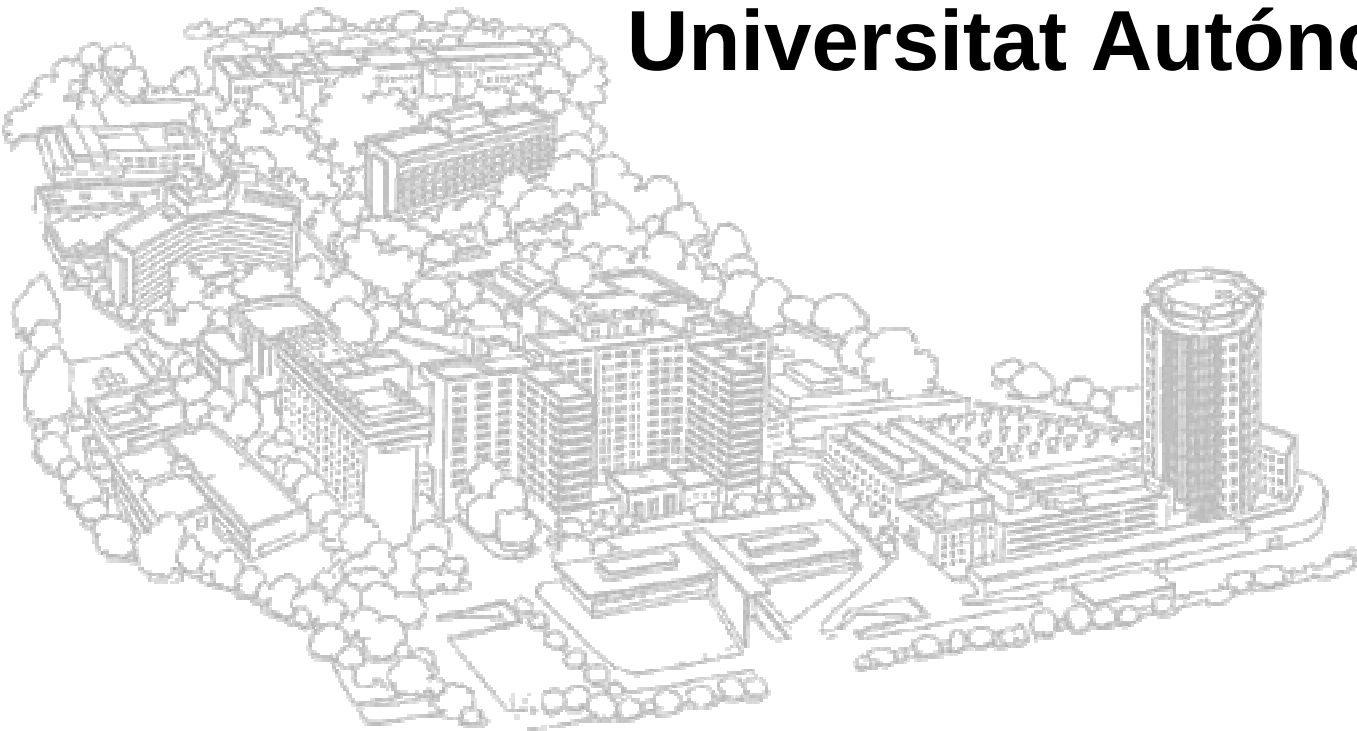


INFECCIÓN TARDIA i T.O.S.

Albert Pahissa

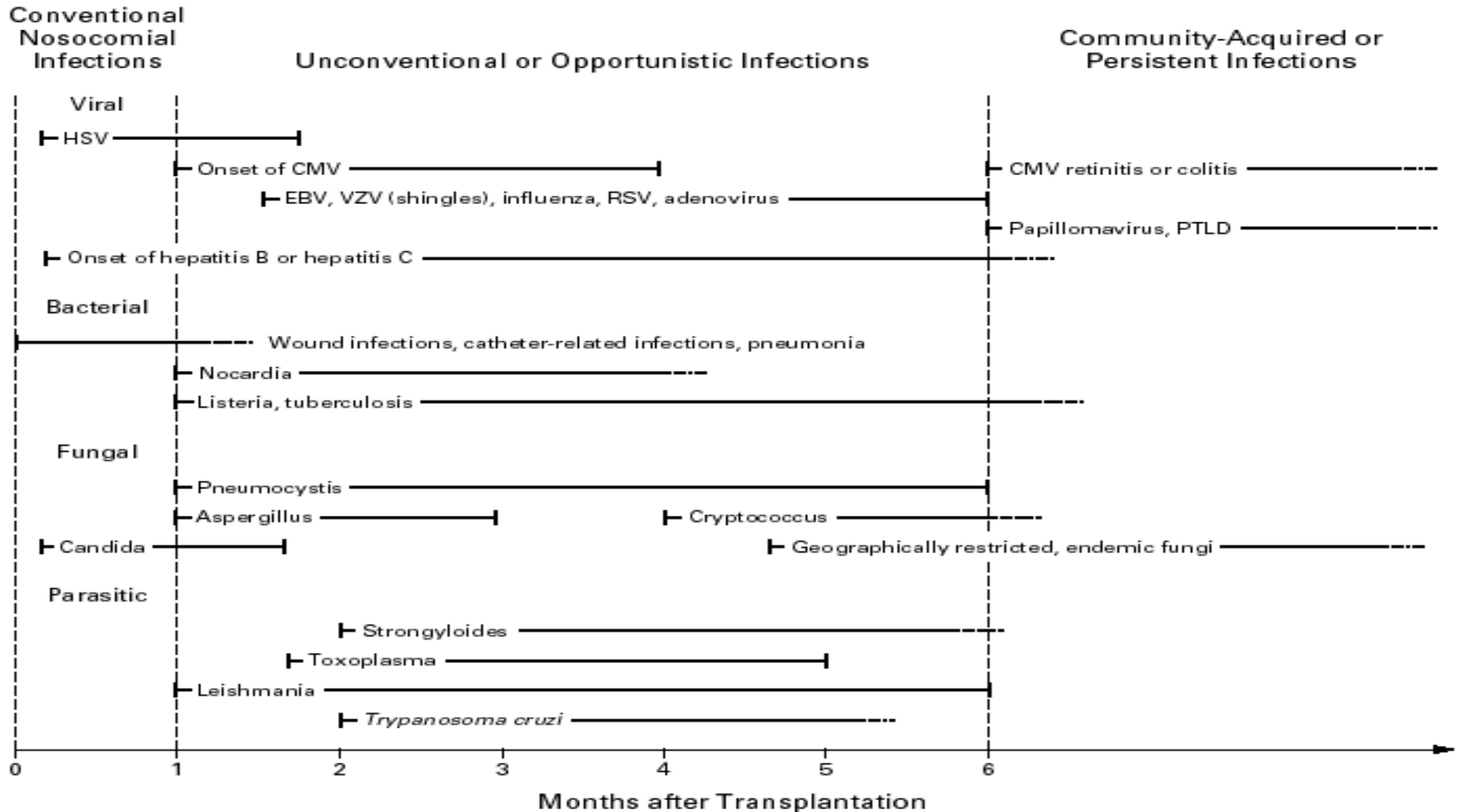
**Servicio Enfermedades Infecciosas. H. Vall d'Hebron
Universitat Autònoma de Barcelona**



Experts, acollidors i solidaris



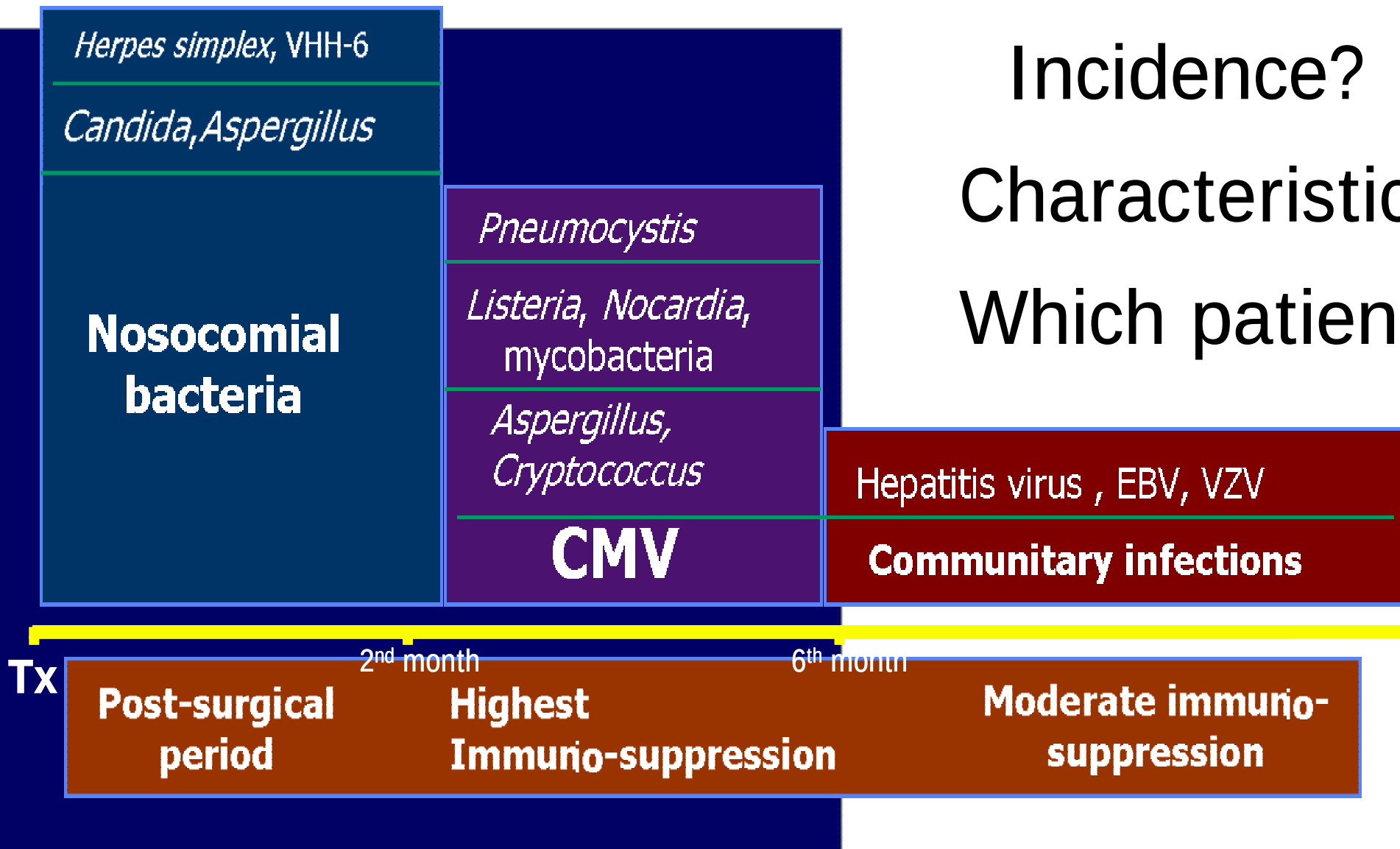
Epidemiologia



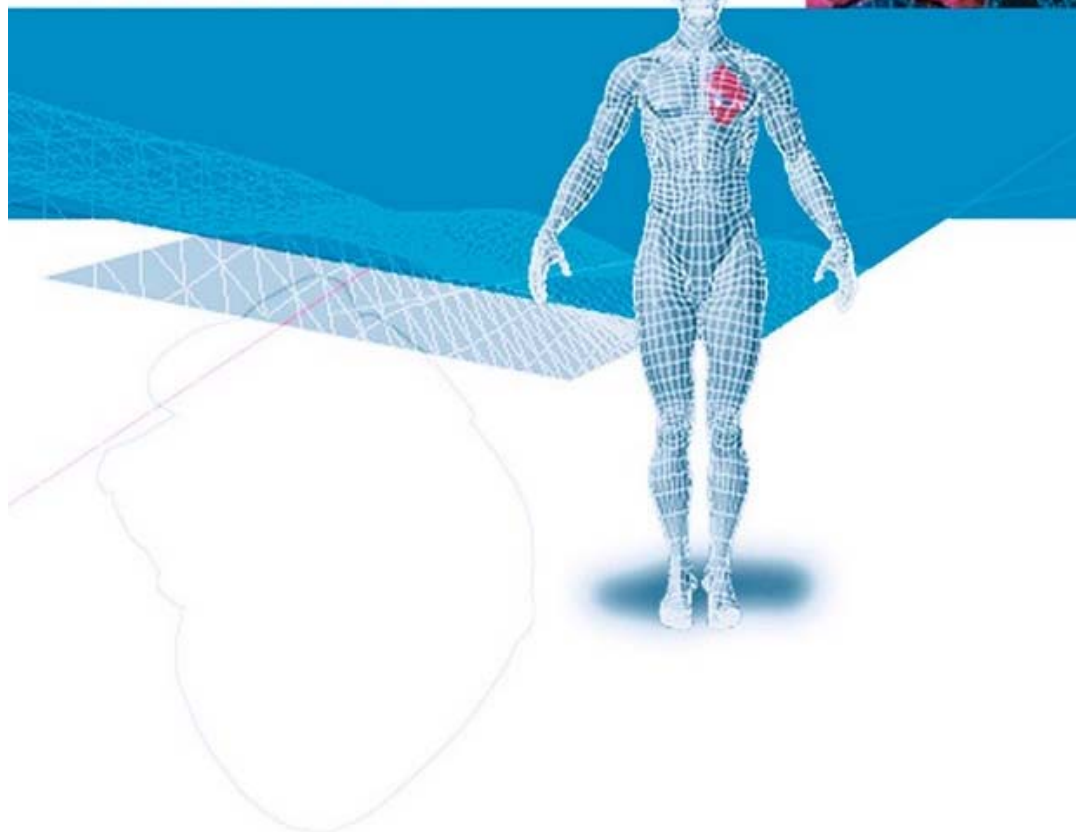
Experts, acol·ladors i solidaris



Incidence?
Characteristics?
Which patients?



Resitra



JUAN
CANALEJO

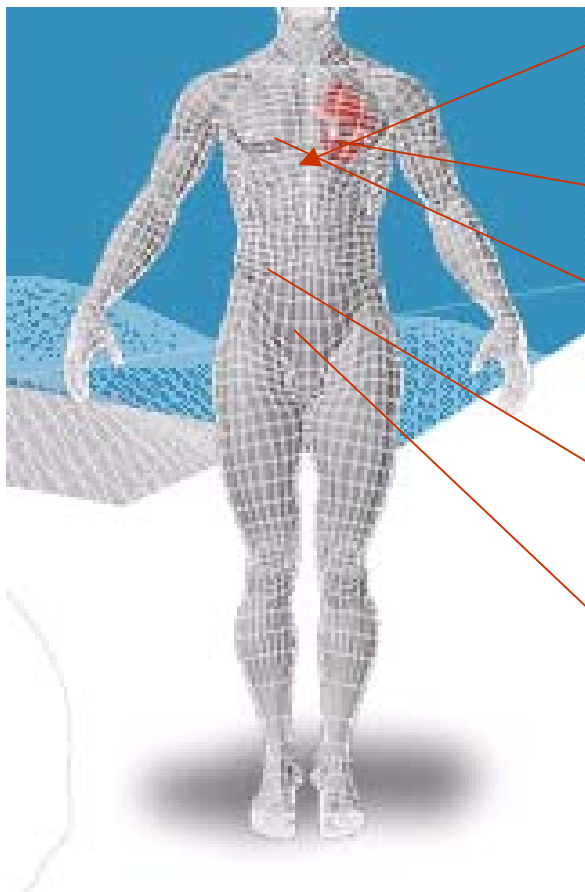
CRUCES

HVH
Clinic
Bellvitge
Sant Pau
Tries i P

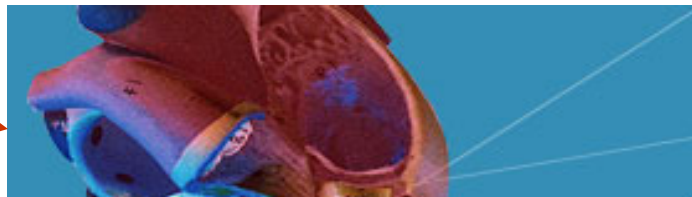
Doce Octubre
Ramón y Cajal
Gregorio Marañón
Puerta de Hi

16 HOSPITALES
7 CCAAs





1364



374



256



1403



1959

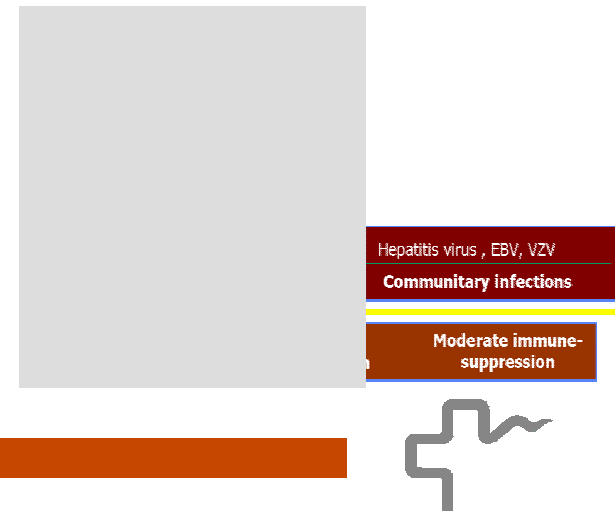
PANCREAS

113



OBJETIVOS DEL TRABAJO.

- **Conocer la incidencia de infección tardía (> 6 m.) en los receptores de un T.O.S. en comparación con el período precoz (< 6 m.)**
- **Describir las características clínicas y analizar los factores de riesgo para el desarrollo de infección tardía**

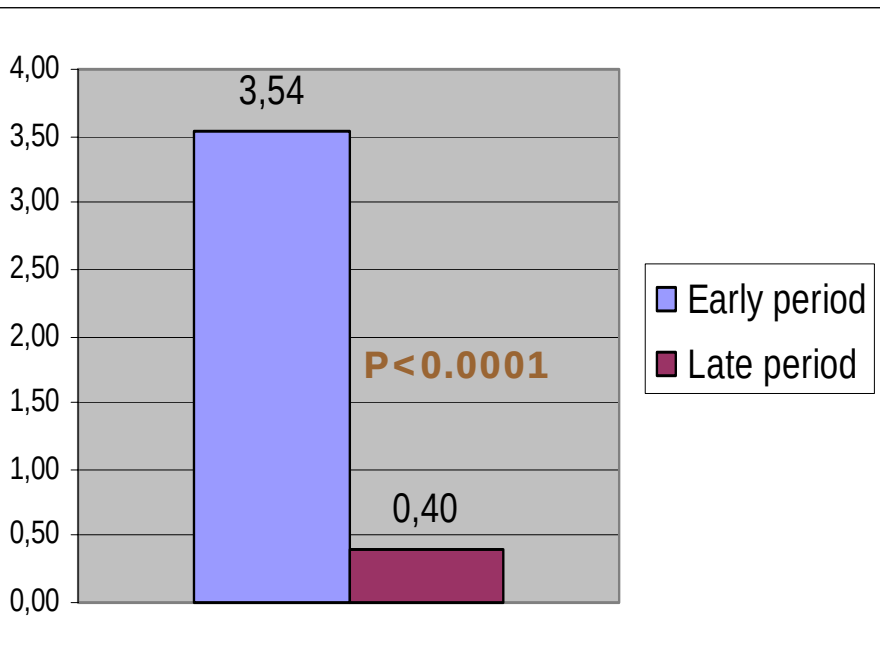


PERÍODO DE TIEMPO VALORADO

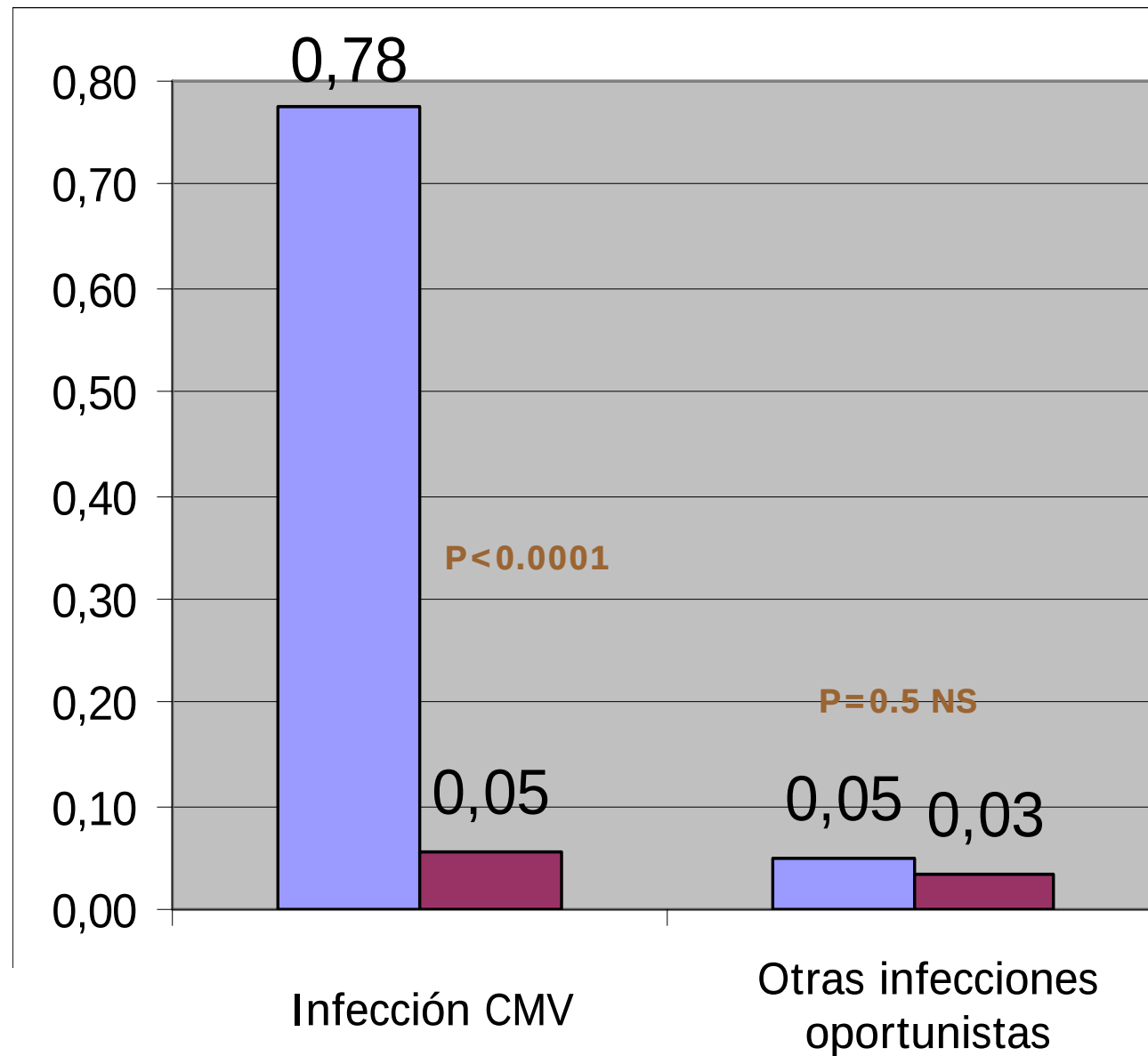
SEPTIEMBRE 2003 – FEBRERO 2005



Incidencia de infección en TOS (Episodios / 1000 d. Trasplante)



Infección global



Otras infecciones oportunistas



Incidencia de infección en TOS

TABLE 2. Comparative incidence of infections between early and late periods in solid organ transplantation (SOT)

	Early period (<6 mo)	Late period (>6 mo)	<i>P</i> value
No. of SOT recipients at risk	2,563	2,169	
No. of patients with infectious episodes (%)	1041 (40.6%)	131 (6%)	
Incidence of global infection			
No infectious episodes/100 SOT recipients	62.2 ^a	8.5	<0.0001
No infectious episodes/1000 transplantation days	3.5	0.4	<0.0001
Cytomegalovirus infection			
No infectious episodes/100 SOT recipients	14 ^a	1.2	<0.001
No infectious episodes/1000 transplantation days	0.	0.0	<0.001
Other opportunistic infections			
No infectious episodes/100 SOT recipients	0.8 ^a	0.7	NS
No infectious episodes/1000 transplantation days	0.05	0.03	NS

NS indicates not significant.

San Juan Garrido et al. Transplantation 2006;82:1457-1462

Resitra 



Pacientes con infección tardia por tipo de trasplante

Type of SOT	Nº Pts	Nº Pts with LI	
		Total (%)	Oport. Inf (%)
<i>Heart</i>	205	14 (6.8%)	4 (2%)
<i>Liver</i>	706	40 (5.7%)	3 (0.4%)
<i>Pancreas</i>	44	4 (9.1%)	3 (7%)
<i>Lung</i>	120	18(15%)	6 (5%)
<i>Kidney</i>	1091	55 (5%)	7 (0.6%)
<i>Total</i>	2166	131 (6%)	23 (1%)

LI: infecció tardia.; Pt: Paciente; OI: infecció oportunista



Incidencia por períodos y tipo de trasplante

Table 1: Incidence of infection per transplant type

Transplant type	Early period		Late period
	First month after Tx Incidence ¹	Second to sixth month after Tx Incidence ¹	Over six months after Tx Incidence ¹
Heart	8.78	2.33	0.34
Liver	11.52	1.90	0.31
Kidney-pancreas	14.47	4.27	0.76
Intestine	13.26	3.29	1.4
Kidney	4.91	2.02	0.28
Other	8.27	2.13	0.37

¹ = transplant.
episodes/1000 transplant-days.

San Juan Garrido et al. Transplantation 2006;82:1457-1462 Resitra 📄



Características de la infección por períodos postrasplante

Table 3: Infectious syndromes distribution and isolated microorganisms in the early and late periods

	Early period		Late period	p-value ¹
	First month after Tx Total: 757 No episodes (%)	Second to sixth month after Tx Total: 838 No episodes (%)	Over 6 months after Tx Total: 176 No episodes (%)	
Infectious syndromes				
Viral symptomatic disease ²	20(2.6%)	119 (14.2%)	7 (4%)	p < 0.0001
Lower respiratory tract infection	165 (21.8%)	96 (11.5%)	45 (25.6%)	p < 0.0001
Skin and soft tissue infection	136 (18%)	96 (11.5%)	19 (10.8%)	
Asymptomatic CMV viraemia requiring treatment	20 (2.6%)	106 (12.6%)	16 (9.1%)	
Genitourinary infection ³	73 (9.6%)	93(11.1%)	19 (10.8%)	
Intraabdominal infection	83 (11%)	71 (8.5%)	19 (10.8%)	
Endovascular infection (also catheter-related)	71 (9.3%)	47 (5.6%)	5 (2.8%)	0.06
Upper respiratory tract infection (including tracheobronchitis)	69 (9.2%)	46 (5.4%)	15(8.5%)	
Bacteremia and/or disseminated infection	57 (7.5%)	48 (5.7%)	10 (5.7%)	
Colitis and/or gastroenteritis	18 (2.5%)	52 (6.2%)	11 (6.3%)	
Stomatitis and/or oesophagitis	24 (3.2%)	38 (4.6%)	4 (2.3%)	
CNS infection	0	3 (0.4%)	0	
Bone and/or joint infection	0	1 (0.1%)	1 (0.6%)	
Others	21(2.7%)	22 (2.6%)	5 (2.8%)	
	Total: 711 No isolates (%)	Total: 640 No isolates (%)	Total: 126 No isolates (%)	
Isolated microorganisms				
Gram-positive bacteria	272 (38.2%)	144 (22.5%)	23 (18.3%)	0.02
CMV	39 (5.4%)	150 (23.4%)	26 (20.6%)	
Enteric bacteria	167 (23.5%)	140 (21.9%)	25 (19.8%)	
NFGNB and other Gram-negative bacteria	135 (19%)	96 (15%)	15(11.9%)	
Other virus apart from CMV ⁴	56 (7.9%)	61(9.5%)	20 (15.9%)	0.002
Yeast	31 (4.4%)	32 (5.1%)	3 (2.4%)	

Incidencia de infección tardía por tipo de trasplante

Table 4: Incidence¹ of infections in the late period per transplant type

	Kidney	Kidney-pancreas	Liver	Heart	Lung
Infectious syndromes	Total: 70	Total: 7	Total: 48	Total: 16	Total: 35
Lower respiratory tract infection	0.06	0.11	0.07	0.11	0.53
Intraabdominal infection	0.01	0.11	0.11	0	0
Skin and soft tissue infection	0.03	0	0.03	0.06	0.16
Genitourinary infection ²	0.05	0.11	0.03	0	0.04
Asymptomatic CMV viraemia requiring treatment	0.03	0	0.01	0.04	0.24
Upper respiratory tract infection (including tracheobronchitis)	0.02	0	0	0.04	0.28
Viral symptomatic disease ³	0.02	0.22	1	0.04	0
Bacteremia and/or disseminated infection	0.01	0.11	0.03	0	0
Colitis and/or gastroenteritis	0.02	0.11	0.02	0.02	0.04
Endovascular infection (also catheter-related)	0.01	0	0.01	0	0
Stomatitis and/or oesophagitis	0.01	0	0	0	0.08

CMV = cytomegalovirus.

¹Episodes/1000 transplant-days.

²Non-complicated cystitis or asymptomatic bacteriuria excluded.

³Includes mostly CMV viral syndrome without organ affectation.



Etiología de la infección tardía por tipo de trasplante

Table 5: Isolated microorganisms distribution in the late period per transplant type

	Kidney (%)	Kidney-pancreas (%)	Liver (%)	Heart (%)	Lung (%)
Microorganisms isolated	Total: 54	Total: 7	Total: 27	Total: 11	Total: 27
Gram-positive bacteria	9 (16.7)	3(43)	4 (14.8)	1 (9.1)	4 (14.8)
CMV ¹	11 (20.4)	1 (11)	0	6 (54.5)	8 (29.6)
Enteric bacteria	12 (22.2)	1 (11)	10 (37)	1 (9.1)	1 (3.7)
NFGNB and other Gram-negative bacteria	4 (7.4)	1 (11)	4 (14.8)	0	6 (22.2)
Other virus apart from CMV ²	19 (18.5)	1 (11)	4 (14.8)	2 (18.2)	3 (11.1)
Yeast	1 (1.9)	0	2 (7.4)	0	1 (3.7)
Other immunosuppression related microorganisms ³	7 (13)	0	3 (11.1)	1 (9.1)	4 (14.8)

CMV = cytomegalovirus.

¹Includes mostly CMV viral syndrome without organ affectation.

²Mostly *Herpes-simplex* and *Herpes-zoster* viruses.

³Includes filamentous fungi, BK virus, mycobacteria, *Listeria*, *Nocardia*, *Legionella*, *P. jirovecii*, *Leishmania*.



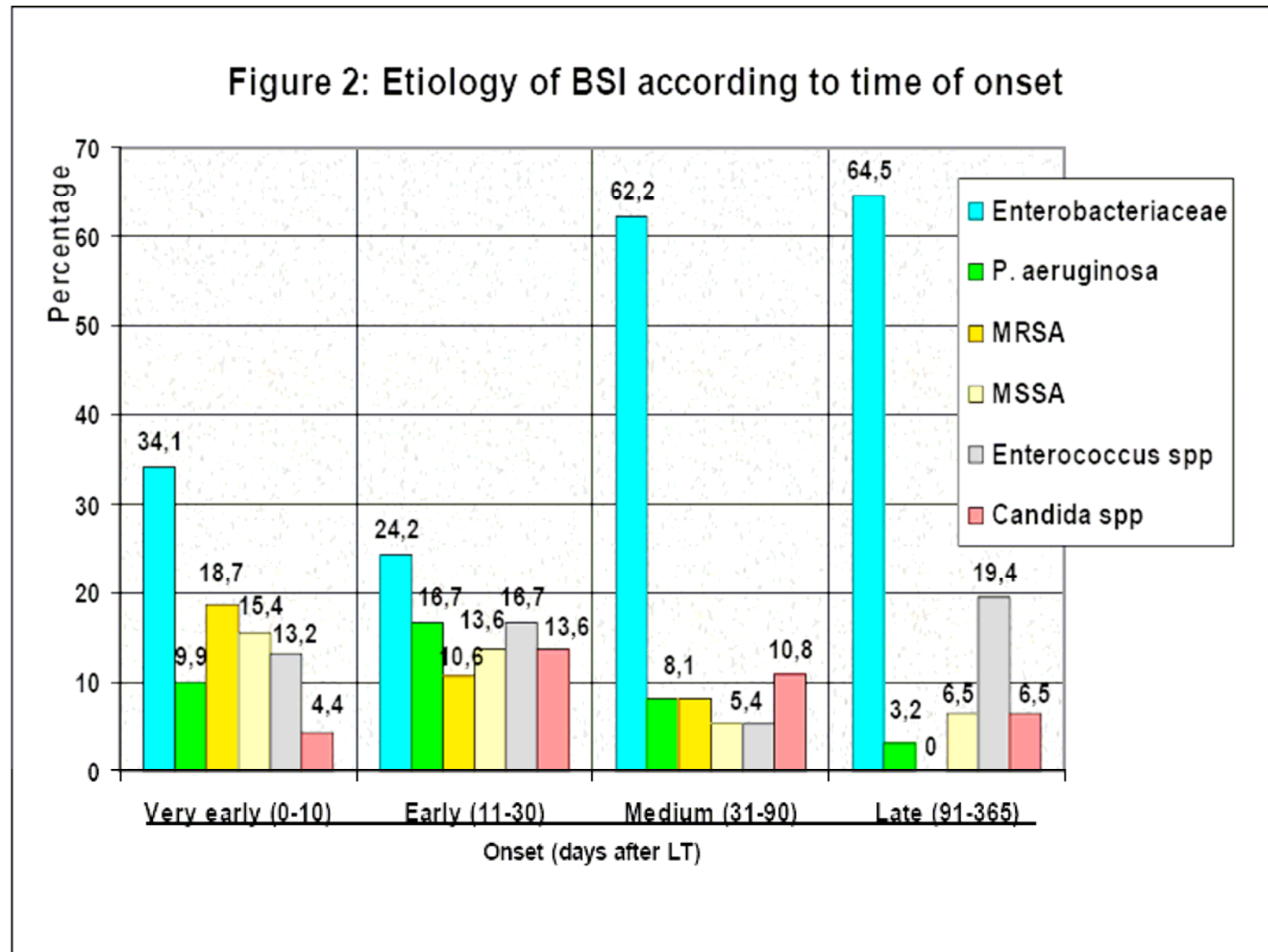
Factores de riesgo de infección tardía en el TOS

	OR	IC 95%
Trasplante de pulmón	8	2,3-28
Al menos dos episodios de infección bacteriana (período precoz)	5	2-12
Episodio previo de insuficiencia renal con necesidad de diálisis	4,7	1,5-15
Mal función crónica del injerto	4,3	1,6-11



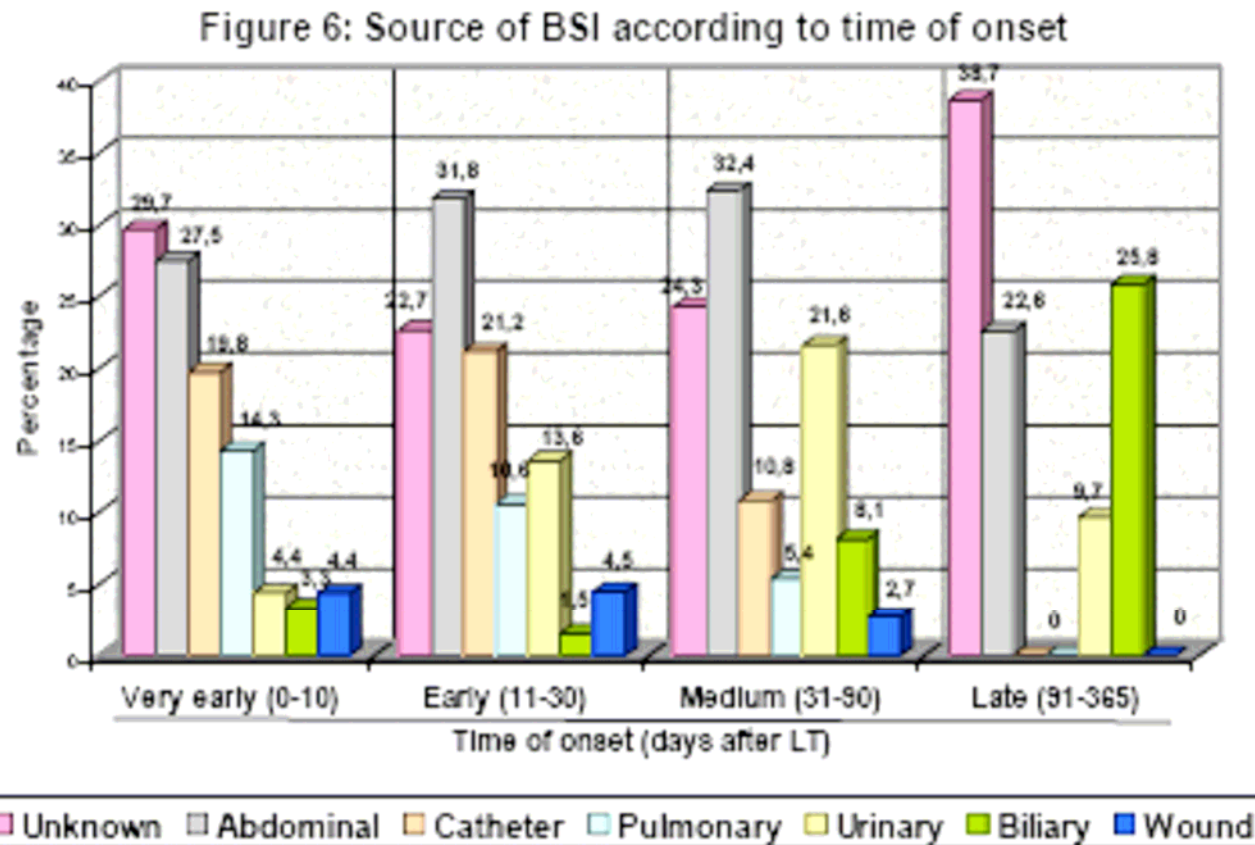
Epidemiología de la bacteriemia en el 1^{er} año postrasplante hepático

F. Bert et al. Póster K-1764. ICAAC 2007



Epidemiología de la bacteriemia en el 1^{er} año postrasplante hepático

F. Bert et al. Póster K-1764. ICAAC 2007



Epidemiologia de las bacteriemias en los TOS

M.S.J. Júnior et al. Póster K-1759. ICAAC 2007

Type of transplant		
Kidney	199	87.2
Kidney-pancreas	18	7.0
Liver	7	3.1
Heart	5	2.6
Kidney-Liver	1	0.1

Site of infection		
Urinary tract infection	78	33.3
Bloodstream	49	21.5
Pneumonia	31	13.6
Abdomen	28	12.3
Wound	18	7.0
Other	28	12.3
Charlson		
≤3	189	82.9
Bacteremia after 100 days	157	58.8
Septic shock after bacteremia	42	18.4

Pathogen	Total (N)	Percentage
Gram negative	159	100
<i>Escherichia coli</i>	68	41.50
<i>Klebsiella pneumoniae</i>	25	15.73
<i>Pseudomonas aeruginosa</i>	21	13.20
<i>Enterobacter aerogenes</i>	20	12.57
<i>Acinetobacter baumannii</i>	12	7.54
<i>Serratia marcescens</i>	5	3.14
<i>Salmonella</i> spp	4	2.51
<i>Providencia</i> spp	2	1.25
<i>Burkholderia cepacia</i>	1	0.62
<i>Stenotrophomonas maltophilia</i>	3	1.88
Gram positive	59	100
<i>Staphylococcus aureus</i>	20	33.89
Coagulase negative <i>Staphylococcus</i>	17	28.81
<i>Enterococcus</i> spp	12	20.33
<i>Listeria monocytogenes</i>	1	1.69
<i>Streptococcus pneumoniae</i>	8	13.55
<i>Streptococcus viridans</i>	1	1.69
Fungal	9	100
<i>Candida albicans</i>	4	44.44
<i>Candida tropicalis</i>	1	11.11
<i>Candida parapsilosis</i>	1	11.11
<i>Candida krusei</i>	1	11.11
<i>Cryptococcus neoformans</i>	2	22.22



Incidencia enfermedad CMV en relación con inicio profilaxis anti CMV

R. San Juan et al. Póster K – 1761. ICAAC 2007

Enero 2003 → Octubre 2006

↓
40 TOS D+ R-

↓
100 d. profilaxis anti CMV

Riesgos infección tardía CMV en D+R-

- 1.- Más frecuente y grave que en D+R+
- 2.- Factor de riesgo de mortalidad
- 3.- Peligro de cepas Ganciclovir R

1 / 2003	12 / 2004	1 / 2005	10 / 2006
Inicio profilaxis inmediato		Inicio profilaxis a partir día 15	

6 / 22 (27 %)

1 / 18 (5 %)

P = 0,08

110 – 246 d.



Etiologia neumonia post-trasplante de pulmón

RESITRA

Microorganism	n (%)	Incidence (Number of episodes per 1.000 LT recipients/year)
BACTERIA	47 (82.7)	398
Gram-negative bacilli:	34 (59.9)	288
<i>Pseudomonas aeruginosa</i>	14 (24.6)	118.6
<i>Acinetobacter baumannii</i>	8 (14)	67.8
<i>Escherichia coli</i>	3 (5.3)	25.4
<i>Klebsiella pneumoniae</i>	3 (5.3)	25.4
<i>Stenotrophomonas maltophilia</i>	3 (5.3)	25.4
<i>Pseudomonas putida</i>	1 (1,8)	8.4
<i>Serratia marcescens</i>	1 (1,8)	8.4
<i>Burkholderia cepacia</i>	1 (1,8)	8.4
Gram-positive cocci:	8 (14)	67.8
<i>Staphylococcus aureus</i>	8 (14)	67.8
<i>Nocardia</i> sp.	2 (3,5)	16.8
Mycobacteria	3 (5,3)	25.4
<i>M. tuberculosis</i>	2 (3,5)	16.8
<i>M. avium</i>	1 (1,8)	8.4
FUNGI	8 (14)	67.8
<i>Aspergillus fumigatus</i>	4 (7)	33.8
<i>Aspergillus niger</i>	1 (1,8)	8.4
<i>Scedosporium prolificans</i>	1 (1,8)	8.4
<i>Acremonium</i> sp.	1 (1,8)	8.4
<i>Mucor</i> sp.	1 (1,8)	8.4
VIRUS	6 (10,4)	50.8
Cytomegalovirus	6 (10,4)	50.8
TOTAL	57 (107)*	

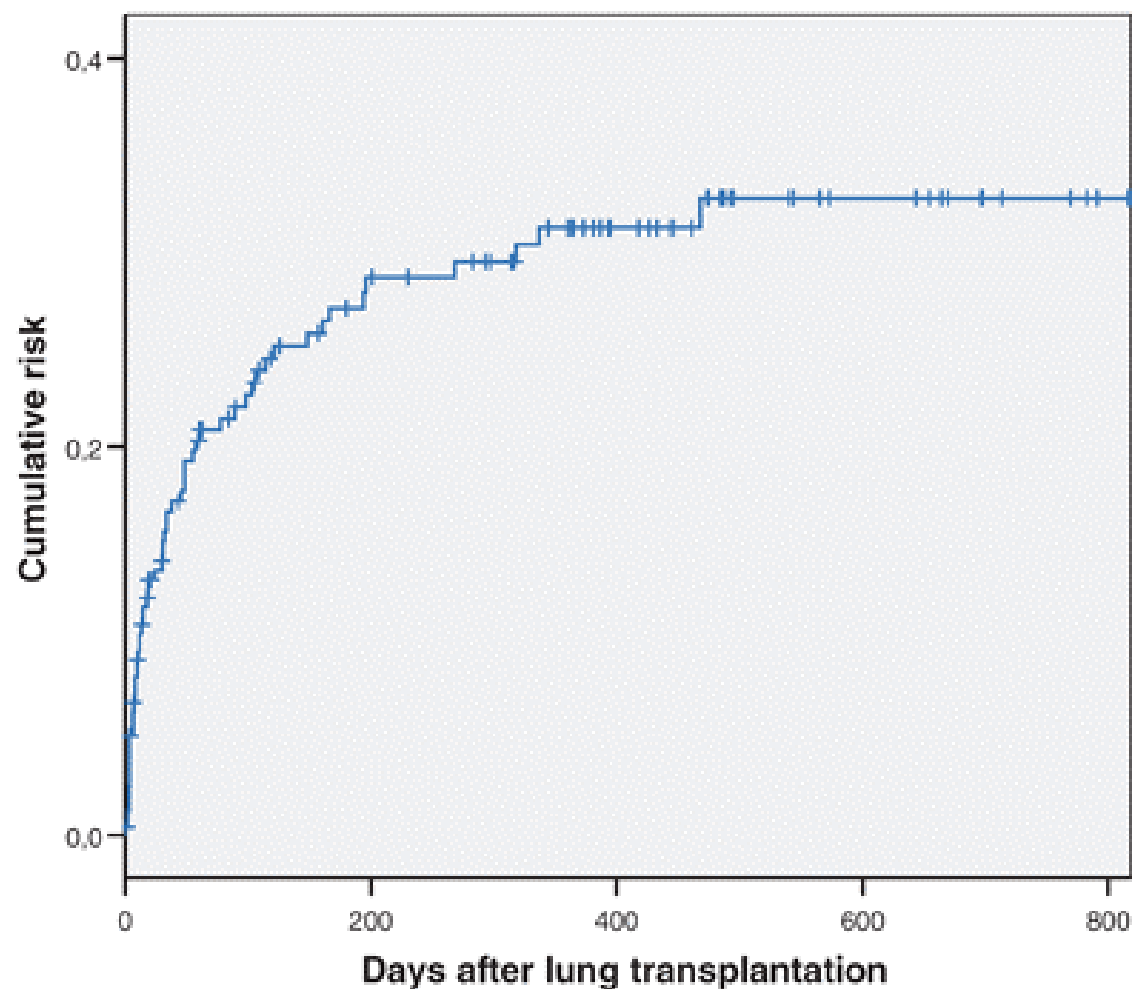
*Four (7%) of 57 cases of pneumonia were polymicrobial: *S. maltophilia* with *A. baumannii* (two cases), *K. pneumoniae* with *P. aeruginosa*, and *K. pneumoniae* with *E. coli*.

Source: Am J Transplant © 2007 Blackwell Publishing

Experts, acollidors i solidaris



Epidemiología neumonía post-trasplante de pulmón. RESITRA



Months	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	≥17
	0.17	0.22	0.24	0.27	0.28	0.30	0.31	0.32	0.33	0.33	0.34	0.34	0.34	0.35	0.35	0.35	0.36

Source: Am J Transplant © 2007 Blackwell Publishing

Experts, acol·lids i solidaris

M. Aguilar-Guisado et al. Am J Transp 2007;7:1989-1996

Resitra



Epidemiología neumonia post-trasplante de pulmón. RESITRA

Medscape®		www.medscape.com	
Month	Number of episodes	Incidence (n° episodes per 100 lung transplant)	
1	40	17	
2	12	5	
3	5	2	
4	7	3	
5	3	1,3	
6	4	1,7	
7	3	1,3	
8	3	1,3	
9	2	0,8	
10	0	0	
11	1	0,4	
12	1	0,4	
>12	4	1,7	
Total	85	36	

Source: Am J Transplant © 2007 Blackwell Publishing



CONCLUSIONES DE LA INFECCIÓN TARDIA

1. Incidencia del 6% vs el 41% en la etapa precoz
2. Por tipos de trasplante, el pulmón es el que tiene un riesgo mayor
3. La etiología de la infección bacteriana que predomina son los BGN, enterobacterias y en el TP son importantes los BGN no fermentadores
4. Importancia de la infección por CMV, especialmente en el D+R-
5. Neumonía poco habitual. En el TP la etiología es compleja
6. Incidencia baja de IFI

