Procalcitonine :

Un marqueur de l'infection bactérienne

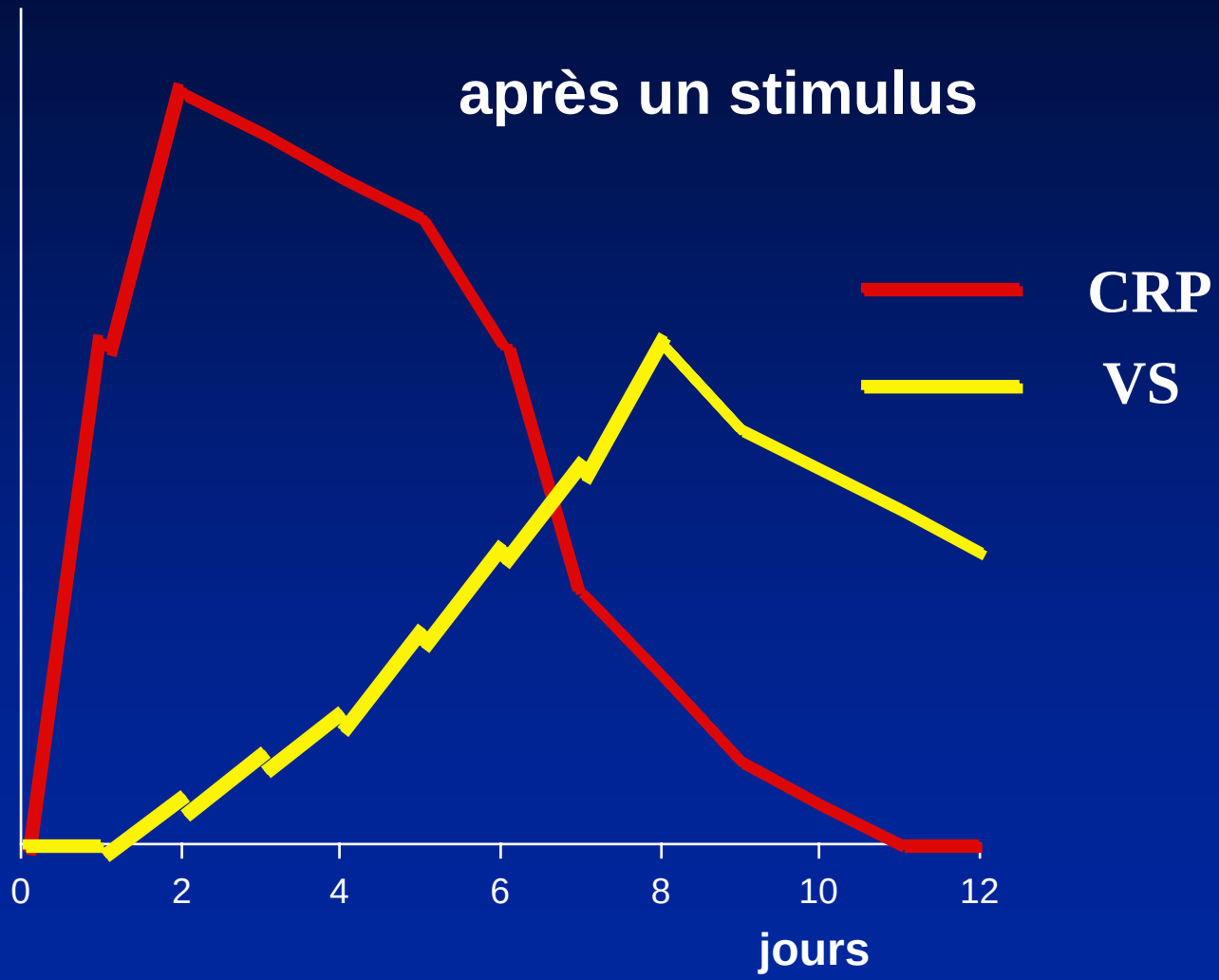
Dominique Gendrel
Saint Vincent de Paul – Cochin, Paris

MARQUEURS DANS LES INFECTIONS

- Spécificité et sensibilité
- Valeurs prédictives positives et négatives
- Facilité de dosage en urgence
- Stabilité à la conservation
- UN MARQUEUR BIOLOGIQUE N ’EST QU ’UNE AIDE A LA CLINIQUE

Variations de VS et CRP

après un stimulus

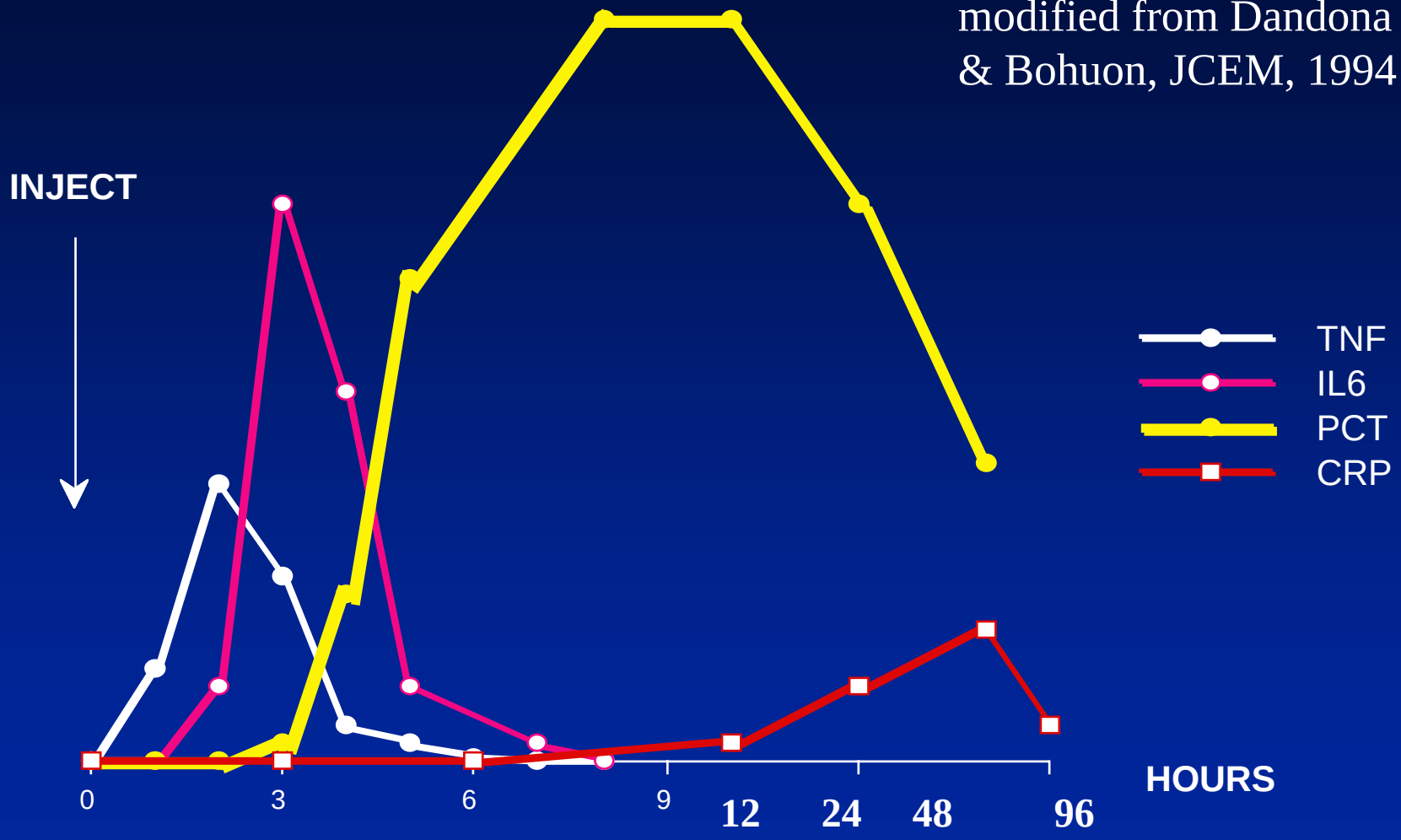


CONCENTRATION PLASMATIQUE DES PROTEINES DE LA PHASE AIGUE DE L ’INFLAMMATION

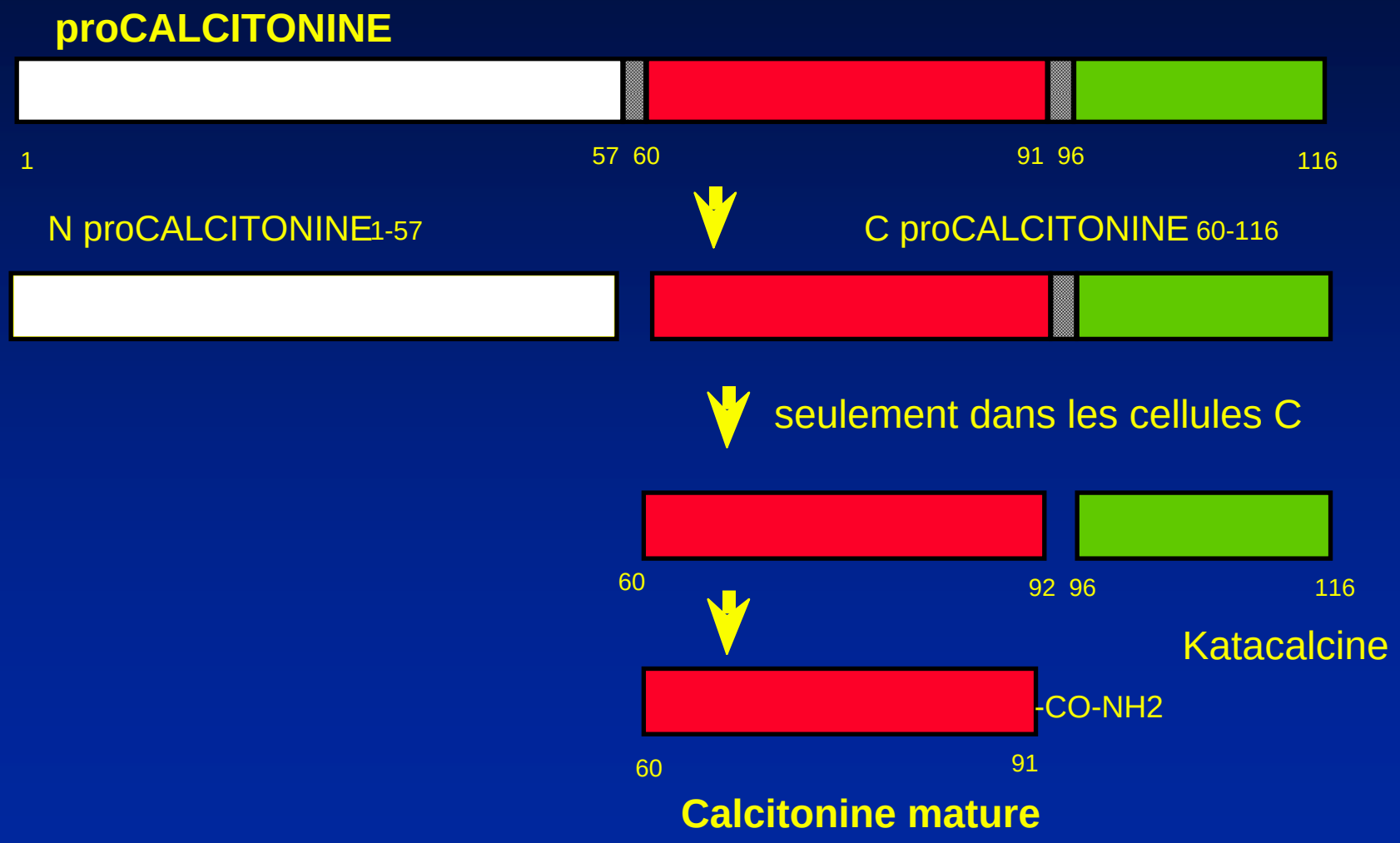
Protéines de la phase aiguë de l ’inflammation	Concentration plasmatique (g/L)		
	Homéostasie	Inflammation	Augmentation
Protéine C réactive (CRP)	**< 0,006**	**0,03-0,4**	**jusqu ’à 100**
Sérum amyloïde A (SAA)	< 0,010	0,05-1,00	jusqu ’à 100
α1-glycoprotéine acide	0,4-0,8	1,2-2,5	2 à 4 fois
α1-antitrypsine	2,0-2,5	4-6	2 à 4 fois
α1-antichymotrypsine	0,3-0,6	1-2	2 à 4 fois
Haptoglobine	0,6-1,8	3-8	2 à 4 fois
Fibrinogène	2,5-4,5	6-10	2 à 4 fois
Céruleoplasmine	0,2-0,5	0,8-1,2	2 à 4 fois

MARKERS after INTRAVENOUS ENDOTOXIN

modified from Dandona & Bohuon, JCEM, 1994



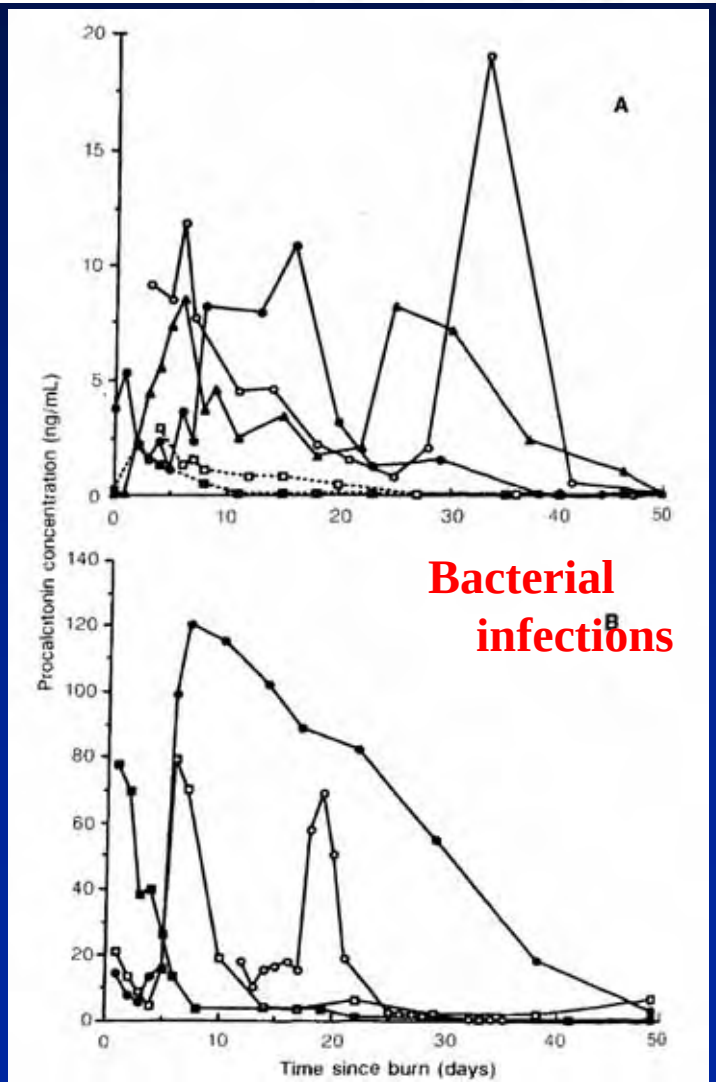
Maturation schèmatique de la CALCITONINE

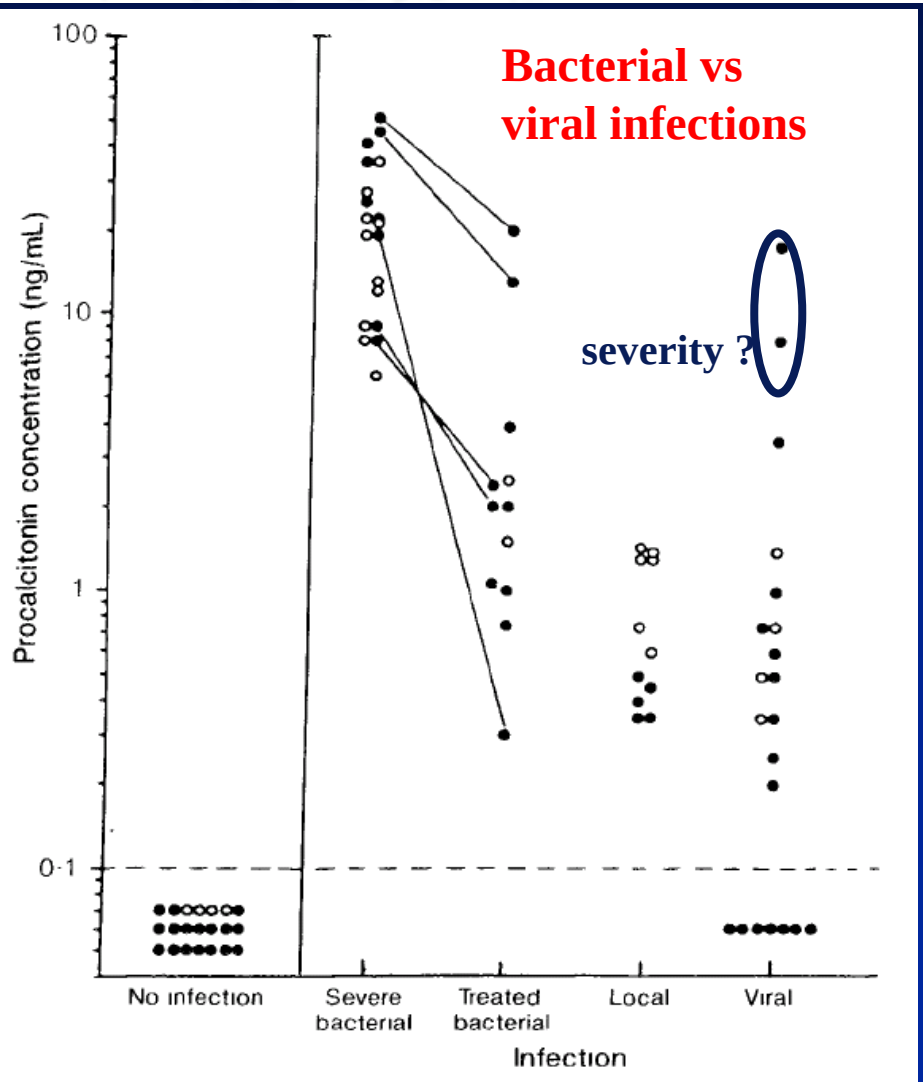


VOL 341: FEB 27, 1993 THE LANCET 515

High serum procalcitonin concentrations in patients with sepsis and infection

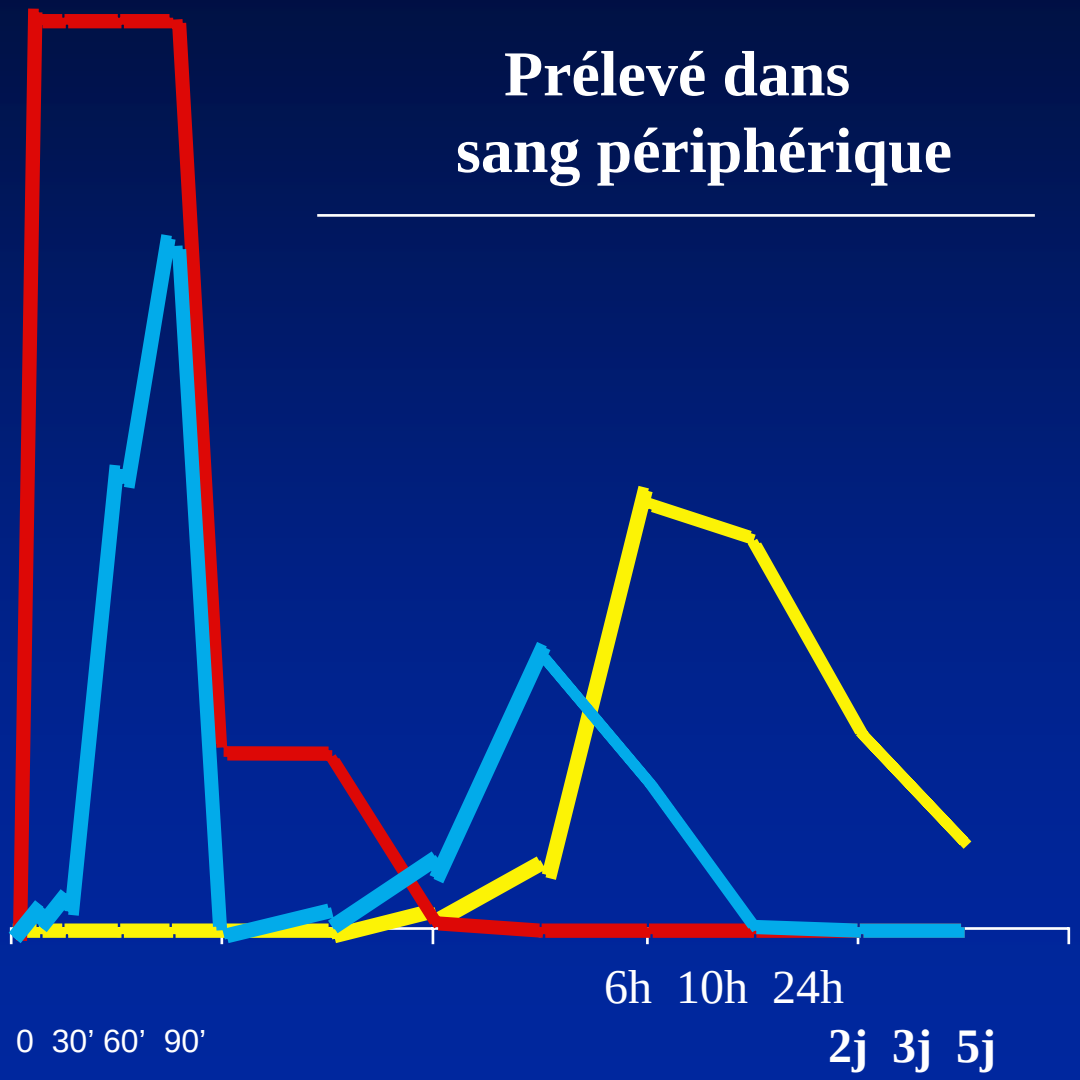
MARCEL ASSICOT DOMINIQUE GENDREL HERVÉ CARSIN
JOSETTE RAYMOND JEAN GUILBAUD CLAUDE BOHUON





Perfusion locale de TNF

Prélevé dans sang périphérique



Swaak & Bohuon, 1996

PROCALCITONIN CHILDREN STUDY IN EMERGENCY ROOM

Objective :

Obtain seric markers to differentiate viral and bacterial infections, trying to reduce non appropriate antibiotic use.

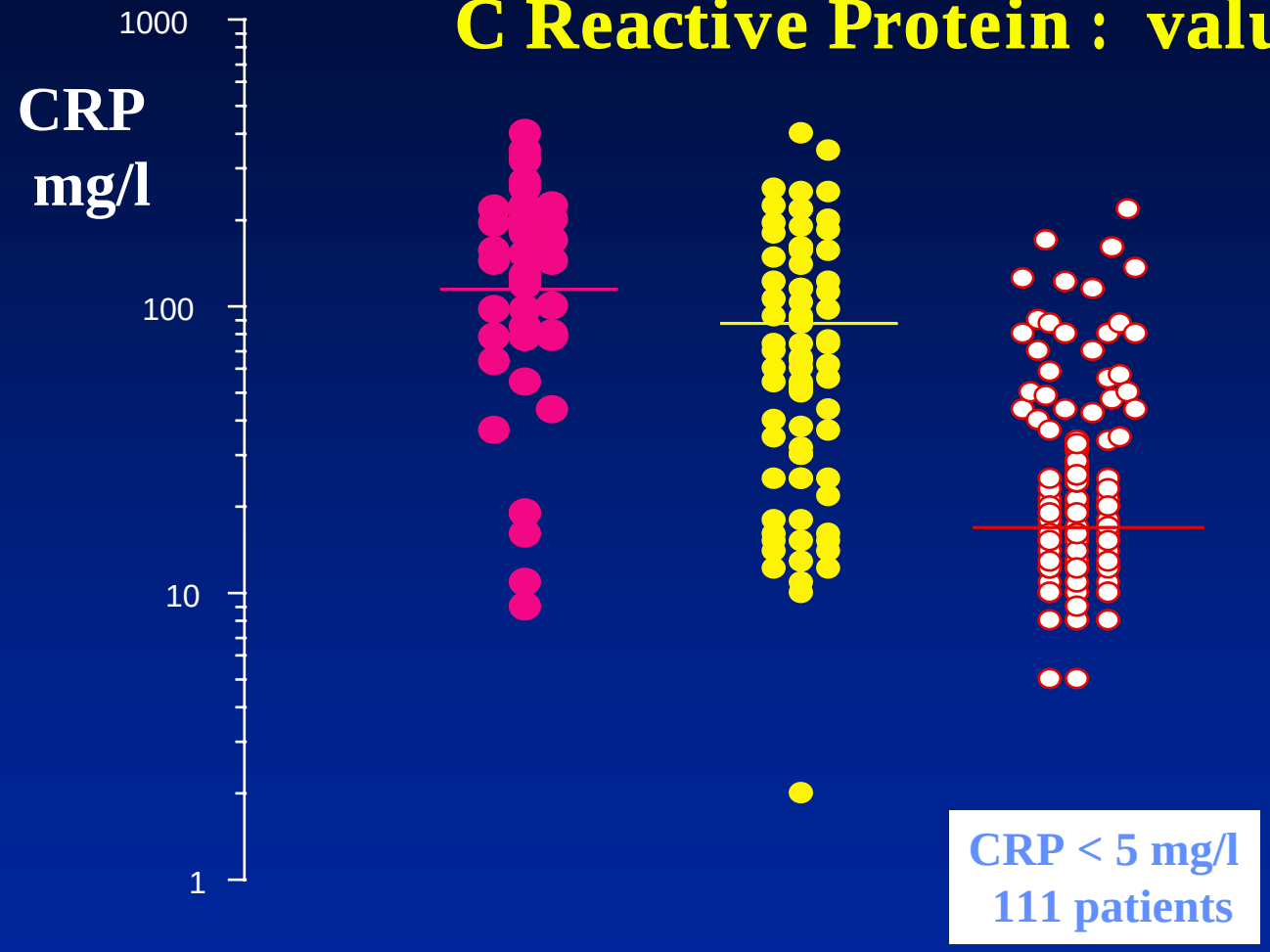
Blood collection in 75O feverish children at hospital admission (St Vincent de Paul Children Hospital, PARIS, France)

- **Procalcitonin** (Immunoluminescence, BRAHMS Co)
- **C Reactive protein** (Nephelemetry)
- **Interferon α** (Biological assay on MBDK cells)
- **Interleukin 6** (ELISA, Medgenix Co)

Gendrel et al,PIDJ 1999

Bacterial vs viral infections in 360 children

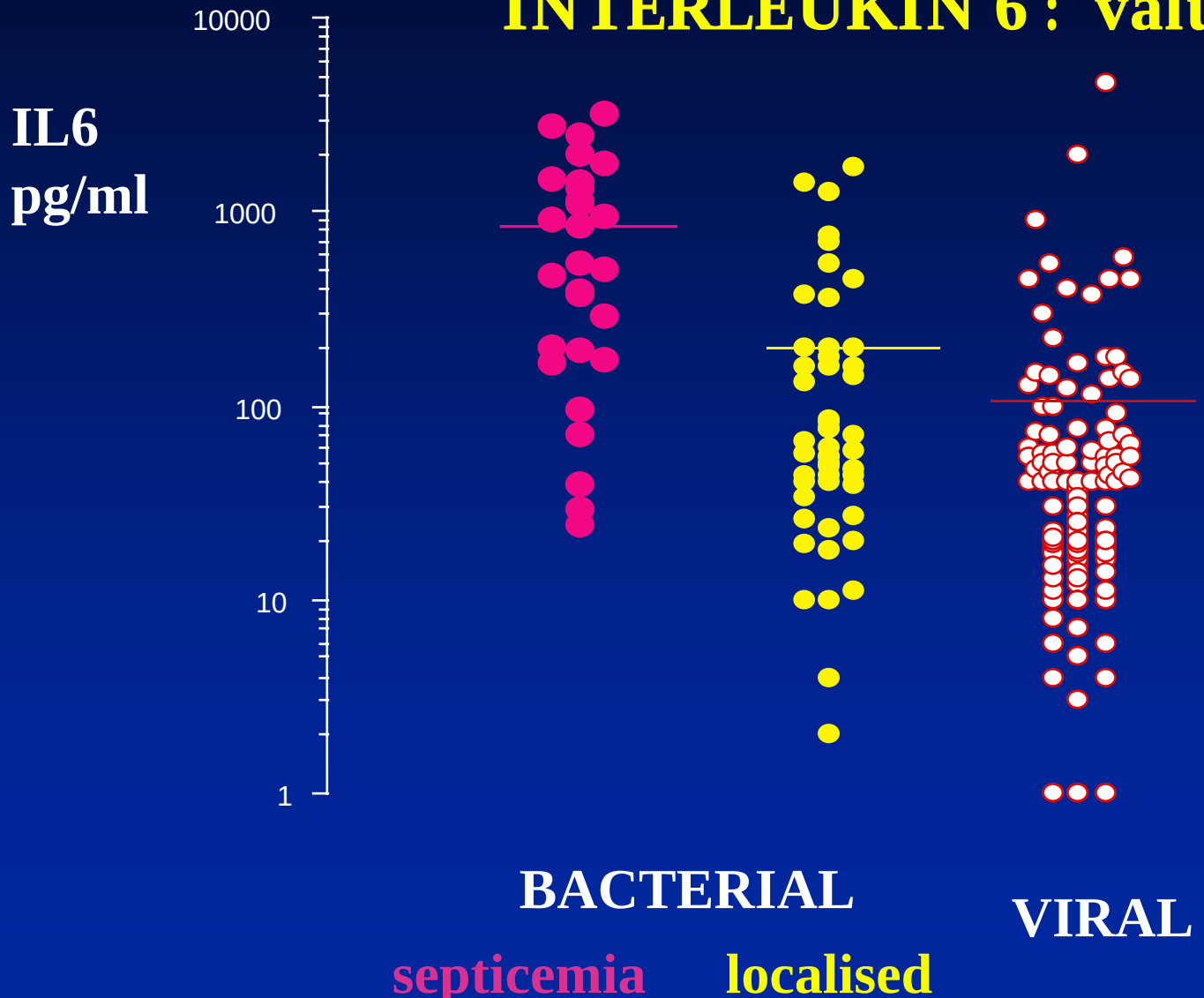
C Reactive Protein : values at admission



Gendrel et al,PIDJ 1999

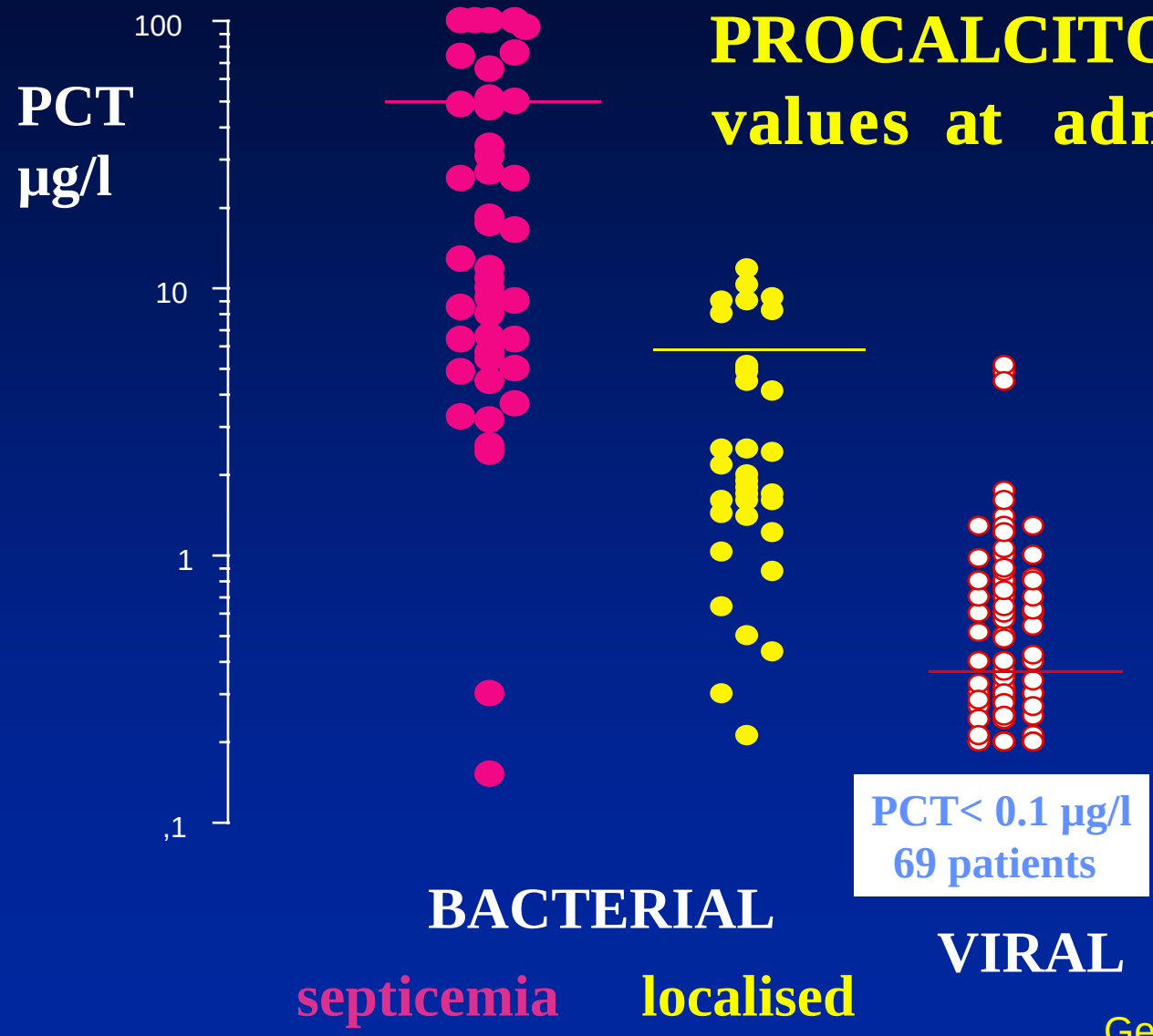
Bacterial vs viral infections in 360 children

INTERLEUKIN 6 : values at admission



Gendrel et al,PIDJ 1999

Bacterial vs viral infections in 360 children

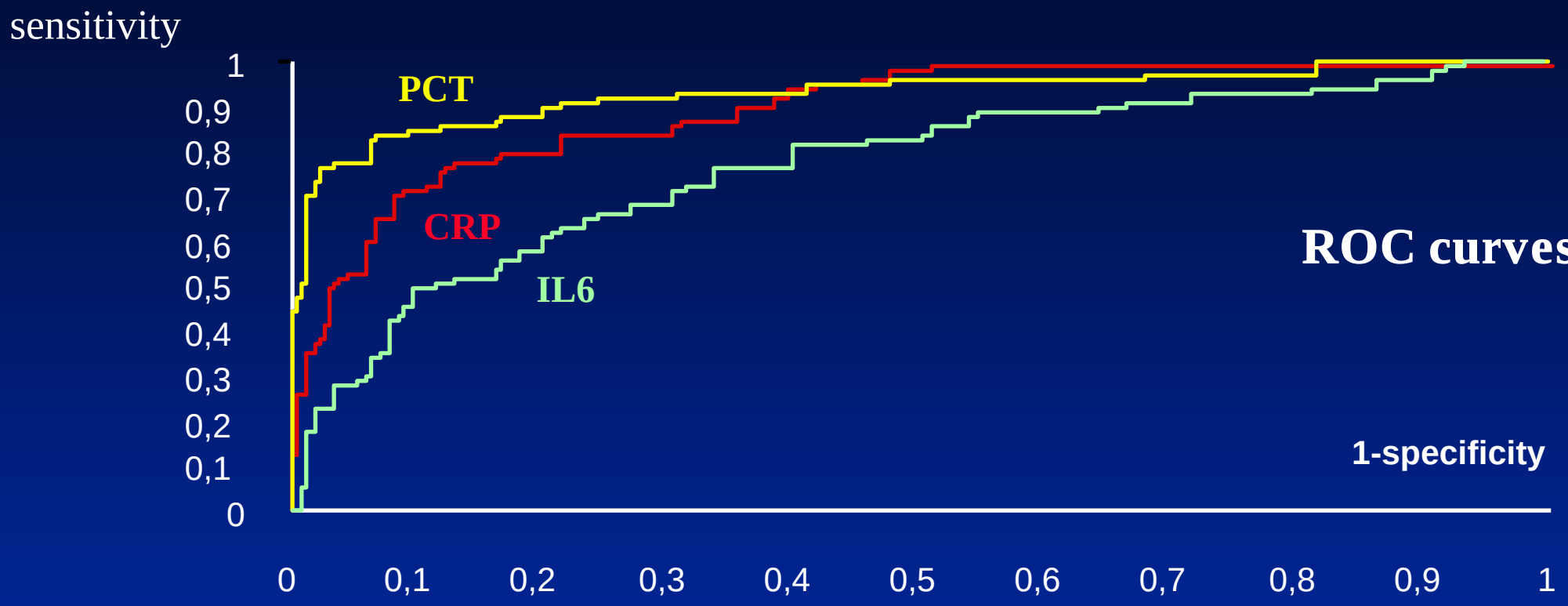


Gendrel et al,PIDJ 1999

BACTERIAL & VIRAL INFECTIONS

	SPECIFICITY	SENSITIVITY	
		SEPTICEMIA	LOCALIZED
PCT > 1 µg/l	93 %	96 %	77 %
PCT > 1,5	98 %	96 %	76 %
CRP > 20 mg/l	74 %	89 %	80 %
CRP > 10	53 %	98 %	97 %
IL_6 > 100 pg/ml	86 %	88 %	34 %

PIDJ 1999



Bacterial vs viral infections in 360 children

PIDJ 1999

BACTERIAL INFECTIONS

SEPTICEMIA or MENINGITIS — PCT: m = 45.9

PCT > 1,5 µg/l : 44 / 46 (96%)

CRP > 20 41 / 46 (89 %) - IL6 > 100 23 / 26 (88 %)

- 6 months, bloody diarrhea, blood culture pos (S. typhimurium)
  PCT 0,15 CRP 129 IL6 29

- 8 mois, otitis media, blood culture pos (S. pneumoniae)
  PCT 0,3 CRP 43 IL6 365

LOCALIZED — PCT : m = 4.2

PCT > 1,5 µg/l : 50 / 77 (65 %)

CRP > 20 62 / 77 (81%) - IL6 > 100 17 / 50 (34 %)

PIDJ 1999

Group 2 : Bacterial localized infections (n = 78)

- **Urinary tract infections : n =22**
  (PCT < 1 µg/l in 3)
  Antibiotic treatment

- **16 other patients PCT < 1 µg/l**
  12/16 were not treated with antibiotics after clinical evaluation

- **39 other patients PCT > 1 µg/l**
  30/39 received antibiotics in admission after clinical evaluation

Nb : PCT results available after 48 h or more

PIDJ 1999

VIRAL INFECTIONS

n = 236

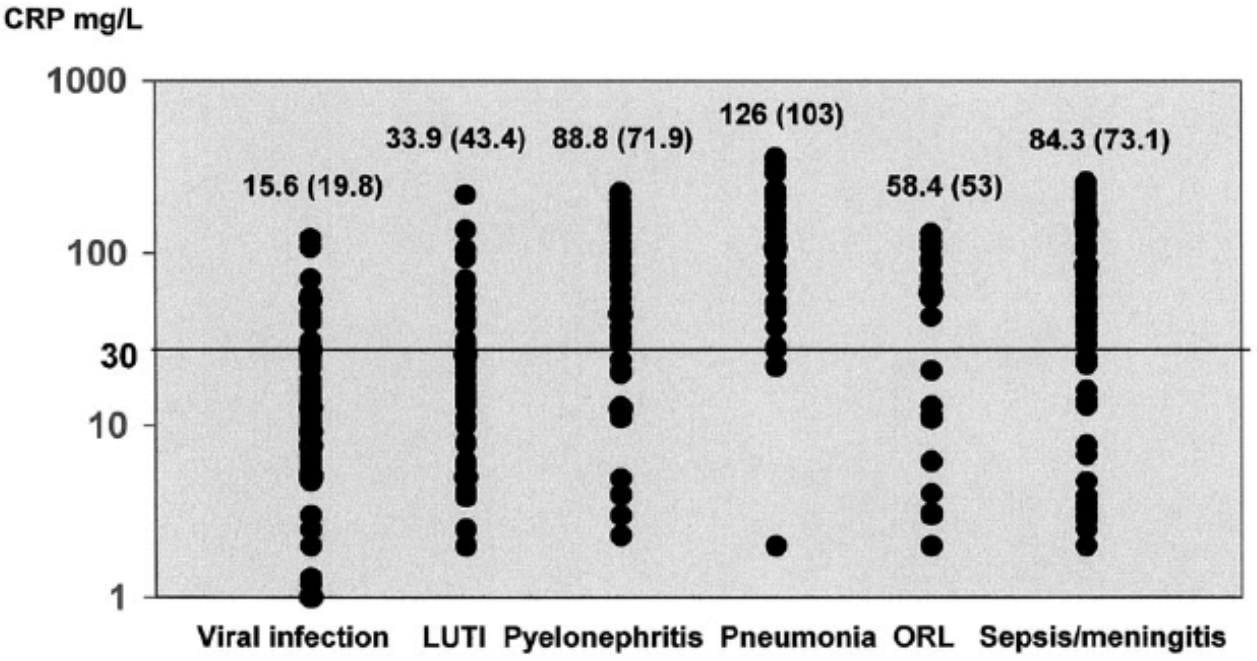
PCT > 1,5 µg/l n = 5 (2.1 %)

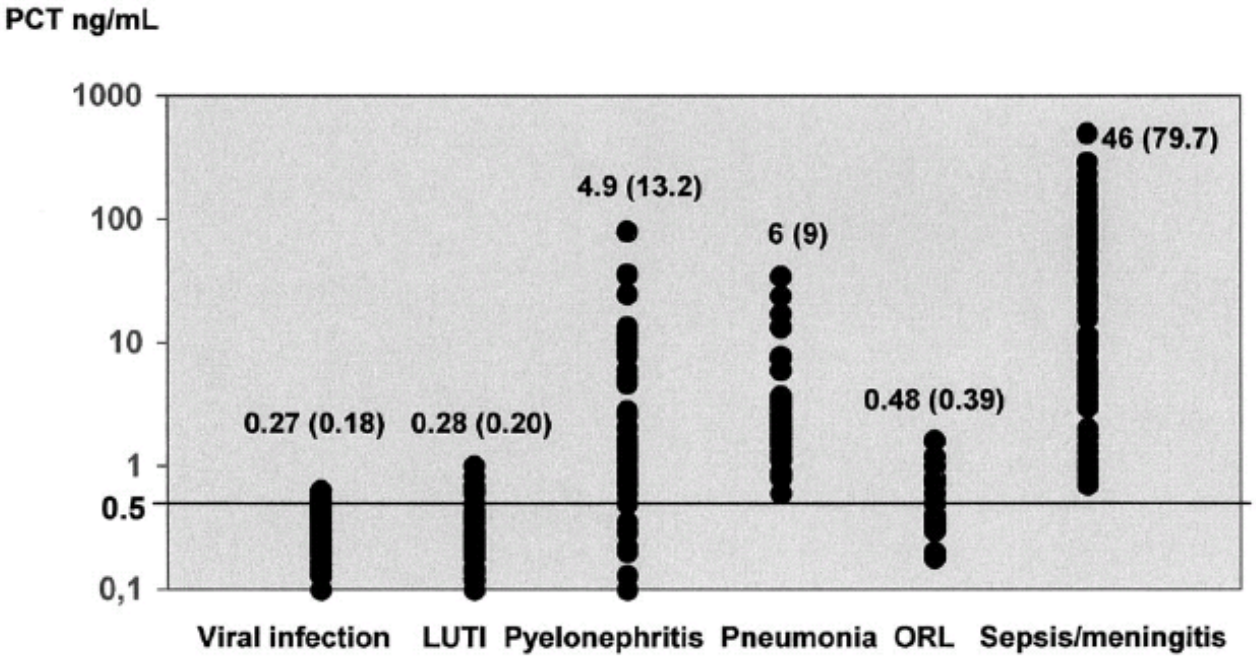
PCT > 1 µg/l n = 16 (6.7 %)

132 / 172 (77%) have positive INFα

	PCT	CRP	IL6	INFα
- 6 months, rotavirus	4,5	16	75	12
- 12 years, EBV + macroph activ	5,2	15	16	25
- 4 years, pneumonia	4,80	169	35	200

PIDJ 1999





PCT-Q (test rapide)
aux Urgences Pédiatriques en Espagne pour rechercher une infection bactérienne invasive

PIDJ 2003; 22 : 895

Procalcitonin secretion is independent of Interferon–α production

Method : biological assay on MBDK cells
no INF-α in serum of normal patients

Viral infections :
132 / 172 are producers of INF-α

Bacterial infections
6 / 70 are producers of INF-α
(viral + bacterial co-infections)

INF-α : Sensitivity 77% Specificity 90 %
for viral vs bacterial infections

PIDJ 1999

Infections virales hospitalisées

5 % des enfants ont des signes de choc

25% ont une CRP > 20 mg/l

5 à 10 % ont une CRP > 50 mg/l

H Peltola , J Pediatr, 1985

Infections virales hospitalisées

5 % des enfants ont des signes de choc

25% ont une CRP > 20 mg/l

PIDJ 1999 :

77% des enfants ont un interferon-alpha serique positif

MAIS :

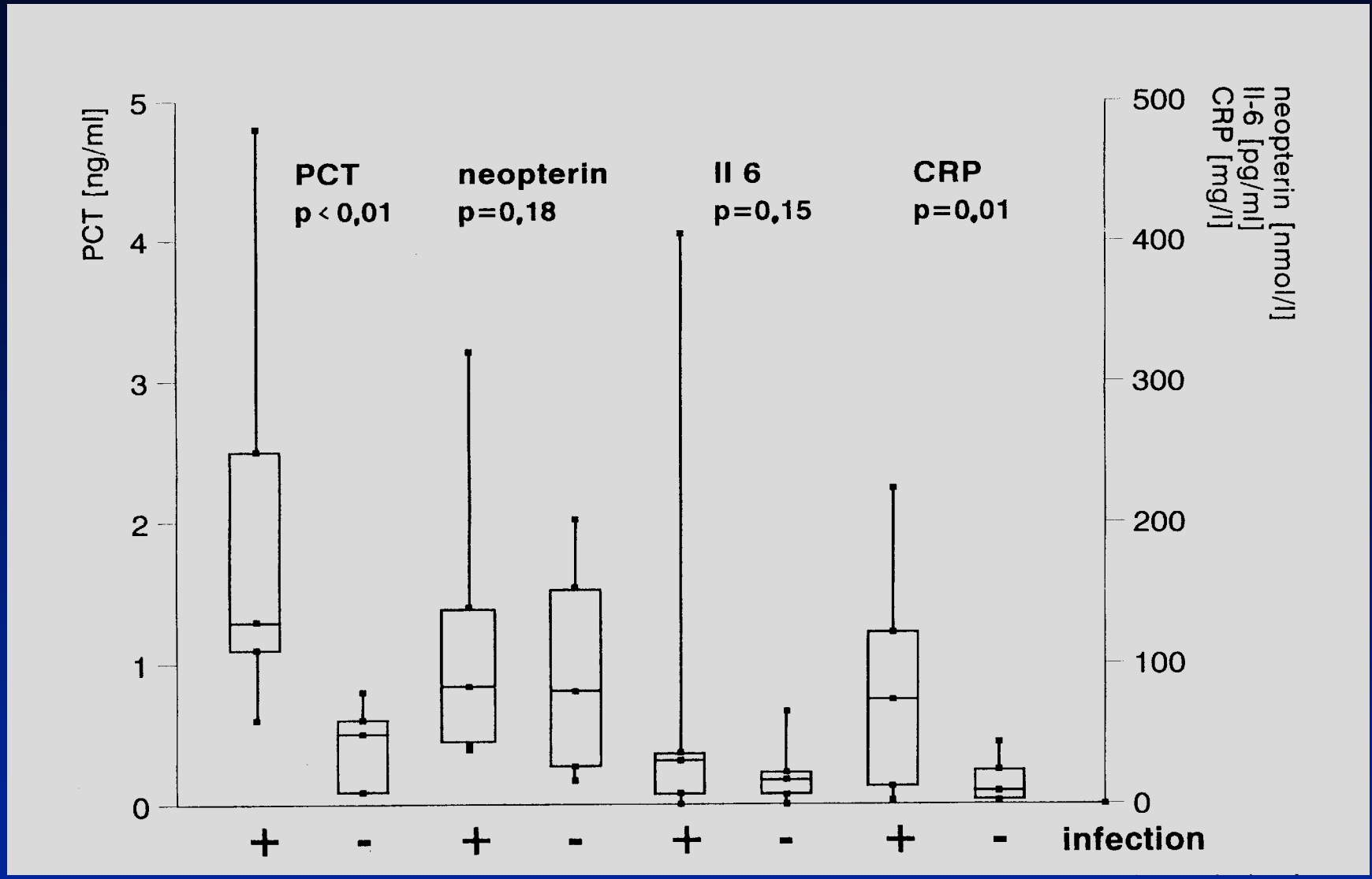
Dosage biologique
48 h d'incubation

donc non adapté à l'urgence

Values of PCT, CRP and IL6 at admission in 10 patients with inflammatory disease and body temperature > 38.5°C

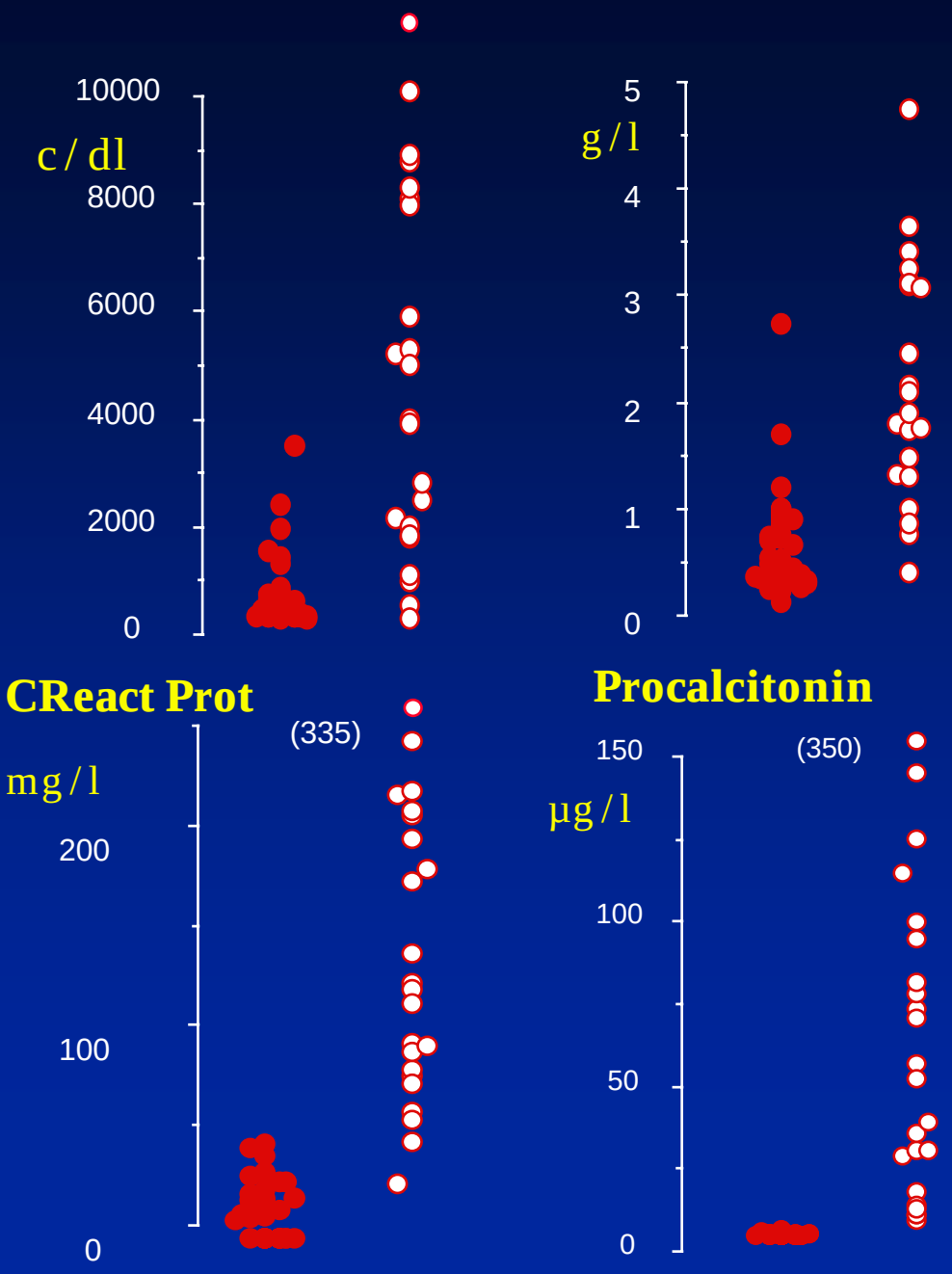
Diagnosis	Age (y)	PCT (µg/l)	CRP (mg/l)	IL6 (pg/ml)
Juven Rheum arthr	12	.11	141	193
Juven Rheum arthr	2	.25	60	-
Juven Rheum arthr	2	.08	88	-
Juven Rheum arthr	3	.01	40	-
Crohn	8	.1	55	100
Sarcoidosis	6	.5	83	-
Metastatic neuroblastoma	3	1.4	125	149
Kawasaki	1.5	0.9	67	56
Kawasaki	1.8	0.6	85	-
Kawasaki	5	5.9	95	65

PIDJ 1999



Lupus erythematosus with or without infection

Eberhard , Arthritis & Rheumatism, 1997

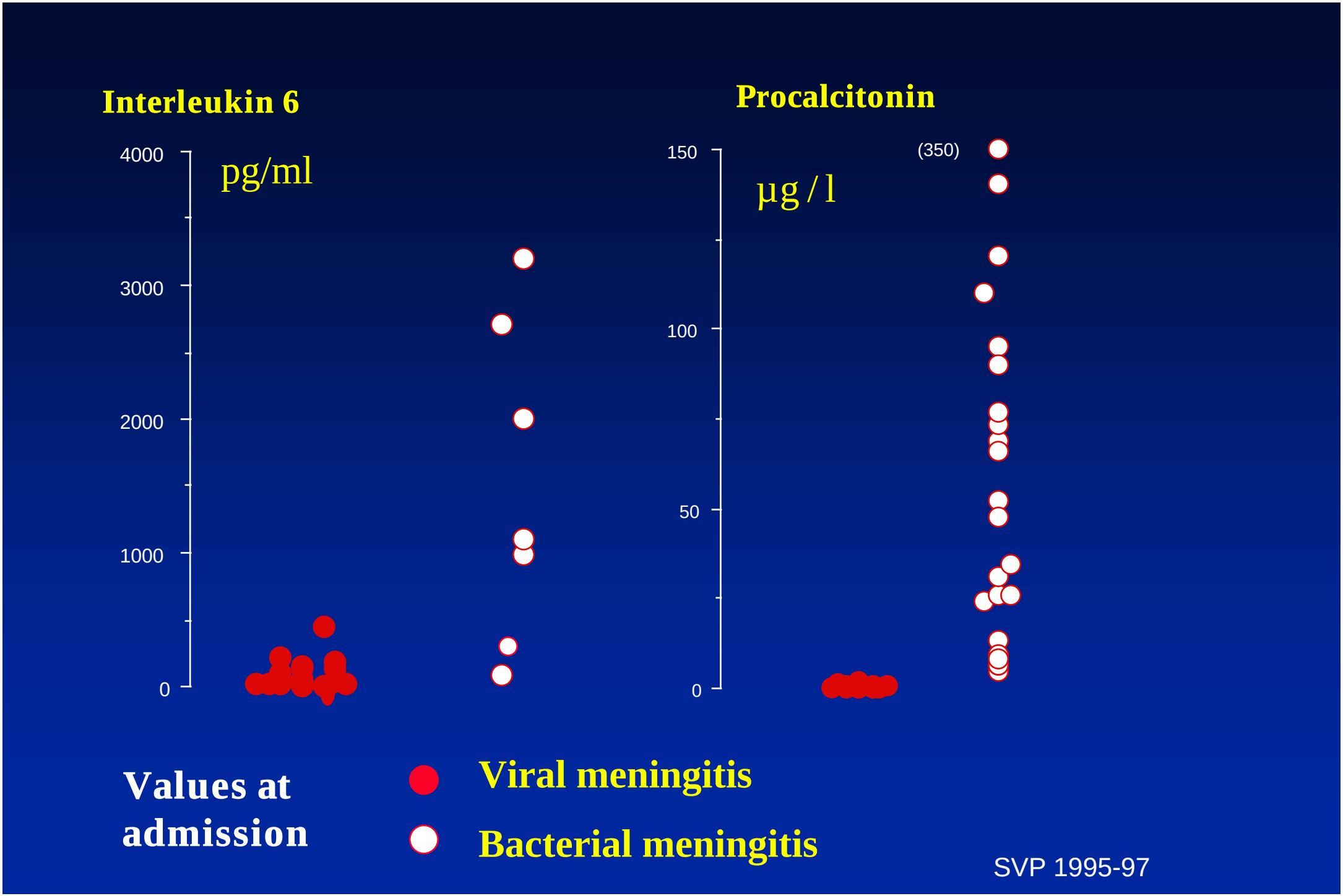


Values at admission in bacterial (n = 23) and viral (n = 60) meningitis

Viral meningitis

Bacterial meningitis

Gendrel et al, Clin Infect Dis 1997


Interleukin 6
pg/ml
4000
3000
2000
1000
0
Procalcitonin
µg / l
150
100
50
0
(350)
Values at admission
Viral meningitis
Bacterial meningitis
SVP 1995-97

INITIAL DATA in CHILDREN MENINGITIS

	CSF cells /mm3	CSF proteins g/l	seric CRP mg/l	proCALCITONIN µg/l
Bacterial meningitis n = 18	5156.3 (250-17500)	2.3 ±1.2 (.4-4. 74)	144.1 ± 69.1 (28-311)	54.5 ± 35.1 (4.8- 110)
Viral meningitis n = 41	390.8 (20-3200)	0.62 ± 0.47 (0.12-2.72)	14.8 ± 14.1 (0-48)	0.32 ± 0.35 (0.0-1.7)

Gendrel et al, Clin Infect Dis 1997

EPIDEMIE DE MENINGITE VIRALE
Printemps 2000

- **1er mai - 30 juin : 58 patients hospitalisés**
  - **50/52 PCR enterovirus positive**
    (culture = 18 Cox B_5, 3 écho 6)

  - **CRP** **17.6 (2-172)** **> 20** **15/58**
  - **Protéines LCR** **0,37 (0,19-0,92)** **> 0,5** **10/58**
  - **Cell LCR** **244 (10-2800)** **> 1000** **4/58**

    PN > 500 :2/58

PCR, INFα 1/semaine, PCT 3/semaine

DECISION ARRET Antibiotiques si PCT < 0.5 ng/ml
et pas de suspicion de méningite décapitée

- **Traités par AB IV : 17/58**

  - **PCT $\leq$ 0,5 ng/ml : 55/58 (un patient 0.7 ng/ml non traité)**
    > 1 ng/ml 2/58

EPIDEMIE PRINTEMPS 2000 : 17/58 traités

- **Patient 1 : 4 ans, OMA sous antibiotiques**
  - LCR Cell 2800 (88% PN), Prot 0.77
  - CRP 172 ng/l, PCT 1,3 ng/ml
  - Traité 4 j IV puis per os (INF 9 UI/ml)

- **Patient 2 : 6 semaines, 1 dose d 'antibiotique**
  - Fièvre, choc (hypo TA, cyanose)
  - J1 : PCT 4.4, CRP 78, Cell 68, Prot 0,24
  - J2 : PCT 2.8, cell 450, Prot 0,96
  - INFα = 6, PCR positive à J7

  Traité 10 jours IV

- **15/17 : arrêt à 24 h : 9, 48 h : 6**
- **soit 35 jours de traitement (et 36 d 'hospitalisation)**

Groupe contrôle (CID 1997)

- 41 méningites virales , 19 traités
  PCT à distance, PCR entérovirus, INF-alpha : 1 fois/semaine

- 4 PCT > 0,5 ng/ml 2 non traités (0,7 et 0,8)

Patient 3	OMA	Prot 1,2	Cell 220	CRP 16	Traité 5 jours (PCT = 1,2)
Patient 4	OMA	Prot 0,83	Cell 20	CRP 16	Traité 4 jours (PCT = 1,72)

- 2 patients considérés comme méningite purulente décapitée :

a)	Pr. 0,32	Cell 3200 (90% PN)	CRP 15	Traité 8 j	PCT 0,01	PCR positive
b)	Pr. 2.72	Cell 2100	CRP	Traité 14 j	PCT 0,34	Culture = écho

- Traitement, durée : 3 j = 7 ; 4 j = 8 ; 5 j = 2 ; 8 et 14 j = 1
  Total 71 jours pour 19 patients versus 35 j pour 17

Soit 3.75 j vs 2.05 j par patient traité, gain : 30 jours d 'hospitalisation ($p<0.01$)

M..... 5 semaines

- Au sein, Carnet de santé = accouchement RAS
- 38°5, bon état, pas de point d ’appel
- Hb 12,8 g, 12800 GB, 75% PN, 719 000 Pl
- CRP 14
- PCT 1,2 ng/ml
- PL hémorragique

Hospitalisée pour attendre les résultats d ’hémoculture et d ’ECBU

M.... 5 semaines

12 h après arrivée :

- **Choc, Convulsions, AB débutés**
- **Hémoc = Strepto B** (Serotype III) **• 2ème PL : Strepto B**
- **24 h après = CRP 113 - PCT 12**

On apprend ensuite (fax du CR de maternité) :

- **Mère porteuse strepto B**
- **RPDE : Amoxicilline 48 h**

- **Découverte de Strepto B dans lait maternel à 5 semaines**

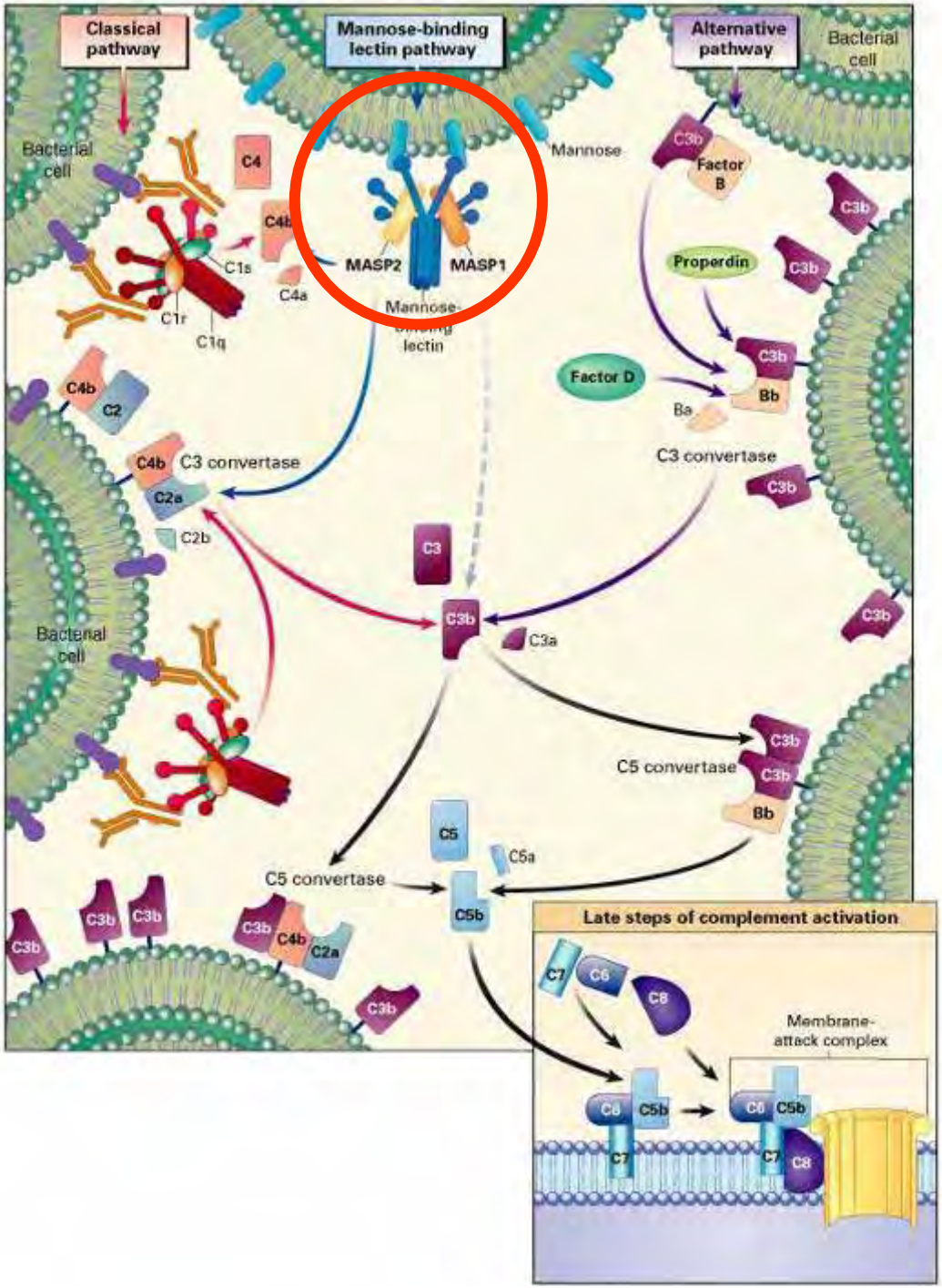


TABLE 2. INITIATORS OF THE THREE ACTIVATION PATHWAYS OF COMPLEMENT.

PATHWAY	INITIATORS
Classical	Immune complexes Apoptotic cells Certain viruses and gram-negative bacteria C-reactive protein bound to ligand
Mannose-binding lectin	Microbes with terminal mannose groups
Alternative	Many bacteria, fungi, viruses, tumor cells

- **Patient 1**, 8 months

Septicemia and meningitis : *Haemophilus influenza non b*

Admission : PCT 0.4 ng/ml,

after 24 h : PCT 5 ng/ml

- **Patient 2**, 6 months

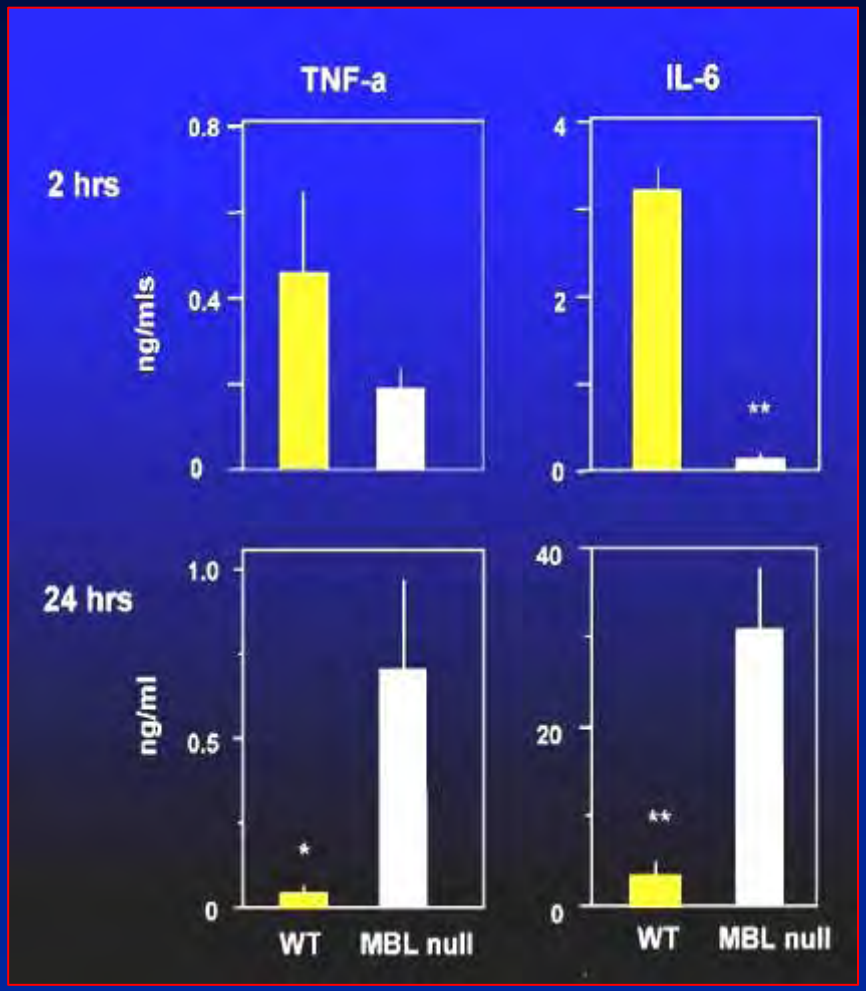
Meningitis : *Strept pneumoniae serogroup 21*

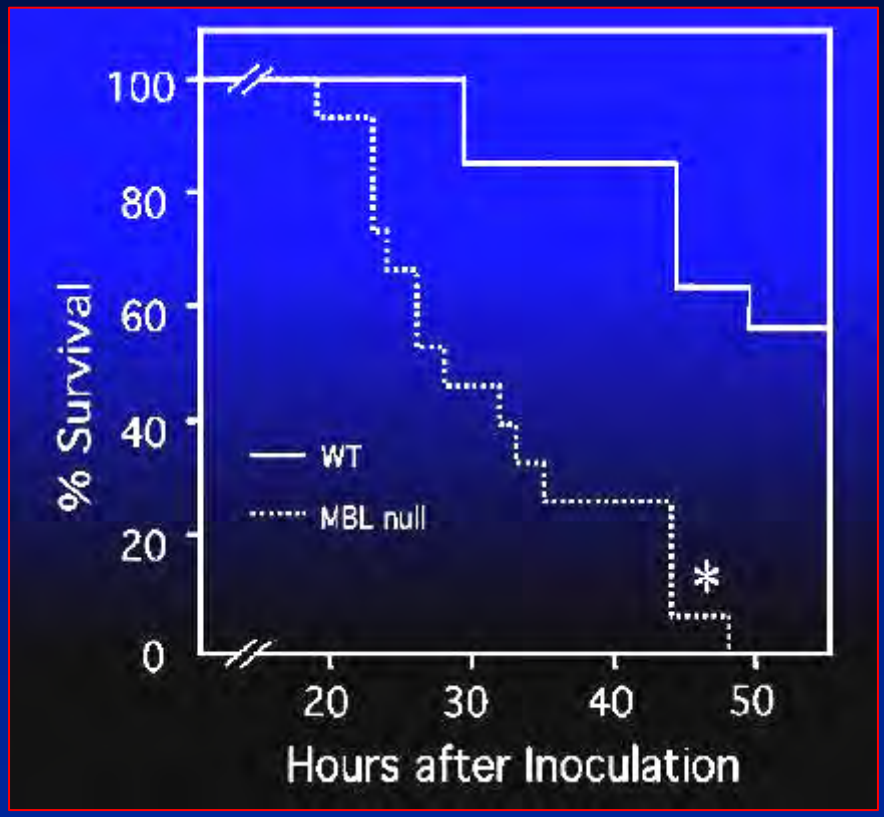
Admission : PCT 0.2 ng/ml,

after 24 h : PCT 12 ng/ml

The 2 infants had MBL gene mutation and low level of circulating MBL

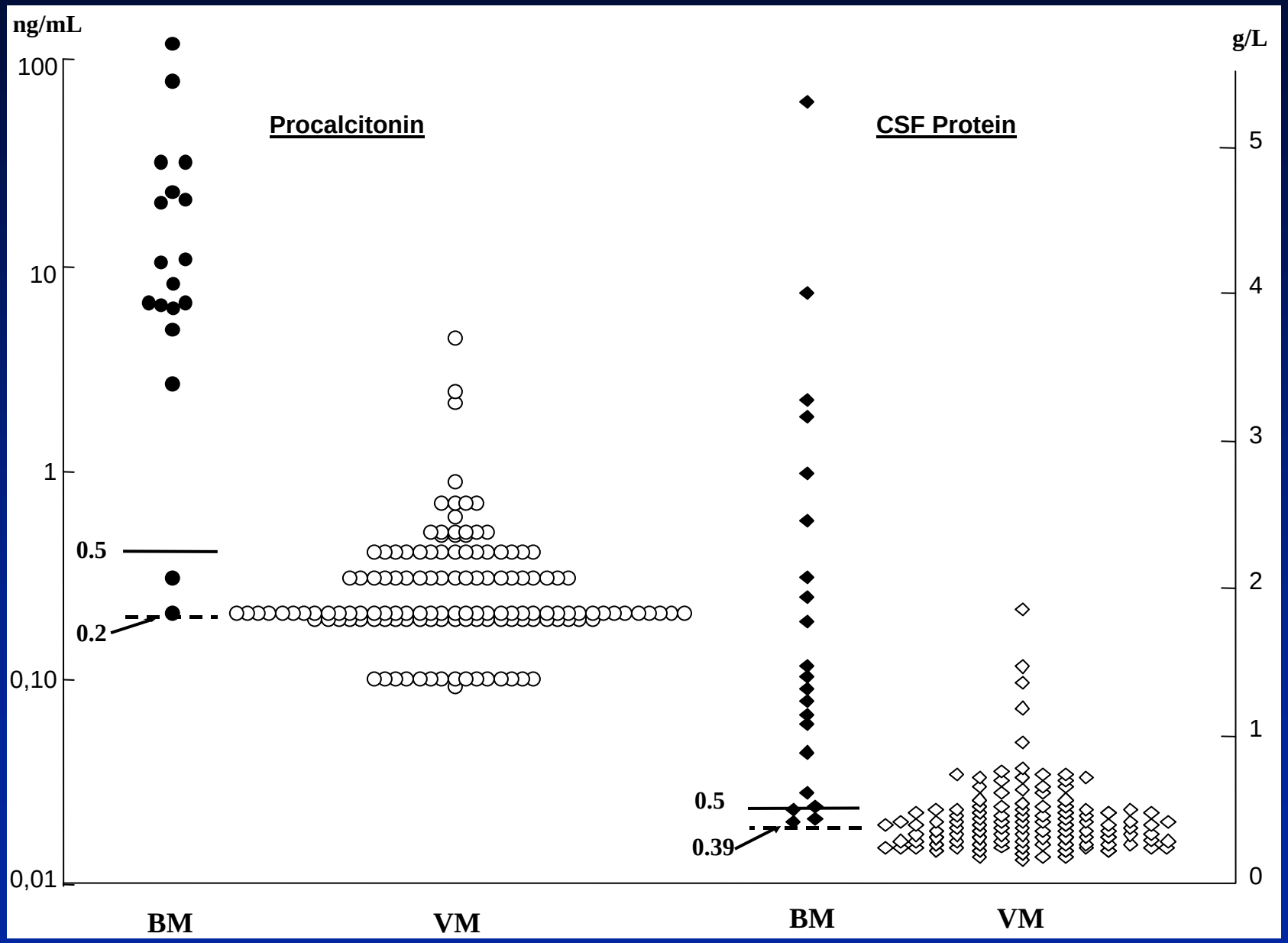
MBL-Deficient Mice and Staphylococcus Infection





Shi L, J Exp Med 2004; 199:1379

Distribution of PCT and CSF protein



SERUM PROCALCITONIN AND OTHER BIOLOGIC MARKERS TO DISTINGUISH BETWEEN BACTERIAL AND ASEPTIC MENINGITIS

FRANCOIS DUBOS, MD, FLORENCE MOULIN, MD, VINCENT GAJDOS, MD, NATHALIE DE SUREMAIN, MD, SANDRA BISCARDI, MD, PIERRE LEBON, MD, JOSETTE RAYMOND, MD, PHD, GERARD BREART, MD, DOMINIQUE GENDREL. MD. AND MARTIN CHALUMEAU, MD, PHD

(J Pediatr 2006;149:72-6)

Conclusion

Best independent predictors	Thresholds for Se = 100%	95% CI
PCT = 0.5 ng/ml	0.2 ng/ml	82-100
CSF prot = 0.5 g/l	0.39 g/l	85-100

Reproductibility of our findings?

Methods

Retrospective study from 6 centers:

Published or unpublished series

Consecutive patients in each center

- **Rzsescow**
- **Firat**
- **Lille**
- **Badalona**
- **Geneva**
- **Madrid**

Inclusion criteria

- Age: 29 days – 18 years

- Acute meningitis
(≥7 cells/mm^3 in CSF)

Exclusion criteria

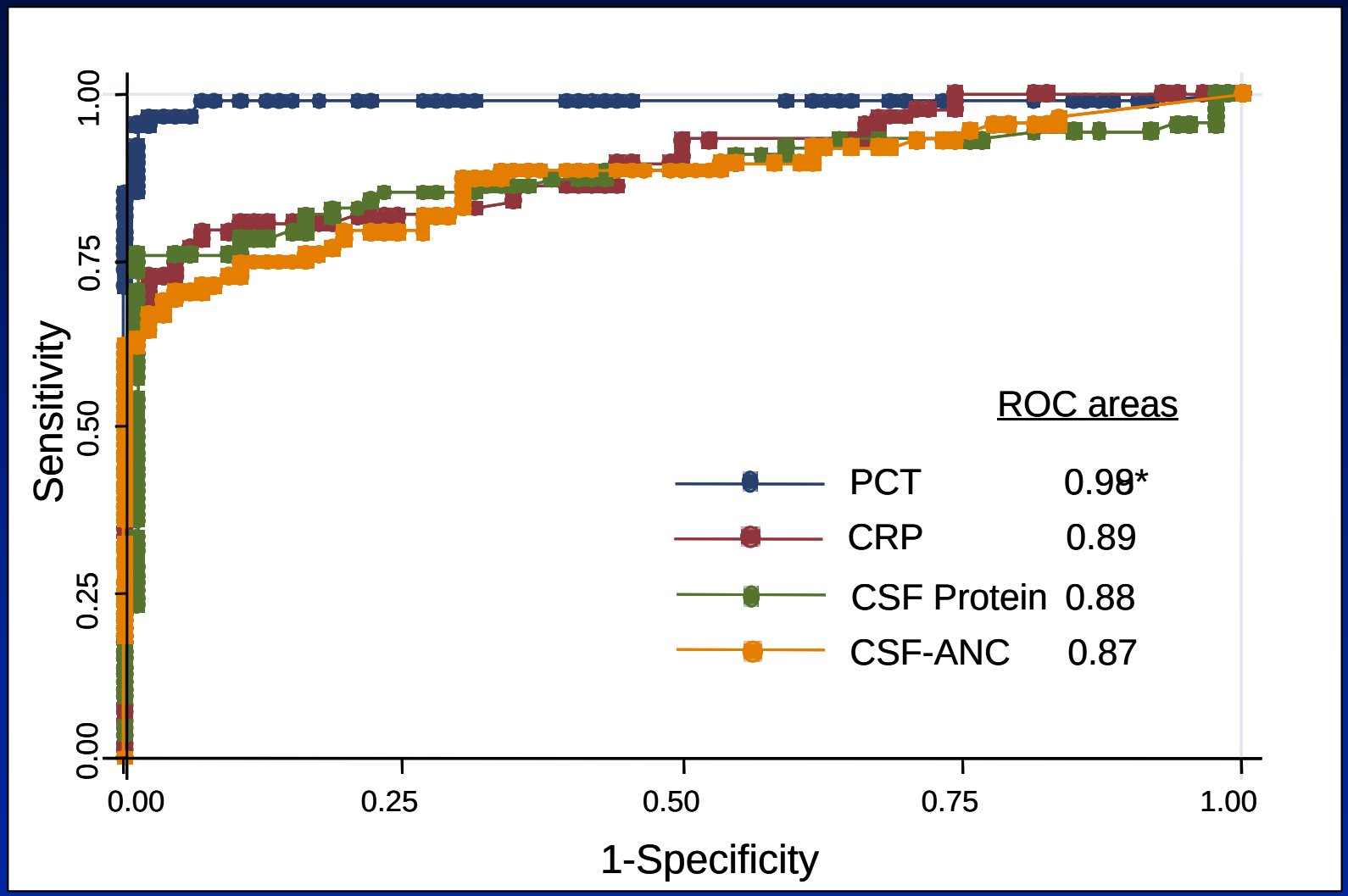
- known neurosurgical history

- known immunosuppression

- ≥10000 RBC count at the CSF puncture

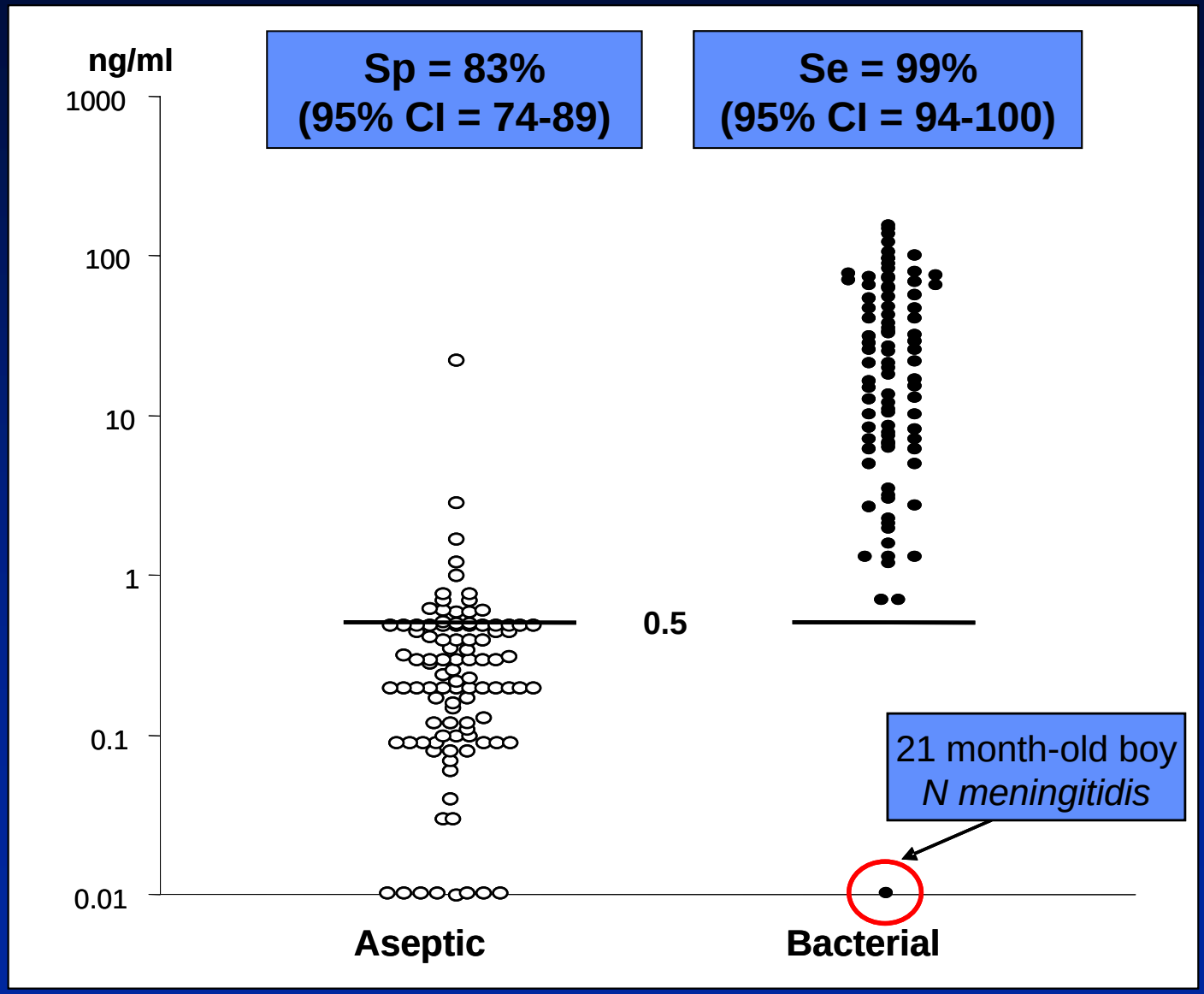
- Patients pre-treated by antibiotics

ROC curve areas comparison



* p<0.05

Distribution of PCT values



Conclusion

PCT at 0.5 ng/ml threshold

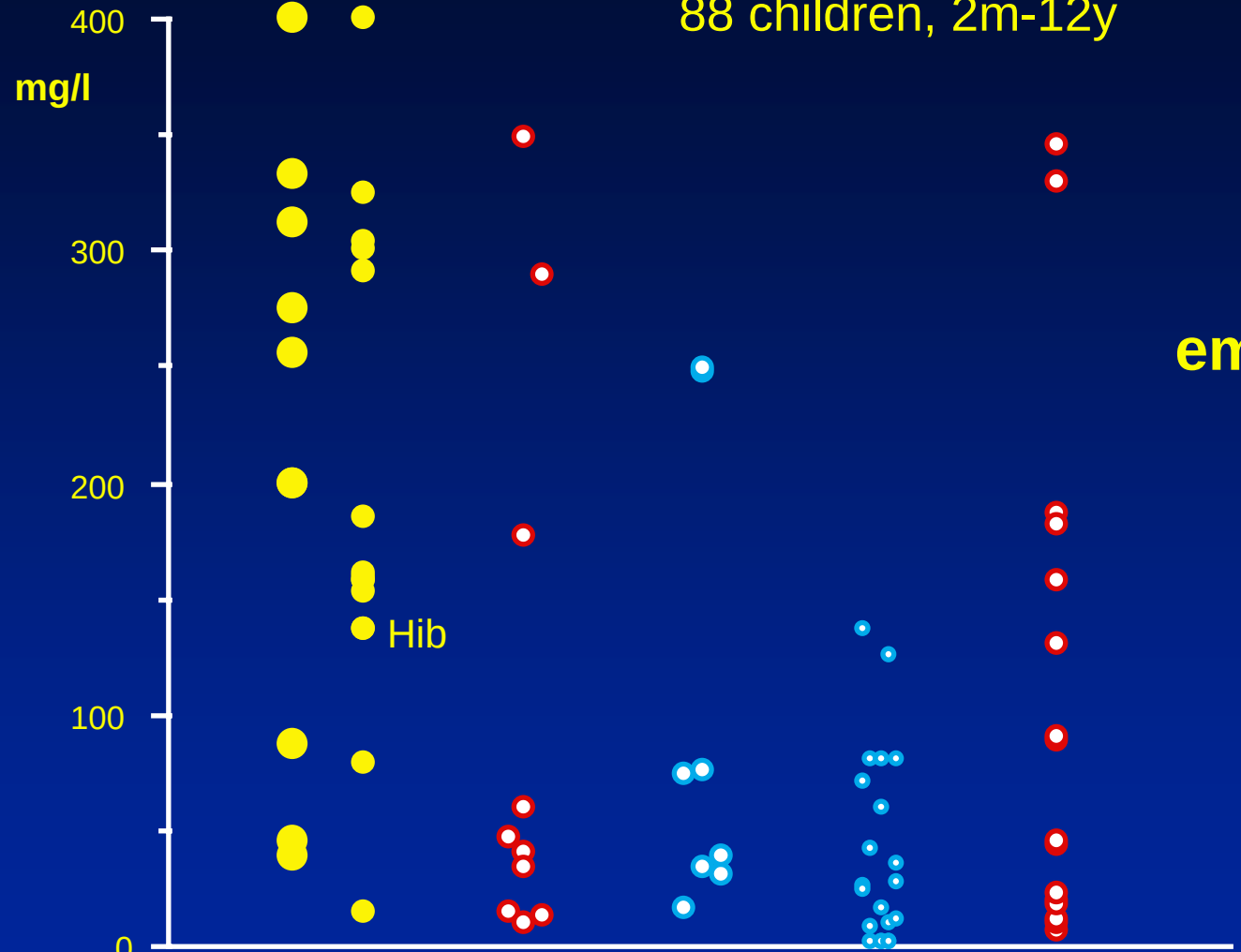
- **Best marker to distinguish early between bacterial and aseptic meningitis, in the emergency department**
- **Not enough alone to detect all bacterial meningitis**
- **Perspectives:**
  - **combination of PCT with other variables (CSF protein?) in a simple clinical decision rule**
  - **prospective validation**

Funding: DRC (CRC 03154) and the URC–Cochin, AP-HP, the Fonds d'Etudes et de Recherche du Corps Médical des Hôpitaux de Paris and the Fondation Bayer Santé.

Potential conflicts of interest: an unrectricted educational grant was received from Brahms (the manufacturer of PCT) for another study.

Community Acquired Pneumonia

88 children, 2m-12y



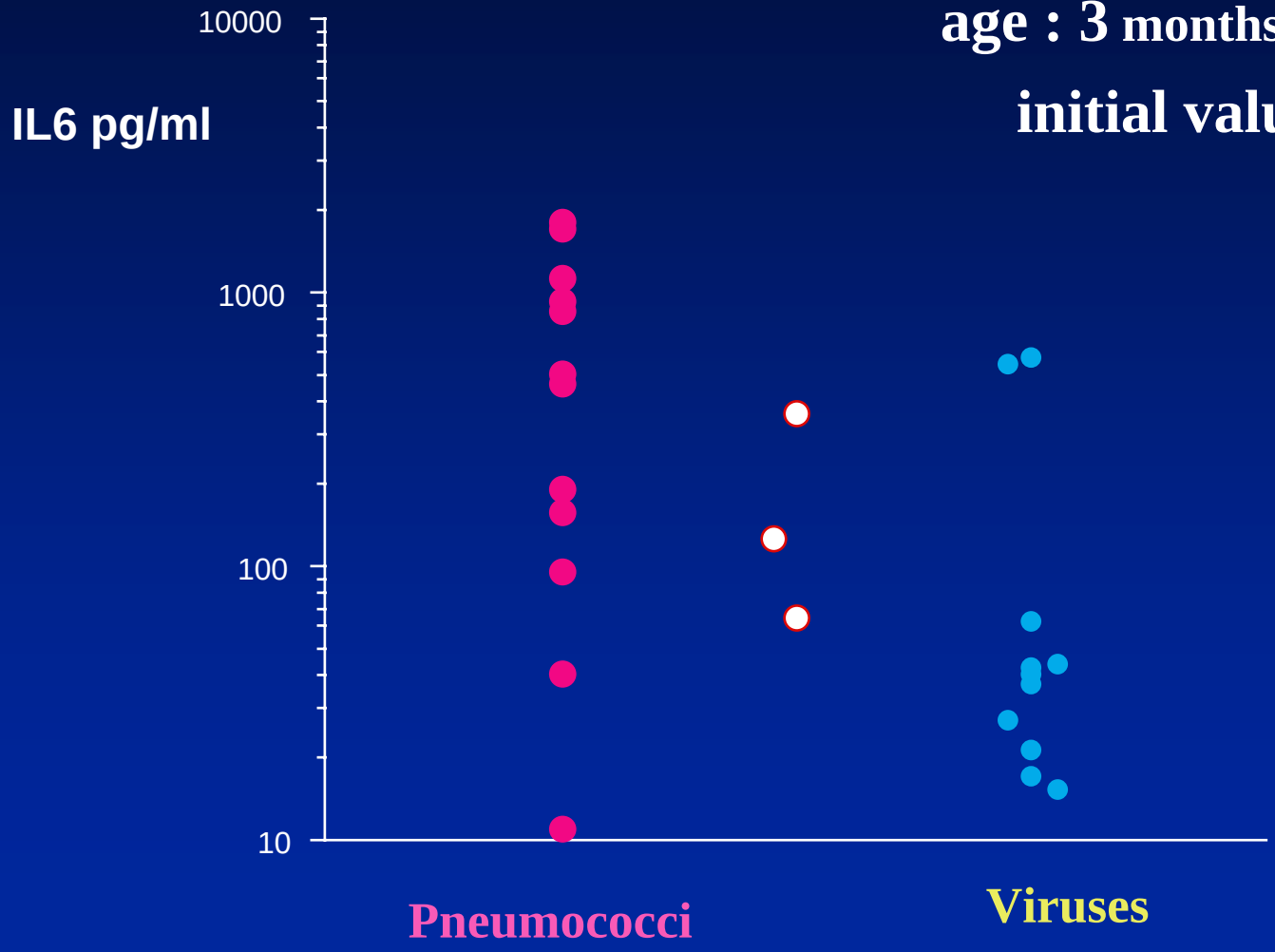
CRP at emergency room

Moulin F, Arch Dis Child 2001

Interleukin 6 in Community acquired pneumonia

age : 3 months to 12 years,

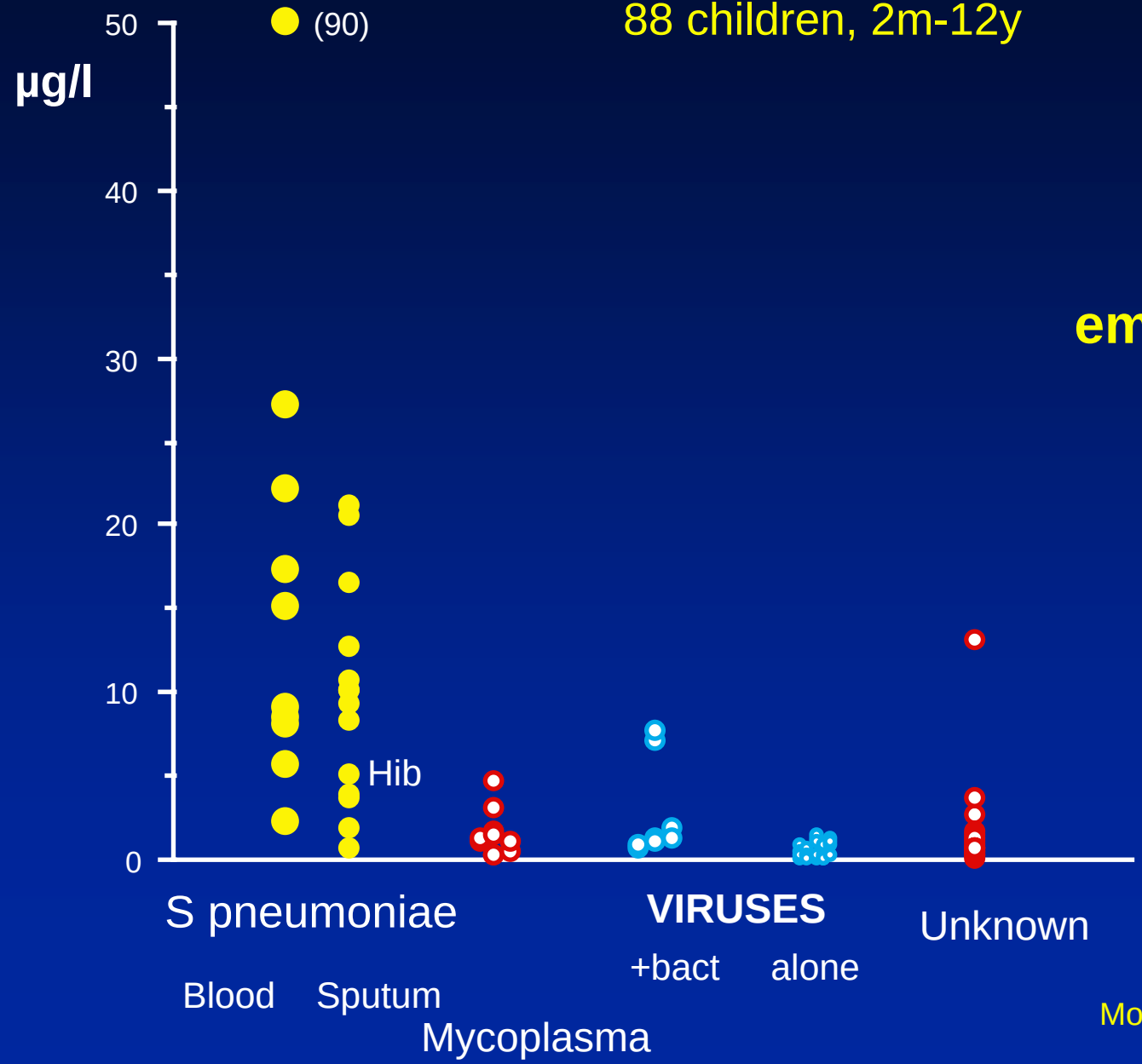
initial values



St Vincent de Paul Hospital

Community Acquired Pneumonia

88 children, 2m-12y



PCT at emergency room

Moulin F, Arch Dis Child 2001

Pediatr Infect Dis J, 2003;22:963–7
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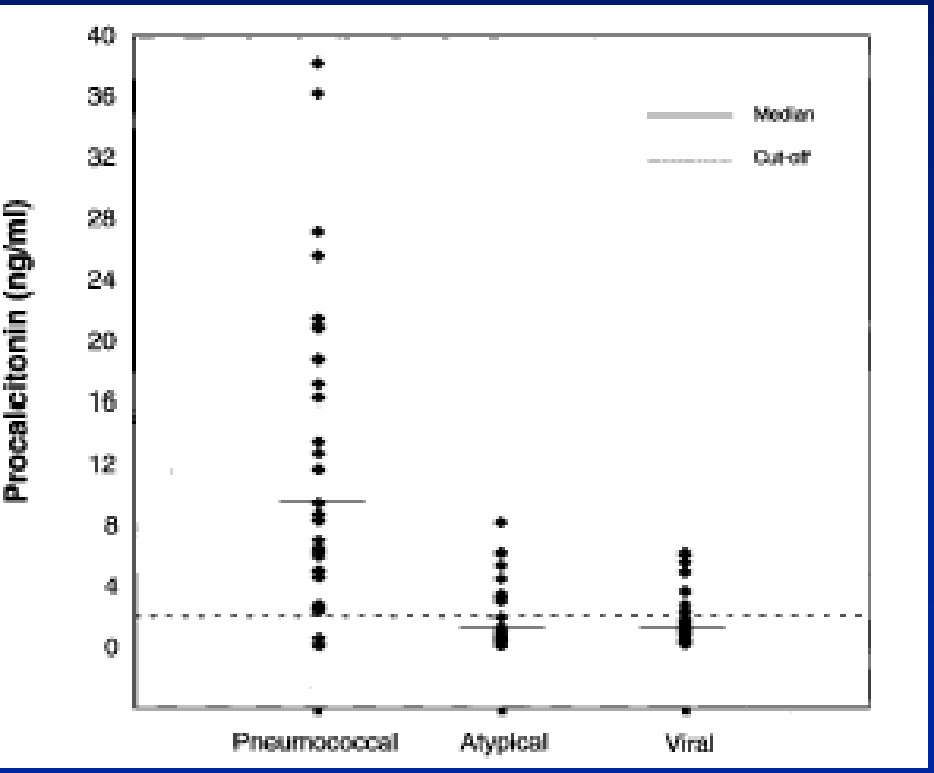
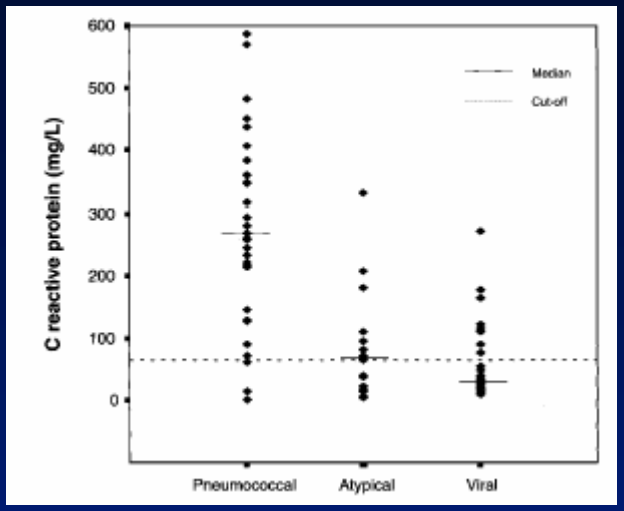
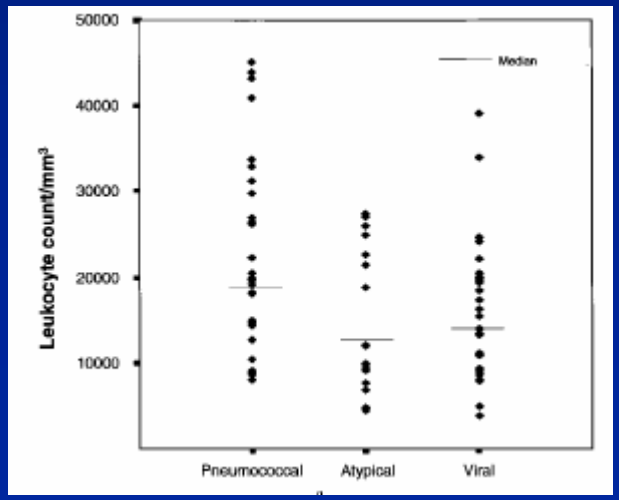
Procalcitonin, C-reactive protein and leukocyte count in children with lower respiratory tract infection

CRISTINA PRAT, MD, JOSEP DOMÍNGUEZ, PHD, CARLOS RODRIGO, MD, PHD, MONTSE GIMÉNEZ, MD, PHD, MARTA AZUARA, MD, ORLANDO JIMÉNEZ, MD, NÚRIA GALÍ, MSC AND VICENÇ AUSINA, MD, PHD







INTERFERON-ALPHA
in lower respiratory tract infections

S. pneumoniae	**1*/3**
H. influenza b	**0/5**
M. pneumoniae	**3*/40**
B. pertussis	**0/4**
S. aureus	**0/1**

RSV	**38/50**
Adenovirus	**9/10**
Parainfluenza	**10/13**
Influenza	**2/2**

* viral infection identified

F. Moulin, PIDJ, 1996

39°C after 2 days amoxicillin trt

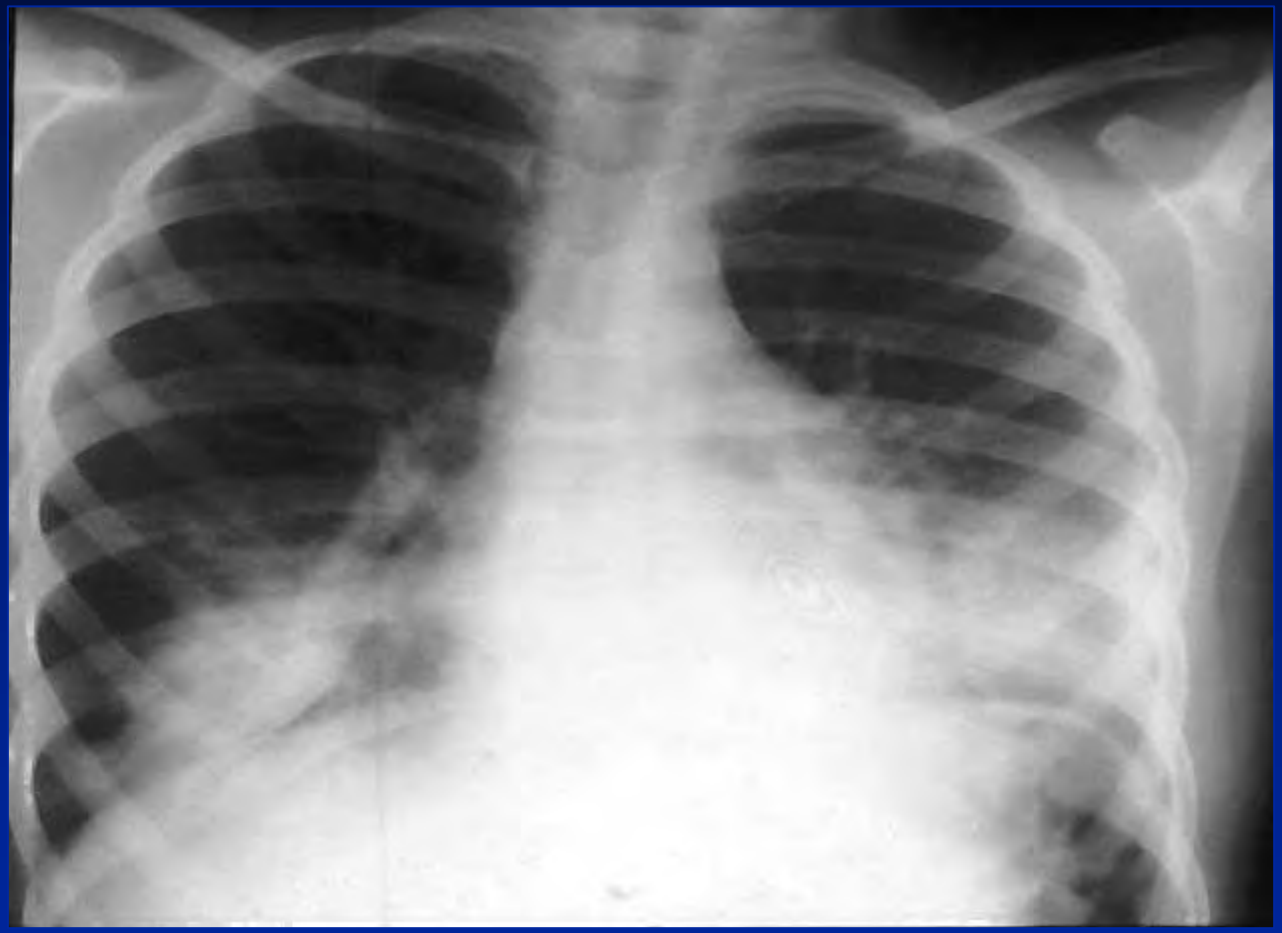
PCT 0.4 ng/ml

RSV in throat

CRP 45 mg/l

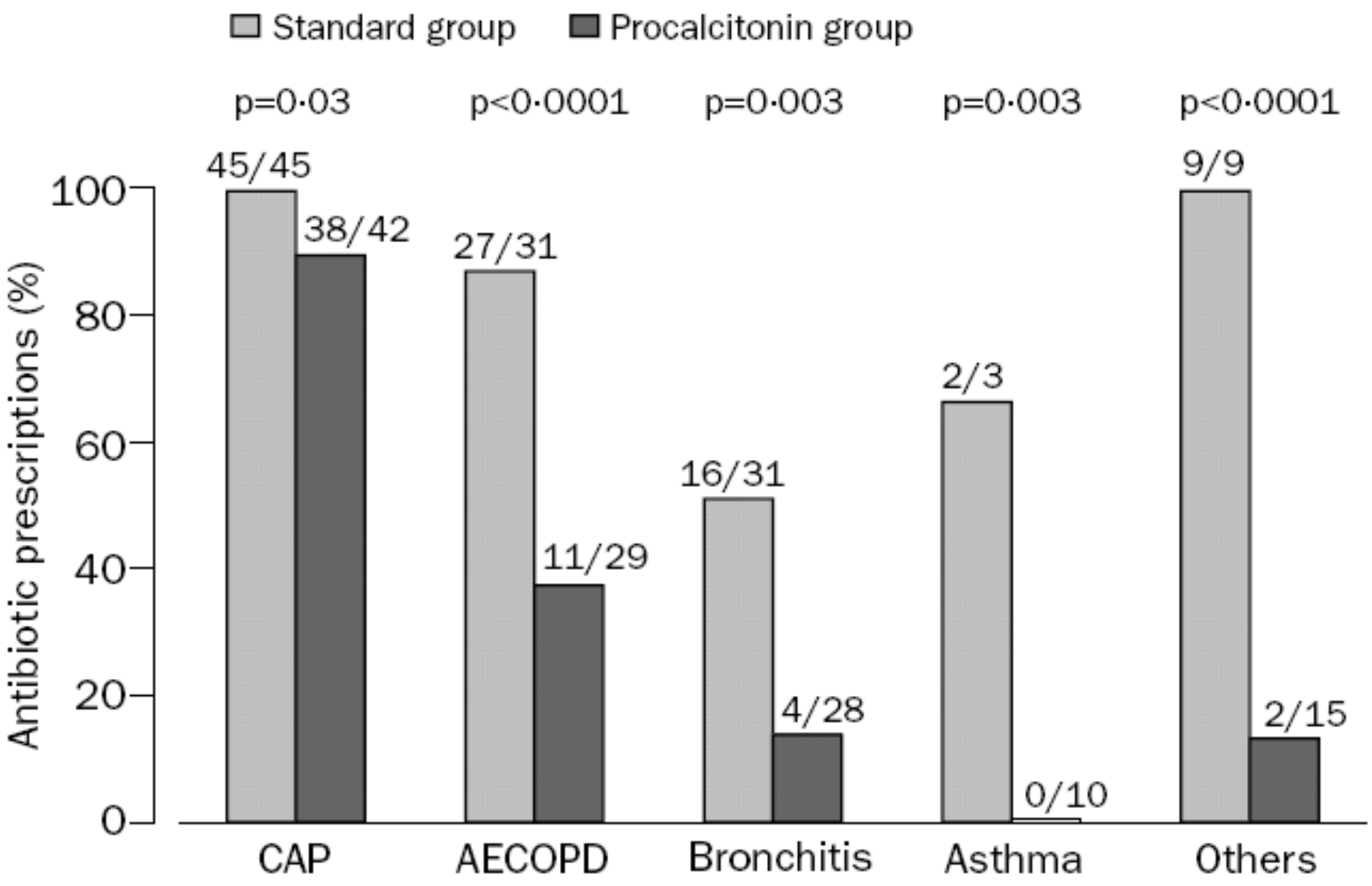
12 years , 39°, cough since 1 day, CRP 70 mg/l

Emergency Room diagnosis : *Mycoplasma pneumoniae*



Blood culture : *Strept pneumoniae*

PCT : 18 ng/ml



Same outcome in the two groups

Lancet 2004

Age	PCT µg/l	CRP mg/l	IL6 pg/ml	Age	PCT µg/l	CRP mg/l	IL6 pg/ml
Hémoculture +, ECBU +				Hémoculture -, ECBU +			
1 m	30,2	9	535	1 m	0,21	87	75
2 m	3,21	19	5	2 m	16	188	1270
2 m	8,5	16	-	4 m	2,4	103	-
3 m	50	11	24	6 m	4,13	160	-
1 a	5,4	225	-	6 m	2	92	-
3 a*	26,9	65	1400	6 m	2,2	32	-
				6 m	5,2	56	-
				7 m	4,91	35	54
				8 m	1,6	21	-
				1 a	0,88	88	-
				1 a	0,65	14	43
				1 a	0,05	14	-
				2 a	1,2	226	-
				8 m	2,50	90	-
				1 m	4,3	60	46
				8 a	16,9	251	-
				4 a	0,6	122	687
				6 a	8	216	160

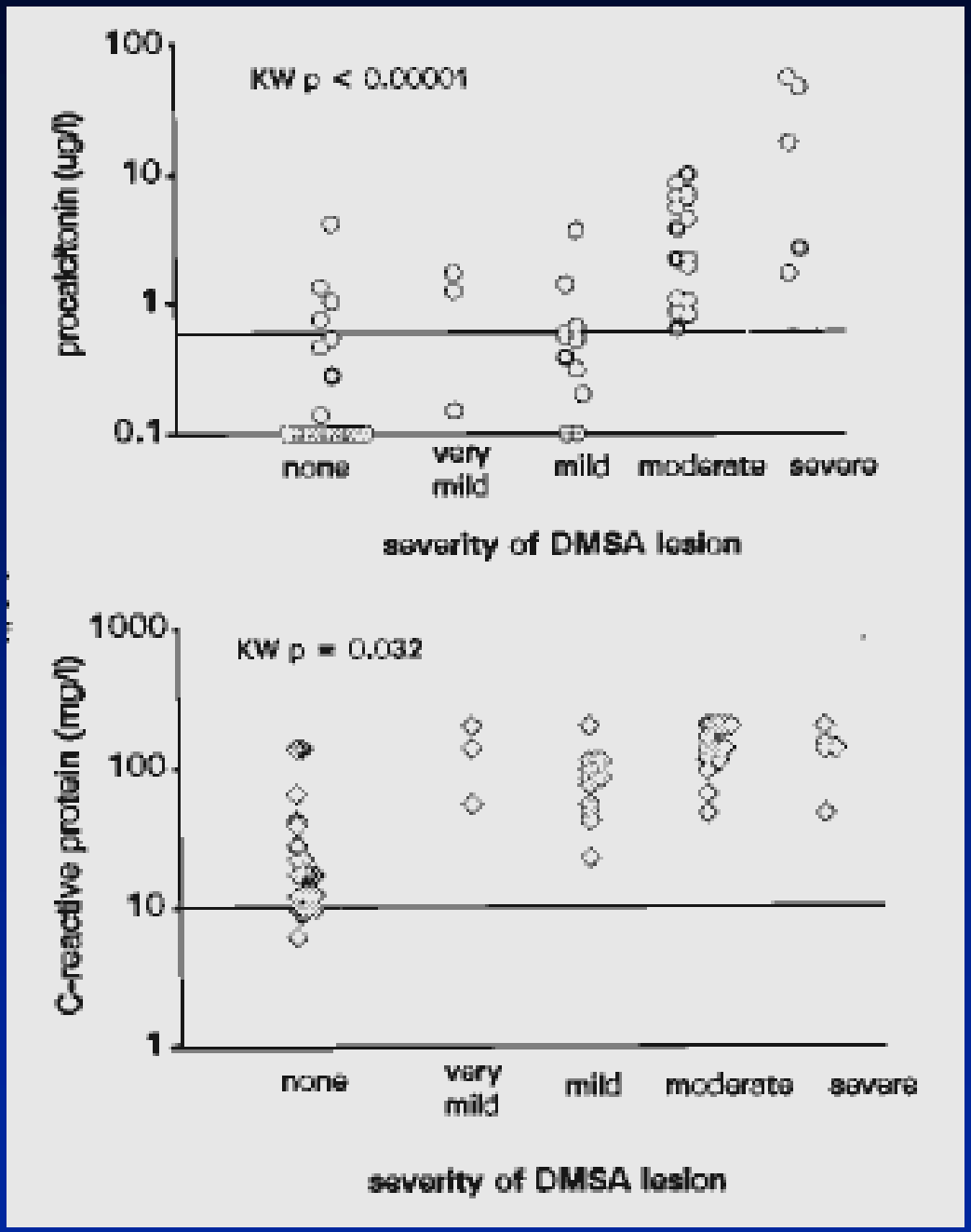
Résultats à l'admission (E. Coli, * entérocoques)

ETUDE GENEVE-PARIS
(Benador, Siegrist, Gendrel et al, Pediatrics Dec 1998)

- 80 enfants 1 an - 15 ans
  - Infection urinaire fébrile

- **Scintigraphie DMSA**
  - 37 ont des lésions en rapport avec l'infection

- **Cicatrices rénales dues à la pyélonéphrite**
  - non corrélées à IL6, IL8, TNF, CRP
  - corrélation très positive avec **PROCALCITONINE**

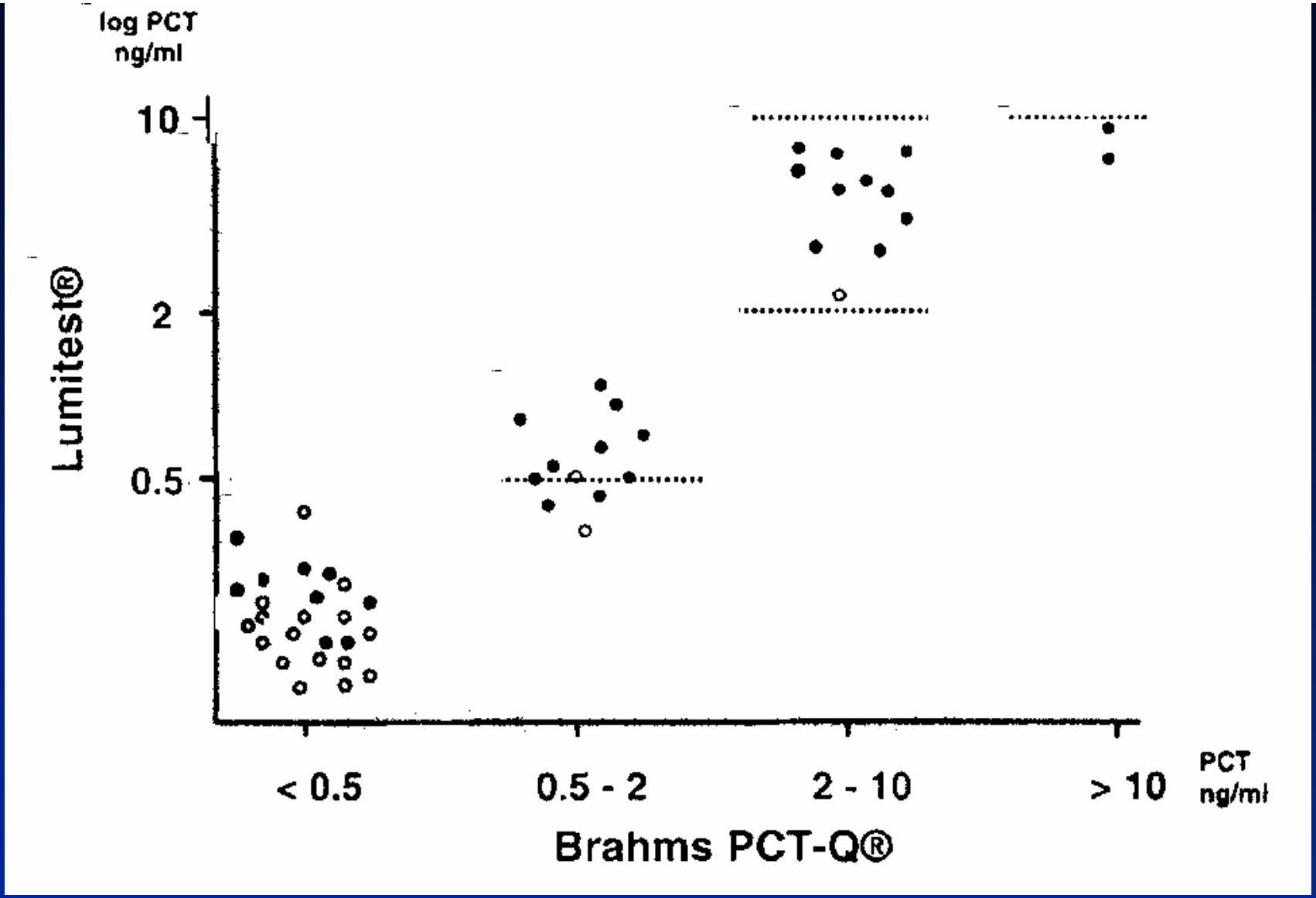


Procalcitonin is a marker of severity of renal lesions in pyelonephritis

Results of initial CRP & PCT and DMSA scintigraphy in 60 children with urinary tract infection (Geneva & Paris)

Importance of renal scars is correlated **with PCT**
and not with CRP, TNF, IL6 and IL8

Benador, *Siegrist*, *Gendrel*, et al
PEDIATRICS, 1998; 102 : 1422



PCT (Lumitest et PCT –Q) dans les infections urinaires
Scinti au DMSA : pos ● neg ○ pour cicatrices

Gervaix , PIDJ 2001

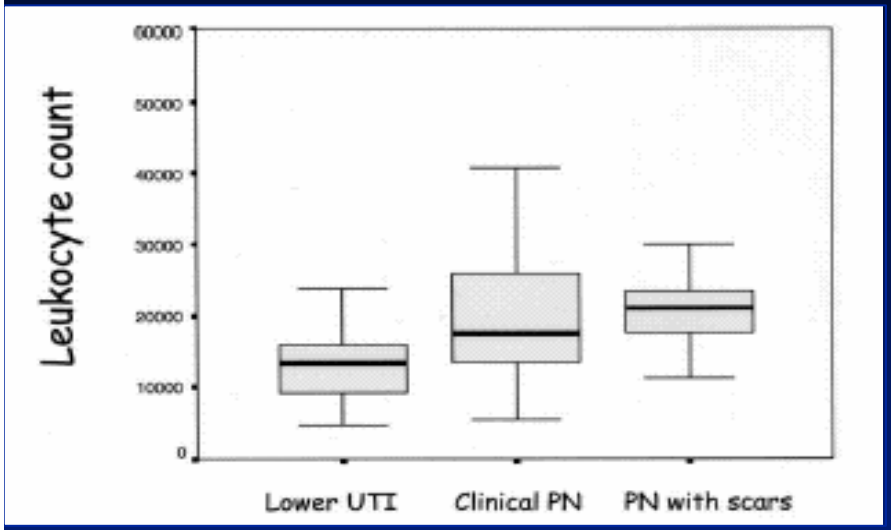
	Lower UTI (*n* = 42)	Pyelonephritis (*n* = 18)	*P* value
Age (months)	**14 (1-35)**	**18 (2-35)**	**0.270**
Gender F/M	**30/12**	**13/5**	**0.470**
WBC:mm^3	**14,600** (8,190-26,470)	**15,910** (10,200-26,900)	**0.340**
CRP (mg/l)	**74.5** (14.5 - 235)	**120** (62 - 249)	**0.012**
PCT (µg/l)	**0.13** (0.02 - 2.15)	**3.41** (0.36 - 12.4)	**<0.0001**

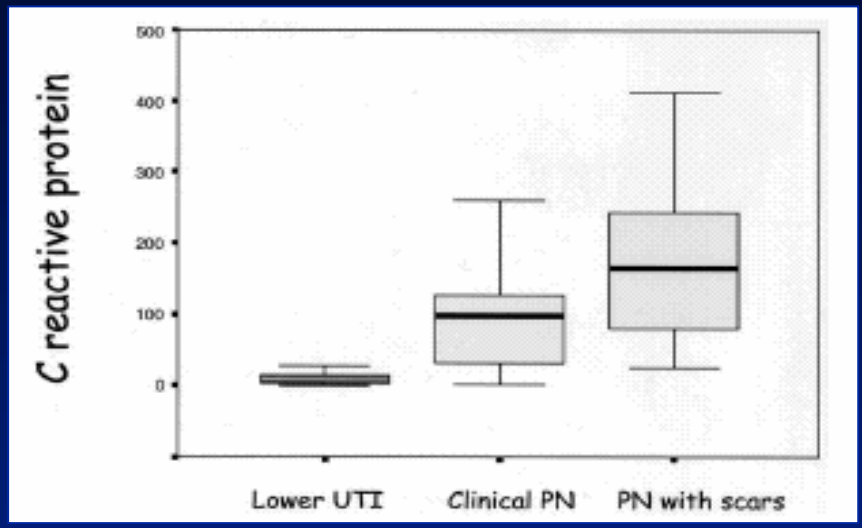
Pyelonephritis	Sens	Spec	NPV	PPV
PCT > 0.5 µg/l	94.1	89.7	97.6	85.7
CRP > 20 mg/l	100	18.5	100	30.9

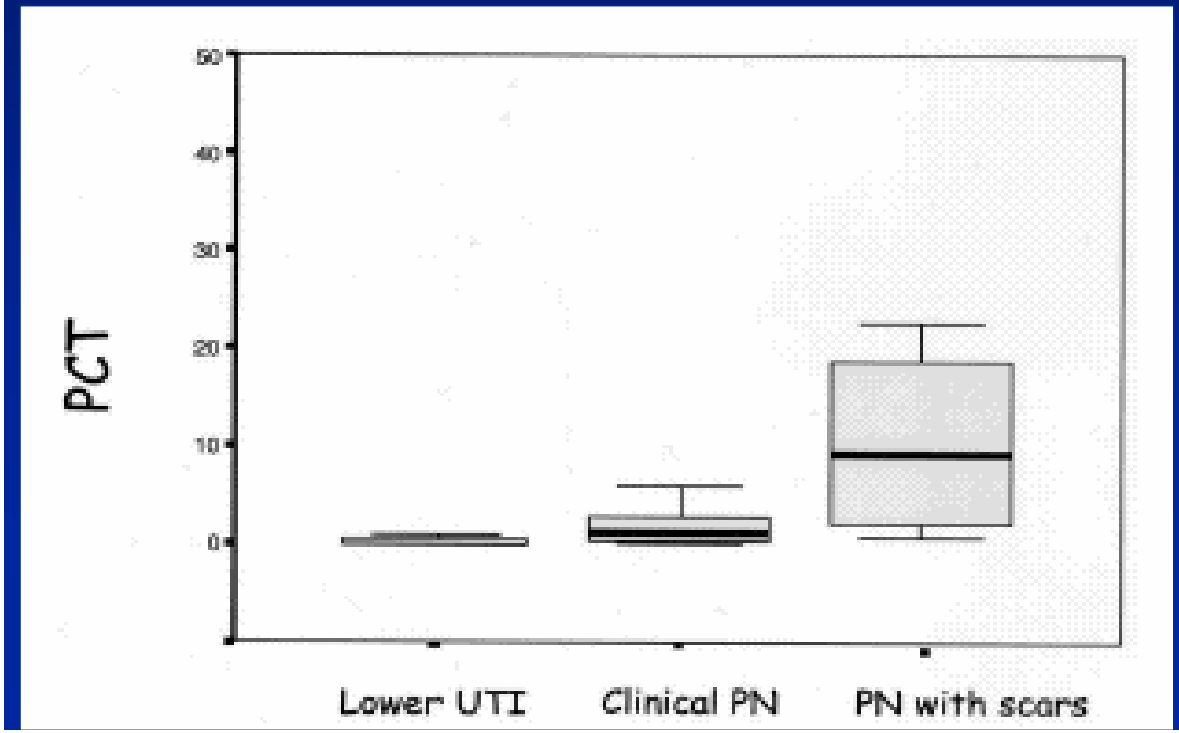
DMSA scintigraphy 2 to 7 days after UTI

Smolkin, Pediatr Nephrol , 2002

DMSA scintigraphy 6 months after UTI



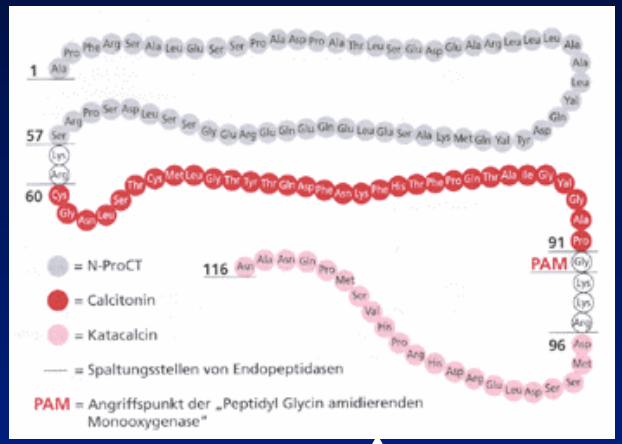




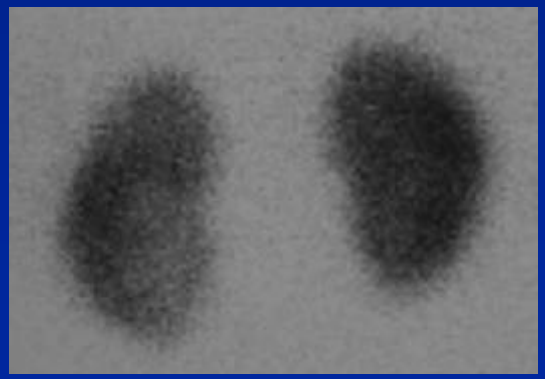
Low PCT indicates
a low risk of renal scarring
in children with UTI

Prat et al , PIDJ 2003

PCT : prédiction du reflux ?



?



Les infections urinaires fébriles

- Fréquentes : 2-7% avant 6 ans
- Reflux vésico-urétéral :
  - 20-40% des enfants après une 1ère IUF
  - récurrence, cicatrices, HTA, IRC
  - traitement possible

Märild, *Acta Paediatr*, 1998
Jacobson, *Acta Paediatr*, 1999

Intérêt d'un dépistage :

- Pathologie fréquente
- Potentiellement grave
- Accessible à un traitement

⇒ ***Cystographie systématique***

Guillot, *Arch Pédiatr*, 1998
Académie américaine, *Pediatrics,* 1999

Douloureuse

Psychological reaction by children of various ages to hospital care and invasive procedures

B Hägglöf

Department of Child and Adolescent Psychiatry, University Hospital of Umeå, Umeå, Sweden

Hägglof, *Acta Paediatr*, 1999

Irradiante

Radiation burden to paediatric patients due to micturating cystourethrography examinations in a Dutch children's hospital

[1]F W SCHULTZ, PhD, [2]J GELEIJNS, PhD, [3]H C HOLSCHER, MD, PhD, [2]J WESTSTRATE, RT, [2,3]H M ZONDERLAND, MD and [1]J ZOETELIEF, PhD

Schultz, *Br J Radiol*, 1999

Risquée

Complications Associated with Cystography in Children[1]

William H. McAlister, M.D., Alexander Cacciarelli, M.D., and Gary D. Shackelford, M.D.

Complications of cystography include infections, especially those associated with intrarenal reflux; complications related to bladder filling; allergic reactions; catheter problems; inflammatory response of the bladder to contrast media; peritoneal spillage of contrast medium *via* the vagina; transurethral reflux of organisms from cleansing procedures; pain from reflux or incorrect catheter placement; radiation effects; temporary anuria; and intrarenal foreign body reaction to contrast media. Fourteen cases are presented, including two patients who died from sepsis. Some considerations for reduction of the complications are discussed.

Mc Alister, *Pediatr Radiol*, 1974

The NEW ENGLAND JOURNAL of MEDICINE

Imaging Studies after a First Febrile Urinary Tract Infection in Young Children

Alejandro Hoberman, M.D., Martin Charron, M.D., Robert W. Hickey, M.D., Marc Baskin, M.D., Diana H. Kearney, R.N., and Ellen R. Wald, M.D.

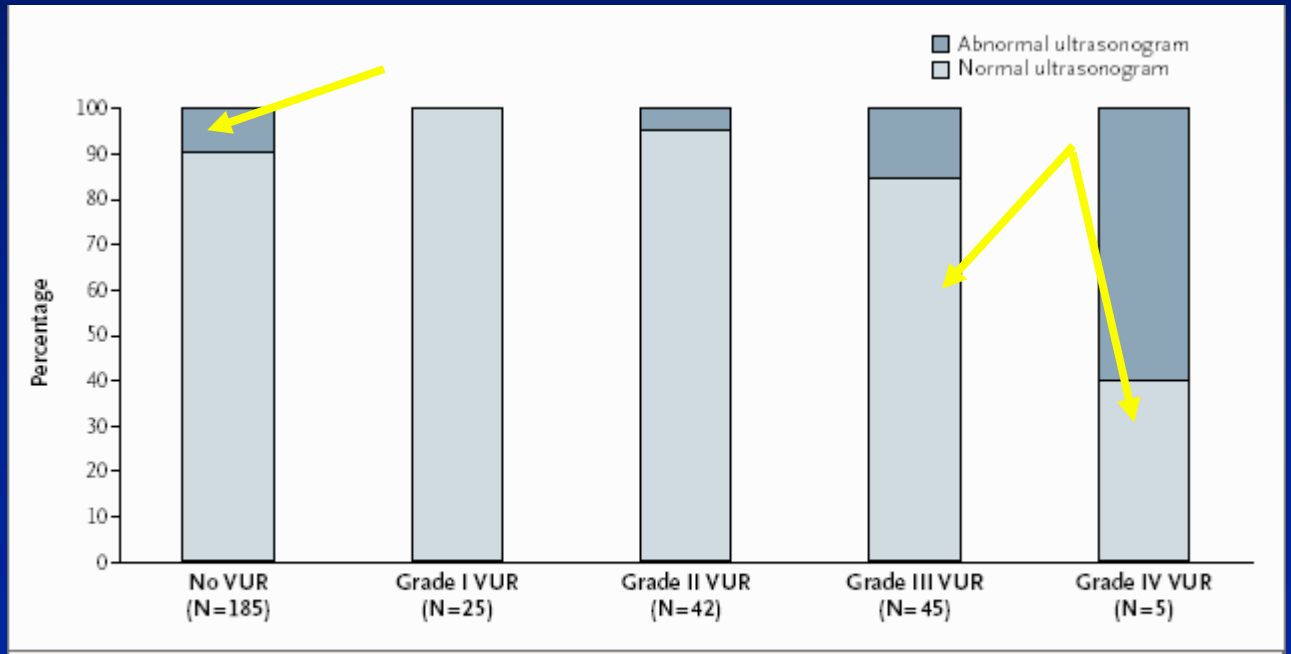
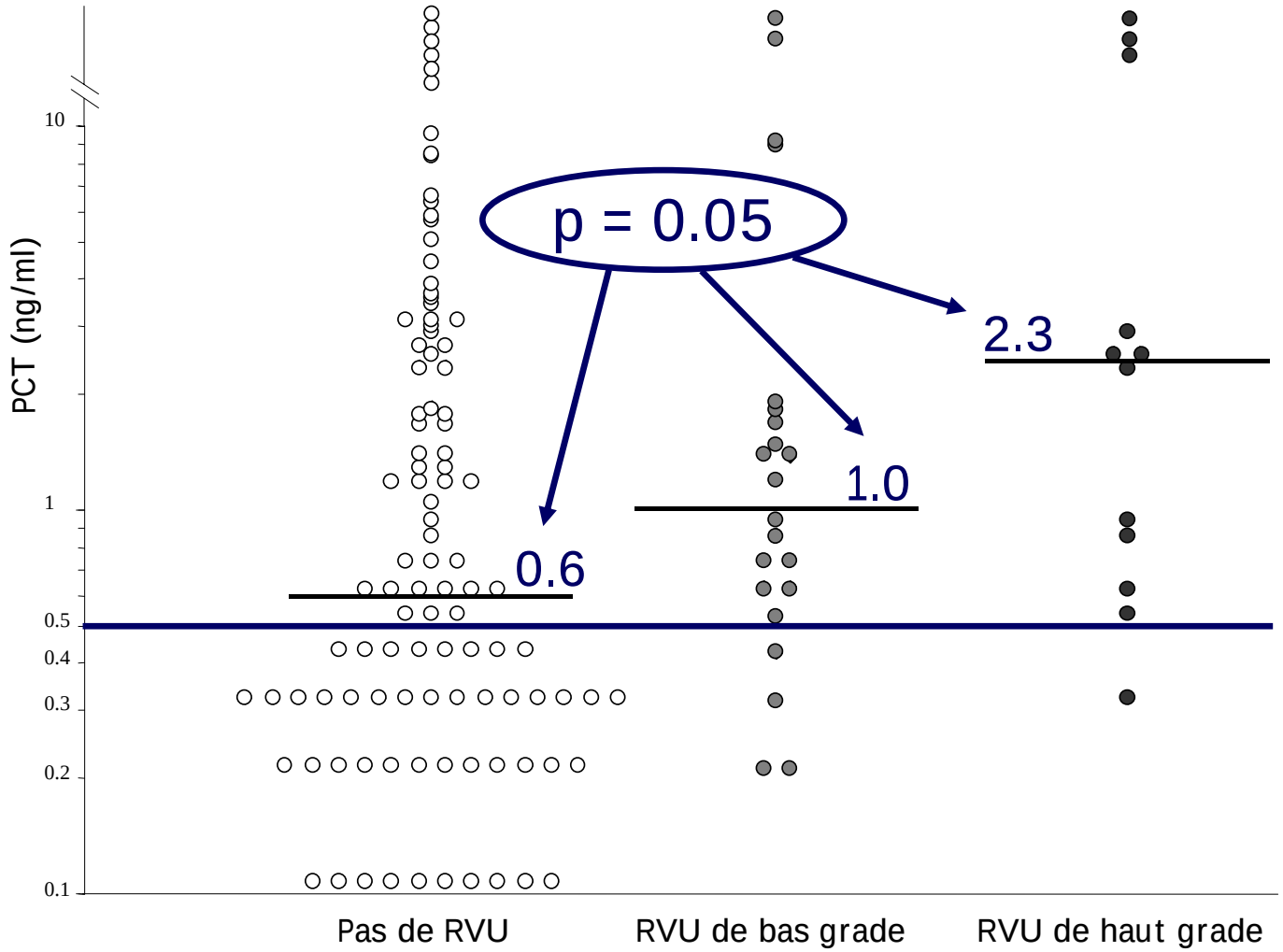


Figure 1. Frequency of Evidence of Dilatation of the Urinary Tract on the Initial Ultrasonogram, According to the Presence or Absence and Degree of Vesicoureteral Reflux (VUR) in Children with a First Urinary Tract Infection.

Distributions de la PCT



Pouvoir discriminant

	RVU (tout grade)		RVU ≥ 3	
	%	IC à 95%	%	IC à 95%
Sensibilité	85	70-94	92	65-99
Spécificité	44	34-55	44	34-55

Conclusions

- Reflux vésico-urétéral : fréquent voire grave

  ⇒ *Cystographie systématique, 'sub-optimale'*
- Stratégies sélectives de cystographies

  ⇒ *peu concluantes*
- La procalcitonine
  - prédicteur fort et indépendant
  - à confirmer
  - à combiner

Results

Centres	Dates	n = 398	% VUR	% VUR ≥ 3
Afula	1999-2000	56	25	11
Badalona	1998-2001	40	38	29
Clamart	2001-2002	23	30	4
Geneva	1998-2002	77	29	13
Paris	2003-2004	42	24	5
Rzeszow	1997-1998 and 2001-2004	49	22	8
Udine	2000-2002	80	19	11
Yvoir	1999-2003	33	21	12
Range			**19–38**	**5–29**
Total	**21 years**		**25**	**12**

Relationship VUR / PCT

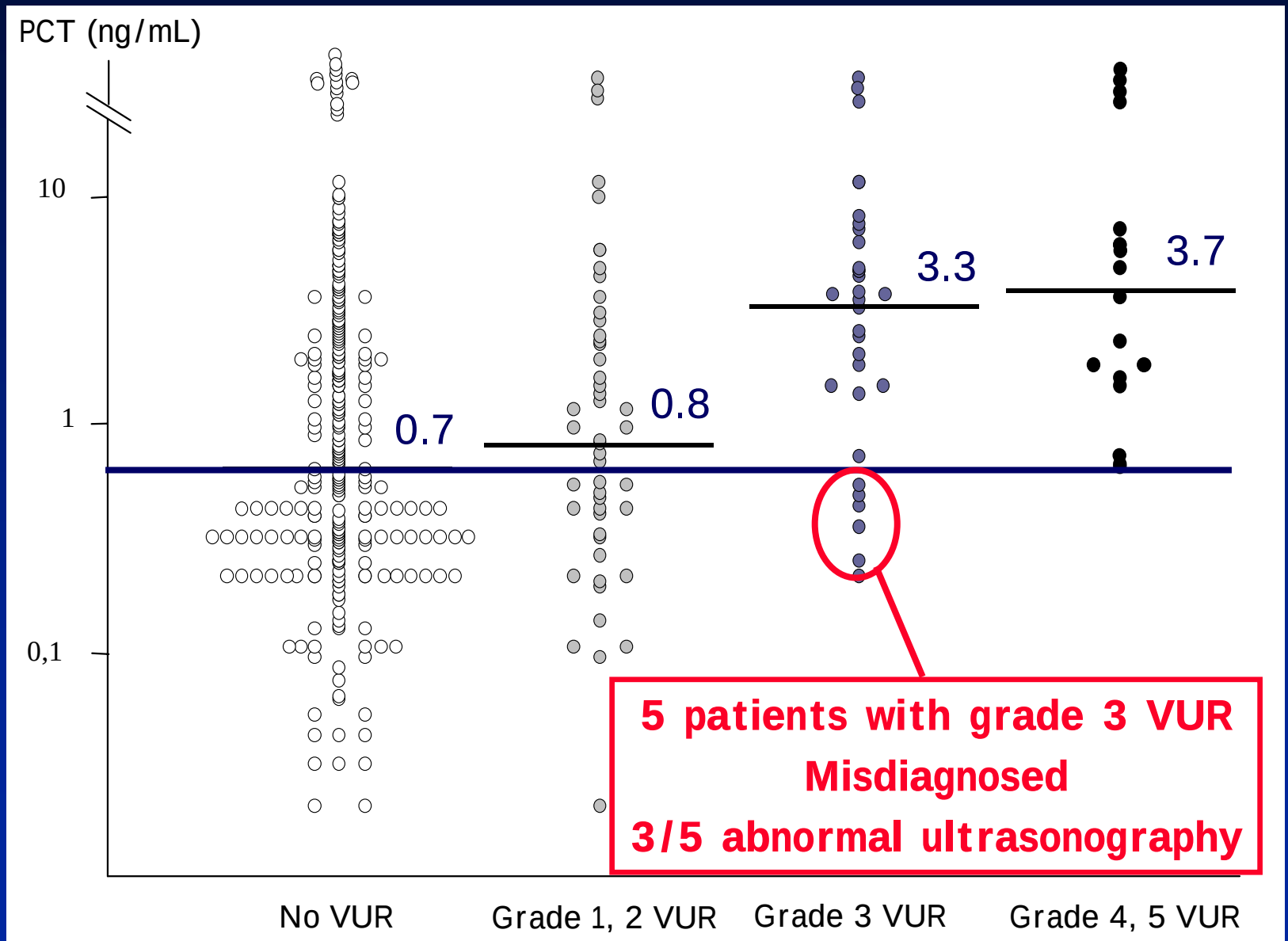
Vur Grade	n (%)	PCT (ng/mL)		OR (95% IC)	p
		<0·5	≥0·5		
None	297 (75)	127 (43)	170 (57)		
All grade	101 (25)	25 (25)	76 (75)	2,3 (1,3–3,9)	0,001
Grade 1, 2	50 (13)	19 (38)	31 (62)	1,2 (0,–2,4)	0,5
Grade 3	30 (8)	5 (17)	25 (83)	3,7 (1,4-12,8)	0,005
Grade 4, 5	16 (4)	0 (0)	16 (100)	24,7 (1,5–415)	< 0,001

χ^2 for trend: p < 0,001

OR*a = 2.4 [1.3-3.9]; p = 0.001

* after adjustment for all potential confounders: young age, male gender, family history of uropathy, dilation of urinary tract on renal US

Distributions of PCT



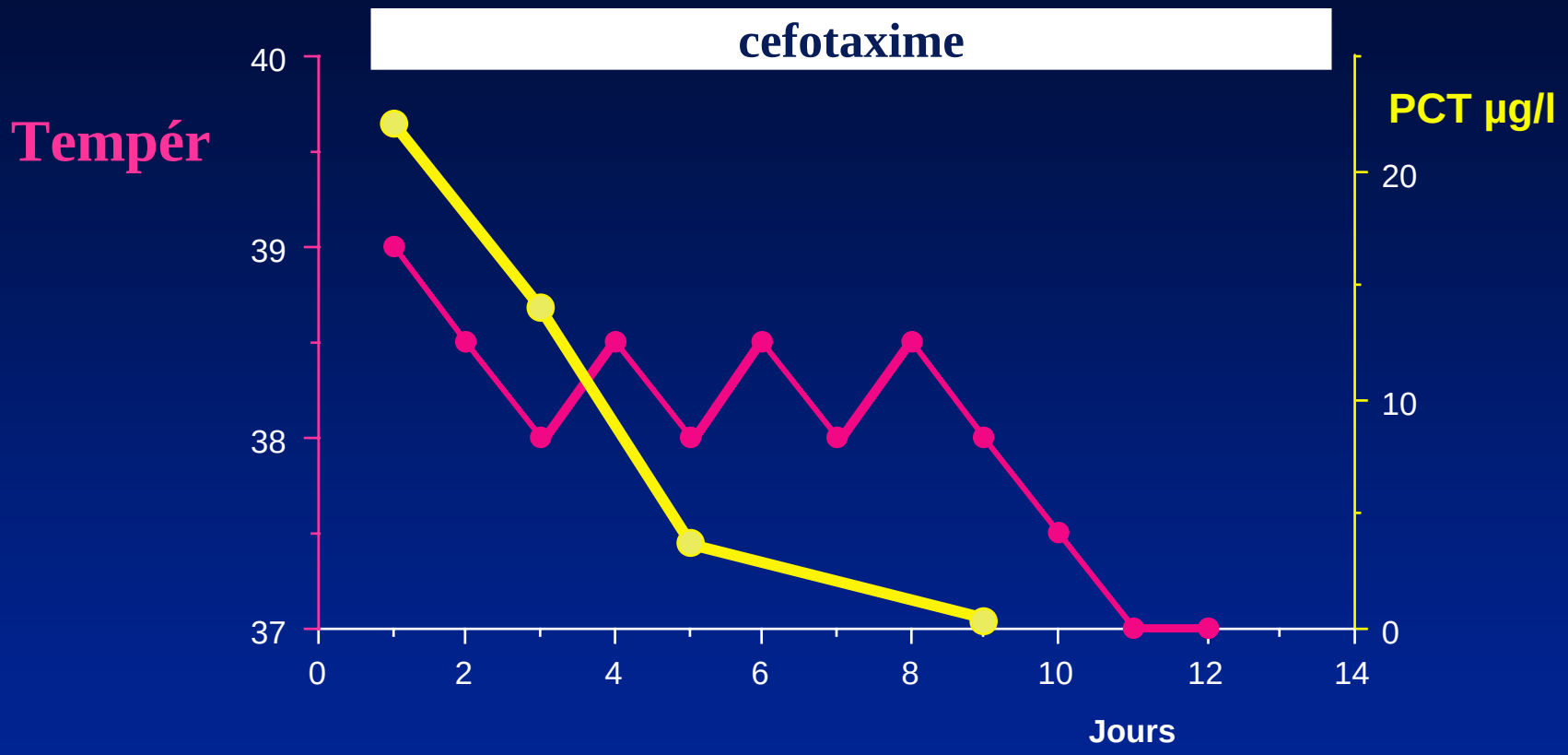
J Pediatr
in press 2006

MARQUEURS PRONOSTIQUES

- **Efficacité du traitement**
- **Evolution à long terme**

* **CRP reste importante mais variations trop lentes**
* **La PCT est supérieure à CRP et IL6**

N..., 6 mois, Meningite à Meningocoque

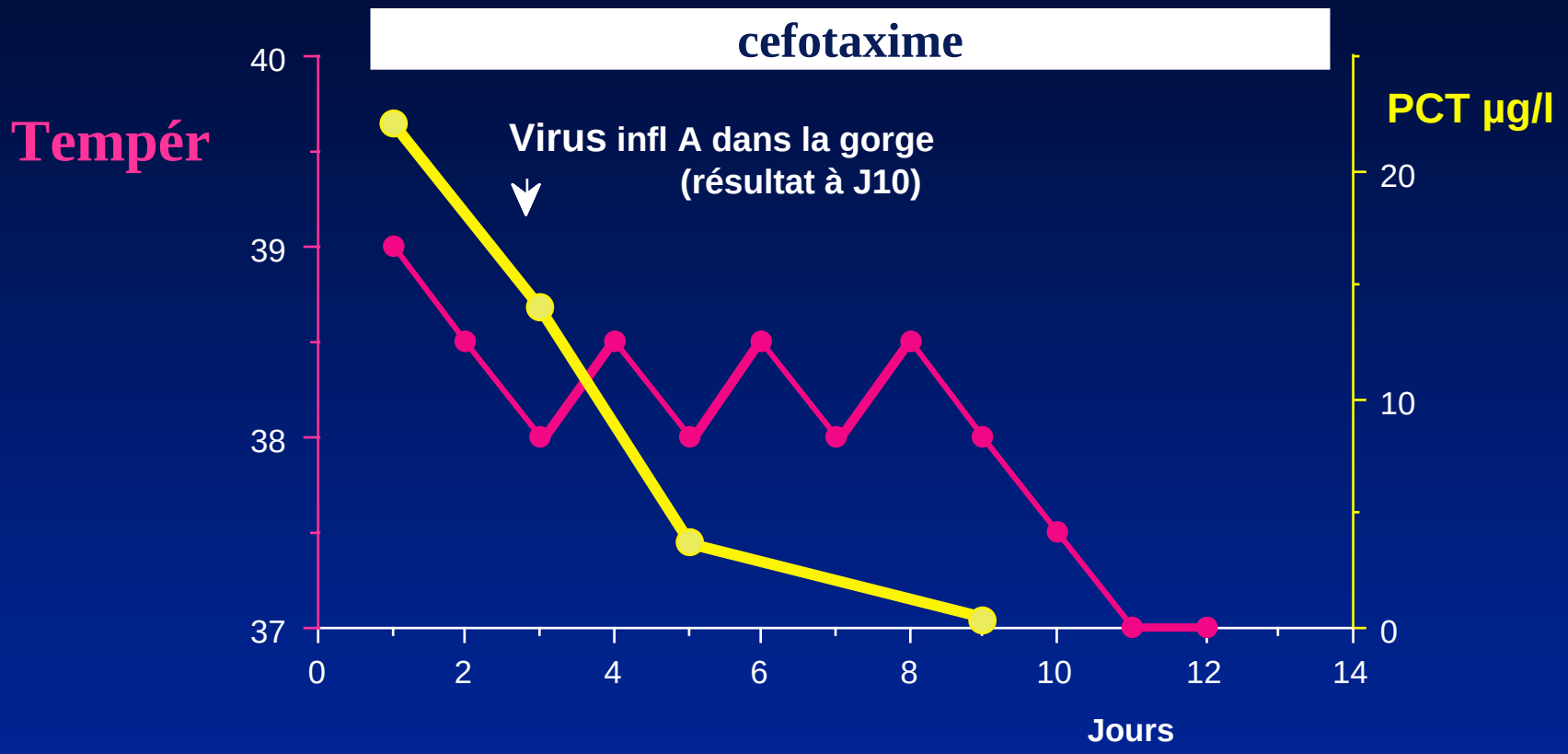


Prot LCR	2,1	0,86		0,40
Cell LCR	600	180		25
PCT	22	14	3,7	0,3
CRP	170	80	31	29

MENINGOCOQUE B
Sensibilité réduite à la Pénicillline
CMI Amox 0,5 mg / l

SVP 1998

N..., 6 mois, Meningite à Meningocoque



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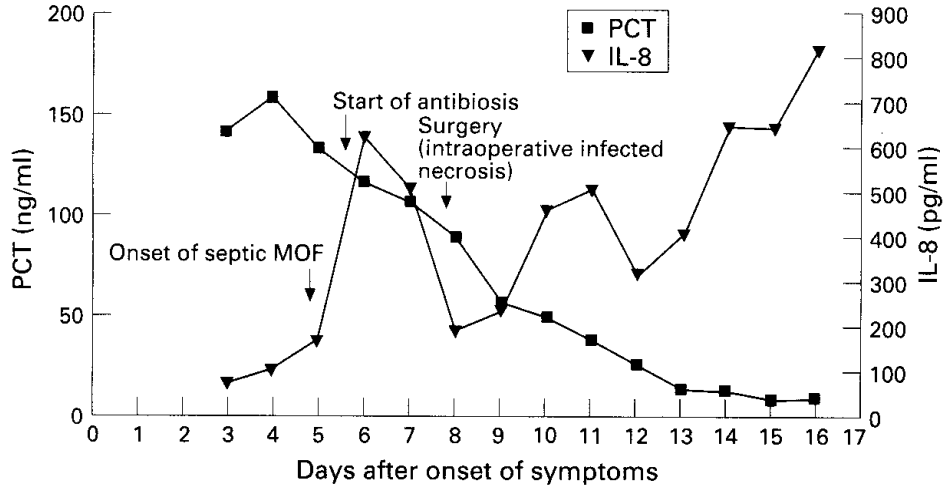


Figure 3: Typical course of PCT and IL-8 in a patient with infected necrosis and severe septic multiple organ failure.

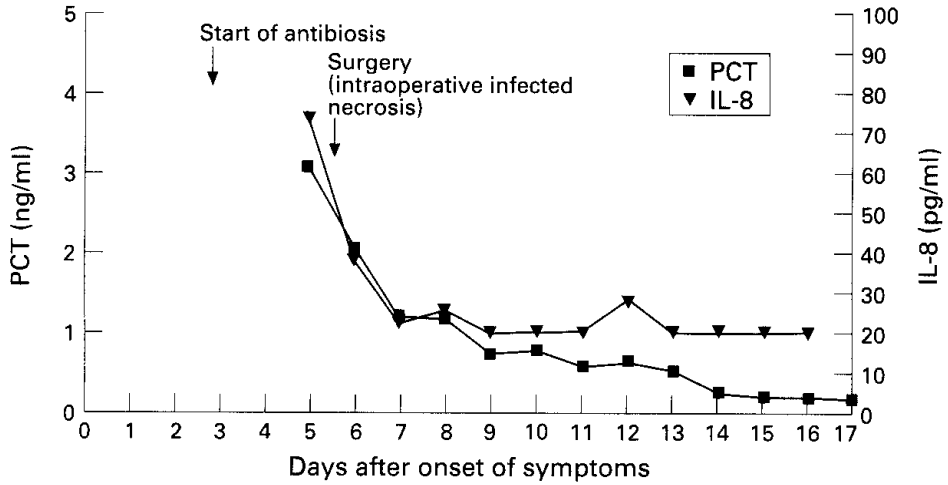
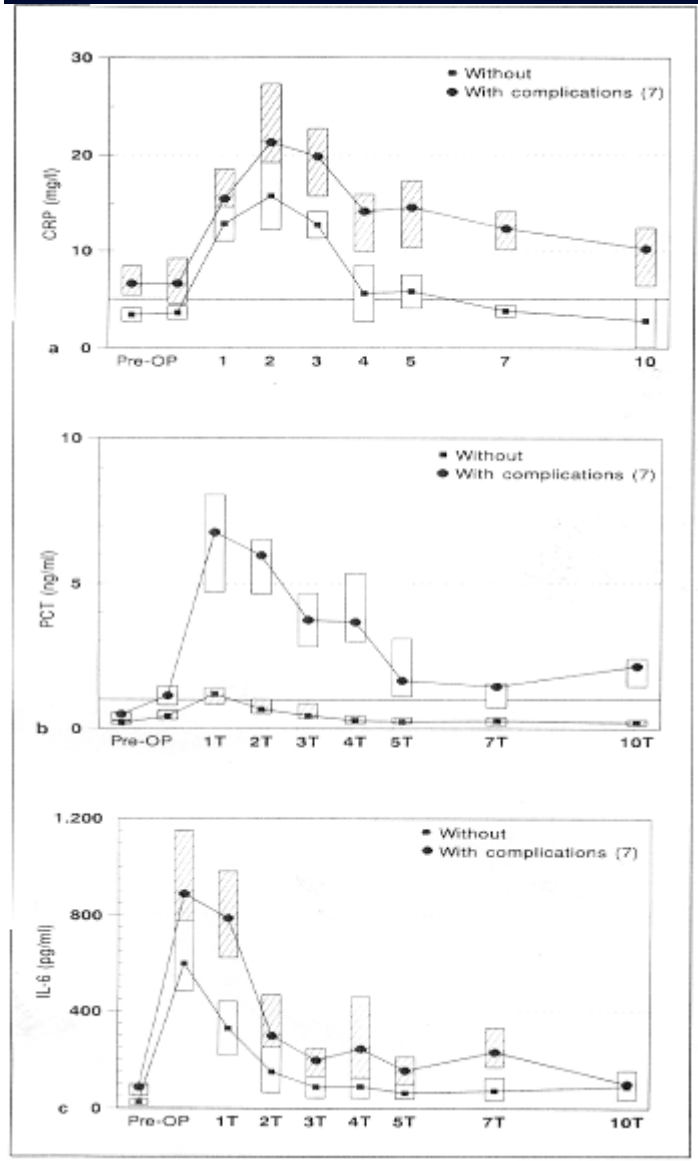
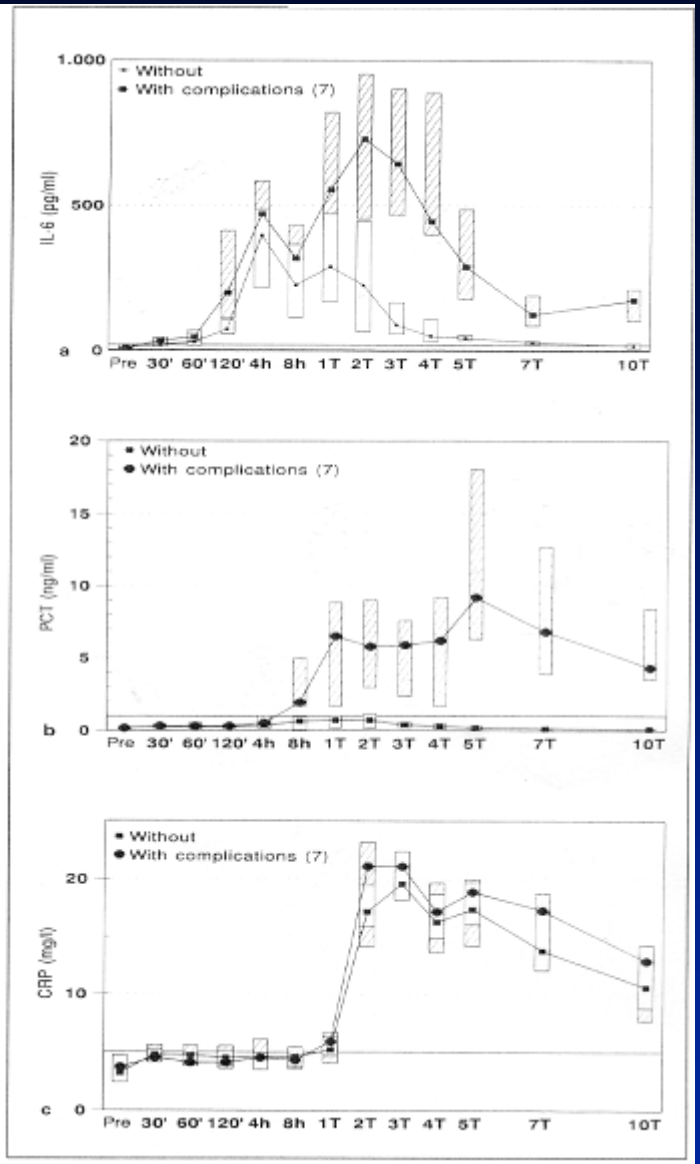


Figure 4: Typical course of PCT and IL-8 in a patient with infected necrosis and an uncomplicated course.

Procalcitonin in acute pancreatitis with infected necrosis

Rau B et al, Gut 1997, 41: 832-40





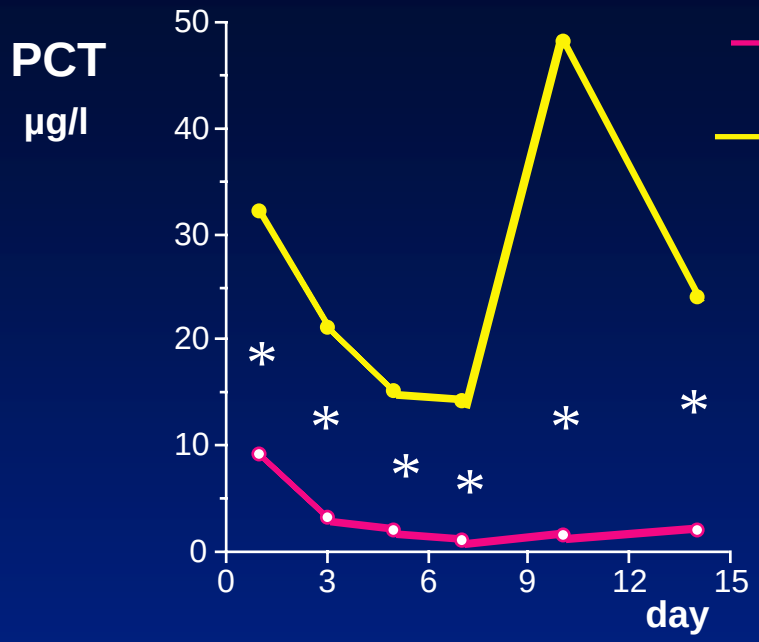
PCT vs CRP and IL6

Procalcitonin in early detection of post operative complications

Reith B,
Digestive Surgery , 1998

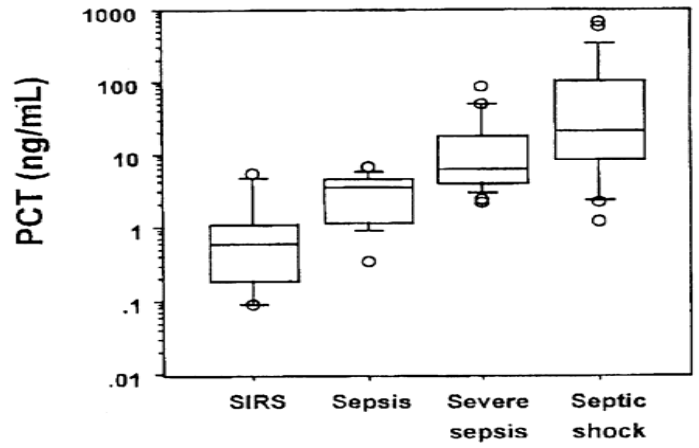
Colorectal surgery

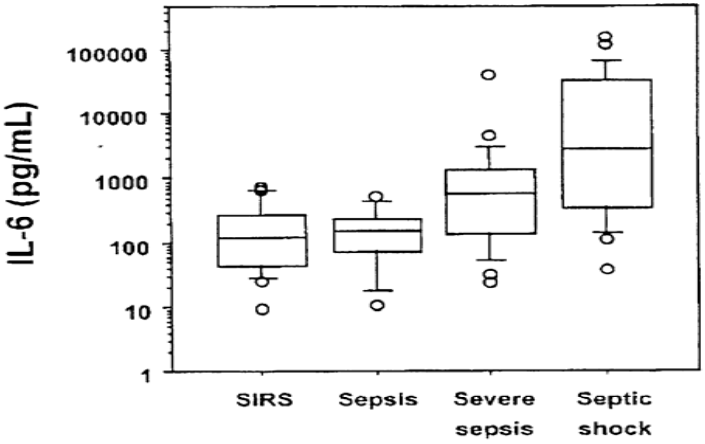
Aortal surgery

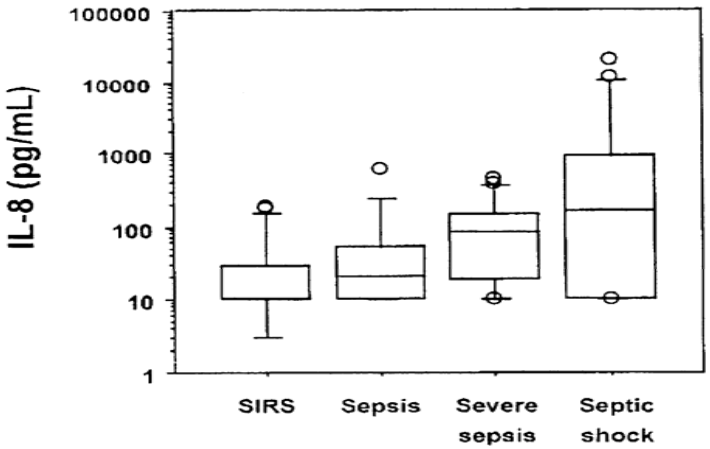


La procalcitonine est un marqueur de sévérité dans le choc septique

Schröder et al
Langenbeck's arch surg 1999; 384 33-8







Genève (J Pugin) :

78 patients consécutifs en réa

Habarth et al, Am J RespCrit Care Med 2001

La PCT est supérieure au TNF, à l'IL6, l'IL8 et aux autres examens biologiques comme marqueur diagnostique et de sévérité des infections bactériennes

Low Serum Procalcitonin Level Accurately Predicts the Absence of Bacteremia in Adult Patients with Acute Fever

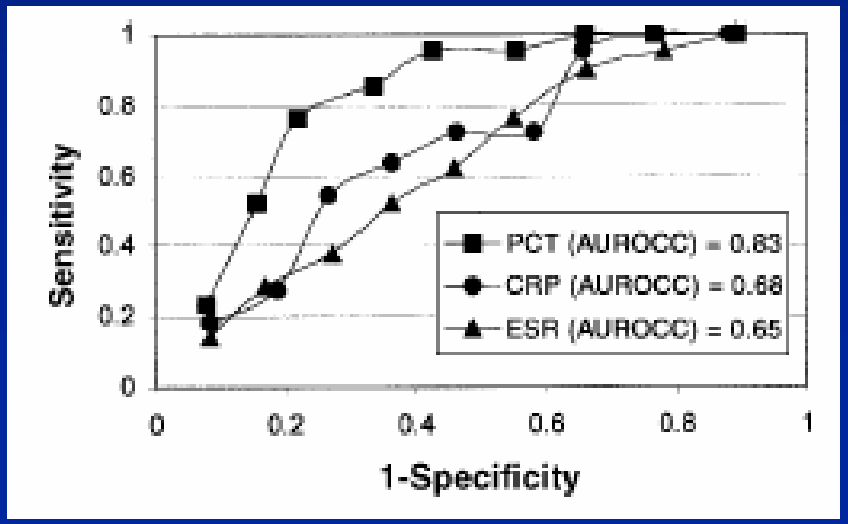
Catherine Chirouze,[1] Hélène Schuhmacher,[2] Christian Rabaud,[3] Helder Gil,[2] Norbert Khayat,[1] Jean-Marie Estavoyer,[1] Thierry May,[2] and Bruno Hoen[1]

[1]Services de Maladies Infectieuses et Tropicales and [2]Service de Médecine Interne, University Hospital of Besançon, Besançon, and [3]University Hospital of Nancy, Nancy, France

Parameter	Bacteremic episode group	Nonbacteremic episode group	*P*
Serum procalcitonin level,[a] ng/mL			
Mean ± SD	32.9 ± 82.9	2.6 ± 10.2	<.001
Range	0.2–353	0.05–87	
C-reactive protein level,[b] mg/L			
Mean ± SD	217 ± 136	141 ± 114	.007
Range	74–560	5–542	
Erythrocyte sedimentation rate,[c] mm/h			
Mean ± SD	59 ± 40	40.17 ± 30	.024
Range	13–151	1–119	

Table 3. Sensitivity, specificity, and positive and negative predictive values of serum procalcitonin (PCT) assessment for the 9 cutoff values that separate the 10 deciles of PCT distribution.

PCT cutoff value, ng/mL	No. of cases under the cutoff value	Sensitivity, %	Specificity, %	Positive predictive value, %	Negative predictive value, %
0.07	15	100	10.6	14.3	100
0.12	33	100	23.4	16.3	100
0.18	48	100	34.0	18.4	100
0.30	64	95.2	44.7	20.4	98.4
0.40	82	95.2	57.4	25.0	98.8
0.55	97	85.7	66.7	27.7	96.9
0.90	115	76.2	78.0	34.0	95.7
2.00	129	52.4	84.4	33.3	92.2
6.20	146	23.8	92.2	31.3	89.0



Chirouze et al, CID 2002

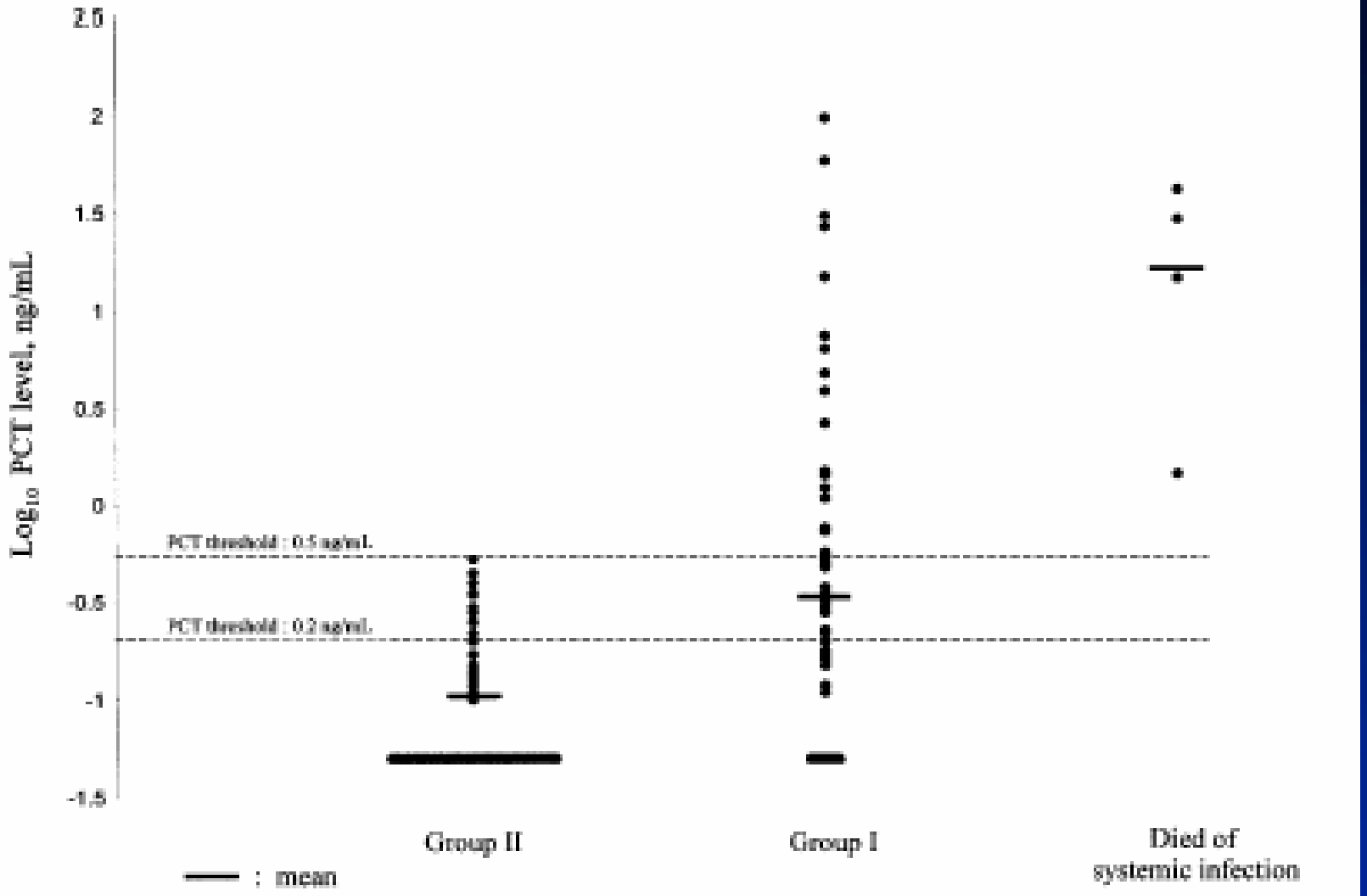
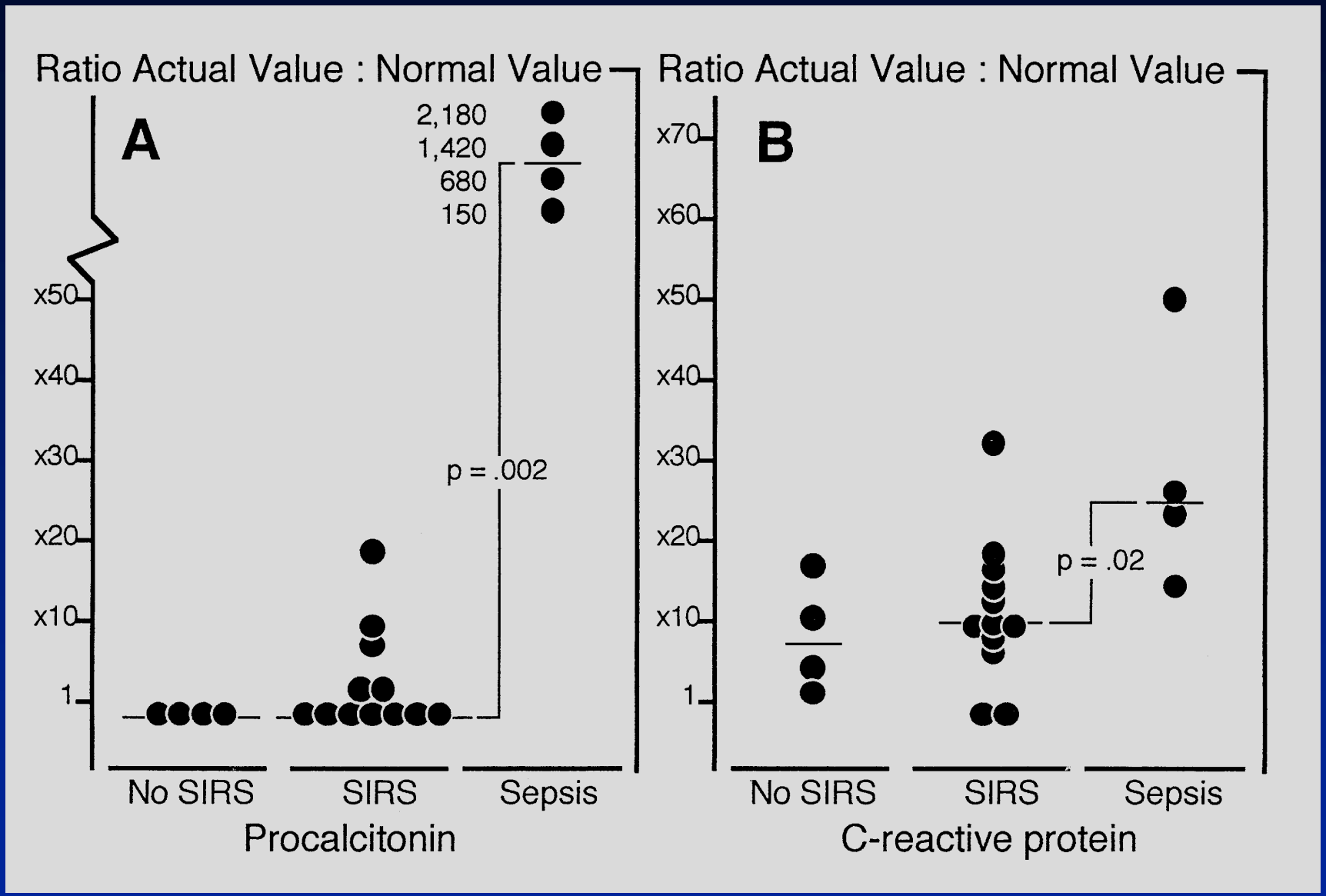


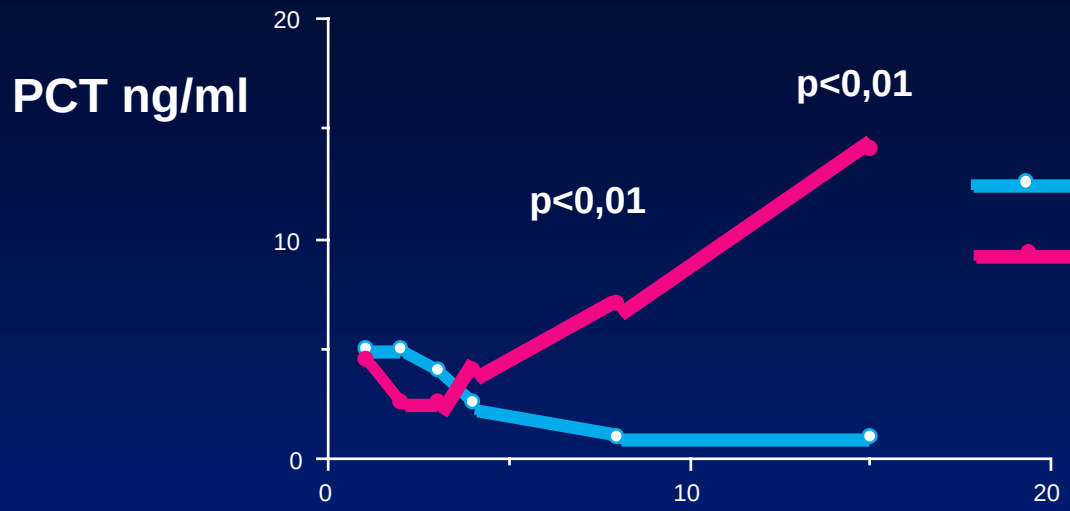
Figure 1. Procalcitonin (PCT) levels for 3 groups of patients. Group I comprised patients with systemic infection; group II comprised patients with systemic infection.

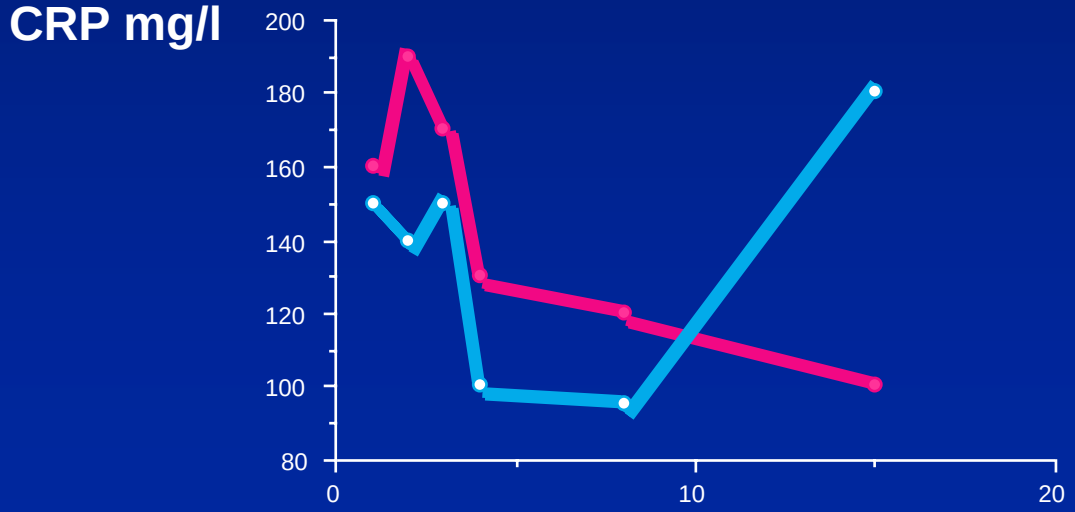
Hausfater et al, CID 2002



Infection after trauma

Mimoz, Intensive Care Med, 1997

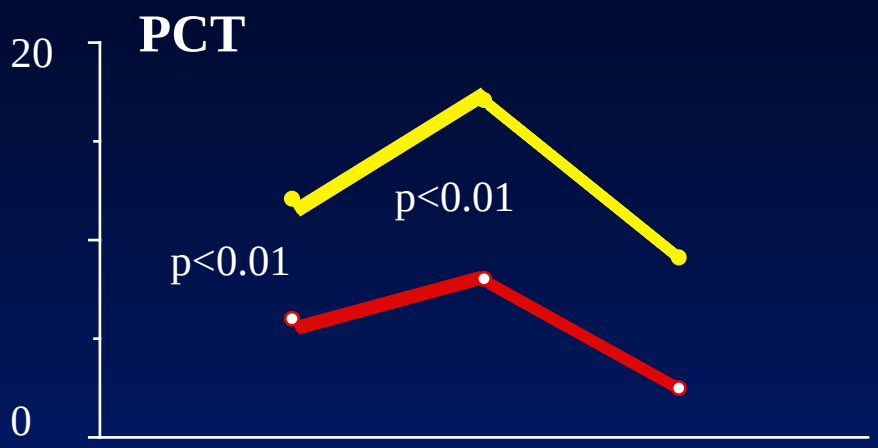




40 patients avec sepsis ou défaillance multiorganique

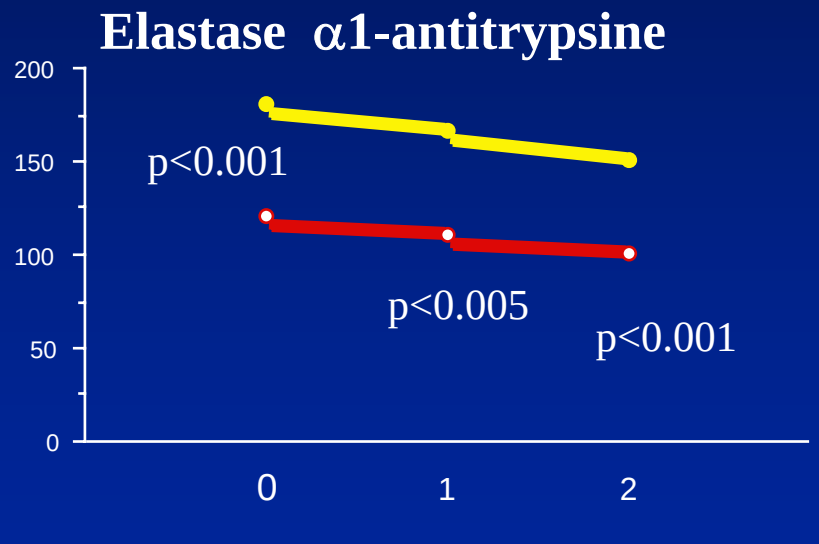
Variations de PCT corrélées
- aux differents SOFA scores
- à l'évolution fatale

Meisner , Critical Care 1999



infection prouvée

infection non prouvée



300 patients adultes fébriles en médecine

Bossink, CID 1999

INFECTION CHEZ LES NEUTROPENIQUES FEBRILES

H Giamarellou, Athènes : 1999-2000

1) **PCT permet de détecter :**

   - **infections sévères (élevée)**
   - **infections localisées (intermédiaire)**

2) **PCT baisse sous traitement AB efficace**
   PCT monte sous traitement AB inefficace

3) **Fièvres d ’origine inconnue répondant aux antibiotiques :**

   - **PCT élevée**

EJ Giamarellosis, CID 2001

INFECTION CHEZ LES NEUTROPENIQUES FEBRILES

Infection	Neutropènie	Fièvre 1er Jour	p
PCT	0,24 (0,16-0,42)	0,52 (0,23-31,6)	0,01
CRP	15 (4-172)	92 (19-430)	0,001
IL6	30 (5-260)	230 (38-4146)	0,001

Fièvre Orig inconn	Neutropènie	Fièvre 1er Jour	
PCT	0,21 (0,11-0,36)	0,23 (0,13-0,46)	NS
CRP	25 (4-106)	44 (30-121)	0,001
IL6	27 (5-82)	83 (44-320)	0,001

Bernard, CID 1998

Episodes fébriles chez des enfants sous chimiothérapie pour tumeur solide ou leucèmie

PCT avec un seuil de 0,5 mg/l

→ **sensibilité et spécificité pour prouver une infection bactérienne supérieures à :**

CRP, IL6, IL8, récepteurs solubles sIL-2R et sTNF II

En particulier pour

- **infections bactériennes *vs* fièvre d ’origine inconnue**
- **épisodes sévères *vs* infections localisées**
- **infections à gram négatifs**

FleischhacK, Brit J Haematol 2000

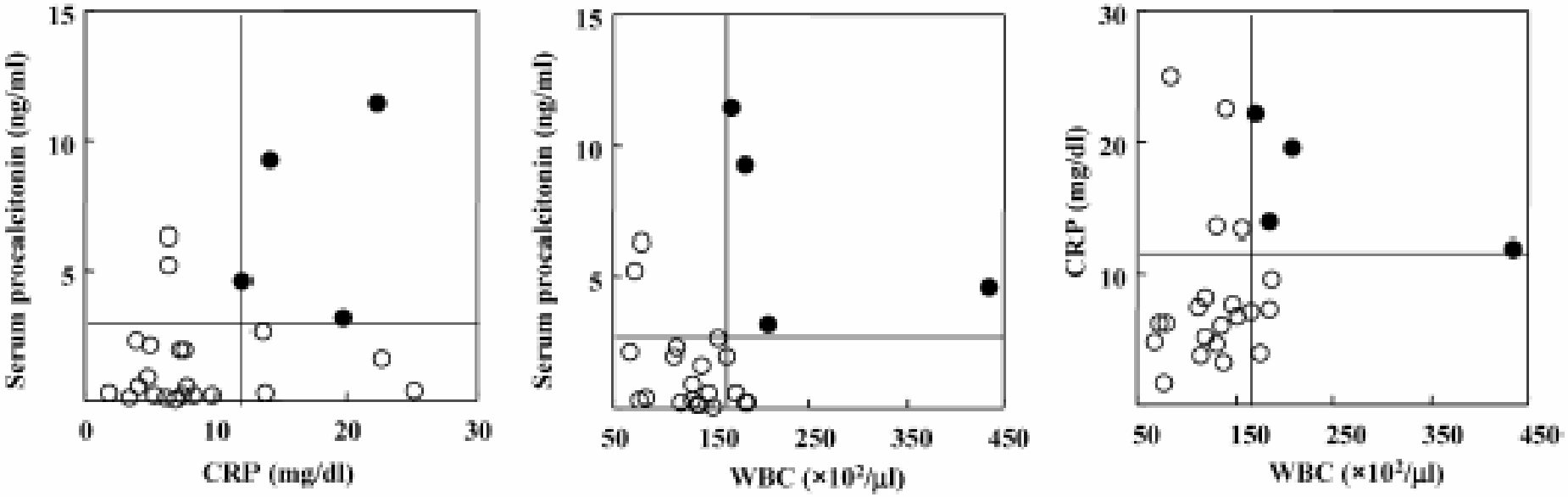
PCT CHEZ LES MALADES TRANSPLANTES

1) Hammer 1998 : coeur et coeur-poumon

- **Augmentation de la PCT (seuil 0.5 et 0.8) en cas d'infection bactérienne, fungique ou à protozoaires**
- **Reste basse en cas de rejet et d'absence de rejet**

2) Caresone 1999 : coeur, rein.

- **Elevation transitoire de PCT après transplantation cardiaque**
- **Augmentation importante dans les infections systémiques**
- **Pas d'augmentation au cours du rejet ou des infections systémiques**



Okada et al , J of Infection , 2004

Saint Vincent de Paul, 1998-2004

22 Kawasaki, 6/22 PCT > 3 ng/ml

3 avec anevrysmes : 2/3 PCT > 3 ng/ml

1/3 PCT = 0.5 ng/ml

Serum Procalcitonin and C-Reactive Protein Levels as Markers of Bacterial Infection: A Systematic Review and Meta-analysis

Liliana Simon,[1] France Gauvin,[2] Devendra K. Amre,[2] Patrick Saint-Louis,[3] and Jacques Lacroix[2]

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19%–96%]). The Q value was higher for PCT markers (0.89 vs. 0.83). PCT markers also had a higher positive likelihood ratio and lower negative likelihood ratio than did CRP markers in both groups. On the basis of this analysis, the diagnostic accuracy of PCT markers was higher than that of CRP markers among patients hospitalized for suspected bacterial infections.

CID 2004

Procalcitonin as an early marker of infection in neonates and children

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

A child or neonate presenting with fever is a common medical problem. To differentiate between those with a severe bacterial infection and those with a localised bacterial or a viral infection can be a challenge. This review provides an overview of neonatal and paediatric studies that assess the use of procalcitonin as an early marker of bacterial infection. Procalcitonin is an excellent marker for severe, invasive bacterial infection in children. However, the use of procalcitonin in the diagnosis of neonatal bacterial infection is complicated, but if correctly used procalcitonin results in a higher specificity than C-reactive protein. In addition, procalcitonin has been shown to correlate with severity of disease (urinary tract infections and sepsis), and can therefore be used as a prognostic marker. Procalcitonin is therefore a useful additional tool for the diagnosis of bacterial disease in neonates and children.

Figure 1. Infant with meningococcal purpura (courtesy of J A Hazelzet, Erasmus Medical Center, Sophia Children's Hospital, Rotterdam, Netherlands).

Lancet Infect Dis 2004; 4: 620–30

En pédiatrie, la procalcitonine est un marqueur majeur d'infection bactérienne

MARQUEURS DE L ’INFECTION

Le plus important est de les utiliser pour les interpréter

- **CRP très répandue :**
  - **limites bien connues**
  - **s ’en servir comme élément de comparaison**
- **PCT et IL_6 récentes**
- **PCT semble supérieure pour le diagnostic et le pronostic**
  - **est plus facile à mesurer (mais le coût ?)**

MARQUEURS DE L ’INFECTION

- **Juger de l’efficacité d’un antibiotique : baisse de la PCT**

- **Instituer un traitement antibiotique :**

  - **la clinique prime**
  - **chez l’adulte, nécessité de marqueurs pronostiques plus que diagnostiques**

- **Arrèter un traitement antibiotique inutile : la PCT est supérieure aux autres marqueurs**

MARQUEURS DE L ’INFECTION

UN MARQUEUR BIOLOGIQUE N ’EST

QU ’UNE AIDE A LA CLINIQUE