	92	98	100	99	94	98	95	91	82	87	98	97	48
Kleb. Oxytoca	48	63	86	98	100	100	98	98	98	98	90	90	100	100	94
P. mirabilis	160	94	98	98	99	99	99	95	94	97	64	52			0

Key to Antibiotics

AM = Ampicillin
AMS=Ampicillin/ Sulbactam
CE = Cefazolin
CFP=Cefipime
CFTZ=Ceftazidime
CXM = Cefuroxime
ER = Erythromycin
LVX=Levofloxacin
OX = Oxacillin
PCN = Penicillin
PP = Piperacillin
TIM=Ticarcillin/Clav
TO = Tobramycin
SxT = Sulfamethoxaz

Antibiotic Selection – Part 2

Day 2: Her sputum has heavy GNRs. She's on levophed. Now what?

Guidelines recommend double coverage for *Pseudomonas aeruginosa*
weak recommendation, very low quality evidence.

They've "limited" the at risk population to:
-- sputum with heavy GNRs
-- bronchiectasis
-- septic shock
-- requiring mechanical ventilation

Antibiotic Coverage III

Sputum culture grows *Pseudomonas aeruginosa* susceptible only to colistimethate.

VAP due to GNR susceptible only to aminoglycosides or polymyxins, they suggest adding inhaled agent in addition to systemic delivery.

Weak recommendation, very low quality evidence.

They also suggest routine testing for polymyxin sensitivity in settings with a high prevalence of extensively resistant organisms.

Guideline Rec's for MDR bugs

MRSA	vanco or linezolid (strong rec)
P. aeruginosa, S only to aminoglycoside/ polymyxin	IV and inhaled drug
P. aeruginosa	not aminoglycoside monotherapy (poor lung penetration, no studies supporting use)
ESBL GNRs	get susceptibility testing
Acinetobacter sp.	get susceptibility testing carbapenem or amp/sulbactam polymyxins do not add tigaycline or rifampacin add inhaled colsitimethate
Carbapenem-R GNRs	IV and inhaled colistimethate

How long to treat?

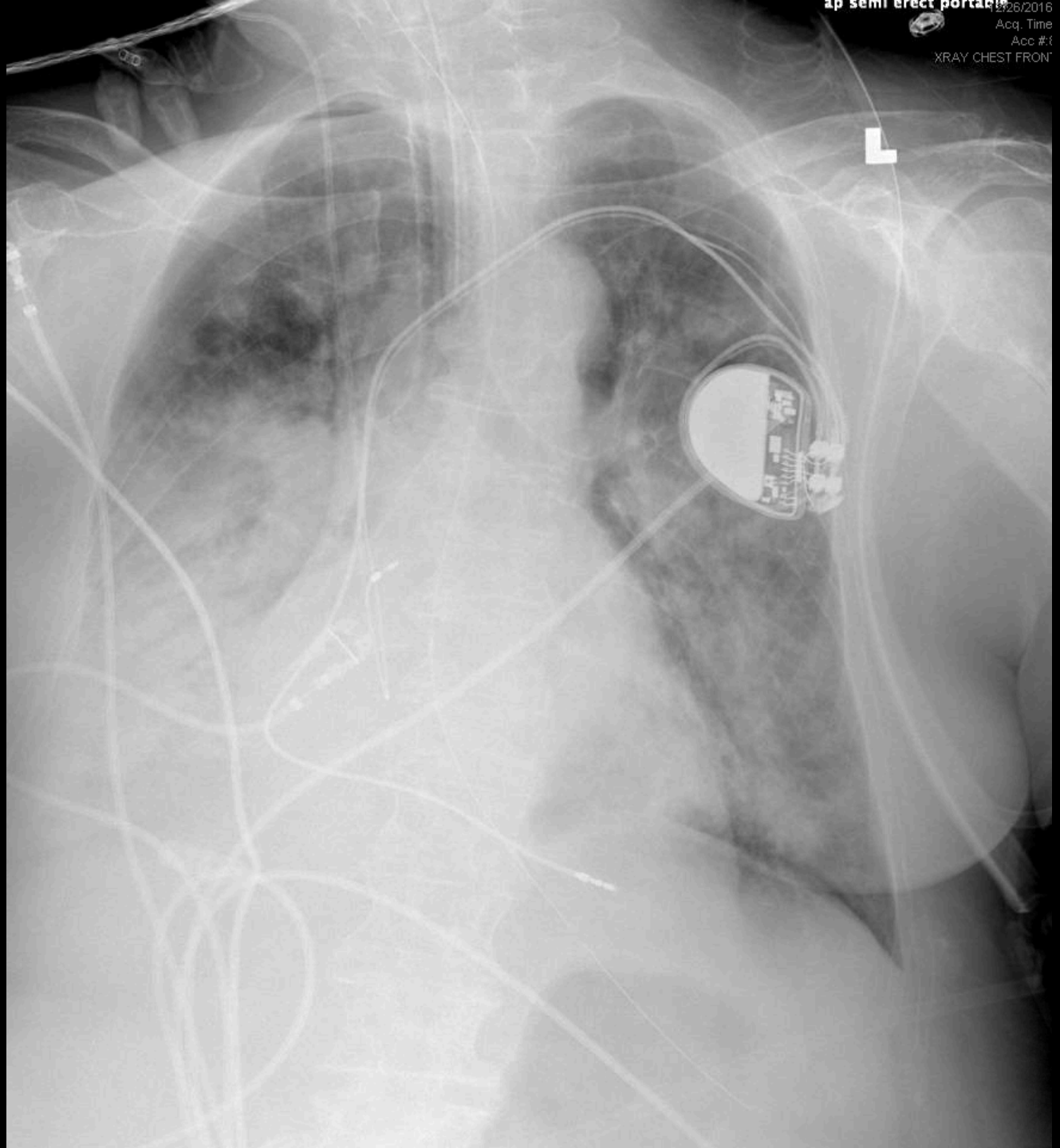
She has been treated for 6 days with pip-tazo for a pan-S *P. aeruginosa.* Afebrile after 2 days of therapy, hemodynamics improved, now extubated.

- Guidelines recommend 7 days of therapy for all organisms, including *P. aeruginosa.*
- Strong rec, very low quality evidence.
- Admits continued therapy for slow responders is reasonable.

Duration of therapy

Guidelines argue that the longer courses of abx for *PsA* treatment was to decrease recurrence rate. No change in mortality, LOS, duration of ventilation. Subsequent studies haven't confirmed the benefit. Also the definition of recurrence was unclear and subjects may have been colonized.

They then conducted their own meta analysis *within* the guideline document. They DO NOT recommend longer therapy for non-fermenting GNRs (mostly *P. aeruginosa)*.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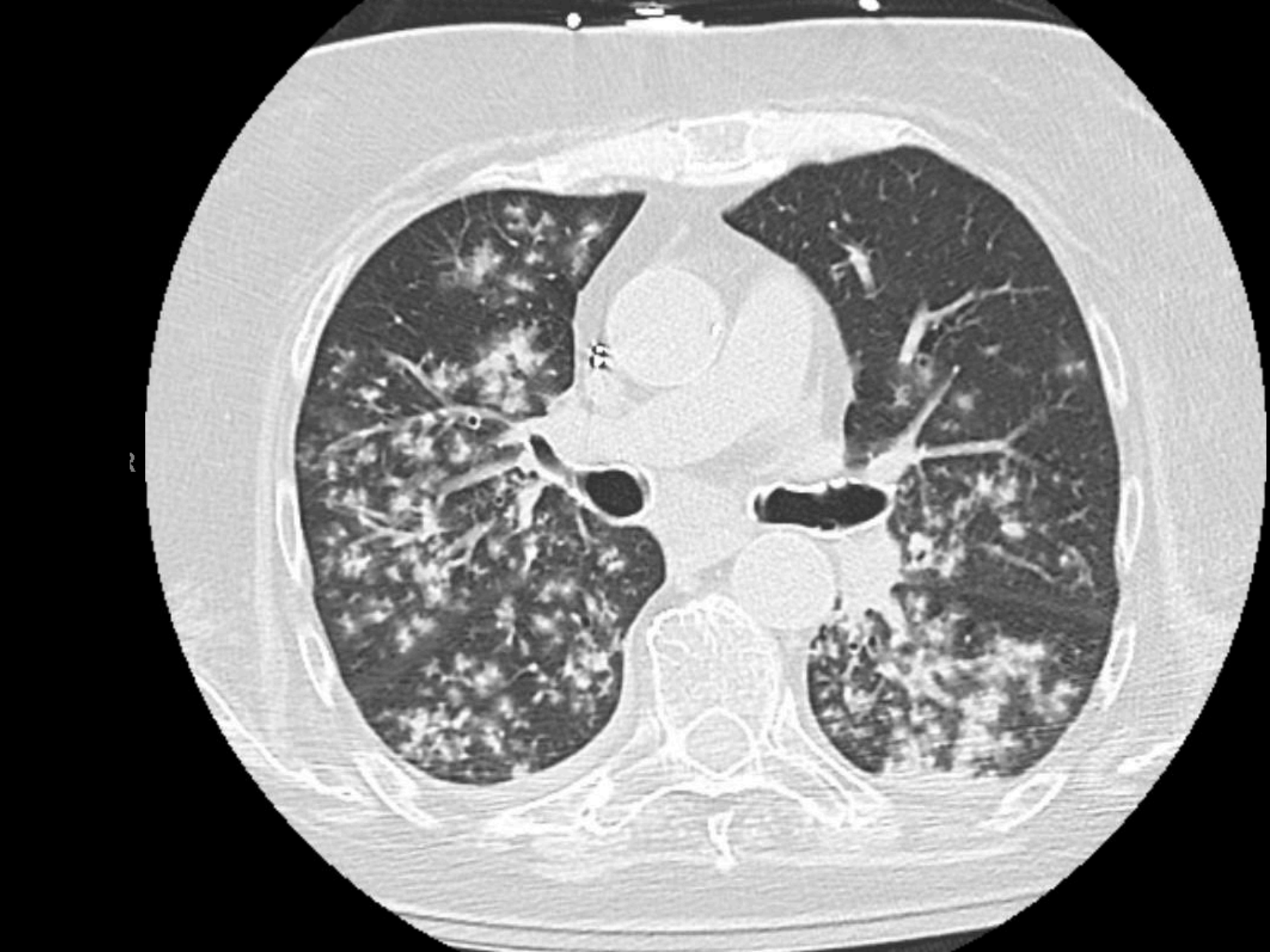


Ventilator Associated Events

CDC statement released Jan 17, 2017

Ventilator-Associated Event: after a period of stability your PEEP or FiO_2 requirement increases.

VAE subtypes

Infection-Related VAC: worsening oxygenation + (fever or leukocytosis) + addition of antibiotic.

Possible Ventilator-Associated Pneumonia: VAC +positive culture or lab certified purulent secretion

Note that radiographic findings are not discussed.

VAP Prevention

A lot of heat, not much light.

Adding “HOB 30%” and “CHX” to a lot of notes…

VAP Pathogenesis vs Proposed Preventive Strategies

Bacterial colonization of the oropharynx and/or stomach

Microaspiration

Pneumonia

Decrease Microaspiration

Reduce oral secretion

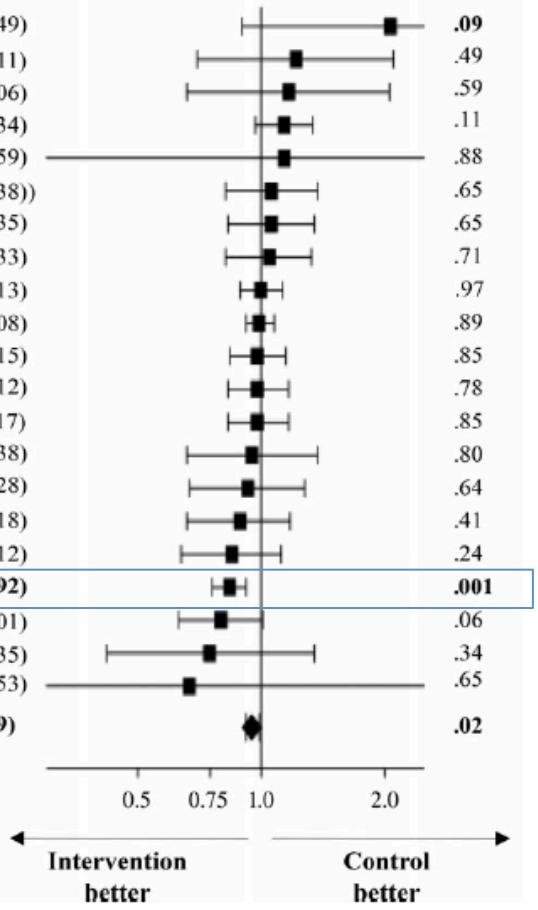
Inhibiting bacterial growth in the mouth or stomach

Studied Methods:

acidified enteral feeds, phytotherapy (ginger), selective digestive decontamination, early enteral feeds, post pyloric enteral feeds, decreased gastric contents, probiotics, ulcer prophylaxis, aerosolized antibiotics, closed suctioning systems, early tracheotomy, humdifiers, physiotherapy, PEEP, coated endotracheal tubes, saline tracheal installation, selective oral decontamination, patient positioning, sinusitis prophylaxsis, subglotic aspiration, tracheal cuff monitoring.

Hospital Mortality Rates

Intervention	No. of RCTs; No. of Patients (N); I^2, %	Relative Risk (95% CI)	*P* Value
Acidified enteral feeding	1; 120; NA	2.07 (.90–4.49)	.09
Tracheal cuff monitoring	2; 264; 0	1.22 (.70–2.11)	.49
PEEP	1; 127; NA	1.17 (.66–2.06)	.59
Silver-coated ET	1; 1509; NA	1.14 (.97–1.34)	.11
Physiotherapy	2; 204; 81	1.14 (.20–6.59)	.88
Patient position	5; 785; 0	1.06 (.82–1.38))	.65
Decreased gastric content	3; 810; 0	1.06 (.83–1.35)	.65
Tracheal saline instillation	1; 262; NA	1.05 (.82–1.33)	.71
Ulcer prophylaxis	16; 3365; 0	1.00 (.89–1.13)	.97
SOD	23; 9666; 0	0.99 (.92–1.08)	.89
Subglottic secretion drainage	9; 2241; 0	0.98 (.84–1.15)	.85
Heat moisture exchanger	13; 2431; 0	0.98 (.86–1.12)	.78
Closed suctioning system	5; 909; 0	0.98 (.83–1.17)	.85
Aerosolized antibiotic	5; 450; 23	0.95 (.66–1.38)	.80
Post pyloric feeding	6; 582; 0	0.93 (.67–1.28)	.64
Probiotic/symbiotic	13; 1569; 23	0.89 (.66–1.18)	.41
Early tracheotomy	6; 1050; 45	0.85 (.64–1.12)	.24
SDD	**30; 10 227; 16**	**0.84 (.76–0.92)**	**.001**
Sinusitis prophylaxis	1; 399; NA	0.80 (.63–1.01)	.06
Early enteral feeding	1; 150; NA	0.75 (.42–1.35)	.34
Phytotherapy	1; 36; NA	0.67 (.13–3.53)	.65
Overall	145; N=37156; 4	0.95 (.92–.99)	.02



CID 2015:60 Roquilly *et al*

What is selective digestive decontamination?

SOD: selective oral decontamination

SDD: selective digestive decontamination

Combination of PO nonabsorbable antibiotics and a short course of IV antibiotics.

For example: 4 days of IV cefotaxime with oral/ topical application of tobramycin, colistin and amphotericin B.

Ongoing Studies

25,000 subject, cluster randomized study in Canada, UK, NZ, AUS ongoing (SuDDICU).

9-nation European study, cluster randomization with crossover comparing SDD, SOD and oral chlorhexidine (RGNOSIS).