PROCALCITONIN: FRIEND OR FOE

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DISCLOSURE

Speaker: Thermo Fisher Scientific

4/2023 - current

OBJECTIVES

- Discuss how procalcitonin is regulated
- Define the role procalcitonin plays in patient management
- Pitfalls in utilizing procalcitonin

CASE #1

- 64 yo male with PMHx COPD, HTN presents with dyspnea x 1 day, subjective fever and productive cough.
  - VS HR 100 RR 24 BP 150/84 98% RA
  - PE: Alert, tachycardic, mild expiratory wheezing, no knee mottling
  - CXR without infiltrates
  - WBC 14k BMP NL
  - CURB-65 score – 0
  - Procalcitonin – 0.1
    - 0.5
    - 5

CASE #2

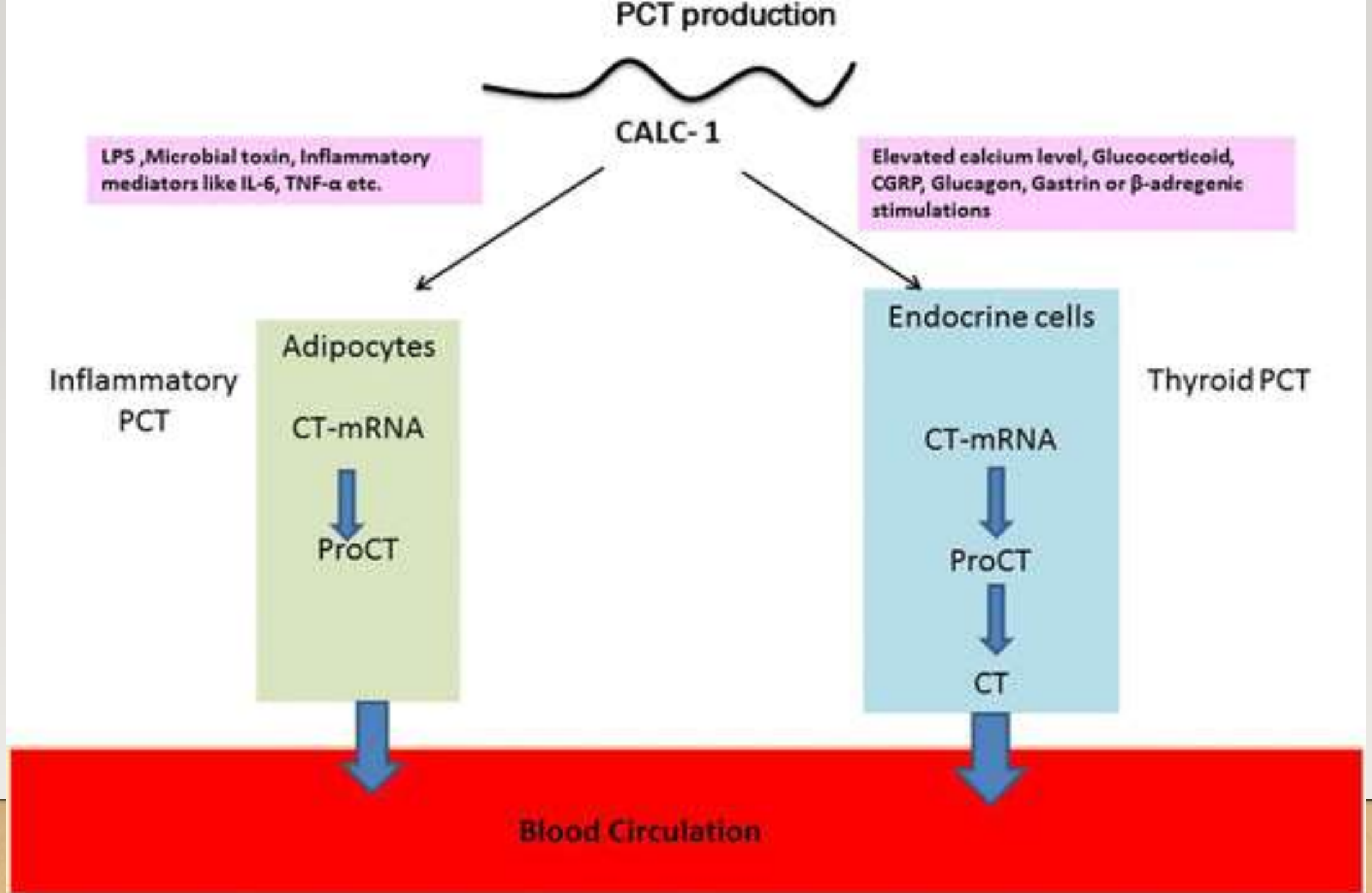
- 56 yo male with mild LLQ abdominal pain and loose stool. PMHx DM, Obesity, HTN, completed levaquine 1 month ago for sinusitis. Denies fevers or vomiting
  - VSS HR 90 RR 18 BP 140/85
  - WBC 10.2 BMP NL
  - CT Abdomen – Mild descending colonic thickening without perforation or bowel obstruction. NL appendix
  - Procalcitonin - < 0.25

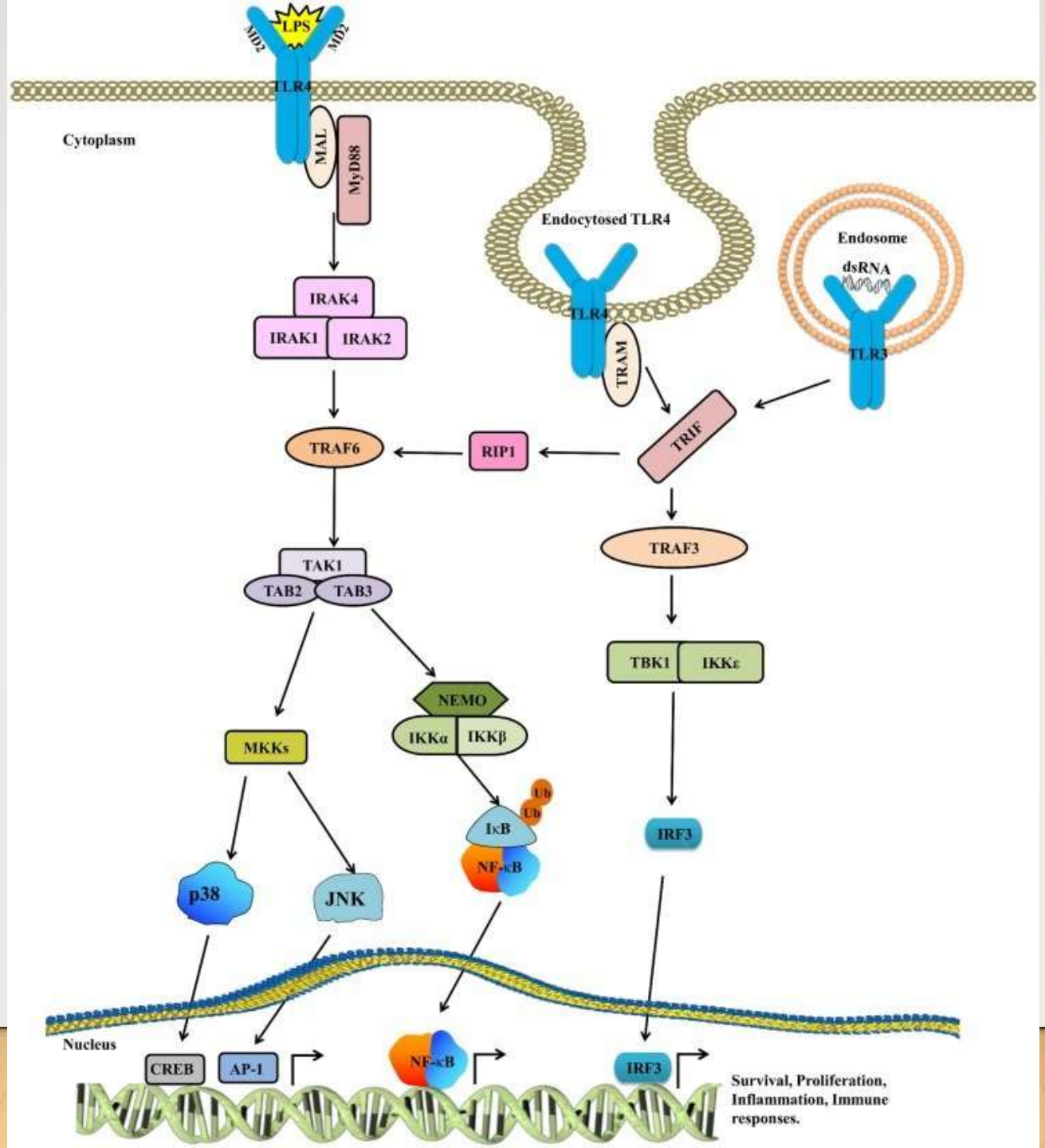
CASE #3

- 45 yo male presents with HA and neck stiffness. Dx with SAH – Hunt Hess grade 2 / Fisher grade 3. Pt is admitted for monitoring and management.
- Pt receives a clipping procedure and close monitoring.
- Postop day 1 – Fever 39 C - Procalcitonin – 20 – No localized infectious process
  - Antibiotics?
- Postop day 5 – afebrile x 24 hrs. HR 95 RR 18 BP 135/84 38.4 C
  - Procalcitonin – 0.1
  - Procalcitonin - 10
- BP 95/50 - ?

PROCALCITONIN

- 116 amino acids
- Stored in extra-thyroidal tissue
  - Lung
  - Liver
  - bowel
- Released in an all or none fashion to stimulus
- Rises in 3-6 hours
- ½ life is 24 hours
- Reduction approximately 30%/day


PCT production
CALC- 1
LPS ,Microbial toxin, Inflammatory mediators like IL-6, TNF-α etc.
Elevated calcium level, Glucocorticoid, CGRP, Glucagon, Gastrin or β-adregenic stimulations
Inflammatory PCT
Adipocytes
CT-mRNA
ProCT
Endocrine cells
CT-mRNA
ProCT
CT
Thyroid PCT
Blood Circulation


LPS
MD2
MD2
TLR4
Cytoplasm
MAL
MyD88
IRAK4
IRAK1
IRAK2
TRAF6
RIP1
TAK1
TAB2
TAB3
MKKs
p38
JNK
NEMO
IKKα
IKKβ
IκB
Ub
Ub
NF-κB
Endocytosed TLR4
TLR4
TRAM
Endosome
dsRNA
TLR3
TRIF
TRAF3
TBK1
IKKε
IRF3
Nucleus
CREB
AP-1
NF-κB
IRF3
Survival, Proliferation,
Inflammation, Immune
responses.

PROCALCITONIN

- Stimulus is bacterial and trauma predominantly
  - Elevation with H1N1 and H7N9
  - Minimal elevation with atypical bacteria
- Baseline levels are < 0.25
- Linear elevation with level of stimulus
  - Level correlates with outcome
  - Failure to decline correlates with higher mortality
- Trauma and surgery will elevate procalcitonin
  - Return to baseline 48-72 hours
- Appears to rise with age, CKD, and cirrhosis

PROCALCITONIN

- What is the role of procalcitonin with fungemia?
  - It does show a small rise in candidemia
    - Usually < 5.5
  - Negative predictive value
    - 100% negative predictive value if > 5.5
    - 65% positive predictive value if < 5.5

History of procalcitonin

- Discovered in 1981
- Evaluated in LRTI/COPD/CAP
- Most recently expanding into early sepsis recognition
- Studies have looked at:
  - Initiation of antibiotics
  - Continuation of antibiotics
  - The need for adding antifungal treatment

Acute phase reactants

- CRP vs ESR vs IL-6 vs Procalcitonin
- CRP
  - Elevated in NON-infectious disease e.a. ITP
  - Obesity, smoking, DM, HTN, depression
- ESR
  - Can be influenced by immunoglobulins, neoplasms, ischemia, trauma
  - ESRD, Anemia, SLE
  - Effected by age and gender
- IL-6
  - Not commercially available
- Procalcitonin
  - Sn 77% Sp 79%

Role for Procalcitonin

- Early diagnosis of systemic bacterial infections
- Effective monitoring of sepsis patients
- Safe antibiotic therapy guidance
  - 3d vs 5d vs 8d vs 10d

Lower respiratory tract infection

- **Procalcitonin-Guided Antibiotic Use vs a Standard Approach for Acute Respiratory Tract Infections in Primary Care**
  - **53 primary care physicians**
  - **458 patients – required antibiotics**
  - **Procalcitonin (< 0.25 vs > 0.25) vs Standard approach**
  - **Follow-up at day 7, 14, 28**
- **Results**
  - **Prescription use decreased 72%**
  - **No difference in morbidity or mortality**

Arch Intern Med. 2008;168(18):2000-2007

COPD EXACERBATION

- 208 consecutive patients admitted for COPD exacerbation
- Procalcitonin guided vs standard antibiotic use
- Results
  - Antibiotic use 40% vs 72%
  - Antibiotic exposure 43% vs 73%
  - No difference in morbidity or mortality during hospitalization and at 6 months
  - Number needed to treat – 3

Chest, Volume 131, Issue 1, January 2007, Pages 1-2

ICU – ANTIBIOTIC USE

- Multicentre, prospective, parallel-group, open-label trial
- Non-surgical ICU with anticipated stay > 3 days
- 307 procalcitonin guided vs 314 standard treatment
- Results
  - mortality at 28 and 60 days
    - Procalcitonin guided was non-inferior
  - Antibiotic exposure
    - 11.6 days vs 14.3 days

Lancet 2010;375:463-74

Guidelines for initiating antibiotics according to PCT value.
Except any situation requiring immediate therapy ...

PCT ...

< 0.25 ng/mL	0.25 - 0.5 ng/mL	0.5 ng/mL < 1ng/mL	>= 1 ng/mL
Antibiotics strongly discouraged	Antibiotics discouraged	Antibiotics encouraged	Antibiotics strongly encouraged

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Guidelines for stopping, continuing or changing antibiotics according to daily measured PCT value.

PCT ...

< 0.25 ng/mL	Decline more than 80% or 80% of peak (maximum) value or ≥ 0.25 to <0.5 ng/mL	Decline of PCT less than 80% of peak value and PCT ≥ 0.5 ng/mL	Increase of PCT above previous and PCT ≥ 0.5 ng/mL
Stopping antibiotics strongly discouraged	Stopping antibiotics encouraged	Continuing antibiotics encouraged	Changing antibiotics strongly encouraged

Lancet 2010;375:463-74

PROGNOSTICATION

- Serial PCT measurement
  - prospective, multi-centre observational clinical trial, the 28-day all-cause mortality was two-fold higher when PCT did not show a decrease of more than 80% from baseline to day 4 (20% vs 10%).
- PCT decrease
- 28-day all-cause mortality:
  - 10% if PCT decrease >80% - Low-risk
  - 20% if PCT decrease ≤80% - High-risk

ANTIBIOTIC GUIDANCE

- LRTI - START
  - PCT cut-off > 0.25 mcg/L
- STOP
  - Change in PCT > 80% reduction
  - PCT cut-off < 0.25 mcg/L

- Sepsis - START
  - PCT cut-off > 0.5 mcg/L
- STOP
  - Change in PCT > 80% reduction
  - PCT cut-off < 0.5 mcg/L

Jury says?

- Meta-analysis
- 14 randomized controlled trials
- 4221 patients
- PCT-guided management
  - Non-inferior

Evid Based Child Health 2013;8:1297-371

ANTIBIOTIC GUIDANCE

- Reduction of initial antibiotic prescription rates
  - 70% vs 86%
- Antibiotic treatment duration
  - 2 days less with no adverse outcome

Jury says?

- Retrospective data analysis
- 1312 ICU patients
- Arbitrary use of PCT-algorithm
- Result
  - Substantial reduction in treatment costs (DRG system)

Eur J Med Res 2011;16:543-8

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QUESTION

- 1) The following is a true statement about procalcitonin.
  a) Procalcitonin rises in 1-2 hours from the time of a stimulus.
  b) Procalcitonin has a half-life of three days.
  c) Procalcitonin is inversely proportional to the level of stimulus.
  d) Procalcitonin levels have a prognostic implication when used with community acquired pneumonia.

QUESTION

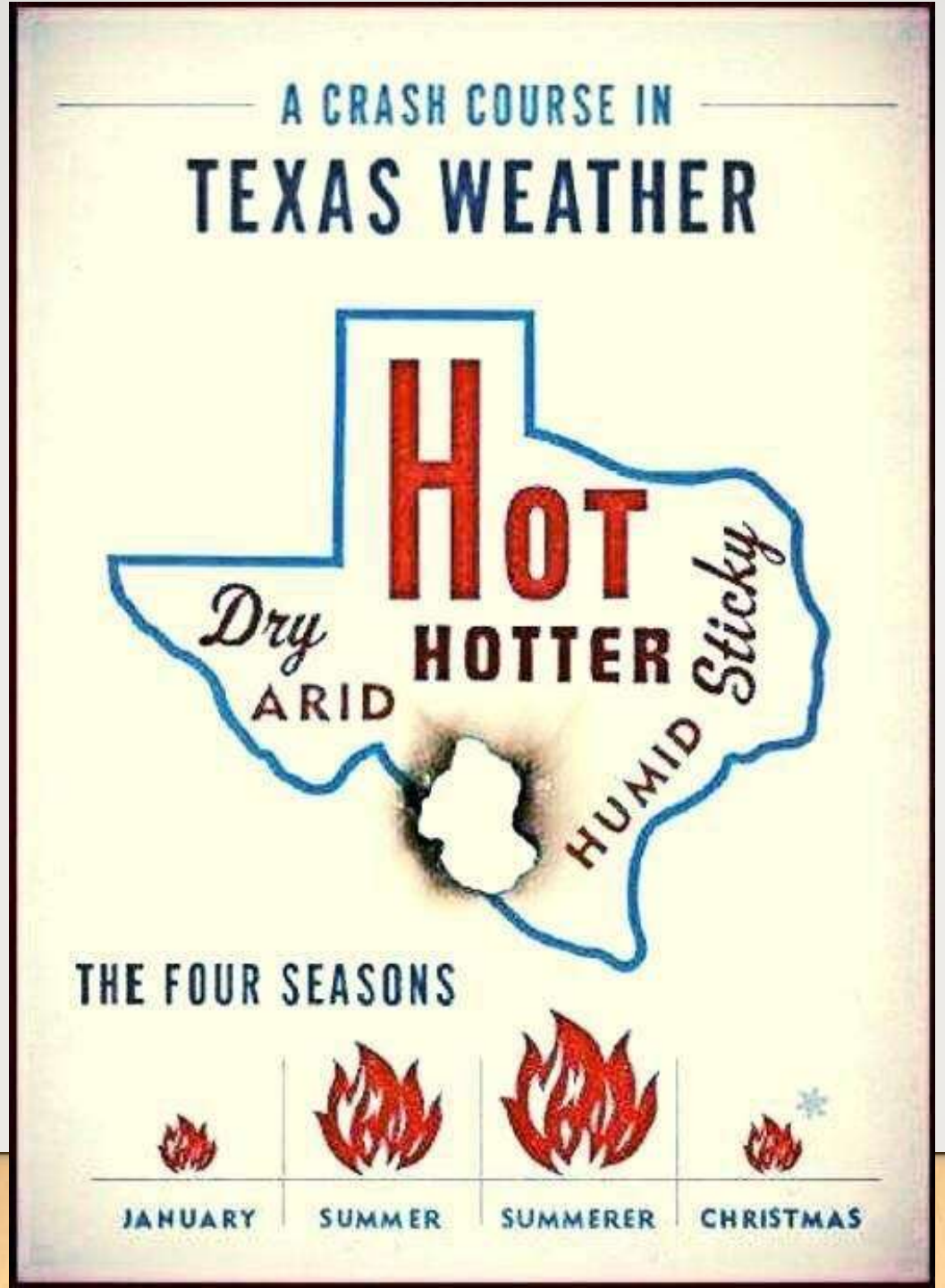
2) Antibiotics can be safely stopped in sepsis when the following is met:

A) When procalcitonin has declined to less than 50% of its highest level.

B) When procalcitonin has declined to less than 40% of its highest level.

C) When procalcitonin has declined to less than 30% of its highest level.

D) When procalcitonin is below 0.5 mcg/L


A CRASH COURSE IN
TEXAS WEATHER
HOT
Dry
ARID
HOTTER
HUMID
Sticky
THE FOUR SEASONS
JANUARY
SUMMER
SUMMERER
CHRISTMAS