

# USE OF PROCALCITONIN TO SUPPORT ANTIMICROBIAL STEWARDSHIP

A Selection of Clinical Cases



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## PREFACE

Overuse of antimicrobials, and largely antibiotics, has been recognized as a main driver for the increase in multi-drug resistant pathogens posing a dramatic threat to global health. Therefore, **reducing antibiotic overuse by improving antimicrobial stewardship** efforts is of high global interest. As clinical signs and symptoms of infection and sepsis may be ambiguous, the identification of **objective diagnostic and prognostic parameters** are needed to improve the decision to start antimicrobial therapy if necessary, and to define the optimal duration. This is particularly true because current treatment duration is mostly based on fixed antibiotic regimens recommended by practice guidelines. Individualizing antibiotic therapy therefore has great potential to improve antimicrobial stewardship and thereby reduce the overall treatment exposure.

In this regard, **procalcitonin (PCT), a serum biomarker** produced in response to bacterial infection, has been found to be most helpful. PCT is upregulated in epithelial cells upon contact with bacterial pathogens within six to twelve hours. Viral infection on the other hand leads to downregulation of its expression, which gives **PCT a diagnostic advantage over other inflammatory markers**. Once the infection is controlled by the host's immune system or by antibiotic therapy, PCT levels halve daily. Thus, PCT helps to discriminate between bacterial and viral infections, thereby helping to define whether antibiotics should be started in patients with unclear clinical pictures, and also provides prognostic information as a marker mirroring the severity of infection and treatment response over time. By tracking the resolution of infection, PCT also allows antibiotic treatment to be discontinued earlier.

Importantly, with the current **COVID-19 pandemic**, respiratory tract infections have again become a main center of attention. While the reduction of antibiotic overuse has been a main goal for PCT-guided antimicrobial stewardship, missing a bacterial sepsis in a patient with suspicion of COVID-19 is also a frequent problem with negative influence on patient outcome. In this case, the **high positive predictive value** of an **increased PCT level in a patient with COVID-19 infection** may help to draw the attention of the treating team to a bacterial infection, thereby improving adequate initial antibiotic management.

It is important to understand the kinetics and also the strengths and limitations of PCT for its safe and effective use in clinical practice. In this context, in addition to reading results of robust research trials, the **discussion of individual patient cases is extremely helpful** to understand the role of PCT in different clinical situations. Within this booklet, we have gathered such **illustrative cases from world-renowned experts** in the field to help readers better understand how PCT may be used most effectively. Cases are also related to specific clinical studies and thereby help make the transition from the theory of clinical studies to the practical aspects of patient management.

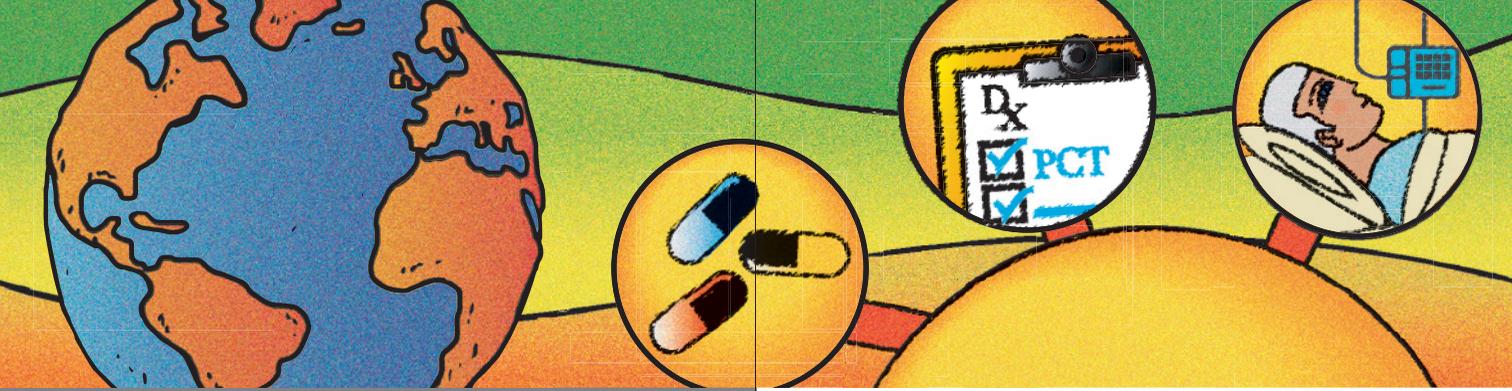
I would like to express my gratitude to all participating experts for sharing their insights with us in order to **further advance the optimal use of PCT for patient care**.



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### DISCLAIMER

This document provides experts' experience and actual case studies regarding the practical use of Procalcitonin (PCT) measurement and interpretation of results to support antimicrobial stewardship. The views presented in this educational resource are the authors' personal opinions and do not necessarily represent the viewpoint, strategy or opinions of bioMérieux.

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# PCT CLINICAL CASES

## SEPSIS



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## EARLY PCT-GUIDED ANTIBIOTIC DISCONTINUATION PROTECTS FROM LONG-TERM INFECTION SEQUELAE



**89-year-old female**

- Past history of chronic heart failure

**On ED admission**



- Patient experienced pain on palpation of the right costovertebral angle
- qSOFA score of 2 (mental confusion and 30 breaths/minute), BP: 128/54 mmHg, T: 37.8°C, pO<sub>2</sub>/FiO<sub>2</sub>: 292mmHg, lactate: 2.6 mmol/L
- **In the ward,** Glasgow Coma Scale: 12, SOFA score: 4, CRP: 41.8 mg/dL, **PCT: 42.3 ng/mL**, total WBC count: 10.57x10<sup>9</sup>/L, pO<sub>2</sub>/FiO<sub>2</sub>: 292 mmHg

➔ **Treatment started with intravenous ciprofloxacin**

**After 24 hours**



- Patient was afebrile
- Results of urine and blood culture revealed *Escherichia coli* with resistance to piperacillin-tazobactam

**After 5 days**



- Patient remained afebrile and hemodynamically stable
- No side effects from the use of antibiotics were observed
- **PCT had decreased to 7.5 ng/mL (Figure 1)**

➔ **Decision to stop antibiotics was taken based on the PCT discontinuation rule: decrease of PCT more than 80% from baseline**

**Patient outcome**



**On day 6, patient remained afebrile without symptoms and was discharged.**

**After one month:**

- follow-up urine culture was sterile,
- surveillance stool culture to monitor for colonization by resistant *E. coli* was negative.

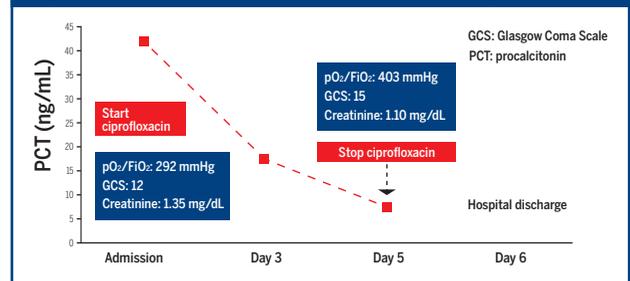
**After six months, patient showed no long-term sequelae from the infection.**



## CONCLUSIONS

- Decrease of long-term infection sequelae for 6 months, namely infections by multidrug-resistant microorganisms (MDROs) and *Clostridioides difficile*, achieved through reduction of the odds for colonization by MDRO and *C. difficile* under the pressure of broad-spectrum antibiotics.
- Decrease of 28-day mortality associated with decrease of antibiotic-associated adverse events (diarrhea and acute renal injury).
- Decrease in the cost of hospital stay.

**Figure 1. Evolution of PCT levels from admission to day 5**



### Supportive literature

- Kyriazopoulou E, Liaskou-Antoniou L, Adamis G, et al. Procalcitonin to reduce long-term infection-associated adverse events in sepsis: a randomized trial. *Am J Respir Crit Care Med.* 2021;203(2):202-210



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# PCT TO SUPPORT CLINICAL DECISION TO DISCONTINUE ANTIBIOTIC THERAPY



## 64-year-old female

- Transferred to ICU for acute myocardial infarction, urogenic sepsis, septic shock
- Then transferred to Cardiovascular Medicine with diagnosis of urinary tract infection, multiple kidney stones and acute myocardial infarction

### At ICU admission



- Temperature: 36.8°C, unconsciousness, speech disorder
- **PCT: >200 ng/mL**, CRP: 332.27 mg/dL, WBC: 37.38x10<sup>9</sup>/L
- Lymphocytes: 3.3%

➔ **Antibiotics started: imipenem/cilastatin sodium**

### On day 3



- Temperature: 37.3°C, listless
- **PCT: 138.1 ng/mL**, CRP: 124.28 mg/dL, WBC: 14.19x10<sup>9</sup>/L
- Lymphocytes: 6.2%

### On day 4



- Temperature: 37.8°C, listless
- **PCT: 72.82 ng/mL**, CRP: N/A, WBC: 10.07x10<sup>9</sup>/L
- Lymphocytes: 11.0%

### On day 5



- Temperature: 37.2°C, listless
- **PCT: 34.73 ng/mL**, CRP: N/A, WBC: 10.70x10<sup>9</sup>/L
- Lymphocytes: 14.0%
- Blood culture: *E. coli*, AST: piperacillin-tazobactam S (MIC: 4)
- Transfer from ICU to Cardiology Department

➔ **Antibiotics de-escalated: piperacillin-tazobactam**

### On day 13



- Temperature: 36.6°C, conscious
- **PCT: 0.97 ng/mL**, CRP: 8.24 mg/dL, WBC: 9.13x10<sup>9</sup>/L
- Lymphocytes: 15.1%

### On day 19



- Temperature: 36.8°C, conscious and stable vital signs
- **PCT: 1.45 ng/mL**, CRP: N/A, WBC: N/A
- Lymphocytes: N/A
- **PCT dropped by >80%** compared with peak level
- No rebound of WBC in urine, no fever

➔ **Antibiotics safely discontinued**

## Patient outcome



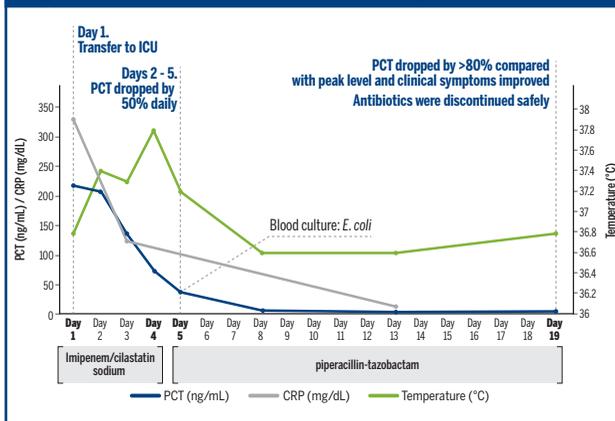
**Patient was discharged and not rehospitalized for infection within 3 months after discharge.**



## CONCLUSIONS

- PCT level was initially higher than 200 ng/mL, indicating severe infection, and allowing clinician to start immediate monitoring.
- Daily PCT dynamic monitoring in ICU decreased by about 50% every day, indicating empirical antibiotic treatment was effective.
- Blood culture results of Gram-negative bacilli were in line with the characteristics of high PCT value. Antibiotics were adjusted according to AST results.
- On Day 19, the PCT level decreased by >80% compared with the peak value, which, combined with the patient's infection index (no rebound of urine white blood cells, no fever) enabled the patient to be discharged safely.

Figure 1. Blood levels of PCT and CRP, and temperature



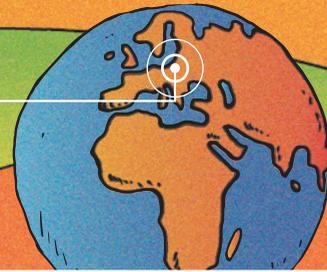
### Supportive literature

- Lee CC, et al. Procalcitonin (PCT)-guided antibiotic stewardship in Asia-Pacific countries: Adaptation based on an expert consensus meeting. *Clin Chem Lab Med.* 2020;58(12):1983-91



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# USING PCT KINETICS TO GUIDE ANTIBIOTIC THERAPY IN THE CRITICALLY ILL



## 46-year-old female

- Admitted to ED with respiratory complaints

### On ED admission



- Looked poorly in general
- SpO<sub>2</sub>: 85% on O<sub>2</sub> face mask (flow: 10L/min)
- Trouble breathing with tachypnea (respiratory rate: 35/min)
- Hemodynamically stable
- Transferred to ICU
- Poor tolerance of non-invasive ventilation. Therefore, decision to perform endotracheal intubation and invasive ventilation after left radial artery catheter insertion.
- First measurements at T<sub>0</sub> are summarized in **Table 1**, page 14

### At ICU admission



- Patient was hemodynamically stabilized with fluid resuscitation only (no need for vasopressors)
  - **PCT level low**
  - Cultures sent for microbiology (due to elevated temperature and acute respiratory failure)
- ➔ **Decision made not to start antibiotics, as no strong evidence of bacterial sepsis and patient not in life-threatening situation**

### On days 1-2



- Patient remained stable and improved slowly over the course of 2 days (**Table 1**: T<sub>24, 48</sub>)
- Microbiology sent at T<sub>0</sub> came back negative on day 2

### On day 3



- **PCT increased almost 3-fold** (Figure 1, T<sub>72</sub>)
  - Vasopressor (noradrenaline, NA) was needed
  - Pulmonary function did not improve from day 2
  - 2<sup>nd</sup> set of cultures sent to the laboratory
- ➔ **Empirical antibiotics started for nosocomial pneumonia (piperacillin-tazobactam + ciprofloxacin)**

### From day 3 to day 5



- 12 hours after starting empirical antibiotics, **PCT increase slowed down** (T<sub>84</sub>)
- 24 hours later, **PCT was decreasing** (Figure 1, T<sub>96</sub>)

### On day 5



- Microbiology revealed *Klebsiella pneumoniae*, susceptible for both empirical antibiotics
- ➔ **De-escalation to ciprofloxacin only was decided, as patient improved from all aspects**
- NA need reduced
  - Gas exchange improved
  - **PCT continued to decrease**

### From day 6 to day 9



- Patient showed continuous improvement
  - NA was stopped (day 6)
  - Patient was extubated (day 9)
  - **PCT showed continuous decrease with kinetics of ~50% per day** (Figure 1)
- ➔ **Antibiotics were stopped on day 8 (i.e. 5 days in total), as PCT decreased by >80% compared to peak value at T<sub>84</sub> and patient's clinical condition remained stable**

### Patient outcome



**On day 9, patient was discharged to high dependency ward, then to a medical ward and later discharged home from hospital on day 14.**

## USING PCT KINETICS TO GUIDE ANTIBIOTIC THERAPY IN THE CRITICALLY ILL

### CONCLUSIONS

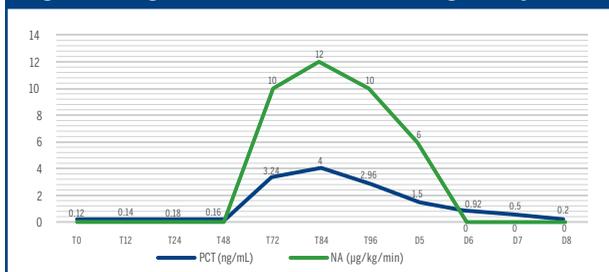
- Putting low PCT values in the context of the clinical picture helps to withhold antibiotics in case of low probability for a bacterial infection in patients who are hemodynamically stable.<sup>1,2</sup>
- Sudden increase of PCT should be a warning signal (red flag) for new onset infection.<sup>3</sup>
- If PCT increase is accompanied with new onset or increasing vasopressor need, starting empirical antibiotics early (within 1 hour) should be considered.<sup>3,4</sup>
- In cases of new onset infections in the ICU, absolute values and/or changes of conventional indicators of infection such as temperature, WBC, and CRP can be false negative.<sup>3</sup>
- Assessment of PCT kinetics after the start of empirical antibiotics (i.e. at 0-12-24 hours) may help to identify antibiotic appropriateness/inappropriateness before microbiology results are available.<sup>5</sup>
- Evaluating daily PCT changes could help to reduce antibiotic exposure, which may have a positive effect on outcomes and costs.<sup>6</sup>

Table 1. Change of condition within first 48 hours

|                             | T <sub>0</sub> | T <sub>24</sub> | T <sub>48</sub> |
|-----------------------------|----------------|-----------------|-----------------|
| <b>Hemodynamics</b>         |                |                 |                 |
| Heart rate (/min)           | 110            | 105             | 95              |
| MAP (mmHg)                  | 66             | 70              | 68              |
| ScvO <sub>2</sub> (%)       | 67             | 71              | 68              |
| Noradrenaline (µg/kg/min)   | -              | -               | -               |
| <b>Respiratory function</b> |                |                 |                 |
| FiO <sub>2</sub>            | 0.8            | 0.7             | 0.6             |
| PEEP (cmH <sub>2</sub> O)   | 10             | 10              | 10              |
| PaO <sub>2</sub> (mmHg)     | 86             | 73              | 78              |
| <b>Inflammation</b>         |                |                 |                 |
| Temp (°C)                   | 38,6           | 37,9            | 37,8            |
| WBC (10 <sup>9</sup> /L)    | 8,6            | 8,8             | 7,8             |
| CRP (mg/dL)                 | 67             | 86              | 153             |
| PCT (ng/mL)                 | 0,12           | 0,18            | 0,16            |

ScvO<sub>2</sub>: central venous oxygen saturation; FiO<sub>2</sub>: fraction of inspired oxygen; PEEP: positive end expiratory pressure; PaO<sub>2</sub>: partial pressure of arterial oxygen; Temp: temperature; WBC: white blood cell; CRP: C-reactive protein; PCT: procalcitonin

Figure 1. Changes in PCT and noradrenaline during the stay in ICU



#### Supportive literature

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# USING PCT TO DIFFERENTIATE VIRAL FROM BACTERIAL INFECTION IN COVID-19 PATIENTS



### 24-year-old male, healthy

- Hospitalized with increasing shortness of breath, dry cough, chest discomfort and diarrhea for 5-6 days
- Presenting with low grade fever increasing to 38.8°C in ER
- Initial oxygen saturation: 85% on room air
- Chest X-ray showed bilateral inflammatory infiltrates and ground glass changes (Figure 1)
- Arterial blood gas showed severe hypoxemia
- pH: 7.42, PaCO<sub>2</sub>: 40.5, PaO<sub>2</sub>: 46.7 on 5 liters of oxygen

### On ICU admission



- Initial inflammatory biomarkers were elevated: CRP: 10 mg/dL, Ferritin: 1554 ng/mL, Il-6: 69 pg/mL
- **PCT was not elevated on admission (0.11 ng/mL), suggesting absence of bacterial infection**
- Urinary antigens for *Streptococcus pneumoniae* and *Legionella pneumoniae* were negative
- Viral PCR was negative for influenza A, B and RSV
- COVID-19 nasal PCR was positive
- Patient was hospitalized due to the severity of illness
- ➔ **Antibiotics started for CAP: cefuroxime, azithromycin and dexamethasone followed by remdesivir for COVID-19 pneumonia**

### After 24 hours



- Patient's oxygen requirements went up
- Transferred to ICU for BiPAP, then very quickly needed intubation for progressive hypoxic respiratory failure
- **PCT remained low: <0.05 ng/mL (Figure 2)**
- ➔ **Antibiotics were discontinued at 48 hours**

### Over next days



- Patient's condition continued to worsen, despite aggressive recruitment maneuvers, including bi-level ventilation and prone ventilation
- PaO<sub>2</sub>/FiO<sub>2</sub> remained <100
- Decision made to insert canulae for veno-venous ECMO (Figure 3)

### Patient outcome



Despite EMCO support, patient continued to have dense bilateral infiltrates and stiff lungs. The outcome was complicated by a MRSA pneumonia with bacteremia and a pneumothorax on right side (Figure 4). While still on ECMO, the patient sustained a cardiac arrest and died 97 days after admission.



## CONCLUSIONS

- Historically, patients with infiltrates were treated with antibiotics as the assumption was that it was almost always a bacterial infection.
- The COVID-19 pandemic has proven that viral infections can produce equally exuberant infiltrates as bacterial infections.
- To prevent overuse and unnecessary duration of antibiotics, using PCT to differentiate bacterial from viral infections is very helpful in appropriate antibiotic stewardship, without compromising patient safety.
- White blood cell count is non-specific in differentiating bacterial from viral infection. CRP is also elevated in both conditions. However, PCT levels do not generally go up with a viral infection even in very severe cases, as illustrated here.
- Therefore, presence of a normal PCT allows for safe discontinuation of antibiotics within 24 to 48 hours if no other evidence for a bacterial infection.
- We feel that the combination of rapid viral PCR testing and a negative PCT allows for greater confidence in safe antibiotic stewardship.

### Supportive literature

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## USING PCT TO DIFFERENTIATE VIRAL FROM BACTERIAL INFECTION IN COVID-19 PATIENTS

Figure 1. Chest X-ray on admission

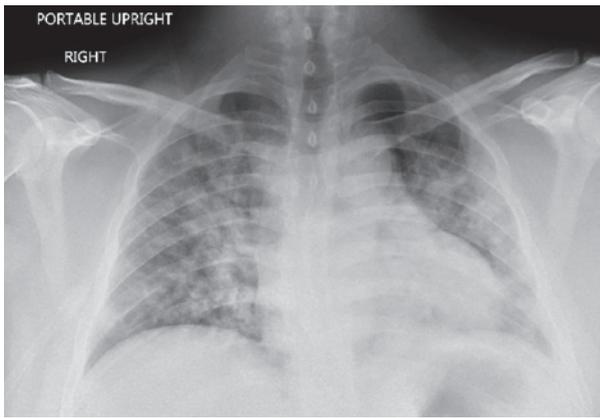


Figure 3. Chest X-ray during ECMO

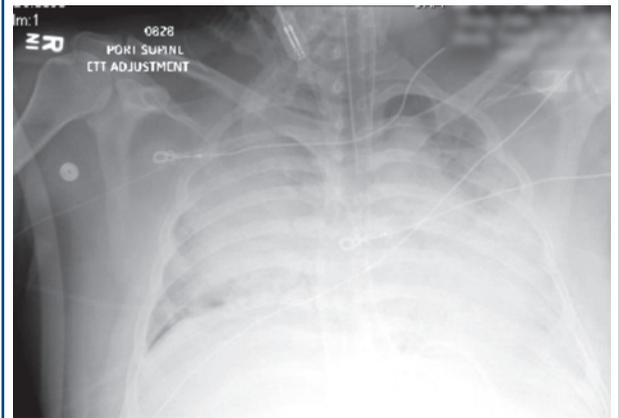


Figure 2. White blood cell count (WBC) and biomarker kinetics

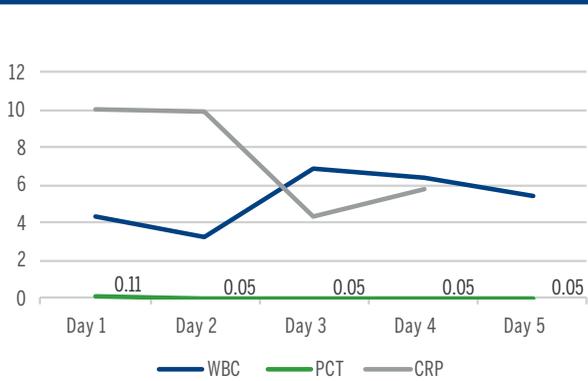
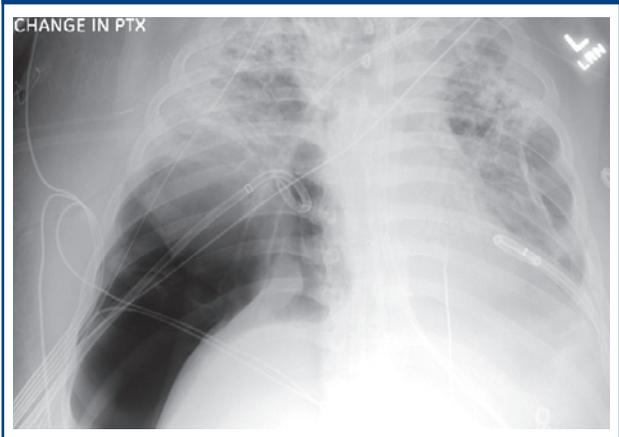
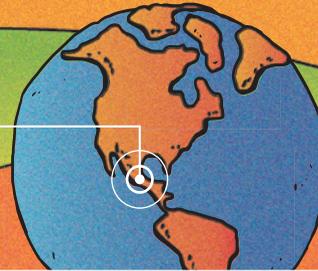


Figure 4. Chest X-ray showing pneumothorax





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## UTILITY OF PCT IN THE COVID-19 ERA FOR DIAGNOSIS OF BACTERIAL SEPSIS



### 44-year-old female

- Presented to the ED with high fever, shortness of breath, diarrhea, distal cyanosis
- BP: 65 mm/Hg, HR: 150/min, SpO<sub>2</sub>: 78%, with ARDS
- Past medical history of systemic hypertension and obstructive sleep apnea syndrome (OSAS) treatment with nocturnal nasal CPAP
- Transfer to ICU with diagnosis of ARDS secondary to COVID-19 and suspicion of pulmonary thromboembolism

### On ICU admission



- Patient required invasive mechanical ventilation
- Chest CT scan showed bilateral hypoperfusion areas and diffuse bilateral pulmonary infiltrates; echocardiogram with TAPSE of 8 and enlarged right ventricle
- BP: 60/25 mm/Hg, metabolic acidosis, lactate: 5.6 mmol/L, creatinine: 4.1 mg/dL, D-dimer: 34,000 ng/mL
- PCR: 24.5 and **PCT: 95.8 ng/mL**, WBC: 12.23x10<sup>9</sup>/L, SOFA: 7
- Patient suffered two cardiac arrests in the ICU
- Due to strong suspicion of pulmonary thromboembolism, thrombolysis with rTPA was given

➔ **Broad spectrum antibiotic coverage was given in the first 2 hours (meropenem plus vancomycin) due to elevated PCT**

### On day 2



- Patient was admitted to respiratory ICU
- PCR for SARS-CoV-2 came back negative
- Blood cultures were obtained in the ED, became positive after 12 hours and the Gram stain showed Gram-negative bacilli
- Abdominal ultrasound and abdominal CT scan were performed and a diagnosis of acute cholecystitis and gallbladder empyema was made
- Patient had a cholecystectomy 48 hours after admission
- After surgery, the patient stabilized
- **PCT levels decreased in the first 48 hours**
- Final blood culture results were *E. coli* ESBL

➔ **Vancomycin was stopped and after 72 hours of meropenem, the patient was de-escalated to ertapenem (i.e. 10 days of antibiotic treatment)**

### Patient outcome



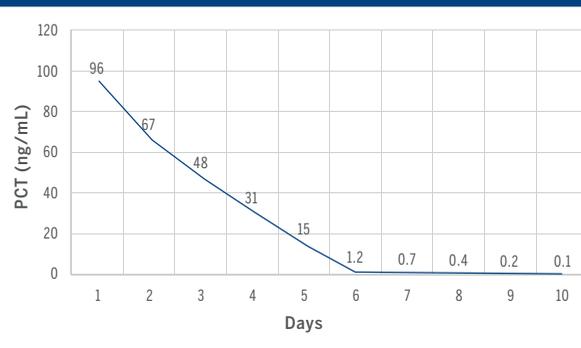
**Patient was discharged 12 days after admission, without any renal or neurological sequelae.**



## CONCLUSIONS

- PCT is a useful marker to determine the severity of illness. The treatment of intra-abdominal infections based on the PCT algorithm shortens the duration of antibiotic treatment and does not pose a risk for recurrence of the infection.
- In this specific clinical case, PCT helped the doctors to look for another source of infection than the lungs.
- Due to the severity of the patient's condition and in the context of the COVID-19 pandemic, the initial diagnosis was COVID-19 and PCT was a key factor in making the diagnosis and prognosis for the patient.
- In the COVID-19 era, not all cases of septic shock are due to COVID-19!

Figure 1. PCT kinetics over hospitalization period



### Supportive literature

- Reith H, Mittelkötter U, Wagner R, et al. Procalcitonin (PCT) in patients with abdominal sepsis. *Intensive Care Med.* 2000;26:S165-S169
- Mahmutaj D, et al. The predictive role of procalcitonin on the treatment of intraabdominal infections. *Open Access Maced J Med Sci.* 2017;5(7):909-914



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# SERIAL PCT TESTING REVEALS BACTERIAL SUPERINFECTION IN SEVERE COVID-19 PNEUMONIA



## 49-year-old male

- Presented to ED with asthenia and dyspnea
- Past medical history included arterial hypertension treated with enalapril
- Myalgia and dry cough reported for the last seven days
- Asthenia and dyspnea developing in the 48 hours prior to medical consultation

## On ED admission (day 1)



- HR: 105 bpm, tachypnea (RR: 24/min)
- Bilateral dry crackles on respiratory auscultation
- SpO<sub>2</sub>: 87% without supplementary oxygen
- Axillary temperature: 37°C
- Community-acquired pneumonia was suspected
- Oxygen therapy was delivered by a Venturi mask, with a fraction of inspired oxygen (FiO<sub>2</sub>) of 0.35
- Blood gas analysis showed PaO<sub>2</sub>: 71 mmHg (FiO<sub>2</sub> 0.35), PaCO<sub>2</sub>: 41 mmHg, Hb: 12 g/dL, lactate: 1.5 mmol/L
- Blood test showed predominantly polymorphonuclear leukocytosis (total WBC count 18x10<sup>9</sup>/L, neutrophil count 16x10<sup>9</sup>/L) with lymphopenia (900x10<sup>9</sup>/L)
- Further blood tests included D-dimer (900 ng/mL), IL-6 (650 pg/mL) and CRP (1.5 mg/dL)
- Chest X-ray showed peripheral alveolar infiltrates; echocardiography and electrocardiogram were normal
- Rapid bacterial and viral diagnostic tests: *S. pneumoniae*, *L. pneumophila*, Gram stain, Influenza were negative
- Nasopharyngeal swab for SARS-CoV-2 was positive
- Suspicion of possible bacterial coinfection

➔ **Ceftriaxone and azithromycin started**

## On day 2



- Patient was hospitalized due to COVID-19 pneumonia and remained stable with sustained oxygen saturation and no increase in oxygen demands
- Sputum culture was negative
- **Serial determinations of PCT performed during first two days of hospitalization gave values <1 ng/mL**

➔ **Empiric antibiotic therapy stopped**

- On day four, patient developed a decrease in oxygen saturation, with increased difficulty breathing and was transferred to ICU

## On day 4



- Patient admitted to ICU
- High-flow oxygen therapy started with FiO<sub>2</sub> 0.8 - 50L/min
- Chest X-rays showed worsening infiltrates
- Progression of the viral pneumonia was suspected
- **PCT remained low (0.8 ng/mL)**

➔ **Antibiotics were not initiated and dexamethasone was added to the treatment**

## On day 5



- Patient condition deteriorated
- Mechanical ventilation required due to acute respiratory failure and increased difficulty breathing
- Bronchoscopy performed, and lower respiratory tract samples obtained
- No clinical signs of bacterial superinfection
- **PCT remained stable**

➔ **Decision to withhold antibiotics, based on low PCT.**

## On day 9



- Patient developed progressive hypoxemia and persistent fever
- Chest X-rays showed condensation in right lower quadrant
- Peripheral blood tests showed polymorphonuclear leukocytosis (total WBC: 20x10<sup>9</sup>/L)
- IL-6 (30000 pg/mL), CRP (15 mg/dL) and **PCT (160 ng/mL)** used as confirmatory biomarkers
- Ventilator-associated pneumonia suspected; blood/respiratory cultures obtained

➔ **Meropenem started as empiric antibiotic therapy**

## SERIAL PCT TESTING REVEALS BACTERIAL SUPERINFECTION IN SEVERE COVID-19 PNEUMONIA

On day 10



- Patient showed progressive respiratory improvement
- Endotracheal aspirate positive for a strain of *Pseudomonas aeruginosa* susceptible to all antibiotics tested

➔ **Antibiotic therapy de-escalated to ceftazidime**

- Within 3 days of antibiotic therapy initiation, **PCT levels decreased to 5 ng/mL**
- After 5 days of antibiotic therapy, **PCT levels had reached baseline levels**

➔ **Antibiotics discontinued**

Patient outcome



**Patient was weaned from mechanical ventilation after 20 days and discharged from ICU on day 24.**

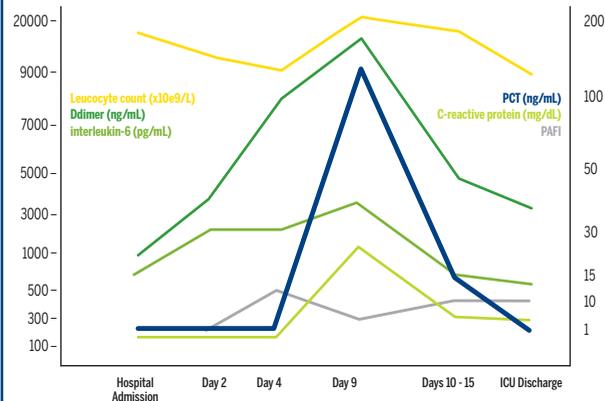


### CONCLUSIONS

- The prevalence of laboratory-confirmed bacterial superinfection in severe COVID-19 patients could be up to 25%,<sup>1</sup> especially in patients admitted to the ICU.<sup>2</sup>
- Several studies have reported that elevated PCT is positively associated with the severity of COVID-19.<sup>3,4</sup> Serial PCT measurements may be of prognostic value<sup>5</sup> in predicting evolution towards a more severe form of the disease and complications such as ventilator-associated pneumonia.



Figure 1. Kinetics of PCT and other blood biomarkers from day 1 to day 24



#### Supportive literature

1. Lansbury L, Lim B, Baskaran V, Lim WS. Co-infections in people with COVID-19: a systematic review and meta-analysis. *J Infect.* 2020;81(2):266–275
2. Garcia-Vidal C, Sanjuan G, Moreno-García E, Martínez JA, Soriano A. Incidence of co-infections and superinfections in hospitalized patients with COVID-19: a retrospective cohort study. *Clin Microbiol Infect.* 2020;S1198-743X(20)30450-X
3. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395:497–506
4. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.* 2020;382:1708–1720
5. Hu R, Han C, Pei S, Yin M, Chen X. Procalcitonin levels in COVID-19 patients. *Int J Antimicrob Agents.* 2020;56(2):106051

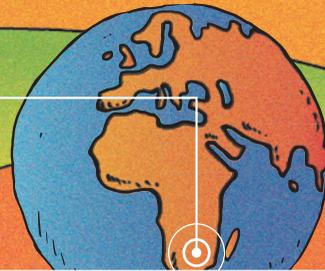


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## PCT TO SUPPORT ANTIBIOTIC STEWARDSHIP IN MAN

## AGEMENT OF PATIENTS WITH COVID-19 PNEUMONIA



### 51-year-old female healthcare worker

- Presented to ED with features of COVID-19 pneumonia confirmed by PCR testing
- Comorbidities: hypertension and obesity (BMI 35)
- Respiratory support administered via non-invasive ventilation
- Received steroids, tocilizumab, empiric antibiotics and therapeutic anticoagulation

### On ICU admission



- Admitted to ICU with worsening dyspnea and hypoxemia
- Patient was intubated and ventilated
- Initial PaO<sub>2</sub>/FiO<sub>2</sub> ratio of 81, CRP: 65 mg/dL, **PCT: 0.08 ng/mL**, blood cultures negative

➔ **Antibiotics stopped based on low PCT result**

### On Day 6



- Patient was extubated post-admission as gases had improved considerably
- However, extubation failed and patient was re-intubated on Day 7 with a PaO<sub>2</sub>/FiO<sub>2</sub> ratio of 85 on an airway pressure release (APRV) mode
- CRP and **PCT remained low**

### On Day 17



- **PCT rose to 10.93 ng/mL** and CRP to 84 mg/dL
- Source of sepsis uncertain
- Appropriate investigations; invasive lines changed

➔ **Empiric antibiotics started: ertapenem and amikacin according to the epidemiology of the unit**

### Day 18



- **PCT: 45.65 ng/mL**
- Blood culture flagged positive for *Klebsiella pneumonia* sensitive to ceftriaxone and ciprofloxacin

➔ **Antibiotics de-escalated**

- Blood cultures repeated

### Day 19



- CRP rose to 225 mg/dL and **PCT decreased to 33.6 ng/mL**

- Blood culture now grew an *Acinetobacter baumannii* species sensitive to colistin

➔ **Antibiotics were left unchanged, however, given the decreasing PCT result**

### On Day 20



- CRP showed no response (222 mg/dL) but **PCT halved to 16.11 ng/mL** and both biomarkers then continued on a downward trajectory

- Patient completed 6 days of ceftriaxone

➔ **Antibiotics stopped when PCT was 1.32 ng/mL and CRP 78 mg/dL**

### Patient outcome



**Patient remained in ICU for 31 days. No further episodes of sepsis occurred. Patient was discharged to ward for rehabilitation post-COVID-19 pneumonia.**



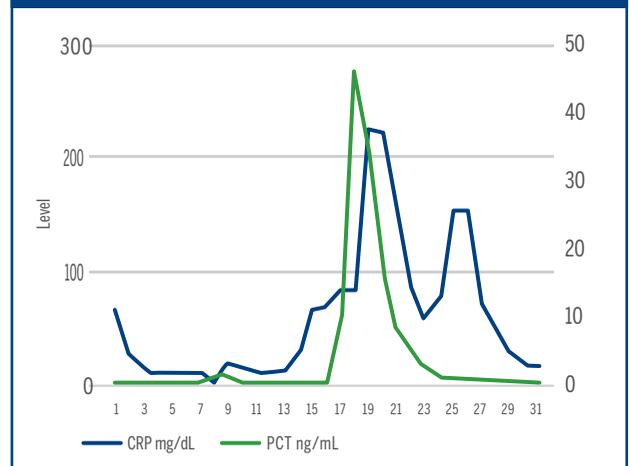
## PCT TO SUPPORT ANTIBIOTIC STEWARDSHIP IN MANAGEMENT OF PATIENTS WITH COVID-19 PNEUMONIA



### CONCLUSIONS

- If performed daily, PCT is of value in deciding on initiation of antibiotics and may also allow earlier discontinuation when the patient has recovered.
- The article by Schuetz et al. *Lancet Infect Dis.* 2018;18(1):95-107 supports this practice. However, it is important that the trend is followed rather than an isolated measurement. In addition, PCT only works as a stewardship tool if the result is believed and acted upon.
- Furthermore, if another more resistant organism is cultured while PCT levels are dropping, escalation of antibiotics may not be necessary. However, PCT should still be measured daily to allow these decisions to be made and patients should be carefully monitored after stopping antibiotic treatment in case of late treatment failure.
- PCT can rise with other causes of inflammation and with trauma. It is important to know the values associated with infection for each specific laboratory as in some laboratories sepsis may only be likely if values >5 or >10 ng/mL occur.
- Access to viral PCR, and in this case, SARS-CoV-2 PCR can significantly reduce antibiotic use.

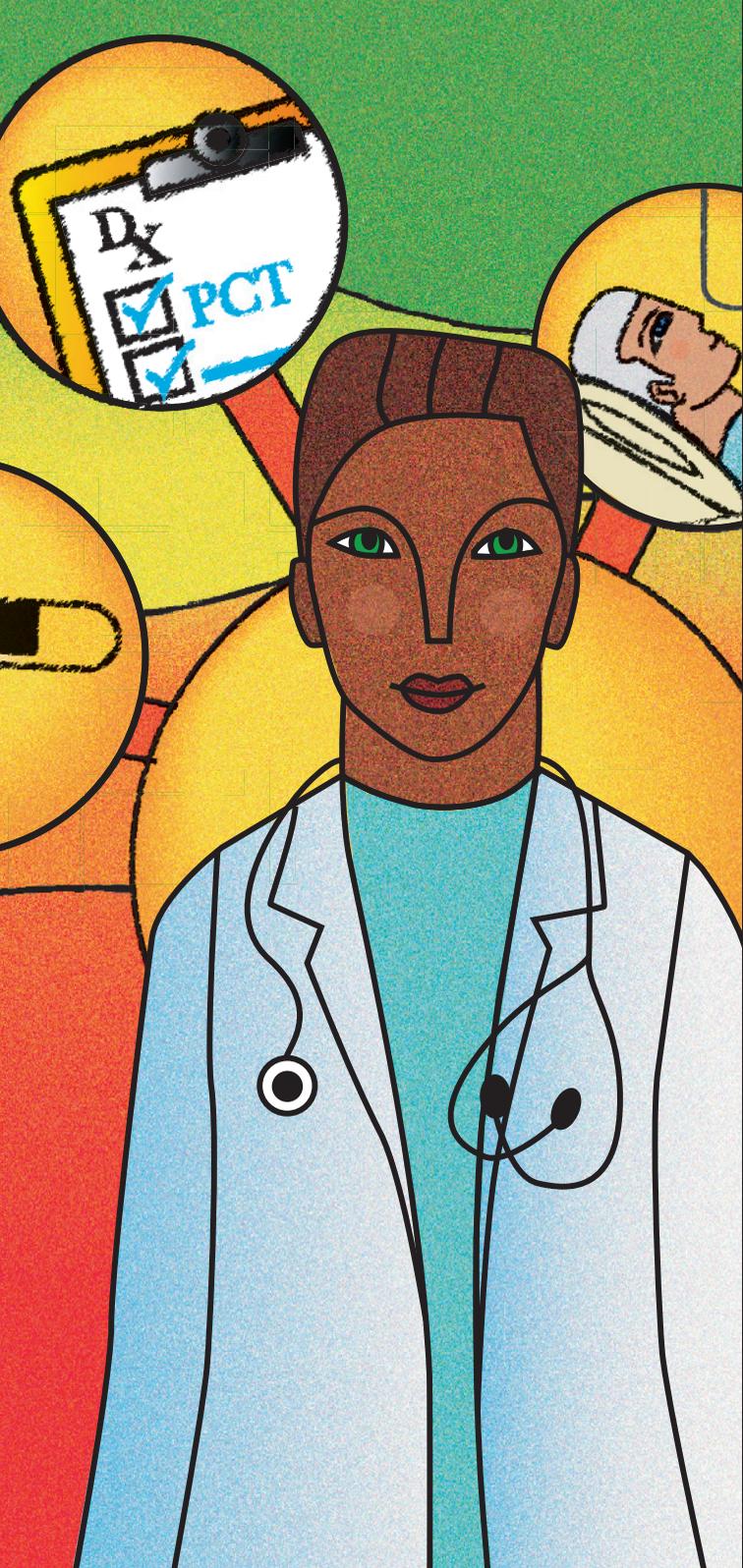
Figure 1. Kinetics of the inflammatory markers: blood levels of PCT and CRP in a case of COVID-19 pneumonia with secondary bacterial sepsis.



- PCT and CRP kinetics are evident in **Figure 1**
- Whereas CRP rose and fell randomly, PCT rose only in association with an episode of sepsis

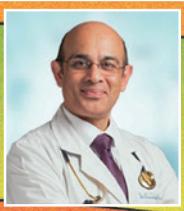
#### Supportive literature

- Torres A, Artigas A, Ferrer R. Biomarkers in the ICU: less is more? No. *Intensive Care Med.* 2020. <https://doi.org/10.1007/s00134-020-06271-4>
- Schuetz P, Wirz Y, Sager R, Christ-Crain M, et al. Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis. *Lancet Infect Dis.* 2018;18(1):95-107
- Hellyer TP, McAuley DF, Walsh TS, Anderson N, et al. Biomarker-guided antibiotic stewardship in suspected ventilator-associated pneumonia (VAPrapid2): a randomised controlled trial and process evaluation. *Lancet Respir Med.* 2020;8(2):182-191
- Moradi T, Bennett N, Shemanski S, Kennedy K, Schlachter A, Boyd S. Use of procalcitonin and a respiratory polymerase chain reaction panel to reduce antibiotic use via an electronic medical record alert. *Clin Infect Dis.* 2020;71(7):1684-9



# **PCT CLINICAL CASES**

## **RESPIRATORY TRACT INFECTIONS**



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## PCT HELPS DIFFERENTIATE BETWEEN VIRAL AND

## BACTERIAL INFECTIONS IN LRTI\*



### 58-year-old male, diabetic

- Presented to the ER
- Fever, vomiting, diarrhea for 7 days
- Breathlessness for 1 day
- Started on piperacillin-tazobactam elsewhere
- Nasopharyngeal swab for SARS-CoV-2 positive

### At ICU admission



- Heart rate: 110 bpm, blood pressure: 130/80 mmHg, O<sub>2</sub> saturation 91% in room air
- CT scan of chest showed peripheral ground glass opacities consistent with COVID-19
- Started on 4 liters oxygen

➔ **Antibiotics started;**  
**remdesivir, enoxaparin, dexamethasone**

- TLC: 5720 mL, **PCT: 0.16 ng/mL**

➔ **Antibiotics stopped**

- **Repeat PCT after 2 days: 0.01 ng/mL**

### On day 5



- Patient developed worsening hypoxia requiring high flow nasal oxygen
- Temperature: 36.8°C, blood pressure: 110/70 mmHg
- TLC: 13200 mL, N: 80%, **PCT: 2.6 ng/mL**

➔ **Started on meropenem**

### From day 6 to discharge



- Patient clinically improved in 48 hours
- **Repeat PCT after 72 hours: 0.56 ng/mL**
- Blood cultures grew *Klebsiella* (ESBL-producer)
- **Repeat PCT after 6 days: 0.12 ng/mL**

➔ **Antibiotics stopped**

### Patient outcome



**Patient was discharged after 12 days of hospitalization.**



## CONCLUSIONS

- PCT helps to differentiate between viral and bacterial infections, especially in the context of lower respiratory tract infections.
- Serial PCT levels are useful to assess response in patients with severe infections.
- Monitoring PCT levels in a patient who is showing clinical response can help to stop antibiotics earlier and thereby reduce antibiotic exposure.

### Supportive literature

- Self WH, Balk RA, Grijalva CG, et al. Procalcitonin as a Marker of Etiology in Adults Hospitalized with Community-Acquired Pneumonia. *Clin Infect Dis.* 2017;65:183
- Schuetz P, Wirz Y, Sager R, et al. Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis. *Lancet Infect Dis.* 2018;18:95

\*LRTI: Lower Respiratory Tract Infection



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## PCT COMBINED WITH PCR TO GUIDE EMPIRIC ANTIBIOTICS IN PATIENTS WITH VIRAL RTIs\*



### 86-year-old female

- Presented to ED with cough, dyspnea and fever of 2 days' duration
- Past medical history of diabetes mellitus, gout, sick sinus syndrome, and congestive heart failure
- On admission, BP: 126/64 mmHg, HR 62 bpm, T: 38.2°C, RR: 22 breaths/minute, SpO<sub>2</sub>: 94% on room oxygen
- Blood test results showed hemoglobin: 11.4 g/dL, WBC: 13,850 x 10<sup>9</sup>/L, lymphocytes: 1662/μL, blood urea: 17.2 mg/dL, creatinine: 1.0 mg/dL and NT-proBNP: 5295 pg/mL
- Chest X-ray was essentially clear, except for mild bilateral hilar infiltrates

### On ED admission



- Suspicion of acute heart failure with superimposed lower respiratory tract infection.
- ➔ **Initiation of ampicillin/sulbactam by injection, diuretic, oxygen therapy, and antipyretics**
- The rapid molecular test showed a positive result for respiratory syncytial virus (RSV) and **a low PCT level of 0.12 ng/mL** confirmed diagnosis of superimposed RSV infection
- ➔ **Due to low PCT result, initial intravenous antibiotic was discontinued**
- Patient was kept on diuretics and oxygen therapy

### After 24 hours



- Fever subsided 24 hours after admission
- Dyspnea improved after diuretics and oxygen therapy

### Patient outcome



**Patient was discharged after 3 days hospitalization.**



## CONCLUSIONS

- Respiratory virus infection is a common cause of acute dyspnea in elderly patients, but superimposed bacterial infection occurs in 10% of patients.
- A low PCT level (<0.25 ng/mL) in a patient with a positive molecular test for respiratory virus may help guide clinicians in withholding use of empiric antibiotics in low-risk patients.

Figure 1. Chest X-ray on admission



### Supportive literature

- Lee CC, Chang JC, Mao XW, et al. Combining procalcitonin and rapid multiplex respiratory virus testing for antibiotic stewardship in older adult patients with severe acute respiratory infection. *J Am Med Dir Assoc.* 2020;21(1):62-67
- Maisel A, Neath SX, Landsberg J, et al. Use of procalcitonin for the diagnosis of pneumonia in patients presenting with a chief complaint of dyspnoea: results from the BACH (Biomarkers in Acute Heart Failure) trial. *Eur J Heart Fail.* 2012;14(3):278-86

\*RTIs: respiratory tract infections



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# PCT TO AID IN TREATMENT OF RTIs\* AND REDUCE ANTIBIOTIC OVER-PRESCRIPTION



## 85-year-old female

- History of hypertension, COPD, tobacco abuse, osteoarthritis and breast cancer
- Chief complaint: increased shortness of breath with cough
- Found to be hypoxic to high 80s on room air
- BP: 114/76 mmHg, Pulse: 75 bpm, RR: 33 breaths/minute
- Suspected condition: respiratory insufficiency with presumptive diagnosis of Community Acquired Pneumonia (CAP)

### On admission



- Patient admitted to medicine floor
  - Chest X-ray revealed patchy infiltrates in mid lobes suspicious for either pulmonary edema or pneumonia
- ➔ **Empiric therapy initiated: ceftriaxone 1 gram IV q24h + azithromycin 500 mg IV q24h**

### After 12 hours



- WBC:  $8.8 \times 10^9/L$ , BNP: 144 pg/mL, **PCT: <0.1 ng/mL**
  - No further chest imaging performed
  - Patient saturations improved to 97% on 1L O<sub>2</sub>
- ➔ **Diagnostic-based therapy decision to discontinue ceftriaxone: based on negative procalcitonin, improvement in O<sub>2</sub> saturations and no fever**
- ➔ **Azithromycin was continued for acute exacerbation of COPD**

### Patient outcome



**Patient quickly recovered and at discharge had O<sub>2</sub> saturations of 97% on room air. No leukocytosis, fever or vital sign abnormalities.**



## CONCLUSIONS

- PCT can help differentiate between a bacterial and non-bacterial cause of respiratory insufficiency. For this patient with initially suspected community-acquired pneumonia, antibiotics were quickly narrowed based on low PCT levels and therefore low clinical suspicion for pneumonia with rapid resolution of patient symptoms.
- At our hospital we draw initial PCT to assess need for antimicrobial therapy in patients presenting with respiratory insufficiency. If clinical suspicion supports use of antibiotics, but is borderline, then we will obtain a 2<sup>nd</sup> level and if still negative will de-escalate as appropriate (see PCT protocol on pages 37/38).

### Supportive literature

Evidence used to discontinue antibiotics was based on Duke Regional Hospital's experience with over 20,000 PCT measurements and aligned with:

- Schuetz P, Briel M, Mueller BI. Clinical outcomes associated with procalcitonin algorithms to guide antibiotic therapy in respiratory tract infections. *JAMA* 2013;309(7):717-718

\*RTIs: respiratory tract infections



## PCT TO AID IN TREATMENT OF RTIs\* AND REDUCE ANTIBIOTIC OVER-PRESCRIPTION

### Procalcitonin protocol in use at Duke Regional Hospital

Protocol and algorithms adapted from Schuetz P, Briel M, Mueller BI. Clinical outcomes associated with procalcitonin algorithms to guide antibiotic therapy in respiratory tract infections. *JAMA* 2013;309(7):717-718

Serum concentrations of PCT are normally  $<0.05$  ng/mL but in circumstances of systemic inflammation, particularly bacterial infection, PCT is produced in large quantities by many body tissues. It is detectable within 2-4 hours and peaks within 6-24 hours.

**Emergency Room:** exacerbations of bronchitis, COPD or CHF  
**Recommended use:** based upon evidence, it is recommended that patients who present with symptoms that mimic LRTIs have a PCT value measured with interpretation based on **Algorithm 1**.

#### Algorithm 1. ER: PCT level in suspected LRTI

| PCT value (ng/mL)             | $<0.1$               | 0.1-0.24    | $\geq 0.25-0.5$ | $>0.5$              |
|-------------------------------|----------------------|-------------|-----------------|---------------------|
| Antibiotic use recommendation | Strongly discouraged | Discouraged | Encouraged      | Strongly encouraged |

Additional algorithms (2 and 3) in use at the Duke Regional Hospital for patients with suspected sepsis/septic shock.

#### Sepsis Initial Antibiotic Use Algorithm.

**Recommended use:** based upon evidence, it is recommended that patients admitted to the ICU with presumed sepsis/septic shock have PCT drawn on admission and that PCT be repeated on the next 2 days. Decisions regarding antibiotic therapy can then be made based upon PCT dynamics, culture data, and patient specific clinical data.

\*RTIs: respiratory tract infections

#### Algorithm 2. Initial PCT level in sepsis

| PCT value (ng/mL)             | $<0.25$              | 0.25-0.49   | $\geq 0.5-1.0$ | $>1.0$              |
|-------------------------------|----------------------|-------------|----------------|---------------------|
| Antibiotic use recommendation | Strongly discouraged | Discouraged | Encouraged     | Strongly encouraged |

**Strongly consider antibiotic initiation in all patients with suspicion of infection**

- Consider alternative diagnosis
- Repeat PCT in 6-12 hours if antibiotics not begun
- If clinically unstable, immune-suppressed or high risk, consider over-ruling

Repeat daily for 3 days to consider early antibiotic discontinuation  
**See algorithm 3**

#### Algorithm 3. Sepsis initial PCT follow-up

| PCT value (ng/mL)             | $<0.25$                       | 0.25-0.49 or drop by $>80\%$ | $\geq 0.5-1.0$ decreased by $<80\%$ | $>1.0$ or not decreasing       |
|-------------------------------|-------------------------------|------------------------------|-------------------------------------|--------------------------------|
| Antibiotic use recommendation | Cessation strongly encouraged | Cessation encouraged         | Cessation discouraged               | Cessation strongly discouraged |

Consider continuation if clinically unstable

- A PCT value which is rising or not declining at least 10% per day is a poor prognostic indicator and suggests infection is not controlled
- Consider expanding antibiotic coverage or further diagnostic evaluation



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## USING PCT TO STOP UNNECESSARY ANTIBIOTIC USE SAFELY



### 89-year-old male

- Referred by Outpatient Clinic Services to ED for unwitnessed fall
- **Medical History:**  
IHD, HTN, HLD, T2DM, anemia with B12 deficiency - baseline Hb 10-11, nocturia BPH
- **Symptoms & Complaints:**  
intermittent cough x 1-2/52, no sore throat/rhinorrhea, no SOB, no fever, no urinary symptoms
- **Suspected Conditions:**
  - ➔ Unwitnessed fall precipitated by: postural hypotension? Hypoglycemia? CBG in ED: 4.1-5.9 mmol, HbA1c: 6.1%, on OHGAs (gliclazide reduced gradually from 160mg BD)
    - CT brain ordered
  - ➔ UTI/Pneumonia?
    - COVID-19 testing ordered
    - CXR, CRP, FBC ordered

### On ED admission



- Temp: 35.7°C, BP: 160/76 mmHg, HR: 92 breaths/minute, SpO<sub>2</sub>: 99% on RA
- Intermittent cough x 1-2/52, no sore throat/rhinorrhea, no SOB, no fever
- No urinary symptoms
- CT brain done: no established territorial infarct, acute intracranial haemorrhage or mass effect, no skull vault fracture
- COVID-19 testing negative, CXR done: minor areas of atelectasis noted in left lower zones
- CBG: 8.7-10.2 mmol/L, FBC ➔ Hb: 11.2 g/dL, WBC: 9.5x10<sup>9</sup>/L, Plt: 314x10<sup>9</sup>/L, CRP: 5 mg/dL

### After 48 hours



- Pain Score: 0, Temp: 36.9°C
- BP: 104/57 mmHg, HR: 59 bpm, RR: 20 breaths/minute, SpO<sub>2</sub>: 95%
- Temp: 38.5°C
- Blood sugar level (mmol/L): 8.7(N) ◀ 9.4(N) ◀ 10.2(N)
- Lab Values: Hb: 11.1 g/dL, WBC: 12.60x10<sup>9</sup>/L (from 9.5 on admission), Plt: 318x10<sup>9</sup>/L
- On examination: well, no complaints, no cough

### From day 3 to day 4



- In view of nosocomial fever and WBC 12.60x10<sup>9</sup>/L, unclear source of infection, blood and urine cultures were sent
- CXR, PCT, CRP, 2<sup>nd</sup> round of COVID-19 testing ordered
- ➔ **Piperacillin-tazobactam 4.5g q6h started**
  - CXR, PCT, CRP, 2<sup>nd</sup> round of COVID-19 testing ordered
  - After 3 hours ➔ CRP: 53 mg/dL (up from 5 on admission), **PCT <0.06 ng/mL**
  - Patient was afebrile
  - CXR report: lungs showed neither congestion nor consolidation
  - COVID-19 testing negative
  - Blood and urine cultures pending

### On day 4



- AMS team review: patient remained afebrile, hemodynamically stable and clinically well
- Only single spike of fever overnight, **PCT normal**, CXR - no consolidation
- Blood and urine cultures negative

### ➔ Decision to discontinue piperacillin-tazobactam

### Patient outcome



**Patient was finally discharged on day 4 evening, after confirmation of negative COVID-19 via two rounds of testing and negative bacterial cultures (blood and urine).**



## CONCLUSIONS

- CRP, WBC and fever are not specific for bacterial infection/pneumonia.
- Use of PCT can rule out bacterial infection with precision, and there is no need to finish a course of antibiotics if bacterial infection is ruled out.
- PCT has value for individual patient management and as part of the hospital AMS program.

### Supportive literature

- Liew YX, Lee W, Loh JC, et al. Impact of an antimicrobial stewardship programme on patient safety in Singapore General Hospital. *Int J Antimicrob Agents.* 2012;40:55-60
- Loo LW, Liew YX, Lee W, Lee LW, Chlebicki P, Kwa AL. Discontinuation of antibiotic therapy within 24 hours of treatment initiation for patients with no clinical evidence of bacterial infection: a 5-year safety and outcome study from Singapore General Hospital Antimicrobial Stewardship Program. *Int J Antimicrob Agents.* 2019;53(5):606-611



## CONCLUDING REMARKS

The cases presented in this booklet give an in-depth view on the best use of PCT, namely, serial testing and in combination with a thorough clinical and laboratory assessment also including diagnostic tests from microbiology.

The **most important rules for use of PCT in clinical practice** may be summarized as follows:

- in the context of a **low-risk situation** and a low pre-test probability for bacterial infections (e.g., bronchitis patient), a **low PCT level <0.25 ng/mL or <0.1 ng/mL aids in ruling-out bacterial infection** and empiric antibiotic therapy may be avoided.
- if PCT is increased or the initial clinical assessment shows a **high suspicion for bacterial infection**, antibiotics should be considered and PCT testing every 24-48 hours can be used to **stop antibiotics if PCT drops to levels  $\leq 0.25$  ng/mL or decreases by 80% or more from its peak (Figure 1, page 43).**
- in the context of a **high-risk patient with sepsis**, it is important that initial antibiotics should be used irrespective of PCT results, but a low PCT value may prompt additional diagnostic measures to rule out other non-bacterial causes of illness. In these situations, **monitoring of PCT over time helps to track resolution of infection and decisions regarding early discontinuation of antibiotic treatment (Figure 2, page 44).**

The algorithms in Figures 1 and 2 are taken from the latest **International Experts Consensus** paper (Schuetz et al. *Clin Chem Lab Med*, 2019) which refined established PCT algorithms by incorporating **severity of illness and probability of bacterial infection**. Furthermore, to simplify practical application, the fixed cut-offs were reduced to only one for **mild or moderate disease (0.25 ng/mL)** and one for **severe disease (0.5 ng/mL)**.

PCT has shown great promise for the personalization of antibiotic treatment, leading to an overall reduction in antibiotic exposure, fewer (or “less”) side effects and improvements in clinical outcomes.

**PCT measurements should always be interpreted in the context of the overall assessment of each patient, and should never delay the initiation of treatment in high-risk patients and critical states.** However, PCT can then be used to monitor resolution of infection and therefore length of treatment.

The use of PCT requires **experience, education and training** as well as **case-based discussions** with experts and health professionals from different areas. For this purpose, this booklet is well suited and will hopefully help provide practitioners with important take-home messages to share with their colleagues.

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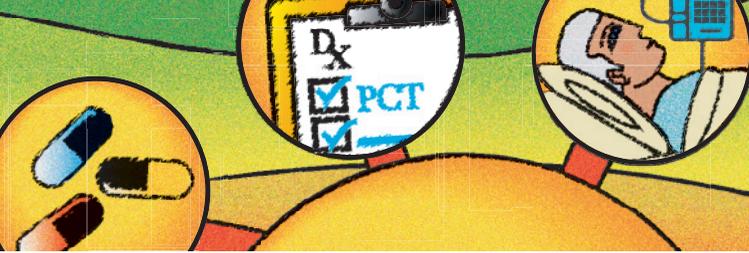


Figure 1. Use of PCT in patients with moderate illness outside the ICU

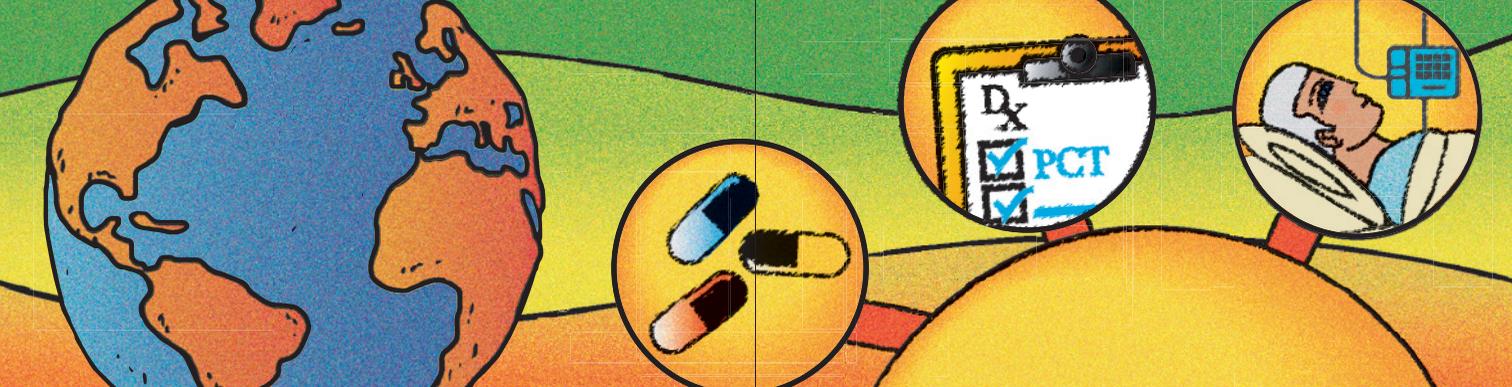
Adapted by Prof. Schuetz from Schuetz P. et al. *Clin Chem Lab Med.* 2019;57(9):1308-18

| Initial clinical assessment (including microbiology)  | BACTERIAL INFECTION UNCERTAIN  |  | BACTERIAL INFECTION SUSPECTED  |  |
|---|--|--|--|--|
|   | <0.25  | ≥0.25  | <0.25  | ≥0.25  |
| PCT (ng/mL)   | <0.25  | ≥0.25  | <0.25  | ≥0.25  |
| Probability of bacterial infection based on PCT level | LOW PROBABILITY  | HIGH PROBABILITY   | LOW PROBABILITY  | HIGH PROBABILITY   |
| PCT interpretation                                    | BACTERIAL INFECTION UNLIKELY   | BACTERIAL INFECTION LIKELY   | BACTERIAL INFECTION POSSIBLE   | BACTERIAL INFECTION HIGHLY LIKELY  |
| Antibiotic Management                                 | Initiate empiric antibiotic regimen based on clinical judgement; consider other diagnostic tests | Initiate empiric antibiotic regimen based on clinical judgement                              | Initiate empiric antibiotic regimen based on clinical judgement; consider other diagnostic tests | Initiate appropriate empiric or targeted antibiotic regimen based on clinical judgement      |
| PCT Monitoring  | Repeat PCT within 6-24h and discontinue antibiotics if PCT still <0.25 ng/mL                     | Repeat PCT every 24-48h and discontinue antibiotics when PCT <0.25 ng/mL or decreases by 80% | Repeat PCT within 6-24h and discontinue antibiotics if PCT still <0.25 ng/mL                     | Repeat PCT every 24-48h and discontinue antibiotics when PCT <0.25 ng/mL or decreases by 80% |

Figure 2. Use of PCT in patients with severe illness in the ICU

Adapted by Prof. Schuetz from Schuetz P. et al. *Clin Chem Lab Med.* 2019;57(9):1308-18

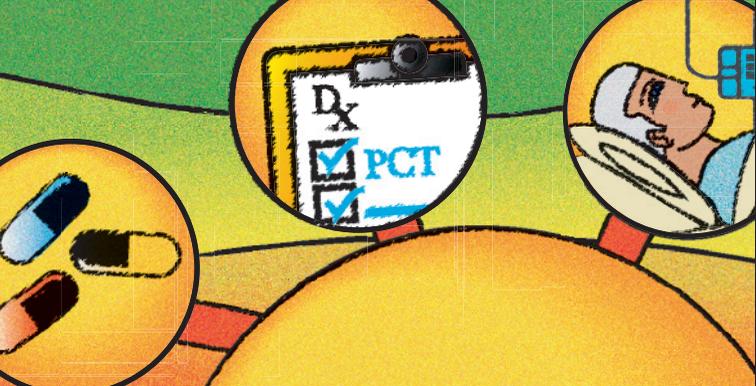
| Initial clinical assessment (including microbiology)  | BACTERIAL INFECTION UNCERTAIN  |   | BACTERIAL INFECTION SUSPECTED  |   |
|---|--|---|--|---|
|   | <0.5   | ≥0.5  | <0.5   | ≥0.5  |
| PCT (ng/mL)   | <0.5   | ≥0.5  | <0.5   | ≥0.5  |
| Probability of bacterial infection based on PCT level | LOW PROBABILITY  | HIGH PROBABILITY  | LOW PROBABILITY  | HIGH PROBABILITY  |
| PCT Interpretation                                    | BACTERIAL INFECTION UNLIKELY   | BACTERIAL INFECTION LIKELY  | BACTERIAL INFECTION POSSIBLE   | BACTERIAL INFECTION HIGHLY LIKELY   |
| Antibiotic Management                                 | Initiate empiric antibiotic regimen based on clinical judgement; consider other diagnostic tests | Initiate empiric antibiotic regimen based on clinical judgement                             | Initiate empiric antibiotic regimen based on clinical judgement; consider other diagnostic tests | Initiate appropriate empiric or targeted antibiotic regimen based on clinical judgement     |
| PCT Monitoring  | Repeat PCT within 24-48h and discontinue antibiotics if PCT still <0.5 ng/mL                     | Repeat PCT every 24-48h and discontinue antibiotics when PCT <0.5 ng/mL or decreases by 80% | Repeat PCT within 24-48h and discontinue antibiotics if PCT still <0.5 ng/mL                     | Repeat PCT every 24-48h and discontinue antibiotics when PCT <0.5 ng/mL or decreases by 80% |



## ABBREVIATIONS AND ACRONYMS

|                 |  |
|-----------------|--|
| <b>AMS</b>      | antimicrobial stewardship              |
| <b>ARDS</b>     | acute respiratory distress syndrome    |
| <b>BiPAP</b>    | bilevel positive airway pressure       |
| <b>BMI</b>      | body mass index                        |
| <b>BNP</b>      | brain natriuretic peptide              |
| <b>BPH</b>      | benign prostatic hyperplasia           |
| <b>BP</b>       | blood pressure                         |
| <b>CAP</b>      | community-acquired pneumonia           |
| <b>CBG</b>      | capillary blood glucose                |
| <b>CHR</b>      | chronic heart failure                  |
| <b>COPD</b>     | chronic obstructive pulmonary disorder |
| <b>COVID-19</b> | coronavirus disease 2019               |
| <b>CPAP</b>     | continuous positive airway pressure    |
| <b>CRP</b>      | C-reactive protein                     |
| <b>CT</b>       | computerized tomography                |
| <b>CVC</b>      | central venous catheter                |
| <b>CXR</b>      | chest X-ray                            |
| <b>ECMO</b>     | extracorporeal membrane oxygenation    |
| <b>ED</b>       | emergency department                   |
| <b>ER</b>       | emergency room                         |
| <b>ESBL</b>     | extended spectrum beta-lactamase       |
| <b>FBC</b>      | full blood count                       |

|                         |  |
|-------------------------|--|
| <b>FiO<sub>2</sub></b>  | fraction of inspired oxygen                        |
| <b>GCS</b>              | Glasgow Coma Scale                                 |
| <b>Hb</b>               | hemoglobin   |
| <b>HLD</b>              | hyperlipidemia                                     |
| <b>HR</b>               | heart rate   |
| <b>HT/HTN</b>           | hypertension                                       |
| <b>ICU</b>              | intensive care unit                                |
| <b>IHD</b>              | ischemic heart disease                             |
| <b>IL-6</b>             | interleukin-6                                      |
| <b>LRTI</b>             | lower respiratory tract infection                  |
| <b>MDRO</b>             | multi-drug resistant organism                      |
| <b>mmHg</b>             | millimeters of mercury                             |
| <b>N</b>                | nitrogen   |
| <b>NA</b>               | noradrenaline                                      |
| <b>NT-proBNP</b>        | N-terminal prohormone of brain natriuretic peptide |
| <b>OHGA</b>             | oral hypoglycemic agent                            |
| <b>OSAS</b>             | obstructive sleep apnea syndrome                   |
| <b>PaCO<sub>2</sub></b> | partial pressure of carbon dioxide                 |
| <b>PaO<sub>2</sub></b>  | partial pressure of arterial oxygen                |
| <b>PCR</b>              | polymerase chain reaction                          |
| <b>PCT</b>              | procalcitonin                                      |
| <b>PEEP</b>             | positive end expiratory pressure                   |



## ABBREVIATIONS AND ACRONYMS

|                         |   |
|-------------------------|---|
| <b>Plt</b>              | platelets                                       |
| <b>PO<sub>2</sub></b>   | partial pressure of oxygen                      |
| <b>qSOFA</b>            | quick Sequential Organ Failure Assessment       |
| <b>RA</b>               | room air  |
| <b>RSV</b>              | respiratory syncytial virus                     |
| <b>rtPA</b>             | recombinant tissue plasminogen activator        |
| <b>RR</b>               | respiratory rate                                |
| <b>SARS-CoV-2</b>       | severe acute respiratory syndrome coronavirus 2 |
| <b>ScvO<sub>2</sub></b> | central venous oxygen saturation                |
| <b>SOB</b>              | shortness of breath                             |
| <b>SOFA</b>             | Sequential Organ Failure Assessment             |
| <b>SpO<sub>2</sub></b>  | oxygen saturation                               |
| <b>T2DM</b>             | type 2 diabetes mellitus                        |
| <b>TAPSE</b>            | tricuspid annular plane systolic excursion      |
| <b>Temp/T</b>           | temperature                                     |
| <b>TLC</b>              | total lung capacity                             |
| <b>URTI</b>             | upper respiratory tract infection               |
| <b>WBC</b>              | white blood cell count                          |



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