



AMERICAN COLLEGE OF SURGEONS

Inspiring Quality: Highest Standards, Better Outcomes

Severe and Tertiary Peritonitis

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**PS204: The Bad Infections: Tools to Keep Ahead of Difficult Infections
and Resistant Organisms
Tuesday October 6, 2015**

Courtesy of American College of Surgeons Division of Education
Clinical Congress 2015

68 yo female admitted to the SICU following and urgent laparotomy

- sigmoid resection and Hartmann's procedure for perforated diverticular abscess**
- partial small bowel resection with primary anastomosis due to dense scarring to the abscess**
- Intraoperatively**
 - diffuse peritonitis**
 - vasopressor support**
 - metabolic acidosis**

68 yo female admitted to the SICU following and urgent laparotomy

On admission:

- Mechanically ventilated
- Levophed
- APACHE II - 17
- Serum albumin 2gm/dL

SICU course:

- Initial improvement
- POD 4 – declining pulmonary function, delirium, persistent leukocytosis
- Bronchoscopic BAL and expanded empiric AB coverage for possible pneumonia on CXR

68 yo female admitted to the SICU following and urgent laparotomy

SICU course continued:

- POD 7 – BAL cultures < 10,000 CFU of normal respiratory flora**
- Contrasted CT scan: diffusely layering intraabdominal fluid without enhancement, no evidence of anastomotic leak**
- POD 9 – Develops a partial fascial dehiscence with drainage of purulent fluid, blood cultures + for enterococcus**
- POD 12 – enterocutaneous fistula presents**
- After a prolonged ICU course, she dies of progressive organ failure**

For this patient:

- Her course was predictable on ICU admission
- Represents failure of source control, which significantly increases risk of mortality
- Signs predicting source control failure were present early in the post operative course
- Prolonged antibiotic therapy will not successfully replace source control
- Resistant pathogens are predicted by source control failure

Disclosures:

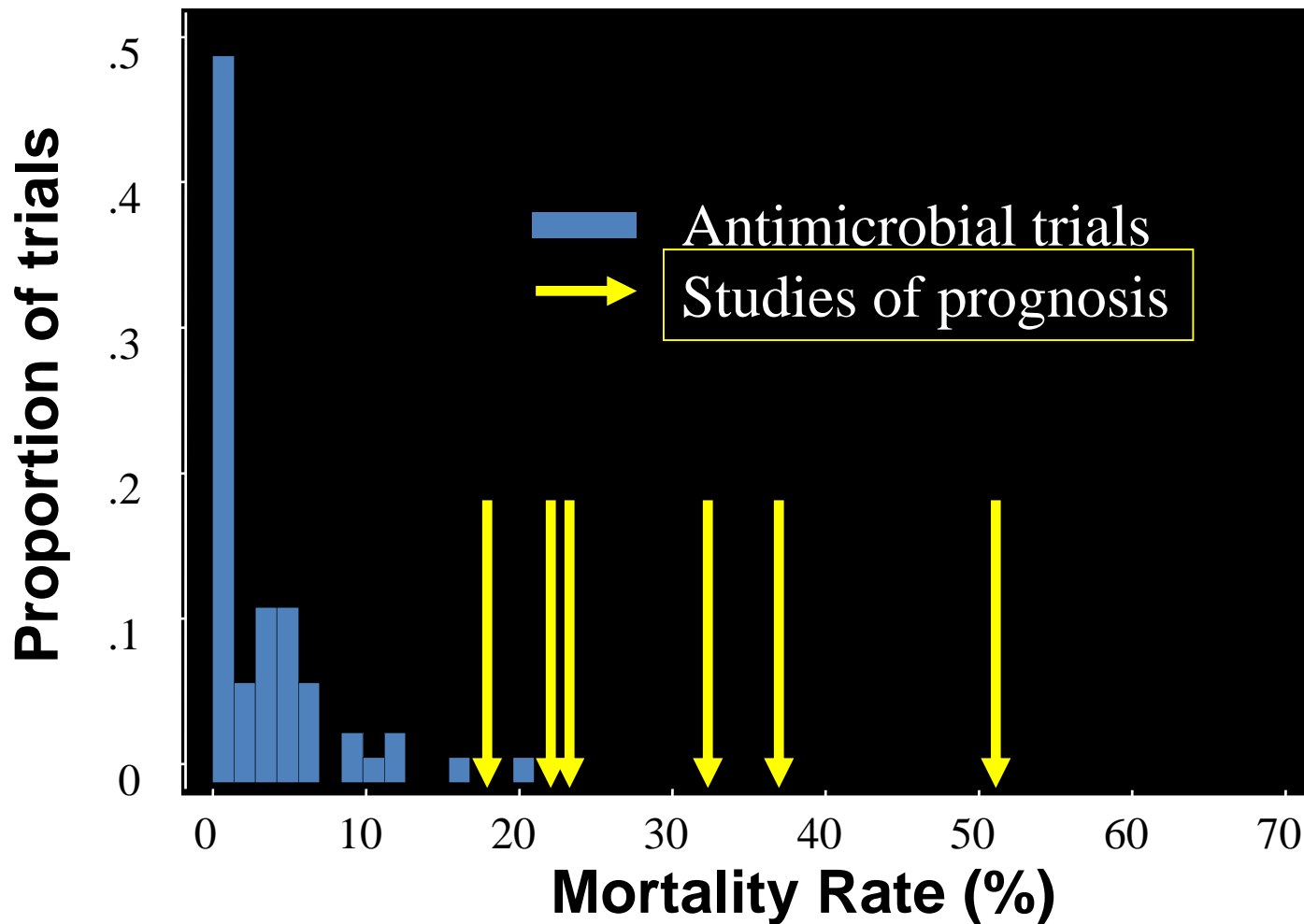
- **Receive research funding and consultant for AtoxBio**
- **Research funding from several pharmaceutical companies**
- **No significant conflicts to disclose for this presentation**

SEVERE SEPSIS: a strong predictor of mortality in peritonitis

- **5% of all patients with peritonitis**
- **Strong predictor of mortality for patients with peritonitis - RR = 19**
- **Predictors of severe sepsis include:**
 - **age greater than 60**
 - **diffuse peritonitis**
 - **pre-existing organ dysfunction**

Anaya DA and Nathens AB. *Surgical Infections*. 2003; 4:355-62

Mortality rates in antimicrobial trials 1990-2000



Components of definitive source control

1. The removal of diseased or non-viable material and control / closure of enterostomies
2. Reinstitution of hollow viscus continuity or stoma creation
3. Reduction of bacterial and toxin load

Critically ill patients are at high risk of recurrent or persistent infection and anastomotic disruption

Failure of SOURCE CONTROL

Traditionally

- Failure of source control viewed as “the surgeon’s” failure

In high risk patients

- Failure of source control is a failure of the host’s ability to eliminate pathogens and heal normally

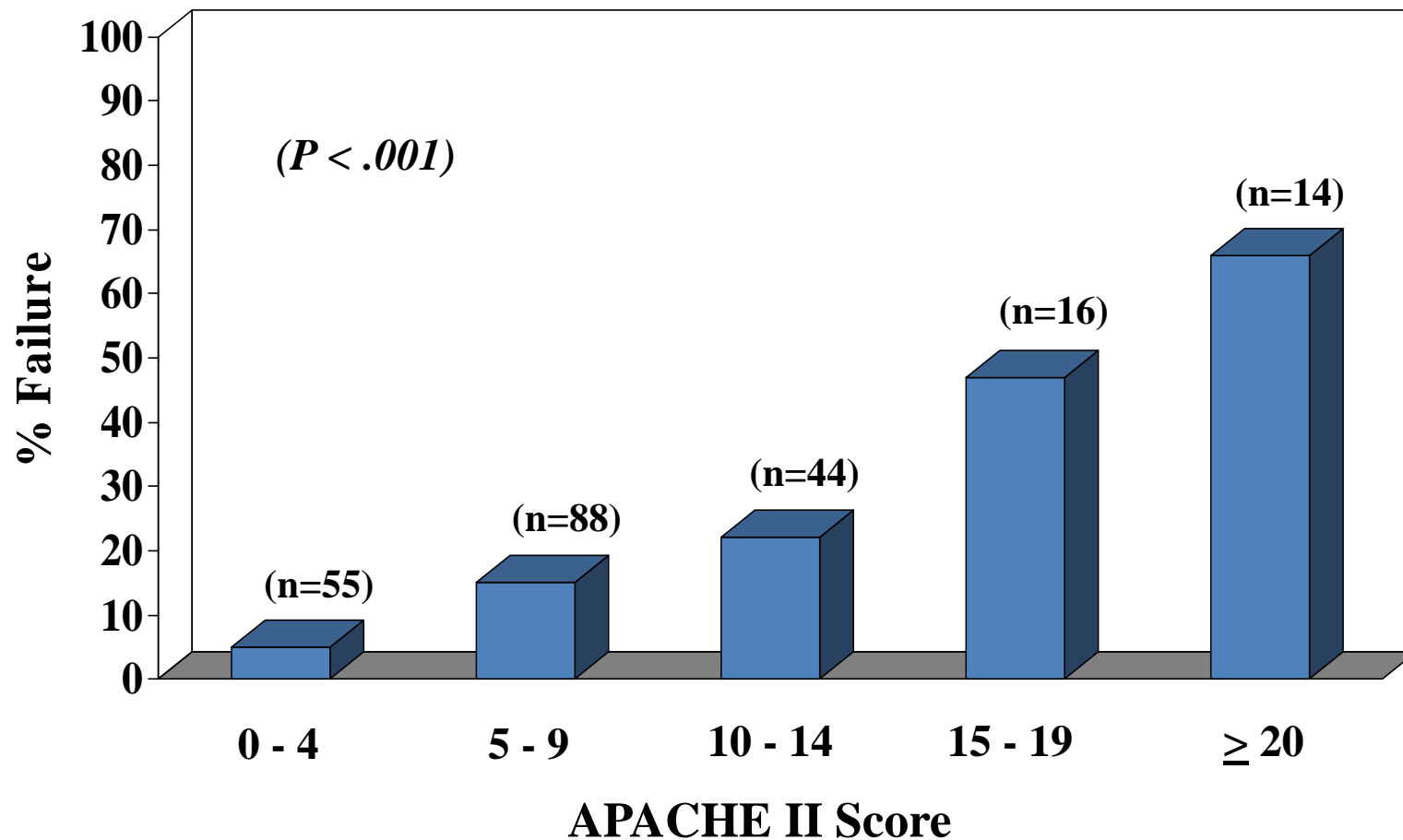
Risk can be assessed on admission

Factors independently associated with failure of source control

- **Advanced age**
- **Severe SIRS, high severity of illness (APACHE II)**
- **Degree of peritoneal involvement (MPI)**
- **Hypoalbuminemia**
- **Comorbidity**
- **BMI > 29**
- **Inability to achieve source control**
- **Time to source control**
- **Inadequate empiric antibiotic coverage**

Relation of illness severity score to failure of source control in intraabdominal infections

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68 yo female admitted to the SICU following and urgent laparotomy

On admission:

- Diffuse peritonitis
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- Metabolic acidosis
- Serum albumin 2gm/dL

Estimated risk for failure of source control - >50%

Re-laparotomy

Scheduled vs On-demand

- Randomized, non-blinded study
- 232 pts with severe secondary peritonitis
 - 7 hospitals in the Netherlands
 - 2001-2005
 - APACHE II > 11
- Excluded packing, discontinuity
- Randomized after 1st laparotomy
- On-demand laparotomy criteria
 - MODS unchanged at 48 hrs (± 2) from previous lap
 - Increase in MODS >4 at any time
 - Emergent indications

Patient characteristics:		
Median /Percent	On-demand (n=114)	Planned (n=115)
Age	65	70
APACHE II	14.5	16
Percent APACHE II > 20	14%	17%
MPI	27	29
Percent comorbid disease	56%	63%
Diffuse peritonitis	61%	62%

Re-laparotomy Scheduled vs On-demand

	On-demand (n=114)	Planned (n=115)	P value
Primary endpoint (%)	57%	65%	0.25
Mortality (%)	29%	36%	0.22
Total re-laparotomies	113	233	<0.001
% Negative re-laparotomy	31%	66%	<0.001
Ventilator days (median)	5	8	0.007
ICU LOS (median)	7	11	0.001
Hospital LOS (median)	25	35	0.008

Van Ruler O. *JAMA* 2007; 298:865-873

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Failure can be predicted by clinical course

Factors independently associated with failure of source control

- Persistent/progressive organ dysfunction
- SAPS2 or MOF/MODS scores day 2 and after
- Elevated CRP – day 2 and after
- Postoperative fever
- Postoperative low P/F ratio
- Postoperative tachycardia
- Postoperative elevated serum Na

SIS Guidelines for Duration of Antimicrobial Therapy

- **AB Rx should be limited to no more than 5 – 7 d**
 - Decision based on operative findings or upon resolution of fever or leukocytosis
- **Continued clinical evidence of infection at the end of AB Rx should prompt a search for residual/recurrent infection rather than prolonged antibiotic Rx**
- **In the absence of adequate source control, extending AB Rx is warranted**

SIS: STOP-IT Trial

- Randomized, multicenter study (23 sites)
- 518 patients with intra-abdominal infections
- Intervention – at source control, AB Rx assigned to:
 - 4 days
 - versus
 - Resolution of clinical signs (WBC, fever, ileus) + 2 days

- Results:
 - 4 days versus 8 days of therapy
 - No difference in mortality (0.8% vs 1.2%)
 - No difference in composite endpoint (23% vs 22%)
(SSI, recurrent IAI, death)

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Is there failure of source control?

Clinical change suggesting infection

- **Differential Dx:**
 1. Infection related to the surgical site
 2. Pneumonia
 3. BSI
- **Others – much lower on differential list**

cholecystitis, ischemic enteritis/colitis, C. difficile, septic thrombophlebitis, valve infection, peri-rectal abscess, urine, etc.
- **Diagnostic workup directed at differential dx list**

Source control failure and mortality

Mortality (%)

	Source control Yes	Source control No	Overall
Johnson:	0	53	17
Kopera:	4	51	14
Solomkin:	6	45	-
Seiler: (diffuse peritonitis)	13	27	14
Grunau: (post-op peritonitis)	19	100	38

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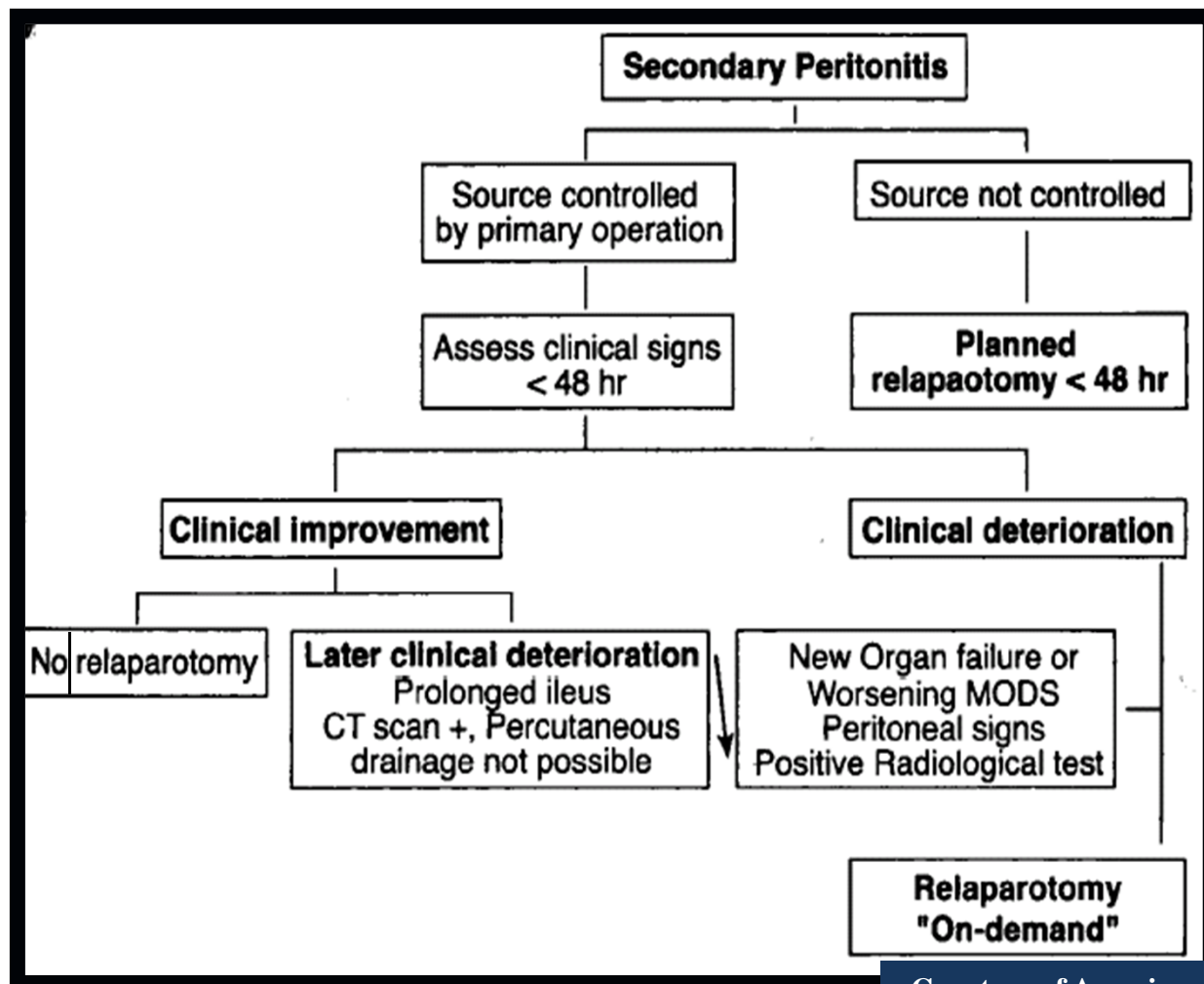
Addressing source control sooner is better

105 patients requiring re-laparotomy for failed source control

Table 3. Mortality differences after relaparotomy for persisting abdominal sepsis according to the preoperative APACHE II score.

APACHE II score	Relaparotomy ≤ 48 hr (%)	Relaparotomy > 48 hr (%)	Significance (<i>p</i>)
≤ 10	0	25	0.09
11–15	0	33	0.02
16–20	0	78	0.002
21–25	57	100	0.02
≥ 26	79	94	0.2
Overall	28	77	0.0001

Prospective surgical strategy for critically ill patients with peritonitis



- Greater severity of illness increases likelihood of lack of source control
- Early deterioration → re-laparotomy
- Late deterioration (> 7 -10 days) → CT scan

Adapted from Lipsett AP in Source Control

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Decisions regarding antibiotic therapy after failure of source control

Tertiary peritonitis:

- **intra-abdominal infection that persists or recurs 48 h initial adequate surgical source control**
- **previous antibiotic use leads to selection of resistant pathogens**
- **immuno-incompetent host enables persistence of relatively non-virulent microorganisms**

Nosocomial IAI and antimicrobial therapy

- **100 consecutive post-operative infections**
- **Shift towards resistant pathogens**
 - resistant Gm negative bacteria
 - MRSA
 - enterococcus
 - fungi
- **relative risk of failure if resistant organisms present - 1.9**
- **single & two drug combinations inadequate ~ 60% of cases**
- **inadequate therapy independent predictor of mortality
(50% vs 26%)**

The Microbiology of Intraabdominal Infection

Secondary

(Polymicrobial)

B. fragilis group

Clostridium sp.

Other anaerobes

E. coli

Klebsiella sp.

Enterobacter sp.

Enterococcus sp.

Streptococcus sp.

Staphylococcus sp.

Candida sp.

Tertiary

(Mono or Polymicrobial)

S. epidermidis

Enterococcus sp.

“SPACE” bugs

MRSA

Candida sp.

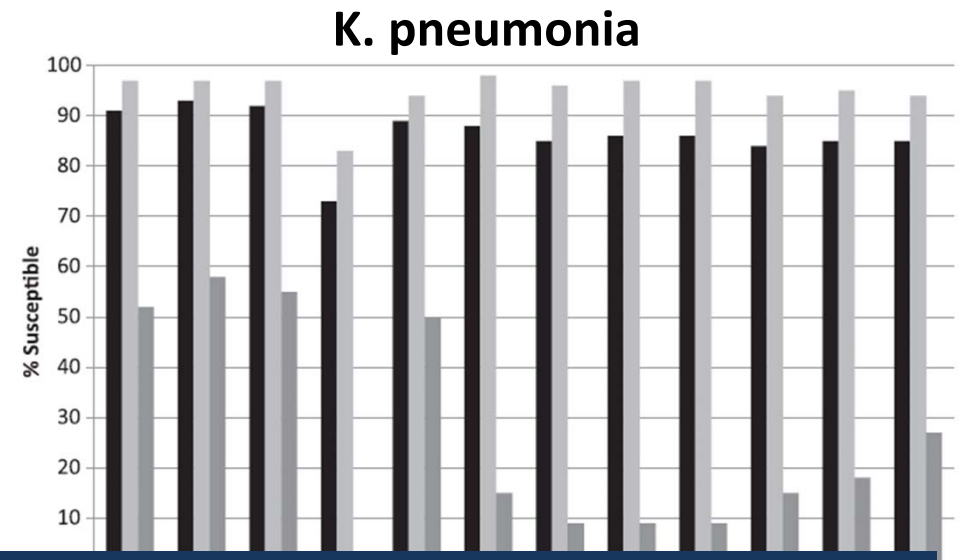
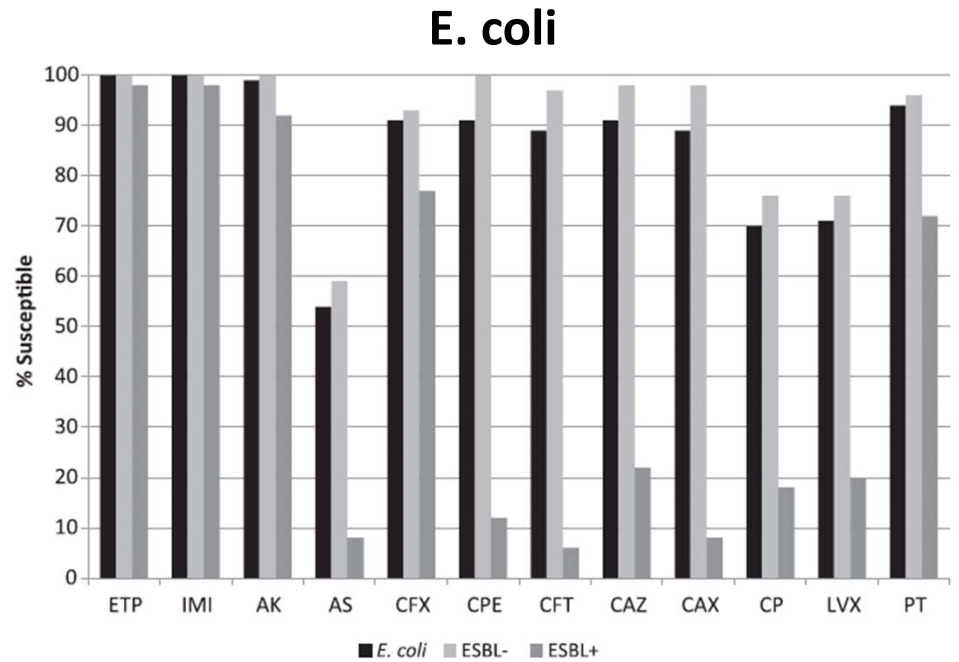
(ESBL & KPC gm- bacilli???)

SMART - 2011

- 1442 IAI gram-negative pathogens
- 19 hospitals in USA
- CA – IAI and HA – IAI pathogens
- E. coli 36% of isolates
 - 9.7% ESBL positive
- K. pneumonia 18.6 % of isolates
 - 12.7% ESBL positive

ESBL positive pathogens

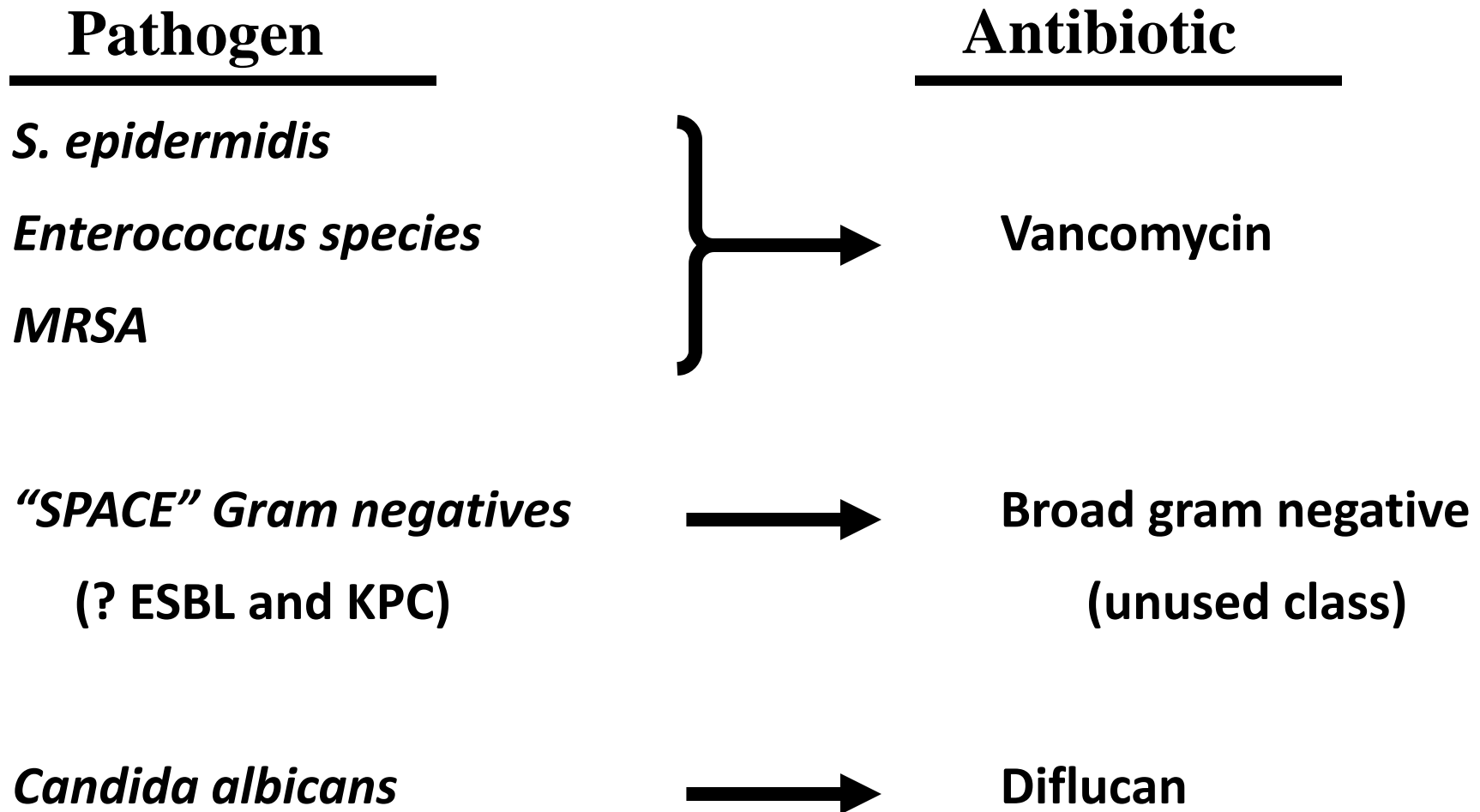
- > 6% of all isolates
- 1 in 17 patients



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Empiric coverage for nosocomial intra-abdominal infections

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Summary

- **Failure of source control in IAI is predictable**
- **Efforts should be directed towards achieving adequate control, once failure is suspected**
- **Patients with tertiary peritonitis will have resistant pathogens - require 3 (possibly 4) agents to ensure adequate empiric coverage**



100+years

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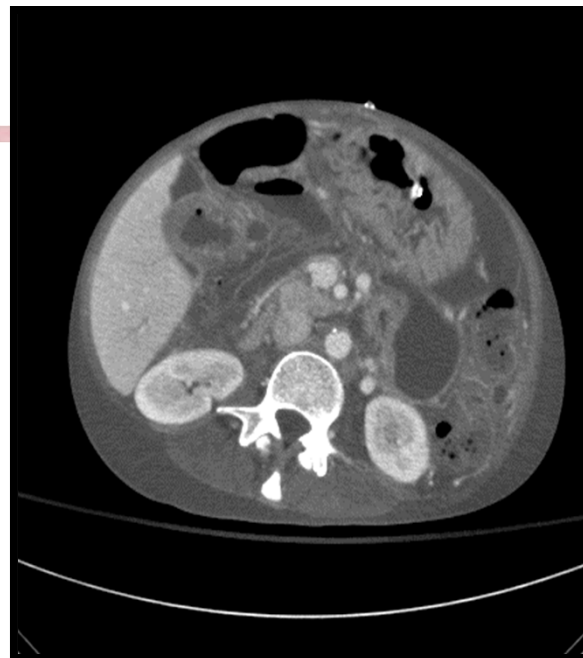
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***Thank you for your
attention***

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Approaches for Abdominal Sepsis

- 55 yo F with admitted for SBO
 - Hx of XRT & chemoRx for SCC of rectum
 - Laparotomy, LOA, and small bowel resection
- POD #6 – fever, tachycardia, hypotension
- CT of abdomen revealed:



Why isn't longer better?

1. Antibiotics cannot be effective if unable to achieve adequate levels!

2. Neutrophils cannot effectively kill bacteria unless they phagocytize or trap them

- neutrophils will continue to degranulate in attempt to do so!

