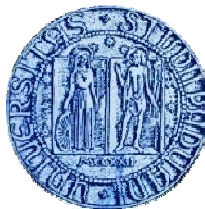


3° CONGRESSO NEWMICRO
...The need for speed: il
laboratorio di Microbiologia e le
Urgenze Infettive



***Le urgenze infettive in Pediatria:
confronto tra Pediatra e Microbiologo
nell'approccio al lattante febbrile***



***Prof.ssa Liviana Da Dalt
Università degli Studi di Padova
U.O.C. di Pediatria, Treviso***

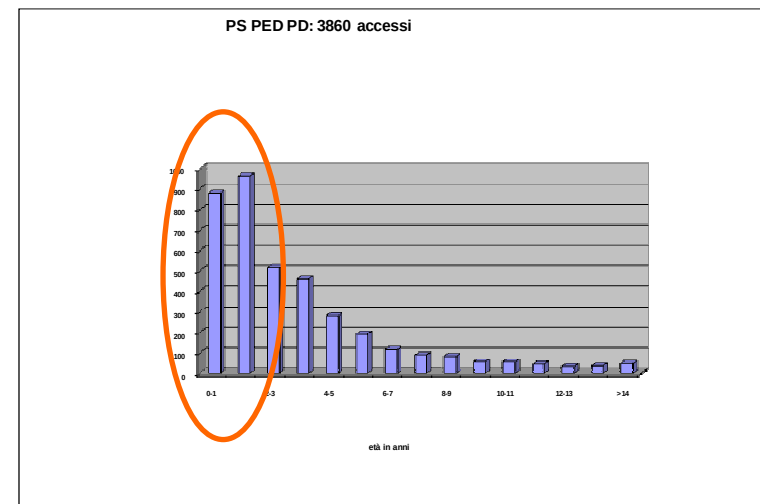


**Padenghe sul Garda (BS)
20-22 Marzo 2013**

La febbre nei primi anni di vita

- ✓ E' un problema comune
 - 15% degli accessi totali al PS, 20% degli accessi non traumatici
 - 30% delle visite ambulatoriali
- ✓ E' nella grande maggioranza dei casi di origine infettiva:
 - virale (70%))
 - batterica (30%)
- ✓ E' più frequente nelle primissime età della vita

Van den Bruel, Lancet 2010
UpToDate 2012

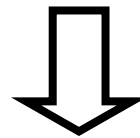


La febbre nei primi anni di vita

• • •

.....e nelle primissime età della vita

- ✓ più che nelle età successive può sottendere un'Infezione Batterica Severa, anche quando le condizioni generali del bambino sono buone
- ✓ e' spesso un sintomo isolato di tali infezioni per la scarsa capacità del bambino a localizzare i segni e i sintomi specifici di malattia



Febbre senza localizzazione

Dimensione del problema

- 408 bambini con FSL di età compresa tra i 7 giorni ed i 36 mesi (Padova Maggio-Ottobre2005)
- 94 (20%) con diagnosi finale di IBS

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

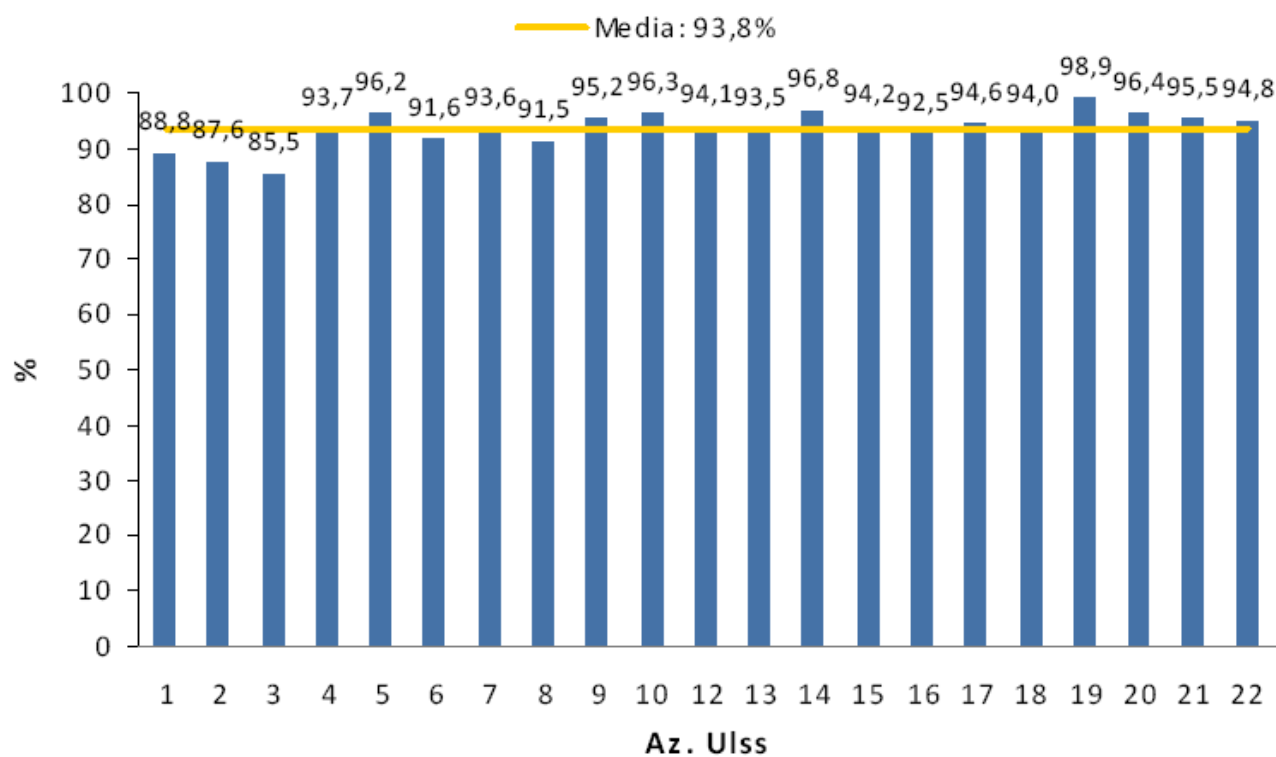
	No. of Patients	%
<u>Pyelonephritis</u>	50	53.2
<u>Pneumonia</u>	24	25.5
Meningitis	7	7.5
Occult bacteremia	6	6.4
Sepsis	3	3.2
Osteomyelitis	2	2.1
Septic arthritis	2	2.1



REGIONE DEL VENETO

REPORT MONITORAGGIO SOSPENSIONE OBBLIGO VACCINALE

Figura 15: Coperture per vaccino contro il pneumococco 7valente nelle Az. Ulss della Regione Veneto. Nati secondo semestre 2008. Dati al 31/03/2009



The NEW ENGLAND JOURNAL of MEDICINE

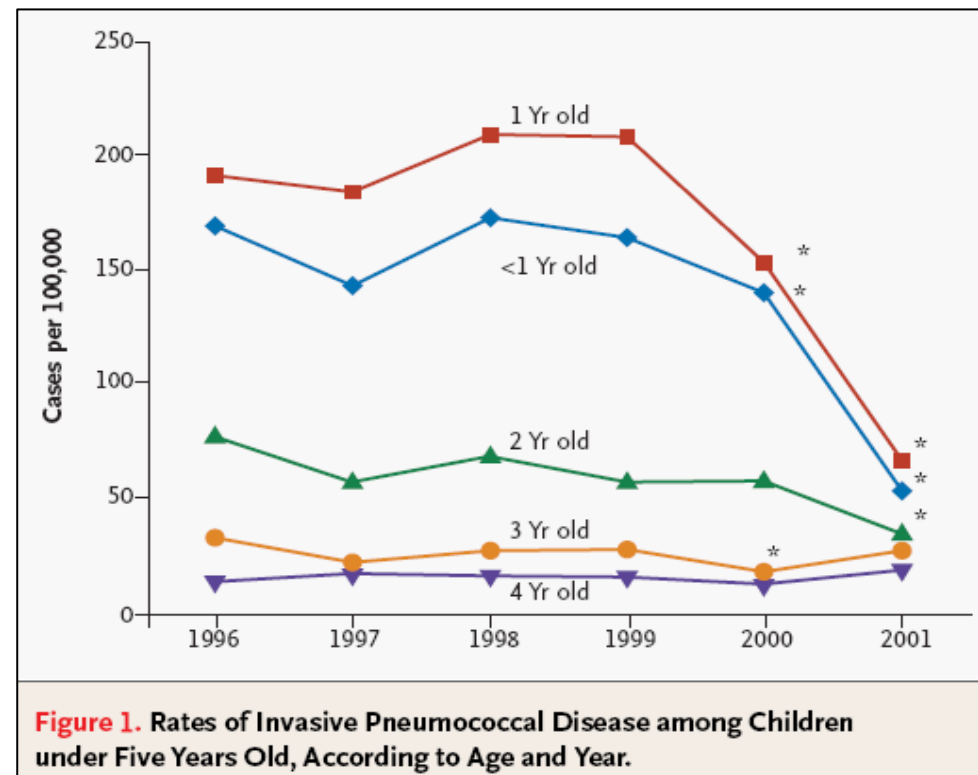
ESTABLISHED IN 1812

MAY 1, 2003

VOL. 348 NO. 18

Decline in Invasive Pneumococcal Disease after the Introduction of Protein–Polysaccharide Conjugate Vaccine

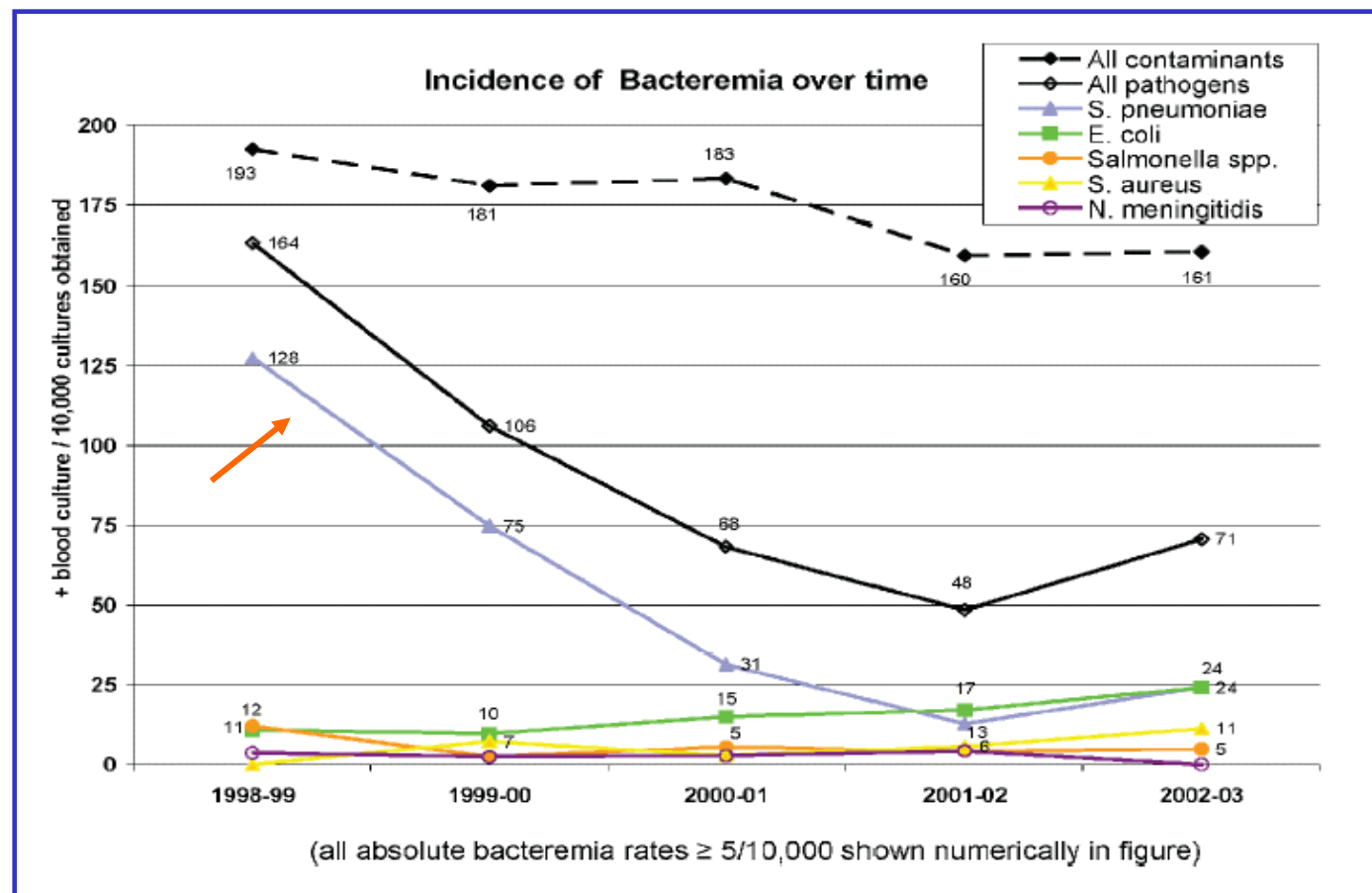
Cynthia G. Whitney, M.D., M.P.H., Monica M. Farley, M.D., James Hadler, M.D., M.P.H., Lee H. Harrison, M.D., Nancy M. Bennett, M.D., Ruth Lynfield, M.D., Arthur Reingold, M.D., Paul R. Cieslak, M.D., Tamara Pilishvili, M.P.H., Delois Jackson, M.S.A., Richard R. Facklam, Ph.D., James H. Jorgensen, Ph.D., and Anne Schuchat, M.D., for the Active Bacterial Core Surveillance of the Emerging Infections Program Network



Changing Epidemiology of Outpatient Bacteremia in 3- to 36-Month-Old Children After the Introduction of the Heptavalent-Conjugated Pneumococcal Vaccine

Arnd M. Herz, MD,* Tara L. Greenhow, MD,† Jay Alcantara,* John Hansen, BA,‡
Roger P. Baxter, MD,§ Steve B. Black, MD,‡ and Henry R. Shinefield, MD‡

The Pediatric Infectious Disease Journal • Volume 25, Number 4, April 2006



ORIGINAL ARTICLE

Effect of Pneumococcal Conjugate Vaccine on Pneumococcal Meningitis

Heather E. Hsu, M.P.H., Kathleen A. Shutt, M.S.,
Matthew R. Moore, M.D., M.P.H., Bernard W. Beall, Ph.D.,
Nancy M. Bennett, M.D., Allen S. Craig, M.D., Monica M. Farley, M.D.,
James H. Jorgensen, Ph.D., Catherine A. Lexau, Ph.D., M.P.H.,
Susan Petit, M.P.H., Arthur Reingold, M.D., William Schaffner, M.D.,
Ann Thomas, M.D., Cynthia G. Whitney, M.D., M.P.H.,
and Lee H. Harrison, M.D.

JANUARY 15, 2009

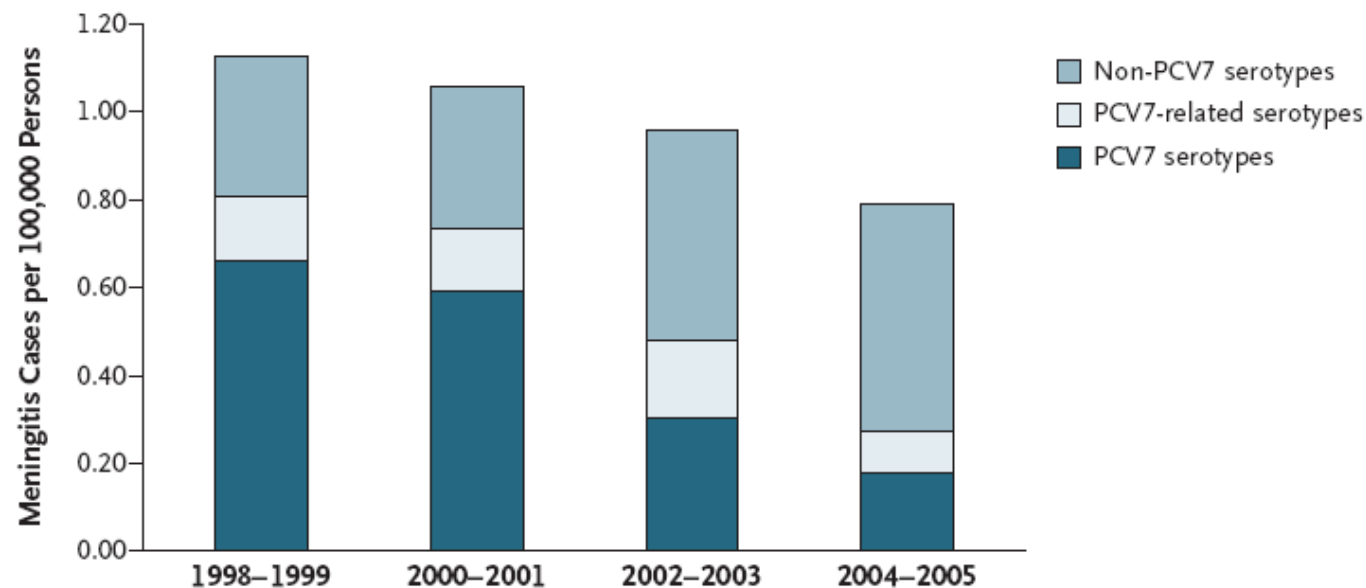


Figure 1. Mean Annual Incidence of Pneumococcal Meningitis, According to Serotype Group and Time Period.

Le dimensioni del problema

PS Pediatrico di PD (magg-nov 2009)
670 bambini 0-3 anni;

Eziologie	Diagnosi	N° casi
Virali (67%)	- Virosi non specificata - Virosi alte vie - Gengivostomatite - Gastroenterite	260 120 22 50
Batteriche localizzate (24%)	- Faringotonsillite / Otite - Cellulite / Linfadenite	150 12
Batteriche severe (9%)	- IVU - Broncopolmonite - Batteriemie - Artrite settica - Osteomielite - Meningite	30 12 3 1 1 1

Bacteremia in feverish children presenting to the emergency department: retrospective study and literature review

Silvia Bressan (silvia.bressan.1@unipd.it)¹, Paola Berlese¹, Teresa Mion¹, Susanna Masiero¹, Antonietta Cavallaro², Liviana Da Dalt¹

1.Department of Pediatrics, University of Padova, Padova, Italy

2.Department of Microbiology and Virology, Padova Hospital, Padova, Italy

Acta Paediatr 2011

Emocolture positive	3/392	0.7%
Emocolture positive Streptococco Pn.	0/392	0%
Emocolture positive 3-36 mesi	1/291	0.34%
Emocolture positive 1-3 mesi	2/101	2%
Contaminanti	15/392	3.8%

Blood Culture and Bacteremia Predictors in Infants Less Than Three Months of Age With Fever Without Source

Borja Gómez, MD, Santiago Mintegi, MD, Javier Benito, MD, Andere Egireun, MD,
Diego Garcia, MD, and Eider Astobiza, MD

Pediatric. Infect Dis.2011

TABLE 1. Final Diagnoses for the 1018 Patients Included in This Study

No SBI	820 (80.6%)
SBI	198 (19.4%)
UTI	172
Occult bacteremia	9
UTI and bacteremia	8
Bacterial meningitis	4
Sepsis	2
Cellulitis	2
Acute otitis media	1

Results are expressed as number (%).

TABLE 3. Bacteria Isolated From Blood Cultures

Bacterium	No. Cases
<i>Escherichia coli</i>	9
<i>Streptococcus pneumoniae</i>	4
Group B <i>Neisseria meningitidis</i>	3
<i>Enterococcus faecalis</i>	3
<i>Streptococcus agalactiae</i>	2
<i>Klebsiella pneumoniae</i>	1
<i>Staphylococcus aureus</i>	1

**Gómez B¹, Bressan S², Mintegi S¹, Da Dalt L³, Olaciregui I⁴, de la Torre M⁵,
Ruano A⁶, Palacios M⁷, Berlese P³, Blázquez D⁸**

*¹Hospital de Cruces, ²University of Padova, ³Ospedale Ca' Foncello, ⁴Hospital Donostia,
⁵Hospital Infantil Universitario Niño Jesús, ⁶Hospital de Basurto, ⁷Complejo Hospitalario de
Navarra, ⁸Hospital 12 de Octubre*

557 well-appearing infants under 3 months of age
with FWS in whom PCT and a BC was performed

122 SBI (21.9%)

Final diagnosis	n	%
Urinary tract infections	110	19.7%
Urinary tract infections + bacteraemia	6	1.1%
Occult bacteraemias	5	0.9%
Bacterial meningitis	1	0.2%

Predicting Severe Bacterial Infections in Well-Appearing Febrile Neonates

Laboratory Markers Accuracy and Duration of Fever

Silvia Bressan, MD, Barbara Andreola, MD, Francesca Cattelan, MD, Tiziana Zangardi, MD,
Giorgio Perilongo, MD, and Liviana Da Dalt, MD

Pediatr Infect Dis J 2010;29:227-232

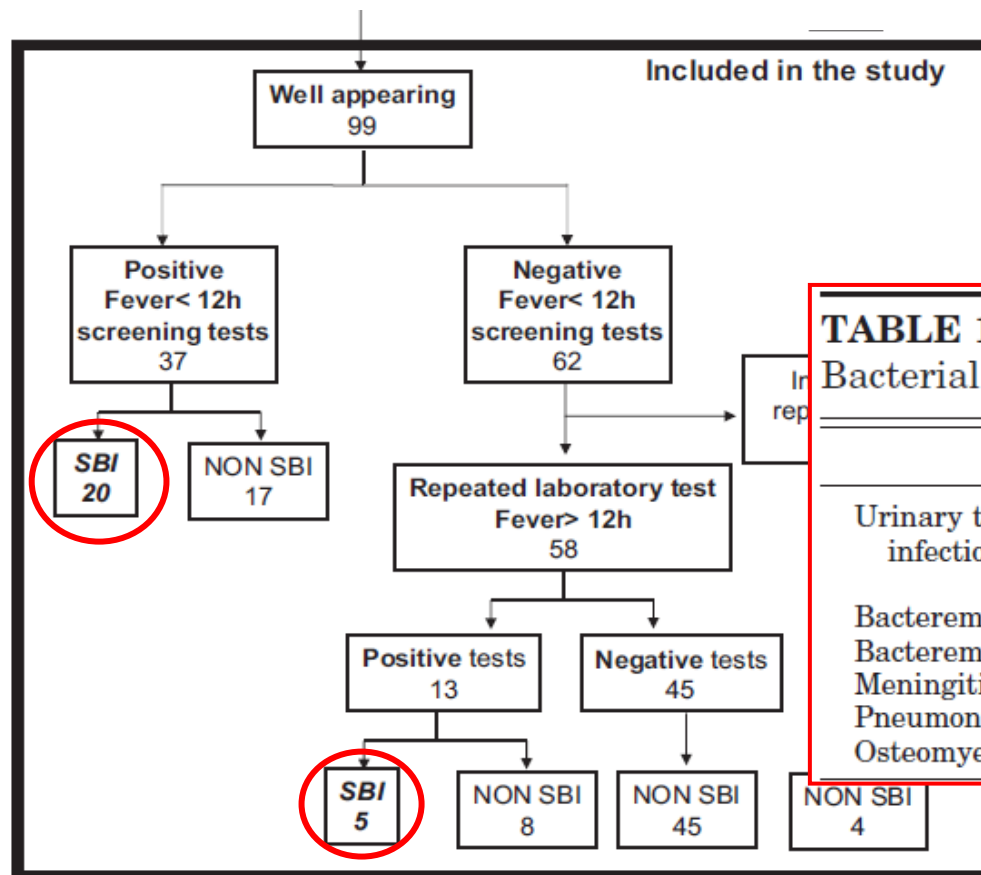


TABLE 1. Final Diagnosis of Patients With Severe Bacterial Infections (n = 25)

	No. Patients	%	Causative Organisms
Urinary tract infections (UTI)	15	60%	13 <i>Escherichia coli</i> 2 Enterococco 1 <i>Klebsiella pneumoniae</i>
Bacteremia	3	12%	3 group B Streptococcus
Bacteremia and UTI	2	8%	2 <i>Escherichia coli</i>
Meningitis	3	12%	3 group B Streptococcus
Pneumonia	1	4%	Not determined
Osteomyelitis	1	4%	Not determined

Approccio tradizionale nel lattante febbrile

- ✓ Ampio utilizzo di esami colturali per la ricerca di infezioni batteriche occulte
- ✓ Ampio utilizzo di terapia antibiotica “empirica”

**PUR IN BAMBINI CON DIAGNOSI FINALE DI INFEZIONE
VIRALE CERTA O PRESUNTA**



Febbre nei primi anni di vita

Quali gli strumenti del Pediatra per una diagnosi accurata in urgenza?

- ✓ **Attenta valutazione clinica**
- ✓ **Esami di screening**





Diagnostic value of clinical features at presentation to identify serious infection in children in developed countries: a systematic review

Ann Van den Bruel, Tanya Haj-Hassan, Matthew Thompson, Frank Buntinx, David Mant, for the European Research Network on Recognising Serious Infection investigators*

Lancet 2010; 373:834-45



30 studi inclusi

Principali predittori di infezione severa (LR >5):

- ✓ rash petecchiale
- ✓ scarsa perfusione periferica
- ✓ polipnea
- ✓ $TC \geq 40^{\circ}C$
- ✓ "parental concern"
- ✓ "clinician instinct"



...

Esami di screening

- ✓ **Esami ematici: - emocromo con Formula**
 - PCR
 - PCT
- ✓ **Esame delle urine**



Diagnostic value of laboratory tests in identifying serious infections in febrile children: systematic review

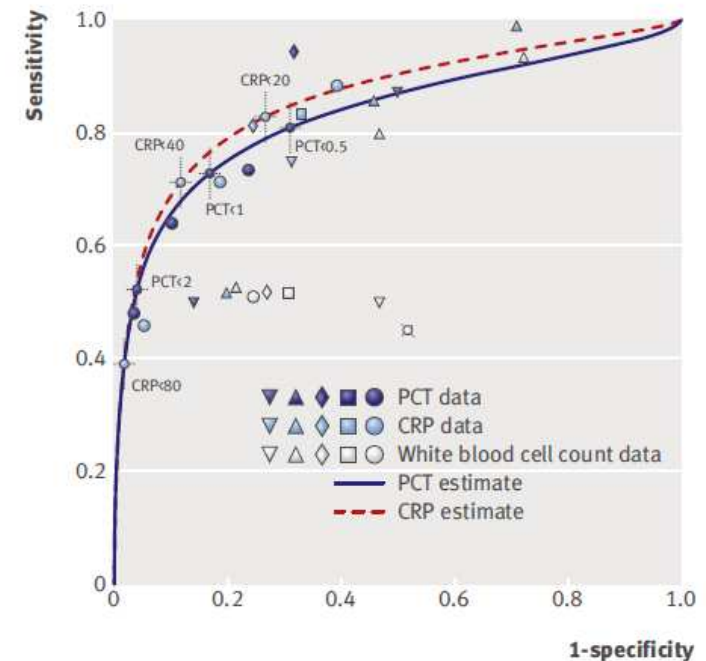
Ann Van den Bruel, academic clinical lecturer,¹ Matthew J Thompson, associate professor,^{1,2} Tanya Haj-Hassan, medical student,³ Richard Stevens, senior statistician,¹ Henriette Moll, professor,⁴ Monica Lakhanpaul, senior lecturer,⁵ David Mant, emeritus professor¹

BMJ 2011;342:d3082

14 studi inclusi

Principali conclusioni:

- ✓ GB: Limitato valore diagnostico
- ✓ PCR e PCT: accuratezza sovrapponibile
- ✓ PCR più vantaggiosa per:
 - minori costi
 - maggior disponibilità
- ✓ PCT: più accurata
 - ✓ nelle fasi precoci della malattia (< 12 ore)



Diagnostic Value of Procalcitonin in Well-Appearing Young Febrile Infants

AUTHORS: Borja Gomez, MD,^a Silvia Bressan, MD,^b Santiago Mintegi, MD,^a Liviana Da Dalt, MD,^c Daniel Blazquez, MD,^d Izaskun Olaciregui, MD,^e Mercedes de la Torre, MD,^f Miriam Palacios, MD,^g Paola Berlese, MD,^h and Aitor Ruano, MD^h

^aCruces University Hospital, Barakaldo, Spain; ^bDepartment of Pediatrics, University of Padova, Padova, Italy; ^cCa' Foncello Hospital, Treviso, Italy; ^d12 de Octubre University Hospital, and ^eNiño Jesús Children's University Hospital, Madrid, Spain; ^fDonostia University Hospital, Donostia, Spain; ^gNavarra Hospital Complex, Pamplona, Spain; and ^hBasurto University Hospital, Bilbao, Spain



WHAT'S KNOWN ON THIS SUBJECT: Procalcitonin is a better marker than white blood cell count and overall comparable to C-reactive protein for identifying children at higher risk of having a serious bacterial infection. However, its value in well-appearing young febrile infants has not been clearly defined.



WHAT THIS STUDY ADDS: In well-appearing young febrile infants, procalcitonin is a better marker than C-reactive protein for identifying patients with an invasive bacterial infection.

Pediatrics Vol 130, Number 5, November 2012

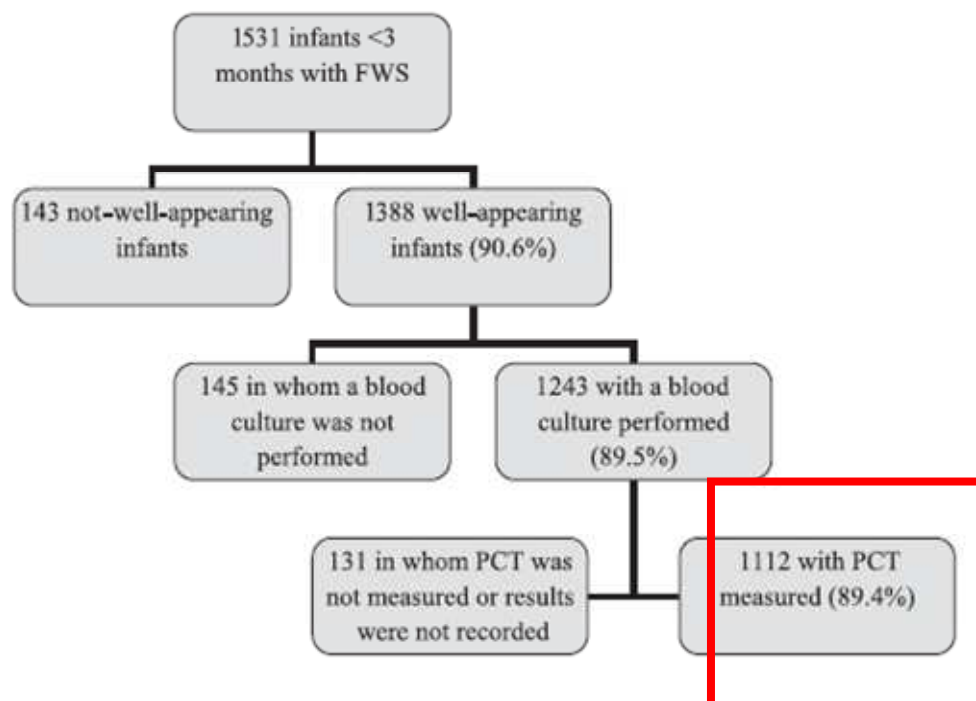


FIGURE 1

Flowchart for identification of infants to be included in the analysis.

Diagnostic Value of Procalcitonin in Well-Appearing Young Febrile Infants

AUTHORS: Borja Gomez, MD,^a Silvia Bressan, MD,^b Santiago Mintegi, MD,^a Liviana Da Dalt, MD,^c Daniel Blazquez, MD,^d Izaskun Olaciregui, MD,^e Mercedes de la Torre, MD,^f Miriam Palacios, MD,^g Paola Berlese, MD,^h and Aitor Ruano, MD^h

^aCruces University Hospital, Barakaldo, Spain; ^bDepartment of Pediatrics, University of Padova, Padova, Italy; ^cCa' Foncello Hospital, Treviso, Italy; ^d12 de Octubre University Hospital, and ^eNiño Jesús Children's University Hospital, Madrid, Spain; ^fDonostia University Hospital, Donostia, Spain; ^gNavarra Hospital Complex, Pamplona, Spain; and ^hBasurto University Hospital, Bilbao, Spain



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WHAT THIS STUDY ADDS: In well-appearing young febrile infants, procalcitonin is a better marker than C-reactive protein for identifying patients with an invasive bacterial infection.

Pediatrics Vol 130, Number 5, November 2012

TABLE 3 Definitive Diagnoses for the 289 Patients Diagnosed With a Definite SBI and Bacteria Isolated in Patients With IBIs

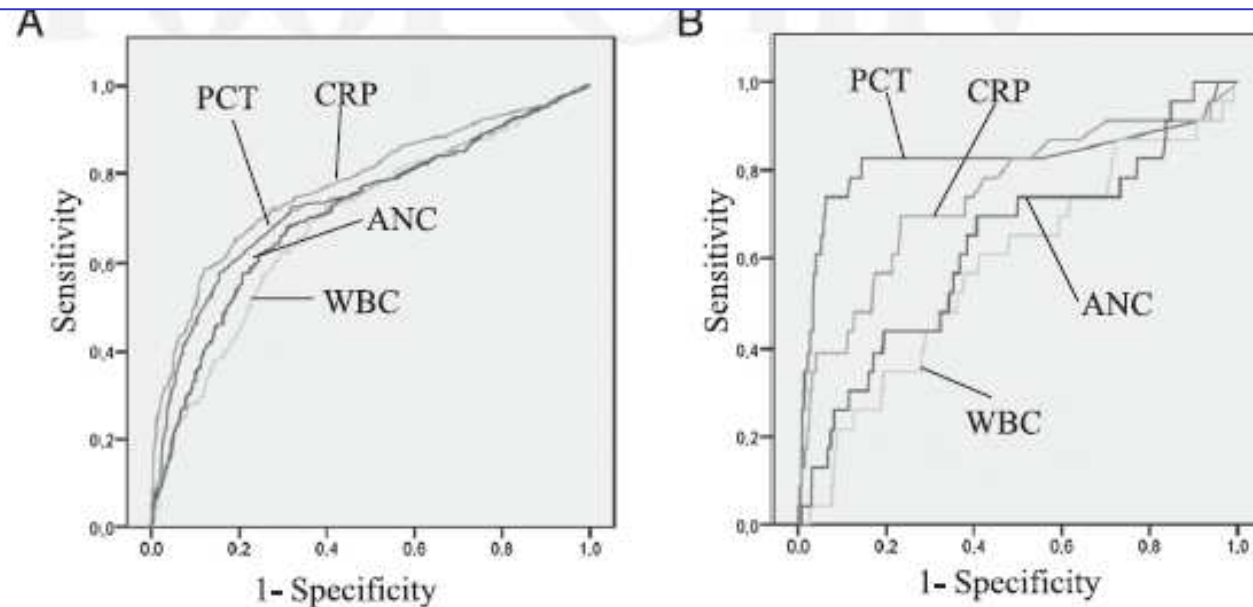
Diagnosis (n)	Bacteria (n)
No IBI	
UTI (264)	—
Bacterial gastroenteritis (2)	—
IBI	
UTI and bacteremia (12)	<i>E. coli</i> (11); <i>S. mitis</i> (1)
Occult bacteremia (10)	<i>S. agalactiae</i> (3); <i>E. faecalis</i> (2); <i>S. aureus</i> (2); <i>E. coli</i> (1); group B <i>N. meningitidis</i> (1); <i>S. pneumoniae</i> (1)
Bacterial meningitis (1)*	<i>S. agalactiae</i> (1)

* The patient diagnosed with bacterial meningitis was a 10-d-old girl who arrived at the PED I h after fever was first noted. PCT was 1.9 ng/mL, and CRP was 7 mg/L; pleocytosis was detected, and no bacteria grew in the CSF culture, but *S. agalactiae* was isolated in the blood culture.

1112 with PCT measured (89.4%)

FIGURE 1

Flowchart for identification of infants to be included in the analysis.



Infection biomarkers

Area Under the ROC Curve (95% CI)

	SBI	IBI
PCT	0.739 (0.702–0.776)	0.825 (0.698–0.952)
CRP	0.776 (0.741–0.811)	0.747 (0.629–0.865)
ANC	0.711 (0.674–0.748)	0.629 (0.506–0.752)
WBC	0.692 (0.655–0.729)	0.583 (0.460–0.706)

FIGURE 2

Receiver operating characteristic (ROC) curves to detect definite (A) SBIs and (B) IBIs.

Diagnostic value of laboratory tests in identifying serious infections in febrile children: systematic review

Ann Van den Bruel, academic clinical lecturer,¹ Matthew J Thompson, associate professor,^{1,2} Tanya Haj-Hassan, medical student,³ Richard Stevens, senior statistician,¹ Henriette Moll, professor,⁴ Monica Lakhanpaul, senior lecturer,⁵ David Mant, emeritus professor¹

BMJ 2011;342:d3082

WHAT THIS STUDY ADDS

C reactive protein and procalcitonin may be useful measures, but different cut-off values should be used for ruling in or ruling out serious infections

White blood cell counts are less useful

No evidence from primary care was identified



CLINICAL PRACTICE GUIDELINE

Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months

PEDIATRICS Volume 128, Number 3, September 2011

Downloaded from

TABLE 1 Sensitivity and Specificity of Components of Urinalysis, Alone and in Combination

Test	Sensitivity (Range), %	Specificity (Range), %
Leukocyte esterase test	83 (67–94)	78 (64–92)
Nitrite test	53 (15–82)	98 (90–100)
Leukocyte esterase or nitrite test positive	93 (90–100)	72 (58–91)
Microscopy, WBCs	73 (32–100)	81 (45–98)
Microscopy, bacteria	81 (16–99)	83 (11–100)
Leukocyte esterase test, nitrite test, or microscopy positive	99.8 (99–100)	70 (60–92)



CLINICAL PRACTICE GUIDELINE

Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months

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Leukocyte esterase or nitrite test positive	93 (90–100)	72 (58–91)
Microscopy, WBCs	73 (32–100)	
Microscopy, bacteria	81 (16–99)	
Leukocyte esterase test, nitrite test, or microscopy positive	99.8 (99–100)	

Nitrite Test

A nitrite test is not a sensitive marker for children, particularly infants, who empty their bladders frequently. Therefore, negative nitrite test results have little value in ruling out UTI. Moreover, not all urinary pathogens reduce nitrate to nitrite. The test is helpful when the result is positive, however, because it is highly specific (ie, there are few false-positive results).³²

Approccio tradizionale nel lattante febbrile

- ✓ Ampio utilizzo di esami colturali per la ricerca di infezioni batteriche occulte
- ✓ Ampio utilizzo di terapia antibiotica “empirica”

**PUR IN BAMBINI CON DIAGNOSI FINALE DI INFEZIONE
VIRALE CERTA O PRESUNTA**



Il caso di Marco, 27 giorni

Il 2.02.2013 viene condotto al PS per febbre 12 ore (T max 38.9 °C ascellare).

Non altra sintomatologia associata.

Nato a termine da parto eutocico. Sierologie e tamponi materni riferite negative. Perinatalità regolare. Allattamento materno esclusivo.

All'arrivo in PS

Condizioni generali buone. Cute calda e rosea. Reattività, suzione e pianto validi.

Obiettività generale non significativa.



Il caso di Marco, 27 giorni

Vengono eseguiti all'ingresso

Esami di screening:

Stick urine: PS 1010, PH 6, Leucociti +/-, resto negativo.

Emocromo: GB 7970/mm³ (N 3030/mm³), GR 3860000/mm³, Hb 11.8 g/L, Htc 46%, MCV 93.5 fL, Ptl 296000/mm³,

PCR: 41 mg/L → 57 mg/L

PCT: 0.1 ug/L → 0.3 ug/L



Il caso di Marco, 27 giorni

Vengono eseguiti all'ingresso

Esami di screening:

Stick urine: PS 1010, PH 6, Leucociti +/-, resto negativo.

Emocromo: GB 7970/mm³ (N 3030/mm³), GR 3860000/mm³, Hb 11.8 g/L, Htc 46%, MCV 93.5 fL, Ptl 296000/mm³,

PCR: 41 mg/L → 57 mg/L

PCT: 0.1 ug/L → 0.3 ug/L

Esami colturali:

Emocoltura....

Urocoltura....

Liquorcoltura....



Il caso di Marco, 27 giorni

Vengono eseguiti all'ingresso

Esami di screening:

Stick urine: PS 1010, PH 6, Leucociti +/-, resto negativo.

Emocromo: GB 7970/mm³ (N 3030/mm³), GR 3860000/mm³, Hb 11.8 g/L, Htc 46%, MCV 93.5 fL, Ptl 296000/mm³,

PCR: 41 mg/L → 57 mg/L

PCT: 0.1 ug/L → 0.3 ug/L

Esami colturali:

Emocoltura....

Urocoltura....

Liquorcoltura....

Terapia antibiotica empirica:

AMPICILLINA + GENTAMICINA



Il caso di Marco, 27 giorni

Per la persistenza di febbre a 48 ore dall'inizio della terapia antibiotica esegue:

- **Aspirato nasofaringeo positivo per Influenza A/H1N1**



Il caso di Marco, 27 giorni

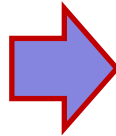
Per la persistenza di febbre a 48 ore dall'inizio della terapia antibiotica esegue:

-Aspirato nasofaringeo positivo per Influenza A/H1N1

Emocoltura....

Urocoltura....

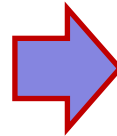
Liquorcoltura....



NEGATIVE



AMPICILLINA + GENTAMICINA



Sospesa dopo 5 giorni

**Diagnosi finale:
INFEZIONE FEBBRILE DA INFLUENZA A/H1N1**

Retrospective Review of Serious Bacterial Infections in Infants Who Are 0 to 36 Months of Age and Have Influenza A Infection

Hannah F. Smitherman, MD; A. Chantal Caviness, MD, MPH; and Charles G. Macias, MD, MPH

Pediatrics, Vol 115, No 3, March 2005

705 bambini 0-6 mesi febbrili:- **163** (23%) Influenza Pos
- **542** (77%) Influenza Neg

TABLE 3. Association Between Influenza A and SBIs

Serious Bacterial Illness	OR*	95% CI for OR
Bacteremia	0.14	0.02–1.04
UTI	0.17	0.04–0.71
SBI including pneumonia	0.28	0.16–0.48
Age 0–28 d	*	
Age 29–90 d	0.21	0.05–0.93
Age 91–1056 d	0.29	0.16–0.53
WBC 0–4999	0.29	0.03–2.69
WBC 5000–14999	0.28	0.14–0.55
WBC ≥15000	0.28	0.09–0.86
SBI excluding pneumonia	0.14	0.04–0.46
Age 0–28 d	*	
Age 29–90 d	0.19	0.03–1.44
Age 91–1056 d	0.17	0.04–0.74
WBC 0–4999	*	
WBC 5000–14999	0.18	0.04–0.77
WBC ≥15000	0.15	0.02–1.16

* Numbers are insufficient to calculate ORs for this stratum.

Conclusions. Febrile children with influenza A had a lower prevalence of bacteremia, urinary tract infections, consolidative pneumonia, or any SBI compared with those without influenza A infection in this study. *Pediatrics 2005;115:710–718; influenza A, fever, serious bacterial infections, recognizable viral syndrome, testable viral syndrome.*

Prevalence of Serious Bacterial Infections in Febrile Infants With Respiratory Syncytial Virus Infection

M. Olivia Titus and Seth W. Wright

Pediatrics 2003;112:282

PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

174 bambini 0-8 settimane RSV+ vs 174 controlli appaiati per età

TABLE 2. Culture Results in Patients With and Without RSV Infection

	RSV-Positive (No. Positive/ No. Tested)	Controls (No. Positive/ No. Tested)
Bacteremia	0/170	5/171
Urinary tract infection	2/147	17/166
Meningitis	0/111	1/153
Overall serious bacterial illness	2/174	22/174*

* One patient had a positive culture from both blood and spinal fluid.

Conclusions. The risk of SBI in febrile infants with RSV infection seems to be very low, particularly in comparison with a control group of RSV-negative infants. These data suggest that full septic evaluations are not necessary in nontoxic-appearing infants with a positive RSV test. It seems to be prudent to examine the urine in these infants, as there is a clinically relevant rate of urinary tract infection. *Pediatrics* 2003;112:282–284; fever, infants, respiratory syncytial virus, septic evaluations.

Serious Bacterial Infections in Febrile Infants 1 to 90 Days Old With and Without Viral Infections

Carrie L. Byington, MD*; F. Rene Enriquez, BS†; Charles Hoff, PhD*; Richard Tuohy, MIBS*; E. William Taggart, BS§; David R. Hillyard, MD§; Karen C. Carroll, MD§; and John C. Christenson, MD*

Pediatrics, Vol 113, No 6 June 2004

- ✓ Prospettico
- ✓ 1779 pz 0 – 90 gg con FSL
- ✓ Sepsis work up + test virologici
(variabili secondo quadro clinico e stagionalità)

Conclusions. Febrile infants with confirmed viral infections are at lower risk for SBI than those in whom a viral infection is not identified. Viral diagnostic data can positively contribute to the management of febrile infants, especially those who are classified as HR. *Pediatrics* 2004;113:1662–1666; febrile infant, viral infection, bacterial infection, Rochester criteria.

Impact of Rapid Influenza Testing at Triage on Management of Febrile Infants and Young Children

Juan Carlos Abanses, MD, M. Denise Dowd, MD, MPH,† Stephen D. Simon, PhD,‡
and Vidya Sharma, MBBS, MPH§*

Pediatric Emergency Care, Vol 22, Number 3, March 2006

1007 bambini 3-36 mesi, Dic 2002 - Marzo 2003
- 719 Influenza Test al Triage
- 288 Non influenza test al Triage

Conclusions: A triage protocol for rapid influenza testing for febrile infants and children appears to significantly decrease additional testing, time in the ED, and charges in children testing positive for influenza.

Outcomes of febrile children without localising signs after pneumococcal conjugate vaccine

E Waddle, R Jhaveri

Arch Dis Child 2009;**94**:144–147.

What this study adds

- ▶ Urinary tract infection is the most common bacterial infection identified in children with fever without a localising source of infection (FWLS).
- ▶ This study validates the UK guidelines that focus on diagnosing urinary tract infection for the management of children with FWLS.
- ▶ US guidelines that still concentrate on the detection and treatment of occult bacteraemia should be changed as this invasive disease is now rare.



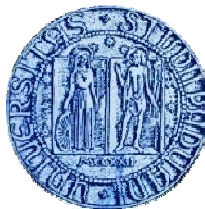
Al fine di contenere la ancora elevata terapia antibiotica empirica:

- ✓ Quanto possono aiutarci i test virologici rapidi?
(quali test disponibili, quale accuratezza, quali tempi di risposta?)
- ✓ Quali sono i tempi minimi per una terapia mirata in caso di sospetta infezione delle vie urinarie?

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Grazie



Prof.ssa Liviana Da Dalt
Università degli Studi di Padova
U.O.C. di Pediatria, Treviso



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89.24.24
PRONTO PAGINEGIALLE
CON TE 24 ORE SU 24

0422 32.43.21

PRONTO

MICRO

CON TE 24 ORE SU 24



- 1. Virus respiratori nei pazienti pediatrici:

- ✓ VIRUS SINCIZIALE RESPIRATORIO- RSV

- ✓ INFLUENZA A, A-H1N1, B

da tampone naso-faringeo, da lavaggi nasali

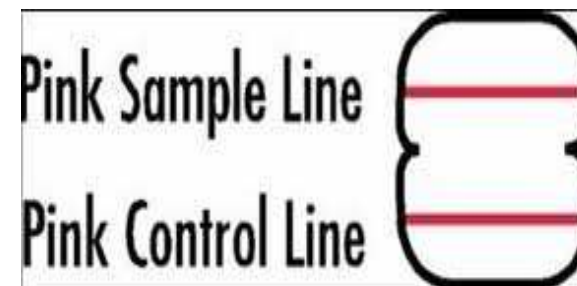
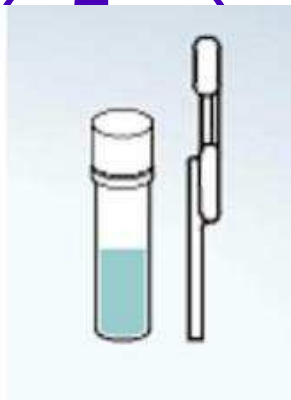


- RSV
- Dosaggio immunocromatografico rapido su membrana: Ag delle proteine di fusione del RSV





- Tempi di preparazione ed esecuzione rapidi
- Durata del test 15 minuti
- Interpretazione risultati semplice
- Validato in pazienti neonatali e pediatrici



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- INFLUENZA A, A-H1N1, B
- Ricerca degli acidi nucleici del virus
mediante RT-PCR in biologia molecolare



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- × Tampone naso-faringeo
- × 300 ul di campione
- × La soluzione fornita nel kit
- × Caricamento nella macchina senza difficili impostazioni
- × Durata 1h e 20 minuti



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GeneXpert PC

09/27/12 02:39:11

Test Report

Patient ID: 39
Sample ID: musaj
Test Type: Specimen
Sample Type:

Assay Information

Assay	Assay Version	Assay Type
Xpert Flu G2	2	In Vitro Diagnostic

Test Result:

Flu A NEGATIVE;
2009 H1N1 NOT DETECTED;
Flu B POSITIVE

Test and Analyte Result

Analyte Name	Ct	EndPt	Analyte Result	Probe Check Result
Flu A	0	1.0	NEG	PASS
2009 H1N1	0	4.0	NEG	PASS
Flu B	20.6	1028.0	POS	PASS
SPC	29.6	207.0	NA	PASS

User: <None>
Status: Done
Reagent Lot ID*: 10201
Expiration Date*: 04/20/14
Cartridge S/N*: 44696413
S/W Version: 4.0c
Notes:
Error Status: OK

Start Time: 09/27/12 01:04:14
End Time: 09/27/12 02:21:30
Module Name: A4
Module S/N: 613362
Instrument S/N: 706904

Tech. Initial/Date

Supervisor Initial/Date

* indicates that a particular field is entered using a barcode scanner

For In Vitro Diagnostics Use Only.

GeneXpert® Dx System Version 4.0c

Page 1 of 4

GeneXpert PC

09/27/12 02:39:11

Test Report

Patient ID: 38
Sample ID: cencio
Test Type: Specimen
Sample Type:

Assay Information

Assay	Assay Version	Assay Type
Xpert Flu G2	2	In Vitro Diagnostic

Test Result:

Flu A POSITIVE;
2009 H1N1 DETECTED;
Flu B NEGATIVE

Test and Analyte Result

Analyte Name	Ct	EndPt	Analyte Result	Probe Check Result
Flu A	19.7	486.0	POS	PASS
2009 H1N1	21.5	715.0	POS	PASS
Flu B	0	1.0	NEG	PASS
SPC	29.5	245.0	NA	PASS

User: <None>
Status: Done
Reagent Lot ID*: 10201
Expiration Date*: 04/20/14
Cartridge S/N*: 44696409
S/W Version: 4.0c
Notes:
Error Status: OK

Start Time: 09/27/12 01:03:21
End Time: 09/27/12 02:20:47
Module Name: A3
Module S/N: 613357
Instrument S/N: 706904

Tech. Initial/Date

Supervisor Initial/Date

* indicates that a particular field is entered using a barcode scanner

For In Vitro Diagnostics Use Only.

GeneXpert® Dx System Version 4.0c

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 Xpert® Flu

PRONTI PER LA NUOVA STAGIONE INFLUENZALE (H3N2)?

Xpert® Flu è un sistema diagnostico in multiplex PCR real time impiegato per l'analisi *qualitativa in-vitro* e per la rapida differenziazione dell'Influenza A, Influenza B e la variante H1N1 2009.

Xpert FLU identifica il ceppo stagionale H3N2v come influenza A POSITIVO.

- **Targets Identificati**
 - o Flu A, Flu B e variante suina H1N1 2009.
- **Tempo di Refertazione**
 - o 75 minuti
- **Manipolazione manuale**
 - o 1 minuto
- **Tipologia di campione**
 - o Tampone naso-faringeo in 3ml UTM (NASL-100N-050)
 - o Lavaggio Naso-Faringeo
- **Conservazione**
 - o CE-IVD 2-28°C
- **Formato: 10 test**
- **Codice: CGXFLUA-B 10 CE**





- I NOSTRI DATI
- Dal 01/01/2013: 230 CAMPIONI:
 - » 19 POSITIVI per INFLUENZA A-H1N1
 - » 29 POSITIVI per INFLUENZA B
 - » 1 POSITIVO SIA PER A-H1N1 CHE B
 - » 20 PEDIATRICI
 - » 2 PEDIATRICI POSITIVI per A-H1N1
 - » 2 PEDIATRICI POSITIVI per B
- SOLO 1 CASO DI INFLUENZA A NON H1N1, DI UNA DONNA DI 60 ANNI RICOVERATA IN RIANIMAZIONE. IL FRATELLO MISSIONARIO IN CINA ERA TORNATO A CASA CON L'INFLUENZA!!



- STUDIO DELL'ISS: SORVEGLIANZA DELLA SICUREZZA DI FARMACI E VACCINI E VALUTAZIONE DELL'EFFICACIA DELLA VACCINAZIONE ANTI-INFLUENZALE IN PEDIATRIA

- ➔ 50 CASI
- ➔ Età compresa tra i 6 mesi e i 18 anni trattenuti in OBI o ricoverati per infezione delle vie respiratorie compatibile con una sindrome influenzale (ILI)
- ➔ sintomi: FEBBRE $>38^{\circ}\text{C}$; almeno un sintomo respiratorio; almeno un sintomo sistemico (mal di testa, astenia, malessere generale)



- **RISULTATI SU 50 PAZIENTI**
- 9 pazienti POSITIVI per A-H1N1
- 13 pazienti POSITIVI per B



- **Simultaneous detection of 15 major respiratory viruses**

- **SEEGENE**

- Parainfluenza virus 1, 2, 3
- Adenovirus A/B/C/D/E
- Coronavirus 229E/NL63
- Coronavirus OC43
- Rhinovirus A/B/C
- Influenza A virus
- Respiratory syncytial virus A
- Respiratory syncytial virus B
- Bocavirus 1/2/3/4
- Influenza B virus
- Metapneumovirus Parainfluenza virus 4
- Enterovirus





• |

- **ARGENE MULTIPLEX PCR**

- Influenza A/B r-gene®
- RSV/hMPV (Metapneumovirus)
- Rhino & EV/Cc r-gene®
- AdV/ hBoV r-gene®
- *Chlamidia/Mycoplasma pneum.*
- HCoV/HPIV (Parainfluenzali)



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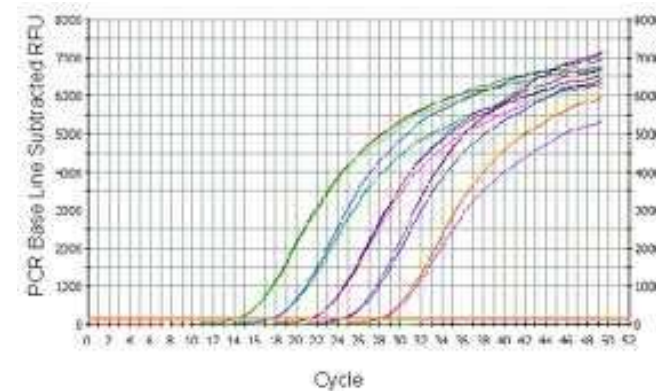
- ESTRAZIONE
- AMPLIFICAZIONE



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- VALIDAZIONE E INTERPRETAZIONE
- DEI RISULTATI



- TEMPI DI RISPOSTA: CIRCA 2 ORE
- PUO' ESSERE METODICA URGENTE NELLA NOSTRA REALTA'?



- *The Open Virology Journal*, 2012, 6, (Suppl 1: M5) 151-159
- **Laboratory Detection of Respiratory Viruses by Automated Techniques**
- Mercedes Pérez-Ruiz*, Irene Pedrosa-Corral, Sara Sanbonmatsu-Gámez and José-María Navarro-Mari
- **Abstract:** Advances in clinical virology for detecting respiratory viruses have been focused on nucleic acids amplification techniques, which have converted in the reference method for the diagnosis of acute respiratory infections of viral aetiology. Improvements of current commercial molecular assays to reduce hands-on-time rely on two strategies, a stepwise automation (semi-automation) and the complete automation of the whole procedure. Contributions to the former strategy have been the use of automated nucleic acids extractors, multiplex PCR, real-time PCR and/or DNA arrays for detection of amplicons. Commercial fully-automated molecular systems are now available for the detection of respiratory viruses. Some of them could convert in point-of-care methods substituting antigen tests for detection of respiratory syncytial virus and influenza A and B viruses. This article describes laboratory methods for detection of respiratory viruses. A cost-effective and rational diagnostic algorithm is proposed, considering technical aspects of the available assays, infrastructure possibilities of each laboratory and clinic-epidemiologic factors of the infection.

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Table 2. Fully-Automated Assays for Detection and Identification of Respiratory Viruses

Assay	Manufacturer	Method	Virus Detected	Hands-On/ Turnaround Times (min)
MariPOC [®] respi test	ArcDia	Antigen detection	Flu A, Flu B, RSV, hMPV, PIV1-3, ADV	< 1 / 20-120
Xpert [®] Flu	Cepheid	Nucleic acid extraction Real-time multiplex RT-PCR	Flu A, Flu B, 2009 H1N1	1 / 60
Simplexa [™] Flu A/B & RSV Direct kit	Focus Diagnostics	Nucleic acid extraction Real-time multiplex RT-PCR	Flu A, Flu B, RSV	1 / 60
Verigene [®] Respiratory virus plus test	Nanosphere	Nucleic acid extraction RT-PCR Nanoparticle probe-based DNA-array hybridization	Flu A, Flu B, RSV A, RSV B, 2009 H1N1, Flu A H1, Flu A H3, oseltamivir-resistant 2009 H1N1 (H275Y mutation)	5 / 150
Verigene [®] Respiratory virus XP test			FluA, FluB, RSV A, RSV B, 2009 H1N1, Flu A H1, Flu A H3, oseltamivir-resistant 2009 H1N1 (H275Y mutation), PIV 1-4, ADV, hMPV, HRV, HEV	5 / 90
Filmarray [®] Respiratory Panel	Idaho technology Inc.	Nucleic acid extraction RT Multiplex nested-PCR Detection by end-point melting curves	ADV, hBoV, HCoV (HKU1, NL63, 229E, OC43), Flu A H1, 2009 H1N1, Flu A H3, Flu B, hMPV, PIV1-4, RSV, HRV/HEV	2 / 60



• Conclusioni:

- Antigen detection methods for RSV and/or Flu may be enough for patients attended at **emergency units** that do not fulfil severity clinical criteria for hospitalisation
- Samples from patients requiring **hospitalisation** with negative RSV or Flu antigen results should be subjected to extended virological study that includes viral culture assays and/or NAAT targeted at more or less RV depending on the severity of the disease and the need for a rapid result.
- Otherwise, other molecular multiplexed methods of low complexity could be performed in certain patients that included hMPV, HRV and PIV detection, depending on patient's age and/or the existence of underlying diseases. More complex NAAT that detect other less frequent RV should be reserved to certain situations such as more severe cases (**ICU patients**) in which previous NAAT for the most prevalent viruses have yielded negative results [60-62].
- In future, automated NAAT may be the alternative of antigen detection methods if costs become comparable and a reduction of turnaround time is achieved.



- 2 . Urinocoltura



- **NEGATIVA:** risposta nel primo
pennello

- **POSITIVA:** semina su piastra



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- 24 ore: Identificazione del germe

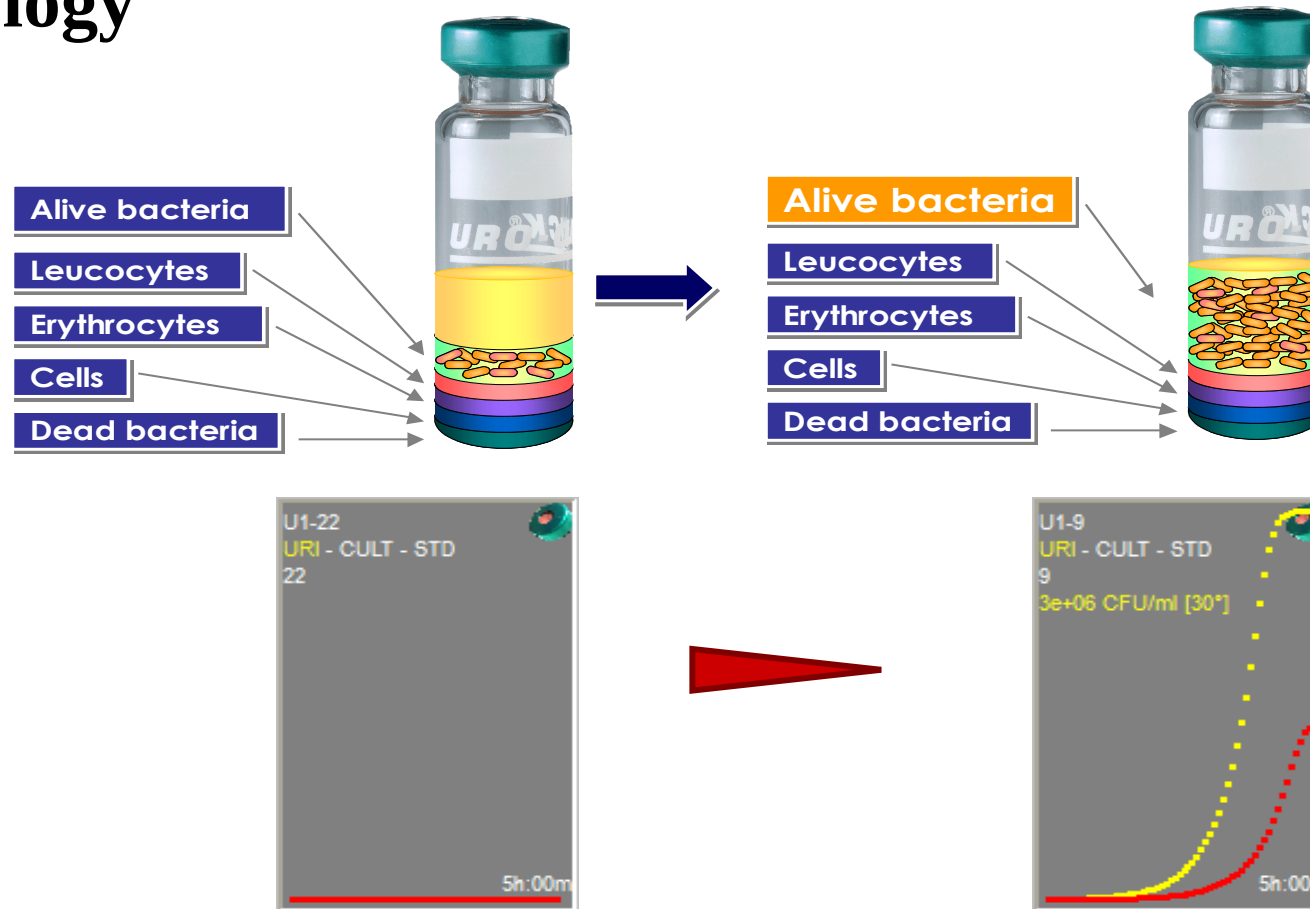


- 48 ore: Antibiotogramma

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Culturing methods / Alifax® Light Scattering Technology





- Dopo max 6 ore se POSITIVA (carica elevata) —————→ IDENTIFICAZIONE
- A 24 ore l'antibiogramma
-  1 GIORNO IN MENO

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- ... *FORMARSI E' BENE,*
- *TRASFORMARSI E' MEGLIO ...*

-

GRAZIE!