

ANTIBIOTERAPIA EN PIE DEL DIABÉTICO

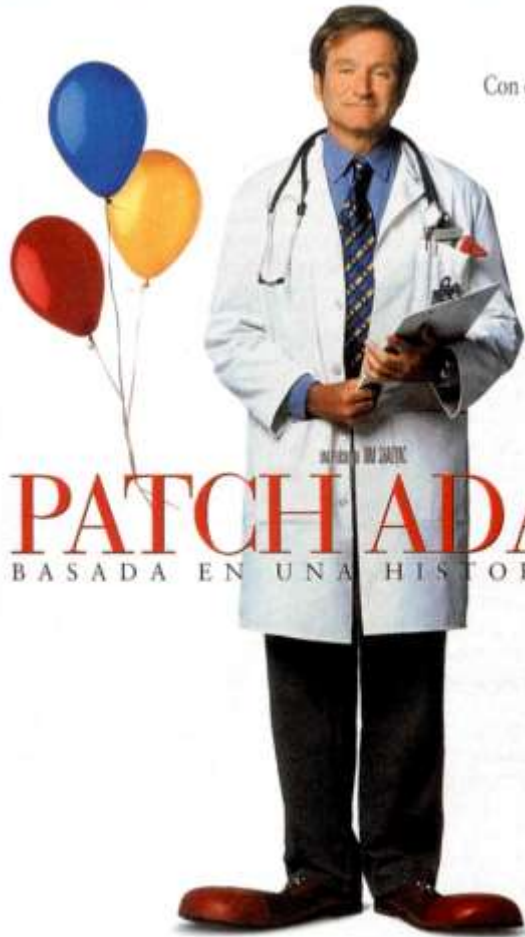
José Elías García Sánchez

**XXVII Curso de Avances en Quimioterapia
Hospital Universitario de La Princesa**



ROBIN WILLIAMS

Con él todo es diferente.

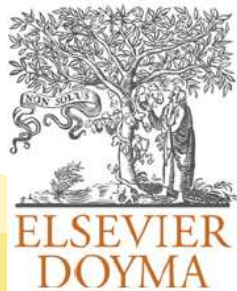


PATCH ADAMS
BASADA EN UNA HISTORIA REAL



- *“Pie diabético en mujer con diabetes tipo 1”.*
- *“Ulceras cutáneas y gangrena”.*
- *“Se recomienda **control de la glucemia** y quizás **antibióticos** y **amputación**”*

Para una correcta antibioterapia es necesario el concurso de la microbiología



Angiología

www.elsevier.es/angiologia



DOCUMENTO DE CONSENSO

Documento de consenso sobre el tratamiento de las infecciones en el pie del diabético[☆]

J.I. Blanes^{a,*}, A. Clará^a, F. Lozano^a, D. Alcalá^b, E. Doiz^a, R. Merino^a,
J. González del Castillo^c, J. Barberán^d, R. Zaragoza^e y J.E. García Sánchez^f

Infecciones del pie diabético

INTRODUCCIÓN

• **Diabetes mellitus**

- Prevalencia elevada \approx 6% de la población
- Prevalencia en no diagnosticados similar
- El 11% en mayores de 65 años
- En los países desarrollados: séptima causa de muerte por causa directa
- Importancia indirecta en la mortalidad cardiovascular
- Tiene complicaciones tardías importante:
 - Arteriosclerosis, neuropatía, retinopatía,...
 - **Úlcera:** frecuente, en un 15% de los casos

Es un hecho dramático e impactante para el paciente, su familia y los facultativos

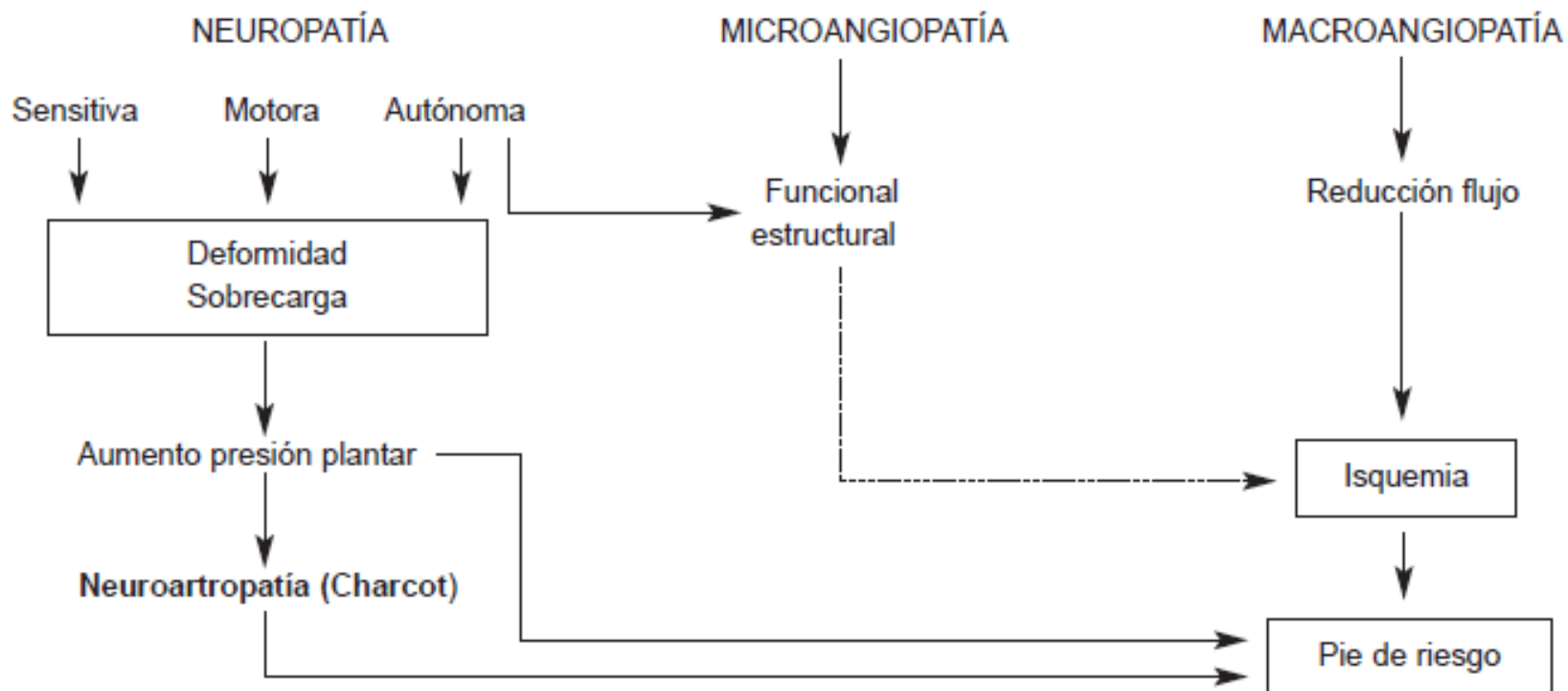




Las infecciones del pie (que pueden afectar a la piel, pates blandos y hueso, con o sin repercusión sistémica) **son la causa más frecuente de hospitalización de los diabéticos (25%), con estancias prolongadas y con frecuencia causa de amputación de la extremidad inferior**



FACTORES PREDISPONENTES



FACTORES DESENCADENANTES

Deformidad + traumatismo



FACTORES AGRAVANTES

Infección
Isquemia
Neuropatía

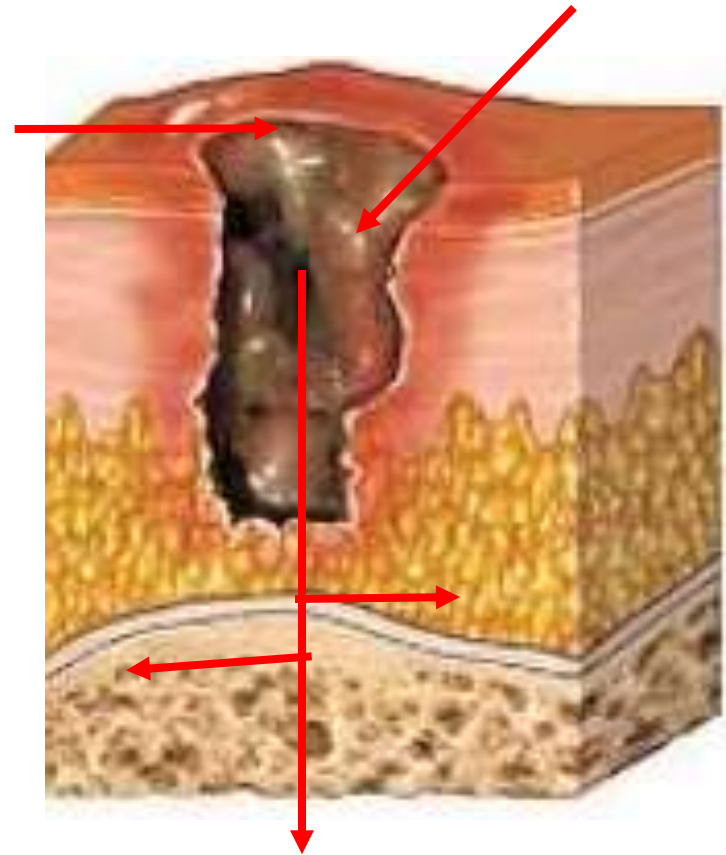


Extensión de la lesión, necrosis



- La úlcera es una puerta abierta para numerosos **“enemigos”** a un territorio comprometido, el diabético

- Siempre se coloniza
 - Quizás una colonización elevada puede retrasar la cicatrización
- Con frecuencia se infecta
 - La infección “contribuye” a la no cicatrización y extensión
- La úlcera infectada debe tratarse con antibióticos sistémicos



Infecciones del pie diabético

LA MICROBIOLOGÍA ¿POR QUÉ?

- **Para conocer los agentes etiológicos**
 - Variables y no siempre predecibles y para...
- **Conocer su sensibilidad a los antimicrobianos**
 - **Muy cambiante**
 - Por el patrón natural de sensibilidad
 - Incremento de resistencia
 - Problema mundial
 - Diferencias geográficas
 - Diferencias locales
- **Permite establecer una terapia racional**

- **Las variaciones se deben:**
 - Al tiempo de evolución
 - A los tratamientos antibióticos previos
 - A los ingresos hospitalarios precedentes
 - A factores geográficos

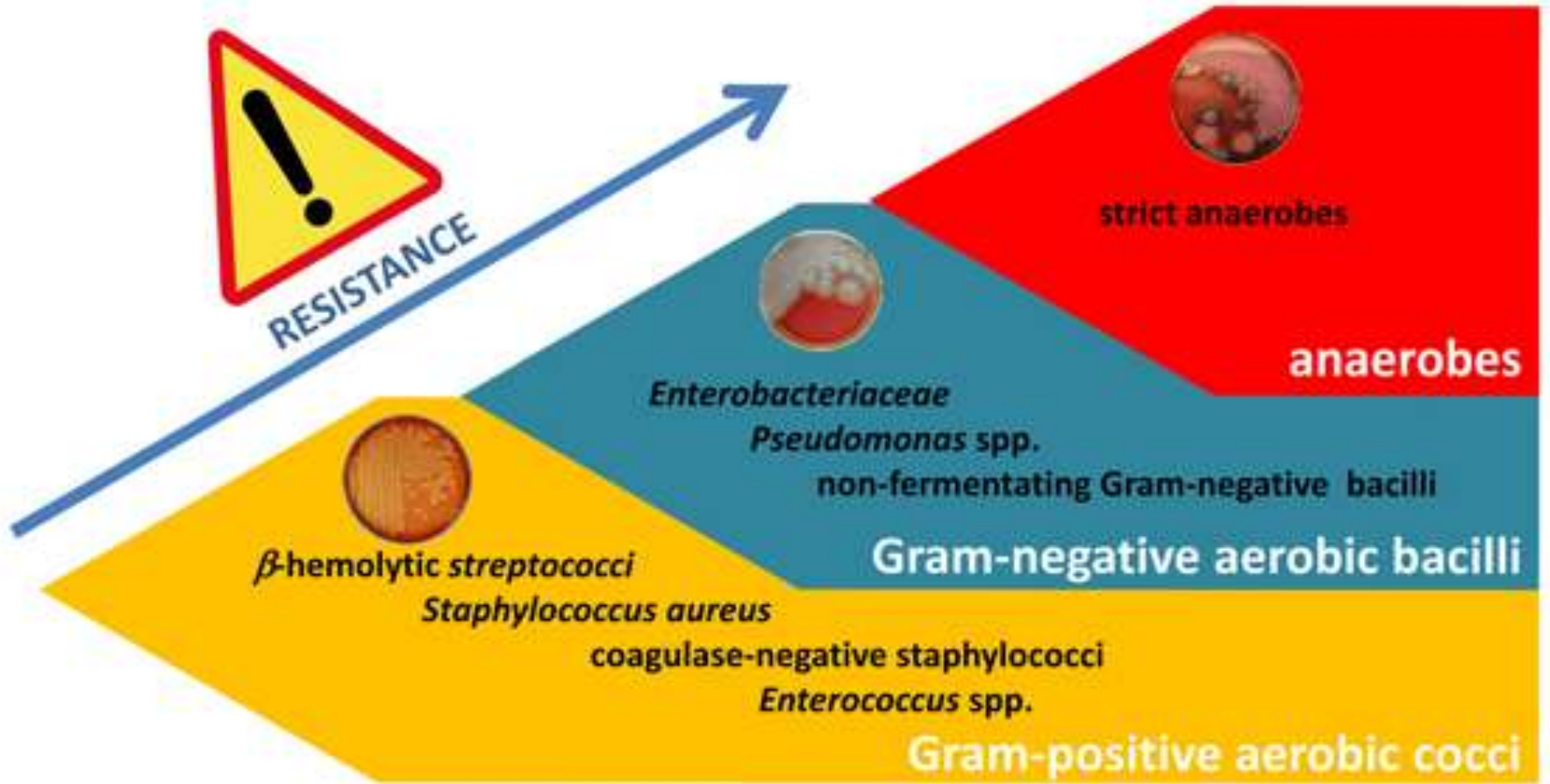
monomicrobial

polymicrobial

species number



RESISTANCE



strict anaerobes

anaerobes

Enterobacteriaceae

Pseudomonas spp.

non-fermentating Gram-negative bacilli

Gram-negative aerobic bacilli

β -hemolytic streptococci

Staphylococcus aureus

coagulase-negative staphylococci

Enterococcus spp.

Gram-positive aerobic cocci

NEUROPATHIC

NEUROISCHEMIC

time

Infecciones del pie diabético

EL DIAGNÓSTICO MICROBIOLÓGICO

- El diagnóstico microbiológico solo está indicado en la **infección clínica** del pie diabético y quizás cuando hay **¿Retraso en la cicatrización?**

- En estos casos hay que hacerlo siempre
 - Es esencial la participación de los clínicos **peticionarios**

1.- Toma de muestras

Los microbiólogos informan de lo que reciben
La muestra y su calidad es esencial



Muestras profundas
Son representativas de la infección



Muestras superficiales
Representan la flora cutánea

1985

Es un tema cuya importancia se ha mantenido en el tiempo

Foot Infections in the Diabetic: A Review of Microbiologic Aspects

Francisco L. Sapico, M.D.

(*Associate Professor of Medicine, University of Southern California, School of Medicine, Los Angeles, California 90033 and Associate Chief, Infectious Diseases Division, Rancho Lee Amigos Medical Center, Downey, California 90242)

SUMMARY

It is clear that the foot infections in the diabetic are generally of polymicrobial origin, and that both aerobes and anaerobes participate in this process. We have shown that anaerobes are as clinically important in this disease entity as are aerobes. Initial empiric therapy in the septic diabetic patient with an infected foot should, therefore, include coverage for the most common microorganisms isolated from deep tissue cultures. Included in this coverage should be gram-negative enteric aerobic bacilli, *Bacteroides fragilis*, enterococci, clostridia, and anaerobic streptococci. [*Phil J Microbiol Infect Dis* 1985; 14(2):52-54]

When concordance was examined quantitatively, **curettage** specimens again yielded **better** results than **swabs as needle aspirates**. In general, swab cultures tended to overestimate and needle aspirates, underestimate, the number of isolates actually present in deep tissue

Senneville E, et al. **Needle puncture and transcutaneous bone biopsy cultures are inconsistent in patients with diabetes and suspected osteomyelitis of the foot.** Clin Infect Dis. 2009;48:888-93.

Background. Needle puncture has been suggested as a method for identifying bacteria in the bones in patients with diabetes with osteomyelitis of the foot. However, no studies have compared needle puncture with concomitant transcutaneous bone biopsy, which is the current standard recommended in international guidelines.

Methods. We conducted a prospective study in 2 French diabetes foot clinics. Transcutaneous bone biopsy specimens, needle puncture specimens, and swab samples were collected on the same day for each patient.

Results. Overall, 31 patients were included in the study from July 2006 through February 2008. Twenty-one bone biopsy specimens (67.7%), 18 needle puncture specimens (58%), and 30 swab samples (96.7%) had positive culture results. *Staphylococcus aureus* was the most common type of bacteria that grew from bone samples, followed by *Proteus mirabilis* and *Morganella morganii*. The mean number of bacteria types per positive sample were 1.35, 1.32, and 2.51 for bone biopsy specimens, needle puncture specimens, and swab samples, respectively. Among the 20 patients with positive bone biopsy specimens (69%), 13 had positive needle puncture samples. Overall, the correlation between microbiological results was 23.9%, with *S. aureus* showing the strongest correlation (46.7%). Results of cultures of bone biopsy and needle puncture specimens were identical for 10 (32.3%) of 31 patients. Bone bacteria were isolated from the needle punctures in 7 (33.3%) of the 21 patients who had positive bone biopsy specimen culture results. If the results of cultures of needle puncture specimens alone had been considered, 5 patients (16.1%) would have received unnecessary treatment, and 8 patients (38.1%) who had positive bone culture results would not have been treated at all.

Conclusions. Our results suggest that needle punctures, compared with transcutaneous bone biopsies, do not identify bone bacteria reliably in patients with diabetes who have low-grade infection of the foot and suspected osteomyelitis.

La biopsia transcutanea es mejor que la aspiración en osteomielitis

Table 1. Distribution of microorganisms isolated from bone biopsy specimens, needle puncture specimens, and swab samples obtained concomitantly from 31 patients with diabetes and suspected osteomyelitis of the foot.

Variable	Bone biopsy specimens (n = 31)	Needle puncture specimens (n = 31)	Swab samples (n = 31)
No. (%) of sterile sample cultures	10 (32.3)	13 (41.9)	1 (3.2)
Total no. of isolates	42	41	78
Mean no. of isolates per sample	1.35	1.32	2.51
Gram-positive cocci	21/42 (50)	21/41 (51.2)	45/78 (57.7)
Staphylococci	17/42 (40.4)	16/41 (39.0)	32/78 (41.0)
<i>Staphylococcus aureus</i>			
All	14/42 (33.3)	8/41 (19.5)	17/78 (21.8)
MRSA	2/14 (14.3)	3/8 (37.5)	3/17 (17.6)
Coagulase-negative staphylococci	3/42 (7.1)	8/41 (19.5)	15/78 (19.2)
Other gram-positive cocci ^a	4/42 (9.5)	5/41 (12.2)	13/78 (16.7)
Gram-negative bacilli	16/42 (38.1)	15/41 (36.6)	26/78 (33.3)
<i>Escherichia coli</i>	2/42 (4.8)	2/41 (4.9)	5/78 (6.4)
<i>Proteus</i> species	6/42 (14.3)	5/41 (12.2)	7/78 (9.0)
<i>Pseudomonas</i> species	1/42 (2.4)	3/41 (7.3)	5/78 (6.4)
<i>Serratia marcescens</i>	2/42 (4.8)	0	3/78 (3.8)
<i>Enterobacter</i> species	1/42 (2.4)	1/41 (2.4)	0
<i>Morganella morganii</i>	3/42 (7.1)	4/41 (9.8)	3/78 (3.8)
<i>Haemophilus</i> species	0	0	1/78 (1.3)
<i>Acinetobacter baumannii</i>	1/42 (2.4)	0	2/78 (2.6)
Anaerobes ^b	5/42 (11.9)	5/41 (12.2)	7/78 (9.0)

NOTE. Data are proportion (%) of isolates, unless otherwise indicated. Percentage values do not add up to 100% because of decimal approximation. MRSA, methicillin-resistant *S. aureus*.

^a Includes group B streptococci, enterococci, and corynebacteria.
^b Includes *Veillonella* species, *Fusobacterium* species, *Bacteroides* species, and *Peptostreptococcus* species.

Table 2. Proportion of microorganisms isolated from bone biopsy specimens and needle puncture specimens obtained concomitantly from 31 patients with diabetes and suspected osteomyelitis of the foot.

Microorganism isolated	No. of cultures				Correlation, ^a %
	Total	Bone biopsy specimen only	Needle puncture specimen only	Bone biopsy and needle puncture specimens	
<i>Staphylococcus aureus</i>	15	7	1	7	46.7
Coagulase-negative staphylococci	11	3	8	0	0
Other gram-positive cocci ^b	8	3	4	1	14.3
Gram-negative bacilli	25	10	9	6	24.0
Anaerobes ^c	8	3	3	2	25.0
Total	67	26	25	16	23.9

^a Percentage of bone biopsy and needle puncture specimens obtained from a given patient that yielded the same pathogen.
^b Includes group B streptococci, enterococci, and corynebacteria.
^c Includes *Veillonella* species, *Fusobacterium* species, *Bacteroides* species, and *Peptostreptococcus* species.

Table 3. Proportion of microorganisms isolated from bone biopsy specimens and swab samples obtained concomitantly from 31 patients with diabetes and suspected osteomyelitis of the foot.

Microorganism isolated	No. of cultures				Correlation, ^a %
	Total	Bone biopsy specimen only	Needle puncture specimen only	Bone biopsy and needle puncture specimens	
<i>Staphylococcus aureus</i>	17	0	3	14	82.3
Coagulase-negative staphylococci	18	3	15	0	0
Other gram-positive cocci ^b	13	0	9	4	30.7
Gram-negative bacilli	28	2	12	14	50.0
Anaerobes ^c	8	1	4	3	37.5
Overall	84	6	43	35	41.7

^a Percentage of bone biopsy and needle puncture specimens obtained from a given patient that yielded the same pathogen.
^b Includes group B streptococci, enterococci, and corynebacteria.
^c Includes *Veillonella* species, *Fusobacterium* species, *Bacteroides* species, and *Peptostreptococcus* species.

2010

Sotto et al. Beneficial effects of implementing guidelines on microbiology and costs of infected diabetic foot ulcers. *Diabetologia*. 2010;53:2249-55.

- **Fundamento: toma de muestras adecuadas**
 - Eliminar las tomas superficiales con torundas
 - Obviar en lo posible las tomas profundas con hisopo
 - Recurrir fundamentalmente a tomas tisulares
- **Estudio de 2003 a 2007**

- **Impacto en la microbiología**

- Disminución significativa del número de especies de bacterias por muestra (de 4,1 se pasó a 1,6)
- Caída drástica de la prevalencia de microorganismos considerados colonizadores del 23,1 al 5,8% (**p < 0,001**)
- Aislamiento de más grampositivos, especialmente ***Staphylococcus aureus***
- Aislamiento de menos gramnegativos, tanto enterobacterias como *P. aeruginosa*
- Mantenimiento de los aislamientos de anaerobios, siempre en niveles bajos (5%).
- Disminución de la prevalencia de microorganismos multirresistentes (35,2 frente 16,3%)
- Disminución de la prevalencia de SAMR (de 52,2 a 18,9%) (**p < 0,001**)

- **El impacto económico**
 - Ahorro de 14.914 € por trabajo microbiológico
 - Ahorro de 109.305 € por disminución de consumo de antimicrobianos
- **Impacto ecológico no valorado**

- **Realizar antes de instaurar el tratamiento antibiótico**
 - Biopsia: muestra de referencia
 - Raspado
 - Aspiración con aguja
 - Hisopo
 - **Hemocultivo (bajo rendimiento)**
 - La bacteriemia es infrecuente
- **Repetir ante mala evolución**



Siempre antes de tomarlas:

**Desbridamiento y limpieza cuidadosa de la herida
(solución salina estéril, incluso con desinfección previa)
o desinfección de la piel (punción)**



- **Herida superficial**
- **Herida profunda sin colección**
- **Hueso**
 - **Biopsia**
 - **Raspado o**
 - **Torunda profunda**



- **Herida profunda con colección**
- **Absceso**
- **Celulitis**
- **Hueso licuado**
 - **Aspiración transcutánea con aguja fina**

**Medio de transporte
Para anaerobio**

- **Torunda o hisopo**

- Es la muestra más utilizada

- **Es de mala calidad**

- Superficial (no raspa el tejido, no toma biofilm)

- Refleja la flora cutánea y quizás la causal

- No es buena para recuperar anaerobios

- El material de la torunda puede inhibir a algunas bacterias

- Debe desaconsejarse en lo posible



2 Transporte de la muestras

- En un sistema adecuado
- Ideal en uno para anaerobios
- Bien identificada
- Enviada rápidamente al laboratorio
- A temperatura ambiente



**Vale de petición correctamente cumplimentado
(Antibióterapia concomitante, alergia a algún antibiótico)**





Procesamiento microbiológico



Infecciones del pie diabético

ETIOLOGIA DE LA INFECCIÓN DEL PIE DEL DIABETICO

Etiología de las infecciones del pie diabético (por cultivo)

Infección	Microorganismos
Celulitis Erisipela	<i>Staphylococcus aureus</i>  Estreptococos β hemolíticos (A, B, C y G)
Ulcera no tratada con antibióticos	<i>Staphylococcus aureus</i>  Estreptococos β hemolíticos (A, B, C y G)
Ulcera tratada con antibióticos o de larga evolución (generalmente polimicrobianas)	<i>S. aureus</i> sensible a meticilina  <i>S. aureus</i> resistente a meticilina  Streptococcus spp. Enterococcus spp. Enterobacterias <i>Pseudomonas aeruginosa</i> ¹ Otros bacilos gramnegativos no fermentadores ² Corynebacterium spp. ² Candida spp. ²
Fasctis necrosante o mionecrosis (generalmente polimicrobianas)	Cocos grampositivos aerobios Enterobacterias Bacilos gramnegativos no fermentadores Anaerobios

¹Especialmente en úlceras maceradas. ² Microorganismos menos prevalentes

Tabla 2. Número de muestras positivas para cada microorganismo aislado

Tabla 2. Número de muestras positivas para cada microorganismo aislado

Tipo de muestra	Exudados	Aspirados	Biopsias	Total
Muestras estudiadas para aerobios	34	34	16	84
Enterobacterias	10 (29)	9 (26)	3 (19)	22 (26)
<i>Escherichia coli</i>	4 (12)	2 (6)	1 (6)	7 (8)
<i>Enterobacter cloacae</i>	–	4	–	4
<i>Klebsiella pneumoniae</i>	2	–	–	2
<i>Klebsiella oxytoca</i>	2	1	–	3
<i>Morganella morganii</i>	–	2	1	3
<i>Citrobacter freundii</i>	–	1	–	1
<i>Citrobacter koseri</i>	–	1	–	1
<i>Proteus mirabilis</i>	2	–	1	3
BGNF	8 (23)	2 (6)	2 (12)	12 (14)
<i>Pseudomonas aeruginosa</i>	6 (18)	2 (6)	2 (12)	10 (12)
<i>Pseudomonas</i> spp.	1	–	–	1
<i>Xanthomonas maltophilia</i>	2	–	–	2
Grampositivos	21 (62)	18 (53)	7 (44)	46 (55)
<i>Staphylococcus aureus</i>	9 (27)	14 (41)	5 (31)	28 (33)
<i>Enterococcus faecalis</i>	7 (20)	–	–	7 (8)
<i>Enterococcus</i> spp.	1	–	–	1
<i>Streptococcus agalactiae</i>	2	1	–	3
<i>Streptococcus viridans</i>	–	1	1	2
Estafilococos coagulasa negativo	3	2	1	6
<i>Corynebacterium</i> spp.	–	1	1	2
Hongos				
<i>Candida albicans</i>	–	1	–	1 (1)
Muestras estudiadas para anaerobios	–	31	14	45
Anaerobios	–	7 (26)	1 (7)	8 (18)
<i>Peptostreptococcus</i> spp.	–	4	1	5
<i>Prevotella</i> spp.	–	2	–	2
<i>Clostridium</i> spp.	–	–	1	1
<i>Bacteroides</i> spp.	–	1	–	–



Martínez-Gómez et al
Infecciones del pie diabético.
Prevalencia de los distintos
microorganismos y
sensibilidad a los
antimicrobianos
Enferm Infecc Microbiol Clin.
2009;27:317-21

96 aislados
48 monomicrobianos
48 polimicrobianos

Infecciones del pie diabético

EPIDEMIOLOGIA DE LA RESISTENCIA

Tabla 4
Resistencia a los antimicrobianos de los principales microorganismos aislados grampositivos

Diciembre de 2001 y diciembre de 2005

Porcentaje de microorganismos aislados resistentes a los antimicrobianos							
Microorganismo (número de aislados)	Penicilina	Oxacilina	Amoxicilina con ácido clavulánico	Eritromicina	Ciprofloxacina	Gentamicina	Vancomicina
<i>Staphylococcus aureus</i>	100	38	38	42	46	8	0

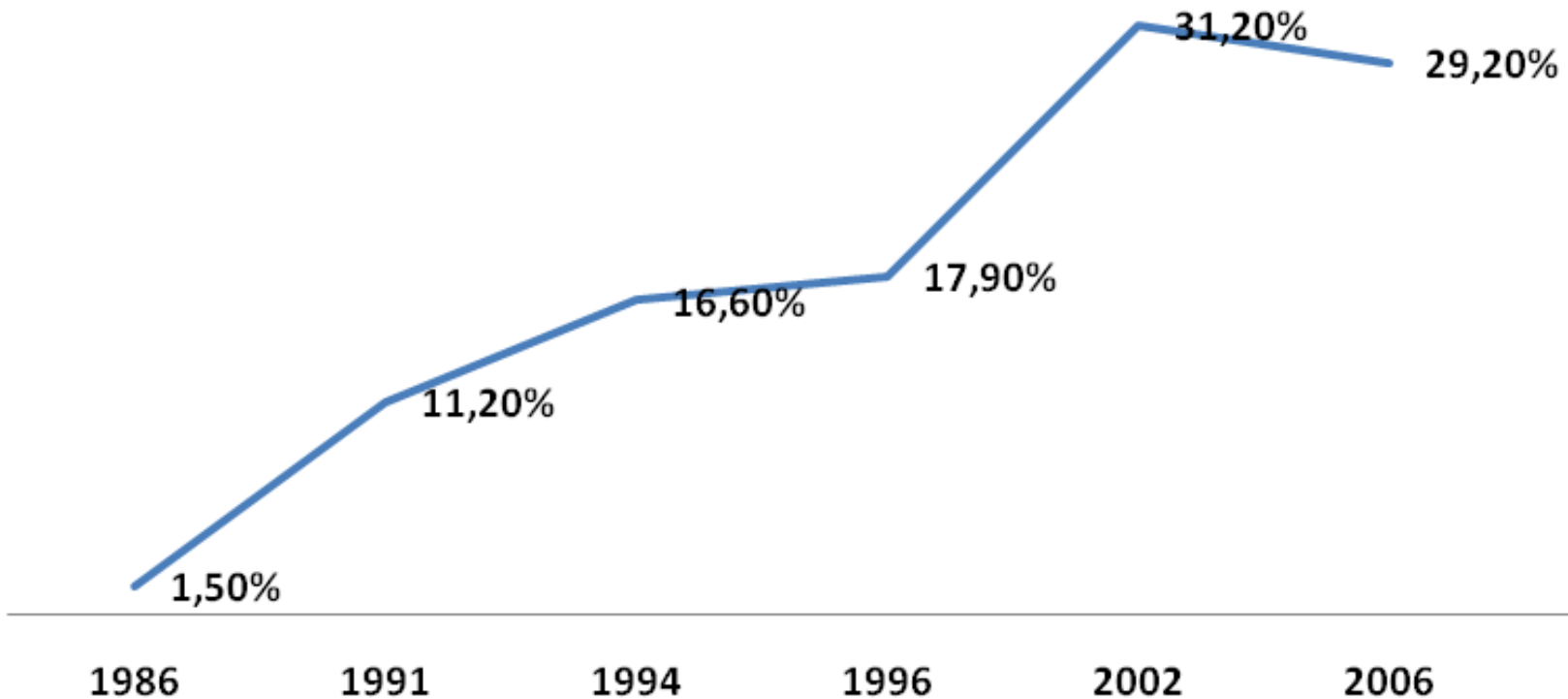


Porcentaje de aislamientos invasivos de *Staphylococcus aureus* resistentes a meticilina en España

2003	2004	2005	2006	2007	2008	2009	2010	2011
24	26	27	25	25	27	26	25	22

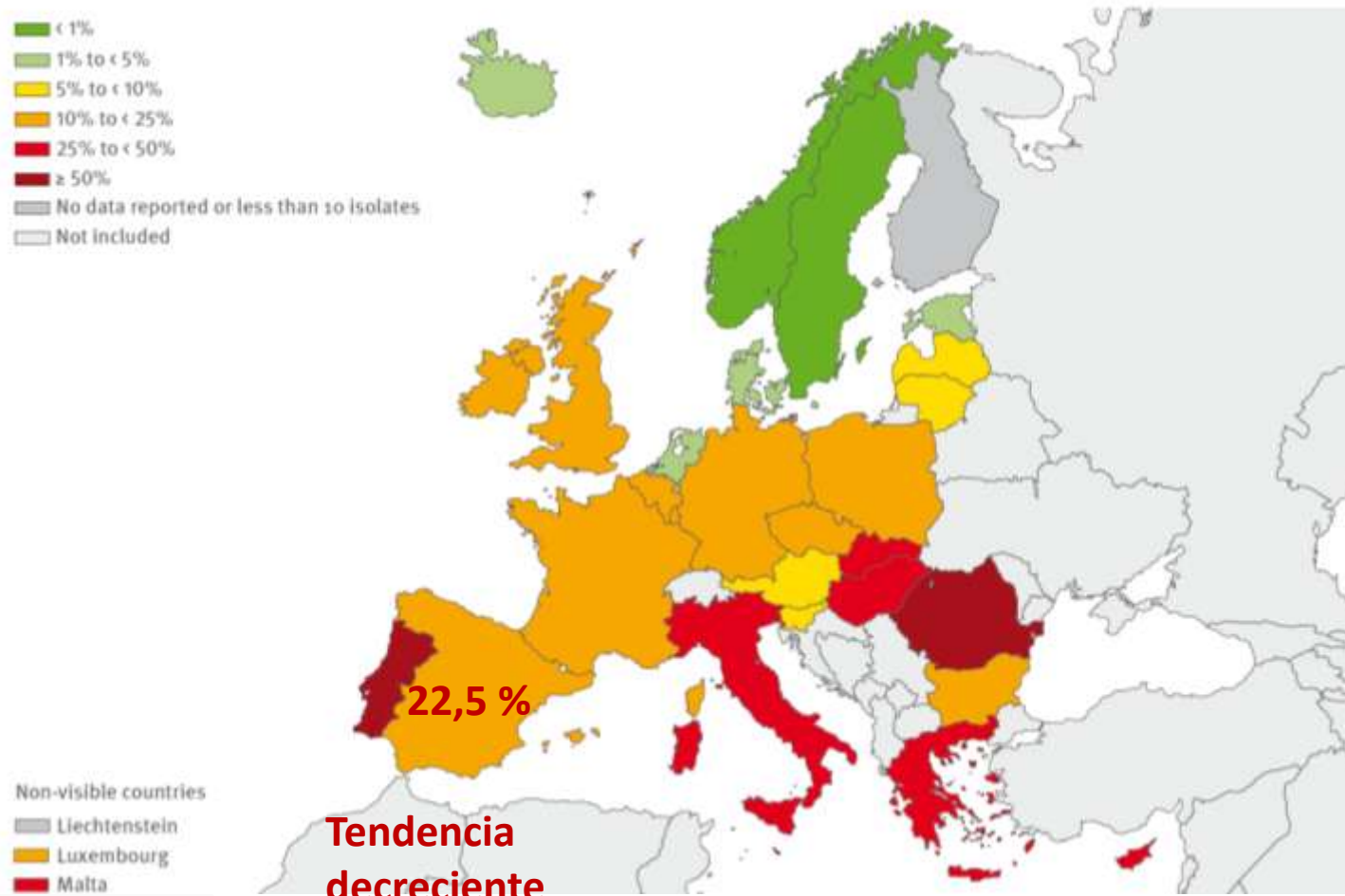
Antimicrobial resistance surveillance en Europe 2009, www.ecdc.europa.eu

Resistencia de *S. aureus* a meticilina en España



Staphylococcus aureus

Figure 4.38: *Staphylococcus aureus*: percentage (%) of invasive isolates resistant to meticillin (MRSA), by country, EU/EEA countries, 2008–2011



Vancomycin: We Can't Get There From Here

Nimish Patel,¹ Manjunath P. Pai,¹ Keith A. Rodvold,⁵ Ben Lomaestro,^{3,4} George L. Drusano,² and Thomas P. Lodise^{1,2}

¹Albany College of Pharmacy and Health Sciences, ²Ordway Research Institute, ³Albany Medical Center Hospital; ⁴Albany Medical College, Albany, New York; and ⁵University of Illinois at Chicago, Chicago, Illinois

(See the article by Kullar et al, on pages 975–981.)

Background. We sought to characterize the pharmacodynamic profile of the more intensive vancomycin dosing regimens currently used in response to the recent vancomycin guidelines.

Methods. A series of Monte Carlo simulations was performed for vancomycin regimens ranging from .5 g intravenous (IV) Q12H to 2 g IV Q12H. The probability of achieving an AUC/MIC ratio ≥ 400 for each dosing regimen was calculated for minimum inhibitory concentrations (MICs) from .5 to 2 mg/L. The risk of nephrotoxicity for each regimen was derived from a previously published vancomycin trough-nephrotoxicity logistic regression function. Restricted analyses were performed that only included subjects with troughs between 15 and 20 mg/L.

Results. At a MIC of 2 mg/L, even the most aggressive dosing regimen considered (2 g every 12 h) only yielded a probability of target attainment (PTA) of 57% while generating a nephrotoxicity probability upward of 35%. At a MIC of 1 mg/L, ≥ 3 g per day provided PTA in excess of 80% but were associated with unacceptable risks of nephrotoxicity. In the restricted analyses of subjects with troughs between 15 and 20 mg/L, all regimens produced a PTA of 100% at MICs ≤ 1 mg/L. The PTA was variable among the regimens at a MIC of 2 mg/L and was highly dependent on the total daily dose administered.

Conclusions. This study indicates that vancomycin may not be useful for treating serious methicillin-resistant *Staphylococcus aureus* (MRSA) infections with MIC values > 1 mg/L where PTA is questionable. Since an AUC/MIC ratio ≥ 400 is target associated with efficacy, one should consider incorporating computation of AUC when monitoring vancomycin.

- Resistencia (VRSA, CMI > 8 mg/L): rarísima
- Resistencia intermedia (VISA) (CMI 4-8 mg/L)
- Resistencia intermedia heterogénea (hVISA)
- Disminución de la sensibilidad (CMI > 1)
 - Deslizamiento de la CMI o “CMI Creep”
 - Incluso durante el tratamiento
- Efecto inóculo
- Tolerancia (disminución del poder bactericida)
 - CMB/CMI ≥ 32

- **Necesidad de fijar nuevo punto de corte más bajo**
- **Es necesario estar seguros de su actividad**
- **Problemas en la detección de la resistencia en el laboratorio**
 - Falta de reproductividad entre distintos métodos
 - Etest /microdilución manual o automatizada/disco placa
 - Dificultad de detectar hVISA

Point: Vancomycin Is Not Obsolete for the Treatment of Infection Caused by Methicillin-Resistant *Staphylococcus aureus*

John F. Mohr¹ and Barbara E. Murray^{1,2}

¹Department of Internal Medicine, Division of Infectious Diseases and Center for Emerging and Re-emerging Pathogens, and ²Department of Microbiology and Molecular Genetics, University of Texas Health Science Center at Houston



Vancomycin MIC, 0.5 µg/mL
Zone diameter, 17 mm

Vancomycin MIC, 2 µg/mL
Zone diameter, 17 mm

Vancomycin MIC, 8 µg/mL
Zone diameter, 17 mm

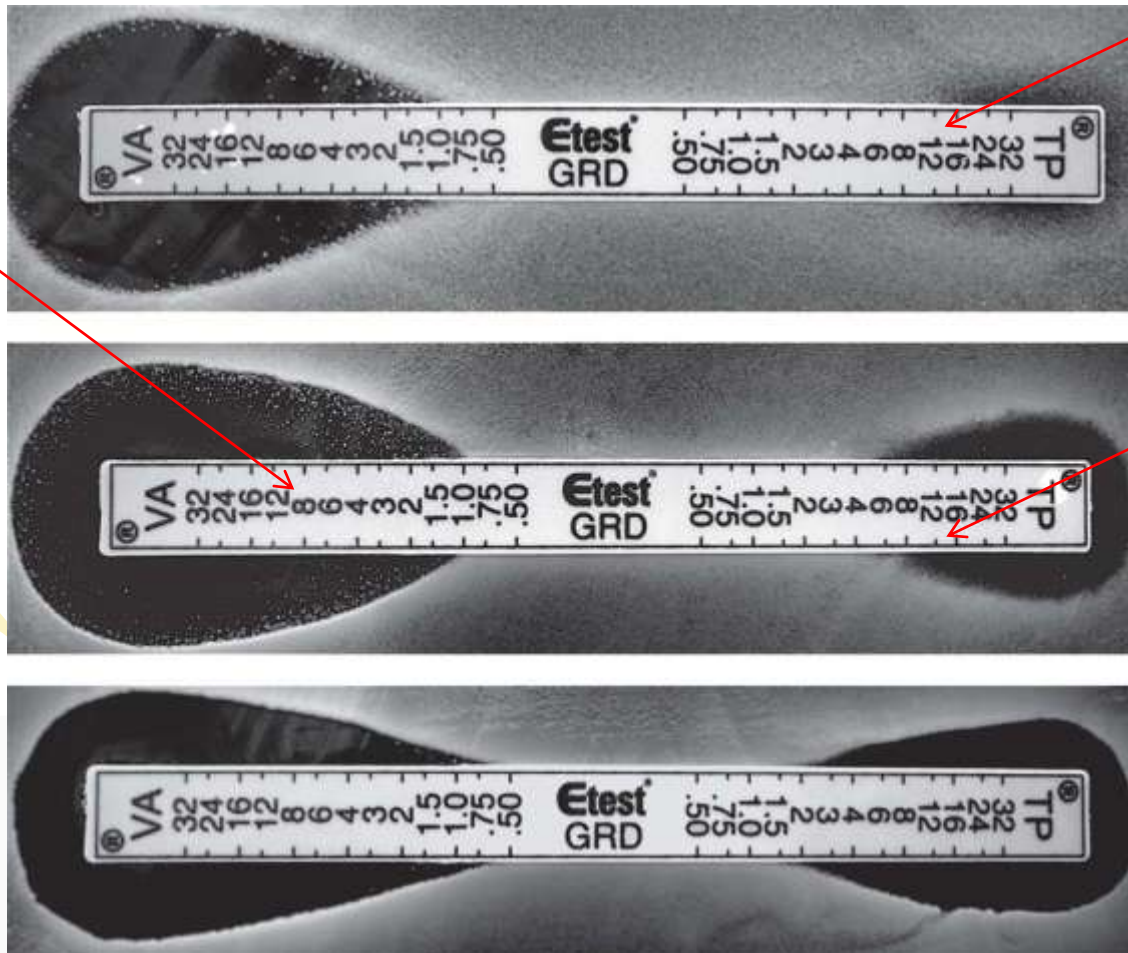


Figure 1. Etest GRD for hVISA Mu3 (a), a clinical hVISA with a positive Etest GRD (b) and a clinical VSSA with a negative Etest GRD (c).

Evolución de la sensibilidad a vancomicina en cepas de *Staphylococcus aureus* procedentes de bacteriemias

CMI (mg/L)	2009	2010	2011	2012
TOTAL	87	83	76	80
SAMS				
≤ 1	51 (91,07%)	56 (91,80%)	39 (68,42%)	35 (67,30%)
2	4 (7,14%)	3 (4,91%)	14 (24,56%)	12 (22,64%)
4	1 (1,78%)	2 (3,27%)	4 (7,01%)	5 (9,61%)
SAMR				
≤ 1	25 (80,64%)	18 (81,81%)	13 (68,42%)	19 (67,85%)
2	5 (16,12%)	3 (13,63%)	5 (26,31%)	9 (32,14%)
4	1 (3,22%)	1 (4,54%)	1 (5,26%)	0

Hospital Universitario de Salamanca. Estudio retrospectivo realizado en un periodo de 4 años (2009-2012).
Congreso SEIMC 2013

Identification and Characterization of a High Vancomycin-Resistant *Staphylococcus aureus* Harboring VanA Gene Cluster Isolated from Diabetic Foot Ulcer

¹Anahita Dezfulian, *²Mohammad Mehdi Aslani, ²Mahvash Oskoui, ²Parisa Farrokh, ¹Masumeh Azimirad, ¹Hossein Dabiri, ¹Mohammad Taghi Salehian, ¹Mohammad Reza Zali

Abstract

Objective(s)

Staphylococcus aureus is a common cause of human infection, and emergence of vancomycin-resistance *S. aureus* is a great concern for treatment of methicillin-resistant *S. aureus* (MRSA) in recent years (MRSA). Here, we report the isolation of high-level VRSA.

Materials and Methods

S. aureus was isolated from foot ulcer of a diabetic woman in Tehran, Iran. Antibiotic susceptibility was determined according to CLSI guidelines. VanA gene cluster PCR was carried out and PCR amplicon of *vanA* was sequenced.

Results

S. aureus had high-level vancomycin-resistant (MIC 512 \geq μ g/ml). Patient's history revealed that VRSA isolate was acquired through community transmission. Only *vanA*, *vanR* and *vanS* genes were amplified in our isolate. Sequencing revealed that the *vanA* sequence had high similarity to the *vanA* sequence of *Tn1546*.

Conclusion

Although VRSA infection continues to be rare, isolation of community-acquired VRSA is a significant issue and it needs the efforts of public health authorities.

Keywords: Community-Acquired Infections, MRSA, Vancomycin Resistance

Tabla 5

Resistencia de los principales microorganismos aislados gramnegativos a los antimicrobianos

Diciembre de 2001 y diciembre de 2005

Porcentaje de microorganismos aislados resistentes a los antimicrobianos									
Microorganismo (número de aislados)	Ampicilina	Amoxicilina y ácido clavulánico	Cefotaxima	Caz	Piperacilina y tazobactam	Imipenem	Gentamicina	Amikacina	Ciprofloxacina
<i>Escherichia coli</i>	71	29	0	0	0	0	0	0	29

Porcentaje de aislamientos resistentes y no sensibles de cepas invasivas de (2003-2011) en España

Patógenos/Antimicrobianos	2003	2004	2005	2006	2007	2008	2009	2010	2011
<i>Escherichia coli</i>									
Fluoroquinolonas R.	21	25	28	28	30	33	31	33	34
Cefalosporinas 3 ^º gen. R.	4	7	8	7	7	9	11	12	13
Carbapenems R.	<1	<1	<1	<1	<1	<1	<1	<1	<1
<i>Klebsiella pneumoniae</i>									
Fluoroquinolonas R.	-	-	11	8	17	15	16	14	17
Cefalosporinas 3 ^º gen. R.	-	-	7	9	10	12	11	10	13
Carbapenems R.	-	-	<1	<1	<1	<1	<1	<1	<1

Antimicrobial resistance surveillance en Europe 2011, www.ecdc.europa.eu

Escherichia coli

Figure 4.2: *Escherichia coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2011

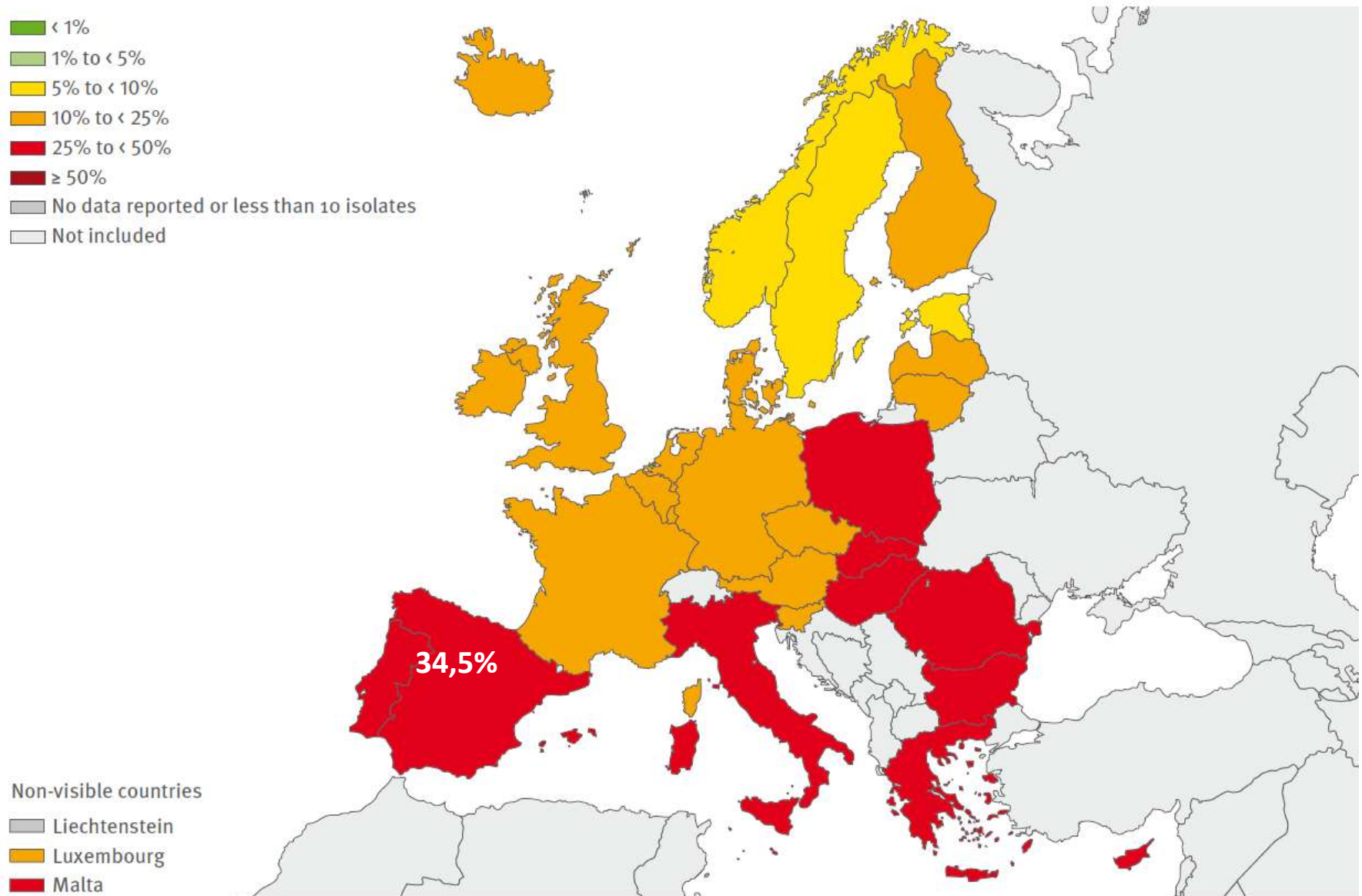
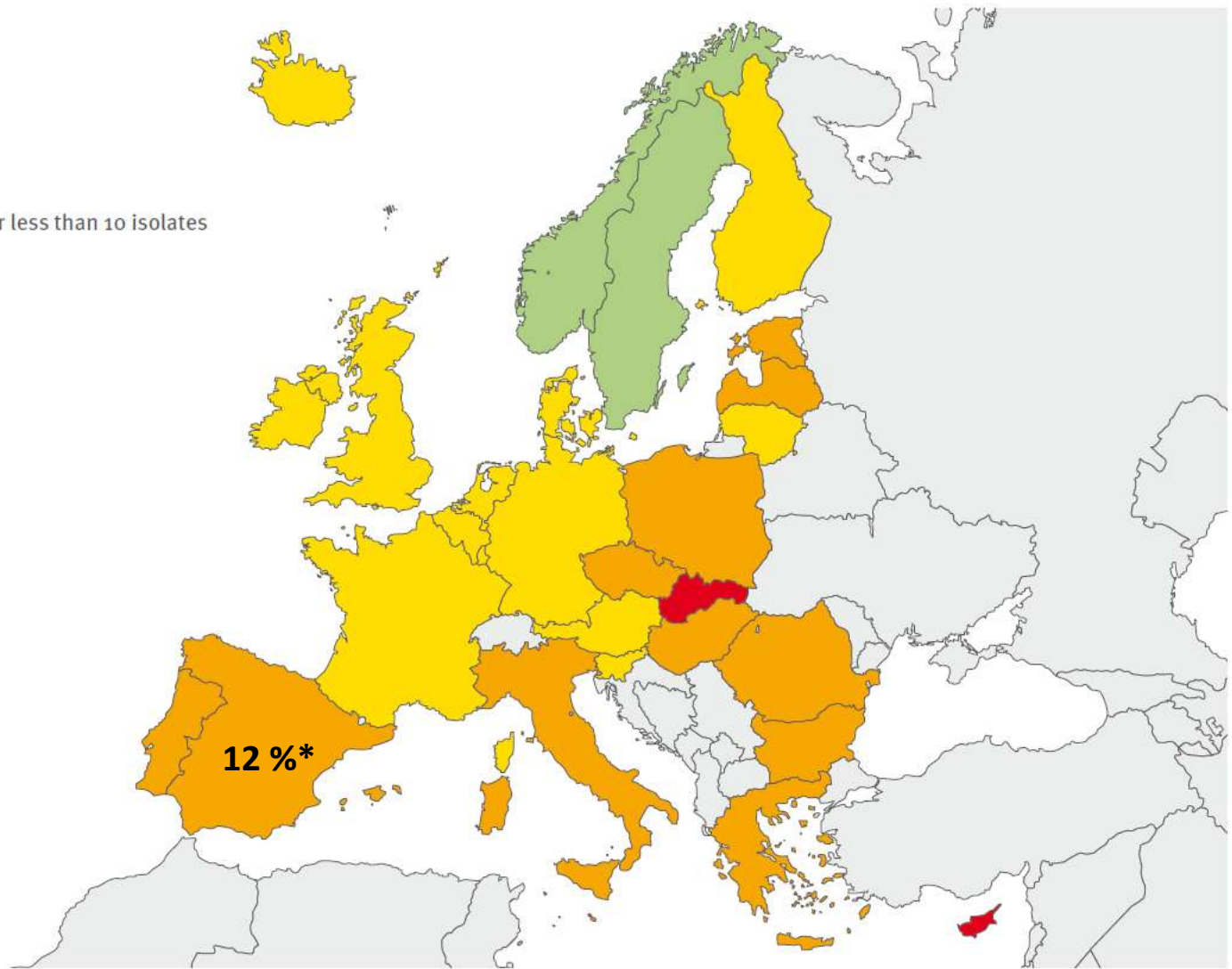


Figure 4.1: *Escherichia coli*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by country, EU/EEA countries, 2011

- < 1%
- 1% to < 5%
- 5% to < 10%
- 10% to < 25%
- 25% to < 50%
- ≥ 50%
- No data reported or less than 10 isolates
- Not included

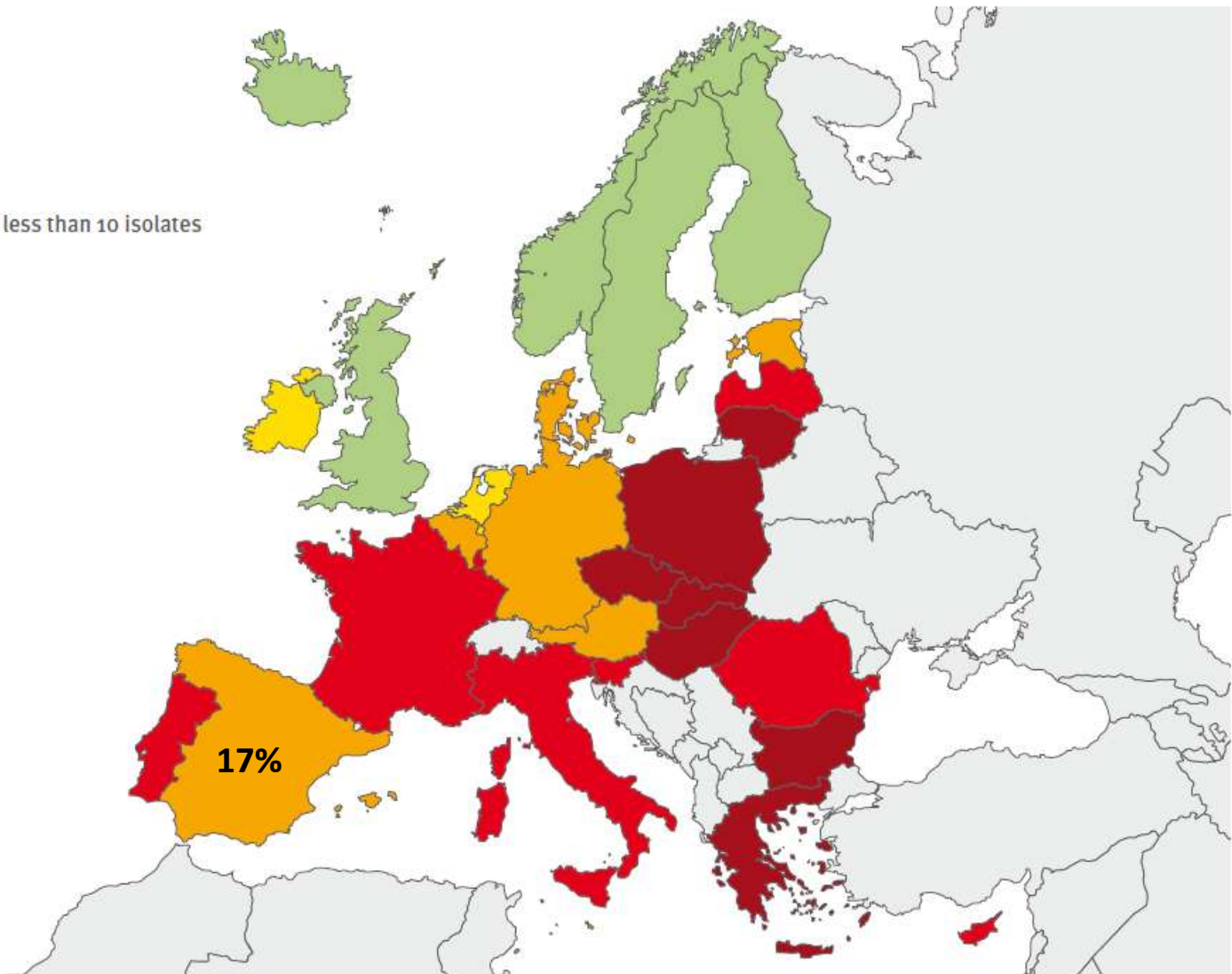


*** El 88.5 % por BLEES**

Resistencia combinada (aminopenicilinas + cefalosporinas de 3ª generación + fluorquinolonas + aminoglicosidos: 8,3%

Klebsiella pneumoniae

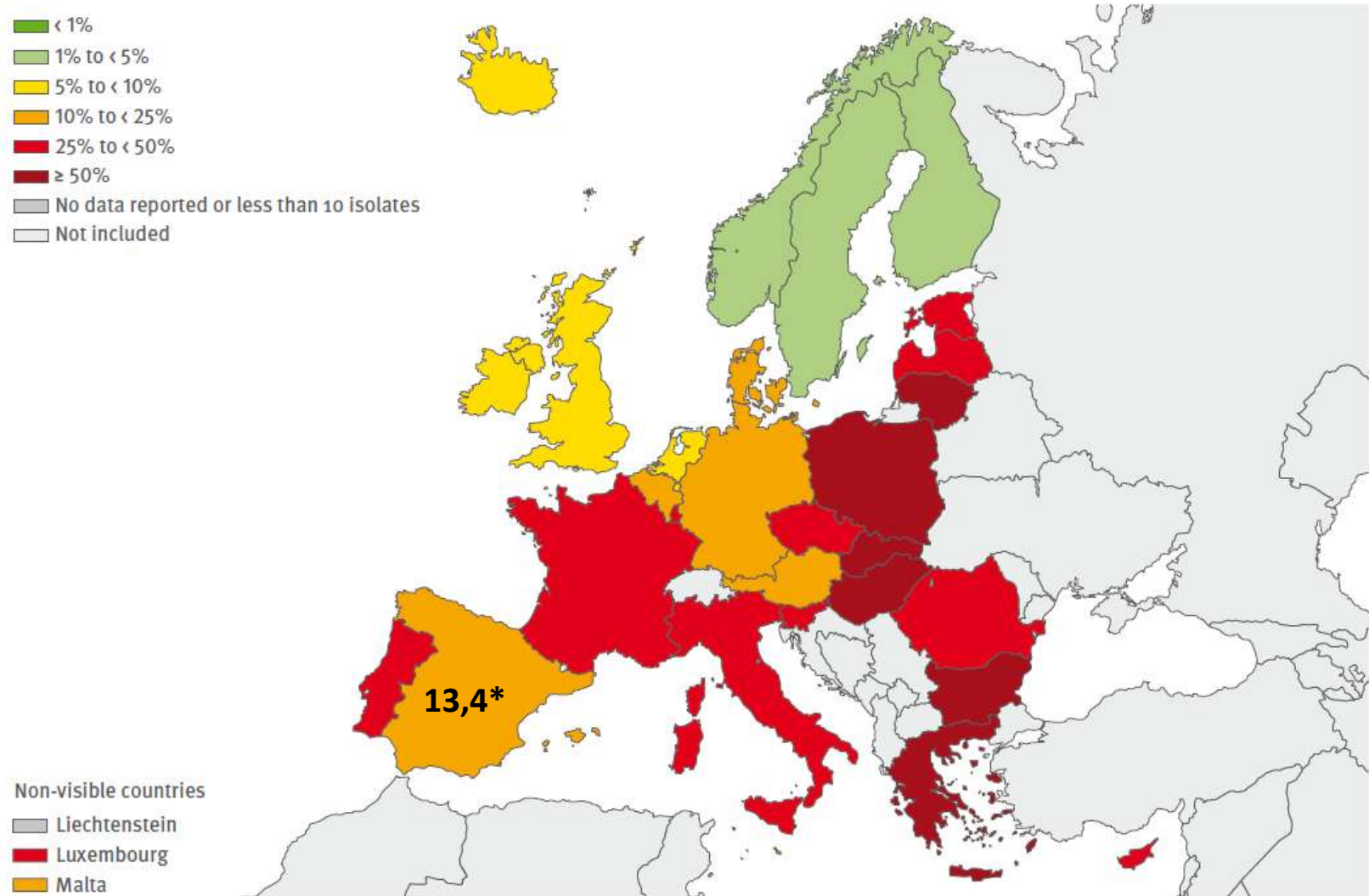
Figure 4.10: *Klebsiella pneumoniae*: percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2011



Non-visible countries

- Liechtenstein
- Luxembourg
- Malta

Figure 4.9: *Klebsiella pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins, by country, EU/EEA countries, 2011



*** El 88.5 % por BLEES**

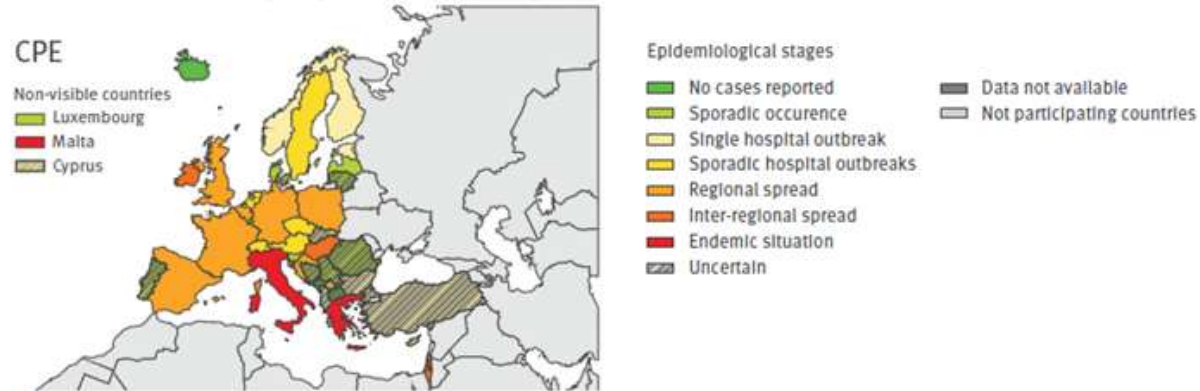
Resistencia a carbapenems: 0,3%

Resistencia combinada: 8,3%

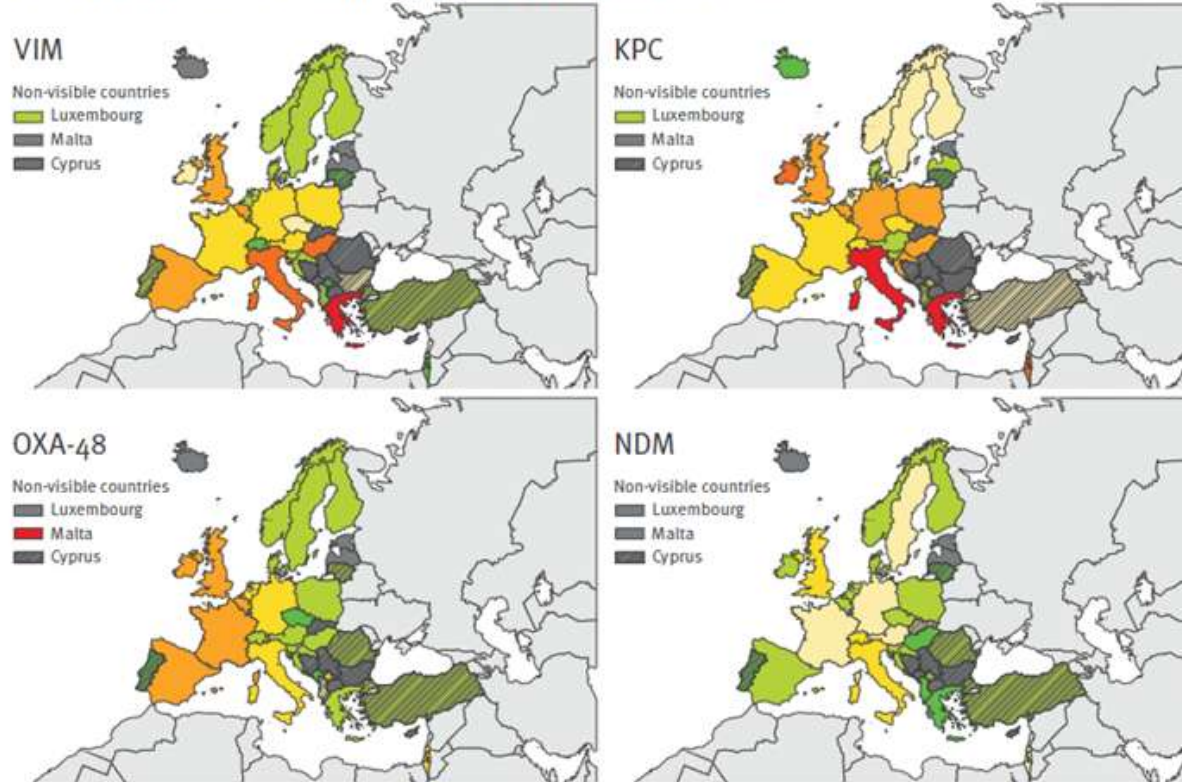
Ambler class	Enzyme	Function	Known organisms
A	KPC ¹	Hydrolyzes all β -lactam antibiotics; inhibited by clavulanate	<i>K pneumoniae</i> , Enterobacteriaceae
B	MBLs ² (NDM, IMP, VIM, GIM, SPM)	Hydrolyze all β -lactams except aztreonam; may be inhibited by clavulanate; require zinc for enzymatic activity; inhibited by EDTA	<i>P aeruginosa</i> , <i>Acinetobacter</i> spp, Enterobacteriaceae
D	OXA	Oxacillin hydrolyzing; less able to hydrolyze carbapenems	<i>P aeruginosa</i> , <i>A baumannii</i> , Enterobacteriaceae

Occurrence of carbapenemase-producing *Enterobacteriaceae* (CPE) in 39 European countries based on self-assessment by respective national experts, 2013

A Overall European situation regarding CPE using an epidemiological scale of nationwide expansion



B Geographic distribution of CPE by resistance mechanism using the same epidemiological scale



KPC: *Klebsiella pneumoniae* carbapenemase-producing *Enterobacteriaceae*; NDM New Delhi metallo-beta-lactamase; OXA-48: carbapenem-hydrolysing oxacillinase-48; VIM: Verona Integron-encoded metallo-beta-lactamase.

The Bacteriology of Diabetic Foot Ulcers, with a Special Reference to Multidrug Resistant Strains

Journal of Clinical and Diagnostic Research. 2013 March, Vol-7(3): 441-445

PRIYADARSHINI SHANMUGAM, JEYA M, LINDA SUSAN S

ABSTRACT

Introduction: A diabetic foot infection is one of the most feared complications of Diabetes mellitus. Many studies have reported on the bacteriology of Diabetic Foot Infections (DFIs) over the past 25 years, but the results have been varied and often contradictory.

Aims and Objectives: This study was carried out to determine the bacterial profiles of infected ulcers and the antibiotic resistance pattern of the isolates.

Materials and Methods: Samples were collected from 50 patients with diabetic foot ulcers by using sterile swabs and they were processed.

Results: A total of 75 bacterial isolates were obtained from 50 patients with diabetic foot ulcers. The age group of these

patients ranged from 35 to 80 years and the maximum number of patients was in the age group of 60 to 65 years. Gram negative bacilli were more prevalent (65.1%) than gram positive cocci (34.9%). The commonest isolate was *Pseudomonas spp* (16%), followed by *Escherichia coli* (14.6%) and *Staphylococcus aureus* (13.3%). The antibiotic sensitivity profiles of the bacteria were also studied. 37.5% of the gram negative bacilli were ESBL producers and 31% were carbapenemase producers.

Conclusion: This study showed a preponderance of gram negative bacilli among the isolates from the diabetic foot ulcers. Knowledge on the antibiotic sensitivity pattern of the isolates will be helpful in determining the drugs for the empirical treatment of diabetic ulcers.

37.5% of the gram negative bacilli were ESBL producers and 31% were carbapenemase producers

Tabla 5
Resistencia de los principales microorganismos aislados gramnegativos a los antimicrobianos

Porcentaje de microorganismos aislados resistentes a los antimicrobianos									
Microorganismo (número de aislados)	Ampicilina	Amoxicilina y ácido clavulánico	Cefotaxima	Caz	Piperacilina y tazobactam	Imipenem	Gentamicina	Amikacina	Ciprofloxacina
<i>Pseudomonas aeruginosa</i>	NA	NA	NA	25	0	0	0	0	33

Diciembre de 2001 y diciembre de 2005

Porcentaje de resistencia de cepas invasivas de *Pseudomonas aeruginosa* en España

Patógeno/Antimicrobianos	2005	2006	2007	2008	2009	2010	2011
<u>Piperacilina o Piper+tazo R.</u>	4	9	8	8	8	6	6
<u>Ceftazidima R.</u>	6	7	10	11	8	7	9
<u>Carbapenems R.</u>	17	12	15	13	16	18	16
<u>Aminoglicósidos R.</u>	4	11	15	18	19	18	19
<u>Fluoroquinolonas R.</u>	14	19	25	23	25	25	24

Antimicrobial resistance surveillance en Europe 2011, www.ecdc.europa.eu

Figure 4.19: *Pseudomonas aeruginosa*: percentage (%) of invasive isolates with resistance to piperacillin±tazobactam, by country, EU/EEA countries, 2011

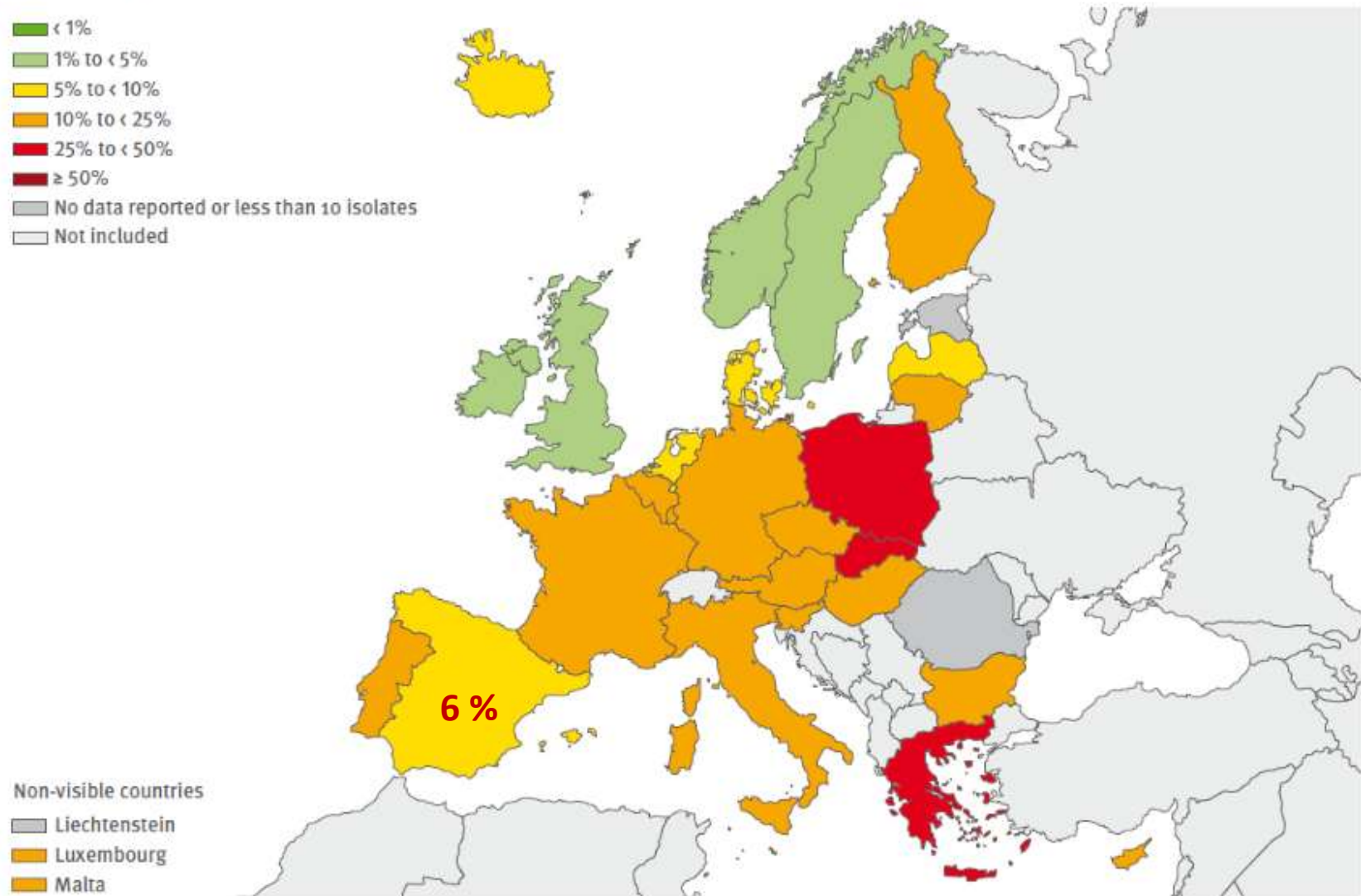


Figure 4.21: *Pseudomonas aeruginosa*: percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2011



Non-visible countries

- Liechtenstein
- Luxembourg
- Malta

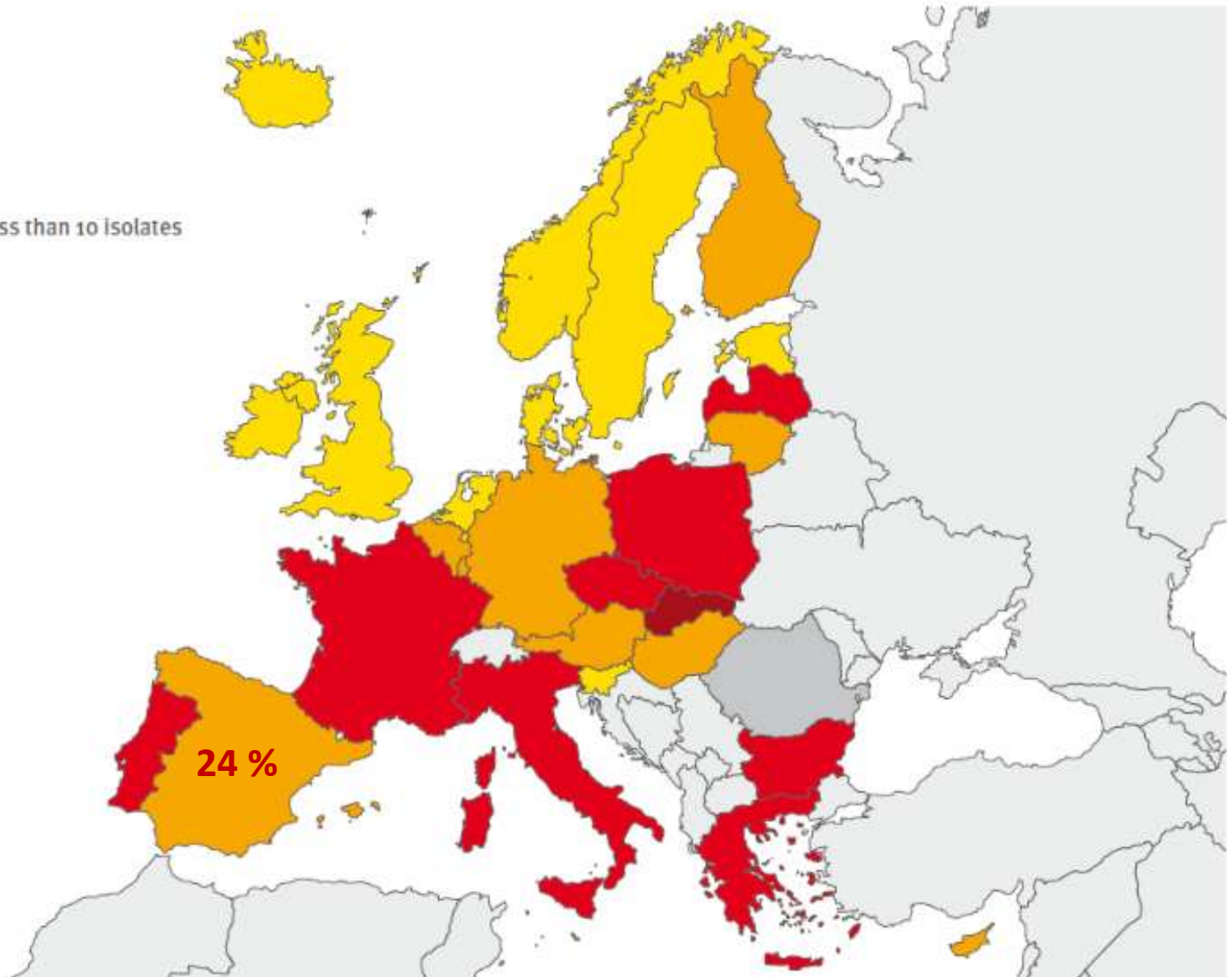


Figure 4.23: *Pseudomonas aeruginosa*: percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2011

- < 1%
- 1% to < 5%
- 5% to < 10%
- 10% to < 25%
- 25% to < 50%
- ≥ 50%

■ No data reported or less than 10 isolates

■ Not included

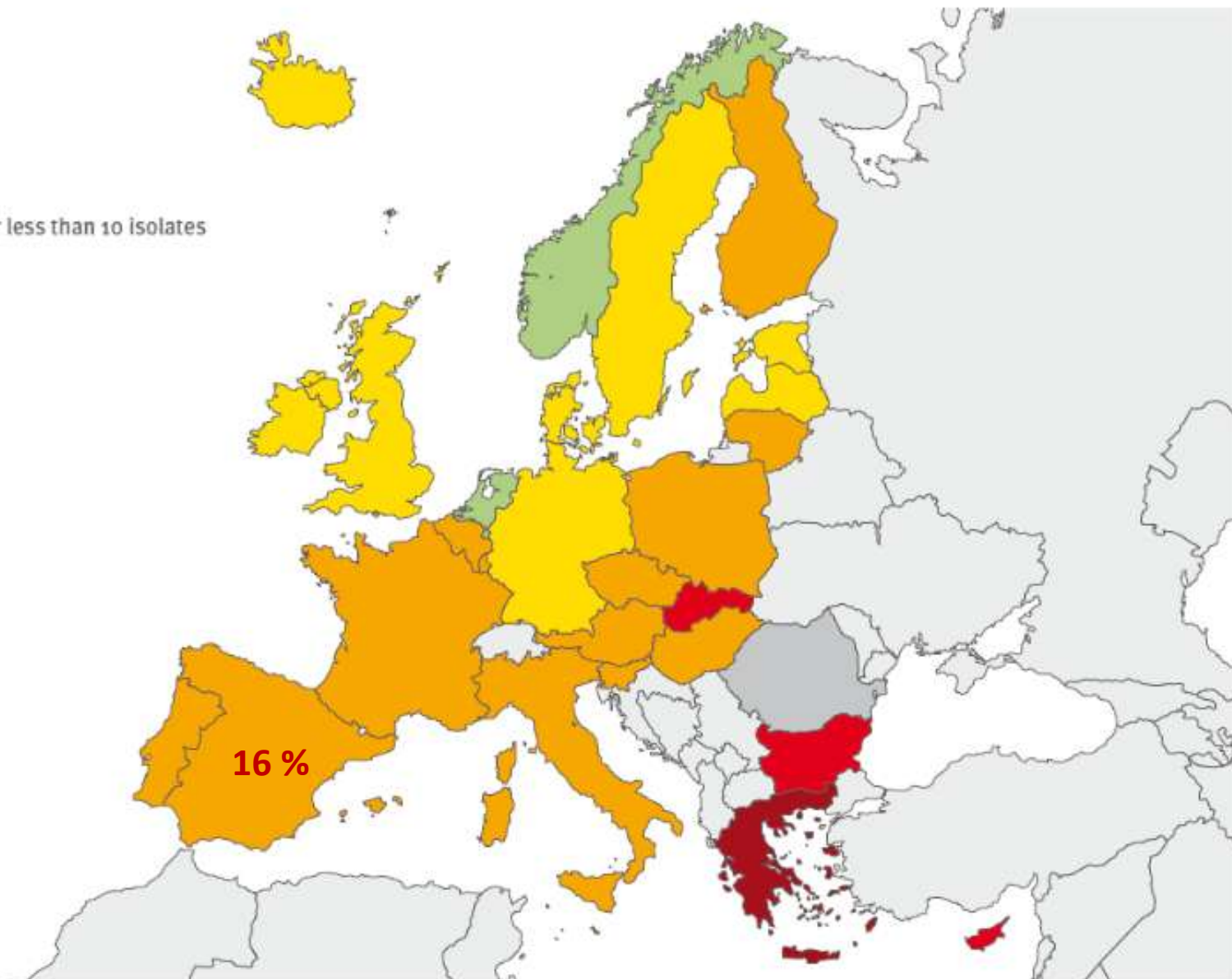
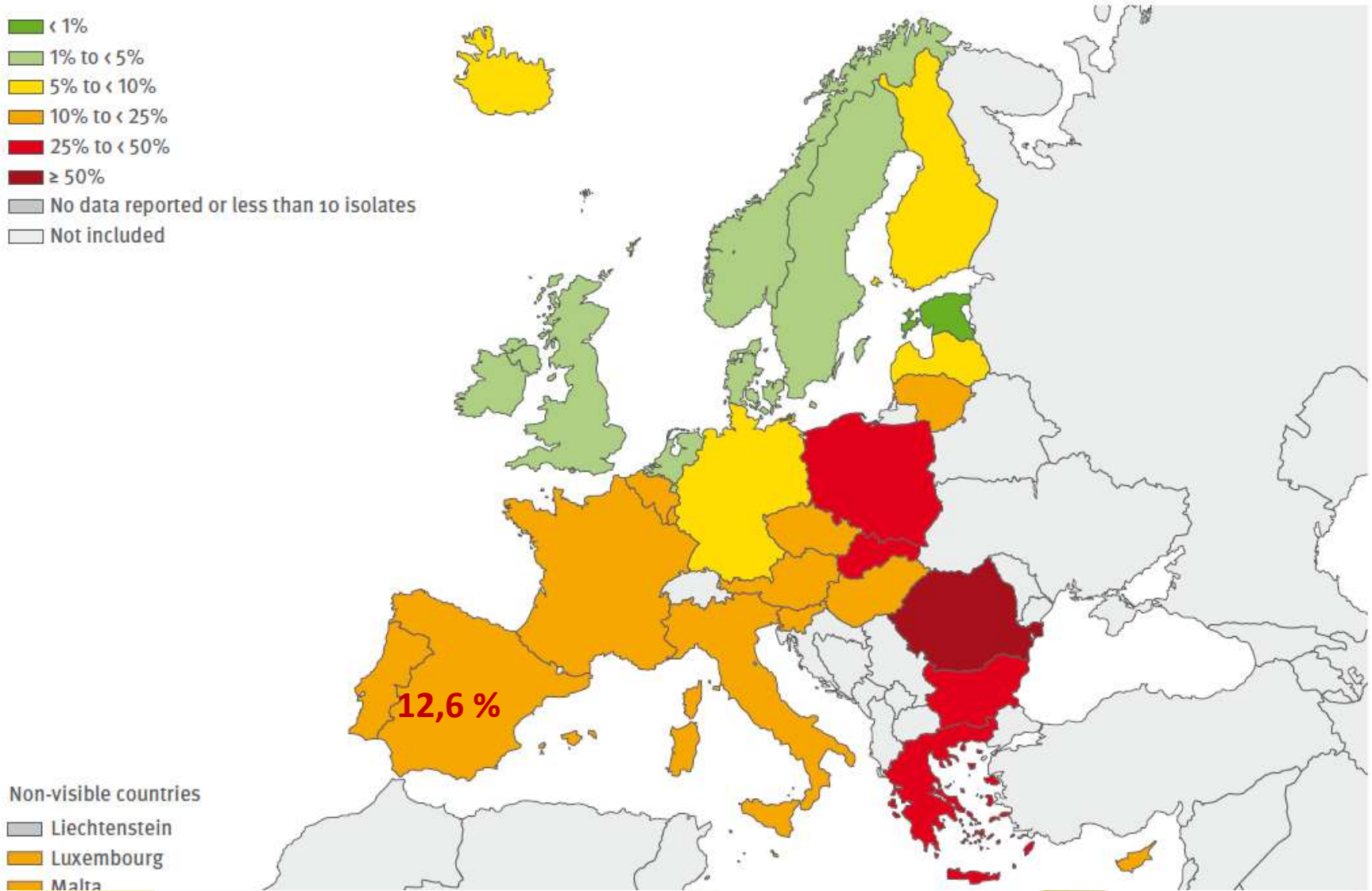


Figure 4.24: *Pseudomonas aeruginosa*: percentage (%) of invasive isolates with combined resistance (resistance to three or more antimicrobial classes among piperacillin (± tazobactam), ceftazidime, fluoroquinolones, aminoglycosides and carbapenems), by country, EU/EEA countries, 2011



Infecciones del pie diabético

TRATAMIENTO ANTIMICROBIANO

Tabla 5 Tratamiento antibiótico empírico de las infecciones del pie diabético

Infección	Primera elección	Alternativa
Leve/Moderada-leve	Amoxicilina - ácido clavulánico v.o.	Levofloxacino o moxifloxacino v.o. clindamicina v.o. cotrimoxazol v.o. linezolid v.o.
Moderada-grave	Ertapenem i.v. ± daptomicina i.v. o linezolid i.v./v.o. o glucopéptido i.v. ^a	Amoxicilina-ácido clavulánico i.v. o cefalosporina de tercera generación i.v. + metronidazol i.v. o fluoroquinolona ^b i.v./v.o. + metronidazol i.v./v.o. o piperacilina-tazobactam i.v. ^c o imipenem i.v. o meropenem i.v. ^c ± linezolid i.v./v.o. o daptomicina i.v. o glucopéptido i.v. ^a
Grave	Imipenem o meropenem i.v. O piperacilina-tazobactam i. v. + linezolid i.v. o daptomicina i.v. o glucopéptido i.v. ^a	Tigeciclina i.v. ^d + fluoroquinolona ^b i.v. o amikacina i.v.

^a Sospecha de SARM.

^b Ciprofloxacino o levofloxacino.

^c Sospecha de *P. Aeruginosa*.

^d Advertencia sobre el uso de tigeciclina (FDA). Disponible en: <http://www.fda.gov/Drugs/DrugSafety/ucm224370.htm>.

Outcome of Diabetic Foot Osteomyelitis Treated Nonsurgically

A retrospective cohort study

ERIC SENNEVILLE, MD¹
AUDREY LOMBART, MD¹
ERIC BELTRAND, MD²
MICHEL VALETTE, MD¹

LAURENCE LEGOUT, MD¹
MARIE CAZAUBIEL, MD¹
YAZDAN YAZDANPANAH, MD, PHD¹
PIERRE FONTAINE, MD, PHD³

OBJECTIVE — The purpose of this article was to identify criteria predictive of remission in nonsurgical treatment of diabetic foot osteomyelitis.

RESEARCH DESIGN AND METHODS — Diabetic patients who were initially treated without orthopedic surgery for osteomyelitis of the toe or metatarsal head of a nonischemic foot between June 2002 and June 2003 in nine French diabetic foot centers were identified, and their medical records were reviewed. Remission was defined as the absence of any sign of infection at the initial or contiguous site assessed at least 1 year after the end of treatment. A total of 24 demographic, clinical, and therapeutic variables including bone versus swab culture–based antibiotic therapy were analyzed.

RESULTS — Fifty consecutive patients aged 62.2 ± 11.1 years (mean \pm SD) with diabetes duration of 16 ± 10.9 years were included. The mean duration of antibiotic treatment was 11.5 ± 4.21 weeks. Bone biopsy was routinely available in four of the nine centers. Overall patient management was similar in the different centers except for the use of rifampin, which was recorded more frequently in patients from centers in which a bone biopsy was available. At the end of a 12.8-month posttreatment mean follow-up, 32 patients (64%) were in remission. Bone culture–based antibiotic therapy was the only variable associated with remission, as determined by both univariate (18 of 32 [56.3%] vs. 4 of 18 [22.2%], $P = 0.02$) and multivariate analyses (odds ratio 4.78 [95% CI 1.0–22.7], $P = 0.04$).

CONCLUSIONS — Bone culture–based antibiotic therapy is a factor predictive of success in diabetic patients treated nonsurgically for osteomyelitis of the foot.

group (3), antibiotic therapy for these patients was based on culture of nonbone specimens such as wound tissues or deep samples taken during debridement of foot lesions (4–7).

The factors associated with success in diabetic patients treated for osteomyelitis of the foot have been assessed in several

- La colaboración entre clínicos y microbiólogos puede mejora el manejo de las infecciones del pie diabético...

did not find any difference in the outcome of patients treated with bone versus nonbone debridement nor in those treated with oral versus oral plus intravenous therapy. The respective roles of an increase in serum creatinine levels and of a fever, identified by Pittet et al. (5) as independent predictive factors of failure in such patients, cannot be applied to bone infections, as deep tissue infection and osteomyelitis were not evaluated separately

