Neumonia Viral Asociada a la Ventilación Artificial

Antoni Torres. Hospital Clinic.Barcelona
Conferència D Experts de la SOCMIC 2015

Severe VIRAL CAP is frequent specially in mixed pneumonias

	S.pneumo	Atypical	Legionella	Virus	Mixed
Outpatients 162/514	35	30	6	9	9
Ward 1050/2521	43	8	8	11	13
ICU 262/488	42	6	8	3	22

Mixed: Bacteria+ virus: 29% out of 208 mixed; atypical + virus: 6%

Cillóniz C et al. Thorax 2012

VAP :WHERE WERE THE VIRUSES in 2002

State of the Art

Ventilator-associat

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 165 2002

Jean Chastre and Jean-Yves Fagon

Service de Réanimation Médicale, Groupe Hospitalier Pitié-Salpêtrière; and Service de Réanimation Médicale, Hôpital Européen Georges-Pompidou, Paris, France

TABLE 5. ETIOLOGY OF VENTILATOR-ASSOCIATED PNEUMONIA AS DOCUMENTED BY BRONCHOSCOPIC TECHNIQUES IN 24 STUDIES FOR A TOTAL OF 1,689 EPISODES AND 2,490 PATHOGENS

Pathogen	Frequency (%)
Pseudomonas aeruginosa	24.4
Acinetobacter spp.	7.9
Stenotrophomonas maltophilia	1.7
Enterobacteriaceae*	14.1
Haemophilus spp.	9.8
Staphylococcus aureus†	20.4
Streptococcus spp.	8.0
Streptococcus pneumoniae	4.1
Coagulase-negative staphylococci	1.4
Neisseria spp.	2.6
Anaerobes	0.9
Fungi	0.9
Others (< 1% each)‡	3.8

* Distribution when specified: *Klebsiella* spp., 15.6%; *Escherichia coli*, 24.1%; *Proteus* spp., 22.3%; *Enterobacter* spp., 18.8%; *Serratia* spp., 12.1%; *Citrobacter* spp., 5.0%; *Hafnia alvei*, 2.1%.

† Distribution when specified: methicillin-resistant *S. aureus*, 55.7%; methicillin-sensitive *S. aureus*, 44.3%.

‡ Including *Corynebacterium* spp., *Moraxella* spp., and *Enterococcus* spp.

The role of viruses in nosocomial pneumonia

Laurent Chiche, Jean-Marie Forel and Laurent Papazian

Table 1 Viruses identified in ICU patients

Virus	Endogenous	Exogenous
Community	HSV, CMV	Influenza, parainfluenza, adenovirus, rhinovirus, RSV, coronavirus, metapneumovirus
Nosocomial	HSV, CMV	Mimivirus, CMV (transfusion), H1N1 pandemic influenza?

CMV, cytomegalovirus; HSV, herpes simplex virus; RSV, respiratory syncytial virus.

Current Opinion in Infectious Diseases 2011, 24:152–156

Virus implicados en la NAV

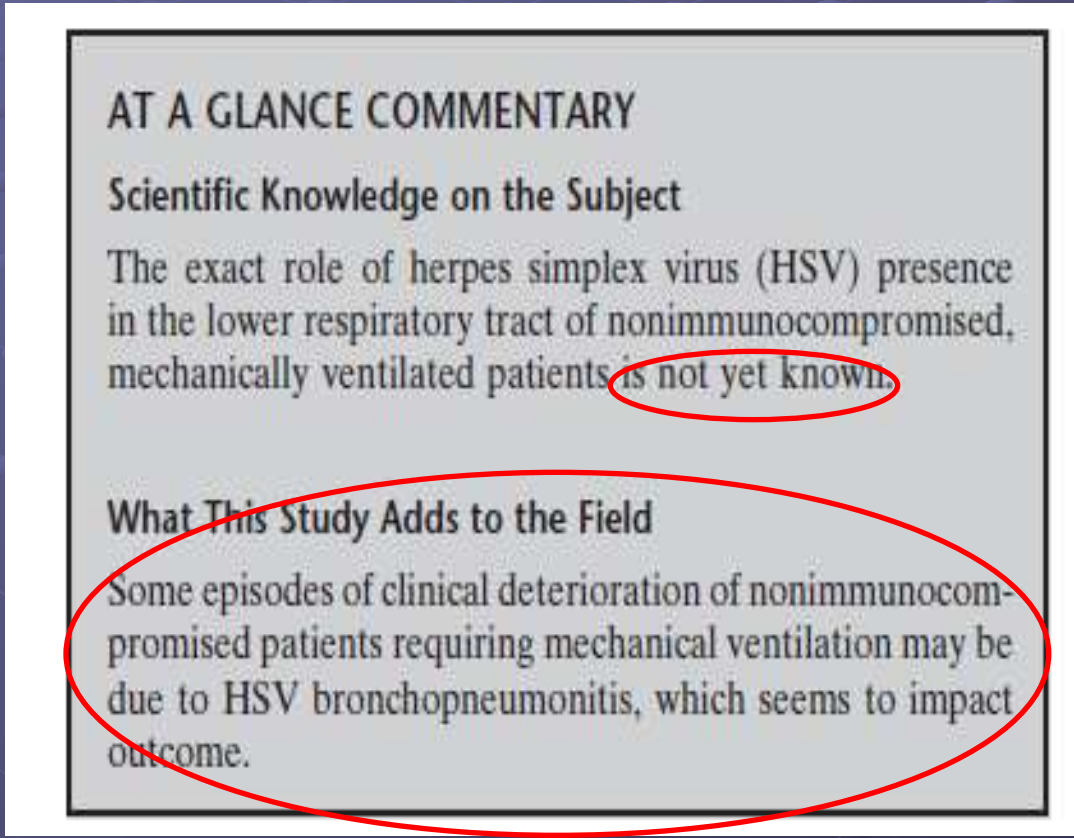
- Herpes-virus
- Citomegalovirus
- Otros:mimivirus

Herpes Simplex Virus Lung Infection in Patients Undergoing Prolonged Mechanical Ventilation

Charles-Edouard Luyt[1], Alain Combes[1], Claire Deback[2], Marie-Hélène Aubriot-Lorton[3], Ania Nieszkowska[1], Jean-Louis Trouillet[1], Frédérique Capron[3], Henri Agut[2], Claude Gibert[1], and Jean Chastre[1]

[1]Service de Réanimation Médicale, [2]Service de Virologie, and [3]Service d'Anatomo-Pathologie, Groupe Hospitalier Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, Université Pierre et Marie Curie, Paris, France

Am J Respir Crit Care Med Vol 175. pp 935–942, 2007



AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

The exact role of herpes simplex virus (HSV) presence in the lower respiratory tract of nonimmunocompromised, mechanically ventilated patients is not yet known.

What This Study Adds to the Field

Some episodes of clinical deterioration of nonimmunocompromised patients requiring mechanical ventilation may be due to HSV bronchopneumonitis, which seems to impact outcome.

Patient Profile

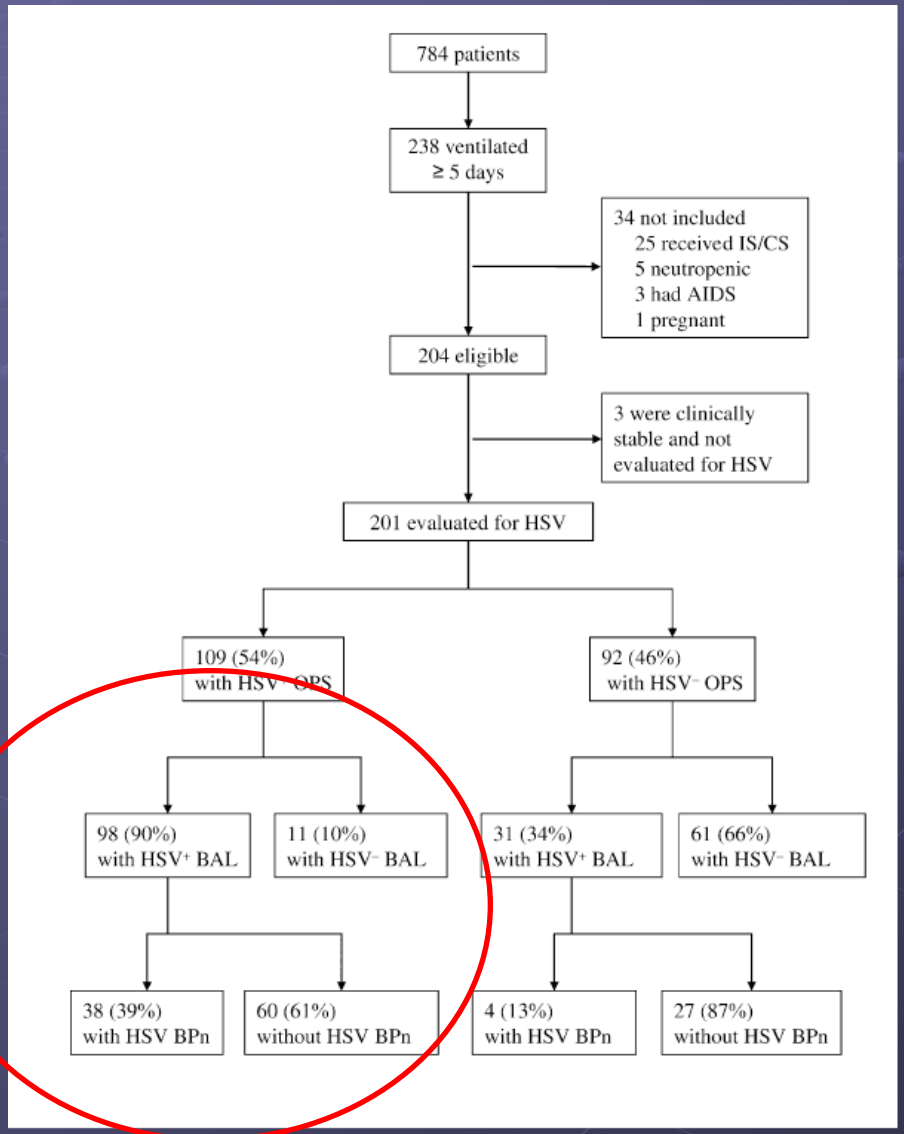


TABLE 1. CHARACTERISTICS OF STUDY POPULATION AT INTENSIVE CARE UNIT ADMISSION AND BASELINE

Parameter	Overall Population ($n = 201$)	HSV Bronchopneumonitis		p Value
		Yes ($n = 42$)	No ($n = 159$)	
Admission				
Age, yr, mean ± SD	59.9 ± 16.1	62.9 ± 13.2	59.2 ± 16.8	0.18
Male sex, no. (%)	136 (68)	30 (71)	106 (67)	0.55
McCabe and Jackson comorbidity score, n (%)				0.45
0	15 (7)	1 (2)	14 (9)	
1	135 (67)	31 (74)	104 (65)	
⩾ 2	51 (25)	10 (23)	41 (26)	
SAPS II, mean ± SD	53.5 ± 14.7	52.9 ± 14.6	53.7 ± 14.8	0.68
Admission category, n (%)				0.03
Medical	87 (43)	11 (26)	76 (48)	
Elective surgery	57 (28)	17 (40)	40 (25)	
Emergency surgery	57 (28)	14 (33)	43 (27)	
Postcardiac surgery, n (%)	105 (52)	29 (69)	76 (48)	0.02
Reason for mechanical ventilation, n (%)				0.18
Acute respiratory failure	55 (27)	7 (17)	48 (31)	
Postoperative respiratory failure	114 (57)	30 (71)	84 (53)	
Neurologic failure	14 (7)	1 (2)	13 (8)	
Acute exacerbation of COPD	1 (0.5)	0	1 (0.6)	
Cardiac arrest	17 (8)	4 (10)	13 (8)	
History of, n (%)				
Tobacco use	66 (33)	12 (29)	54 (34)	0.51
COPD	25 (12)	7 (17)	18 (11)	0.35
Asthma	5 (2)	1 (2)	4 (3)	0.96
Diabetes	41 (20)	8 (19)	33 (21)	0.81
Chronic corticosteroid use*	17 (8)	7 (17)	10 (6)	0.09
Acute corticosteroid use	33 (16)	6 (14)	27 (17)	0.67
Alcohol use	16 (8)	4 (10)	12 (8)	0.92
Cirrhosis	3 (1)	0	3 (2)	0.85
Baseline (Day 5 of MV)				
SAPS II, mean ± SD	47.3 ± 15.6	46.4 ± 14.6	47.5 ± 15.8	0.83
ODIN score, mean ± SD	2.6 ± 1.2	2.5 ± 1.1	2.6 ± 1.3	0.75
SOFA score, mean ± SD	10.0 ± 4.9	10.0 ± 4.7	10.0 ± 4.9	0.87
Organ/system failure,† n (%)				
Respiratory	104 (52)	25 (60)	79 (50)	0.27
Cardiovascular	102 (51)	21 (50)	81 (51)	0.91
Renal	78 (39)	21 (50)	57 (36)	0.09
Central nervous	31 (15)	4 (10)	27 (17)	0.23
Hepatic	35 (17)	7 (17)	28 (18)	0.89
Coagulation	27 (13)	4 (10)	23 (14)	0.41
Temperature, °C, mean ± SD	37.8 ± 1.2	37.7 ± 1.2	37.8 ± 1.2	0.43
WBC count, $\times 10^9$/L, mean ± SD	15.2 ± 10.0	15.1 ± 8.7	15.2 ± 10.4	0.81
Neutrophil count	12.9 ± 8.3	13.2 ± 8.3	12.8 ± 8.3	0.72
Lymphocyte count	1.0 ± 0.7	0.9 ± 0.6	1.0 ± 0.8	0.87
Pa_{O_2}/FI_{O_2} ratio, mean ± SD	199 ± 83	186 ± 85	204 ± 82	0.11
Radiologic score, mean ± SD	6.5 ± 3.4	7.3 ± 3.4	6.3 ± 3.3	0.08
HSV-positive serology, n (%)	182 (91)	42 (100)	140 (88)	0.02

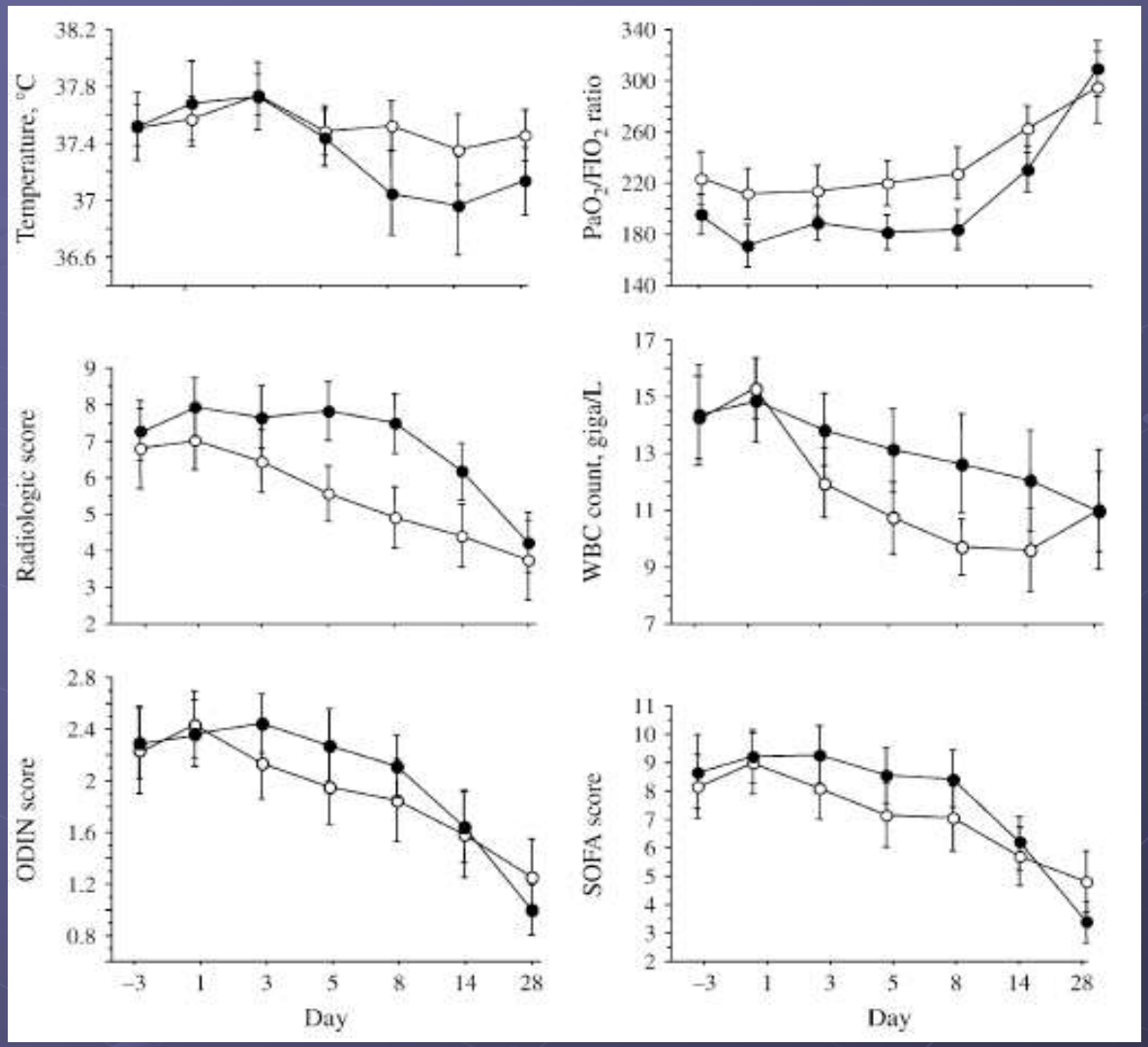
Definition of abbreviations: COPD = chronic obstructive pulmonary disease; HSV = herpes simplex virus; MV = mechanical ventilation; ODIN = Organ Dysfunction(s) and/or Infection; SAPS = Simplified Acute Physiology Score; SOFA = Sepsis-related Organ Failure Assessment; WBC = white blood cells.

* Defined as prednisone or its equivalent at less than 0.5 mg/kg per day for more than 1 month.

† Organ/system failure was deemed present when the corresponding SOFA score was greater than 2.

Differences HSV yes/no bronchopneumonitis

- Type of admission: More medical
- More post-cardiac surgery
- HSV positive serology



Ta

Rx score

ODIN

Kinetics of clinical parameters 3 days after and follow-up
Closed circles: HSV; open circles: HSV + bacterial VAP

Risk factors for HSV Pneumonitis

TABLE 2. RISK FACTORS FOR HERPES SIMPLEX VIRUS BRONCHOPNEUMONITIS

Parameter	HSV Bronchopneumonitis: Yes (*n* = 42)	HSV Bronchopneumonitis: No (*n* = 159)	p Value
ARDS, n (%)	23 (55)	62 (39)	0.06
Oral–labial lesions, n (%)	23 (55)	25 (16)	< 0.0001
Labial vesicles	10 (43)	19 (76)	< 0.0001
Gingivostomatitis	13 (57)	6 (24)	< 0.0001
HSV in throat, n (%)	38 (90)	71 (45)	< 0.0001
HSV in lower respiratory tract, n (%)			
PCR positive	42 (100)	87 (55)	< 0.0001
Culture positive	37 (88)	32 (20)	< 0.0001
Macroscopic bronchial lesions, n (%)	32 (76)	77 (48)	0.001
HSV-specific inclusions on biopsies	12 (38)	0	< 0.0001

Definition of abbreviations: ARDS = acute respiratory distress syndrome; HSV = herpes simplex virus; PCR = polymerase chain reaction.

TABLE 3. UNIVARIABLE AND MULTIVARIABLE LOGISTIC REGRESSION ANALYSES: FACTORS ASSOCIATED WITH HERPES SIMPLEX VIRUS BRONCHOPNEUMONITIS

Factor	Univariable Analysis: OR (95% CI)	Univariable Analysis: p Value	Multivariable Analysis: OR (95% CI)	Multivariable Analysis: p Value
Age, per year	1.01 (0.99–1.04)	0.19		
Male sex	1.25 (0.59–2.64)	0.56		
McCabe and Jackson score ≥ 2	1.11 (0.50–2.46)	0.78		
Reason for MV				
Medical	1			
Elective surgery	2.25 (0.94–5.39)	0.06		
Emergency surgery	2.94 (1.26–6.87)	0.01		
SAPS II at admission	0.99 (0.97–1.02)	0.77		
Postcardiac surgery	2.44 (1.18–5.03)	0.01		
Acute corticosteroid use	0.81 (0.31–2.12)	0.68		
Chronic corticosteroid use*	2.48 (0.85–7.29)	0.09		
ARDS	1.89 (0.95–3.76)	0.07		
Oral–labial lesions	6.48 (3.09–13.64)	< 0.0001	2.57 (1.11–5.94)	0.03
HSV in throat	11.78 (4.01–34.56)	< 0.0001	8.46 (2.68–26.69)	0.0003
Endoscopic bronchial lesions	3.41 (1.57–7.41)	0.002	3.03 (1.29–7.14)	0.01
Baseline radiologic score	1.09 (0.99–1.22)	0.07		
Baseline Pa_{O_2}/Fi_{O_2} ratio	1.0 (0.99–1.01)	0.22		

Definition of abbreviations: ARDS = acute respiratory distress syndrome; CI = confidence interval; HSV = herpes simplex virus; MV = mechanical ventilation; OR = odds ratio.

* Defined as prednisone or its equivalent at less than 0.5 mg/kg per day for more than 1 month.

Outcomes of the Patients: Overall population and case-control study

TABLE 4. OUTCOMES OF PATIENTS DURING THE STUDY

Parameter	HSV Bronchopneumonitis: Yes (*n* = 42)	HSV Bronchopneumonitis: No (*n* = 159)	p Value
Total duration of MV, d	36.7 ± 27.5	30.0 ± 27.1	0.03
VAP episodes/patient, n	1.5 ± 1.0	1.1 ± 1.1	0.03
ICU length of stay, d	40.1 ± 27.8	32.1 ± 28.1	0.01
In-hospital mortality, n (%)	20 (48)	66 (42)	0.5

Definition of abbreviations: ICU = intensive care unit; VAP = ventilator-associated pneumonia.

Plus/minus values represent means ± SD.

TABLE 5. CHARACTERISTICS AND OUTCOMES OF THE POPULATION INCLUDED IN THE CASE-CONTROL STUDY

Parameter	HSV Bronchopneumonitis: Yes (*n* = 42)	HSV Bronchopneumonitis: No (*n* = 42)
Age, yr, mean ± SD	62.9 ± 13.2	62.2 ± 12.9
Male sex, n (%)	30 (71)	29 (69)
SAPS II score, mean ± SD	52.9 ± 14.6	55.4 ± 13.6
McCabe and Jackson comorbidity score ≥ 2, n (%)	10 (24)	10 (24)
Reason for MV, n (%)		
Acute respiratory failure	7 (17)	9 (22)
Postoperative respiratory failure	30 (71)	30 (71)
Neurologic failure	1 (2)	2 (5)
Cardiac arrest	4 (10)	1 (2)
Postcardiac surgery, n (%)	29 (69)	29 (69)
History of, n (%)		
Tobacco use	12 (29)	15 (35)
COPD	7 (17)	4 (10)
Asthma	1 (2)	1 (2)
Diabetes	8 (19)	8 (19)
Chronic corticosteroid use*	6 (14)	6 (14)
Acute corticosteroid use	6 (14)	7 (17)
Alcohol abuse	4 (10)	2 (5)
Cirrhosis	0	1 (2)
Total number of days of MV, mean ± SD†	36.7 ± 27.5	21.8 ± 11.8
Length of ICU stay, d, mean ± SD†	40.1 ± 27.8	24.1 ± 12.5
No. of bacterial VAP episodes, mean ± SD	1.5 ± 1.0	1.1 ± 0.8
In-hospital mortality, n (%)	20 (48)	15 (36)

HSV Type 1 Detection is Associated with poor prognosis in Critically ill patients

Journal of Medical Virology 72:121–125 (2004)

Herpes Simplex Type 1 Shedding Is Associated With Reduced Hospital Survival in Patients Receiving Assisted Ventilation in a Tertiary Referral Intensive Care Unit

G.M. Ong,[1] K. Lowry,[2] S. Mahajan,[2] D.E. Wyatt,[1] C. Simpson,[3] H.J. O'Neill,[1] C. McCaughey,[1] and P.V. Coyle[1]*

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Intensive Care Med (2008) 34:2202–2209
DOI 10.1007/s00134-008-1231-4

ORIGINAL

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Herpes simplex virus load in bronchoalveolar lavage fluid is related to poor outcome in critically ill patients

Herpes virus bronchopneumonitis is a late-onset VAP

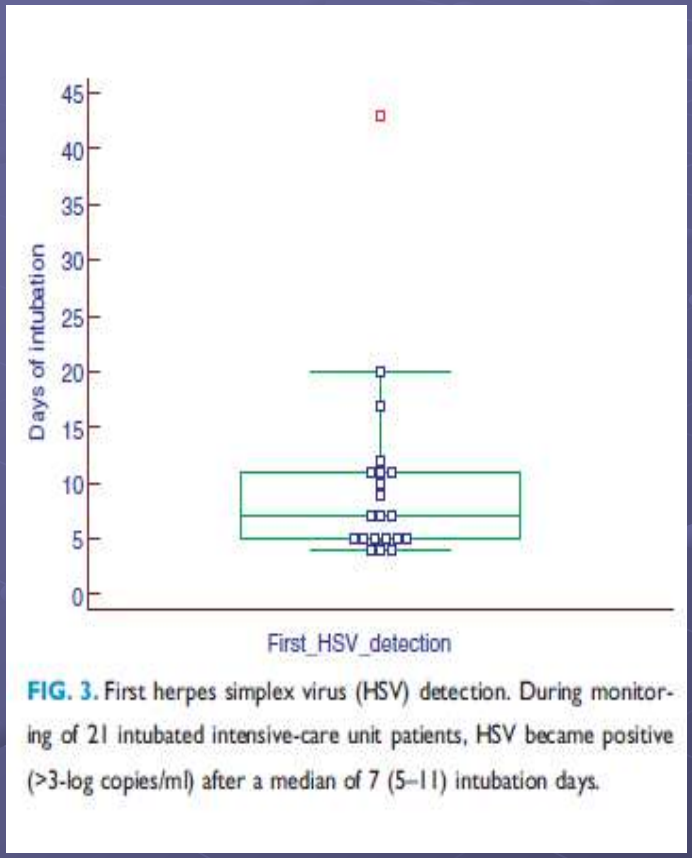

FIG. 3. First herpes simplex virus (HSV) detection. During monitoring of 21 intubated intensive-care unit patients, HSV became positive (>3-log copies/ml) after a median of 7 (5–11) intubation days.

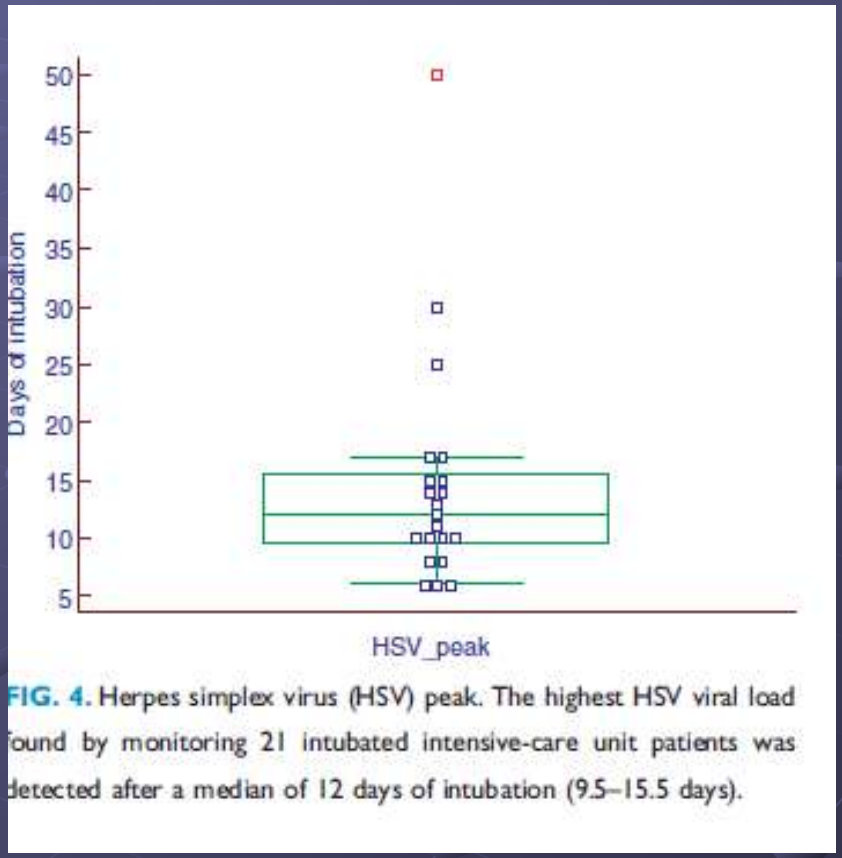

FIG. 4. Herpes simplex virus (HSV) peak. The highest HSV viral load found by monitoring 21 intubated intensive-care unit patients was detected after a median of 12 days of intubation (9.5–15.5 days).

ORIGINAL ARTICLE 10.1111/j.1469-0691.2009.02704.x

Monitoring of herpes simplex virus in the lower respiratory tract of critically ill patients using real-time PCR: a prospective study

N. De Vos[1,*], L. Van Hoovels[1,*], A. Vankeerberghen[1], K. Van Vaerenbergh[1], A. Boel[1], I. Demeyer[2], L. Creemers[1] and H. De Beenhouwer[1]

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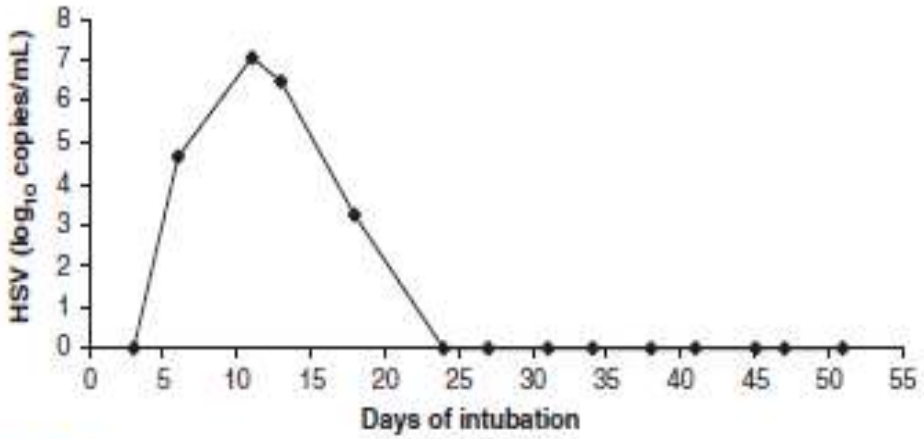


FIG. 2. Typical herpes simplex virus (HSV) kinetic pattern. Monitoring of HSV in the lower respiratory tract of a critically ill patient shows an exponential HSV increase of 1 log copies/mL per day and a high HSV peak of 10^7 copies/mL.

Virus implicados en la NAV

- Herpes-virus
- Citomegalovirus
- Otros:mimivirus

Continuing Medical Education Article

Prevalence and mortality associated with cytomegalovirus infection in nonimmunosuppressed patients in the intensive care unit*

Andre C. Kalil, MD; Diana F. Florescu, MD

Crit Care Med 2009 Vol. 37, No. 8

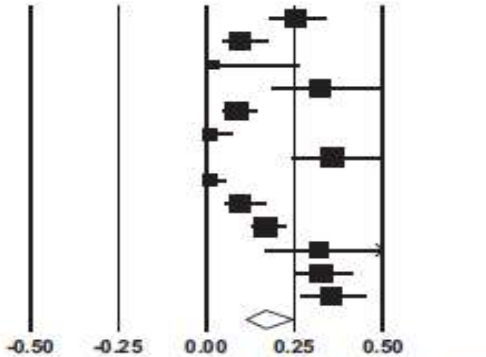
Table 1. The 13 studies selected for analysis

Study	Sample Size	Seropositive for CMV	Male/Female	Study Design	Only Surgical Patients	Only Mechanically Ventilated	Only Severe Sepsis	Only Septic Shock
Domart et al (6)	115	22	97/18	Prospective	Yes	No	No	No
Papazian et al (7)	86	NA	NA	Retrospective	No	Yes	No	No
Stephan et al (8)	23	23	14/9	Prospective	No	Yes	No	No
Kutza et al (9)	34	31	27/7	Prospective	Yes	No	Yes	No
Cook et al (10)	142	NA	NA	Retrospective	Yes	No	No	No
Desachy et al (11)	96	NA	66/30	Prospective	No	No	No	No
Heininger et al (12)	56	56	35/21	Prospective	Yes	Yes	No	No
Razonable et al (13)	120	NA	72/48	Prospective	No	No	No	No
Cook et al (14)	104	76	62/42	Prospective	Yes	No	No	No
Jaber et al (15)	237	NA	55/25	Retrospective	No	Yes	No	No
von Muller et al (16)	25	25	15/10	Prospective	Yes	No	Yes	Yes
Limaye et al (17)	120	120	73/47	Prospective	No	No	No	No
Ziemann et al (18)	99	41	67/33	Retrospective	Yes	No	No	No

NA, not applicable.

Active CMV* Infection - Overall ICU Rate

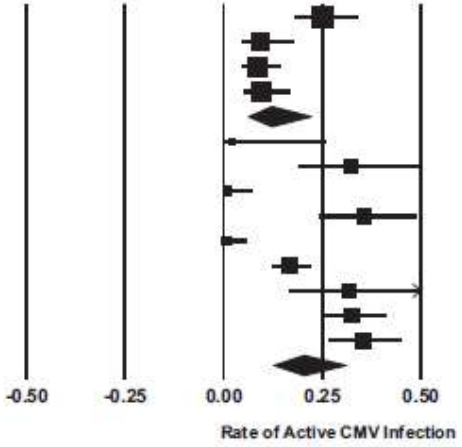
Study name	Event rate	Lower limit	Upper limit	Total
Domart Y 1990	0.25	0.18	0.34	29 / 115
Papazian L 1996	0.09	0.05	0.18	8 / 86
Stephan F 1996	0.02	0.00	0.26	1 / 24
Kutza A 1998	0.32	0.19	0.50	11 / 34
Cook CH 1998	0.08	0.05	0.14	12 / 142
Desachy A 2001	0.01	0.00	0.07	1 / 96
Heininger A 2001	0.36	0.24	0.49	20 / 56
Razonable R 2002	0.01	0.00	0.06	1 / 120
Cook C 2003	0.10	0.05	0.17	10 / 104
Jaber S 2005	0.17	0.13	0.22	40 / 237
von Muller L 2006	0.32	0.17	0.52	8 / 25
Limaye A 2008	0.33	0.25	0.41	39 / 120
Ziemann M 2008	0.35	0.27	0.45	35 / 99
	0.17	0.11	0.24	215 / 1258



*Cytomegalovirus. Z=6.69; P<0.0001; Q=87.07; I2=86%

b Active CMV* Infection Rate by Diagnostic Method

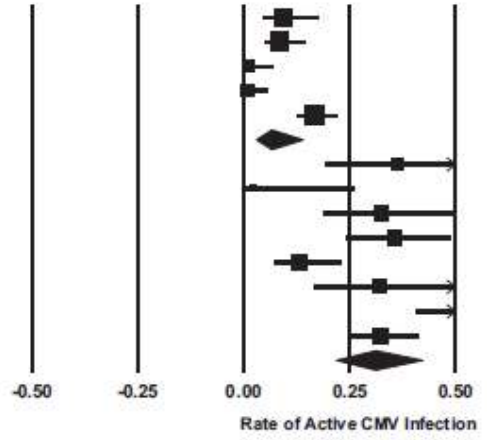
Group by CMV Diagnostic Method	Study name	Event rate	Lower limit	Upper limit	Total
Viral Culture	Domart Y 1990	0.25	0.18	0.34	29 / 115
Viral Culture	Papazian L 1996	0.09	0.05	0.18	8 / 86
Viral Culture	Cook CH 1998	0.08	0.05	0.14	12 / 142
Viral Culture	Cook C 2003	0.10	0.05	0.17	10 / 104
Viral Culture		0.12	0.06	0.22	59 / 447
Viral DNA or Antigen	Stephan F 1996	0.02	0.00	0.26	1 / 24
Viral DNA or Antigen	Kutza A 1998	0.32	0.19	0.50	11 / 34
Viral DNA or Antigen	Desachy A 2001	0.01	0.00	0.07	1 / 96
Viral DNA or Antigen	Heininger A 2001	0.36	0.24	0.49	20 / 56
Viral DNA or Antigen	Razonable R 2002	0.01	0.00	0.06	1 / 120
Viral DNA or Antigen	Jaber S 2005	0.17	0.13	0.22	40 / 237
Viral DNA or Antigen	von Muller L 2006	0.32	0.17	0.52	8 / 25
Viral DNA or Antigen	Limaye A 2008	0.33	0.25	0.41	39 / 120
Viral DNA or Antigen	Ziemann M 2008	0.35	0.27	0.45	35 / 99
Viral DNA or Antigen		0.20	0.13	0.31	156 / 811



*Cytomegalovirus. Z=7.05; P<0.0001; Q=87.07; I2=86%

a Active CMV* Infection Rate by CMV Serology

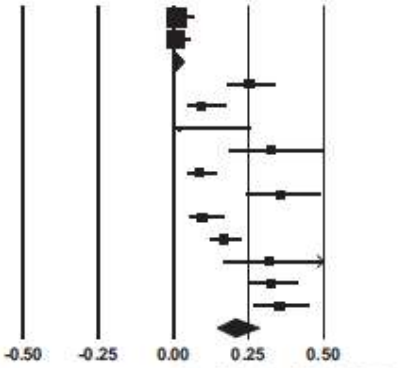
Group by CMV Serology at Baseline	Study name	Event rate	Lower limit	Upper limit	Total
Not Reported	Papazian L 1996	0.09	0.05	0.18	8 / 86
Not Reported	Cook CH 1998	0.08	0.05	0.14	12 / 142
Not Reported	Desachy A 2001	0.01	0.00	0.07	1 / 96
Not Reported	Razonable R 2002	0.01	0.00	0.06	1 / 120
Not Reported	Jaber S 2005	0.17	0.13	0.22	40 / 237
Not Reported		0.07	0.03	0.14	62 / 681
Positive	Domart Y 1990	0.36	0.19	0.58	8 / 22
Positive	Stephan F 1996	0.02	0.00	0.26	1 / 24
Positive	Kutza A 1998	0.32	0.19	0.50	11 / 34
Positive	Heininger A 2001	0.36	0.24	0.49	20 / 56
Positive	Cook C 2003	0.13	0.07	0.23	10 / 76
Positive	von Muller L 2006	0.32	0.17	0.52	8 / 25
Positive	Ziemann M 2008	0.56	0.41	0.70	23 / 41
Positive	Limaye A 2008	0.33	0.25	0.41	39 / 120
Positive		0.31	0.22	0.42	120 / 398



*Cytomegalovirus. Z=5.94; P<0.0001; Q=96.66; I2=87%

b Active CMV* Infection Rate: Screening for > 5 ICU Days

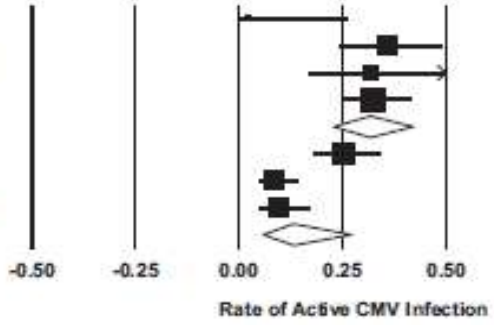
Group by ICU > 5 Days	Study name	Event rate	Lower limit	Upper limit	Total
No	Desachy A 2001	0.01	0.00	0.07	1 / 96
No	Razonable R 2002	0.01	0.00	0.06	1 / 120
No		0.01	0.00	0.04	2 / 216
Yes	Domart Y 1990	0.25	0.18	0.34	29 / 115
Yes	Papazian L 1996	0.09	0.05	0.18	8 / 86
Yes	Stephan F 1996	0.02	0.00	0.26	1 / 24
Yes	Kutza A 1998	0.32	0.19	0.50	11 / 34
Yes	Cook CH 1998	0.08	0.05	0.14	12 / 142
Yes	Heininger A 2001	0.36	0.24	0.49	20 / 56
Yes	Cook C 2003	0.10	0.05	0.17	10 / 104
Yes	Jaber S 2005	0.17	0.13	0.22	40 / 237
Yes	von Muller L 2006	0.32	0.17	0.52	8 / 25
Yes	Limaye A 2008	0.33	0.25	0.41	39 / 120
Yes	Ziemann M 2008	0.35	0.27	0.45	35 / 99
Yes		0.21	0.15	0.29	213 / 1042



*Cytomegalovirus. Z=7.81; P<0.0001; Q=87.06; I2=86%

a Active CMV Infection Rate by Disease Severity

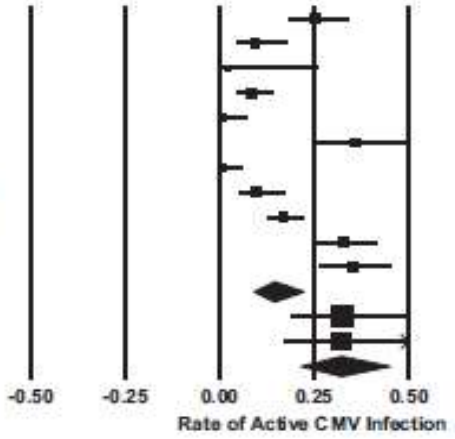
Group by Disease Severity	Study name	Event rate	Lower limit	Upper limit	Total
High	Stephan F 1996	0.02	0.00	0.26	1 / 24
High	Heininger A 2001	0.36	0.24	0.49	20 / 56
High	von Muller L 2006	0.32	0.17	0.52	8 / 25
High	Limaye A 2008	0.33	0.25	0.41	39 / 120
High		0.32	0.23	0.42	68 / 225
Low	Domart Y 1990	0.25	0.18	0.34	29 / 115
Low	Cook CH 1998	0.08	0.05	0.14	12 / 142
Low	Cook C 2003	0.10	0.05	0.17	10 / 104
Low		0.13	0.06	0.27	51 / 361



*High Severity: APACHE II>20, SAPS>40, SOFA>10. Z=-6.26; P<0.0001; Q=11.15; I2=65%

b Active CMV* Infection Rate by Severe Sepsis Status

Group by Severe Sepsis Only	Study name	Event rate	Lower limit	Upper limit	Total
No	Domart Y 1990	0.25	0.18	0.34	29 / 115
No	Papazian L 1996	0.09	0.05	0.18	8 / 86
No	Stephan F 1996	0.02	0.00	0.26	1 / 24
No	Cook CH 1998	0.08	0.05	0.14	12 / 142
No	Desachy A 2001	0.01	0.00	0.07	1 / 96
No	Heininger A 2001	0.36	0.24	0.49	20 / 56
No	Razonable R 2002	0.01	0.00	0.06	1 / 120
No	Cook C 2003	0.10	0.05	0.17	10 / 104
No	Jaber S 2005	0.17	0.13	0.22	40 / 237
No	Limaye A 2008	0.33	0.25	0.41	39 / 120
No	Ziemann M 2008	0.35	0.27	0.45	35 / 99
No		0.15	0.09	0.22	196 / 1199
Yes	Kutza A 1998	0.32	0.19	0.50	11 / 34
Yes	von Muller L 2006	0.32	0.17	0.52	8 / 25
Yes		0.32	0.22	0.45	19 / 59



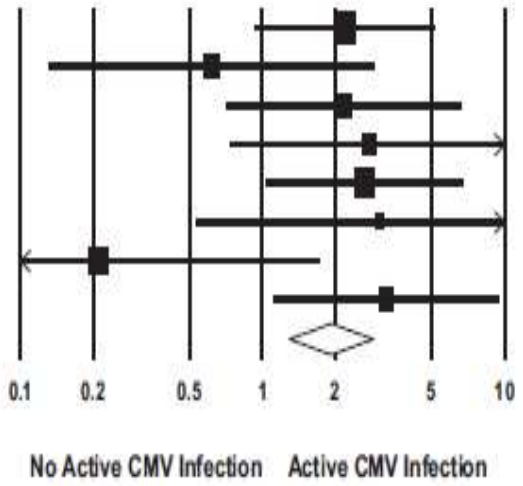
*Cytomegalovirus. Z=6.59; P<0.0001; Q=67.07; I2=86%

Figure 5. Active cytomegalovirus (*CMV*) infection rate by *(a)* disease severity and *(b)* severe sepsis status.

MORTALIDAD CRUDA E INFECCION POR CMV

Active CMV* Infection: All-Cause Mortality

Study name	Statistics for each study				Deaths / Total	
	MH odds ratio	Lower limit	Upper limit	p-Value	Active CMV Infection	No Active CMV Infection
Domart Y 1990	2.18	0.93	5.13	0.073	16 / 29	31 / 86
Kutza A 1998	0.62	0.13	2.88	0.540	7 / 11	17 / 23
Heininger A 2001	2.16	0.71	6.58	0.174	11 / 20	13 / 36
Cook C 2003	2.76	0.74	10.35	0.132	5 / 10	25 / 94
Jaber S 2005	2.64	1.04	6.69	0.041	20 / 40	11 / 40
von Muller L 2006	3.06	0.53	17.46	0.209	5 / 8	6 / 17
Limaye A 2008	0.21	0.03	1.72	0.146	1 / 39	9 / 81
Ziemann M 2008	3.26	1.11	9.54	0.031	10 / 35	7 / 64
	1.93	1.29	2.88	0.001	75 / 192	119 / 441



*Cytomegalovirus. Z=3.21; P=0.001; Q=8.38; I2=16.5%

Active cytomegalovirus infection is common in mechanically ventilated medical intensive care unit patients*

Laurent Chiche, MD; Jean-Marie Forel, MD; Antoine Roch, MD, PhD; Christophe Guervilly, MD; Vanessa Pauly, PhD; Jérôme Allardet-Servent, MD; Marc Gainnier, MD, PhD; Christine Zandotti, MD; Laurent Papazian, MD, PhD

Crit Care Med 2009 Vol. 37, No. 6

Table 2. Characteristics of the study population within the first 24 hrs of admission

	Overall Population (n = 242)	CMV Infection		p
		Yes (n = 39)	No (n = 203)	
Invasive mechanical ventilation, n (%)	219 (90.5)	35 (90)	184 (90.6)	0.86
Maximum temperature (°C), mean ± SD	37.6 ± 3.8	37.5 ± 1.5	37.6 ± 4.1	0.08
Pa_{O_2}/Fi_{O_2} ratio, median (IQR)	181 (123–277)	160 (90–226)	185 (125–280)	0.17
Weinberg's radiologic score, median (IQR)	4 (2–6)	5 (4–7)	3 (2–5)	<0.001
Modified CPIS score, median (IQR)	5 (4–6)	4.5 (4–6)	5 (4–6)	0.56
Hemoglobin (g/dL), mean ± SD	10.8 ± 2.4	10.2 ± 2.4	10.9 ± 2.4	0.09
White blood cell count (g/L), mean ± SD	15.2 ± 8.4	14.7 ± 6.6	15.3 ± 8.8	0.92
Neutrophils (%), mean ± SD	82 ± 13	78 ± 19	82 ± 12	0.48
Lymphocytes (%), mean ± SD	9 ± 7	9 ± 6	9 ± 7	0.65
Platelet (g/L), median (IQR)	240 (158–327)	202 (156–265)	250 (160–338)	0.13
Creatinine (µmol/L), median (IQR)	92 (64–154)	115 (66–169)	84 (63–143)	0.16
ASAT (UI/L), median (IQR)	32 (20–71)	30 (19–83)	33 (20–70)	0.82
ALAT (UI/L), median (IQR)	26 (17–54)	24 (13–90)	27 (17–54)	0.63
Bilirubin (µmol/L), median (IQR)	12 (7–19)	10 (8–14)	12 (7–21)	0.37
CMV-positive serology (IgG), n (%)	182 (75)	35 (89)	147 (72)	0.04
Vasopressors, n (%)	146 (60)	25 (64)	121 (60)	0.74

CMV, cytomegalovirus; IQR, interquartile range; CPIS, Clinical Pulmonary Infection Score; ASAT, aspartate aminotransferase; ALAT, alanine aminotransferase.

Risk Factors and Outcome of Cytomegalovirus Infection in MV patients

Table 7. Characteristics of the patients during hospitalization in ICU: Risk factors

	CMV Infection		
	Yes (n = 39)	No (n = 203)	*p*
Gastric bleeding prevention, n (%)	38 (97)	172 (85)	0.059
Proton pump inhibitors	38 (97)	167 (82)	0.031
Anti-H2	0 (0)	5 (3)	0.71
Corticosteroid therapy, n (%)	31 (79)	128 (63)	0.071
Replacement therapy with hydrocortisone for septic shock	23 (59)	106 (52)	0.55
Corticosteroids	3 (8)	12 (6)	0.95
Both	5 (13)	10 (5)	0.13
Blood products transfusion, n (%)	35 (90)	124 (61)	0.001
RBC, n (%)	34 (87)	121 (60)	0.002
Fresh-frozen plasma, n (%)	8 (20)	19 (9)	0.08
Platelet, n (%)	7 (18)	17 (8)	0.13
Receiving vasopressors, n (%)	36 (92)	150 (74)	0.022
Antibiotics during the preceding 90 d, n (%)	20 (51)	81 (40)	0.25
Prior admission in other wards, n (%)	31 (79)	112 (55)	0.008
Intrahospital transport, n (IQR)	2 (1–3)	2 (1–3)	0.48
Enteral feeding, n (%)	26 (67)	72 (35)	<0.001

ICU, intensive care unit; CMV, cytomegalovirus; RBC, red blood cell; IQR, interquartile range.

Virus implicados en la NAV

- Herpes-virus
- Citomegalovirus
- Otros:mimivirus

MIMIVIRUS

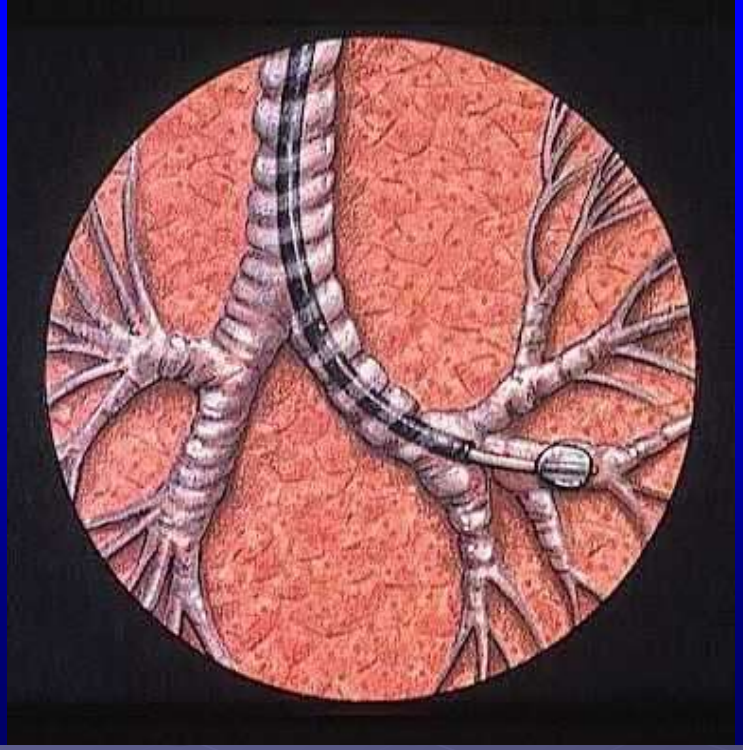
Clinical significance of a positive serology for mimivirus in patients presenting a suspicion of ventilator-associated pneumonia

Crit Care Med 2009 Vol. 37, No. 1

Agnès Vincent, MD; Bernard La Scola, MD, PhD; Jean-Marie Forel, MD; Vanessa Pauly, PhD; Didier Raoult, MD, PhD; Laurent Papazian, MD, PhD

Table 7. Comparison of outcomes according to the serology of mimivirus

Outcome	Cases (n = 55)	Controls (n = 55)	*p*
Further nosocomial infection, n (%)	35 (64)	30 (55)	0.44
Further ventilator-associated pneumonia, n (%)	26 (47)	25 (45)	NS
Further bacterial ventilator-associated pneumonia, n (%)	22 (40)	22 (40)	0.83
Further septicemia, n (%)	17 (31)	9 (16)	0.12
Shock, n (%)	22 (40)	24 (44)	0.86
Acute respiratory distress syndrome, n (%)	12 (22)	8 (15)	0.45
Acute renal failure, n (%)	9 (16)	10 (18)	NS
Duration of mechanical ventilation, days, median (IQR)	38 (20–53)	23 (15–44)	0.005
Duration of mechanical ventilation in the 23 concordant surviving pairs, days, median (IQR)	35 (20–60)	23 (18–45)	0.11
Duration of intensive care unit stay, days, median (IQR)	40 (27–61)	25 (20–47)	0.004
Death, n (%)	19 (35)	25 (46)	0.26



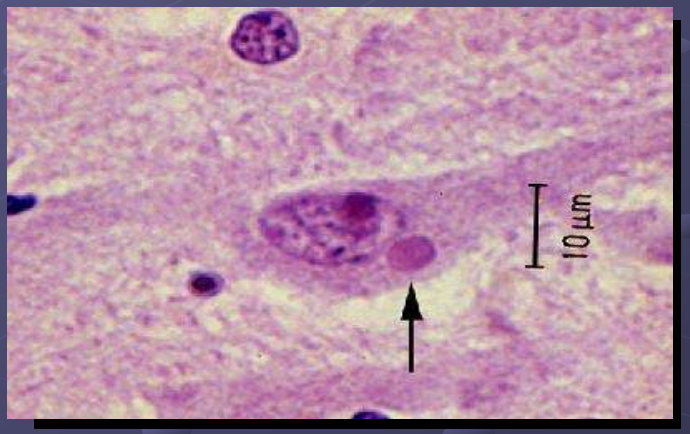
DIAGNOSIS

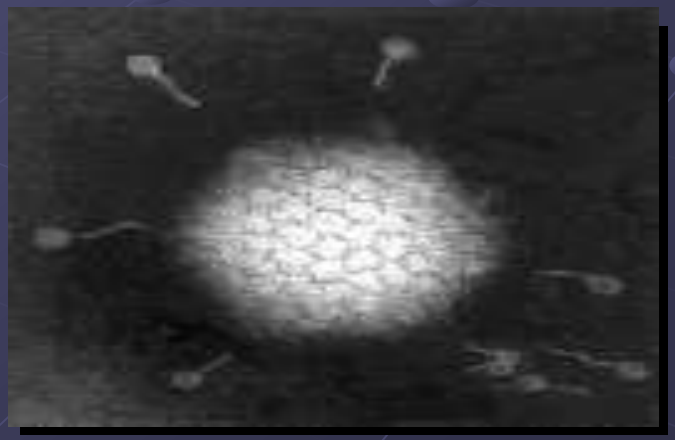
Table 3. Virologic diagnosis of CMV for the 39 patients presenting with an active CMV infection

Diagnostic Technique	
Weekly systematic screening	
Antigenemia	
Positivity rate, n (%)	33 (85)
Time from ICU admission (d), median (IQR)	17 (7–26)
No. cells at diagnosis (d), median (IQR)	2 (1–4)
Seroconversion or reactivation[a]	
Positivity rate, n (%)	16 (41)
Time after ICU admission (d), median (IQR)	16 (7–28.5)
Oriented screening (VAP suspected)	
BAL shell-vial culture	
Positivity rate, n (%)	10 (26)
Time after ICU admission (d), median (IQR)	17 (2–33)
Cytopathogenic effect on BAL	
Positivity rate, n (%)	1 (3)

Viral Diagnosis (I)

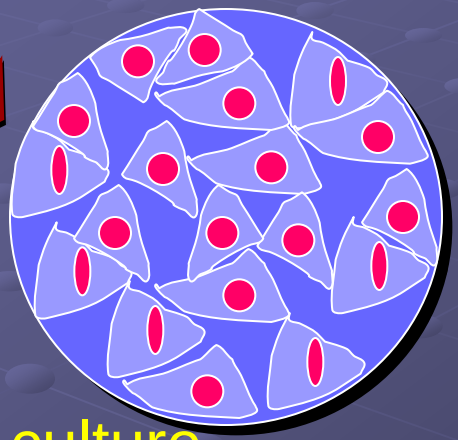
- **Visualization**
  - Conventional microscopy
  - Electronic microscopy

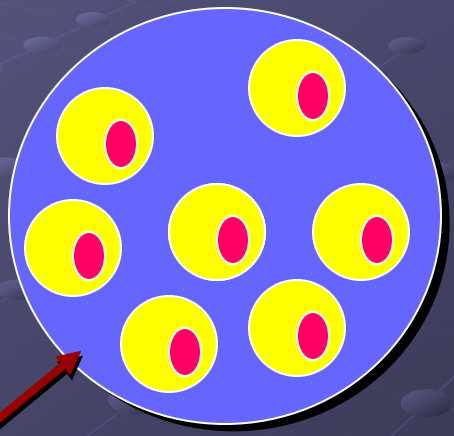




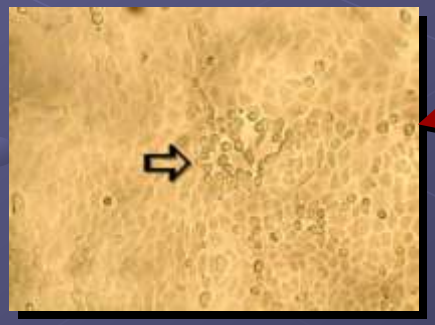
Viral Diagnosis (II)

Isolation and culture

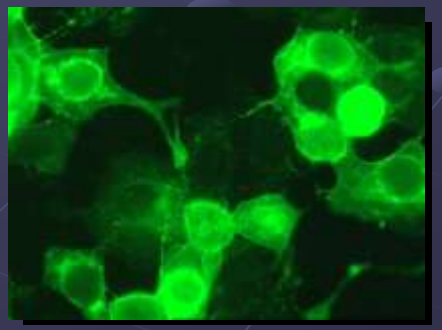




Celular culture



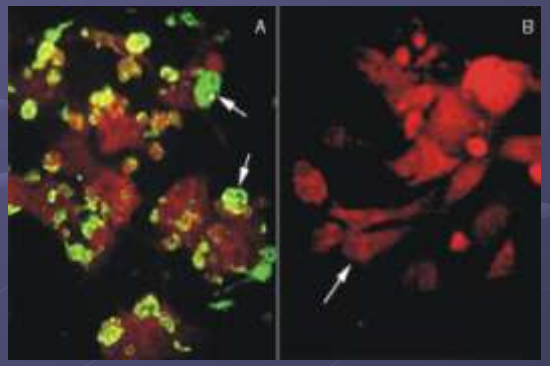
Cytopatic Effect



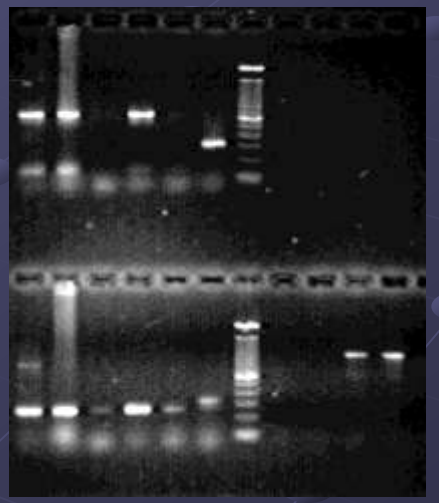
Immunofluorescence
(Monoclonal antibodies)

Viral Diagnosis (III)

- Antigen detection
  - Direct Inmunofluorescence
  - Immunocromatography



- Nucleic acid detection
  - Hibridation Assays
  - Genétic Amplifixcation



- Polimerase Chain Reaction (PCR)
  - nested-PCR, “Real-Time”

Treatment

- Recommendation: To treat these viral infection since prognosis is worsened when present:
- 1Herpes : Acyclovir
- 2Cytomegalovirus:Gancyclovir/Valancyclovir/Foscarnet
- 3The use steroids is controversial or even detrimental

Steroid Treatment

- Varicella pneumonia:
  - Observational studies
    - Mer Chest 1998: Clinical improvement
    - Adhami Respirology 2006: Oxygenation improvement
- Hantavirus
    - Riquelme Emerg Infect Dis 2003: 20 vs 53% (p: ns)
- SARS:
    - Ho Am J Respir Crit Care Med 2003: Rx improvement
    - Peiris Lancet 2003: Clinical improvement (pulse dosing)
- H1N1: Increased mortality

Aportación del laboratorio de microbiología al diagnóstico de la neumonía asociada a la ventilación mecánica

Emilio Bouza[a], María V. Torres[a] y Almudena Burillo[b]

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cabe duda de que algunos herpesvirus se aíslan con frecuencia en muestras respiratorias de pacientes con y sin NAVM[20,21]. En nuestra propia institución (Bouza et al, manuscrito en preparación), tras una búsqueda sistemática y prospectiva en pacientes ventilados mecánicamente, el 6,8% (28 enfermos) de los pacientes sin NAVM y el 13,4% (19 casos) de todos los enfermos con NAVM tenían *Herpes simplex* aislado en el cultivo de muestras del TRI. Su presencia es un marcador de gravedad pero la información disponible no permite conocer el potencial papel de estos virus como causa de NAVM.

El citomegalovirus se ha descrito como causa de NAVM en pacientes inmunocompetentes sin enfermedades hematológicas y es posible que este cuadro esté subdiagnosticado, ya que las técnicas para recuperación de virus no son parte sistemática de la investigación de la NAVM[22].

La adquisición de gripe en pacientes sometidos a ventilación mecánica es muy poco frecuente[23].

Conclusiones

- No se conoce exactamente en profundidad el papel de los virus en la NAV
- Herpes virus y citomegalovirus se detectan con relativa frecuencia
- Los parámetros evolutivos son peores y la mortalidad global está aumentada por lo que se aconseja tratarlos
- Se requieren ensayos clinicos con tratamiento antiviral


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