

## PROCALCITONIN: A REVIEW

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## DISCLOSURES

- I have had no financial relationship over the past 12 months with any commercial sponsor with a vested interest in this presentation

## LEARNING OBJECTIVES

- Pharmacist
  - Identify non-infectious causes of elevated procalcitonin levels
  - Identify patient populations in which evidence supports the utilization of procalcitonin levels to assist in clinical decision making
- Technician
  - Identify non-infectious causes of elevated procalcitonin levels
  - Describe advantages of de-escalation of antibiotics

## BACKGROUND

## PROCALCITONIN

- Prohormone of calcitonin
  - Elevated serum calcium levels
  - Invasion of bacteria or some fungi
- Production
  - Detectable in serum within 4 hours
  - Serum levels peak in 12-48 hours
  - Rarely occurs in response to pure viral infection

Gilbert 2010

## ELEVATED PROCALCITONIN LEVELS

- Bacterial infection
  - Pneumonia
  - Sepsis
- Other infection
  - Candidiasis
  - Aspergillosis
- Physiologic stressors
  - Cardiogenic shock
  - Severe burns
  - Pancreatitis
- Medullary thyroid cancer

Patient population	ProCT level (ng/mL)
Stable MTC	3.6
Newly diagnosed MTC	13.8
Recurrent/metastatic MTC	241.7

Algeciras-Schimmich 2009

## PROCALCITONIN AND INFECTIOUS DISEASE

- Why is procalcitonin potentially useful?
  - Assist with determination of causal pathogen
  - De-escalation of antibiotic regimens
- Antibiotic de-escalation
  - Decrease healthcare costs
  - Decreased parenteral compounding
  - Decrease development of antibiotic resistance

SHEA 2012

## GUIDELINES

- IDSA Antimicrobial Stewardship Guideline:
  - “In adults in ICUs with suspected infection, we suggest the use of serial PCT measurements as an ASP intervention to decrease antibiotic use” (weak recommendation, moderate-quality evidence)

Barlam 2016

## SAMPLE PROTOCOL

PCT <0.1 ng/mL	PCT 0.1-0.25 ng/mL	PCT 0.26-0.5 ng/mL	PCT >0.5 ng/mL
• Antibiotic therapy strongly discouraged	• Antibiotic therapy discouraged	• Antibiotic therapy recommended	• Antibiotic therapy strongly recommended

- Clinical considerations
  - Consider antibiotic therapy for high-risk patients
  - Significantly elevated PCT on presentation:
    - Decline >80% of peak: stop recommended
    - Decline >90% of peak: stop strongly recommended
  - Recommend serial PCT levels

Albrich 2012



## LOWER RESPIRATORY TRACT INFECTIONS

- ProHOSP trial (2009)

Outcome	ProCT (IQR)	Control (IQR)	Rate difference (95% CI)
Antibiotic exposure	5.7 (1-8)	8.7 (6-11)	-34.8 (-40.3 to -28.3)
Antibiotic adverse event rate	19.8%	28.1%	-8.2 (-12.7 to -3.7)
Length of stay	9.4 (4-12)	9.2 (4-12)	1.8 (-6.9 to 11.0)

Schuetz 2009

## LOWER RESPIRATORY TRACT INFECTIONS

- Cochrane Review (2017)

Outcome	ProCT	Control	Difference (95% CI)
28-day Mortality	8.6%	10.0%	OR = 0.83 (0.7 – 0.99)
Antibiotic use	8.0 days	9.4 days	-1.83 days (-2.15 to -1.5)
Antibiotic adverse effects	16.3%	22.1%	OR = 0.68 (0.57 – 0.82)

Schuetz 2017

## CRITICALLY ILL PATIENTS

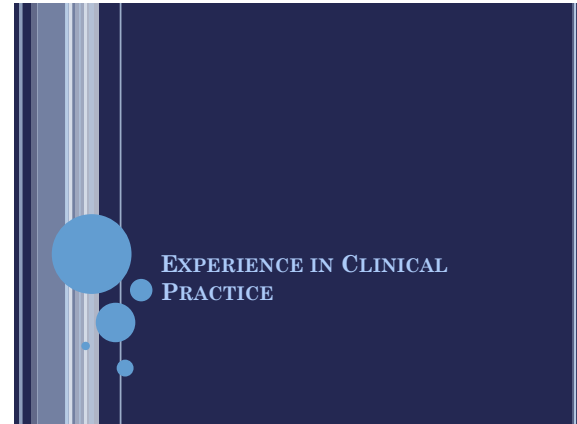
### o PRORATA trial (2010)

Outcome	ProCT group	Control group	P-value
Days without antibiotics	14.3 (SD = 9.1)	11.6 (SD = 8.2)	<0.0001
28-day mortality	21.2%	20.4%	NS
60-day mortality	30%	26.1%	NS

### o SAPS trial (2016)

Outcome	ProCT (IQR)	Control (IQR)	P-value
Antibiotic days	5 (3-9)	7 (4-11)	<0.0001
28-day mortality	20%	25%	0.012
365-day mortality	35%	41%	0.007

Bouadma 2010; De Jong 2016



## LOWER RESPIRATORY TRACT INFECTIONS

### o Albrich, et al (2012)

- Assessed clinical outcomes in the “real world” as compared to a clinical trial
- Primary endpoint:

Outcome	ProCT	Control	Absolute difference (95% CI)
Antibiotic exposure	5.9 days	7.4 days	-1.51 (-2.04 to -0.98)

- Safety endpoints
  - No significant differences found in multiple safety endpoints
  - Fewer antibiotic-associated adverse events in the ProCT group

Albrich 2012

## CRITICALLY ILL PATIENTS

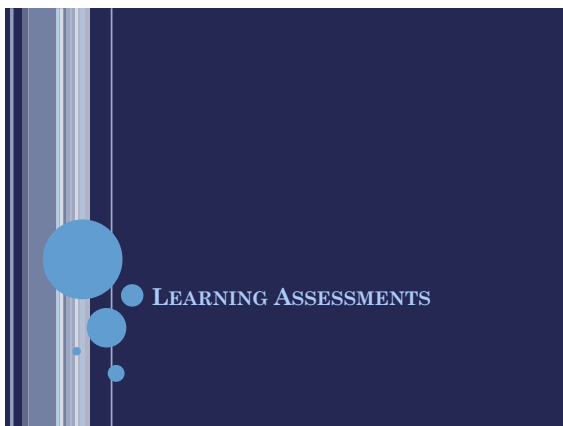
### o Chu, et al (2017)

Outcome	Risk	95% CI
Days of antibiotic therapy	aRR = 1.17	1.15 – 1.18
C. difficile infection	aOR = 1.42	1.09 – 1.85
Mortality	HR = 1.05	0.93 – 1.19

### o Discussion

- Procedures in this study were not consistent with clinical trials
- Study occurred in different countries – potential for differences in clinical practice

Chu 2017



## PHARMACIST LEARNING ASSESSMENT

- Which of the following disease states could cause an elevated serum procalcitonin level?
  - Congestive heart failure
  - Medullary thyroid cancer
  - Asthma
  - Osteoporosis
- In the literature, utilization of serum procalcitonin levels to guide therapy in septic patients has resulted in which of the following outcomes?
  - Decreased 30-day mortality
  - Decreased 90-day mortality
  - Decreased duration of antibiotic therapy
  - Increased length of hospital stay

## TECHNICIAN LEARNING ASSESSMENT

- Which of the following disease states could cause an elevated serum procalcitonin level?
  - a) Congestive heart failure
  - b) Medullary thyroid cancer
  - c) Asthma
  - d) Osteoporosis
- Which of the following benefits are gained from de-escalating antibiotic therapy?
  - a) Decreased healthcare costs
  - b) Decreased likelihood of antibiotic resistance
  - c) Decreased risk of secondary infection for patients
  - d) All of the above

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