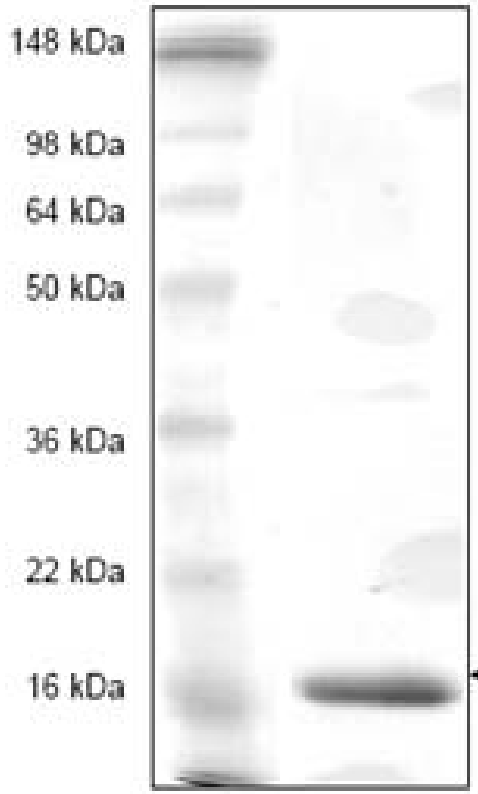
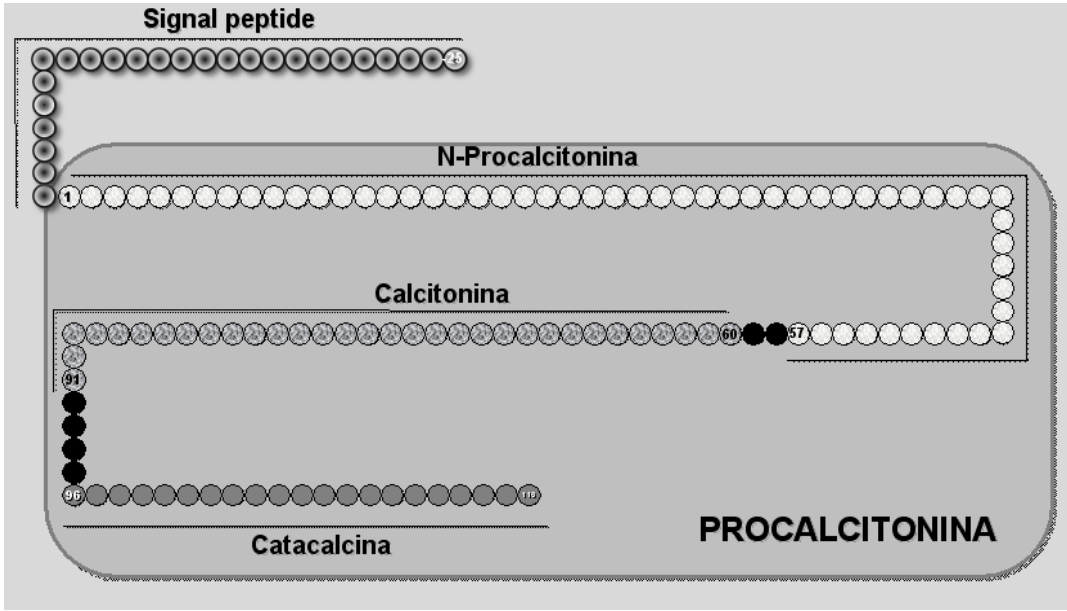
Assicot M, Gendrel D, Carsin H, Raymond J, Guilbaud J, Bohoun C. High serum procalcitonin concentrations in patients with sepsis and infection. Lancet 1993;341:515–8.





13 kDalton

Procalcitonin (PCT) was first described as a sepsis-induced protein detectable in the plasma of patients with sepsis and infection in the early 1990s [1].

Biochem. J. (1988) **256**, 245–250 (Printed in Great Britain)

Structural characterization of a high-molecular-mass form of calcitonin [procalcitonin-(60–116)-peptide] and its corresponding *N*-terminal flanking peptide [procalcitonin-(1–57)-peptide] in a human medullary thyroid carcinoma

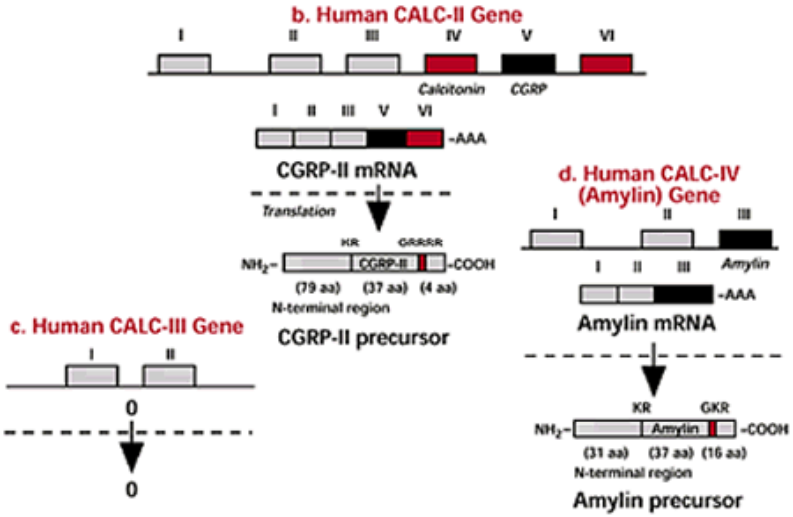
J. Michael CONLON,*§ Lars GRIMELIUS† and Lars THIM‡

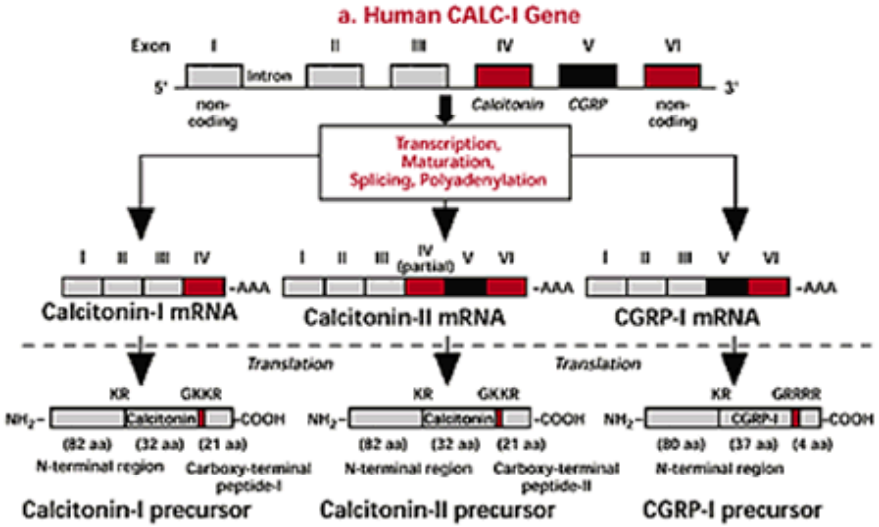
Table 2. Determination of the primary structures of procalcitonin-(1–36)-peptide, procalcitonin-(37–57)-peptide and procalcitonin (60–116)-peptide by automated Edman degradation

PE-Cys refers to the vinylpyridine derivative of cysteine. Residue 36 in procalcitonin-(1–36)-peptide was homoserine lactone, which was not quantified.

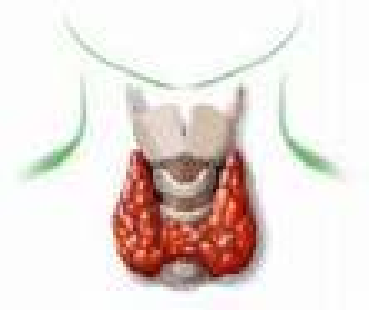
	Procalcitonin-(1–36)		Procalcitonin-(37–57)		Procalcitonin-(60–116)			Procalcitonin-(1–36)		Procalcitonin-(60–116)	
Cycle No.	Amino acid	Yield (pmol)	Amino acid	Yield (pmol)	Amino acid	Yield (nmol)	Cycle no.	Amino acid	Yield (pmol)	Amino acid	Yield (nmol)
1	Ala	1943	Lys	591	PE-Cys	6.7	29	Leu	93	Val	1.6
2	Pro	1767	Ala	873	Gly	7.8	30	Val	73	Gly	1.4
3	Phe	1877	Ser	279	Asn	10.0	31	Gln	52	Ala	1.6
4	Arg	200	Glu	581	Leu	10.5	32	Asp	31	Pro	1.4
5	Ser	607	Leu	610	Ser	3.5	33	Tyr	41	Gly	1.2
6	Ala	1275	Glu	622	Thr	1.8	34	Val	47	Lys	1.8
7	Leu	1207	Gln	412	PE-Cys	4.7	35	Gln	30	Lys	2.4
8	Glu	981	Glu	548	Met	7.0	36			Arg	1.1
9	Ser	356	Gln	378	Leu	6.6	37			Asp	1.1
10	Ser	351	Glu	441	Gly	4.5	38			Met	1.0
11	Pro	509	Arg	204	Thr	1.2	39			Ser	0.4
12	Ala	612	Glu	387	Tyr	4.9	40			Ser	0.4
13	Asp	390	Gly	256	Thr	1.4	41			Asp	0.6
14	Pro	403	Ser	121	Gln	4.3	42			Leu	0.5
15	Ala	409	Ser	131	Asp	4.6	43			Glu	0.4
16	Thr	84	Leu	163	Phe	4.8	44			Arg	0.4
17	Leu	314	Asp	187	Asn	3.4	45			Asp	0.5
18	Ser	105	Ser	61	Lys	5.0	46			His	0.2
19	Glu	206	Pro	99	Phe	3.9	47			Arg	0.4
20	Asp	137	Arg	66	His	2.2	48			Pro	0.3
21	Glu	145	Ser	33	Thr	0.8	49			His	0.3
22	Ala	180			Phe	2.7	50			Val	0.2
23	Arg	92			Pro	2.1	51			Ser	0.1
24	Leu	118			Gln	2.1	52			Met	0.2
25	Leu	225			Thr	0.6	53			Pro	0.2
26	Leu	135			Ala	1.9	54			Gln	0.2
27	Ala	96			Ile	1.6	55			Asn	0.03
28	Ala	123			Gly	1.4	56			Ala	0.1
							57			Asn	0.03

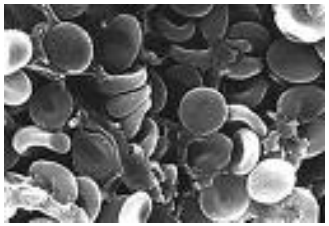
Four genes with nucleotide sequence homologies corresponding to *calcitonin* are known. These genes are collectively called the "***calcitonin gene family***", but they do not all produce the peptide hormone calcitonin. The "**CALC-1**" gene is responsible for the production of calcitonin and its precursor protein, procalcitonin. This gene may be responsible for the generation of inflammatory induced PCT.

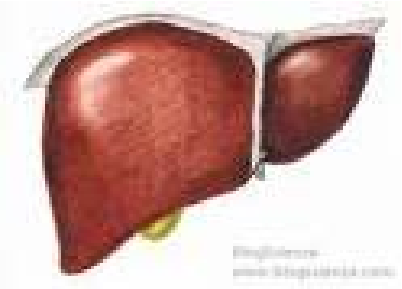




The **CALC-II** gene has a similar structure to CALC-I, but sequence analysis indicates that the synthesis of calcitonin mRNA is unlikely codes only for a precursor and differs from CGRP-I in 3 aminoacids). The **CALC-III** gene is a untranscribed pseudogene. The **CALC-IV gene** contains only 3 exons and codes for amylin (a functional opponent of insulin).





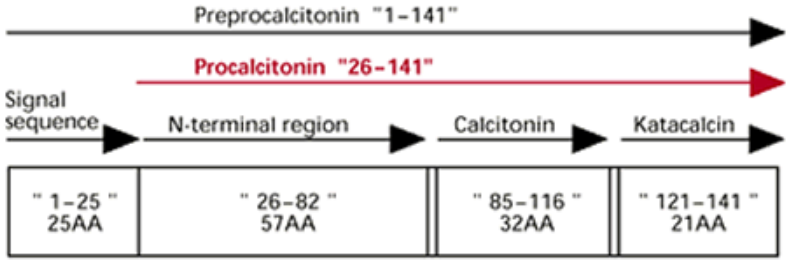


Tyroid (C cells) →

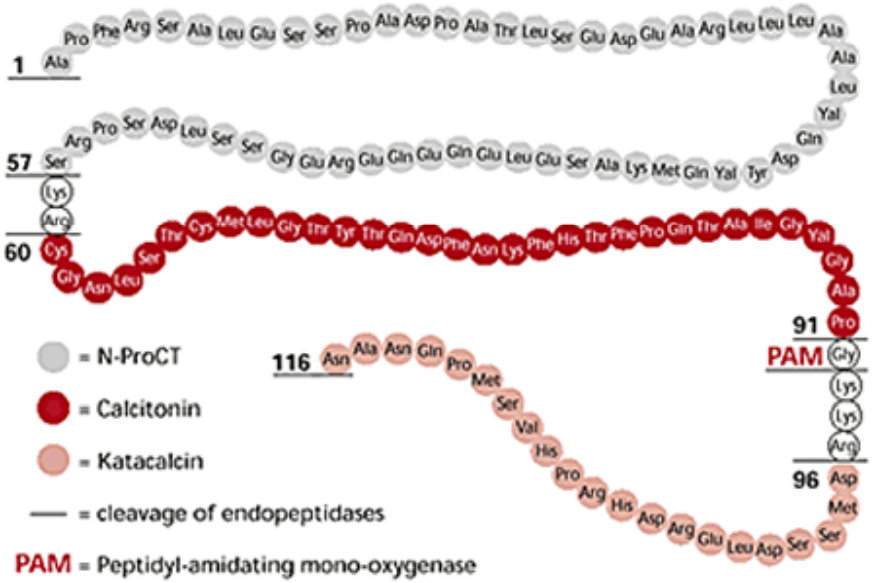
Leucocytes? →

Liver (histiocytes) →

Procalcitonin



Procalcitonin (PCT) is a 116 amino acid protein with a sequence identical to that of the prohormone of calcitonin (32 amino acids). Under normal metabolic conditions, hormonally active *calcitonin* is produced and secreted in the C-cells of the thyroid gland after specific intracellular proteolytic procession of the prohormone procalcitonin.

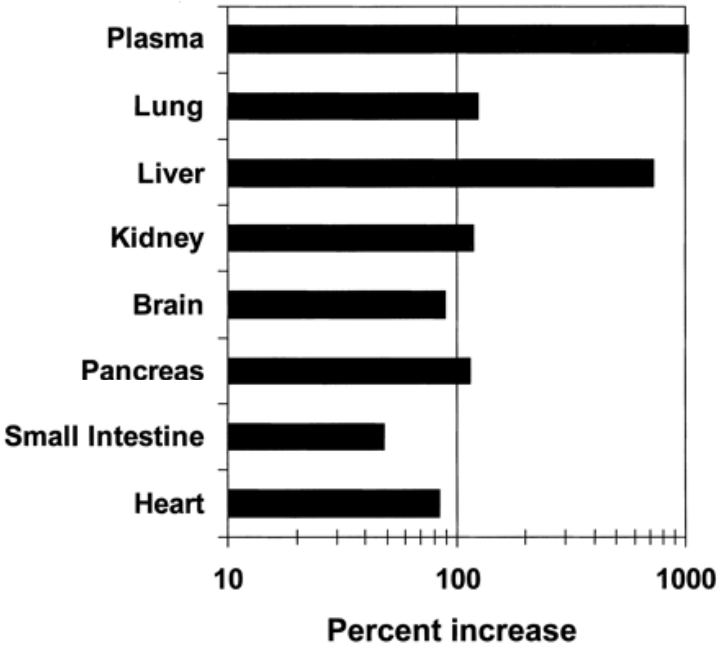


In **severe bacterial infections and sepsis**, however, *intact procalcitonin* is found in blood. Current research indicates that the orgin of procalcitonin in these conditions is **extrathyroidal**.

(*J Clin Endocrinol Metab* 86: 396–404, 2001)

Ubiquitous Expression of the Calcitonin-I Gene in Multiple Tissues in Response to Sepsis*

BEAT MÜLLER, JON C. WHITE, ERIC S. NYLÉN, RICHARD H. SNIDER, KENNETH L. BECKER, AND JOEL F. HABENER†



Increase of plasma and tissue content in sepsis.

Homologies to human preprocalcitonin sequence:	
Rat	74,5 %
Mouse	73,8 %
Sheep	60,3 %
Chicken	45,4 %
Salmon	42,6 %

The large degree of conservation of the gene in various species indicates that it may have biologically important functions…


European Journal of Internal Medicine 22 (2011) 460–465

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Review article

Inflammatory biomarkers for the diagnosis, monitoring and follow-up of community-acquired pneumonia: Clinical evidence and perspectives

Giuseppe Lippi [a,*], Tiziana Meschi [b], Gianfranco Cervellin [c]

Various groups have attempted to uncover specific biological functions of PCT, especially immunologic functions.

- PCT has some effect on plasma calcium levels
- PCT may function as a co-factor capable of modulating various effects during endotoxin shock
- In vitro experiments have shown that it has a weak influence on cytokine expression
- Low or moderately elevated PCT concentrations significantly suppressed TNF-α and IFN-γ-stimulated production of cDNA of iNOS in smooth muscle cells, but not high concentrations.

Review article

Pathobiochemistry and clinical use of procalcitonin

Michael Meisner*

Clinica Chimica Acta 323 (2002) 17–29

- Two groups of receptors of the calcitonin gene family, calcitonin receptors (CR) and calcitonin receptor-like receptors (CRLR), may play a role in mediating PCT-related functions.

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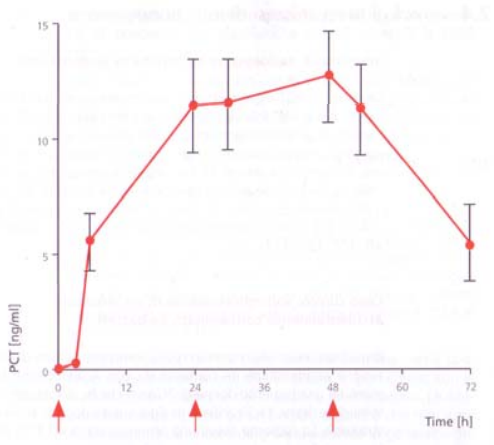
- Molecola stabile (in vivo $t_{1/2}$ 24 ore)
- In seguito a stimolo raggiunge il picco in 3-4 ore ed il plateau in 6-12 ore
- Dopo la fine dello stimolo persiste in circolo per circa 24 ore



- Non sono richiesti particolari accorgimenti per il prelievo e la conservazione del campione
- I valori di PCT sono fisiologicamente aumentati nei primi due giorni di vita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Review article

Inflammatory biomarkers for the diagnosis, monitoring and follow-up of community-acquired pneumonia: Clinical evidence and perspectives

Giuseppe Lippi [a,*], Tiziana Meschi [b], Gianfranco Cervellin [c]

CATABOLISM

- Like other plasma proteins, PCT is probably degraded by proteolysis.
- Renal excretion of PCT plays a minor role. Clinical data have shown that PCT does not accumulate in cases of severe renal dysfunction. The fall in plasma PCT concentrations observed in patients with renal dysfunction does not differ significantly from that of subjects with normal renal function.

Scandinavian Journal of Clinical & Laboratory Investigation
Vol. 69, No. 6, October 2009, 703–707

informa
healthcare

ORIGINAL ARTICLE

Procalcitonin values after dialysis is closely related to type of dialysis membrane

MARTINA MONTAGNANA[1], GIUSEPPE LIPPI[1], NICOLA TESSITORE[2], GIAN LUCA SALVAGNO[1], ELISA DANESE[1], GIOVANNI TARGHER[3], ANTONIO LUPO[2] & GIAN CESARE GUIDI[1]

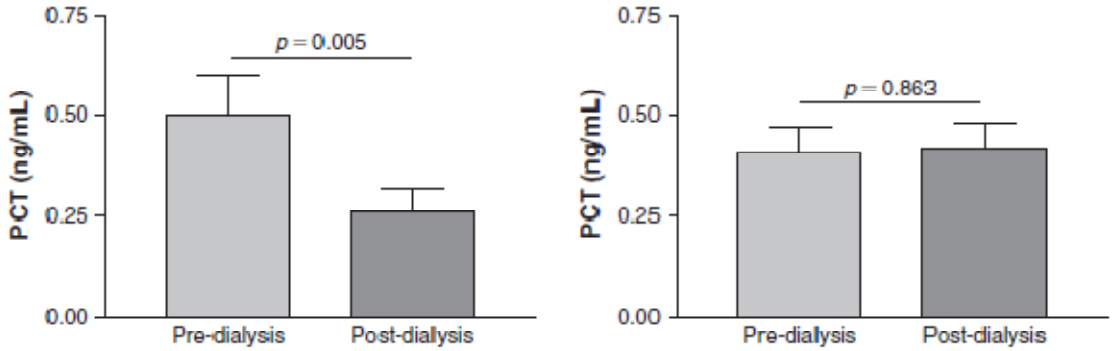


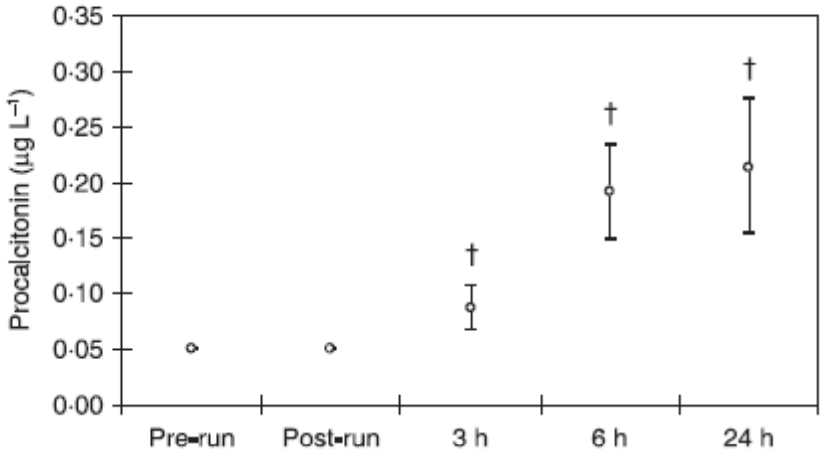
Figure 1. CRP and PCT values in HD patients treated with high-flux (A) and low-flux (B) membranes. Pre- and post-HD measurements were compared using the Wilcoxon matched-pairs test.

DOI: 10.1111/j.1365-2362.2008.02015.x

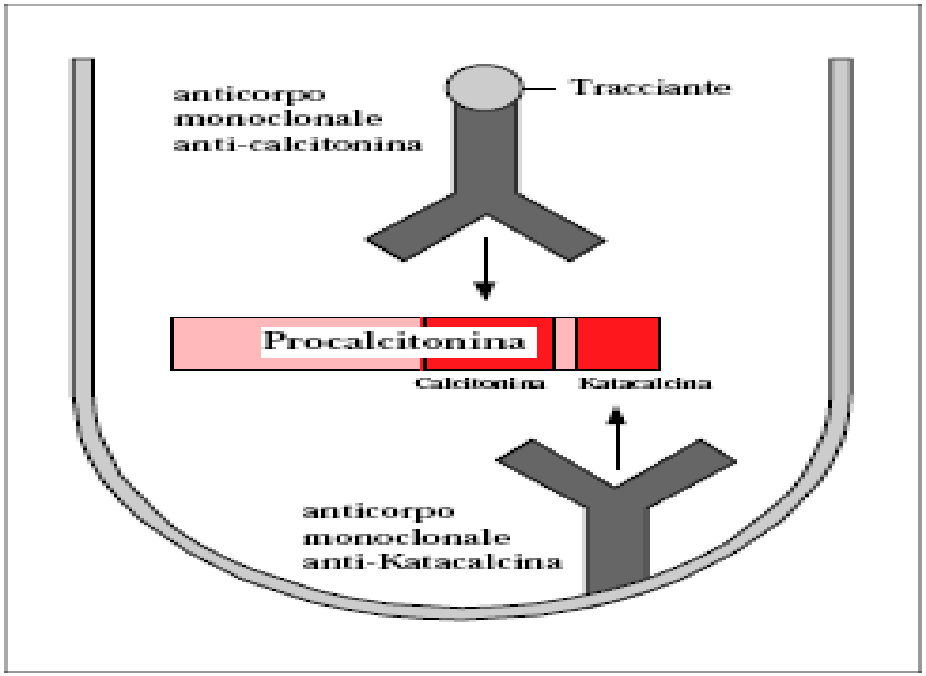
Acute influence of aerobic physical exercise on procalcitonin

G. Lippi,
University of Verona, Italy

Eur J Clin Invest 2008; 38 (10): 784–785



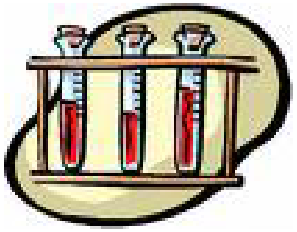
Dosaggio immunoluminometrico (ILMA) - LUMItestPCT



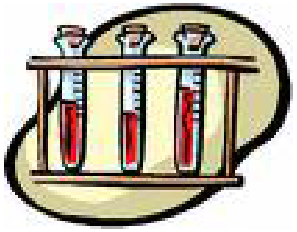
LUMItest PCT è un dosaggio immunoluminometrico (ILMA) quantitativo utilizzato per dosare quantitativamente la PCT nel siero e nel plasma umano. Due anticorpi monoclonali antigene- specifici che legano la PCT (antigene) in due siti leganti differenti (i segmenti della calcitonina e della catakalcina) sono aggiunti in eccesso. Uno di questi anticorpi è marcato con una sostanza luminescente (tracciante) mentre l'altro è fissato sulla parete all'interno della provetta (sistema coated tube).

Durante l'incubazione, entrambi gli anticorpi reagiscono con le molecole di PCT del campione per dare un "complesso sandwich". Il risultato è che l'anticorpo marcato con la sostanza luminescente si lega sulla superficie interna del tubo. A reazione completata, l'eccesso di tracciante viene rimosso totalmente dall'interno del tubo.

Successivamente si determina la quantità di tracciante rimasto sulle pareti all'interno del tubo di reazione misurando il segnale luminescente con un luminometro e con i reagenti LUMItest Basiskit. L'intensità del segnale luminescente (RLU) è direttamente proporzionale alla concentrazione di PCT nel campione. Si costruisce una curva utilizzando standard a concentrazione nota di antigene (standard calibrati contro PCT umana intatta sintetica). Le concentrazioni incognite della PCT contenuta nel siero o nel plasma dei pazienti possono essere determinate per estrapolazione dalla curva.



Ditta	Immunodosaggio	Strumentazione	Range di misura	Sensibilità analitica	Sensibilità funzionale	TAT
BRAHMS GmbH	BRAHMS PCT Sensitive assay	Kriptor	0.02-50 ng/ml	0.02 ng/mL	0.06 ng/mL	19 min
Siemens	BRAHMS PCT	Advia Centaur	0.05-75.0 ng/ml	-	0.05 ng/ml	26-29 min
Roche	BRAHMS PCT	Elecsys/E170	0.06-100 ng/ml	0.02 ng/ml	0.06 ng/ml	18 min
Biomerieux	BRAHMS PCT	Vidas	0.09-200 ng/ml	0.05 ng/mL	0.09 ng/ml	20 min
DiaSorin	BRAHMS PCT	Liaison	0.1-500 ng/ml	0.04 ng/mL	0.3 ng/mL	20 min
BRAHMS GmbH	BRAHMS PCT-Q	Manuale	Risultati semiquantitativi	0.50 ng/mL	0.50 ng/mL	30 min



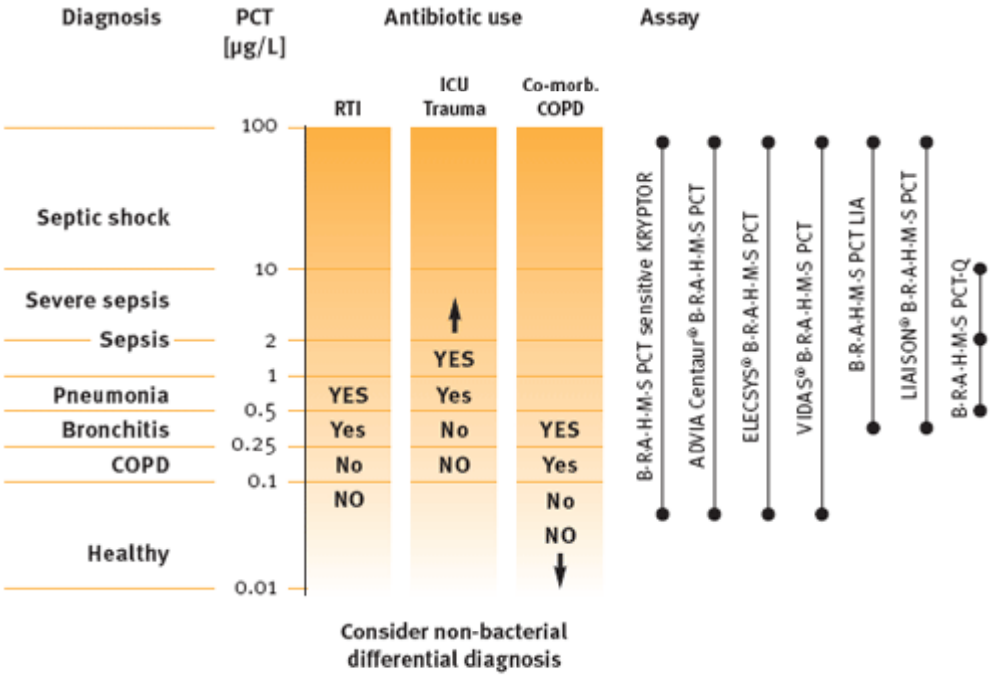
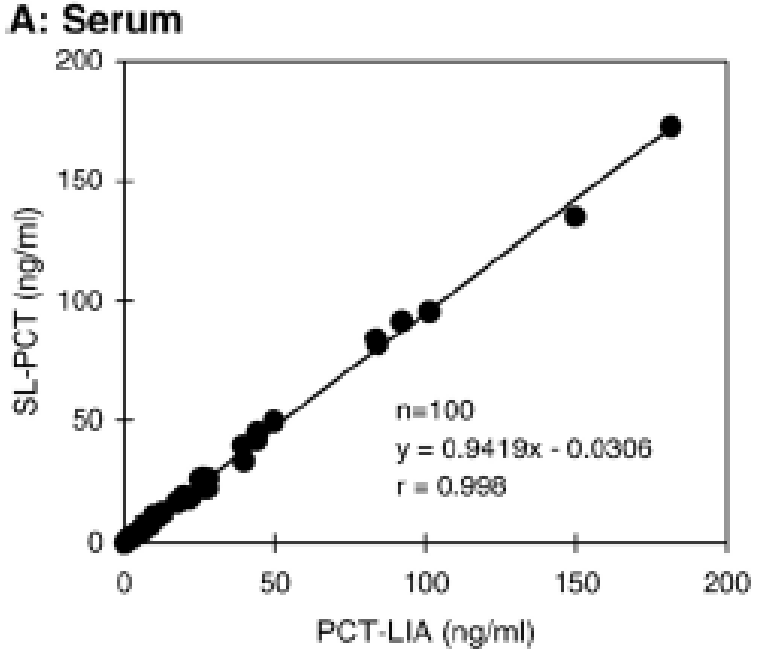


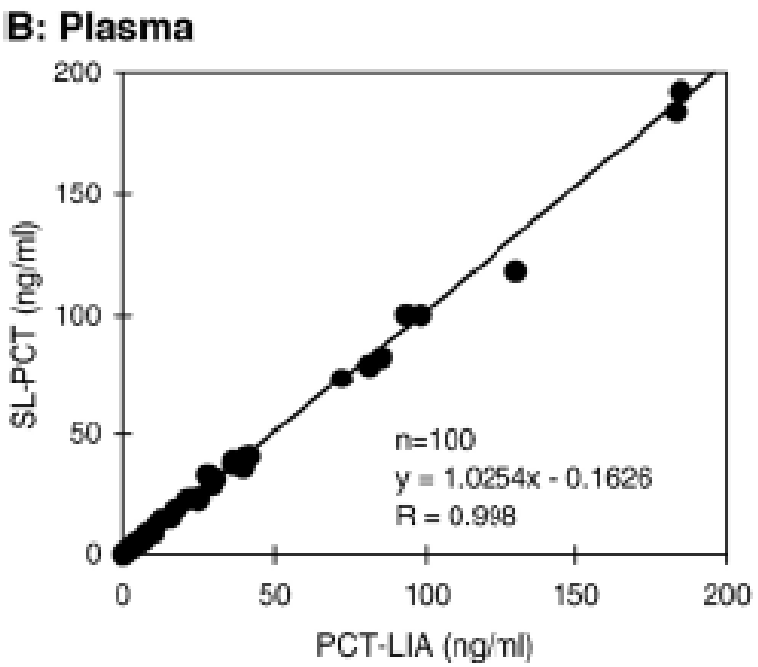
Fig.: Application of available PCT assays for various clinical settings *(adapted from Christ-Crain & Müller (2005)*

Determination of procalcitonin concentration using the SphereLight 180 clinical auto-analyzer

Hiroyuki Yamada *, Shinjiro Matsuda, Yoshihiro Ushio, Kenji Nakamura, Shinzo Kobatake, Shinji Satomura, Shuji Matsuura

patients treated by antibiotic therapy. Interference by endogenous substances, anticoagulants, a glycolysis inhibition agent and drugs was not observed, and correlation studies with the PCT-LIA were highly significant without evidence of assay bias in both of serum and plasma studies.





Clinica Chimica Acta 388 (2008) 38–40

The stability of PCT in blood samples

- Unlike most cytokines, PCT is highly stable in collected blood samples.
- In vitro plasma PCT concentrations fall by approximately 12% at room temperature and by 6% at a temperature of 4C after 24-hr.
- PCT can be collected with routine laboratory specimens.
- The samples should be stored in a refrigerator or, if storage or transport times are prolonged or if any additional influence on the samples is to be avoided during the scope of the studies being implemented, deep frozen until required for analysis.
- Both the type of anticoagulation and the use of plasma or serum have no effect on PCT measurements.
- **However, a standardized collection technique, anticoagulation process and storage procedures should be used for each hospital in order to minimize any discrepancy in the values obtained.**