Attualità in Infettivologia 2013
Le Infezioni Associate alle Cure Sanitarie
Ferrara 20 giugno 2013

Aspetti epidemiologici e clinici nell'ospite immunocompromesso da HIV e da altre condizioni

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Outline

-**The past: HIV and healthcare associated infections**

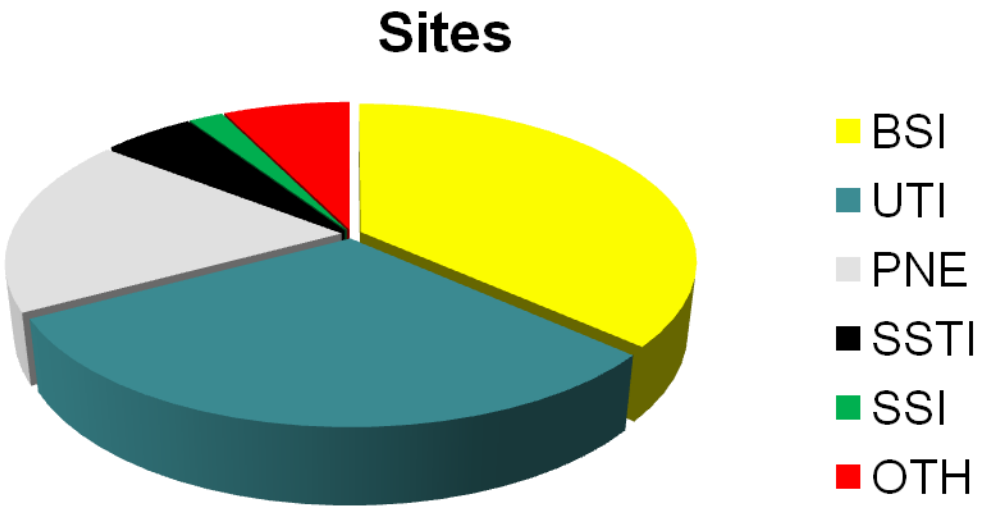
-**New treatments new infectious risks: the case of biological agents**

-**The new immunocompromised and the new MDR.**

Nosocomial infections in HIV infected patients

Multicentre prospective study on consecutive HIV-infected patients admitted to 19 Italian acute-care infectious disease wards

•A total of 344 NI occurred in 4330 admissions, with at least one NI in 273 admissions (6.3%). The incidence rate of NI was 3.6 per 1000 patient days (95%CI, 3.2–4.1].



Petrosillo N et al.AIDS 1999, 13:599–605

Nosocomial infections in HIV infected patients

Table 1. Organisms isolated in vascular catheter-related bloodstream nosocomial infections (CR-BSI) and urinary catheter related infections (UCRI).

Organism	CR-BSI		UCRI	
	n	%	n	%
Staphylococcus epidermidis	17	30.9	4	4.8
Staphylococcus aureus	13	23.7	3	3.6
Enterococcus species	2	3.6	16	19.3
Other Gram positive	2	3.6	–	–
Pseudomonas aeruginosa	3	5.5	21	25.3
Pseudomonas species	1	1.8	1	1.2
Proteus mirabilis	1	1.8	1	1.2
Escherichia coli	2	3.6	23	27.7
Enterobacter species	1	1.8	2	2.4
Candida species	4	7.3	7	8.5
Other Gram negative	–	–	3	3.6
Negative/not performed	9	16.4	2	2.4
Total	55	100.0	83	100.0

Petrosillo N et al.AIDS 1999, 13:599–605

Nosocomial infections in HIV infected patients

Table 2. Factors associated with nosocomial infections (NI) in HIV-infected patients. Univariate and multivariate analysis.

Factors	NI/total (%)	Crude OR (95%CI)	Adjusted OR* (95%CI)
Sex			
Male	203/3333 (6.1)	1	–
Female	70/997 (7.0)	1.16 (0.87–1.56)	–
CD4 T-lymphocytes (× 10^6/l)			
> 199	25/1085 (2.3)	1	1
< 200	248/3245 (7.6)	3.51 (2.28–5.45)†	2.21 (1.35–3.62)†
HIV stage			
A	10/443 (2.2)	1	1
B	43/1109 (3.9)	1.75 (0.84–3.74)	0.99 (0.46–2.12)
C	220/2778 (7.9)	3.72 (1.91–7.51)*	0.96 (0.45–2.01)
Karnofsky Performance Status			
80–100	39/1752 (2.2)	1	1
40–70	183/2226 (8.2)	3.93 (2.73–5.68)†	1.59 (0.94–2.70)
10–30	51/352 (14.5)	7.44 (4.72–11.75)†	1.89 (1.28–2.78)†
Injecting drug use			
No	107/1548 (6.9)	1	–
Yes	166/2782 (6.0)	0.85 (0.66–1.11)	–
White cells (× 10^6/l)‡			
> 2000	222/3761 (5.9)	1	1
1001–2000	40/468 (8.5)	1.49 (1.05–2.00)†	1.38 (0.82–2.33)
< 1001	11/93 (11.8)	2.14 (1.06–4.21)†	1.05 (0.39–2.81)
Neutrophils‡			
> 1000	228/3740 (6.1)	1	1
501–1000	30/422 (7.1)	1.18 (0.78–1.78)	0.85 (0.48–1.52)
< 501	15/136 (11.0)	1.91 (1.05–3.41)†	1.04 (0.43–2.48)
TMP–SMX‡			
Yes	126/1830 (6.9)	1	–
No	136/2349 (5.8)	0.85 (0.66–1.09)	–
Antiretrovirals			
No	137/1981 (6.9)	1	–
Yes	136/2349 (5.8)	0.83 (0.64–1.06)	–
Therapy with corticosteroids			
No	194/3703 (5.2)	1	1
Yes	79/627 (12.6)	2.61 (1.96–3.47)†	1.78 (1.29–2.45)†
Interferon			
No	272/4310 (6.3)	1	–
Yes	1/20 (5.0)	0.78 (0.12–5.37)	–
Central venous catheter			
No	135/3695 (3.6)	1	1
Yes	138/635 (21.7)	7.32 (5.63–9.53)†	3.24 (2.41–4.35)†
Urinary catheter			
No	122/3790 (3.2)	1	1
Yes	151/540 (28.0)	11.67 (8.92–15.27)†	6.53 (4.81–8.86)†
Surgery			
No	243/4139 (5.9)	1	1
Yes	30/191 (15.7)	2.99 (1.94–4.58)†	3.13 (1.90–5.15)†
Ventilation			
No	259/4278 (6.1)	1	1
Yes	14/52 (26.9)	5.72 (2.91–11.07)†	1.18 (0.55–2.50)
In-hospital days§			
2–8	65/1508 (4.3)	1	1
9–30	154/2199 (6.4)	1.67 (1.23–2.28)†	1.25 (0.89–1.74)
> 30	54/623 (8.7)	2.11 (1.43–3.11)†	0.87 (0.57–1.34)

Petrosillo N et al.AIDS 1999, 13:599–605

Nosocomial Bloodstream Infections among Human Immunodeficiency Virus–Infected Patients: Incidence and Risk Factors

•65 NBSIs (4.7%) occurred in 1379 admissions, for an incidence of 2.45 NBSIs per 1000 patient-days.

•Twenty-nine NBSIs were catheter-related bloodstream infections,
•with a rate of 9.6 central venous catheter–associated infections per 1000 device-days.

•Multivariate analysis indicated that variables independently associated with NBSIs included active injection drug use, a Karnofsky Performance Status score of <40, presence of a central venous catheter, and length of hospital stay.

•Mortality rates were 24.6% and 7.2% among patients with and without NBSIs, respectively (*P <.00001).*

Petrosillo N et al. Clin Infect Dis 2002; 34:677–85

Surgical Site Infections in HIV-infected Patients: Results from an Italian Prospective Multicenter Observational Study

C.M.J. Drapeau, A. Pan, C. Bellacosa, G. Cassola, M.P. Crisalli, M. De Gennaro, S. Di Cesare, F. Dodi, G. Gattuso, L. Irato, P. Maggi, M. Pantaleoni, P. Piselli, L. Soavi, E. Rastrelli, E. Tacconelli, N. Petrosillo

Infection 2009

- **A 1-year observational prospective multicenter surveillance study was conducted in 11 ID centres from which 305 consecutive HIV infected patients undergoing different surgical procedures were enrolled.**

- **SSI occurred in 29 of 305 (9.5%) patients, of which 17 (58.6%) SSI occurred during hospital stay, and 12 (41.4%) occurred during the postdischarge period.**

- **Superficial 72.4%, deep 13.8%, organ/space 3.4%, and sepsis 10.3%.**

Surgical Site Infections in HIV-infected Patients: Results from an Italian Prospective Multicenter Observational Study

Table 4
Risk factors for SSI in HIV-infected patients.

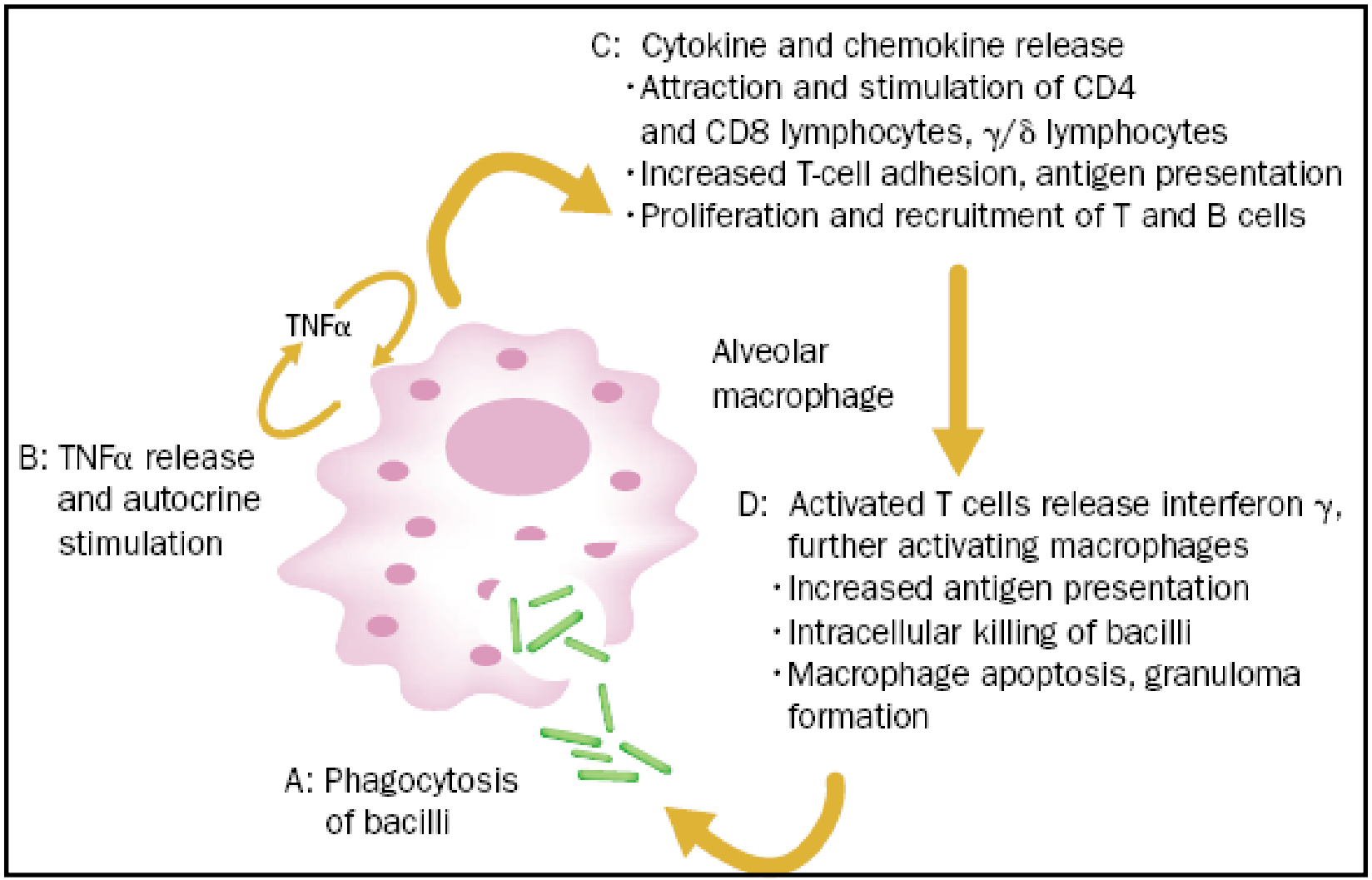
Characteristics	Total, n (%)	SSI infection, n (%)	Odds ratio (95% CI)	MLR-OR[a] (95% CI)
Gender				
Male	132	16 (12.1)	1	
Female	173	13 (7.5)	0.6 (0.3–1.3)	
Age (years)				
<45	210	15 (7.1)	1	1
≥45	95	14 (14.7)	2.2 (1.0–4.9)	2.0 (0.9–4.5)
HCV infection				
No	166	9 (5.4)	1	1
Yes	139	20 (14.4)	2.9 (1.3–6.7)	2.7 (1.2–6.3)
HIV viral load				
Undetectable	185	15 (8.1)	1	
Detectable	120	14 (11.6)	1.5 (0.7–3.2)	
CD4 cell count (/mm^3)				
≥200	230	20 (8.7)	1	
<200	75	9 (12.0)	1.4 (0.6–3.3)	
WBC number pre-intervention (/mm^3)				
≥4,000	258	22 (8.5)	1	
<4,000	47	7 (14.9)	1.9 (0.8–4.7)	
Preoperative hospital stay				
0–1	236	22 (9.3)	1	
>1	69	7 (10.1)	1.1 (0.5–2.7)	
NNIS risk index score				
0	157	10 (6.4)	1	
1–3	148	19 (13.0)	2.2 (1.0–4.8)	
Body mass index				
Underweight	38	4 (10.5)	1.4 (0.4–4.3)	
Normal	200	16 (8.0)	1	
Overweight	47	6 (12.8)	1.7 (0.6–4.6)	
Obesity	20	3 (15.0)	2.0 (0.5–7.7)	
Diabetes				
No	285	25 (8.8)	1	
Yes	20	4 (20.0)	2.6 (0.8–8.4)	
HBV infection				
No	286	28 (9.8)	1	
Yes	19	1 (5.3)	0.5 (0.1–4.0)	
Lipodistrophy				
No	252	21 (8.4)	1	
Yes	53	8 (15.1)	2.0 (0.8–4.7)	
Perioperative prophylaxis				
No	69	9 (13.0)	1	
Yes	236	21 (8.9)	0.7 (0.3–1.8)	

OR Odds ratio; *MLR-OR* multiple logistic regression odds ratio; [a] backward stepwise elimination procedure

Drapeau CMJ et al. Infection 2009

TNF-a is a pro-inflammatory cytokine that is involved in the immune protection against infection, and it is therefore possible that TNF-a neutralisation may favour the development of infection.

Meccanismo d'azione

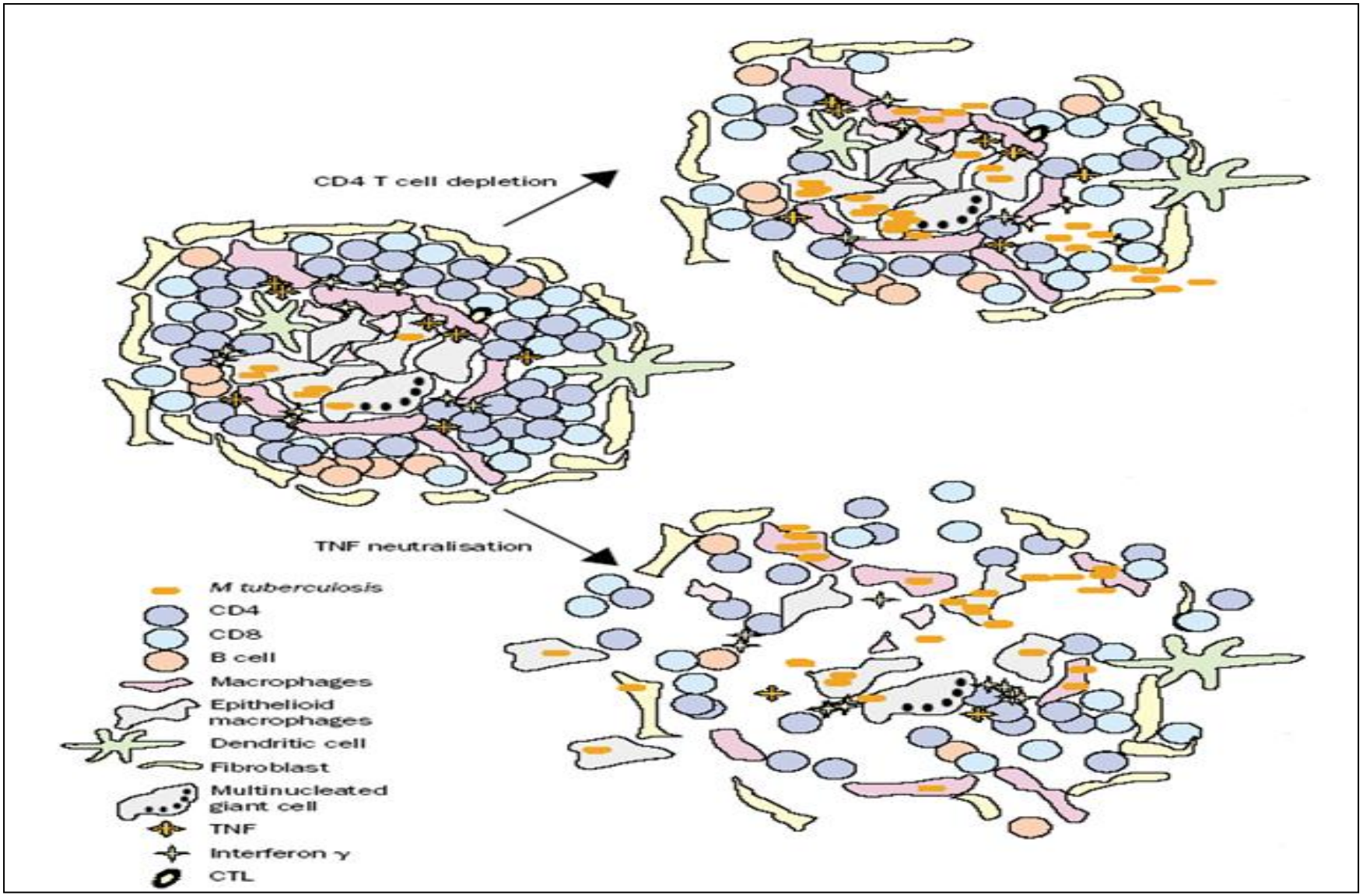


Gardam MA, et al. *Lancet* 2003:**3**;148-155.

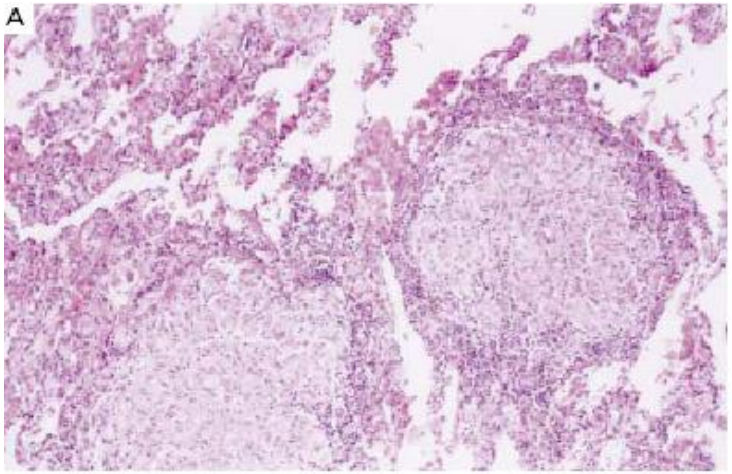
Si stima che circa 1 milione di pazienti siano stati trattati con antagonisti del TNF-α per le seguenti indicazioni:

- **Artrite reumatoide**
- **Malattia infiammatoria intestinale**
- **Artrite psoriasica**
- **Artrite cronica giovanile**
- **Psoriasi**
- **Spondilite anchilosante**

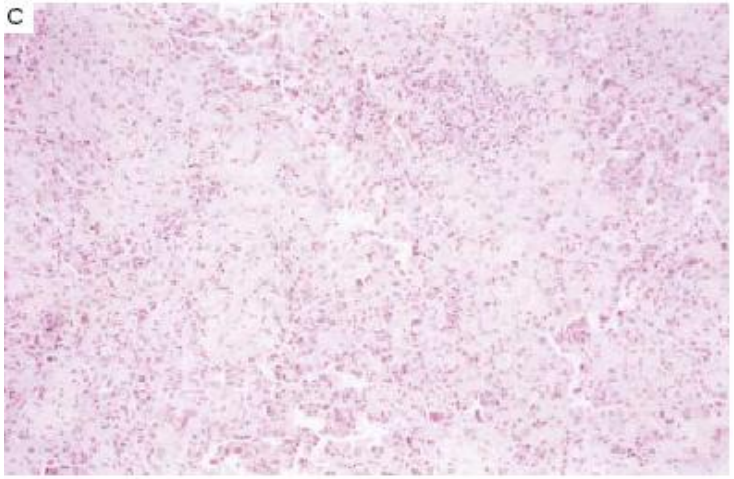
Ruolo del TNF nella formazione del granuloma



Ruolo del TNF nella formazione del granuloma



Senza INFLIXIMAB



Con INFLIXIMAB

Keane J et al. *N Engl J Med* 2001; **345**: 1098-104

Clin Vaccine Immunol. 2008 March; 15(3): 506–512. Published online 2007 December 26. doi: 10.1128/CVI.00401-07.

Reduction of Chemokine Secretion in Response to Mycobacteria in Infliximab-Treated Patients

The development of tuberculosis in infliximab-treated patients is

- **not directly related to the mycobactericidal effects of TNF**
- **but may be due to inhibition of TNF-dependent chemokine gradients disrupting cellular migration necessary to maintain the integrity of the granuloma.**

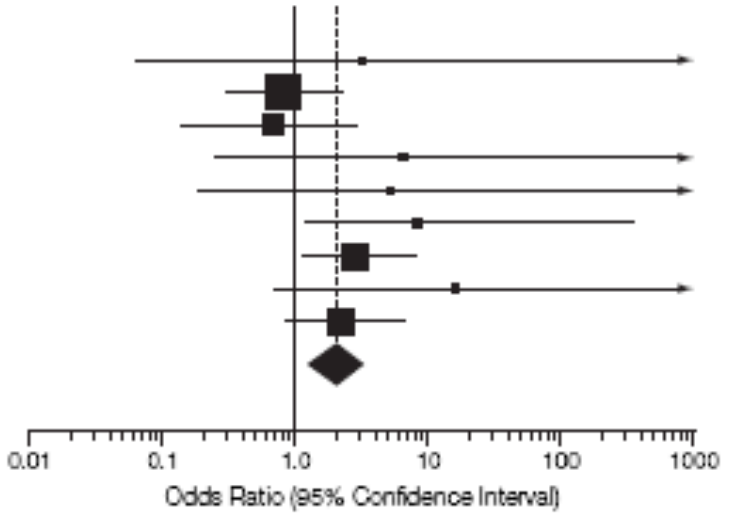
Anti-TNF Antibody Therapy in Rheumatoid Arthritis and the Risk of Serious Infections and Malignancies

Systematic Review and Meta-analysis of Rare Harmful Effects in Randomized Controlled Trials

Figure 3. Effect of Anti-TNF Antibody Therapy vs Control Therapy on Occurrence of 1 or More Serious Infections in Patients With Rheumatoid Arthritis

Source	Serious Infections, No./Total: Anti-TNF	Serious Infections, No./Total: Placebo	Odds Ratio (95% Confidence Interval)
Maini et al,[32] 1999	2/87	0/14	3.13 (0.06-Infinity)
Lipsky et al,[9] 2000	21/342	7/86	0.76 (0.30-2.18)
Furst et al,[6] 2003	4/318	6/318	0.66 (0.14-2.63)
Van de Putte et al,[10] 2003	4/214	0/70	6.33 (0.30-Infinity)
Weinblatt et al,[11] 2003	3/209	0/62	4.93 (0.19-Infinity)
Keystone et al,[6] 2004	16/419	1/200	7.90 (1.21-332.96)
St Clair et al,[7] 2004	40/749	6/291	2.68 (1.11-7.81)
Van de Putte et al,[33] 2004	11/434	0/110	15.34 (0.71-Infinity)
Westhovens et al,[34] 2004	25/721	6/361	2.13 (0.84-6.39)
Total	**126/3493**	**26/1512**	**2.01 (1.31-3.09)**

Test for overall effect:
Mantel-Haenszel $\chi^2 = 9.1$; $P = .002$



TNF indicates tumor necrosis factor. Size of the data markers is proportional to the statistical weight of the trial.

Bongartz T et al. JAMA 2006; 295: 2275-85

Adverse effects of biologics: a network meta-analysis and Cochrane overview (Review)

Table 5. Overall results of biologics versus control

Outcome	Effect estimate, OR (95% CI)
Serious adverse effects	1.11 (0.94, 1.31)
Serious infections	1.19 (0.94, 1.52)
Total adverse events	1.19 (1.09, 1.30)
Withdrawals due to adverse events	1.32 (1.06, 1.64)
TB reactivation	4.68 (1.18, 18.60)
Lymphoma	0.53 (0.17, 1.66)
Congestive heart failure	0.69 (0.18, 2.69)

Singh JA et al. Cochrane Database of Systematic Reviews 2011, issue2.

Risk of Tuberculosis in Patients Treated With Tumor Necrosis Factor Antagonists Due to Incomplete Prevention of Reactivation of Latent Infection

Table 3. Incidence rate (IR) of active tuberculosis stratified by tumor necrosis factor (TNF) antagonist after September 2003*

TNF antagonist	Patient-years	Cases	IR per 100,000 (95% CI)
Infliximab	1,303	5	383 (159–921)
Etanercept	1,740	2	114 (28–459)
Adalimumab	565	1	176 (24–1,254)

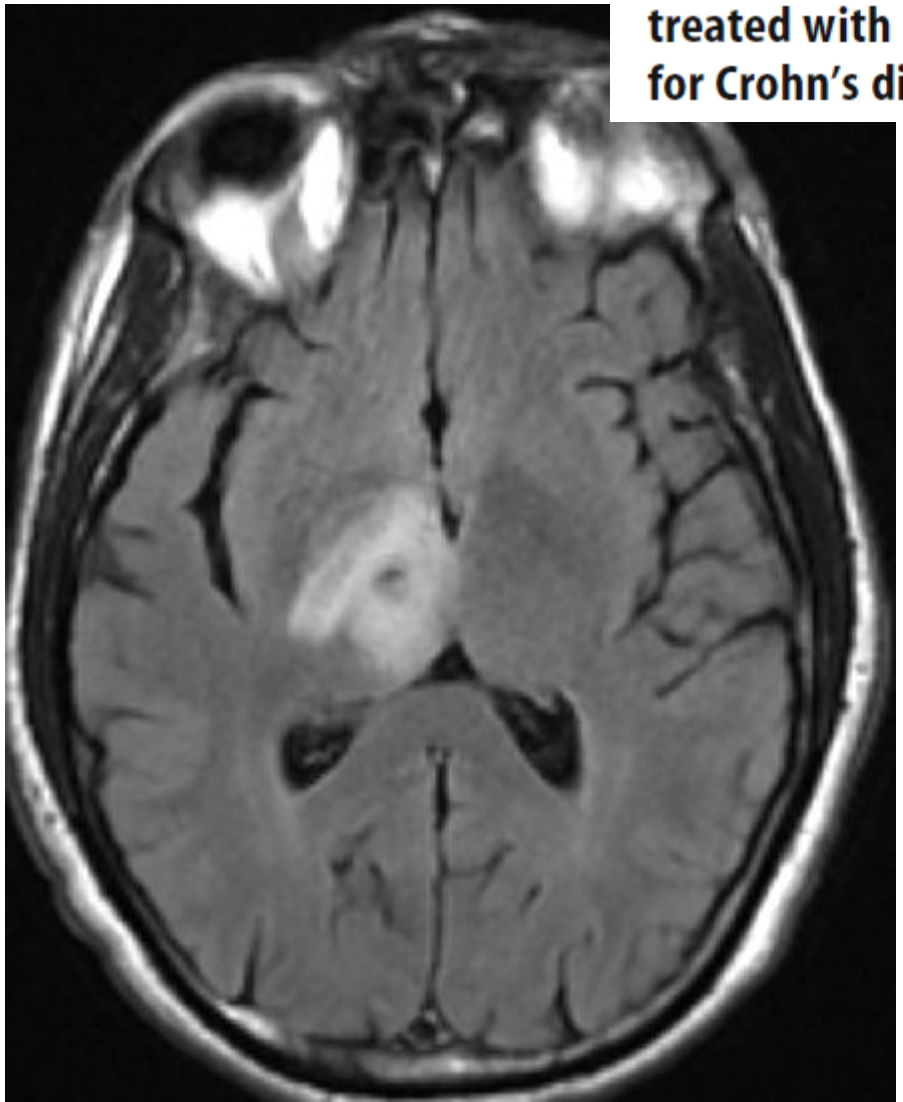
* 95% CI = 95% confidence interval.

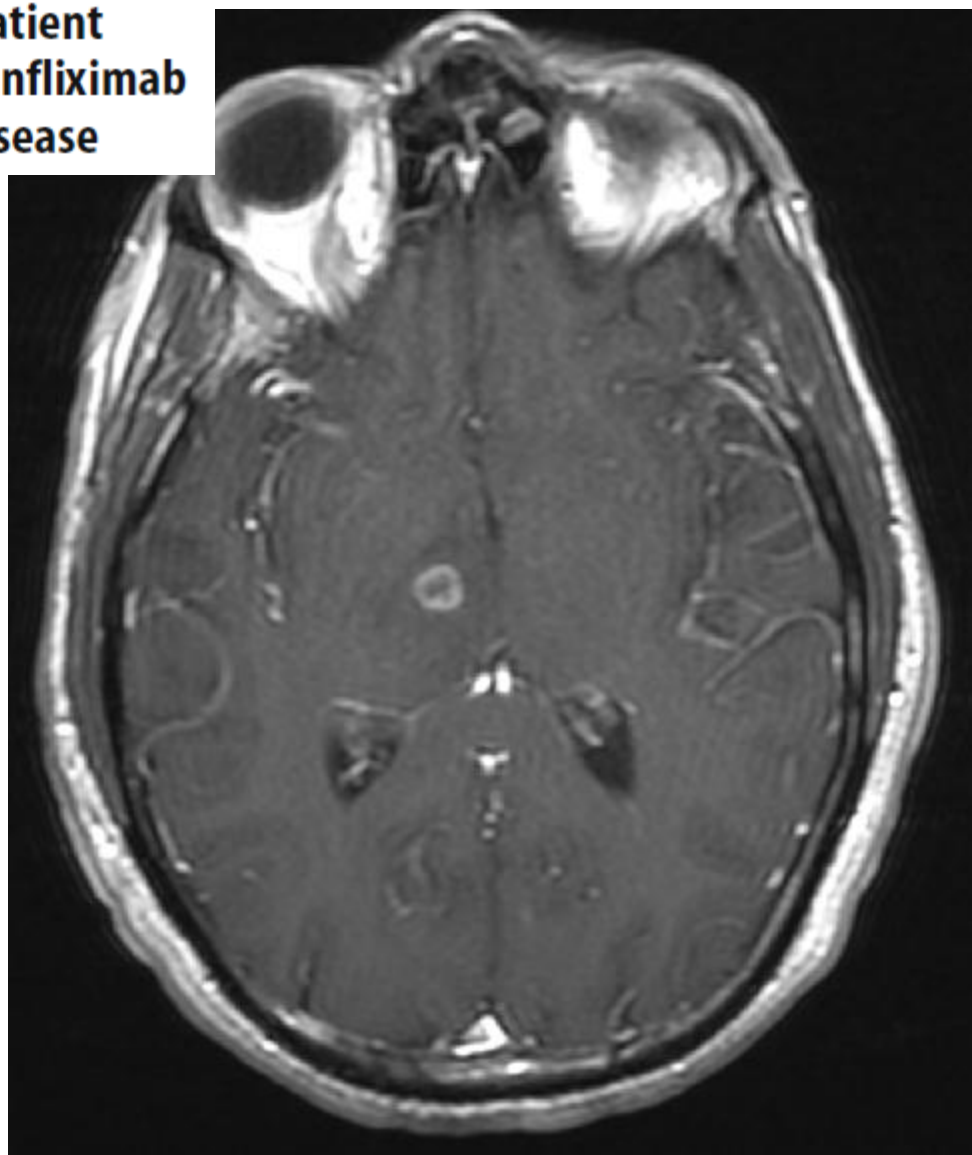
Gomez-Reino JJ et al. Arthtritis Rheum 2007; 57: 756-61

V. Galati
E. Grilli
E. Busi Rizzi
C. Prantera
N. Petrosillo

J Neurol (2008) 255:1981–1982

Cerebral tubercular lesions in a patient treated with Infliximab for Crohn's disease





Effectiveness of Recommendations to Prevent Reactivation of Latent Tuberculosis Infection in Patients Treated With Tumor Necrosis Factor Antagonists

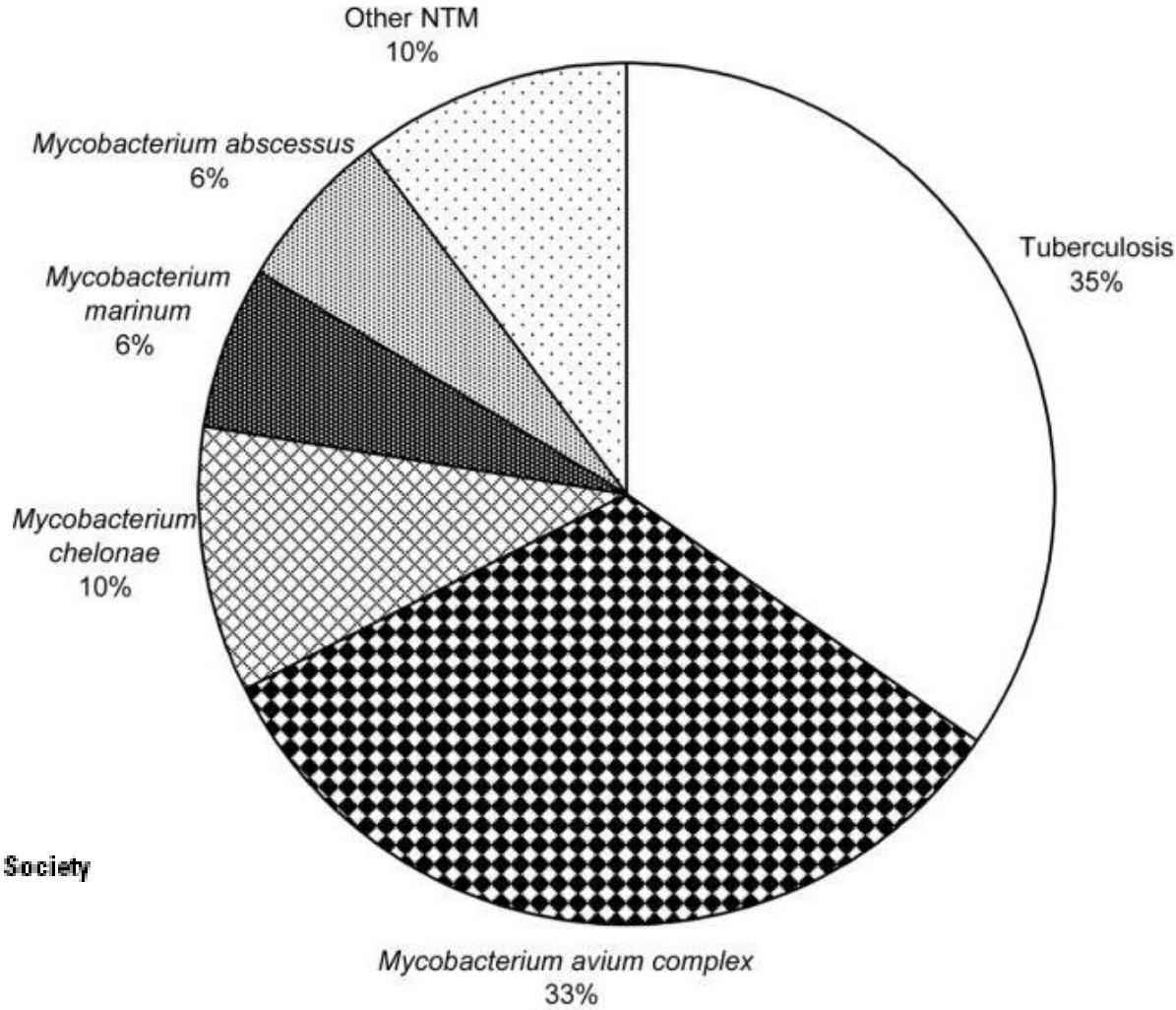
Table 2. Rate of active TB in the BIOBADASER cohort before and after the specific recommendations, and risk ratio for the incidence of active TB compared with the risk in the background Spanish population and in the EMECAR patients*

	Patient-years of exposure to TNF antagonists	No. of active TB cases	Active TB rate per 100,000 (95% CI)	IRR versus background (95% CI)	IRR versus EMECAR (95% CI)†
All TB cases					
Pre-OR	6,126	32	522 (369–738)	20.9 (12.0–36.8)	–
Post-OR	1,699	2	117 (29–470)	4.7 (0.5–18.9)	–
$IRR_{recommendations}$‡	–	–	0.22 (0.03–0.88)	–	–
TB cases with RA only					
Pre-OR	4,780	27	564 (387–823)	22.6 (12.6–40.6)	6.2 (2.6–16.9)
Post-OR	1,049	1	95 (13–676)	3.8 (0.1–23.3)	1.0 (0.02–8.2)
$IRR_{recommendations}$‡			0.17 (0.004–1.02)	–	–

* TB = tuberculosis; IRR = incidence risk ratio; 95% CI = 95% confidence interval (see Table 1 for other definitions).
† EMECAR patients were patients with rheumatoid arthritis (RA) who were not treated with TNF antagonists and were followed up for 5 years in the Morbidity and Clinical Expression of Rheumatoid Arthritis study.
‡ $IRR_{recommendations}$ = incidence risk ratio comparing the rates of active TB before (pre-OR) and following (post-OR) the official recommendations implemented on March 1, 2002 for the management of latent TB infection.

Carmona L et al. Arthritis Rheum 2005; 52: 1766-72

Mycobacterial and Other Serious Infections in Patients Receiving Anti–Tumor Necrosis Factor and Other Newly Approved Biologic Therapies: Case Finding through the Emerging Infections Network



Kevin L. Winthrop,[1] S. Yamashita,[1] S. E. Beekmann,[2] and P. M. Polgreen,[2] on behalf of the Infectious Diseases Society of America Emerging Infections Network

Subfulminant hepatitis B after infliximab in Crohn's disease: Need for HBV-screening?

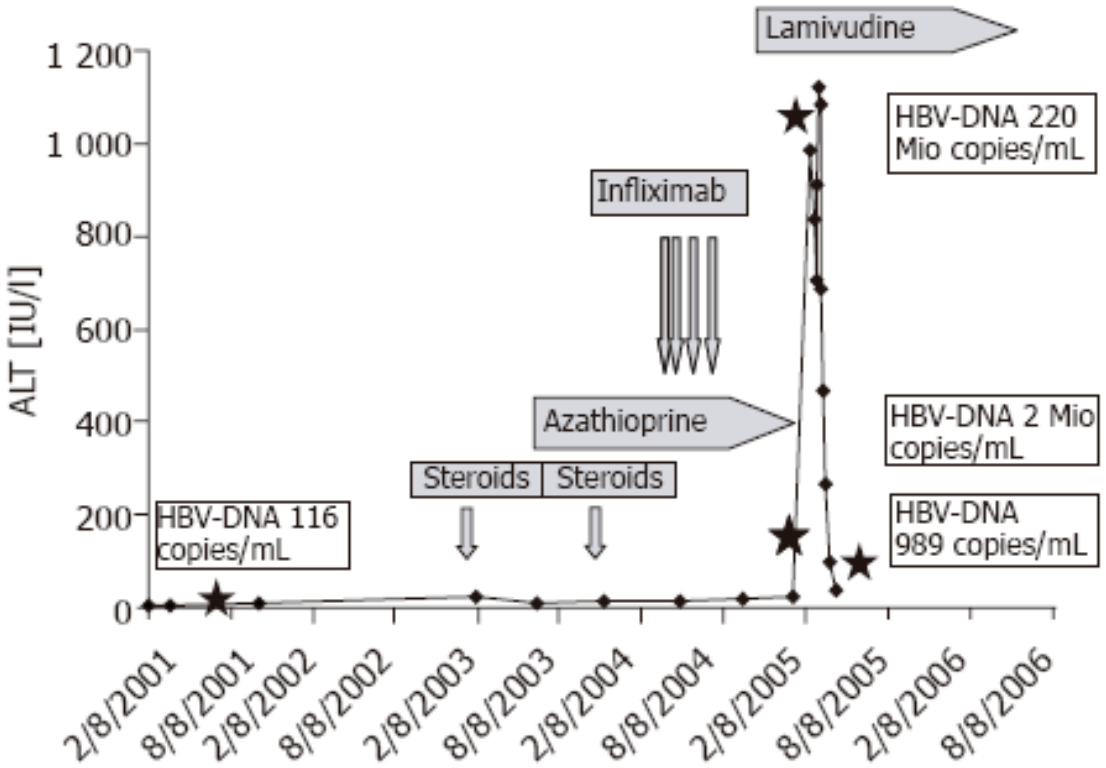


Figure 1 ALT remained within the normal range during therapy with prednisolone, azathioprine and during the infusions with infliximab. Only after the fourth infusion of infliximab, the patient developed a fulminant hepatitis with ALT up to 1 100 IU/L. HBV-DNA ( ) quantification showed 220 mio copies/mL. Lamivudine (150 mg/d) was started and led to a rapid decrease in transaminases and HBV-DNA.

Millonig G et al. World J Gastroenterol 2006;12:974-6.

P2054-ECCMID 2013

Risk factors for *Acinetobacter baumannii* colonization and infection among patients admitted to Intensive Care Units

M. Giannella*, S. Di Bella, G. D'Este, M.E. Halgass, A. Lappa, M.G. Tolusso, P. Orsi, M. Tronci, E. Grilli, N. Corradetti and N. Petrosillo.

National Institute for Infectious Diseases "L. Spallanzani", Rome, Italy

- 6 ICUs
- Screening at admission and during the stay (once weekly) if >48h
- 434 pts [20 (4.6%) colonized at admission]
- 17 pts (3.9%) became Ab infected during the ICU stay

Risk factors for MDR *A. baumannii* infection among ICU patients: P2054

Table 2	Univariate analysis HR (95% CI)	p	Multivariate analysis HR (95% CI)	P
Age	0.97 (0.95-1.01)	0.14		
Male sex	0.51 (0.16-1.61)	0.25		
APACHE II score	0.89 (0.79-1.01)	0.06		
Prior antibiotic therapy (30 d)	0.78 (0.23-2.61)	0.69		
Days of hospitalization before ICU admission	1.00 (0.98-1.02)	0.68		
ICU admission for medical condition	1.11 (0.33-3.68)	0.87		
Any infection at the time of ICU admission	1.41 (0.45-4.45)	0.55		
Antibiotic therapy during ICU stay				
Carbapenems	4.86 (1.42-16.58)	0.01	3.96 (1.14-13.76)	0.03
Cephalosporin 2nd/3th gen	0.23 (0.03-1.77)	0.16		
Piperacillin/tazobactam	1.12 (0.35-3.53)	0.85		
Fluoroquinolones	0.68 (0.15-3.14)	0.62		
AB colonization at the time of ICU admission	32.99 (8.19-133)	<0.001	24.29 (5.96-99.96)	<0.001

Infection control measures for Gram neg colonized patients

- Hand hygiene
- Physical separation of patients
- Education
- Detection/surveillance
- Environmental cleaning
- Antimicrobial stewardship
- Cohort patients' and staff
- Multifaceted approaches

Courtesy E Tacconelli-ESCMID/SHEA guidelines

An effective intervention to limit the spread of an epidemic carbapenem-resistant *Klebsiella pneumoniae* strain in an acute care setting: From theory to practice

The multidisciplinary intervention involved 3 key elements:
(1) guidelines for cohorting, cleaning, and screening;
(2) education and training; and
(3) Automatic instructions and CRKP alerts.

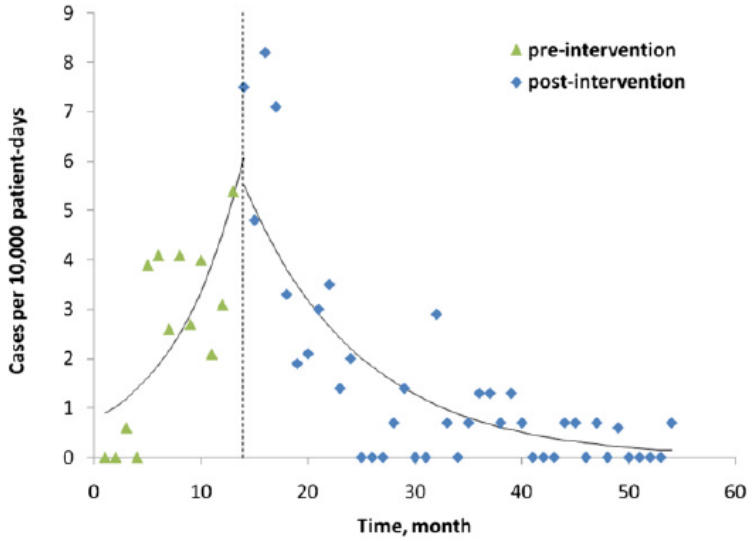


Fig 1. Monthly incidence of clinical CRKP cases per 10,000 patient-days at KMC from January 2006 through June 2010. The preintervention period was

Ciobotaro P et al. Am J Infect Control 2011;39:671-7.)

Clostridium difficile infection in Italian urban hospitals: data from 2006 through 2011

Stefano Di Bella[1], Maria Musso[1], Maria A Cataldo[1], Marcello Meledandri[2], Eugenio Bordi[1], Daniela Capozzi[3], Maria C Cava[4], Patrizia Chiaradonna[5], Grazia Prignano[6] and Nicola Petrosillo[1*]

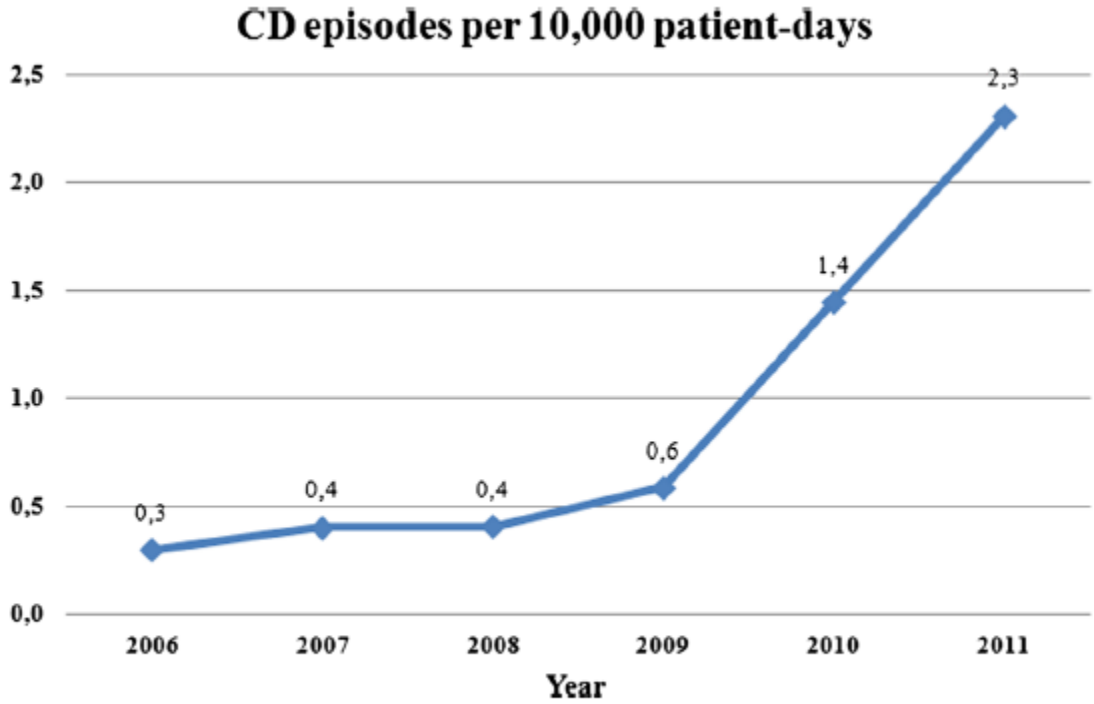


Figure 1 Distribution of Clostridium difficile infection (CDI) episode incidence per 10,000 patient-days from 2006 to 2011. Six hospitals in Rome, Italy.

Clostridium difficile infection in Italian urban hospitals: data from 2006 through 2011

Stefano Di Bella[1], Maria Musso[1], Maria A Cataldo[1], Marcello Meledandri[2], Eugenio Bordi[1], Daniela Capozzi[3], Maria C Cava[4], Patrizia Chiaradonna[5], Grazia Prignano[6] and Nicola Petrosillo[1*]

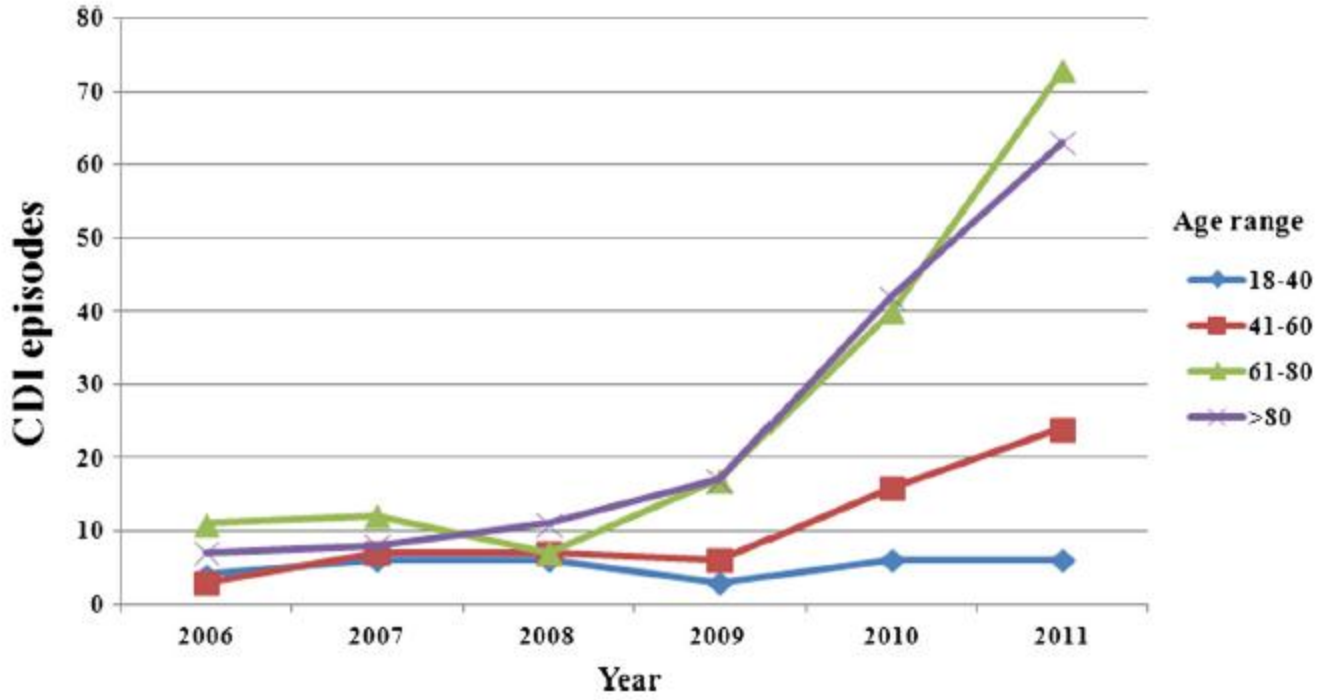
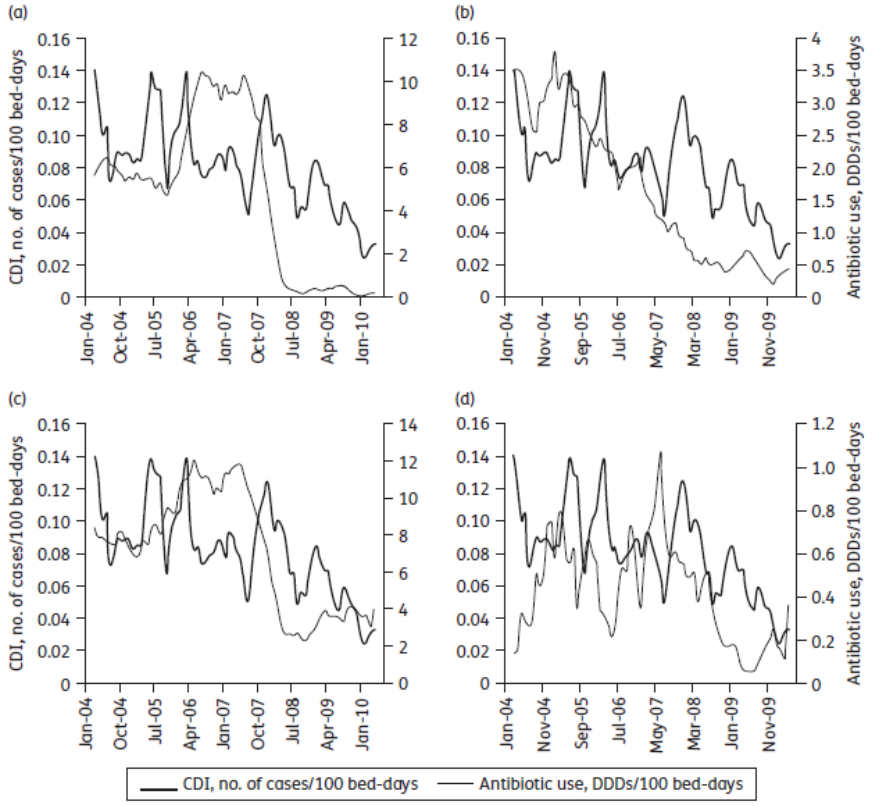


Figure 2 Clostridium difficile infection (CDI) episodes by year and age group.

J Antimicrob Chemother 2012; **67**: 2988–2996
doi:10.1093/jac/dks330 Advance Access publication 16 August 2012

Journal of Antimicrobial Chemotherapy

An evaluation of the impact of antibiotic stewardship on reducing the use of high-risk antibiotics and its effect on the incidence of *Clostridium difficile* infection in hospital settings



Aldeyab MA et al. JAC 2012

Rationale for Antibiotic Optimizaton: Balancing The Needs of Patient and Society

Inappropriate antibiotic therapy associated with higher mortality

Indiscriminate use of broad-spectrum antibiotics driving resistance

Richards GA. *Clin Microbiol Infect*. 2005;11(suppl):18-S22.

Antimicrobial Stewardship Programs in the ICU

ASPs are designed

- to optimize antimicrobial therapy for ICU patients,
- to improve patients' outcomes,
- ensure cost-effective therapy and
- reduce adverse effects associated with antimicrobial use, including antimicrobial resistance

MacDougall C et al. *Clin Microbiol Rev 2005; 18; 638–656*
Lesprit P et al. *Curr Opin Infect Dis 2008:21; 344–349*

Antimicrobial Stewardship Programs in the ICU

A variety of studies have demonstrated that systematic means to optimize antimicrobial use result in:

- improved patient safety,
- increased probability of minimizing antimicrobial resistance,
- fewer instances of unnecessary antimicrobial use, and
- **as a side effect of these, they reduce cost .**

Owens RC. *Infect Dis Clin N Am 2009; 23: 683–702 .*

Box 1. Elements to minimize the spread of and to adequately manage patients with multidrug-resistant organisms in intensive care.

Prevention of spread

- Reducing the antibiotic pressure
- Antimicrobial stewardship programs
- Infection control

Clinical management

- Timeliness, appropriateness and adequacy of the initial antibiotic regimen
- De-escalation therapy
- MIC-driven therapy
- Maximizing antimicrobial exposure at the infection site
- Better understanding of pharmacokinetic–pharmacodynamic relationships and the pattern of bactericidal activity

Petrosillo N. et al. *Expert Rev Anti Infect Ther 2010;* 8: 289–302.

Show Me the Money: Long-Term Financial Impact of an Antimicrobial Stewardship Program

Beardsley JR et al. ***Infect Control Hosp Epidemiol 2012;33:398-400***

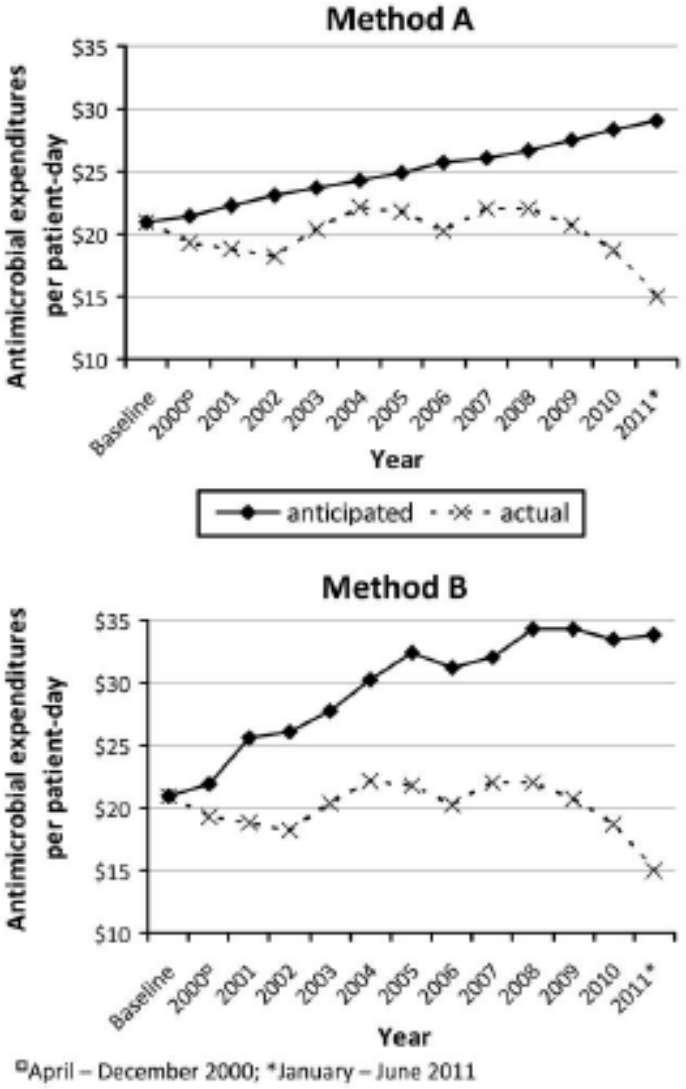


FIGURE 1. Comparison of anticipated versus actual antimicrobial expenditures per patient-day since the implementation of an antimicrobial stewardship program titled the Center for Antimicrobial Utilization Stewardship and Epidemiology, determined using an inflation rate based on the US consumer price index for medical care commodities (method A) and an anti-infective-specific index (method B).

TABLE 1. Summary of Annual Savings Associated with the Implementation of the Center for Antimicrobial Utilization Stewardship and Epidemiology, Determined Using an Inflation Rate Based on the US Consumer Price Index for Medical Care Commodities (Method A) and an Anti-Infective-Specific Index (Method B)

Year	Method A	Method B
2000[a]	158,161	229,076
2001	548,002	1,267,638
2002	806,393	1,446,883
2003	473,174	1,354,129
2004	244,160	1,555,048
2005	419,613	2,005,202
2006	983,690	2,172,756
2007	675,036	1,990,967
2008	817,503	2,557,972
2009	1,278,301	2,782,519
2010	2,175,927	3,456,373
2011[b]	1,770,827	2,406,399
Yearly average	920,070	2,064,441
Total savings	10,350,787	23,224,961

NOTE. Data are US dollars.

$$\text{annual savings} = [(\text{AE/pt-day}_{\text{anticipated}} - \text{AE/pt-day}_{\text{actual}}) \times \text{pt-days}] - \text{labor costs}.$$

IDSA STEWARDSHIP GUIDELINES

Dellit et al. CID 2007; 44:159-77

- **Feedback and audit**
- **Education**
- **Guidelines and clinical pathways**
- **Antimicrobial Management Teams**
- Antimicrobial cycling
- Antimicrobial order forms
- Combination therapies
- Pre-authorisation
- De-escalation-review; post-prescription review
- Dose optimisation
- Parenteral to oral conversion [IV-oral switch]

- Prospective audit with intervention and feedback to reduce inappropriate antimicrobial use (A-I)
- Formulary restriction and pre-authorization leading to reductions in antimicrobial use and cost (A-II)

ID Consultation

	P1	P2	P
Infections	205	197	
Appropriate therapy	141 (68.8%)	165 (83.7%)	0.0004
Adherence to the local guidelines for empirical antimicrobial therapy	63.4%	83.8%	0.0001

- shorter duration of antibiotic treatment ($P < .0001$), mechanical ventilation ($P < .0001$), ICU stay ($P < .0001$), and reduced in-hospital mortality ($P = .006$).

Raineri et al. Am J Infect Control 2008; 36:283-90

Impact of antimicrobial stewardship in critical care: a systematic review

IMPACT OF STEWARDSHIP ON SAFETY?

.“The reductions in antimicrobial utilization associated with stewardship interventions have not been associated with any worsening in nosocomial infection rates, length of stay or mortality among intensive care patients.”

“Stewardship interventions were associated with … fewer antibiotic adverse events.”

Kaki R et al. J Antimicrob Chemother 2011; 66: 1223–1230