IL LABORATORIO ED IL PRONTO SOCCORSO PEDIATRICO

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Il Laboratorio ed il PSP

- ✓ **Nella pratica clinica di ogni giorno la principale sfida per il medico di Pronto Soccorso è di giungere tempestivamente a una corretta diagnosi e di dare avvio alla gestione più appropriata del paziente**

- ✓ **Nel fare questo egli deve integrare le informazioni che vengono da una accurata anamnesi, da un accurato esame obiettivo e, quando necessario, da un corretto uso e da una corretta interpretazione degli esami di laboratorio**

Il Laboratorio ed il PSP

- ✓ **In un'epoca in cui la "medicina praticata" è sempre più sostituita da una "medicina basata su evidenze scientifiche" anche l'utilizzo degli esami di laboratorio non può prescindere da una attenta conoscenza della loro accuratezza diagnostica, intesa, in senso molto generale, come la capacità di un test di predire la presenza di malattia se positivo e, al contrario, di escludere la malattia se negativo**

- ✓ **Deve quindi essere viva la consapevolezza di quanto i risultati degli esami richiesti possano cambiare la probabilità di diagnosi di malattia e di qui le decisioni successive sul paziente in termini di ulteriori esami, di decisioni di ricovero, di avvio di terapie**

Il Laboratorio ed il PSP

- ✓ **Le informazioni relative all'accuratezza di un test sono sempre derivate da studi clinici condotti in specifiche condizioni di malattia**

MA

- ✓ **nella pratica clinica è facile generalizzare i parametri di accuratezza di un test ricavati da una specifica situazione clinica estendendoli a popolazioni cliniche diverse, con l'inevitabile conseguenza di errori importanti nell'interpretazione dei risultati**

L'esempio: I markers di flogosi

- ✓ **Globuli bianchi**
- ✓ **Proteina C reattiva**
- ✓ **Procalcitonina**

Possibili scenari clinici

Accuratezza dei markers di flogosi :

- ✓ **nel lattante e piccolo bambino con febbre senza localizzazione**
- ✓ **nella diagnosi eziologica delle polmoniti acquisite in comunità**
- ✓ **nella diagnosi di appendicite acuta nei bambini con dolore addominale**

Febbre senza localizzazione

- ✓ **La febbre è una tra le cause più comuni di accesso al PS (> 10% degli accessi)**
- ✓ **Circa 1 bambino ogni 3 presenta febbre senza localizzazione**
- ✓ **Il problema è particolarmente rilevante nei primi 3 anni di vita quando:**
  - **è più elevata l'incidenza di Infezioni Batteriche Severe (> 10% nel primo mese di vita)**
  - **è minore l'abilità del bambino nel localizzare segni e sintomi di malattia e quindi i dati clinici sono meno predittivi**

Quale l'accuratezza degli indici di flogosi nel predire la presenza di IBS?

Vanessa, 7 mesi

- Viene portata al PS per febbre da poche ore e due vomiti dopo assunzione di latte.
- Bambina nata a termine, PN 3.120 g, perinatalità regolare, allattata al seno con buona crescita, sviluppo PM nella norma.
- Eseguite 2 dosi di vaccino esavalente+antipneumococco.

EO all'ingresso

- TC 38°C, FC 150 bpm nel pianto, FR 30 apm, sat 98% in a.a., TR<2 sec.
- Colorito roseo, vigile, reattiva anche se la madre la descrive come più irritabile del solito.
- FA 2x2 cm, normotesa.

Accertamenti eseguiti in PS:

- GB 7.620/mmc (N 5.880/mmc)
- PCR 12 mg%
- Elettroliti, glicemia, funzionalità renale ed epatica nella norma

Esami di Screening "Tradizionali"

Positività

EMOCROMO

- GB > 15.000/mm3 o < 5.000/mm3
- Neutrofili > 10.000/mm3
- Band cells >1500

ESAME URINE

- Esterasi leucocitaria positiva
- Nitriti positivi
- GB > 10/ campo al microscopio

KlassenTP, *J Pediatrics 1992C*
Baker MD, *NEJM 1993*
Baraff LJ, *Pediatrics 1993*

Esami di Screening "Tradizionali"

E' stato infatti dimostrato che nel lattante febbrile, nei primi 3 mesi di vita, in buone condizioni generali, il rischio di IBS si modifica in rapporto al risultato di tali esami.

	ESAMI NON NOTI	ESAMI DI SCREENING POSITIVI	ESAMI DI SCREENING NEGATIVI
RISCHIO IBS	8.6%	24.3%	1.4%
RISCHIO BATTERIEMIA	2%	12.8%	1.1%
RISCHIO MENINGITE	1%	3.9%	0.5%

Baraff LJ, *Ped Infect Dis 1992*

Fever in the new millennium: a review of recent studies of markers of serious bacterial infection in febrile children

Allen L. Hsiao and M. Douglas Baker

Curr Opin 2005, 17:56-61

Much progress has been made in recent years in finding more accurate indicators of Severe Bacterial Infection than White Blood Cells .

Globuli Bianchi

Table 2. Sensitivities and specificities for proposed white blood cell count cutoff for detecting SBI: summary of studies examining white blood cell count and SBI

Study	Optimum WBC cutoff K/mm^3	WBC % sensitivity	WBC % specificity
Bonsu	15.0	45.0	78.0
Carrol	15.0	69.0	67.0
Fernandez-Lopez	16.5	50.9	79.2
Galetto-Lacour	15.0	52.0	74.0
Pulliam	15.0	80.0	69.0

WBC, white blood cell count.

One of the first indicators of SBI examined by researchers, the white blood cell count (WBC) is ubiquitous with infant fever work-ups. It is universally available and historically useful as an indicator of serious infections. Algorithms commonly used to evaluate young infants with fever include the interpretation of WBC. However, studies in the past have indicated that WBC is not a reliable indicator of SBI in febrile infants.

Hisiao AL, Curr Opin 2005, 17:56-61

PCR

Table 3. Sensitivities and specificities for proposed CRP cutoff for detecting SBI: summary of studies examining C-reactive protein and SBI

Study	Optimum CRP (cutoff (mg/l)	CRP sensitivity	CRP specificity
Carrol*	30.0	81.0	89.0
Fernandez-Lopez	27.5	63.5	84.2
Gendrel	10.0	98.0	50.0
Galetto-Lacour 2001	40.0	89.0	75.0
Galetto-Lacour 2003	40.0	79.0	79.0
Pulliam	70.0	79.0	91.0

*Meningococcal disease only. CRP, C-reactive protein.

Although the range of proposed cutoff values for CRP is rather large, it appears to have potential as a reliable indicator of bacterial infection in pediatric populations.

Hisiao AL, Curr Opin 2005, 17:56-61

PCR

Systematic Review of the Diagnostic Accuracy of C-Reactive Protein to Detect Bacterial Infection in Nonhospitalized Infants and Children with Fever

Sharon Sanders, BSc(Pod), MPH, Adrian Barnett, BSc(Statistics), PhD, Ignacio Correa-Velez, MBBS, PhD, Mark Coulthard, MBBS, FRACP, and Jenny Doust, BA, BEcons, MBBS, FRACGP, Grad Dip Clin Epi, PhD

J Pediatrics 2008; 153:570-4

For differentiating between serious bacterial infection and benign or nonbacterial infection (6 studies), the pooled estimate of sensitivity was 0.77 (95% CI, 0.68, 0.83); specificity, 0.79 (95% CI, 0.74, 0.83); positive likelihood ratio, 3.64 (95% CI, 2.99, 4.43); and negative likelihood ratio, 0.29 (95% CI, 0.22, 0.40).

Conclusions: **CRP provides moderate and independent information for both ruling in and ruling out serious bacterial infection in children with fever at first presentation. Poor sensitivity means that CRP cannot be used to exclude all bacterial infection.**

PCR

Table III. Performance of CRP for the detection of serious bacterial infection and bacterial infection

Study, year published	CRP cut-off	Prevalence	TP	FN	TN	FP	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR− (95%CI)
CRP for the detection of serious bacterial infection										
Isaacman and Burke, 2002 (14)	4.4 mg/dL	11%	18	11	184	43	62 (44, 80)	81 (76, 86)	3.28 (2.22, 4.85)	0.47 (0.29, 0.75)
Pulliam et al, 2001 (12)	7.0 mg/dL	18%	11	3	57	6	79 (57, 100)	90 (83, 98)	8.25 (3.68, 18.52)	0.24 (0.09, 0.65)
Lacour et al, 2001* (13)	40 mg/L	23%	25	3	72	24	89 (78, 100)	75 (66, 84)	3.51 (2.47, 5.17)	0.15 (0.05, 0.42)
Galetto-Lacour et al, 2003 (15)	40 mg/L	29%	23	6	55	15	79 (65, 94)	79 (69, 88)	3.70 (2.28, 6.02)	0.26 (0.13, 0.54)
Berger et al, 1996* (16)	20 mg/L	24%	25	5	65	32	83 (70, 97)	67 (58, 76)	2.53 (1.82, 3.49)	0.25 (0.11, 0.56)
Andreola et al, 2007* (17)	>40 mg/L	23%	67	27	258	56	71 (61, 80)	81 (76, 85)	3.79 (3.05, 5.03)	0.35 (0.25, 0.48)
		Pooled likelihood ratios							3.64 (2.99, 4.43)	0.29 (0.22, 0.40)
CRP for the detection of bacterial infection										
McCarthy et al, 1978*§ (19)	Positive†	28%	48	60	250	40	44 (35, 54)	86 (82, 90)	3.22 (2.26, 4.60)	0.64 (0.54, 0.77)
Tejani et al, 1995‡ (20)	>2 mg/dL	82%	33	118	32	2	22 (15, 28)	94 (86, 100)	3.72 (0.94, 14.75)	0.83 (0.74, 0.94)
Cobben et al, 1990 (21)	35 mg/L	35%	28	20	87	4	58 (44, 72)	96 (91, 100)	13.3 (4.94, 36.0)	0.44 (0.31, 0.61)

*Some children <1 month of age.
†Positive test indicates level of >6 mg/L or >10 mg/L, depending on the test kit or reagent used.
‡Bacterial only and mixed viral bacterial versus nonbacterial.
§Deep, superficial, and possible bacterial combined versus nonbacterial infection.

J Pediatrics 2008; 153:570-4

Procalcitonina

Table 4. Sensitivities and specificities for proposed procalcitonin cutoff for detecting SBI: summary of studies examining procalcitonin and SBI

Study	Age range	Optimum PCT cutoff (ng/ml)	PCT % sensitivity	PCT % specificity
Fernandez-Lopez	1 mo to 36 mo	0.53	65.5	94.3
Galetto-Lacour	7 days to 36 mo	0.9	93.0	78.0
Galetto-Lacour	7 days–36 mo	0.5	93.0	74.0
Gendrel	1 mo–15 yr	1	83.0	93.0
Carrol*	.07–15.9 yr	2	94.0	93.0

*Meningococcal vs non-meningococcal disease only. PCT, procalcitonin.

Overall, PCT appears to be a superior single screening test for bacterial infections, with generally better sensitivity and specificity than WBC or CRP. However, findings from different studies range widely.

Hisiao AL, Curr Opin 2005, 17:56-61

Procalcitonin and C-Reactive Protein as Diagnostic Markers of Severe Bacterial Infections in Febrile Infants and Children in the Emergency Department

Barbara Andreola, MD, Silvia Bressan, MD,* Silvia Callegaro, MD,* Anna Liverani, MD,† Mario Plebani, MD,† and Liviana Da Dalt, MD**

Pediatric Infect Dis 2007

Setting: Pronto Soccorso Pediatrico Padova

Periodo: Maggio 2005 – Ottobre 2006

Popolazione: 408 Lattanti febbrili 7 gg – 36 mesi di età

TABLE 1. Final Diagnosis of Patients With Severe Bacterial Infections (n = 94)

	No. of Patients	%
Pyelonephritis	50	53.2
Pneumonia	24	25.5
Meningitis	7	7.5
Occult bacteremia	6	6.4
Sepsis	3	3.2
Osteomyelitis	2	2.1
Septic arthritis	2	2.1

Andreola B, Pediatric Infect Dis 2007

TABLE 2. Clinical Characteristics and Laboratory Findings of Patients With SBI and Non-SBI

Variable	SBI (n = 94)	Non-SBI (n = 314)	*P*
Age (mo)	8 (2–20)	9 (2–16)	NS
Sex (F/M)	52/42	153/161	NS
Fever duration (h)			NS
<8	14	31	
8–24	31	67	
>24	49	216	
Max temperature (°C)	39.2 ± 0.8	39.0 ± 0.8	0.004
Yale Score (n)			0.0001
<10	46	225	
10–16	40	82	
>16	8	7	
PCT (ng/mL)	1.9 (0.5–10.7)	0.2 (0.1–0.5)	0.0001
CRP (mg/L)	68.5 (39.0–120.0)	13 (3–31)	0.0001
WBC (mm^3)	15,850 (12,040–20,250)	10,770 (7,050–14,960)	0.0001
ANC (mm^3)	9,522 (6,830–14,154)	5,119 (3,108–8,295)	0.0001

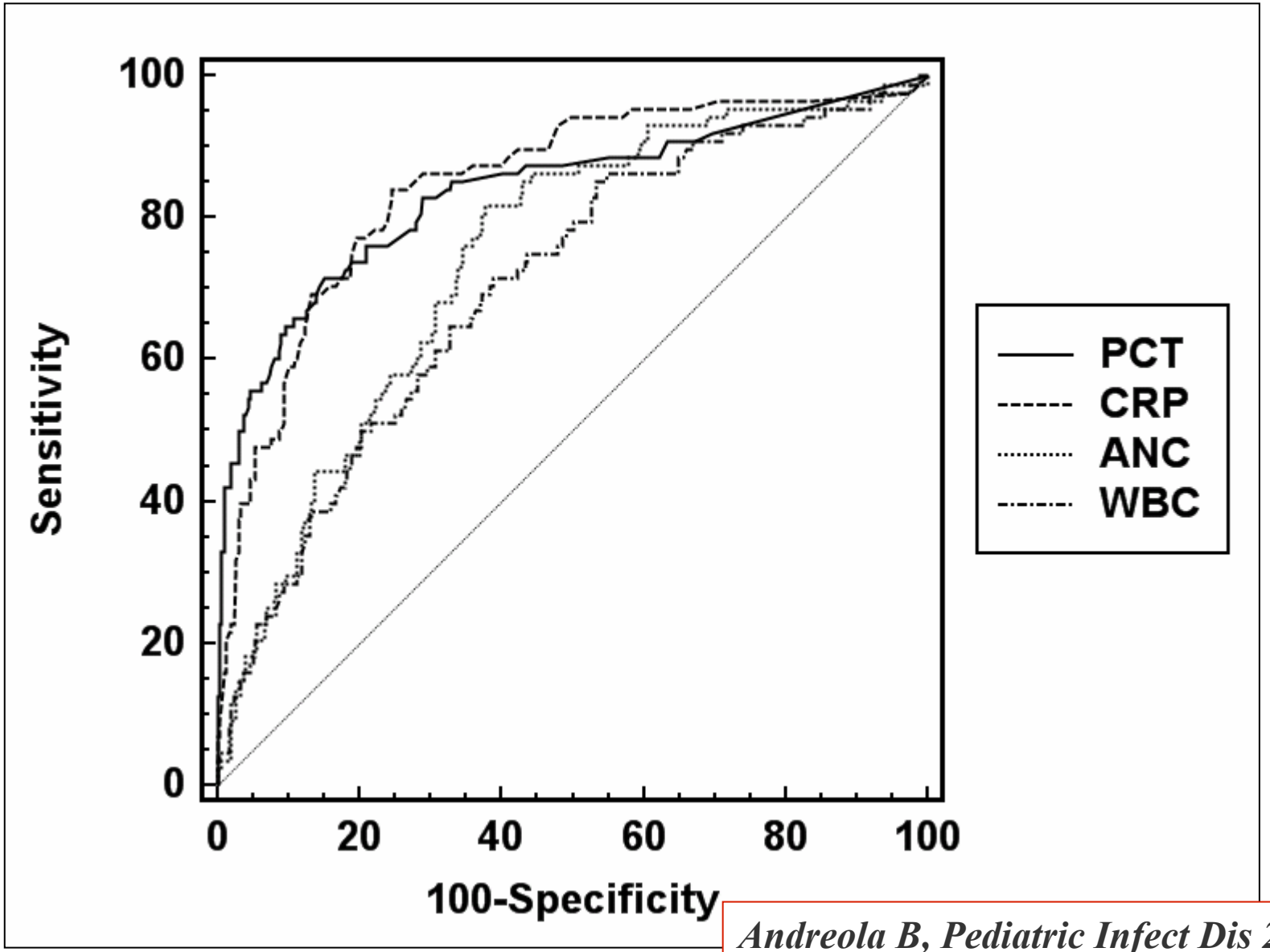
Data are median and interquartile range except for temperature values which are mean ± SD.
NS indicates nonsignificant.

Andreola B, Pediatric Infect Dis 2007

TABLE 3. Sensitivity, Specificity, Positive and Negative Likelihood Ratio Values of PCT, CRP, WBC, ANC, and Yale Observation Score for SBI Prediction

	Sensitivity (% [95% CI])	Specificity (% [95% CI])	Likelihood Ratio+	Likelihood Ratio−
PCT				
>0.5 ng/mL	73.4 (63.3–82.0)	76.4 (71.3–81.0)	3.10	0.35
>1 ng/mL	63.8 (53.3–73.5)	89.8 (85.9–92.9)	6.24	0.40
>2 ng/mL	47.9 (37.5–58.4)	96.5 (93.8–98.2)	13.62	0.54
CRP				
>20 mg/L	88.3 (80.0–94.0)	60.8 (55.2–66.3)	2.25	0.19
>40 mg/L	71.3 (61.0–80.1)	81.2 (76.4–85.4)	3.79	0.35
>80 mg/L	46.0 (36.4–57.4)	94.6 (91.5–96.8)	8.65	0.56
WBC				
>15,000/mm^3	51.6 (41.0–62.1)	75.5 (70.3–80.2)	2.11	0.64
ANC				
>10,000/mm^3	29.9 (20.5–40.6)	78.4 (73.3–82.9)	1.38	0.89
Yale Observation Score				
YOS >10	38.3 (28.5–48.9)	67.8 (62.4–73.0)	1.19	0.91

Andreola B, Pediatric Infect Dis 2007



Andreola B, Pediatric Infect Dis 2007

PCT vs invasività infezione

PCT and CRP values related to the severity of infection.

	PYELONEPHRITIS (n = 50)	LOBAR PNEUMONIA (n = 24)	OCCULT BACTEREMIA (n = 6)	INVASIVE INFECTIONS* (n=10)	*P*
PCT (ng/ml)	0.82 (0.30-2.68)	4.35 (1.44-11.7)	6.55 (3-10.94)	38.65 (31.0-52.6)	0.0000
CRP (mg/l)	57.5 (37–120)	120.0 (60.5-148)	89 (52 -110)	96.5 (14-219)	0.1770

*sepsis and meningitis
Data are median and interquartile range

Severity of Infections. **When serum PCT and CRP concentration were analyzed across various SBI categories, only PCT differed significantly in relation to different organ involvement (*P* 0.0001) with the highest values found in sepsis and meningitis.**

Andreola B, *Pediatric Infect Dis 2007*

PCT e PCR vs invasività infezione

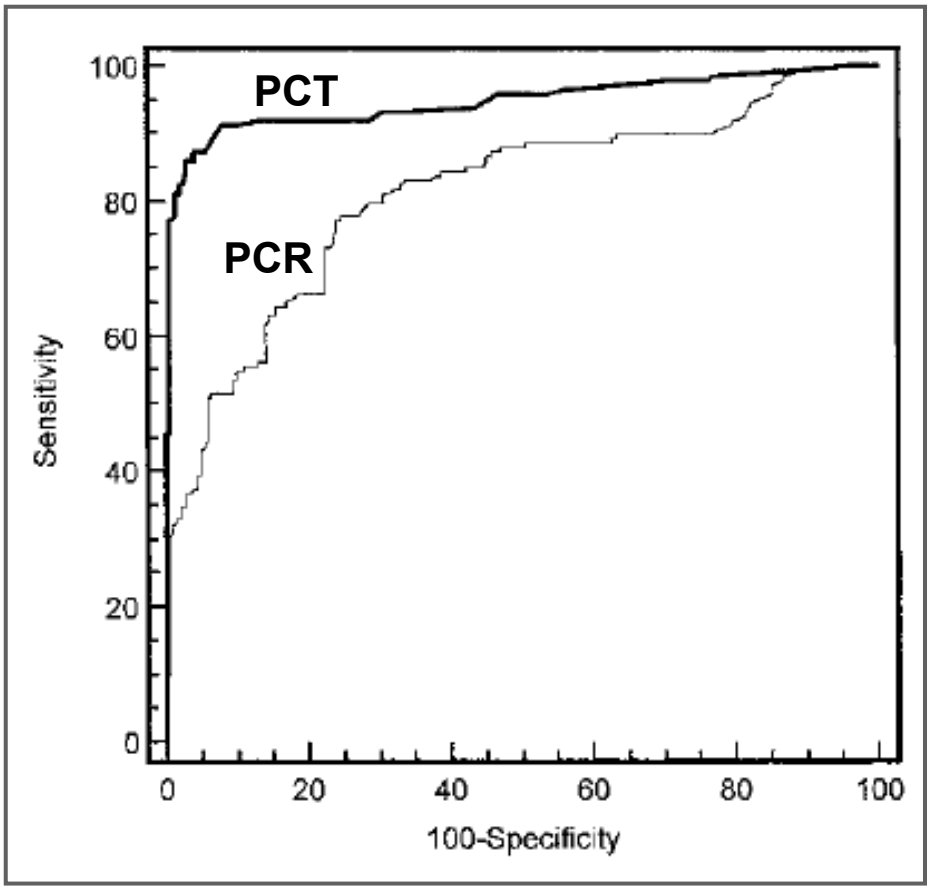


FIG. 3. ROC curves for CRP and PCT for differentiation between invasive and non invasive infections.

Infezioni Invasive
vs
Non Invasive

	PCT	CRP
Area	0.95 (0.01)	0.81 (0.02)

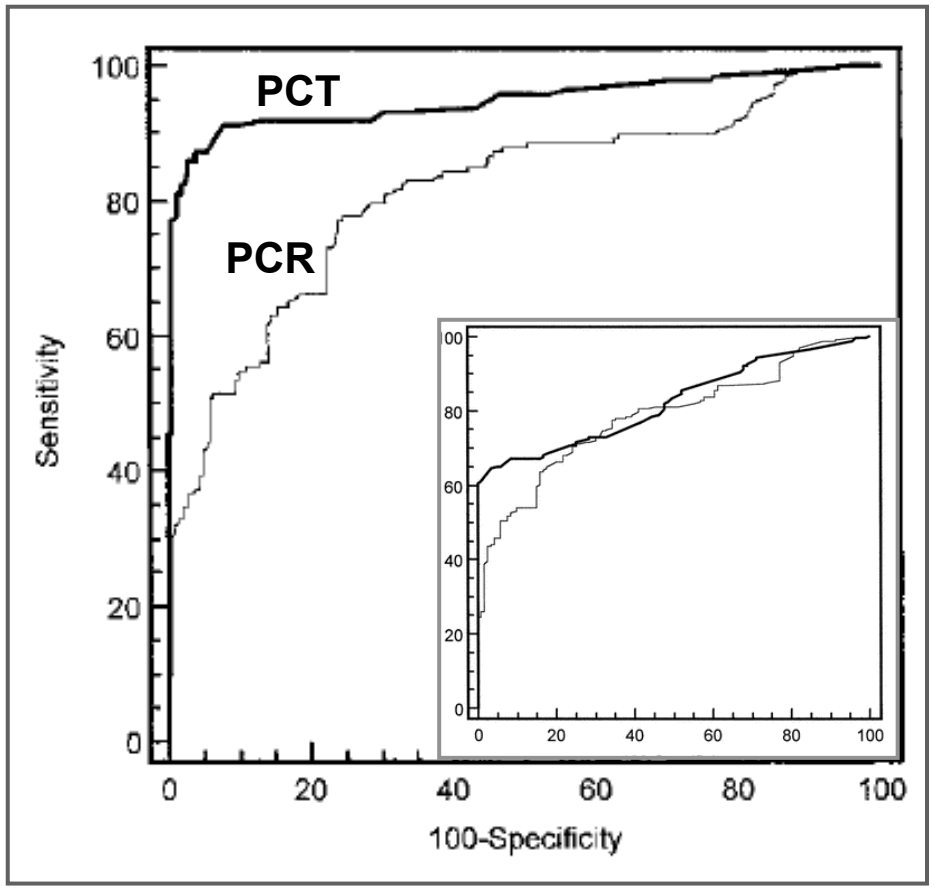
445 bambini

1-36 m

multicentrico

Fernandez Lopez,
Pediatric Infect Dis J 2003

PCT e PCR vs invasività infezione



Infezioni Invasive
vs
Non Invasive

	PCT	CRP
Area	0.95 (0.01)	0.81 (0.02)

Infezioni Batteriche
vs
Infezioni Virali

	PCT	CRP
Area	0.82 (0.02)	0.78 (0.02)

FIG. 3. ROC curves for CRP and PCT for differentiation between invasive and non invasive infections.

Fernandez Lopez,
Pediatric Infect Dis J 2003

Procalcitonin: A Marker of Severity of Acute Pyelonephritis Among Children

Paolo Pecile, MD*; Elisabetta Miorin, MD*; Carla Romanello, MD*; Edmondo Falleti, MD‡; Francesca Valent, MD§; Francesco Giacomuzzi, MD‖; and Alfred Tenore, MD*

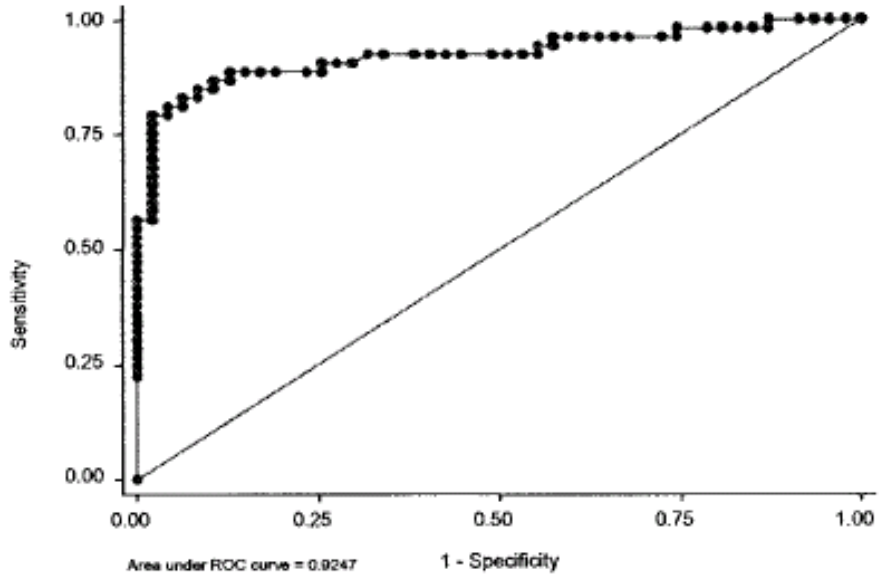


Fig 1. Receiver operating characteristic curve for specificity and sensitivity of PCT measurements.

TABLE 2. Sensitivity, Specificity, PPV, and NPV of PCT and CRP Measurements for Prediction of Acute Pyelonephritis (Cutoff Values of 0.8, 0.5, or 1 ng/mL for PCT and 20 or 50 mg/L for CRP)

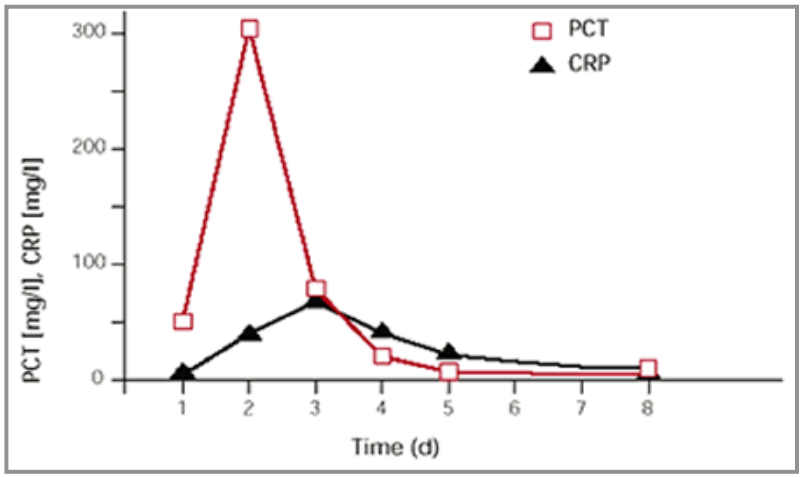
	Sensitivity, %	Specificity, %	PPV, %	NPV, %
PCT, ≥0.8 ng/mL	83.3	93.6	93.7	83.0
PCT, ≥0.5 ng/mL	90.7	70.2	77.7	86.8
PCT, ≥1 ng/mL	81.4	93.6	93.6	81.4
CRP, ≥20 mg/L	94.4	31.9	61.4	83.3
CRP, ≥50 mg/mL	74.0	76.6	78.4	72.0

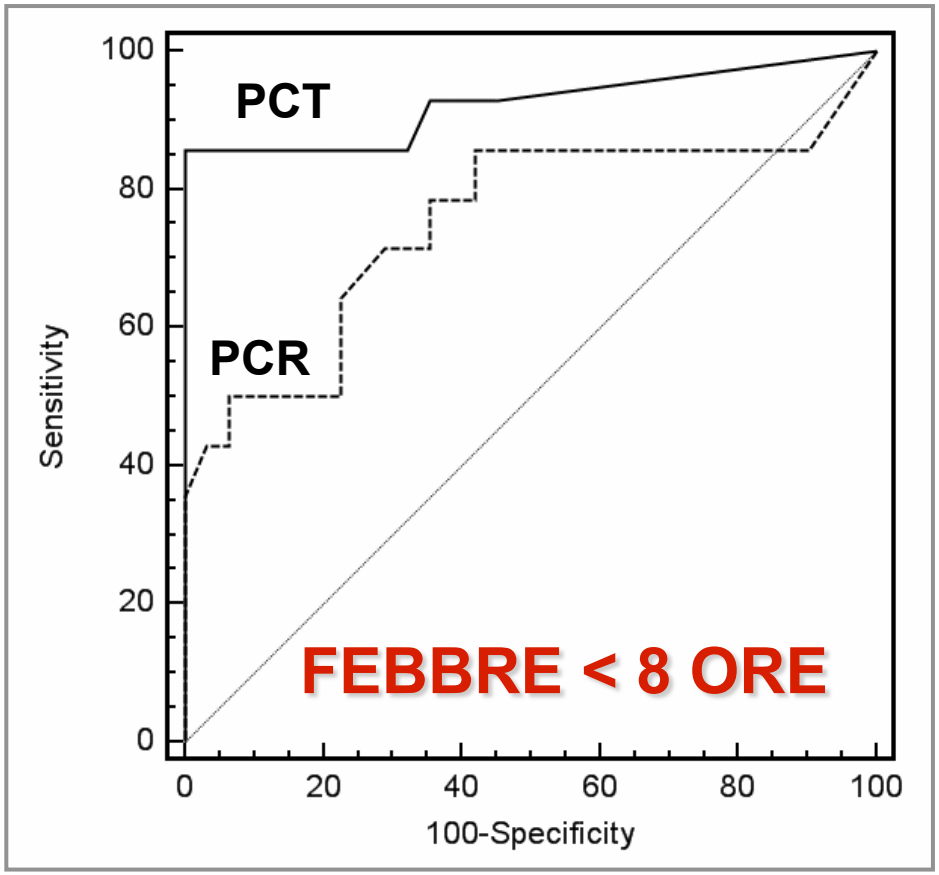
PPV, positive predictive value; NPV, negative predictive value.

CONCLUSIONS

These data indicate that PCT is an accurate biological marker with high sensitivity and specificity for the prediction of acute pyelonephritis among infants and children, compared with the low specificity of CRP measurements. This parameter is correlated with the severity of renal involvement at the time of diagnosis of febrile UTI and also with the risk of permanent scarring. Therefore, PCT measurements could be a valuable tool for the treatment of children with febrile UTIs.

PCT vs PCR: precocità diagnostica





AUC *

PCR: 0.75 (0.60-0.87)

PCT: 0.92 (0.80-0.98)

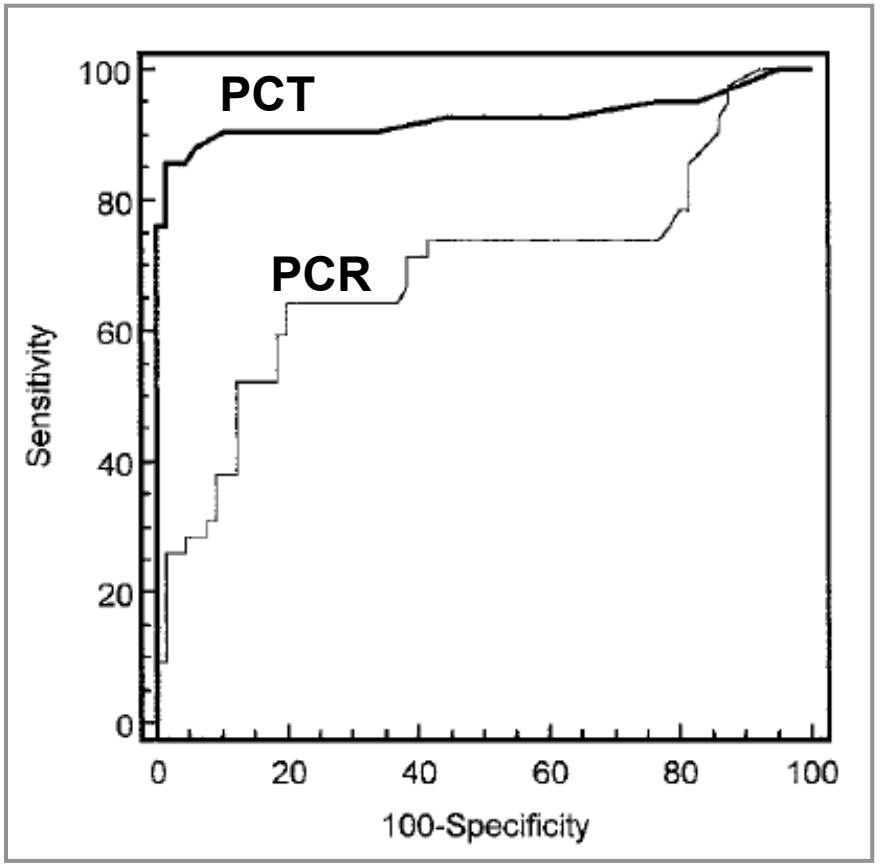
GB: 0.69 (0.54-0.82)

***45 pazienti**

Andreola B, Pediatric Infect Dis J 2007

PCT vs PCR: precocità diagnostica

Optimal cut-off PCT: > 0.69 ng/mL	
Sensitivity: 85.7 %	PPV: 96.9 %
Specificity: 98.5 %	NPV: 89.7 %
Optimal cut-off CRP: > 19 mg/L	
Sensitivity: 61.3 %	PPV: 65.8 %
Specificity: 80 %	NPV: 76.5 %



FEBBRE < 12 ORE

***AUC* ***

PCR: 0.69 (SD 0.03)

PCT: 0.93 (SD 0.05)

***104 pazienti**

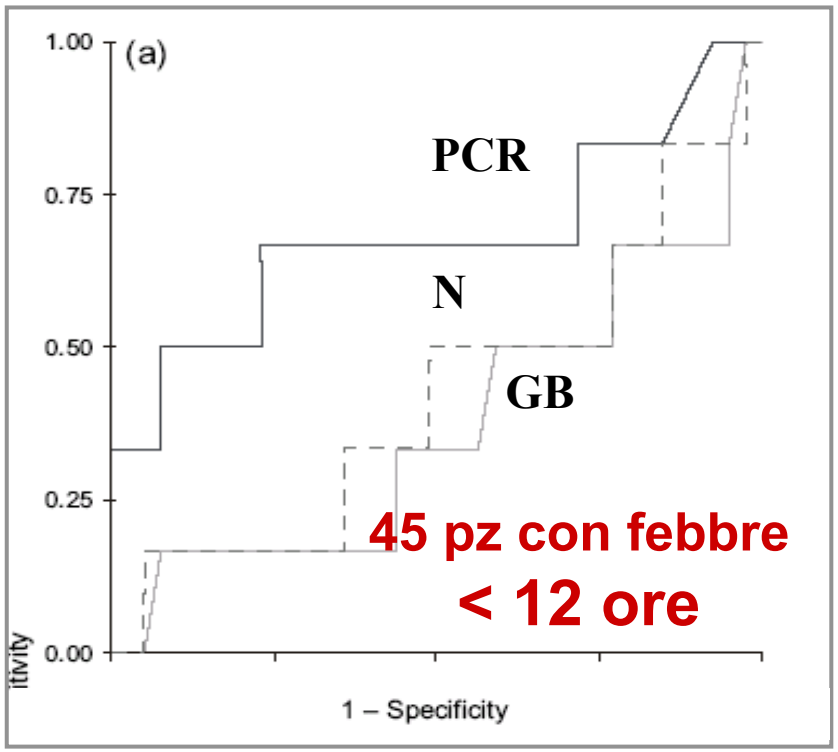
Fernandez Lopez,
Pediatric Infect Dis J 2003

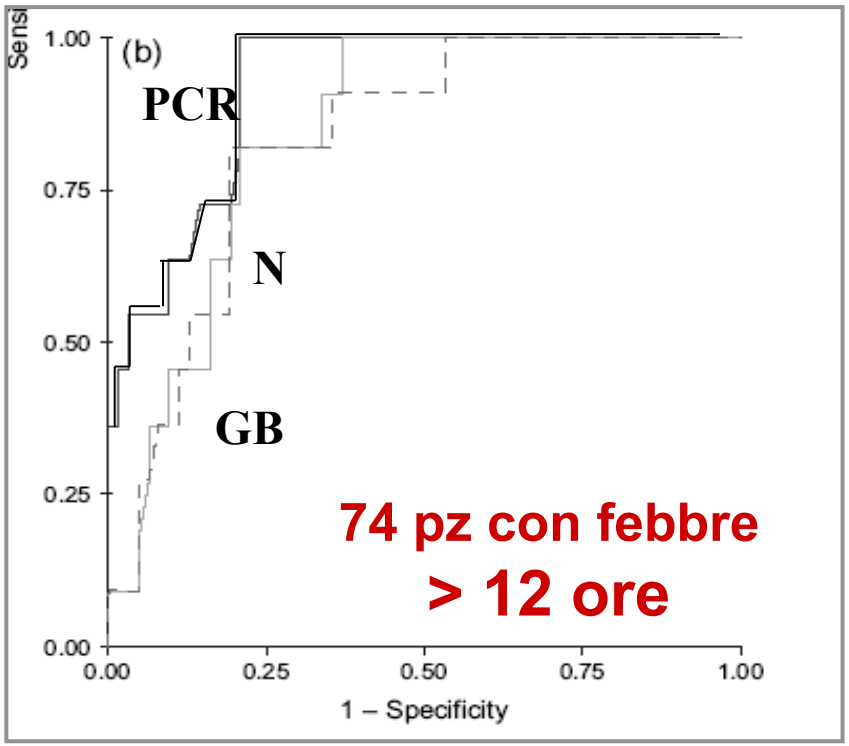
PCR: precocità diagnostica

Duration of fever and markers of serious bacterial infection in young febrile children

Pratt A, Pediatric International 2007

Bambini 1-36 m





Duration of fever and markers of serious bacterial infection in young febrile children

Pratt A, ***Pediatric International 2007***

Conclusion

Bacterial markers performed significantly better when the fever duration was >12 h. All markers had extremely poor sensitivities at the currently utilized cut-off points when fever was ≤12 h. This finding potentially has significant clinical and legal ramifications. Physicians should be cautious when relying on these screening methods when evaluating young children early in the course of their febrile illness. Of note, CRP has better sensitivity and specificity than either WBC or ANC regardless of fever duration and is a useful laboratory screening tool in young patients with fever and no source of infection.

Title:

Predicting Severe Bacterial Infections in well-appearing febrile neonates: laboratory markers accuracy and duration of fever

Bressan S, *Pediatric Infect Dis – In Press*

TABLE 1. Final Diagnosis of Patients with Severe Bacterial Infections (n= 25/99)

	No. of Patients	%	Causative Organisms
Urinary tract infections (UTI)	15	60%	13 E. Coli 2 Enterococco 1 Klebsiella Pneumoniae
Bacteremia	3	12%	3 Group B Streptococcus
Bacteremia and UTI	2	8%	2 E.Coli
Meningitis	3	12%	3 Group B Streptococcus
Pneumonia	1	4%	Not determined
Osteomyelitis	1	4%	Not determined

TABLE 3. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratio (LR) values for the most commonly recommended cut offs of WBC, ANC and CRP for SBI prediction in relation to fever duration.

	Sensitivity (% [95% C.I.])	Specificity (% [95% C.I.])	PPV (% [95% C.I.])	NPV (% [95% C.I.])	LR+ (% [95% C.I.])	LR - (% [95% C.I.])
Initial determination : fever < 12 h (All patients)						
WBC						
< 5000/mm^3 OR >15000/mm^3	28 (14.3-47.6)	87.7 (78.2-93.4)	43.75 (23.1-66.8)	78.1 (68.0-85.6)	2.3 (0.9-5.8)	0.8 (0.7-0.9)
ANC						
> 10000/mm^3	20.0 (8.9-39.1)	97.3 (90.6-99.3)	71.4 (35.9-91.8)	78.0 (68.5-85.3)	7.3 (0.6-93.3)	0.8 (0.7-0.9)
CRP						
> 20 mg/L	48.0 (30.3-66.5)	93.2 (85.1-97.1)	70.6 (46.9-86.7)	84.2 (74.7-90.5)	7.1 (4.0-12.5)	0.6 (0.5-0.7)
Repeated determination: fever > 12 h (58 patients)						
WBC						
< 5000/mm^3 OR >15000/mm^3	80.0 (37.6-96.4)	90.6 (79.7-95.9)	44.4 (18.9-73.3)	98.0 (89.3-99.6)	8.5 (5.1-14.2)	0.2 (0.0-1.6)
ANC						
> 10000/mm^3	80.0 (37.6-96.4)	100 (93.2-100)	100 (51.0-100)	98.2 (90.2-99.7)	undefined	0.2 (0.0-1.4)
CRP						
> 20 mg/L	100 (56.6-100)	96.2 (87.2-99.0)	71.4 (35.9-91.8)	100 (93-100	26.5 (9.9-79.6)	0.0

CONCLUSIONS: In well-appearing neonates with early onset FWS, laboratory markers are more accurate and reliable predictors of SBI when performed after >12 hours of fever duration. ANC and especially CRP resulted better markers than the traditionally recommended WBC .

Bressan S, ***Pediatric Infect Dis – In Press***

Markers that predict serious bacterial infection in infants under 3 months of age presenting with fever of unknown origin

Izaskun Olaciregui, Unai Hernández, José Ángel Muñoz, José I. Emparanza and José J. Landa

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Conclusions

PCT, CRP, and leucocyte count have intrinsic predictive value for SBI in febrile infants under 3 months of age. The diagnostic value of PCT is greater than CRP for more invasive bacterial infections and for fever of short duration.

Vanessa, 7 mesi

- Viene portata al PS per febbre da poche ore e due vomiti dopo assunzione di latte.
- Bambina nata a termine, PN 3.120 g, perinatalità regolare, allattata al seno con buona crescita, sviluppo PM nella norma.
- Eseguite 2 dosi di vaccino esavalente+antipneumococco.

EO all'ingresso

- TC 38°C, FC 150 bpm nel pianto, FR 30 apm, sat 98% in a.a., TR<2 sec.
- Colorito roseo, vigile, reattiva anche se la madre la descrive come più irritabile del solito.
- FA 2x2 cm, normotesa.

Accertamenti eseguiti in PS:

- GB 7.620/mmc (N 5.880/mmc)
- PCR 12 mg%
- Elettroliti, glicemia, funzionalità renale ed epatica nella norma

Probabile virosi - osservazione

Nelle 12 ore successive:

- 2 vomiti alimentari
- Sempre irritabile
- Comparsa di piccole petecchie agli arti, natiche e tronco
- Tachicardia (FC 180 bpm)

Esami ripetuti a distanza di 12 ore:

- GB 21.660/mmc (N 21.670/mmc)
- PCR 131 mg%
- Procalcitonina 21 ug/L
- Esame chimico-fisico del liquor: proteine 0,52 g/L, GB 880/uL (essenzialmente PMN)
- **Emocoltura e liquorcoltura positive per Neisseria Meningitidis di tipo B**

Take home messages

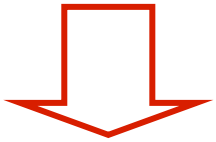
Febbre senza localizzazione

La PCR trova indicazione come “migliore” esame di screening nel lattante e nel piccolo bambino con febbre senza localizzazione.

La PCT sembra essere più accurata nelle febbri di recente insorgenza e nelle infezioni altamente invasive.

Polmoniti Acquisite in Comunità

- ✓ **Le CAP sono causa importante di morbilità in tutti i paesi industrializzati**
- ✓ **I virus sono la causa più comune in tutte le età;**
- ✓ **Tra i batteri lo Streptococco Pneumoniae è la principale causa sotto i 5 aa ed il Mycoplasma Pneumoniae sopra i 5 aa**
- ✓ **La diagnosi microbiologica è difficile e non "cost-effective"**
- ✓ **I dati clinici e la radiografia del torace sono spesso non orientativi**



Quale l'accuratezza degli indici di flogosi nell'orientare verso l'eziologia?

Epidemiology and Clinical Characteristics of Community-Acquired Pneumonia in Hospitalized Children

Ian C. Michelow, Kurt Olsen, Juanita Lozano, Nancy K. Rollins, Lynn B. Duffy, Thedi Ziegler, Jaana Kauppila, Maija Leinonen and George H. McCracken, Jr

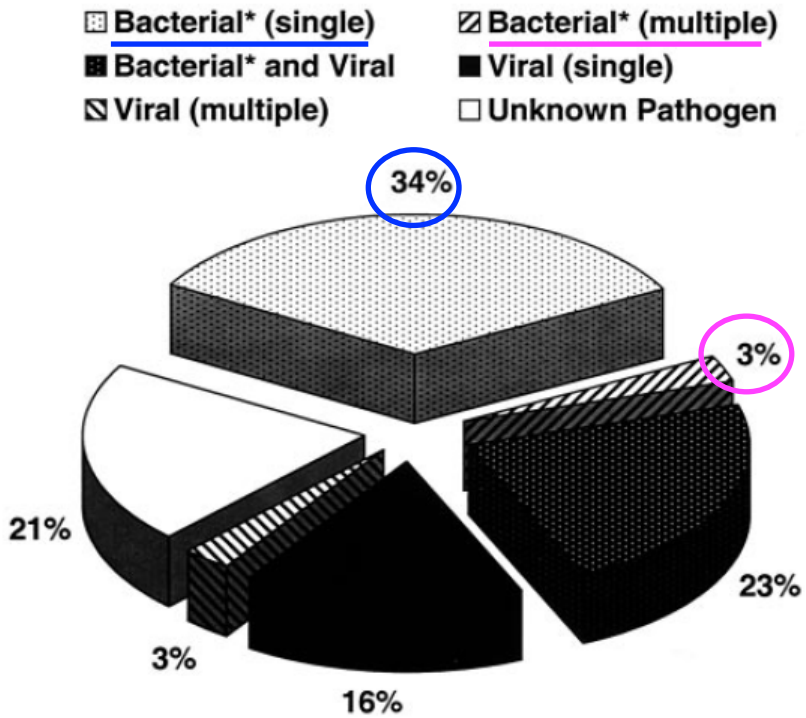


Fig 1. Etiology of LRIs in 154 hospitalized children. Pneumococcal disease was detected by blood or pleural fluid cultures or PCR assays. The asterisk denotes typical respiratory bacterial pathogens (*M pneumoniae*, *C pneumoniae*, and *M tuberculosis*).

Pediatrics 2004;113;701-707

TABLE 2. Demographic and Clinical Characteristics of 154 Hospitalized Children With Community-Acquired LRIs Associated With Bacterial, Viral, or Unknown Pathogens

Characteristics	Type of Lower Respiratory Pathogens					*P* Value
	Typical Bacteria[a]	*M pneumoniae* or *C pneumoniae*[b]	Viruses[c]	Mixed Bacteria/Viruses[d]	Unknown	
No. of patients, %	40 (26)	17 (11)	29 (19)	36 (23)	32 (21)	
Age, mo (range)[e]	39.5 (2.3–209)	60.2 (9–155)[f]	18.5 (2.2–194)[fg]	27.6 (2–134)	41.4 (4–158)[g]	.015
Age <5 y, %	70	47	76	78	63	.17
Gender, % male	73[f]	47	69	44[f]	72	.04
Duration of symptoms before admission, days[e]	6.0	3.5	7.0	5.0	4.0	.41
Antibiotic therapy during preceding 2 weeks, %	33	24	55	44	38	.20
Temperature on admission, °C[h]	39.4	39.1	39.0	39.2	39.1	.46
Maximum temperature ≤72 hours after admission, °C[h]	38.4[fg]	37.5[gi]	37.6[fj]	38.5[ij]	37.9	.001
Wheeze, %	13[f]	41	41[fg]	14[g]	31	.01
Lobar or segmental consolidation ± effusion, %	75	53	45	69	53	.06
Pleural effusion, %	50[fgj]	6[f]	10[g]	39	19[j]	0002
WBC count, × 10^9/L[e]	16.1	12.3	14.5	15.6	14.4	.76
Band forms, %[e]	6.5	1.5[f]	1.0[g]	11.5[fg]	3.0	.038
Band forms (proportion >10%)	39	8[f]	27	56[fg]	19[g]	.006
S pneumoniae NP colonization, %	20	12	35	22	22	.48
Procalcitonin, ng/mL[e]	2.4[f]	0.7[fg]	0.6[j]	2.6[gj]	1.3	.014
Procalcitonin, proportion ≥0.75 ng/mL	68[f]	41	32[fgj]	66[g]	67[j]	.012
Paired serum available, %	78	82	79	94	69	.08
Macrolide/azalide included in regimen, %	8	18	17	11	22	.44
Duration of oxygen therapy, days[e]	1.2	1.0	1.8	2.0	1.8	.28
Duration of hospitalization, % >5 days[ek]	62[fg]	24[f]	31	59[j]	23[gj]	.001
No. ventilated/died/readmitted within 30 days of discharge	1/0/0	1/0/0	3/0/1	3/2/2	2/0/1	ND

The value of clinical features in differentiating between viral, pneumococcal and atypical bacterial pneumonia in children

Matti Korppi (matti.korppi@uta.fi)[1], Massimiliano Don[2], Francesca Valent[3], Mario Canciani[2]

Table 4 Logistic regression: predictive factors associated with the aetiology of CAP

Factor	Bacterial (N = 41) vs. viral (N = 20)	Typical (N = 17) vs. atypical (N = 24)
Crackles	0.5 (0.1–1.8)	2.1 (0.5–8.5)
Alveolar infiltration	0.7 (0.2–2.6)	0.6 (0.1–2.2)
PCT ≥1.0 ng/mL	4.1 (1.0–16.6)	0.9 (0.2–4.1)
Age ≥5 years	20.3 (2.1–195.8)	0.6 (0.2–2.7)
Variable of interaction: PCT ≥1.0 ng/mL and alveolar infiltration	1.8 (0.1–22.2)	0.5 (0.03–7.3)

The results are expressed as adjusted odds ratios and 95% confidence intervals.

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In conclusion, no clinical or radiological characteristic was helpful in the separation between viral, pneumococcal and atypical bacterial aetiology of CAP in children. Elevated PCT >1.0 ng/mL and age >5 years were significant in distinction of bacterial from viral CAP, but not anymore in distinction of pneumococcal from atypical bacterial CAP.

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Procalcitonin as an early marker of infection in neonates and children

A M C van Rossum, R W Wulkan, and A M Oudesluys-Murphy

It is currently not possible to determine whether a patient should be given antibiotics solely on the basis of procalcitonin concentration, but high values indicate the presence of bacterial infection. Further studies with an adequate definition of bacterial lower respiratory infection, and without pretreatment with antibiotics, should be done.

Lancet Infect Dis 2004; **4:** 620–30

Table 3. Respiratory infections

Study, year	Population	Number in study	Age (years)	Aim of study*	Gold standard	AUC ROC curves		Cut-off		Sensitivity (%)		Specificity (%)		PPV (%)		NPV (%)	
						CRP	PCT	CRP (mg/L)	PCT (ng/mL)	CRP	PCT	CRP	PCT	CRP	PCT	CRP	PCT
Korppi et al,[64] 2003	Radiologically confirmed CAP	190	0–15	1	Chest radiograph, positive bacterial/ atypical/viral isolates	..	0·58	60	0·5 1	.. ..	46 24	.. ..	52 90	.. ..	65 79	.. ..	.. ..
Resch et al,[63] 2003	Infants admitted to hospital with bronchiolitis	48	0·04–1	2	Rapid RSV test on nasopharyngeal aspirate; bacterial blood culture	..	..	..	..	..	..	..	..	..	..	..	..
Prat et al,[65] 2003	ER clinical signs of lower RTI	85	0·5–10	3 4	Blood cultures, nasopharyngeal aspirate for viral studies	0·78 0·88	0·76 0·87	65	2	79 90	69 90	67 60	79 74	..	..	..	..
Hatzistilianou et al,[66] 2002	Hospital admission for clinical signs of lower RTI	73	2–14	4	Chest radiograph, positive bacterial/ atypical/viral isolates	..	..	2	2	96	100	38	98	42	93	..	..
Korppi et al,[67] 2001	Hospital admission for clinical signs of lower RTI	58	3 (mean)	5	Chest radiograph, positive bacterial/ atypical/viral isolates	..	0·61	..	0·5 1 2	..	55 32 8	..	71 88 95	..	..	..	..
Moulin et al,[68] 2001	Hospital admission for clinical signs of lower RTI	72	0·2–13	4	Positive bacterial/ atypical/viral isolates, seroconversion	0·84	0·93	20 60	0·5 1 2	88 70 ..	95 86 63	40 52 ..	80 90 96	72 81 ..	80 90 96	67 58 ..	88 80 60
Toikka et al,[69] 2000	Hospital admission for clinical signs of lower RTI	126	0·1–17	3, 5	Positive bacterial/ atypical/viral isolates, seroconversion	..	..	80 150	2 7	59 31	50 19	68 88	80 98	.. ..	.. ..	.. ..	.. ..

*To use procalcitonin (PCT) to differentiate between: 1=viral and bacterial causes of community acquired pneumonia (CAP) in the primary healthcare setting; 2=viral and bacterial causes of bronchiolitis; 3=viral and bacterial or atypical causes of CAP; 4=viral or atypical and bacterial causes of CAP; 5=viral and bacterial or mixed causes of CAP. AUC ROC=area under the curve, receiver operating characteristic; CRP=C-reactive protein; ER=emergency room; NPV=negative predictive value; PPV=positive predictive value; RSV=respiratory syncytial virus; RTI=respiratory tract infection; ..=not available.

The Utility of Serum C-Reactive Protein in Differentiating Bacterial from Nonbacterial Pneumonia in Children

A Meta-Analysis of 1230 Children

Robert G. Flood, MD, Jennifer Badik, MD,† and Stephen C. Aronoff, MD**

TABLE 2. Summary of Studies

	Age Range (yr)	Total Enrollment (n)	Etiology of Pneumonia: Bacterial Alone (n)	Etiology of Pneumonia: Bacterial + Viral (n)	Etiology of Pneumonia: Nonbacterial (n)	Incidence of Bacterial Infection
Isaacs, 1989[19]	0.08–12	56	3	1	52	0.07
Babu et al, 1989[21]	0.25–12	65	30	0	35	0.46
Korppi and Kroger, 1992[8]	<15	209	64	46	99	0.53
Nohynek et al, 1995[20]	0.33 to 15	121	30	24	67	0.45
Heiskanen-Kosma and Korppi, 2000[22]	0.25–15	193	100*	0	93	0.52
Moulin et al, 2001[17]	0.15–13	72	35	8	29	0.6
Virkki et al, 2002[16]	"children"	215	134	0	81	0.62
Lala et al, 2002[23]	0.12–5	299	19	6	274	0.084
Overall		1230	415	85	730	0.41

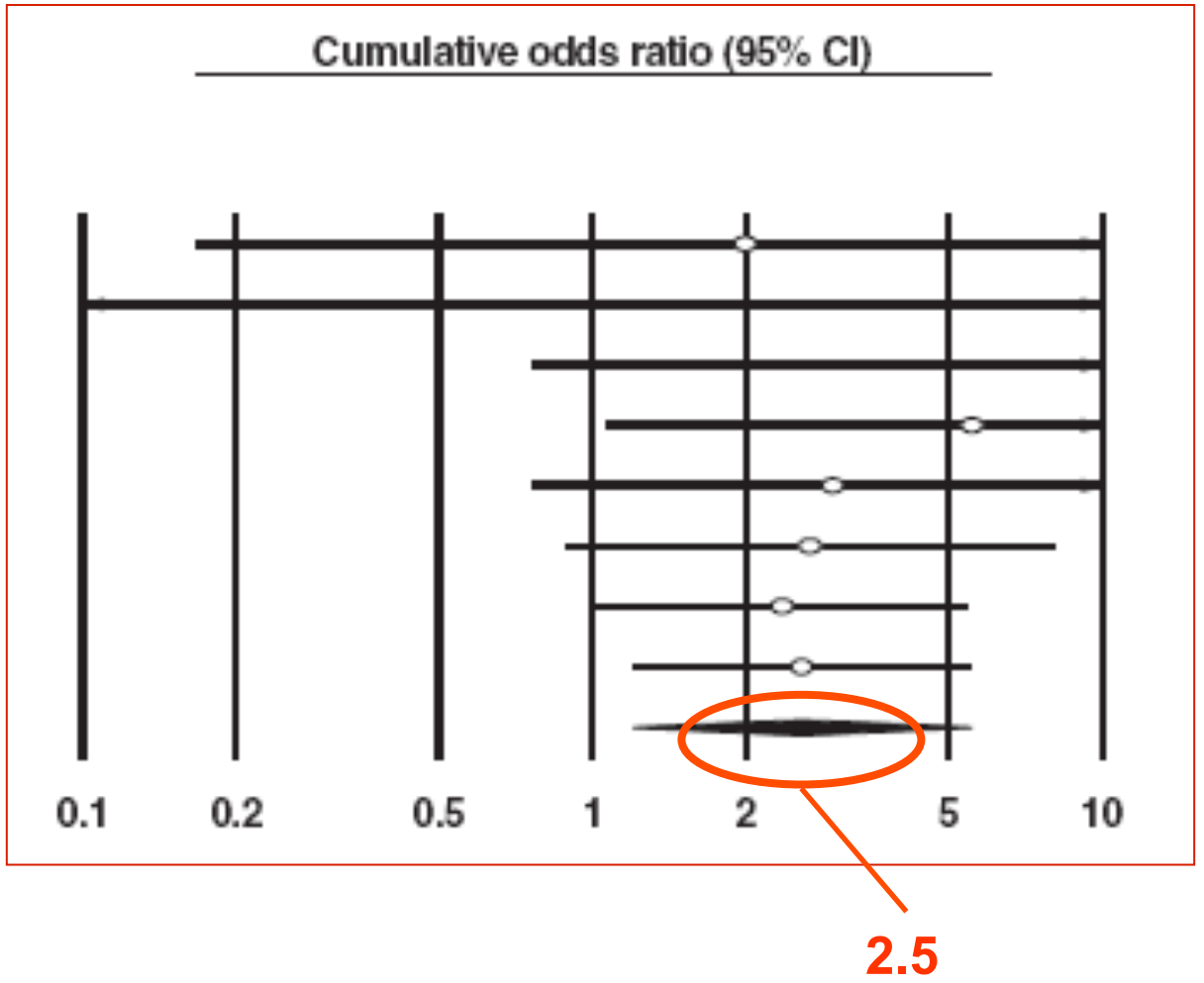
*Includes 43 patients with Chlamydia or Mycoplasma infection.

Pediatr Infect Dis J 2008;27: 95–99

TABLE 3. Sensitivity and Specificity of C-Reactive Protein as Predictor of Bacterial/Mixed Penumonia

	C-RP Cutoff (mg/L)	Sensitivity	Specificity	Odds Ratio
Isaacs, 1989[19]	50	0.75	0.4	2
Babu et al, 1989[21]	35	1	1	2500
Korppi and Kroger, 1992[8]	40	0.35	0.88	3.9
Nohynek et al, 1995[20]	40	0.41	0.63	1.2
Heiskanen-Kosma and Korppi, 2000[22]	40	0.17	0.83	0.55
Moulin et al, 2001[17]	60	0.7	0.52	2.5
Virkki et al, 2002[16]	40	0.66	0.53	2.2
Lala et al, 2002[23]	40	0.76	0.6	4.7

Pediatr Infect Dis J 2008;27: 95–99



Pediatr Infect Dis J 2008;27: 95–99

In summary, this meta-analysis showed that children with serum concentrations exceeding 40–60 mg/L were more likely to have bacterial pneumonia than children with lower serum concentrations. Given an a priori probability of 41% for bacterial pneumonia among children presenting with febrile lower respiratory illnesses, a child with clinical and radiographic pneumonia and a high serum CRP has a 64% probability of a bacterial infection.

Pediatr Infect Dis J 2008;27: 95–99

Differentiation of bacterial and viral community-acquired pneumonia in children

Massimiliano Don,[1] Francesca Valent,[2] Matti Korppi[3] and Mario Canciani[1]

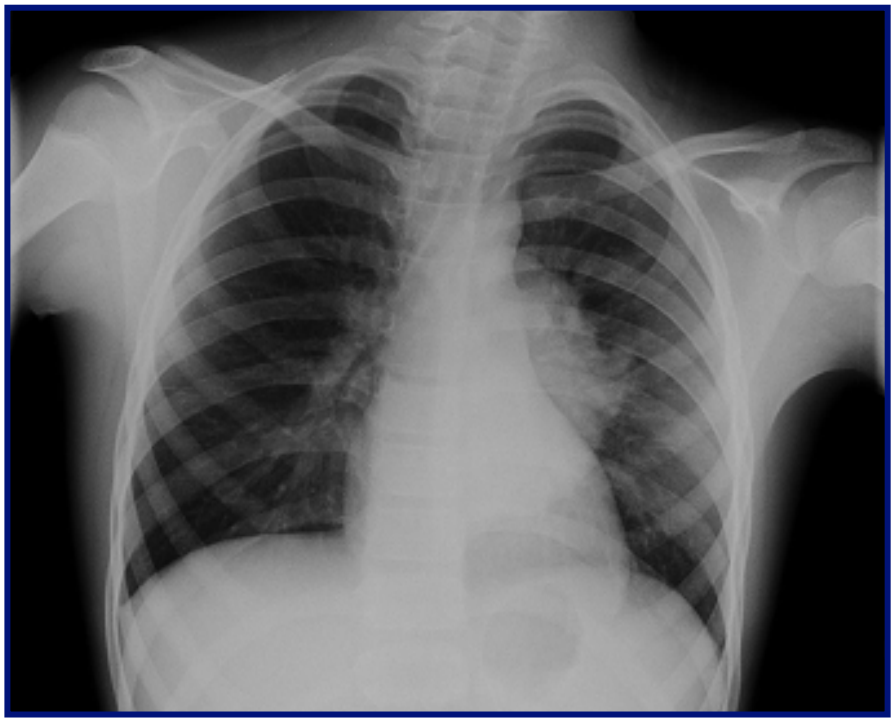
In conclusion, the four non-specific inflammatory markers, CRP, PCT, ESR, WBC count and their combinations have a limited role in the separation of bacterial from viral pneumonia in children. Any combination, however, was sufficiently sensitive and specific to be used routinely. In particular, low levels considered as typical for viral infections were not able to rule out bacterial infection. In everyday clinical practice, both microbe-specific and non-specific laboratory test results must always be interpreted together with other clinical observations, such as medical history, findings on clinical examination and chest radiograph.

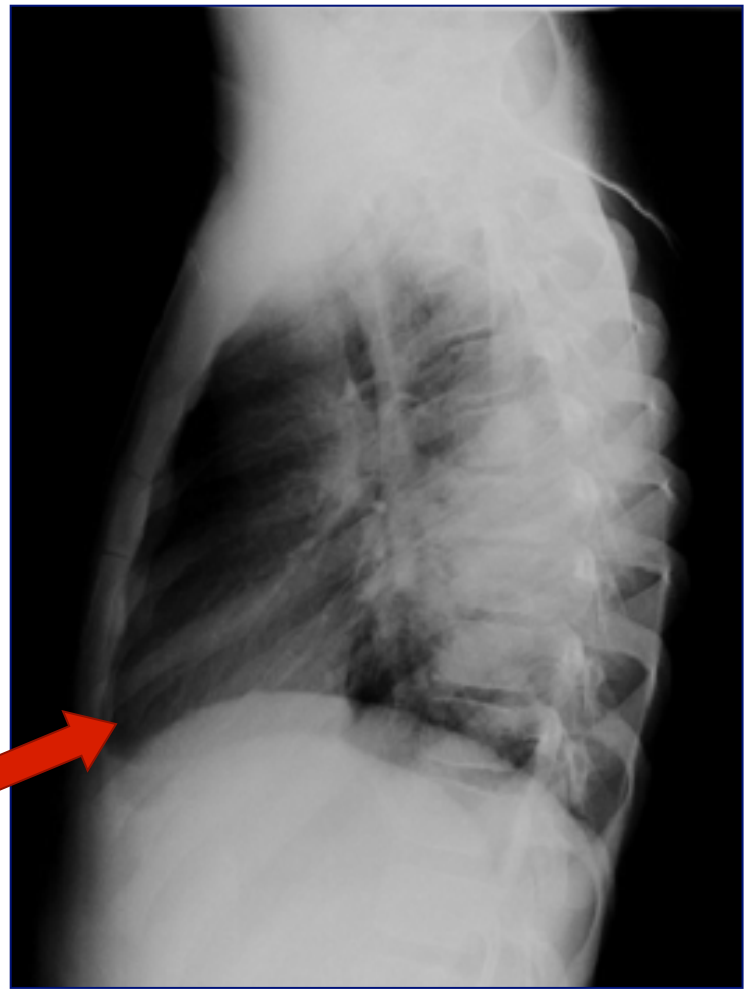
Pediatrics International (2009) **51**, 91–96

Lorenzo, 12 anni

- Febbre da 2 gg con TC max 39°C, associata a dolore addominale e cefalea frontale
- Comparsa da 24 ore di dolore toracico a barra
- Bambino abbattuto in relazione alla sintomatologia dolorosa presentata
- FR 25 apm, FC 89 bpm, sat O2 100% in a.a.
- Riduzione di ingresso aereo all'emitorace sx → soffio bronchiale ai campi medi

Lorenzo, 12 anni





Opacamento parenchimale nel lobo inferiore di sx, posteriormente, a limite superiore netto in corrispondenza della scissura

Accertamenti eseguiti:

- GB 13.930/mmc (N 12.350/mmc),
- PCR 120 mg/L , PCT 1,2 u/L

- IgM rapide per Mycoplasma +
- Emocoltura: negativa
- Buona risposta alla terapia con claritromicina

Take home messages

Febbre senza localizzazione

La PCR trova indicazione come “migliore” esame di screening nel lattante e nel piccolo bambino con febbre senza localizzazione.

La PCT sembra essere più accurata nelle febbri di recente insorgenza e nelle infezioni altamente invasive.

Polmonite

Gli indici di flogosi hanno un ruolo limitato nella diagnosi eziologica delle polmoniti e non vanno utilizzati come esami routinari.

Una concordanza nell’aumento di tutti gli indici di flogosi è indicativa di una forma batterica, ma la loro negatività non esclude tale diagnosi.

Dolore addominale acuto

- ✓ **Il dolore addominale è motivo frequente di accesso al PS (5%)**
- ✓ **le malattie in causa sono molteplici; l'eziologia è chirurgica in meno del 10% dei casi, prevalentemente rappresentata dall'appendicite acuta**
- ✓ **la valutazione clinica è talora difficile e ciò tanto più quanto più piccolo è il bambino**
- ✓ **La sensibilità dei dati clinici per la diagnosi di appendicite alla prima visita si aggira intorno al 70%**
- ✓ **L'ecografia aumenta tale sensibilità al 90%, ma tale esame non è sempre disponibile ed è operatore dipendente**

Quale l'accuratezza degli indici di flogosi per la diagnosi di appendicite?

Does This Child Have Appendicitis?

David G. Bundy, MD, MPH, **Julie S. Byerley, MD**, **E. Allen Liles, MD**, **Eliana M. Perrin, MD, MPH**, **Jessica Katznelson, MD**, and **Henry E. Rice, MD**

JAMA. 2007 July 25; 298(4): 438–451. doi:10.1001/jama.298.4.438.

Accuracy of symptoms, signs, and basic laboratory tests for diagnisis appendicitis in children*

Symptom, signs, or test	Number of studies(n)	Sensitivity (range)	Specificity (range)	+LR (summary value or range)	-LR (summary value or range)
Fever	1 (246)† 4 (1738)	75% 26% to 93%	78% 29% to 75%	3.4 1.2	0.32 0.53
Vomiting	1 (246)† 4 (1017)	79% 63% to 86%	64% 34% to 69%	2.2 1.4	0.33 0.57
RLQ pain	3 (2021)	62% to 96%	5% to 63%	1.2	0.56
Pain migrating to RLQ	2 (744)	45% to 68%	76% to 78%	1.9 to 3.1	0.41 to 0.72
Localised tenderness	1 (246)†	21%	81%	1.1	1.0
RLQ tenderness	4 (2200)	80% to 97%	5% to 52%	1.3	0.45
Rebound tenderness	3 (883)	53% to 88%	76% to 86%	3.0	0.28
Rectal tenderness	4 (1092)	27% to 55%	60% to 90%	2.3	0.70
Involuntary guarding	2 (744)	62% to 86%	63% to 67%	1.6 to 2.6	0.21 to 0.61
White blood cell count (>10.000/uL)	**4 (1912)**	**50% to 92%**	**29%to 76%**	**2.0**	**0.22**
C-reactive protein (>8-10 mg/L)	**3 (522)**	**64% to 85%**	**33% to 82%**	**1.3 to 3.6**	**0.44 to 0.47**
Alvarado score (≥7)	3 (847)	72% to 93%	81% to 82%	4.0	0.20
*Diagnostic terms defined in glossary; RLQ=right lower quadrant.†Level 1 study (unselected children with abdominal pain); all other study are level 3 (selected patient					

P.C. Wyer, *Arch. Dis. Child. Ed. Pract. 2009; 94;95*

Review: symptoms, signs,and lab tests have moderate accuracy for detecting appendicitis in children

The most useful single feature for diagnosis appendicitis in children with abdominal pain was fever in unselected children and rebound tenderness in selected children.

P.C. Wyer, ***Arch. Dis. Child. Ed. Pract. 2009; 94;95***

Giulia, 2 anni

- Anamnesi personale e fisiologica negative.
- Completato 1° ciclo vaccinale con esavalente e anti-pneumococco.
- Viene condotta in PS perché da 24 ore presenta febbre, scariche liquide, vomiti e crisi di pianto che la madre attribuisce al dolore addominale.

EO all'ingresso

- TC 39°C, FC 150 bpm, FR 30 apm, sat 98% in a.a., TR<2 sec.
- Colorito roseo,non segni di disidratazione, vigile, reattiva anche se irritabile ma consolabile dalla madre.
- Addome trattabile, peristalsi presente.

Giulia, 2 anni

Accertamenti eseguiti in PS:

- GB 9.800/mmc (N 7.000/mmc)
- PCR 20 mg%
- Elettroliti, glicemia, funzionalità renale ed epatica nella norma
- Esame urine negativo

Dimissione con diagnosi di gastroenterite

Nei giorni successivi..

- Bambina ancora febbrile (TC 38-38,5°C), 1-2 vomiti al giorno, non scarica, secondo la madre continua ad avere dolore addominale.

- Dopo 4 giorni peggioramento improvviso della condizioni generali per cui viene ricondotta in PS.

EO all'ingresso

- TC 36.7°C, FC 200 bpm, FR 80 apm, sat 98% in a.a., TR>3 sec, con estremità fredde e marezzate, polsi iposfigmici.
- Iporeattiva, risponde poco agli stimoli.
- Addome teso alla palpazione con peristalsi torpida.

Stato di shock

A questo punto:

- Ossigeno
- Accesso vascolare
- 2 boli di fisiologica (20 mL/kg)
- Intubazione
- Antibiotici
- Monitoraggio intensivo

Accertamenti eseguiti in PS:

- GB 23.240/mmc (N 18.300/mmc)
- PCR >120 mg%
- Emogas: pH 7,20, pCO2 22 mmHg, HCO3 15, EB -10.
- Creatinina 133 mmol/L, azotemia 12,5 mmol/L
- Ecografia addominale: anse immobili con pareti inspessite, falda liquida nel piccolo bacino

Giulia, 2 anni

La diagnosi

Diagnosi clinica

Shock settico da appendicite acuta con peritonite

Diagnosi chirugica

appendicite acuta
peritonite diffusa

Diagnosi istologica

appendicite acuta
periviscerite

Take home messages

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La PCR trova indicazione come “migliore” esame di screening nel lattante e nel piccolo bambino con febbre senza localizzazione.

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Gli indici di flogosi hanno un ruolo limitato nella diagnosi eziologica delle polmoniti e non vanno utilizzati come esami routinari.

Una concordanza nell’aumento di tutti gli indici di flogosi è indicativa di una forma batterica, ma la loro negatività non esclude tale diagnosi.

Appendicite

Gli indici di flogosi non hanno un ruolo nella diagnosi di appendicite acuta non complicata.

Grazie per l'attenzione