Resistenza agli antibiotici

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Rianimazione

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Clin Infect Dis. 2008 Jan 15;46(2):155-64

- **The epidemic of antibiotic-resistant infections: a call to action for the medical community from the Infectious Diseases Society of America.**

- Spellberg B1, Guidos R, Gilbert D, Bradley J, Boucher HW, Scheld WM, Bartlett JG, Edwards J Jr; Infectious Diseases Society of America.

Abstract

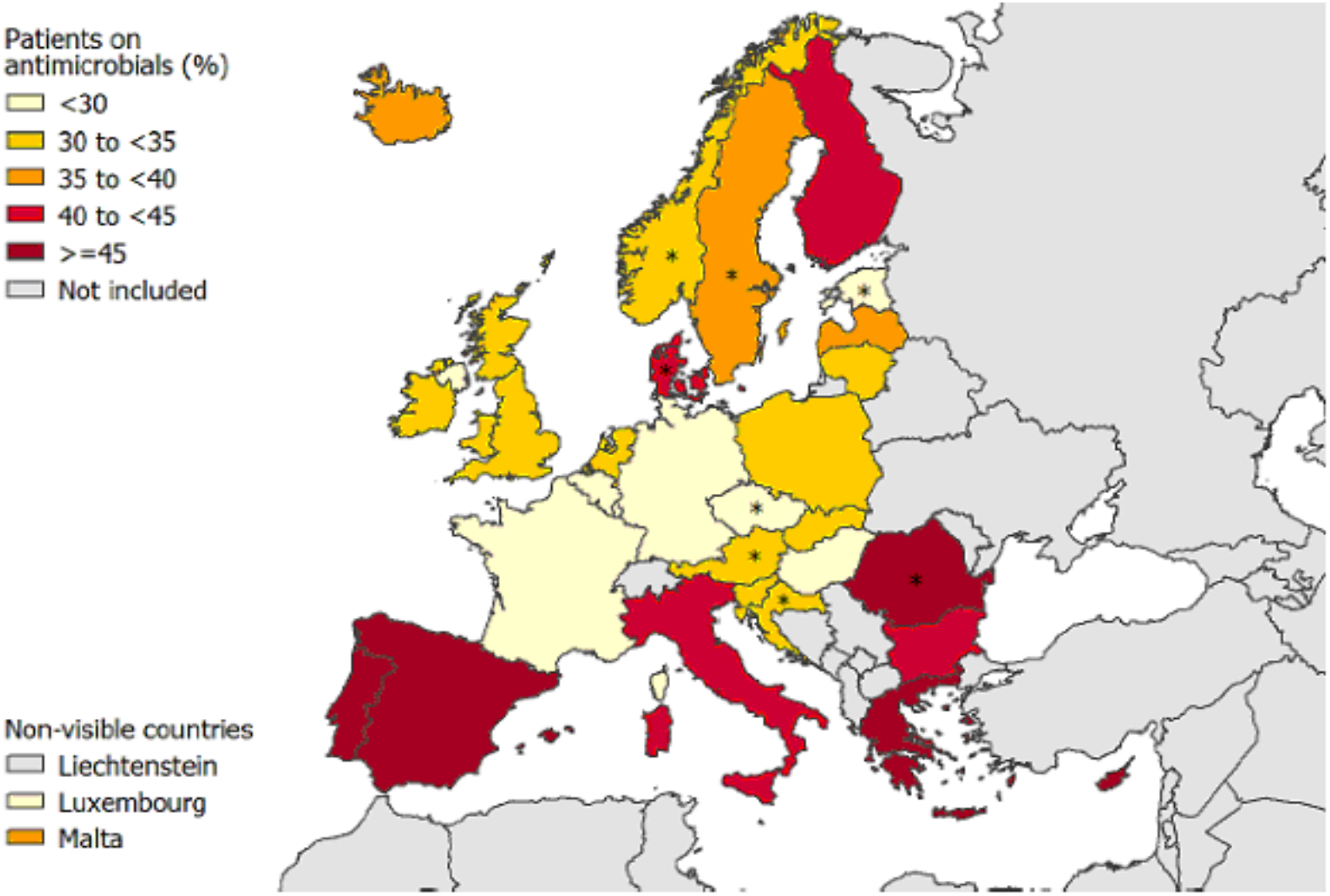
- The ongoing explosion of antibiotic-resistant infections continues to plague global and US health care. Meanwhile, an equally alarming decline has occurred in the research and development of new antibiotics to deal with the threat. In response to this microbial "perfect storm," in 2001, the federal Interagency Task Force on Antimicrobial Resistance released the "Action Plan to Combat Antimicrobial Resistance; Part 1: Domestic" to strengthen the response in the United States. The Infectious Diseases Society of America (IDSA) followed in 2004 with its own report, "Bad Bugs, No Drugs: As Antibiotic Discovery Stagnates, A Public Health Crisis Brews," which proposed incentives to reinvigorate pharmaceutical investment in antibiotic research and development. The IDSA's subsequent lobbying efforts led to the introduction of promising legislation in the 109 th US Congress (January 2005-December 2006). Unfortunately, the legislation was not enacted. During the 110 th Congress, the IDSA has continued to work with congressional leaders on promising legislation to address antibiotic-resistant infection. Nevertheless, despite intensive public relations and lobbying efforts, it remains unclear whether sufficiently robust legislation will be enacted. In the meantime, microbes continue to become more resistant, the antibiotic pipeline continues to diminish, and the majority of the public remains unaware of this critical situation. The result of insufficient federal funding; insufficient surveillance, prevention, and control; insufficient research and development activities; misguided regulation of antibiotics in agriculture and, in particular, for food animals; and insufficient overall coordination of US (and international) efforts could mean a literal return to the preantibiotic era for many types of infections. If we are to address the antimicrobial resistance crisis, a concerted, grassroots effort led by the medical community will be required.

Clin Infect Dis. 2009 Jan 1;48(1):1-12.

- **Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America.**
- Boucher HW1, Talbot GH, Bradley JS, Edwards JE, Gilbert D, Rice LB, Scheld M, Spellberg B, Bartlett J.

Abstract

- The Infectious Diseases Society of America (IDSA) continues to view with concern the lean pipeline for novel therapeutics to treat drug-resistant infections, especially those caused by gram-negative pathogens. Infections now occur that are resistant to all current antibacterial options. Although the IDSA is encouraged by the prospect of success for some agents currently in preclinical development, there is an urgent, immediate need for new agents with activity against these panresistant organisms. There is no evidence that this need will be met in the foreseeable future. Furthermore, we remain concerned that the infrastructure for discovering and developing new antibacterials continues to stagnate, thereby risking the future pipeline of antibacterial drugs. The IDSA proposed solutions in its 2004 policy report, "Bad Bugs, No Drugs: As Antibiotic R&D Stagnates, a Public Health Crisis Brews," and recently issued a "Call to Action" to provide an update on the scope of the problem and the proposed solutions. A primary objective of these periodic reports is to encourage a community and legislative response to establish greater financial parity between the antimicrobial development and the development of other drugs. Although recent actions of the Food and Drug Administration and the 110th US Congress present a glimmer of hope, significant uncertainly remains. Now, more than ever, it is essential to create a robust and sustainable antibacterial research and development infrastructure--one that can respond to current antibacterial resistance now and anticipate evolving resistance. This challenge requires that industry, academia, the National Institutes of Health, the Food and Drug Administration, the Centers for Disease Control and Prevention, the US Department of Defense, and the new Biomedical Advanced Research and Development Authority at the Department of Health and Human Services work productively together. This report provides an update on potentially effective antibacterial drugs in the late-stage development pipeline, in the hope of encouraging such collaborative action.

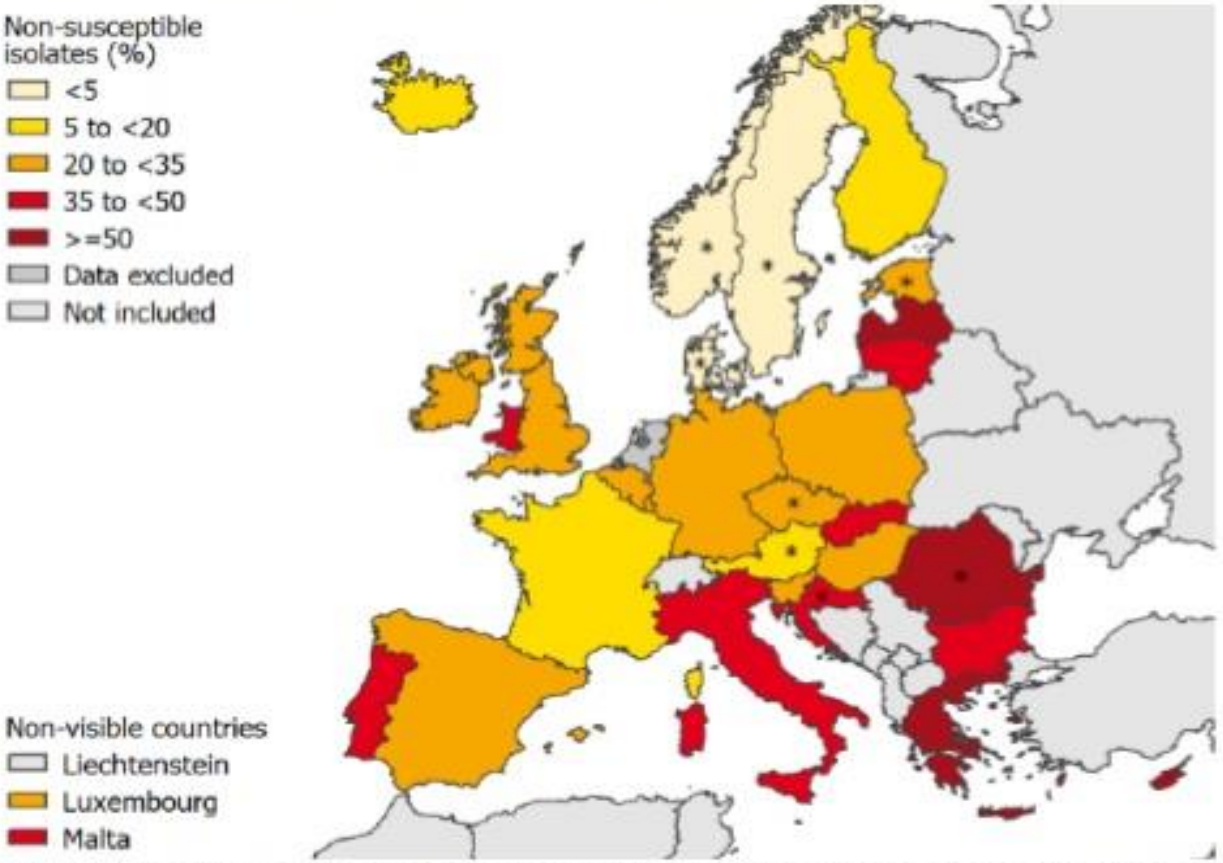


**PPS data representativeness was poor in Austria, Croatia, Czech Republic, Estonia, Norway and Romania and very poor in Denmark and Sweden.*

High ESKAPE composed index of resistance

Extracted from ECDC PPS 2011-2012

DGS desde 1899 Direção-Geral da Saúde



First-level antimicrobial resistance markers in PPS: MRSA, VRE, Enterobacteriaceae non-susceptible to third-generation cephalosporins, Pseudomonas aeruginosa *and* Acinetobacter baumannii *non-susceptible to carbapenems. Data from the Netherlands were excluded for reasons explained above.*

In Ospedale

- In che cosa sbagliamo

a) Cattivo utilizzo degli antibiotici
b) Mancata aderenza alle misure di precauzione da contatto

- Cosa possiamo fare per migliorare

a) Antibiotic stewardship
b) Usare al meglio ciò che abbiamo
c) Diagnostica microbiologica rapida

Il cattivo utilizzo in profilassi

- Profilassi chirurgica

- molecole sbagliate
- durata eccessiva

- Profilassi medica

- indicazioni troppo ampie
- molecole sbagliate
- durata eccessiva

Il cattivo utilizzo in terapia

- Terapia empirica

- Mancato passaggio alla terapia mirata
- Molecole sbagliate
- Dosaggi troppo bassi

- Terapia mirata

- Durata eccessiva (PCT ?)

Cosa ci può aiutare

- Antibiotic stewardship
- Microbiologia: tecniche diagnostiche rapide (biologia molecolare, MALDI-TOF MS)
- T.D.M., pK/pD

Antibiotic stewardship

razionale:ridurre la pressione selettiva causata da uso inappropriato degli antibiotici

obiettivo: ridurre il tasso di esposizione dei pazienti

Antibiotic stewardship

- Stabilire se il malato deve o non deve essere trattato
- Stabilire la terapia empirica iniziale
- De-escalation
- Abbreviare la durata del trattamento

Microbiologia “rapida”

Le tecniche di biologia molecolare (identificazione de germe tramide DNA) e il MALDI-TOF MS (identificazione dal profilo proteico) permettono:

- Identificazione rapida del germe
- Identificazione rapida della presenza di meccanismi di resistenza

RIDUZIONE della durata della TERAPIA EMPIRICA

- Sarà sempre necessario avere l’ABG ?
- Costi elevati
- Dariservare solo ad alcuni pazienti ?

Appropriatezza

Appropriatezza: solo la molecola “giusta” o anche la “posologia giusta” ?

Variazioni del profilo pK nei pazienti con infezione grave (Volume di distribuzione, legame proteico vs albuminemia, clearance)

Appropriatezza posologica

- Meccanismo di “killing” e posologia

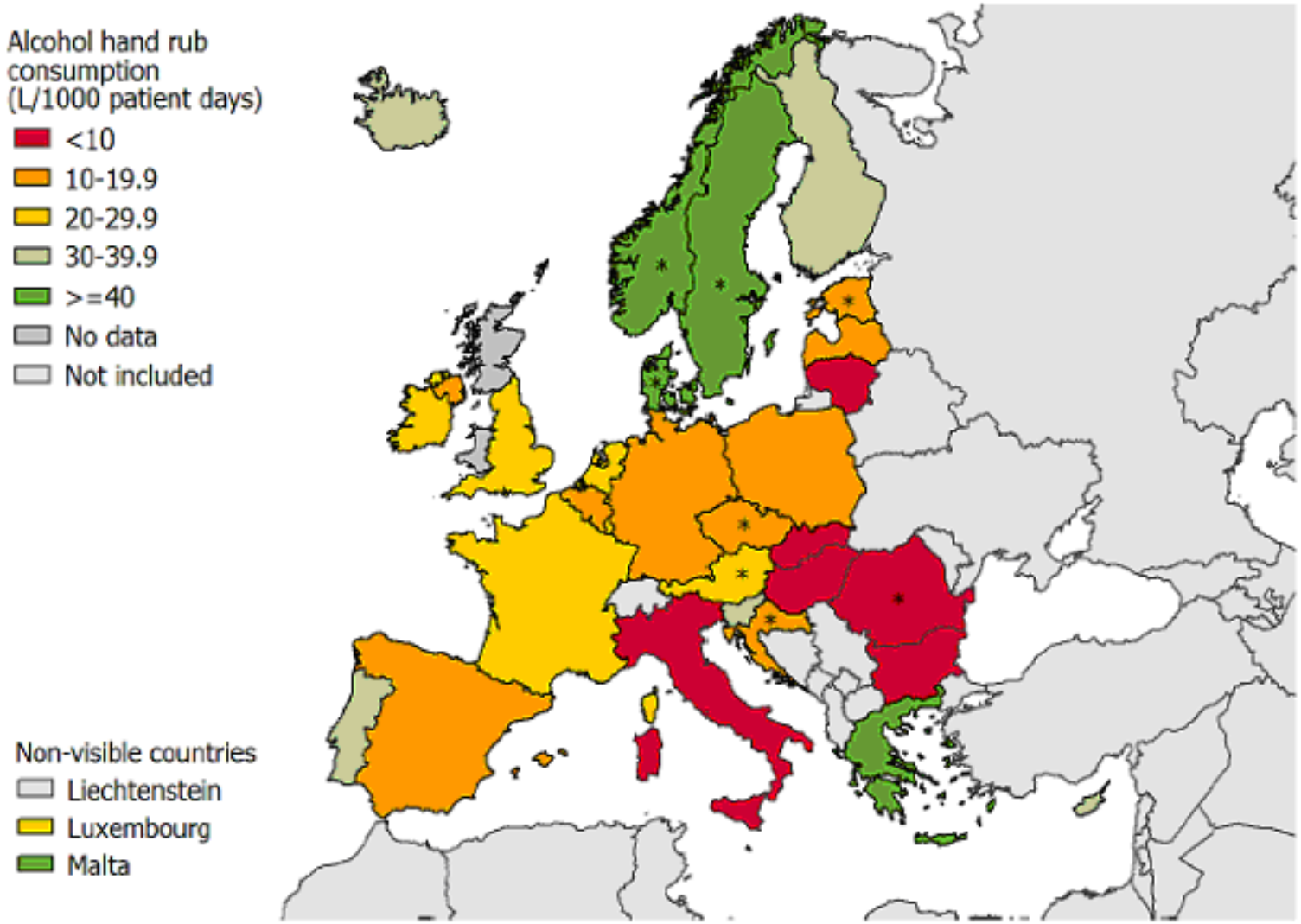
  (infusione continua, infusione estesa, monodose quotidiana)
- M.I.C. e posologia

  (utilizzo dei carbapenemi nelle infezioni da KPC)
- T.D.M. e posologia

La diffusione di MDR per cross-contaminazione

- Colture di sorveglianza

- Precauzioni da contatto



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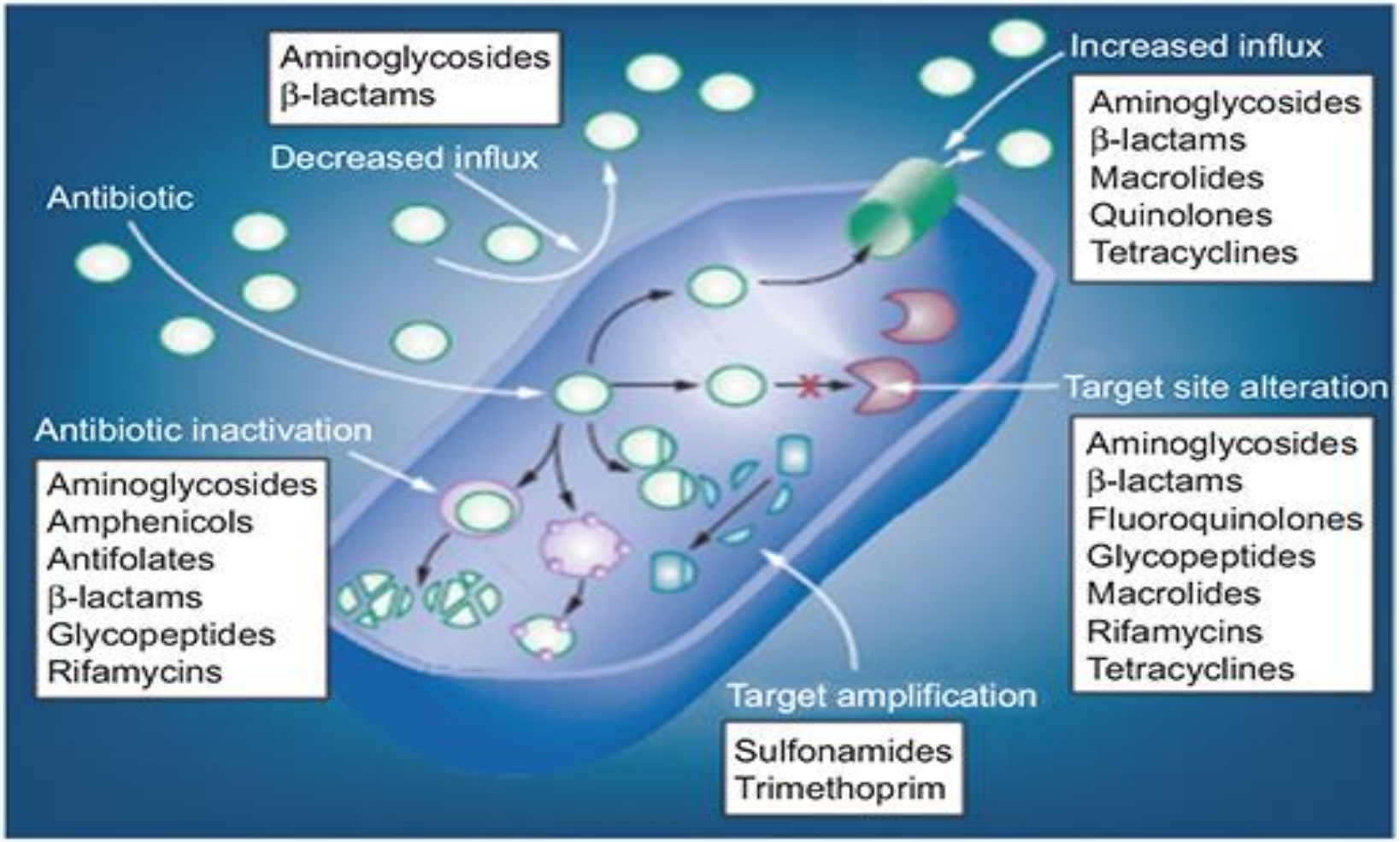

Fig. 2 - Meccanismi di antibiotico resistenza. Nei riquadri sono riportate le classi di antibiotico interessate da ogni meccanismo (Schmieder and Edwards, 2012).