EVMS Emergency Medicine Journal Club January 28th 2008
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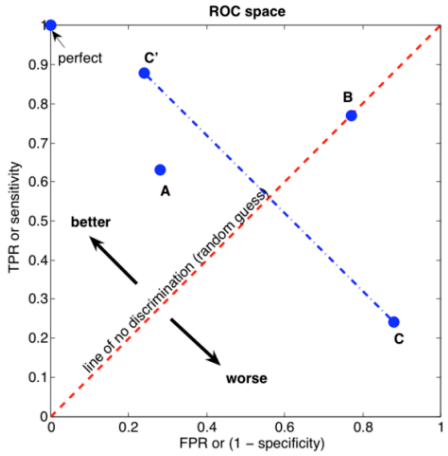
Search strategy: Medline, Cochrane, PubMed, Google.

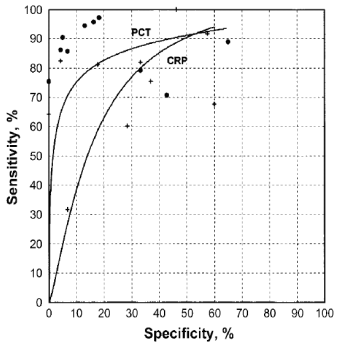
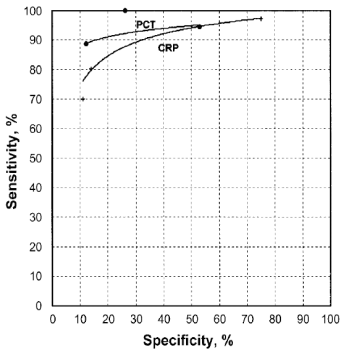
P: In the diagnosis of infection
I: does the measuring of C-reactive protein or Procalcitonin
C: compared to CBC and other traditional indicators of infection
O: provide greater diagnostic accuracy?

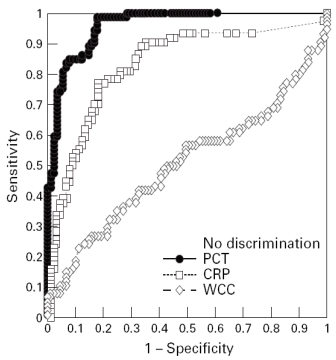
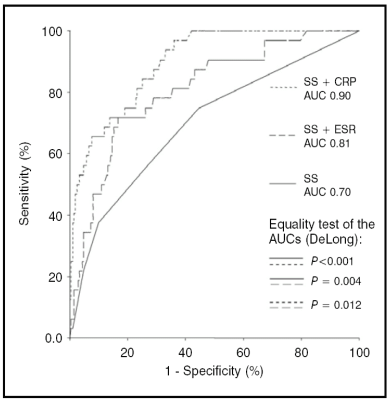
C-Reactive Protein: CPR is an acute phase that is produced by the liver in response to the elevated levels of the cytokines, such as interleukin-6 that accompany acute inflammation. CRP levels rise within 6 h of an inflammatory stimulus and double every 8–9 h thereafter. The clearance rate of CRP is constant, with a serum half-life of about 24h.

Procalcitonin: PCT is the prehormone of calcitonin. Normally negligible serum PCT concentrations are detected. It is believed that PCT is produced by the liver and modulated by lipopolysaccharides and sepsis-related cytokines. It has no known physiological function. PCT levels may start to rise within 2 hours, plasma $T_{½}$ of 25-30 h.

Receiver operating characterisic curve: To draw a ROC curve, only the true positive rate (TPR) and false positive rate (FPR) are needed. An ROC space is defined by FPR and TPR as *x* and *y* axes respectively, which depicts relative trade-offs between true positive (benefits) and false positive (costs). Each prediction result or one instance of a confusion matrix represents one point in the ROC space. The best possible prediction method would yield a point in the upper left corner or coordinate (0,1) of the ROC space, representing 100% sensitivity (all true positives are found) and 100% specificity (no false positives are found). A completely random guess would give a point along a diagonal line (the so-called *line of no-discrimination*) from the left bottom to the top right corners.



Study	Type	Patients	Results	Conclusions	Graphs and limitations
Clinical Infectious Diseases 2004; 39:206–17 Serum Procalcitonin and C-Reactive Protein Levels as Markers of Bacterial Infection	Systematic Review and Meta-analysis of prospective studies in Medline 1970 to 2002 evaluating both CRP and Procalcitonin for diagnosis of bacterial infections	Hospitalized patients in various clinical settings	351 articles found, 12 included. **Differentiating bacterial from noninfective causes of inflammation**: PCT level more sensitive 88% (80%–93%) vs. 75% (62%–84%) and more specific 81% (67%–90%) vs. 67%(56%–77%) than CRP **Differenting bacterial from viral infections**: PCT more sensitive (92% (86%–95%) vs. 86% (65%–95%); specificities were comparable (73% (42%–91%) vs. 70% (19%–96%).	The overall accuracy of PCT markers is higher than that of CRP markers both to differentiate bacterial infections from viral infections and to differentiate bacterial infections from other noninfective causes of systemic inflammation.	Variable clinical settings Not EM studies (1 study on adults with cirrhosis in ED and 1 on children in ED with fever)  **Figure 1.** Summary receiver operating characteristic (SROC) curves comparing serum procalcitonin (PCT; ●) and C-reactive protein (CRP; +) markers for detection of bacterial infections versus noninfective causes of inflammation. Each point contributing to the SROC curve represents 1  **Figure 2.** Summary receiver operating characteristic (SROC) curves comparing serum procalcitonin (PCT; ●) and C-reactive protein (CRP; +) markers for bacterial infections versus viral infections. Each point con-
Arch Dis Child	Prospective	175 Critically ill children	Admission PCT was	In critically ill	Children already known to be critically ill.

1999;81:417–421 Diagnostic markers of infection: comparison of procalcitonin with C reactive protein and leucocyte count.	observational study	admitted to PICU Median age 16 months. Patients classified as: non-infected controls (43); viral infection (14); localised bacterial infection without shock (25); bacterial meningitis/encephalitis (10); or septic shock (77).	significantly higher in children with septic shock median 94.6; (3.3–759.8 ng/ml), compared with localised bacterial infection (2.9; 0–24.3 ng/ml), viral infection (0.8; 0–4.4 ng/ml), and non-infected controls (0; 0–4.9 ng/ml). Area under the ROC curve was 0.96 for procalcitonin, 0.83 for C reactive protein, and 0.51 for leucocyte count. A PCT > 2 ng/ml identified all patients with bacterial meningitis or septic shock	children the admission procalcitonin concentration is a better diagnostic marker of infection than C reactive protein or leucocyte count. A procalcitonin concentration of 2 ng/ml might be useful in differentiating severe bacterial disease in infants and children.	 *Figure 1 Receiver operating characteristic (ROC) curves comparing admission procalcitonin (PCT), C reactive protein (CRP), and leucocyte count (WCC) for prediction of septic shock (all patients). The area under the curve was*
Lancet 2004; 363: 600–07 Effect of procalcitonin-guided treatment on antibiotic use and outcome in lower respiratory tract infections: cluster-randomised, single-blinded intervention trial	Prospective, cluster-randomised, controlled, single-blinded intervention trial	243 patients admitted with suspected LRTI randomly assigned standard care (n=119) or PCT-guided treatment (n=124). On the basis of serum procalcitonin concentrations, use of antibiotics was more or less discouraged (<0·1 _g/L or <0·25 _g/L) or encouraged (_0·5 _g/L or _0·25 _g/L), respectively. Reevaluation was possible after 6–24 h in both groups. Primary endpoint was use of antibiotics and analysis was by intention to treat.	In the procalcitonin group, the adjusted relative risk of antibiotic exposure was 0·49 (95% CI 0·44–0·55; p<0·0001) compared with the standard group. Antibiotic use was significantly reduced in all diagnostic subgroups. Clinical and laboratory outcome was similar in both groups and favourable in 235 (97%).	Procalcitonin guidance substantially reduced antibiotic use in lower respiratory tract infections. Withholding antimicrobial treatment did not compromise outcome. Treatment based on procalcitonin measurement could have important clinical and financial implications.	
British Journal of General Practice 2003, 53, 358-364. Contributions of symptoms, signs, erythrocyte sedimentation rate, and C-reactive protein to a diagnosis of pneumonia in acute lower respiratory tract infection	Prospective observational study	246 adult patients presenting to GP with symptoms and signs of LRTI **Cough less than 29 days** **At least 1 of 4:** - -SOB -Wheezing -CP -Abnormal breath sounds **At least 1 of 4:** -Fever over 38°C, -Perspiring -HA -myalgia **GP diagnosis of LRTI** **CXR on day 3 determined if pneumonia**	Dry cough, diarrhoea, and a temperature of ≥38°C were independent and statistically significant predictors of pneumonia, but abnormal pulmonary auscultation and clinical diagnosis of pneumonia by the GPs were not. ESR and CRP had higher diagnostic odds ratios than any of the symptoms and signs. Applying a prediction rule for low-risk patients, including a CRP of <20, 80 of the 193 antibiotic prescriptions could have been prevented with a maximum risk of2.5% of missing a pneumonia case.	Most symptoms and signs traditionally associated with pneumonia are not predictive of pneumonia in general practice. The prediction rule for low-risk patients presented here, including a CRP of <20, can considerably reduce unjustified antibiotic prescribing.	None  *Figure 2. Multiple logistic regression analysis. ROC curves of the three final models: 'symptoms and signs' model (SS), 'symptoms and signs + ESR' model (SS+ESR), and 'symptoms and signs +*

Clinical Bottom Line: CRP and Procalcitonin:

- are superior in diagnostic accuracy to other laboratory markers of infection
- may be more accurate than all other symptoms and signs of infections
- are probably most useful in risk stratifying patients with intermediate or low probability and uncertain symptoms and signs
- have been more studied in pediatric population and ICU
- more research on use in ED is needed to evaluate accuracy and cost effectiveness
- further research of diagnostic use has the potential to decrease the use of antibiotics