

Introduction to ichromaTM PCT

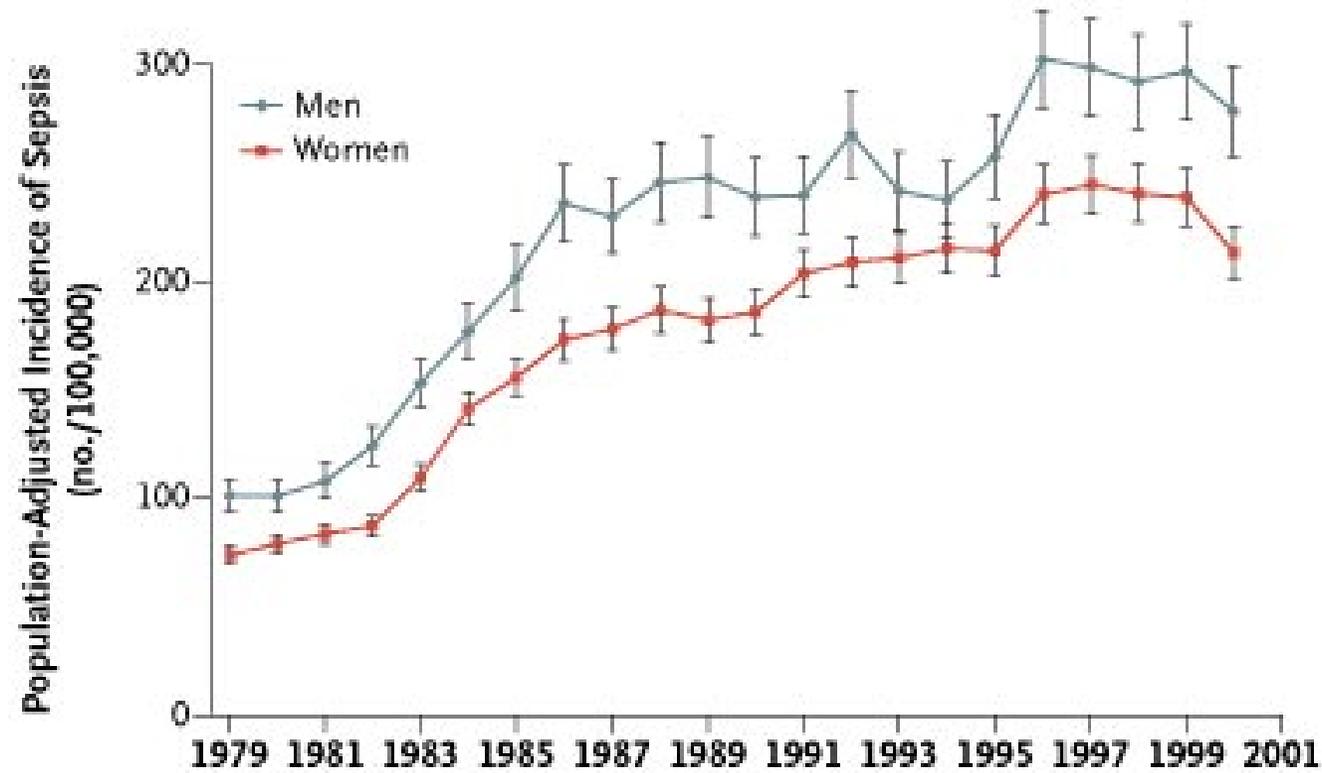
Boditech Med Inc.

March 13 2014

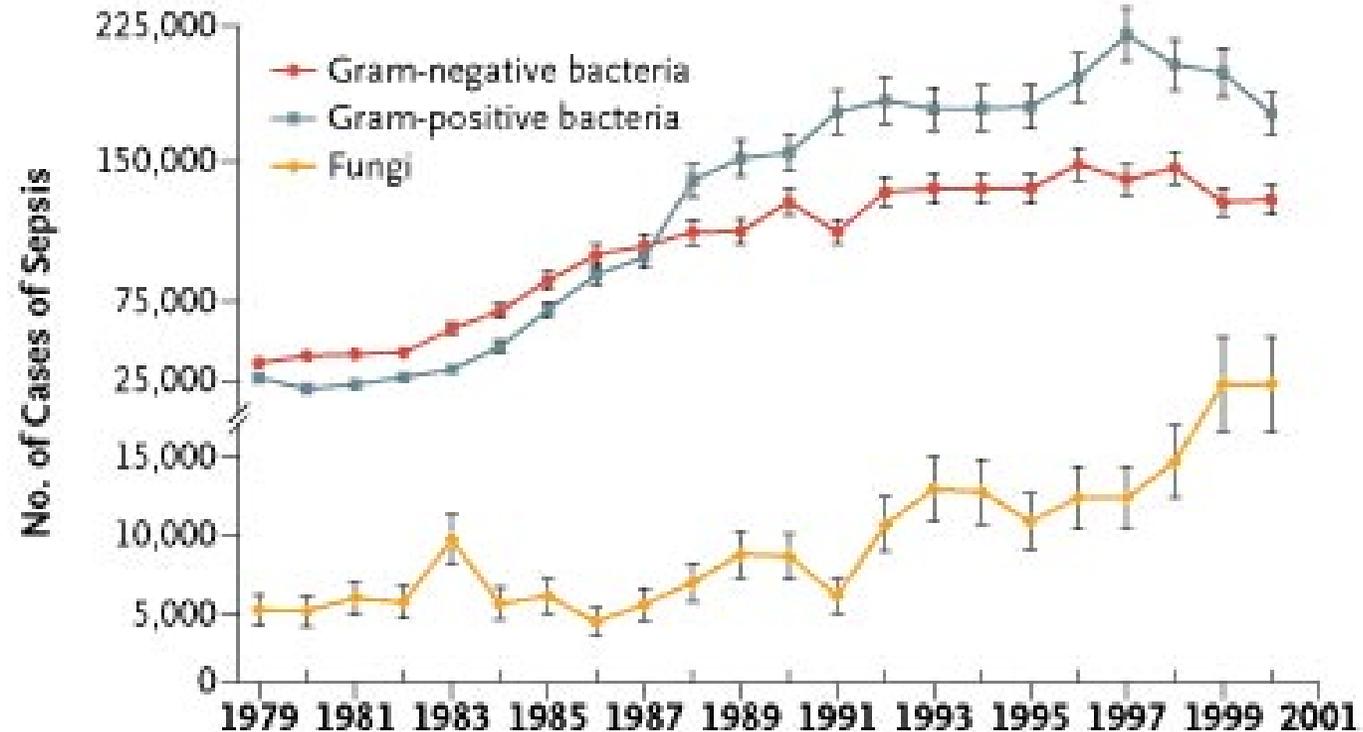
Sepsis is a serious problem



Population adjusted incidence of sepsis increases steadily in USA



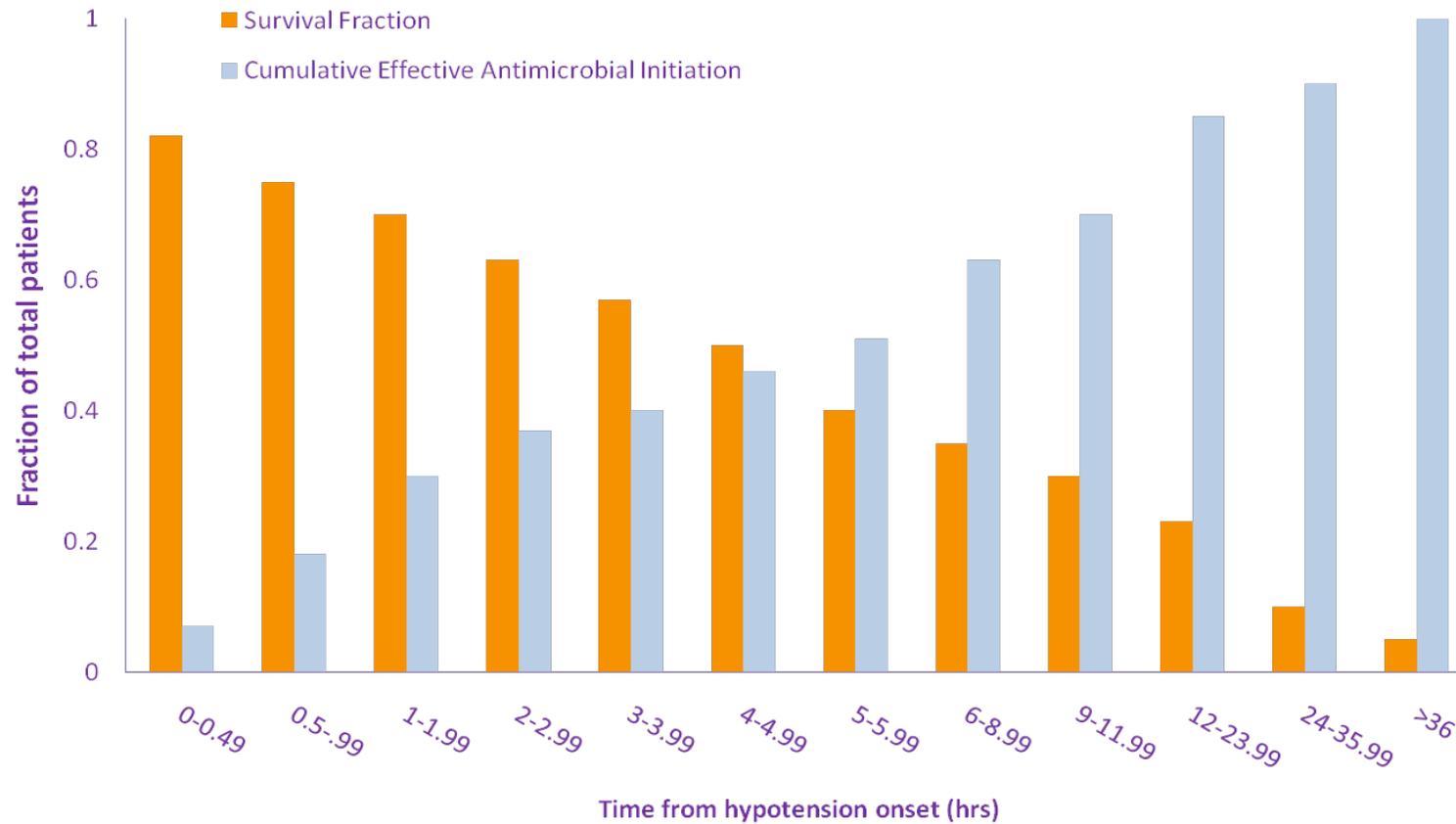
Infection by bacteria is the main cause of sepsis



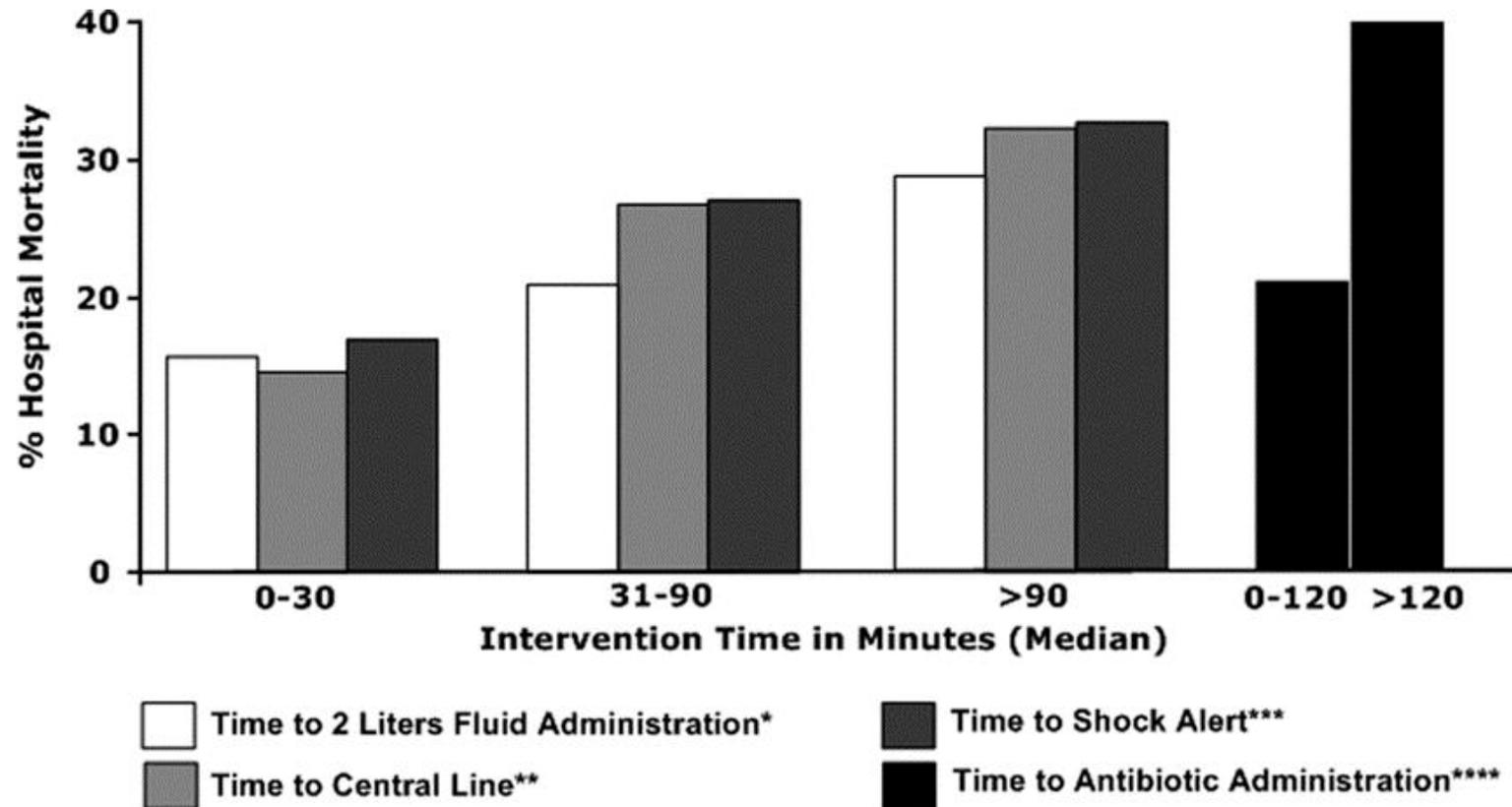
Difficulties in Diagnosis and Treating Sepsis in the Emergency Department

- Scoring systems and commonly available diagnostic tools provide limited value in determining which patients will have a poor outcome.
- Initial vital signs can be incomplete, an accurate core temperature can be lacking.
- These limitations often result in the delayed diagnosis of sepsis which in turn delays treatment, increases hospital length-of-stay, increases costs and leads to increased preventable mortality.

Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock



Failure to Intervene Quickly Can Be Fatal



**Sepsis can be defined by SIRS
with a bacterial origin**



What is sepsis?

Whole Body Inflammatory State triggered by Infection

Systemic Inflammatory Response Syndrome (SIRS)

Systemic inflammatory response to a variety of severe clinical insults, manifested by two or more of the following:

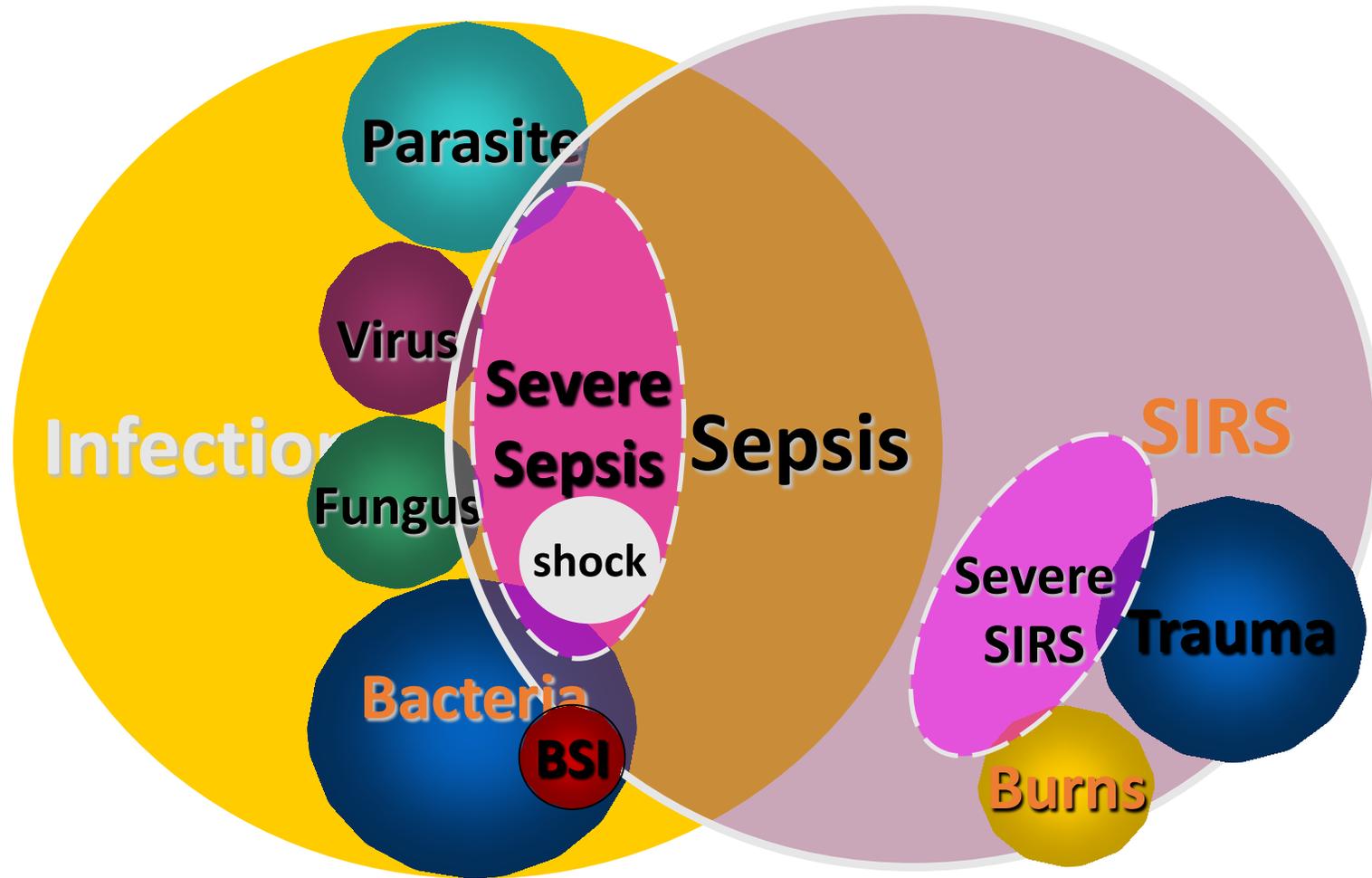
- Temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$
- Heart rate >90 beats/min
- Respiratory rate >20 breaths/min or $\text{PaCO}_2 <32$ mm Hg
- WBC $>12,000/\text{mm}^3$, $<4000/\text{mm}^3$, or $>10\%$ immature (band) forms

ACCP/SCCM Consensus Statement. Chest. 1992;101:1644-1655.

Sepsis: ACCP/SCCM definition

- Sepsis
 - Systemic response to infection – i.e., confirmed or suspected infection plus ≥ 2 SIRS criteria
 - Severe Sepsis
 - Sepsis associated with organ dysfunction, hypoperfusion, or hypotension
- Septic Shock
 - Severe Sepsis that cannot be resuscitated or stabilized with IV fluids alone

Sepsis Category



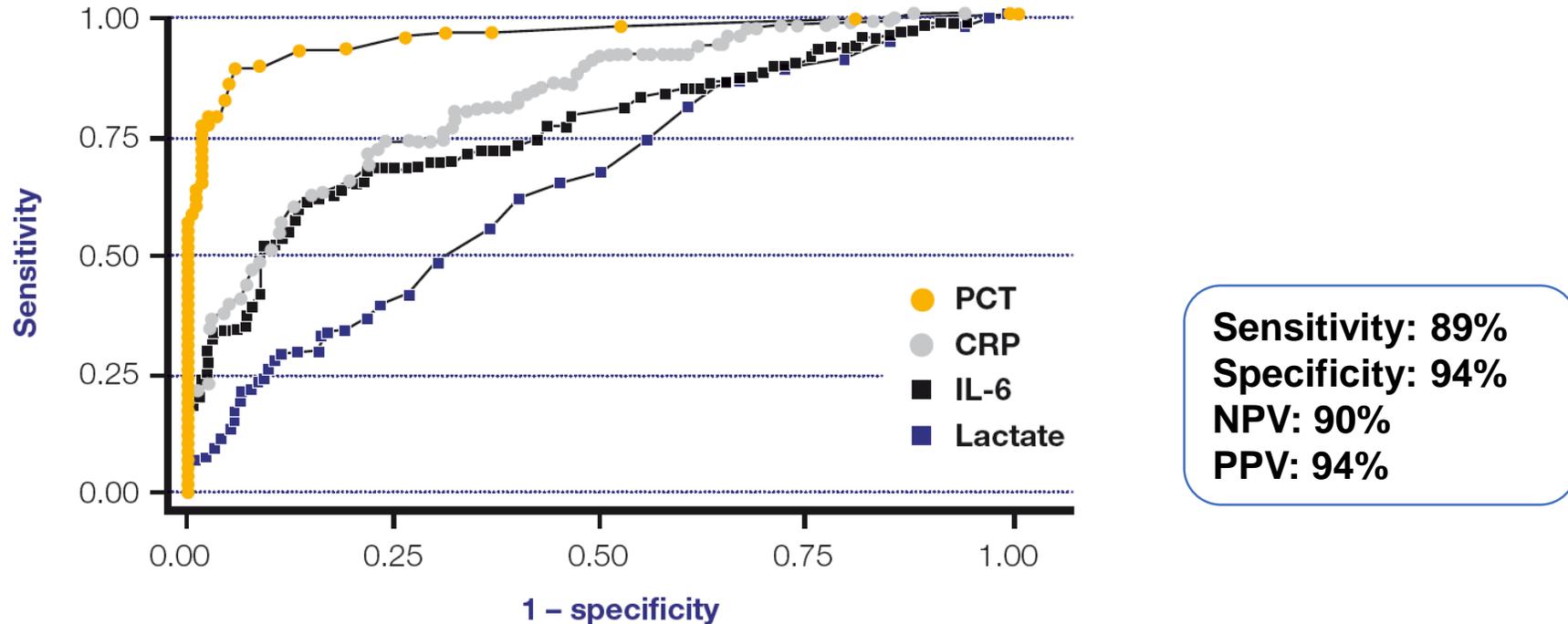
Several biomarkers can be used to diagnose sepsis



BENEFITS AND LIMITATIONS OF OTHER SEPSIS DIAGNOSTIC TOOLS

Microbiology (Blood Culture)		Standard of care, time consuming
Imaging (X-Ray, Hr-CT)		Availability, costs, variability of source detection
Molecular Biological Testing		Availability, costs, time consuming
Biopsy		Invasive, relatively expensive
Biomarker Testing (PCT)		Easy to measure, not invasive, relatively inexpensive
C-Reactive Protein (CRP)		Slow kinetics, suppressed by corticosteroids, relatively inexpensive

PCT is superior to other biomarkers used in sepsis



- PCT levels accurately differentiate sepsis from noninfectious inflammation*
- PCT has been demonstrated to be the best marker for differentiating patients with sepsis from those with systemic inflammatory reaction not related to infectious cause

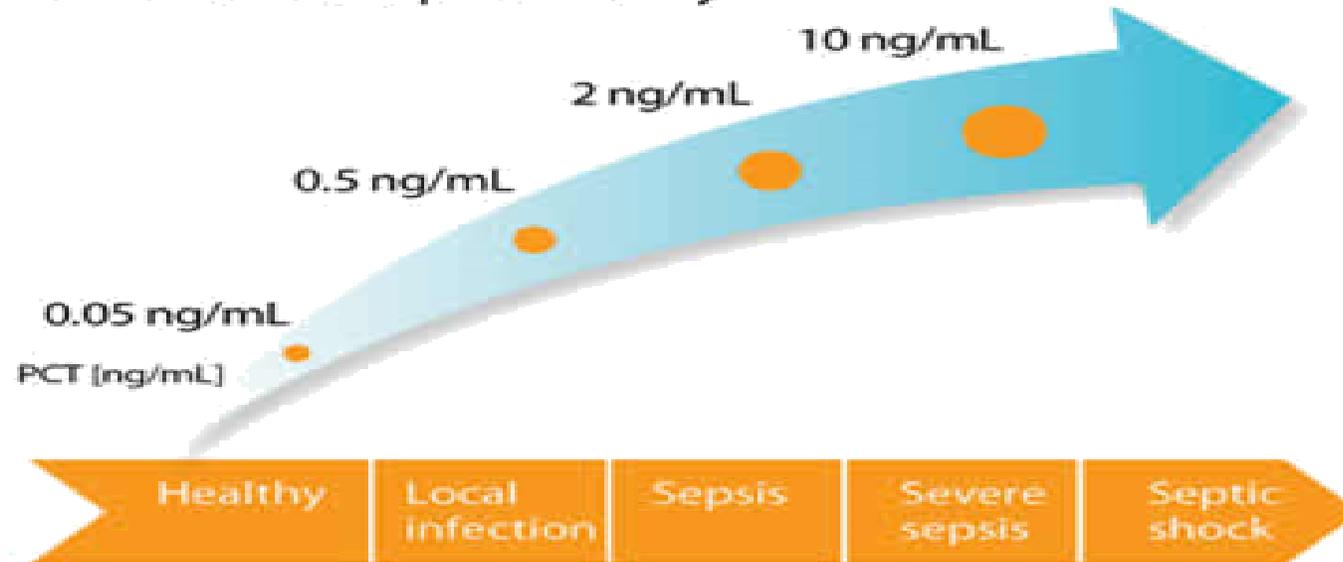
Simon L. et al. Clin Infect Dis. 2004; 39:206-217.

Procalcitonin (PCT) test is currently the best markers for sepsis diagnosis



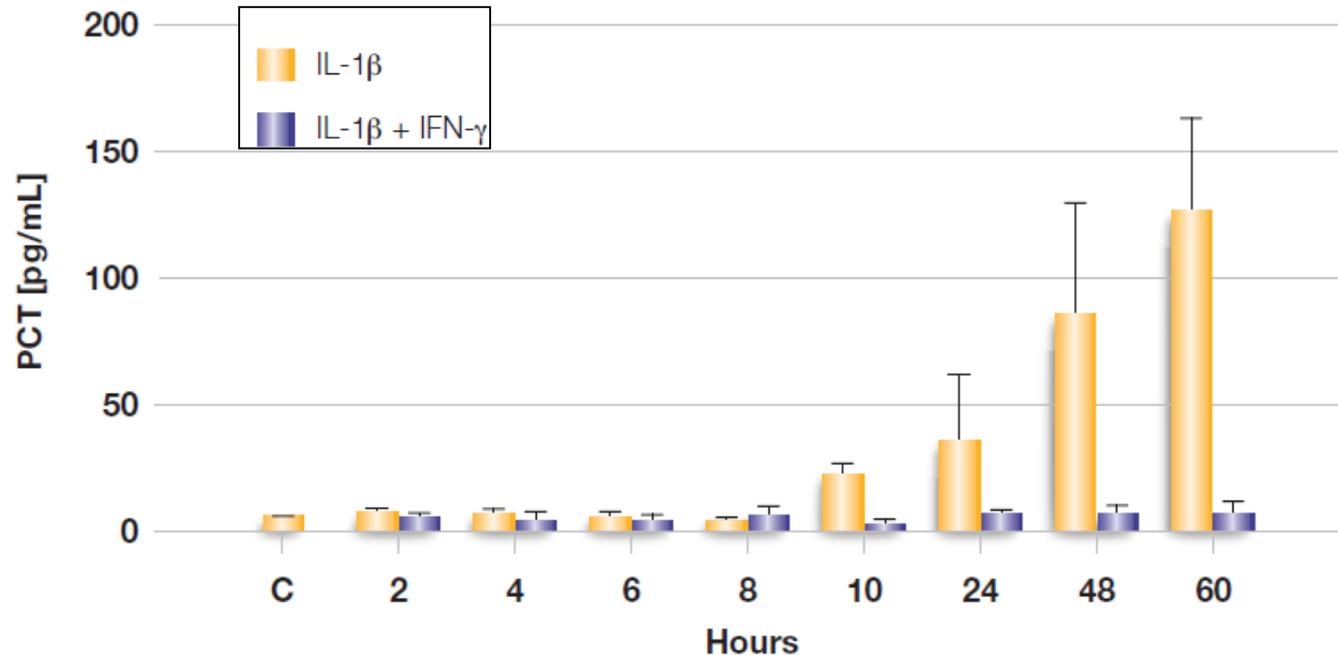
The level of PCT can predict the severity of sepsis

Procalcitonin (PCT) values rise in relation to sepsis severity.



- In critically ill patients, **PCT levels** elevate in correlation to the severity of bacterial infection.
- **In healthy people**, PCT concentration are found below 0.05 ng/ml.
- **Concentrations exceeding 0.5 ng/ml** can be interpreted as abnormal.

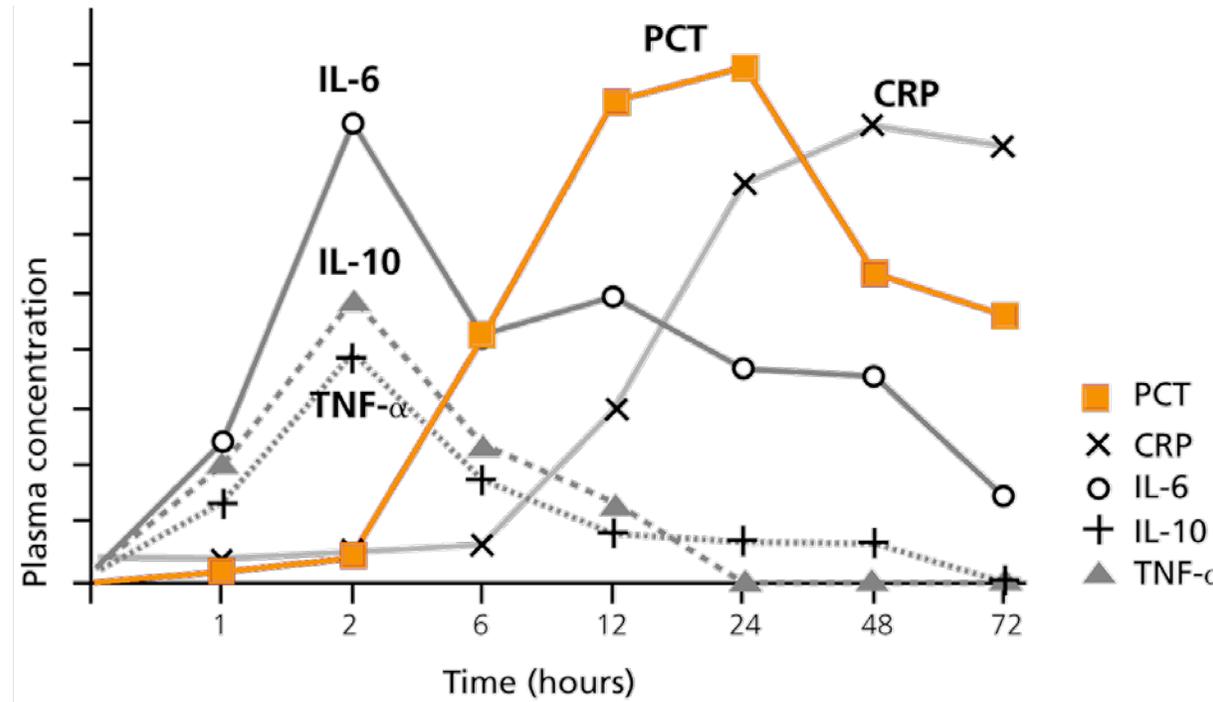
Induction and release of PCT is specific to bacterial infection



- IFN- γ blocks the PCT production.
- IFN- γ produced during viral infection could block the production of PCT.

Adapted from Christ-Crain et al. 2005

PCT KINETICS PROVIDE IMPORTANT INFORMATION ON PROGNOSIS OF SEPSIS PATIENTS

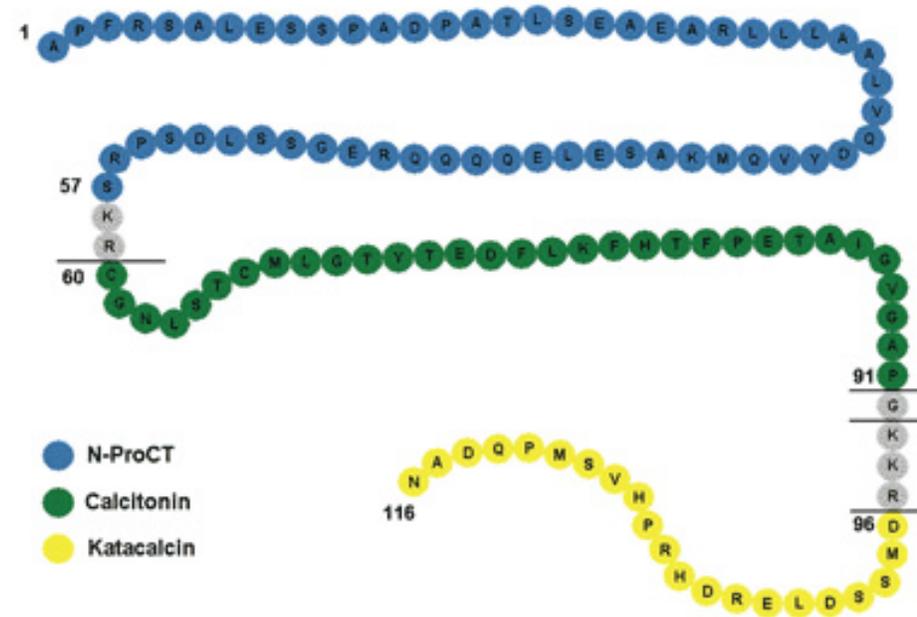


- Clinical symptoms alone are often insufficient for early and accurate diagnosis.
- PCT levels, can be observed within 3-6 hours after an infectious challenge with a peak up to 1000 ng/ml after 6-12 hrs. Half-life: approximately 24hrs
- Specific to bacterial origin of infection and reflects the severity of the infection

What is PCT?

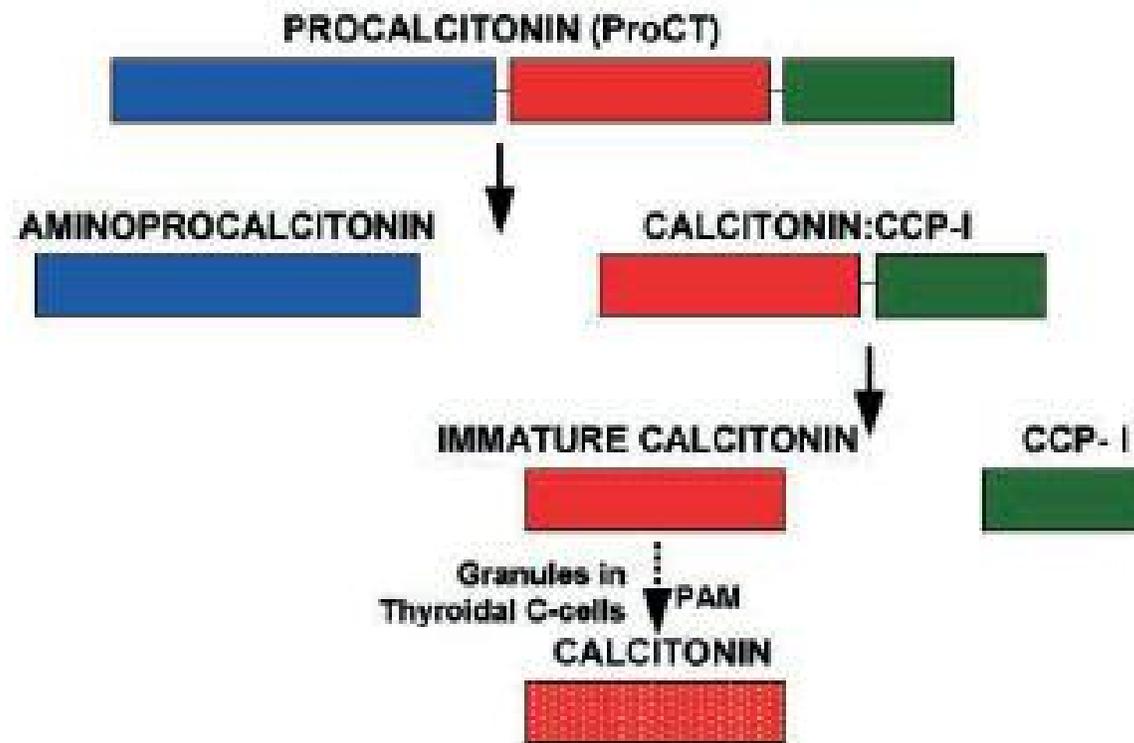


Procalcitonin: A biomarker for severe bacterial infection and sepsis

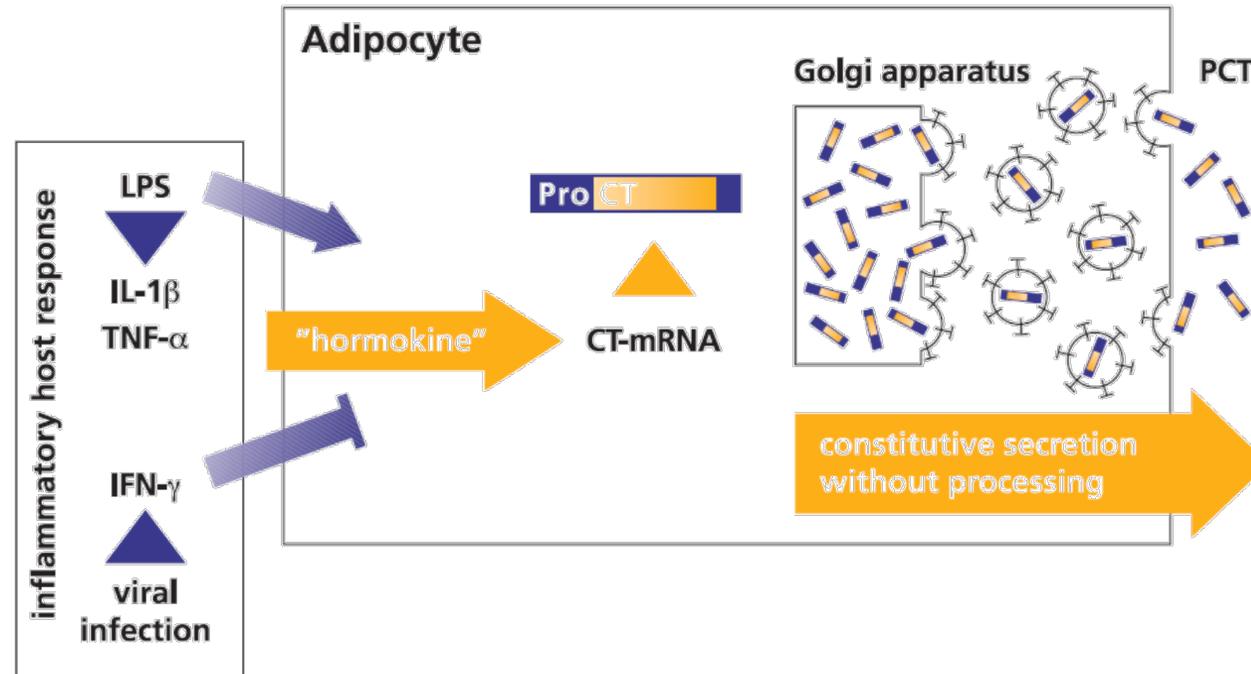


- **Simple blood test** specific for bacterial infection
- During severe bacterial infections and sepsis, **blood levels rise rapidly** (up to x100K)-no elevation from viral infections
- Is the **Standard of Care** for much of Europe in the management of infection and sepsis

Procalcitonin: normally an intermediate product in the synthesis of calcitonin



Procalcitonin-presence of bacterial infection stimulates PCT production



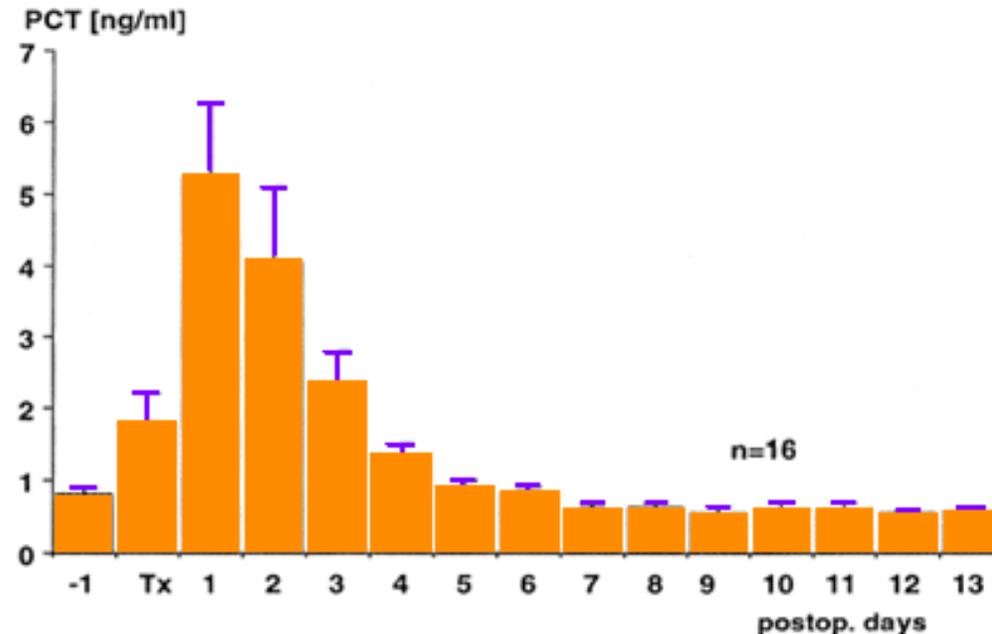
Alternative synthesis of PCT

- Bacterial toxins (gram+/-) and cytokines stimulate production of PCT in all parenchymal tissues
- PCT is immediately released into bloodstream
- This process can be blocked during viral infections

**Not only sepsis diagnosis,
diagnosis of bacterial cause of
other conditions can be determined
by PCT test**

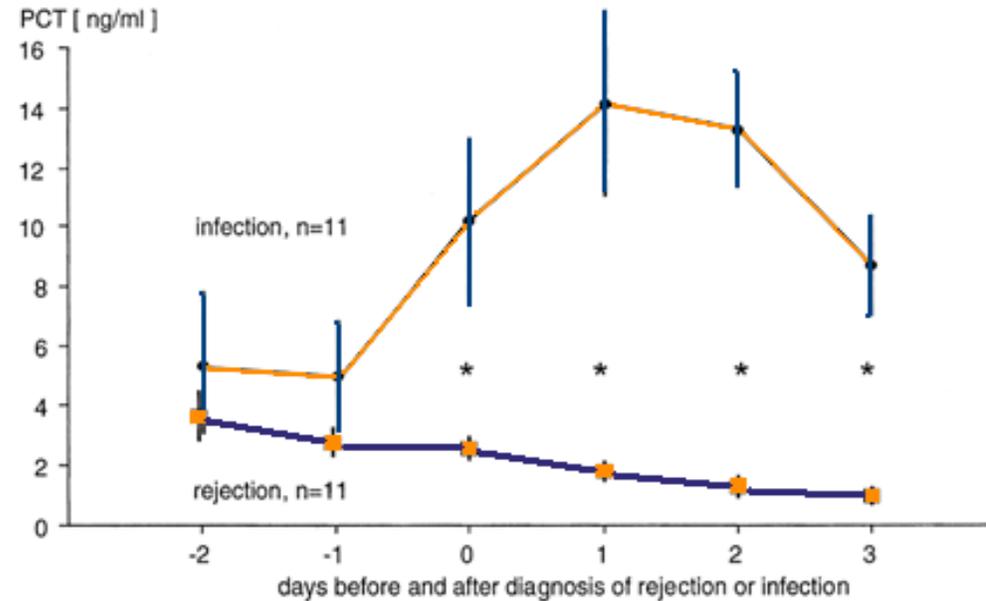


Adding PCT test improves the accuracy of clinical diagnosis of infection post organ transplant



PCT plasma concentrations in 16 patients without postoperative complications after Liver-Transplantation, *Tx*: day of transplantation.

Adding PCT test improves the accuracy of the early clinical diagnosis of infection post organ transplant

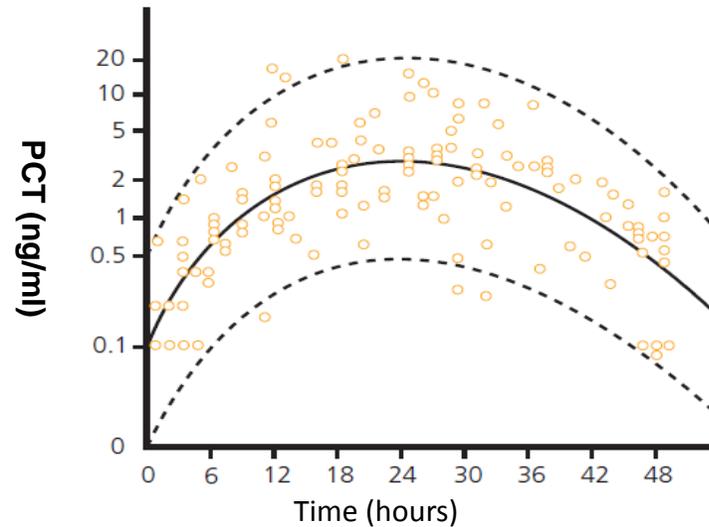


PCT plasma concentrations in infection and rejection (n = 11), *day 0*: day of diagnosis

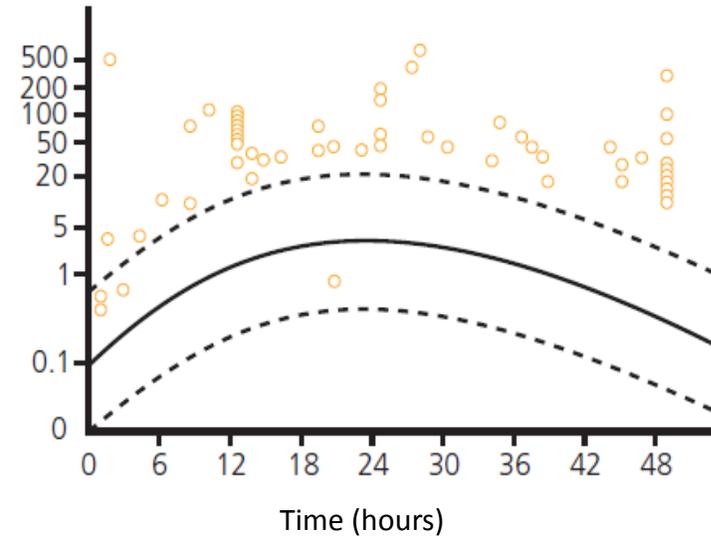
PCT used in early **detection** of infection after liver transplantation-**differentiation** from rejection

ADDING PCT RESULTS TO CLINICAL ASSESSMENT IMPROVES THE ACCURACY OF THE EARLY CLINICAL DIAGNOSIS OF SEPSIS IN NEONATES

UNINFECTED



INFECTED

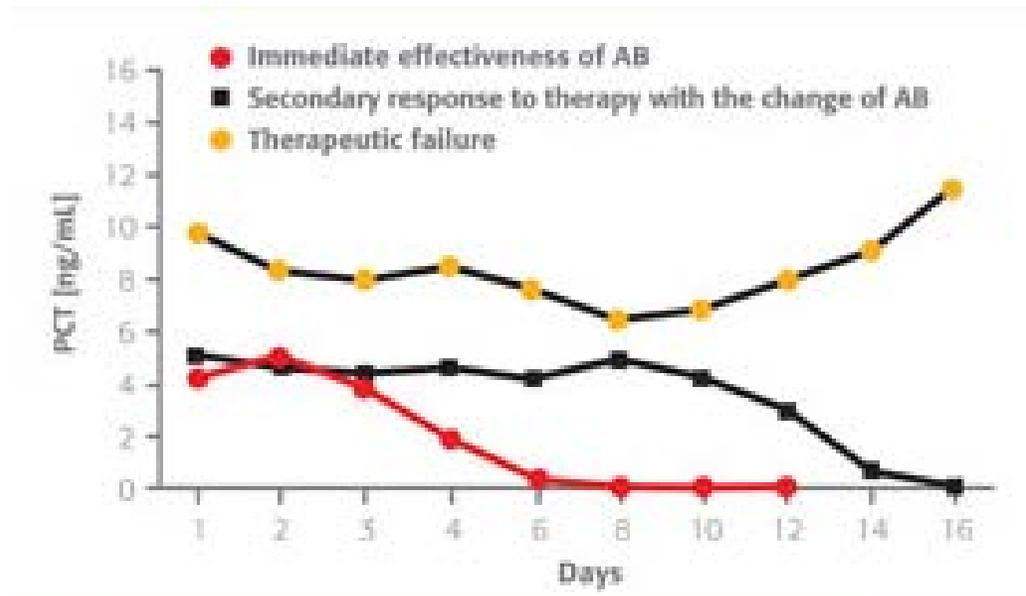


- In early onset neonatal sepsis **PCT** provides a **clear differentiation** of infected from uninfected neonates in the first **2 days** of life
- In neonates the **PCT** values are physiologically and in relation to their age increased.
- A **peak** is reached at 24 h with median at 2 ng/ml and 95% at 20 ng/ml.
- After 3 days **the normal values** for children and adults apply.

**Prescription decision of
antibiotics can be determined
by PCT test**



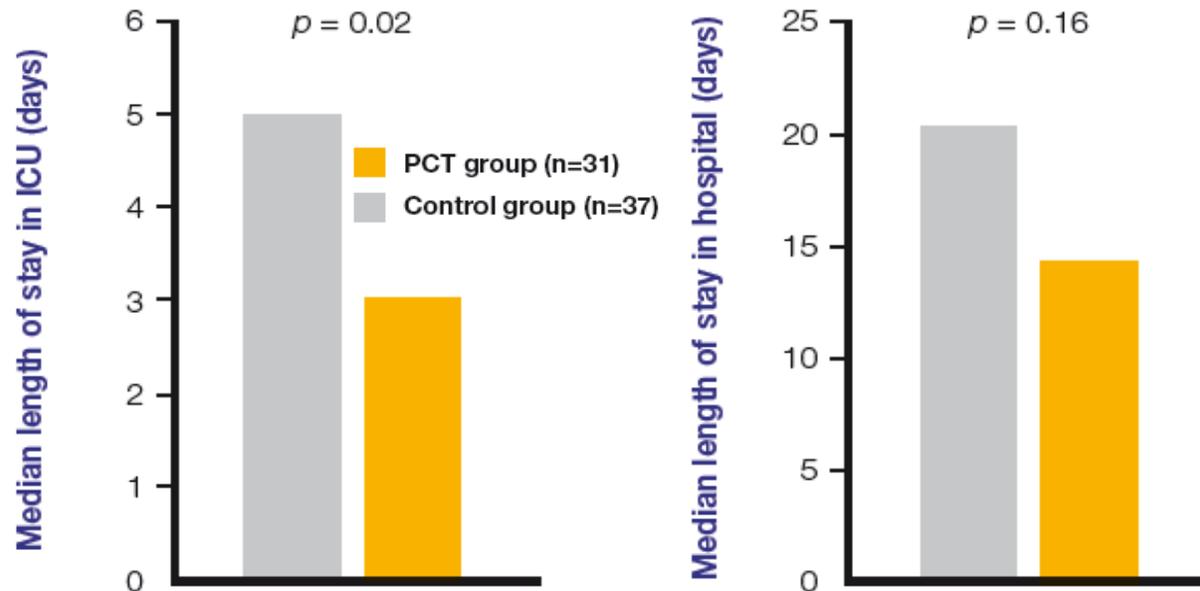
PCT provides a clearer picture of the patient's response to antibiotic treatment.



- **Decreasing PCT levels** in patients with sepsis indicate effective treatment of the underlying infection
- **Persistently elevated PCT levels** indicate a possible treatment failure
- **When integrated into the management of septic patients, PCT** can help clinicians to manage septic patients more efficiently

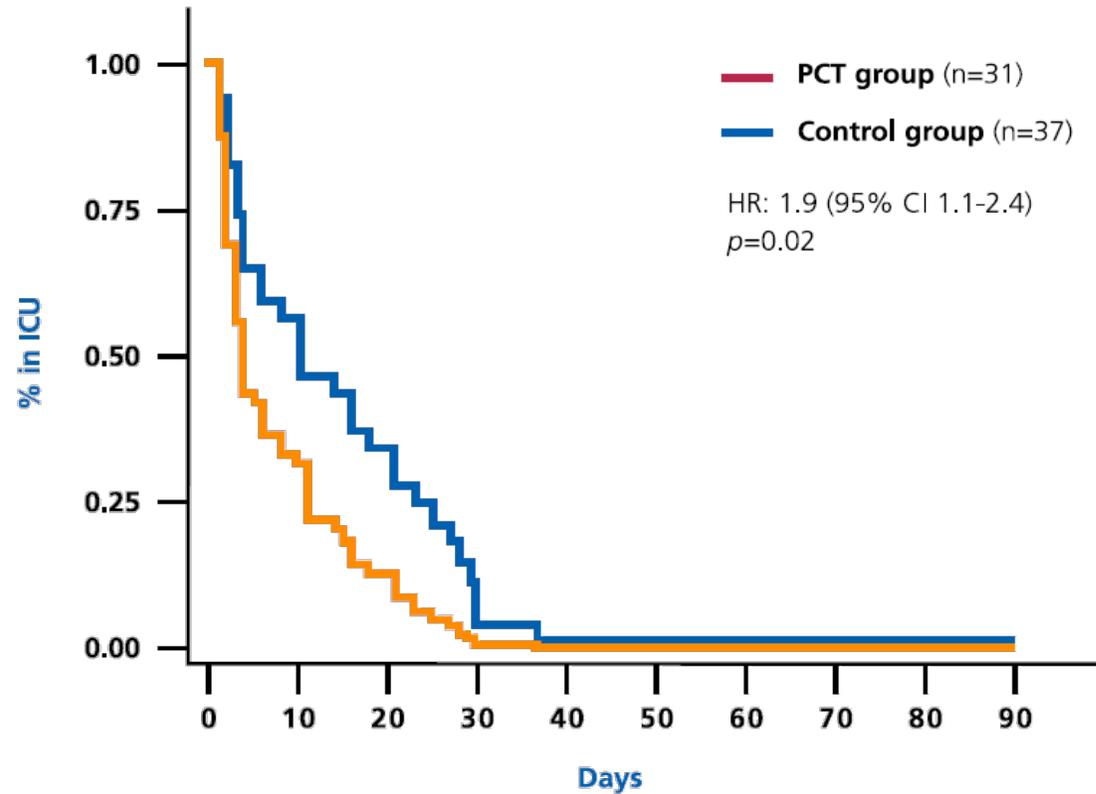
PCT guidance in antibiotic usage

Effects on length of stay



Effect of PCT-guided management in patients with sepsis on ICU length of stay

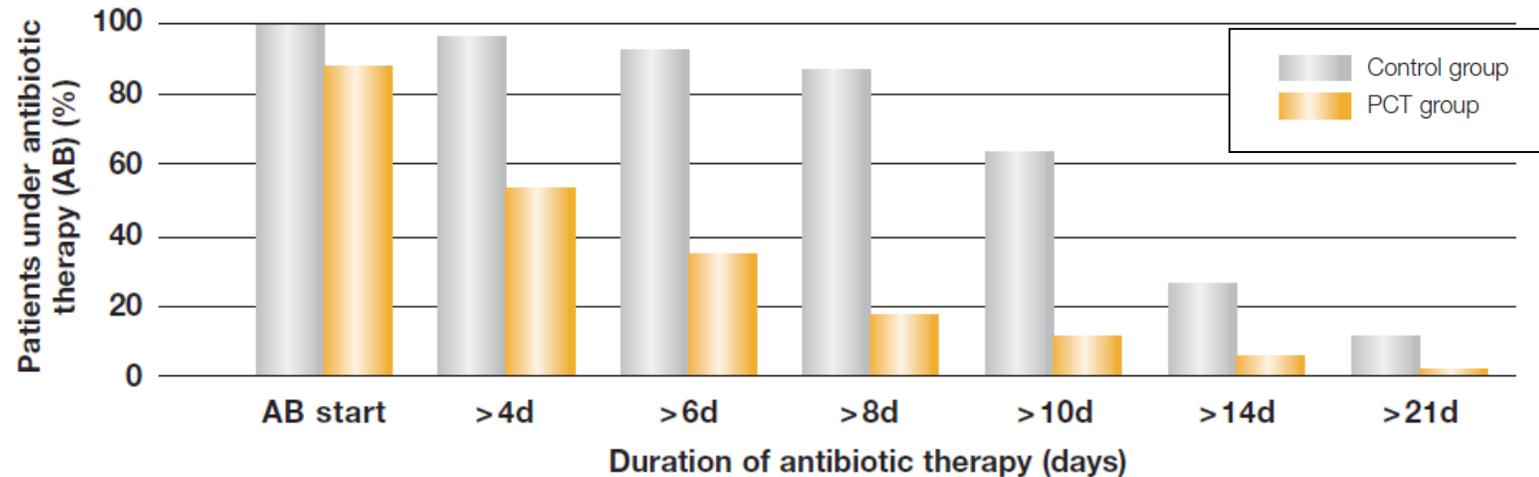
PCT Guidance on effect on length of ICU stay



Effect of PCT-guided management in patients with sepsis on ICU length of stay

PCT guidance in antibiotic usage shorten the time patients need to be on antibiotics

Duration of antibiotic therapy in the control group (n=151) and PCT group (n=151)



Tailoring of AB treatment using PCT to the individual patient needs safely led to a reduction of average treatment duration from 12 to 5 days with same outcome

ichroma α TM PCT



ichroma™ PCT

- ichroma™ PCT along with ichroma™ Reader is a fluorescence immunoassay for quantitative determination of PCT in human sample
- Whole blood, serum or plasma can be used as a sample. PCT testing with whole blood provides distinctive advantage in neonatal & general ICU, or emergency department for diagnosing sepsis
- Provides quantitative result in only 12 minutes with small volume of sample
- ichroma™ PCT test allows diagnosis of sepsis & bacterial infection and helps prescription decision of antibiotics
- ichroma™ PCT test can be conducted with ichroma™ reader, ichroma™ SMART Single and ichroma™ SMART multi

ichroma™
SMART Multi



ichroma™
SMART Single

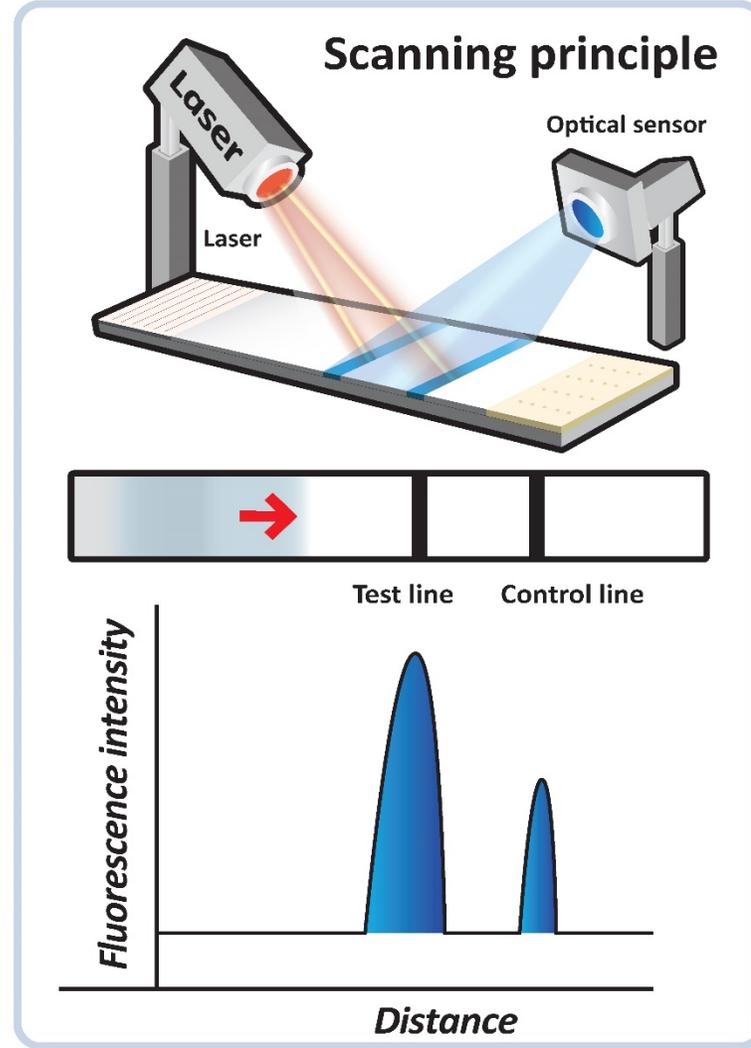
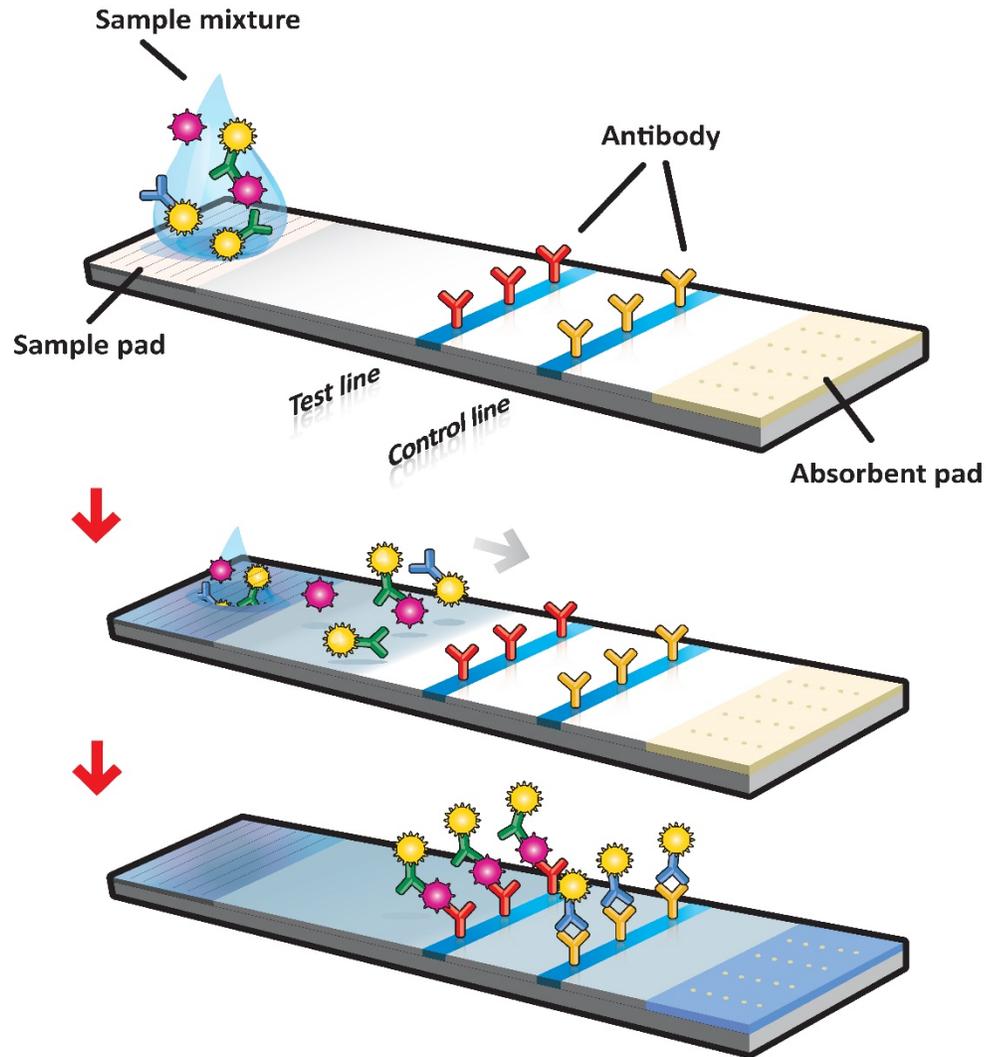


ichroma™



ichromaTM Technology

Lateral flow reaction



ichromaTM reader