



ACTUALIZACIÓN EN
LAS INFECCIONES RELACIONADAS
CON LA **ATENCIÓN SANITARIA**

PREVENCIÓN CON PROA

Dra. Silvia Gómez-Zorrilla

Servicio Enfermedades Infecciosas. Hospital del Mar-IMIM

sgomezzorrilla@psmar.cat

¿POR QUÉ?

Hiperconsumo generalizado de antibióticos



El plástico ya invade el océano Ártico



Científicas recogiendo muestras en el hielo del Ártico. / Alfred-Wegener-Institut / M. Tekman



Plastic pollution in the Arctic

Melanie Bergmann¹, France Collard², Joan Fabres^{3,4}, Geir W. Gabrielsen², Jennifer F. Provencher⁵, Chelsea M. Rochman⁶, Erik van Sebille^{7,8} and Mine B. Tekman¹

Abstract | Plastic pollution is now pervasive in the Arctic, even in areas with no apparent human activity, such as the deep seafloor. In this Review, we describe the sources and impacts of Arctic plastic pollution, including plastic debris and microplastics, which have infiltrated terrestrial and aquatic systems, the cryosphere and the atmosphere. Although some pollution is from local sources — fisheries, landfills, wastewater and offshore industrial activity — distant regions are a substantial source, as plastic is carried from lower latitudes to the Arctic by ocean currents, atmospheric transport and rivers. Once in the Arctic, plastic pollution accumulates in certain areas and affects local ecosystems. Population-level information is sparse, but interactions such as entanglements and ingestion of marine debris have been recorded for mammals, seabirds, fish and invertebrates. Early evidence also suggests interactions between climate change and plastic pollution. Even if plastic emissions are halted today, fragmentation of legacy plastic will lead to an increasing microplastic burden in Arctic ecosystems, which are already under pressure from anthropogenic warming. Mitigation is urgently needed at both regional and international levels to decrease plastic production and utilization, achieve circularity and optimize solid waste management and wastewater treatment.



Understanding drivers of antibiotic resistance genes in High Arctic soil ecosystems

Clare M. McCann^{a,b}, Beate Christgen^b, Jennifer A. Roberts^c, Jian-Qiang Su^d, Kathryn E. Arnold^e, Neil D. Gray^b, Yong-Guan Zhu^d, David W. Graham^{a,*}

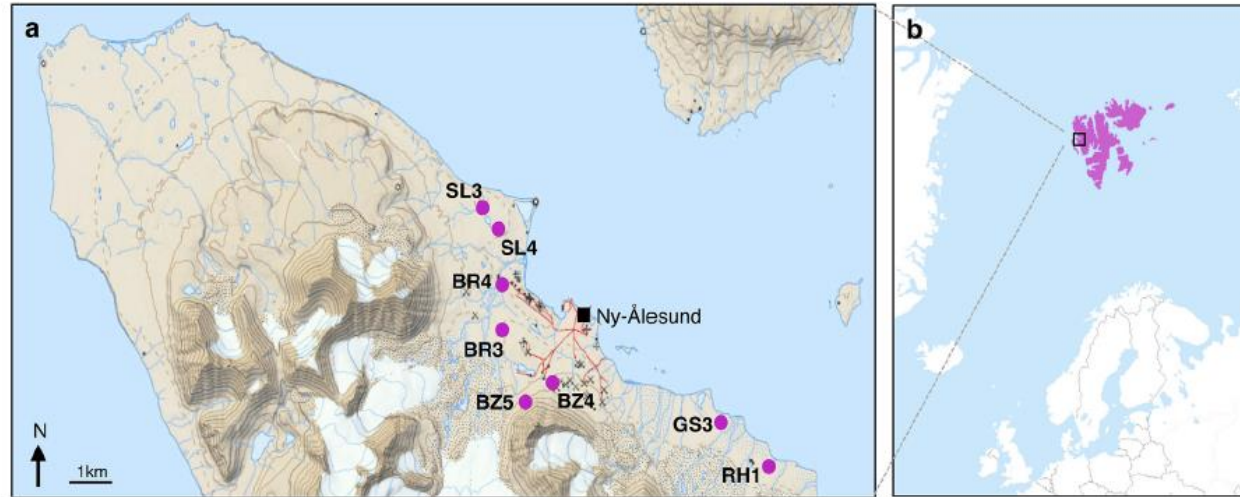


Fig. 1. Sampling locations of (a) the eight soil clusters in Kongsfjorden and (b) the geographical location of Svalbard, High Arctic. Topographic map has been adapted from the Norwegian Polar Institute.

away from the inlet (e.g., bla_{NDM-1} in five clusters). This observation is noteworthy because this study used samples collected in 2013, less than three years after the first detection of bla_{NDM-1} in surface seeps in urban India (Walsh et al., 2011). Although levels of bla_{NDM-1} are comparatively localized in Kongsfjorden (with the exception of SL3) and pose no health threat, its detection reinforces how rapidly AR can globalize. Results here underscore the value of characterizing remote locations with minimal “impact”, providing a baseline for quantifying the spread of AR around the world.

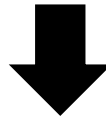


Características especiales de los antibióticos



Emergencia de patógenos multirresistentes a nivel mundial

- ✓ Escaso desarrollo de nuevos antibióticos
- ✓ Ausencia de opciones terapéuticas efectivas



Responsabilidad de utilizar los antibióticos de forma racional

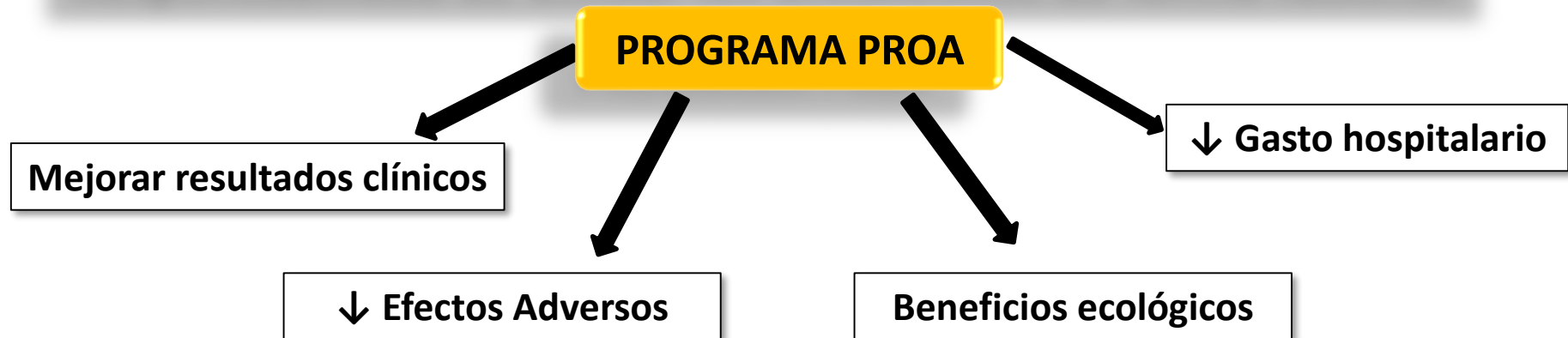
PROGRAMA PROA

Mejorar resultados clínicos

↓ Efectos Adversos

Beneficios ecológicos

↓ Gasto hospitalario



What is Antimicrobial Stewardship?

Thus, we will define an antimicrobial stewardship program as an ongoing effort by a health care institution to optimize antimicrobial use among hospitalized patients in order to improve patient outcomes, ensure cost-effective therapy, and reduce adverse sequelae of antimicrobial use (including antimicrobial resistance).

C MacDougall and RE. Polk. Clinical Microbiological Review, 2005

ANTIMICROBIAL STEWARDSHIP

A coherent set of actions which promote using antimicrobials in ways that ensure sustainable access to effective therapy for all who need them.

¿CÓMO?

A black sign with white text is mounted on a black pole. The sign is split into two horizontal sections. The top section contains the word "LESS" in large, bold, white capital letters, followed by the word "IS" in smaller, white capital letters. The bottom section contains the word "MORE" in large, bold, white capital letters. The background is a clear blue sky with scattered white clouds.

LESS IS MORE

What is Antimicrobial Stewardship?

Coordinated interventions designed to improve and measure the appropriate use of antibiotic agents by promoting the selection of the optimal drug regimen including **dosing, duration of therapy, and route of administration**".

The benefits of antibiotic stewardship include improved patient outcomes, reduced adverse events including *Clostridium difficile* infection (CDI), improvement in rates of antibiotic susceptibilities to targeted antibiotics, and optimization of resource utilization across the continuum of care.

Guideline for Implementing an Antibiotic Stewardship Program, IDSA. CID 2016;62:e51e77

THE FUTURE OF **ANTIBIOTICS** DEPENDS ON ALL OF US



Importancia del
diagnóstico
microbiológico

Reevaluar necesidad
de antibiótico

Espectro
antibiótico

Secuenciación

Dosis

Duración

SECUENCIACIÓN ORAL

XI. Should ASPs Implement Interventions to Increase Use of Oral Antibiotics as a Strategy to Improve Outcomes or Decrease Costs?

Recommendation

12. We recommend ASPs implement programs to increase both appropriate use of oral antibiotics for initial therapy and the timely transition of patients from IV to oral antibiotics (*strong recommendation, moderate-quality evidence*).

Comment: Programs to increase the appropriate use of oral antibiotics can reduce costs and length of hospital stay. IV-to-oral conversion of the same antibiotic is less complicated than other strategies and is applicable to many health-care settings. The conduct of those programs should be integrated into routine pharmacy activities. ASPs should implement strategies to assess patients who can safely complete therapy with an oral regimen to reduce the need for IV catheters and to avoid outpatient parenteral therapy.

SECUENCIACIÓN ORAL

- **ESCALAS PARA EVALUAR LA ESTABILIDAD CLÍNICA**

CRITERIOS HALM

Temperatura $\leq 37.8^{\circ}\text{C}$

FC ≤ 100 bpm

FR ≤ 24 bpm

TAS ≥ 90 mm Hg

Sat $\geq 90\%$ or $\text{paO}_2 \geq 60$ mm Hg

Nivel de consciencia conservado

Tolerancia ingesta oral

CRITERIOS ATS

Mejoría sintomatología respiratoria (tos, disnea)

$\leq 37.8^{\circ}\text{C}$ durante >8 h

Normalización leucocitosis ($\downarrow 10\%$ respecto días previos)

Posibilidad toma v.o. medicación

- **UTILIDAD DE BIOMARCADORES:** Asociados a criterios clínicos (PCR, PCT...)

An evaluation of clinical stability criteria to predict hospital course in community-acquired pneumonia

A. R. Akram¹, J. D. Chalmers¹, J. K. Taylor², J. Rutherford², A. Singanayagam¹ and A. T. Hill¹

TABLE 2. Time taken to achieve clinical stability (median (IQR)) in all patients and stratified by CURB-65

Stratification	N	30-day mortality n (%)	Halm's criteria	ATS criteria	CURB	CRP 50% reduction
All patients	1079	93 (8.6%)	3 (2–6)	3 (2–5)	3 (0–5)	3 (3–6)
CURB-65	N	30-day mortality	Halm's criteria	ATS criteria	CURB	CRP 50% reduction
0	199	2 (1.0%)	2 (0–3)	2 (1–3)	0	3 (2–4)
1	243	9 (3.7%)	2 (1–4)	2 (1–4)	1 (0–3)	3 (2–5)
2	286	15 (5.2%)	3 (1–6)	3 (2–5)	3 (2–6)	3 (3–6)
3	206	25 (12.1%)	4 (2–7)	3 (2–7)	4 (2–6)	4 (3–8)
4	119	31 (26.1%)	7 (3–8)	5 (3–8)	5 (3–8)	6 (3–8)
5	26	11 (42.3%) [#]	8 (7–8) [#]	8 (5–8) [#]	6 (3–8) [#]	7 (3–8) [#]

[#]p < 0.001 across CURB-65 severity class (Kruskal–Wallis test).

TABLE 3. Time taken to achieve clinical stability (median (IQR)) stratified by PSI

PSI	N	30-day mortality	Halm's criteria	ATS criteria	CURB	CRP 50% reduction
1	121	0 (0%)	1 (0–3)	2 (1–3)	0	3 (2–3)
2	228	2 (0.9%)	2 (1–3)	2 (1–4)	1 (0–4)	3 (2–4)
3	212	6 (2.8%)	3 (1–5)	2 (1–4)	2 (0–4)	3 (3–6)
4	317	31 (9.8%)	3 (2–7)	3 (2–6)	3 (1–6)	4 (3–7)
5	201	54 (26.9%) [#]	7 (5–8) [#]	7 (3–8) [#]	5 (3–8) [#]	6 (4–8) [#]

[#]p < 0.001 across PSI severity class (Kruskal–Wallis test).

Time taken to achieve clinical stability

The median time taken to achieve clinical stability for each criterion stratified by the Pneumonia Severity Index (PSI) and CURB-65 class on admission are shown in Tables 2 and 3. The median time to clinical stability was 3 days for all criteria (Table 2 and 3). Patients with more severe pneumonia on admission assessed by both CURB-65 and PSI took a significantly longer time to reach clinical stability. This association was true for all the methods available to assess clinical stability (p < 0.001 for all criteria).

DURACIÓN ANTIBIÓTICOTERAPIA

Duración excesiva → responsable la mayoría de los efectos adversos de los antibióticos

Potential advantages of short-duration antibiotic therapy

Decreased risk of:

- Catheter-associated complications, including bloodstream infection
- Antibiotic-associated infections (*Clostridium difficile* diarrhoea, candidiasis)
- Antibiotic resistance development
- Antibiotic-associated organ toxicity
- Drug interactions

Decreased costs

Improved convenience and treatment compliance

DURACIÓN ANTIBIÓTICOTERAPIA

- Numerosos ensayos clínicos randomizados avalan la utilización de pautas cortas
- Individualizar duración vs. “duraciones estándar”

Table 2. Meta-analyses and Examples of Randomized Clinical Studies Comparing Shorter Versus Longer Duration of Antibiotics

Reference	Clinical Condition/Population	Treatment Duration, d	Clinical Outcome ^a
Meta-analyses			
Dimopoulos et al, 2008 [123]	Adults and children with CAP	3–7 vs 5–10	Clinical success, relapse, mortality, adverse events
Pugh et al, 2011 [124]	Adults with VAP	7–8 vs 10–15	Antibiotic-free days ^b , recurrence ^b
Dimopoulos et al, 2013 [125]	Adults with VAP	7–8 vs 10–15	Relapse, mortality, antibiotic-free days ^c
Randomized clinical trials			
Chastre et al, 2003 [127]	Adults with VAP	8 vs 15	Mortality, recurrent infections ^d
El Moussaoui et al, 2006 [128]	Adults with CAP	3 vs 5	Clinical and radiological success
Greenberg et al, 2014 [129]	Children with CAP	5 vs 10	Treatment failure ^e
Hepburn et al, 2004 [130]	Adults with cellulitis	5 vs 10	Clinical success
Sandberg et al, 2012 [131]	Adult females with acute pyelonephritis	7 vs 14	Clinical efficacy, adverse events
Talan et al, 2000 [132]	Women with acute uncomplicated pyelonephritis	7 vs 14	Bacteriologic and clinical cure ^f
Runyon et al, 1991 [133]	Adults with spontaneous bacterial peritonitis	5 vs 10	Mortality, bacteriologic cure, recurrence
Saini et al, 2011 [134]	Neonatal septicemia	2–4 vs 7 (with sterile culture)	Treatment failure
Sawyer et al, 2015 [135]	Adults with intra-abdominal infection	4 vs ≤10	Composite of surgical site infection, recurrent intra-abdominal infection, or death
Bernard et al, 2015 [136]	Adults with vertebral osteomyelitis	42 vs 84	Cure at 1 y by independent committee and secondary outcomes

Comparison of Short-Course (5 Days) and Standard (10 Days) Treatment for Uncomplicated Cellulitis

MAJ Matthew J. Hepburn, MC, USA; COL David P. Dooley, MC, USA;
MAJ Peter J. Skidmore, MC, USA; MAJ Michael W. Ellis, MC, USA;
MAJ William F. Starnes, MSC, USA; LTC William C. Hasewinkle, MC, USA

Background: Cellulitis is a condition routinely encountered in the primary care setting. No previous study has compared a short (5 days) vs standard (10 days) course of therapy of the same antibiotic in patients with uncomplicated cellulitis.

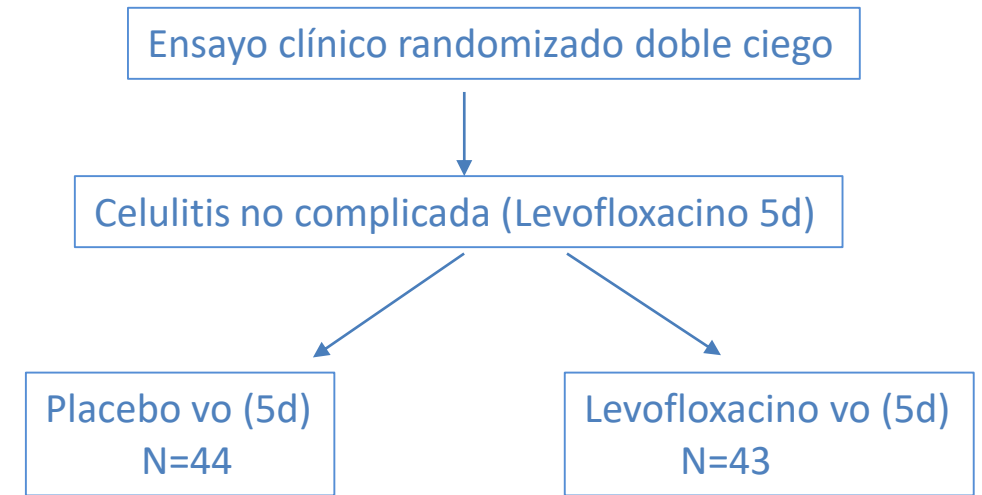
Methods: We performed a randomized, double-blind, placebo-controlled trial to determine if 5 days of therapy has equal efficacy to 10 days of therapy for patients with cellulitis. Of 121 enrolled subjects evaluated after 5 days of therapy for cellulitis, 43 were randomized to receive 5 more days of levofloxacin therapy (10 days total antibiotic treatment), and 44 subjects to receive 5 more days of placebo therapy (5 days of total antibiotic treatment). Levofloxacin was given at a dose of 500 mg/d. Subjects were not randomized if they had worsening cellulitis, a persistent nidus of infection, a lack of any clinical im-

provement, or abscess formation within the first 5 days of therapy. The main outcome measure was resolution of cellulitis at 14 days, with absence of relapse by 28 days, after study enrollment.

Results: Eighty-seven subjects were randomized and analyzed by intention to treat. There was no significant difference in clinical outcome between the 2 courses of therapy (success in 42 [98%] of 43 subjects receiving 10 days of antibiotic, and 43 [98%] of 44 subjects receiving 5 days of antibiotic) at both 14 and 28 days of therapy.

Conclusion: In patients with uncomplicated cellulitis, 5 days of therapy with levofloxacin appears to be as effective as 10 days of therapy.

Arch Intern Med. 2004;164:1669-1674



Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America

Dennis L. Stevens,¹ Alan L. Bisno,² Henry F. Chambers,³ E. Patchen Dellinger,⁴ Ellie J. C. Goldstein,⁵ Sherwood L. Gorbach,⁶ Jan V. Hirschmann,⁷ Sheldon L. Kaplan,⁸ Jose G. Montoya,⁹ and James C. Wade¹⁰

Therapy for typical cases of cellulitis should include an antibiotic active against streptococci (Table 2). A large percentage of patients can receive oral medications from the start for typical cellulitis [56], and suitable antibiotics for most patients include penicillin, amoxicillin, amoxicillin-clavulanate, dicloxacillin, cephalexin, or clindamycin. In cases of uncomplicated cellulitis, a 5-day course of antimicrobial therapy is as effective as a 10-day course, if clinical improvement has occurred by 5 days [57]. In a

Ciprofloxacin for 7 days versus 14 days in women with acute pyelonephritis: a randomised, open-label and double-blind, placebo-controlled, non-inferiority trial

Torsten Sandberg, Gunilla Skoog, Anna Bornefalk Hermansson, Gunnar Kahlmeter, Nils Kuylenstierna, Anders Lannergård, Gisela Otto, Bo Settergren, Gunilla Stridh Ekman

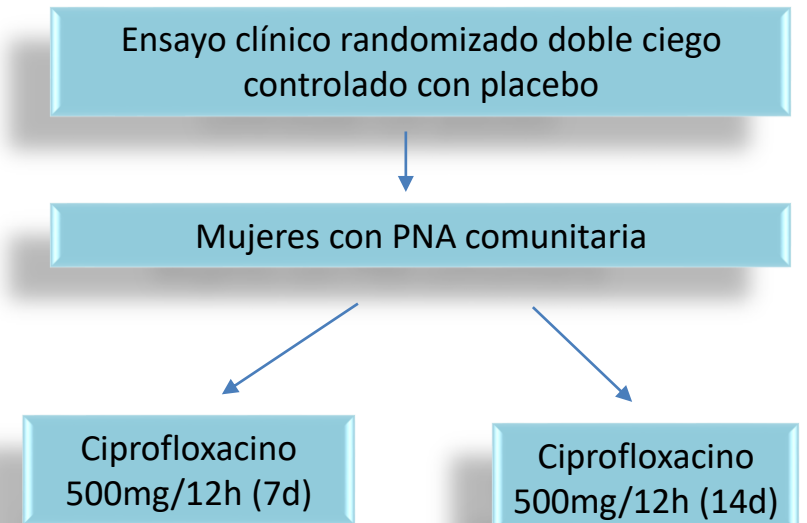
Summary

Background Acute pyelonephritis is a common infection in adult women, but there is a paucity of controlled trials of its treatment and the optimum duration of antibiotic treatment has not been properly defined. We compared the efficacy of ciprofloxacin for 7 days and 14 days in women with community-acquired acute pyelonephritis.

Methods In a prospective, non-inferiority trial undertaken at 21 centres of infectious diseases in Sweden, women (aged ≥ 18 years) who were not pregnant and had a presumptive diagnosis of acute pyelonephritis were randomly assigned to oral treatment with ciprofloxacin 500 mg twice daily for 7 days or 14 days. The first week was open label. A computer-generated randomisation list in block sizes of two was used for treatment allocation in a 1:1 ratio. The study was double-blind and placebo-controlled during the second week of treatment, which was either continuation of ciprofloxacin 500 mg or placebo tablets twice daily according to the randomisation code. Patients, carers, site investigators, and trial coordinating centre staff were masked to group assignment. The primary endpoint was the clinical and bacteriological outcome 10–14 days after completion of treatment with active drug. Analysis was by per protocol. This trial is registered with EudraCT, number 2005-004992-39, and ClinicalTrials.gov, number ISRCTN73338924.

Findings 126 of 248 patients were randomly assigned to 7 days and 122 to 14 days of ciprofloxacin. 73 and 83 patients, respectively, were analysed. Short-term clinical cure occurred in 71 (97%) patients treated with ciprofloxacin for 7 days and 80 (96%) treated for 14 days (difference -0.9% ; 90% CI -6.5 to 4.8 ; $p=0.004$; non-inferiority test). Cumulative efficacy at long-term follow-up was 93% in each group (68 of 73 vs 78 of 84; -0.3% ; -7.4 to 7.2 ; $p=0.015$). Both regimens were well tolerated. Two patients discontinued ciprofloxacin because of myalgia with 7 days of treatment and itching exanthema with 14 days. Four (5%) of 86 patients assigned to 7 days of treatment who complied with study criteria and six (6%) of 93 assigned to 14 days reported an adverse event after the first week of treatment that was possibly or probably related to the study drug. In those assigned to 7 days, no patient had mucosal candida infection after the first week versus five treated for 14 days ($p=0.036$).

Interpretation Our results show that acute pyelonephritis in women, including older women and those with a more severe infection, can be treated successfully and safely with oral ciprofloxacin for 7 days. Short courses of antibiotics should be favoured in an era of increasing resistance.



Panel: Research in context

Systematic review

We identified references for this study by searching PubMed with the terms “acute pyelonephritis” with “treatment”, “clinical trials”, and “female”. Few controlled trials have been done to define the optimum duration of treatment for women with acute pyelonephritis. For many years, 10–14 days was the appropriate treatment as per guideline recommendations. Shorter duration is desirable in an era of increasing antibiotic resistance. In one study, a ciprofloxacin course of 7 days was efficacious for treatment of young women with uncomplicated pyelonephritis in an outpatient setting. Whether short treatment courses are applicable to older women or those with a more severe infection has not been settled.

Interpretation

The results of this randomised, double-blind, and placebo-controlled trial confirm and extend the findings from a previous study of young women with uncomplicated pyelonephritis. Our findings show that a regimen of ciprofloxacin 500 mg twice daily for 7 days was not inferior to a course of 14 days in women with acute pyelonephritis, neither at early or long-term follow-up. Our results are also valid for older women in whom positive blood cultures were more common and for those with a more severe infection. The findings should not be extrapolated to other classes of antibiotics.

	Ciprofloxacin for 7 days	Ciprofloxacin for 14 days	Difference (90% CI)	Non-inferiority test p value
Short-term efficacy	73	83		
Cure	71 (97%)	80 (96%)	-0.9% (-6.5 to 4.8)	0.004
Clinical failure or recurrent symptomatic urinary tract infections	2 (3%)	3 (4%)	..	
Cumulative efficacy	73	84		
Cure	68 (93%)	78 (93%)	-0.3% (-7.4 to 7.2)	0.015
Clinical failure or recurrent symptomatic urinary tract infections	5 (7%)	6 (7%)	..	

Data are number (%), unless otherwise indicated.

Table 3: Clinical outcomes in the per-protocol population

Trial of short-course antimicrobial therapy for intraabdominal infection (Study to Optimize Peritoneal Infection Therapy: STOP-IT)

- 518 pacientes con infección intraabdominal complicada con control adecuado de foco

Tratamiento antibiótico de corta duración (4±1 d)
N=258



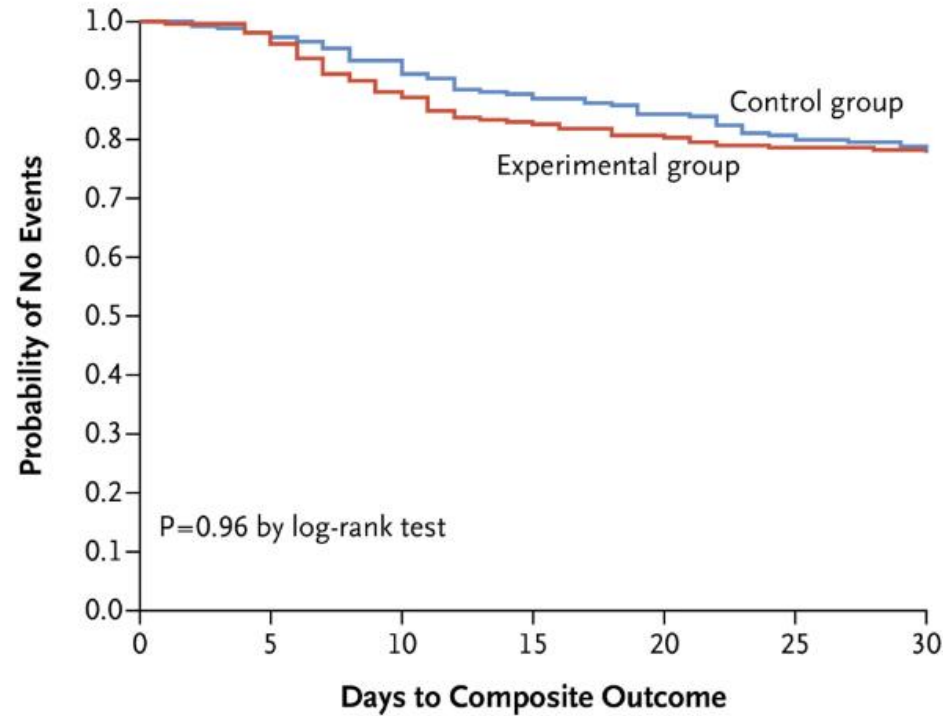
Tratamiento antibiótico hasta 48h después de resolución síntomas/signos FIL
N= 260

Baseline Demographic and Clinical Characteristics, According to Study Group.*

Variable	Control Group (N = 260)	Experimental Group (N = 258)
Age — yr	52.2±1.0	52.2±1.0
Male sex — no. (%)	145 (55.8)	144 (55.8)
Organ of origin — no. (%)		
Colon or rectum	80 (30.8)	97 (37.6)
Appendix	34 (13.1)	39 (15.1)
Small bowel	31 (11.9)	42 (16.3)
Source-control procedure — no. (%)		
Percutaneous drainage	86 (33.1)	86 (33.3)
Resection and anastomosis or closure	69 (26.5)	64 (24.8)
Surgical drainage only	55 (21.2)	54 (20.9)
Resection and proximal diversion	27 (10.4)	37 (14.3)
Simple closure	20 (7.7)	12 (4.7)
Surgical drainage and diversion	3 (1.2)	4 (1.6)

STOP-IT Clinical Trial New England 2015 21, 372:1996-2005

* Plus-minus values are means ±SE. There were no significant differences between the groups (P<0.05).



No. at Risk								
Control group	260	255	243	228	219	210	205	
Experimental group	258	253	227	214	208	203	202	

Figure 2. Kaplan-Meier Time-to-Event Curves for the Composite Primary Outcome, According to Treatment Group
 The composite primary outcome was surgical-site infection, recurrent intraabdominal infection, or death.

Primary and Major Secondary Outcomes.*

Variable	Control Group (N = 260)	Experimental Group (N = 257)	P Value
Primary outcome: surgical-site infection, recurrent intraabdominal infection, or death — no. (%)	58 (22.3)	56 (21.8)	0.92
Surgical-site infection	23 (8.8)	17 (6.6)	0.43
Recurrent intraabdominal infection	36 (13.8)	40 (15.6)	0.67
Death	2 (0.8)	3 (1.2)	0.99
Time to event — no. of days after index source-control procedure			
Diagnosis of surgical-site infection	15.1±0.6	8.8±0.4	<0.001
Diagnosis of recurrent intraabdominal infection	15.1±0.5	10.8±0.4	<0.001
Death	19.0±1.0	18.5±0.5	0.66
Secondary outcome			
Surgical-site infection or recurrent intraabdominal infection with resistant pathogen — no. (%)	9 (3.5)	6 (2.3)	0.62
Site of extraabdominal infection — no. (%)			
Any site [†]	13 (5.0)	23 (8.9)	0.11
Urine	10 (3.8)	13 (5.1)	0.65
Blood	3 (1.2)	5 (1.9)	0.71
Lung	3 (1.2)	3 (1.2)	0.99
Area of skin other than surgical site	1 (0.4)	4 (1.6)	0.36
Vascular catheter	0 (0)	2 (0.8)	0.47
<i>Clostridium difficile</i> infection — no. (%)	3 (1.2)	5 (1.9)	0.71
Extraabdominal infection with resistant pathogen — no. (%)	6 (2.3)	2 (0.8)	0.29
Duration of outcome — days			
Antimicrobial therapy for index infection			<0.001
Median	8	4	
Interquartile range	5–10	4–5	
Antimicrobial-free days at 30 days			<0.001
Median	21	25	
Interquartile range	18–25	21–26	
Hospitalization after index procedure			0.48
Median	7	7	
Interquartile range	4–11	4–11	
Hospital-free days at 30 days			0.22
Median	23	22	
Interquartile range	18–26	16–26	

* Plus-minus values are means ±SE.

Seven Versus 14 Days of Antibiotic Therapy for Uncomplicated Gram-negative Bacteremia: A Noninferiority Randomized Controlled Trial

- Hospital GNB bacteremia at day 7 of covering antibiotic therapy, if hemodynamically stable and afebril for ≥ 48 h

Ensayo clínico randomizado de no inferioridad

Pacientes hospitalizados con bacteriemia BGN día 7 (estables ≥ 48 h y control de foco)

Intervención (7d)

Control (14 d)

CRITERIOS EXCLUSIÓN:

- Foco no controlado
- Otros focos
- Polimicrobiano
- Inmunosupresión

Variable	Short-duration Arm (7 d) (n = 306)	Long-duration Arm (14 d) (n = 298)
Patient characteristics		
Age, y, median (IQR)	71 (61.8–81)	71 (61–80)
Sex, female	156 (51.0)	163 (54.7)
Appropriate empirical therapy administered within 48 h	260 (85.0)	242 (81.2)
Bacteria type ^c		
<i>Escherichia coli</i>	186 (60.8)	194 (65.1)
<i>Klebsiella</i> spp	47 (15.3)	33 (11.1)
Other Enterobacteriaceae	40 (13.1)	43 (14.4)
<i>Acinetobacter</i> spp	2 (0.7)	4 (1.3)
<i>Pseudomonas</i> spp	28 (9.2)	20 (6.7)
Other	3 (1)	4 (1.3)
MDR gram-negative bacteremia ^d	58 (18.9)	51 (17.1)
Source of bacteremia		
Urinary tract	212 (69.3)	199 (66.8)
Primary bacteremia	23 (7.5)	28 (9.4)
Abdominal	37 (12.1)	34 (11.4)
Respiratory	14 (4.6)	10 (3.4)
Central venous catheter	15 (4.9)	23 (7.7)
Skin and soft tissue	5 (1.6)	4 (1.3)

Seven Versus 14 Days of Antibiotic Therapy for Uncomplicated Gram-negative Bacteremia: A Noninferiority Randomized Controlled Trial

Dafna Yahav,^{1,2} Erica Franceschini,³ Fidi Koppel,⁴ Adi Turjeman,^{2,5} Tanya Babich,^{2,5} Roni Bitterman,⁴ Ami Neuberger,^{4,6} Nesrin Ghanem-Zoubi,⁴ Antonella Santoro,³ Noa Eliakim-Raz,^{1,2} Barak Pertzov,⁵ Tali Steinmetz,⁵ Anat Stern,⁴ Yaakov Dickstein,⁴ Elias Maroun,⁴ Hiba Zayyad,⁴ Jihad Bishara,^{1,2} Danny Alon,⁷ Yonatan Edel,^{2,8} Elad Goldberg,⁹ Claudia Venturelli,³ Cristina Mussini,³ Leonard Leibovici,^{2,5} Mical Paul^{4,6}; for the Bacteremia Duration Study Group^a

¹Infectious Diseases Unit, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, and ²Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel; ³Clinic of Infectious Diseases, University of Modena and Reggio Emilia, Italy; ⁴Infectious Diseases Institute, Rambam Health Care Campus, Haifa, ⁵Department of Medicine E, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, ⁶The Ruth and Bruce Rappaport Faculty of Medicine, Technion–Israel Institute of Technology, Haifa, and ⁷Department of Medicine B, ⁸Department of Medicine C, and ⁹Department of Medicine F, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, Israel

(See the Editorial Commentary by Daneman and Fowler on pages 1099–100.)

Background. Gram-negative bacteremia is a major cause of morbidity and mortality in hospitalized patients. Data to guide the duration of antibiotic therapy are limited.

Methods. This was a randomized, multicenter, open-label, noninferiority trial. Inpatients with gram-negative bacteremia, who were afebrile and hemodynamically stable for at least 48 hours, were randomized to receive 7 days (intervention) or 14 days (control) of covering antibiotic therapy. Patients with uncontrolled focus of infection were excluded. The primary outcome at 90 days was a composite of all-cause mortality; relapse, suppurative, or distant complications; and readmission or extended hospitalization (>14 days). The noninferiority margin was set at 10%.

Results. We included 604 patients (306 intervention, 298 control) between January 2013 and August 2017 in 3 centers in Israel and Italy. The source of the infection was urinary in 411 of 604 patients (68%); causative pathogens were mainly Enterobacteriaceae (543/604 [90%]). A 7-day difference in the median duration of covering antibiotics was achieved. The primary outcome occurred in 140 of 306 patients (45.8%) in the 7-day group vs 144 of 298 (48.3%) in the 14-day group (risk difference, –2.6% [95% confidence interval, –10.5% to 5.3%]). No significant differences were observed in all other outcomes and adverse events, except for a shorter time to return to baseline functional status in the short-course therapy arm.

Conclusions. In patients hospitalized with gram-negative bacteremia achieving clinical stability before day 7, an antibiotic course of 7 days was noninferior to 14 days. Reducing antibiotic treatment for uncomplicated gram-negative bacteremia to 7 days is an important antibiotic stewardship intervention.



AMERICAN
SOCIETY FOR
MICROBIOLOGY

Antimicrobial Agents
and Chemotherapy®

Systematic Review and Meta-analysis of the Efficacy of Short-Course Antibiotic Treatments for Community-Acquired Pneumonia in Adults

Giannoula S. Tansarli,^a Eleftherios Mylonakis^a

Short-course antibiotic treatment → ≤6 days
Long-course antibiotic treatment → ≥7 days

Inclusión de 21 ensayos clínicos con NAC (manejo ambulatorio y hospitalario)

-4861 pacientes

- 19 randomizados, 18 multicéntricos, 10 doble ciego

- Cursos antibiótico cortos incluyen: Azitromicina, FQ, ceftriaxona, amoxicilina

Systematic Review and Meta-analysis of the Efficacy of Short-Course Antibiotic Treatments for Community-Acquired Pneumonia in Adults

Giannoula S. Tansarli,^a Eleftherios Mylonakis^a

- **CURACIÓN CLÍNICA:** No diferencias significativas entre los dos grupos
 - Análisis global de los pacientes
 - Subanálisis de pacientes manejo hospitalario vs. ambulatorio
 - Subanálisis según gravedad neumonía (según Fine)
- **RECIDIVAS:** No diferencias significativas
- **MORTALIDAD:** Menor mortalidad en tto cortos (2.4% vs. 5.2%)
 - RR=0.53 [95% CI, 0.33-0.82]
- **EFFECTOS ADVERSOS:**
 - Menor AE en tratamientos cortos (8.2% vs. 11.2%)
 - RR=0.73 [95% CI, 0.55-0.97]
 - Menos SAE (Reacciones alérgicas graves, Nefrotoxicidad, arritmias, infección CD)

ESPECTRO ANTIBIÓTICO

Aminoglycoside or Polymyxin Monotherapy for Treating Complicated Urinary Tract Infections Caused by Extensively Drug-Resistant *Pseudomonas aeruginosa*: A Propensity Score-Adjusted and Matched Cohort Study


Inmaculada López Montesinos  · Silvia Gómez-Zorrilla · Zaira Raquel Palacios-Baena · Nuria Prim · Daniel Echeverría-Esnal · María Pilar Gracia · María Milagro Montero · Xavier Durán-Jordà · Elena Sendra · Luisa Sorli · Roberto Guerri-Fernandez · Eduardo Padilla · Santiago Grau · Juan Pablo Horcajada on behalf of PROA PSMAR group

Table.3 Crude and adjusted associations between different variables and 30- and 90-day mortality in overall and propensity-matched cohorts

	Overall cohort			Propensity-matched cohorts	
	Crude HR (95% CI)	aHR (95% CI)	p value	aHR (95% CI)	p value
30-day mortality					
Age (years), m (IQR)	1.05 (0.99–1.12)	1.09 (1.01–1.19)	0.033*	1.12 (1.01–1.25)	0.046*
Charlson comorbidity index, m (IQR)	1.21 (0.99–1.49)	1.36 (1.07–1.73)	0.012*	1.73 (1.01–2.99)	0.049*
SOFA score, m (IQR)	1.36 (1.05–1.78)	1.37 (1.02–1.83)	0.036*	1.24 (0.75–2.06)	0.398
Amikacin or CMS treatment	0.73 (0.2–2.57)	1.25 (0.29–5.45)	0.763	0.93 (0.17–5.08)	0.937
Propensity score	0.16 (0.02–1.67)	0.27 (0.01–7)	0.438		
90-day mortality					
Age (years), m (IQR)	1.01 (0.98–1.05)	1.04 (0.99–1.09)	0.113	1.07 (0.99–1.15)	0.065
Charlson comorbidity index, m (IQR)	1.3 (1.14–1.49)	1.37 (1.17–1.59)	< 0.001*	1.59 (1.13–2.22)	0.007*
SOFA score, m (IQR)	1.22 (1.03–1.45)	1.22 (1.01–1.48)	0.037*	1.32 (0.88–1.98)	0.177
Amikacin or CMS treatment	0.59 (0.26–1.34)	0.96 (0.36–2.54)	0.933	0.68 (0.20–2.31)	0.534
Propensity score	0.2 (0.48–0.82)	0.34 (0.06–2.03)	0.236		

Key Summary Points

Aminoglycosides or polymyxin monotherapy might be an alternative for urinary tract infections (UTIs) caused by extensively drug-resistant (XDR) *P. aeruginosa*.

Aminoglycosides or polymyxin monotherapy was not associated with poor outcomes compared to other antibiotic regimens.

Patients treated with antibiotic regimens other than aminoglycosides or polymyxin monotherapy were more likely to have *Clostridioides difficile* infection

These results may be useful for antimicrobial stewardship activities.

CONCLUSIONES

- **Los antibióticos son un bien colectivo que debemos proteger porque su efectividad depende de su buen uso.**
- **Uso responsable de antibióticos es esencial para controlar el desarrollo de resistencias y para asegurar que nuestros pacientes reciban el tratamiento adecuado.**
- **Todos los días se nos presentan varias ocasiones en las que se optimizar los tratamientos antibióticos**

A person is sitting in a meditative pose on a wooden pier that extends over a calm lake. The scene is captured at sunrise or sunset, with a soft, golden light reflecting on the water. In the background, there are misty mountains and a forest. The overall atmosphere is peaceful and serene. The text is overlaid on the left side of the image.

all you need is less.

less complexity.

less things.

less clutter.

less stress.

... and less antibiotics.