



Sistema Socio Sanitario



Regione
Lombardia

ASST Santi Paolo e Carlo

Switch from Intravenous to Oral Antibiotic Therapy in the Treatment of Infective Endocarditis

Speakers: Lorenzo Brando Lundgren, Lorenzo Albertini

Background

Current international guidelines (such as **ESC 2015** and **AHA 2015**) for the management of infective endocarditis (IE) suggest 4 to 6 weeks of intravenous (IV) antibiotic therapy^{1,2}.

1. Habib, G. *et al.* 2015 ESC Guidelines for the management of infective endocarditis. *European Heart Journal* vol. 36 3075–3123 Preprint at <https://doi.org/10.1093/eurheartj/ehv319> (2015).
2. Baddour, L. M. *et al.* Infective endocarditis in adults: Diagnosis, antimicrobial therapy, and management of complications: A scientific statement for healthcare professionals from the American Heart Association. *Circulation* vol. 132 1435–1486 Preprint at <https://doi.org/10.1161/CIR.0000000000000296> (2015).

Cases description:

We retrospectively analyzed patients diagnosed with IE at our center (San Paolo and San Carlo Hospital, Milan, Italy:

- from January 2018 to July 2022
- identifying patients switching to OT for different reasons
- collecting demographic and clinical data from clinical records

Parameters	IE, N = 136	IV IE N = 127	OT IE, N = 9
Age, years, median (IQR)	76 (61-81)	76 (62-82)	74 (56-80)
Gender, Male, n (%)	72 (52,9%)	67 (52,8%)	5 (55,6%)
Age Adjusted Charlson score, median (IQR)	4 (3-7)	5 (4-7)	5 (4-7)
Bacteria, n (%)			
MSSA	28 (20,6%)	25 (19,7%)	3 (33,3%)
MRSA	19 (14%)	15 (11,8%)	4 (44,4%)
Staphylococci CoNS	6 (4,4%)	6 (4,4%)	
Streptococci Viridans	13 (9,6%)	12 (9,4%)	1 (11,1%)
Enterococci Amp ⁱ S	17 (12,5%)	16 (12,6%)	1 (11,1%)
Enterococci Vanco ^S	2 (1,4%)	2 (1,4%)	
Enterococci Vanco ^R	1 (0,7%)	1 (0,7%)	
Streptococcus Bovis	4 (2,9%)	4 (2,9%)	
Altri Str	7 (5,1%)	7 (5,1%)	
HACEK	1 (0,7%)	1 (0,7%)	
Non HACEK Gram neg	7 (5,1%)	7 (5,1%)	
Negative blood cultures	31 (22,8%)	31 (22,8%)	

Parameters	IE, N = 136	IV IE N = 127	OT IE, N = 9
Infective endocarditis type, n (%)			
Native valve (NVEI)	90 (66,1%)	82 (64,6%)	8 (88,9%)
Prosthetic valve (PVEI)	44 (32,5%)	44 (36,6%)	1 (11,1%)
Cardiovascular device	2 (1,4%)	1 (0,8%)	-
Community acquired (CA)	89 (65,4%)	87 (68,5%)	2 (22,2%)
Hospital acquired (HA)	47 (36,6%)	40 (31,5%)	7 (77,8%)
Vegetation dimension, mm, median (IQR)			
TT echocardiography	8 (6-12)	8 (6-12)	12 (10-15)
TE echocardiography	10 (7-15)	10 (7-15)	12 (8-12)
Biomarkers			
WBC (at diagnosis), 10 ³ cells/uL, median (IQR)	12 (8-15)	12 (8-15)	11 (10-14)
WBC (at oral switch), 10 ³ cells/uL, median (IQR)	-	-	5 (5-7)
WBC (at therapy end), 10 ³ cells/uL, median (IQR)	7 (5-10)	8 (5-10)	5 (5-6)
PCR (at diagnosis), mg/L, median (IQR)	72 (64-110)	71 (63-110)	76 (33-95)
PCR (at oral switch), mg/L, median (IQR)	-	-	13 (8-28)
PCR (at therapy end), mg/L, median (IQR)	37 (26-57)	40 (26-57)	5 (5-6)

Parameters	IE, N = 136	IV IE N = 127	OT IE, N = 9
Complications, n (%)	40 (29,4%)	34 (26,8%)	6 (66,7%)
Septic embolization	21 (51,5%)	19 (55,6%)	2 (33,3%)
Pneumonia	4 (10%)	2 (5,9%)	2 (33,3%)
Chordal rupture	6 (15%)	5 (14,7%)	1 (16,7%)
Stroke	1 (2,5%)	1 (2,9%)	
Valve regurgitation	2 (5%)	1 (2,9%)	1 (16,7%)
Vertebral osteomyelitis	6 (15%)	6 (17,6%)	
Blood culture's clearance, days, median (IQR)	7 (5-11)	7 (5-11)	4 (3-4)
Treatment, n (%)			
Medical	99 (72,8%)	91 (71,7%)	8 (88,9%)
Surgery	37 (27,2%)	36 (28,3%)	1 (11,1%)
Total antibiotic treatment duration, days, median (IQR)	28 (16-42)	26 (14-42)	43 (48-50)
Outcome at hospital discharge, n (%):			
Recovery	109 (80,1%)	100 (78,7%)	9 (100%)
Deaths	27 (19,9%)	27 (21,3%)	-
Outcome at 28 days, n (%):			
Recovery	98 (72,1%)	89 (70,1%)	9 (100%)
Deaths	38 (27,9%)	38 (29,9%)	-

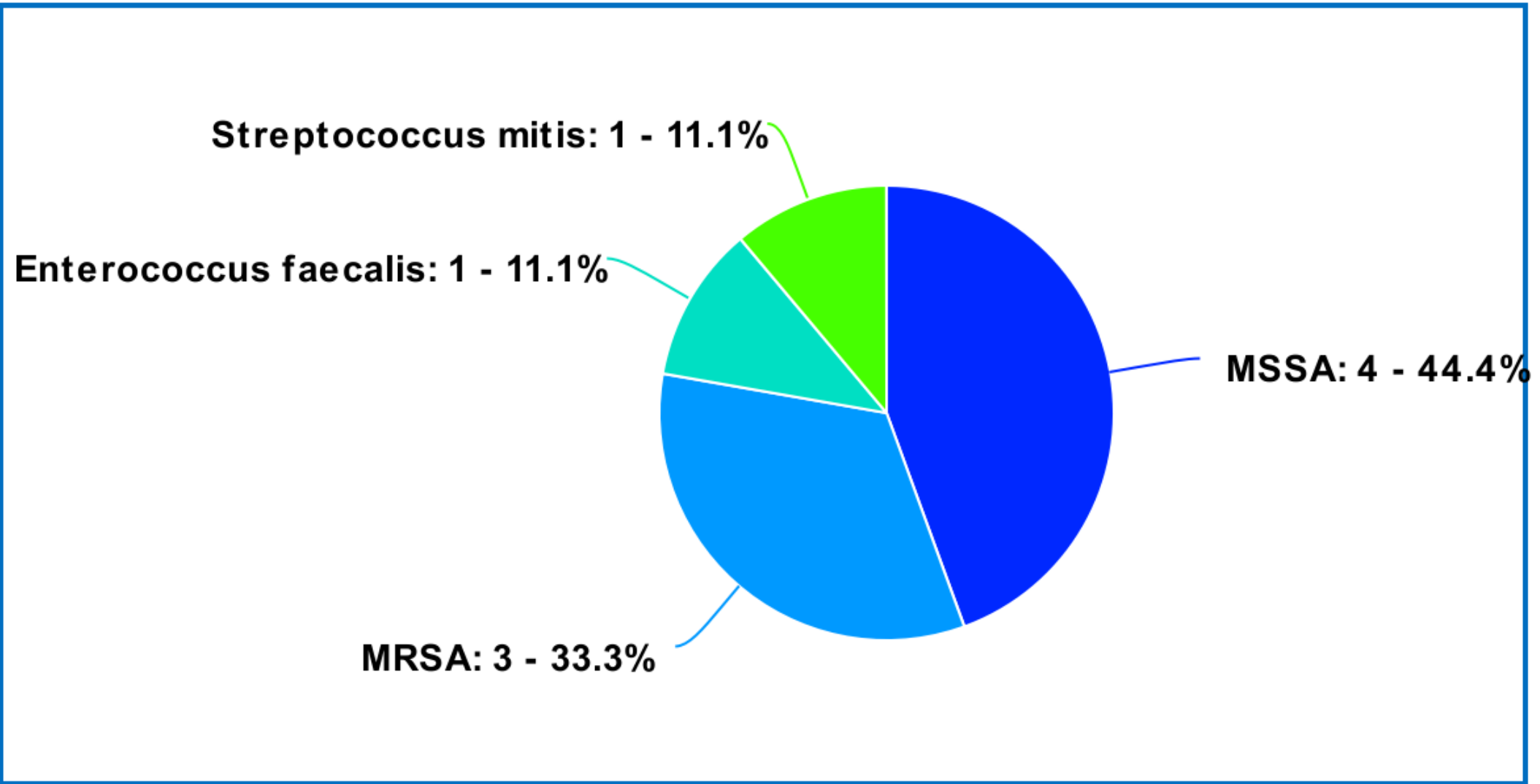
LEGEND: IE, infective endocarditis; IV IE, IE treated with intravenous antibiotics – OT IE, IE treated with step-down to oral antibiotics.

Among **136 IE** patients diagnosed and cared at our center, **9 switched to an OT** after IV antimicrobial treatment:

- Median age: 74 years (IQR 56-80)
- Gender: 5 males, 4 females
- Median Age-Adjusted Charlson Score: 5 (IQR 4-7)
- IE type:
 - 8 NVIE & 1 PVIE
 - 8 left-sided IE & 1 right-sided IE

- All patients underwent initial IV-administered antibiotic therapy and were switched to OT in a clinically stable state, being afebrile, hemodynamically stable, with cleared bacteremia and evidence of inflammatory markers reduction.
- Before switching, CT scans ruled out septic embolization or any further episodes and echocardiography documented no disease progression.

Microbiology



■ MSSA ■ MRSA ■ Enterococcus faecalis ■ Streptococcus mitis

Antibiotic therapy

- All 9 cases were initially treated with IV antibiotics for a median duration of 23 (IQR 16-38) days and were then switched to OT for a median of 18 (IQR 12-23) days.
- Total days of treatment: median of 48 (IQR 43-50)

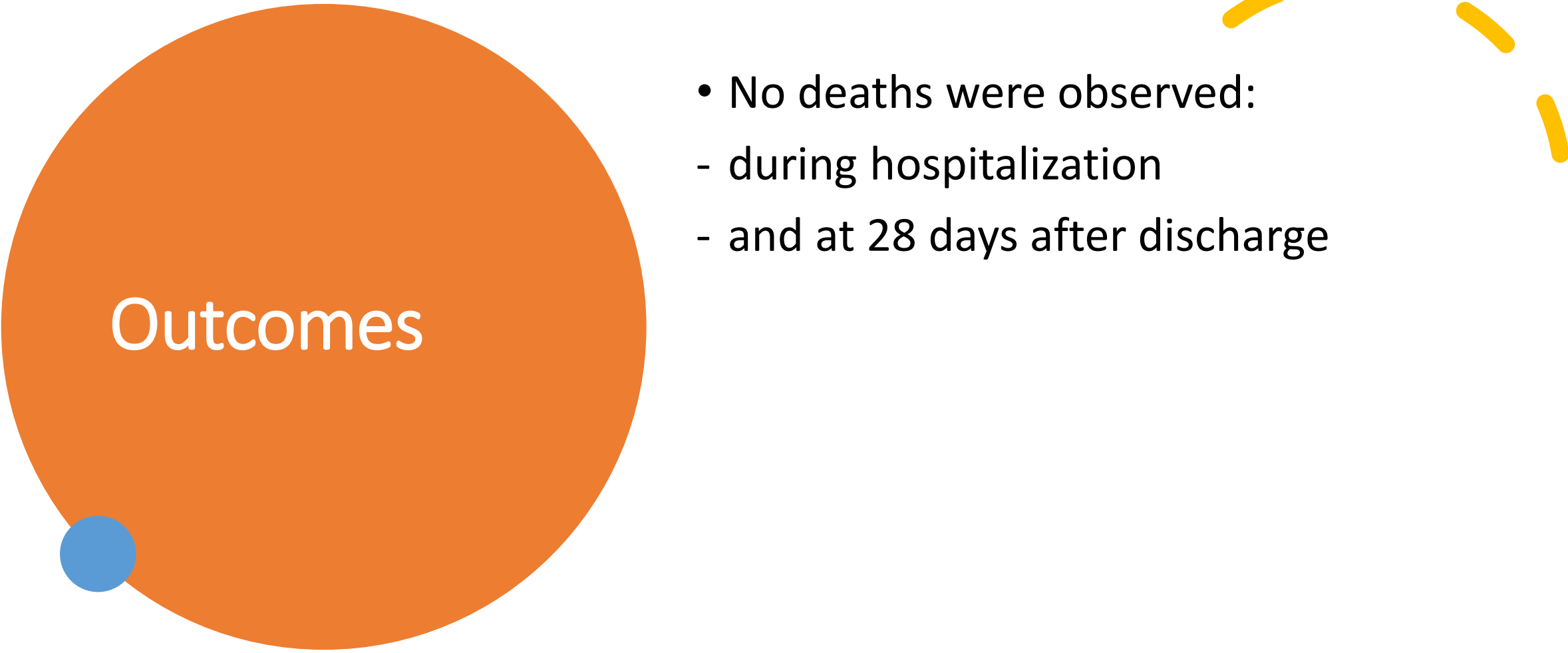
Why switch? And with what?

Reasons for switching to OT were:

- lack of venous access (5 patients)
- improvement of patients' adherence or patients' wish (4 cases)
- IV antibiotics toxicity (1 case).

Oral antibiotic:

- in 8 cases linezolid
- in 1 case amoxicillin/clavulanate.



Outcomes

- No deaths were observed:
 - during hospitalization
 - and at 28 days after discharge

Endocarditis	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9
Age, years	25	82	74	72	80	56	23	79	89
Gender	F	M	M	M	F	M	F	M	F
Risks factor for endocarditis	Heart valve/structural disease	Cardiac device	No	No	No	IVDU HIV/AIDS	No	-Previous endocarditis -Dental operation	No
Bacterial isolates	Streptococcus mitis	Enterococcus faecalis	MRSA	MSSA	MSSA	MSSA	MRSA	MRSA	MRSA
Localization of endocarditis	Native mitral valve	Prosthetic aortic valve	Native aortic valve	Native aortic valve	Native aortic valve	Native tricuspid valve	Native mitral valve	Native aortic valve	Native aortic valve
Complications	Chordal rupture Septic embolization	No	No	Septic embolization	No	Pneumonia Vertebral osteomyelitis	Pneumonia	No	No
IV antimicrobial treatment	Ampicillin + gentamicin	Ampicillin + ceftriaxone	Vancomycin	Oxacillin	Daptomycin	Cefazolin	Vancomycin	Vancomycin	Vancomycin
IV antimicrobial treatment time, days	36	23	16	15	10	55	30	20	40
Reason for oral switch	Source control to surgery	Lack of venous access	Lack of venous access	Will of the patient	Will of the patient	Lack of venous access	Lack of venous access	Lack of venous access	EV drug toxicity
Oral antimicrobial treatment	Amoxicillin/clavulanate	Linezolid	Linezolid	Linezolid	Linezolid	Linezolid	Linezolid	Linezolid	Linezolid
Oral antimicrobial treatment time, days	12	22	26	42	16	11	18	23	≥10

DISCUSSION

- Patients may need to switch to OT in a real-life setting because of a variety of reasons including:
 - a lack of venous access
 - drug-related toxicity
 - patients' will in order to achieve better compliance.
- OT requires patients to have a normal gastrointestinal function to uptake orally administered antibiotics and allow adequate serum concentrations properly. All 9 patients had no malabsorption issues.
- High orally bioavailable molecules need to be selected.

DISCUSSION

- We focused on OT step-down following initial IV-administred antibiotic therapy in 9 selected cases of IE in a real-life setting.
- In all cases, a clinical cure was reached at the time of discharge, and no intra-hospital all-cause mortality was observed. This was also observed 28 days after discharge.
- OT was generally well tolerated with no reported toxic events.

Limitations

- Small number of patients involved
- Clinical heterogeneity with both left and right heart IE, multiple bugs involvement, and different comorbidities.
- Absence of clinical records about antibiotic TDM following the OT switch
- Absence of a structured follow-up program after discharge
- Different time of IV- and OT antibiotic administration



Switch dalla terapia antibiotica endovenosa alla terapia orale nelle endocarditi infettive

Proposta di PTDA

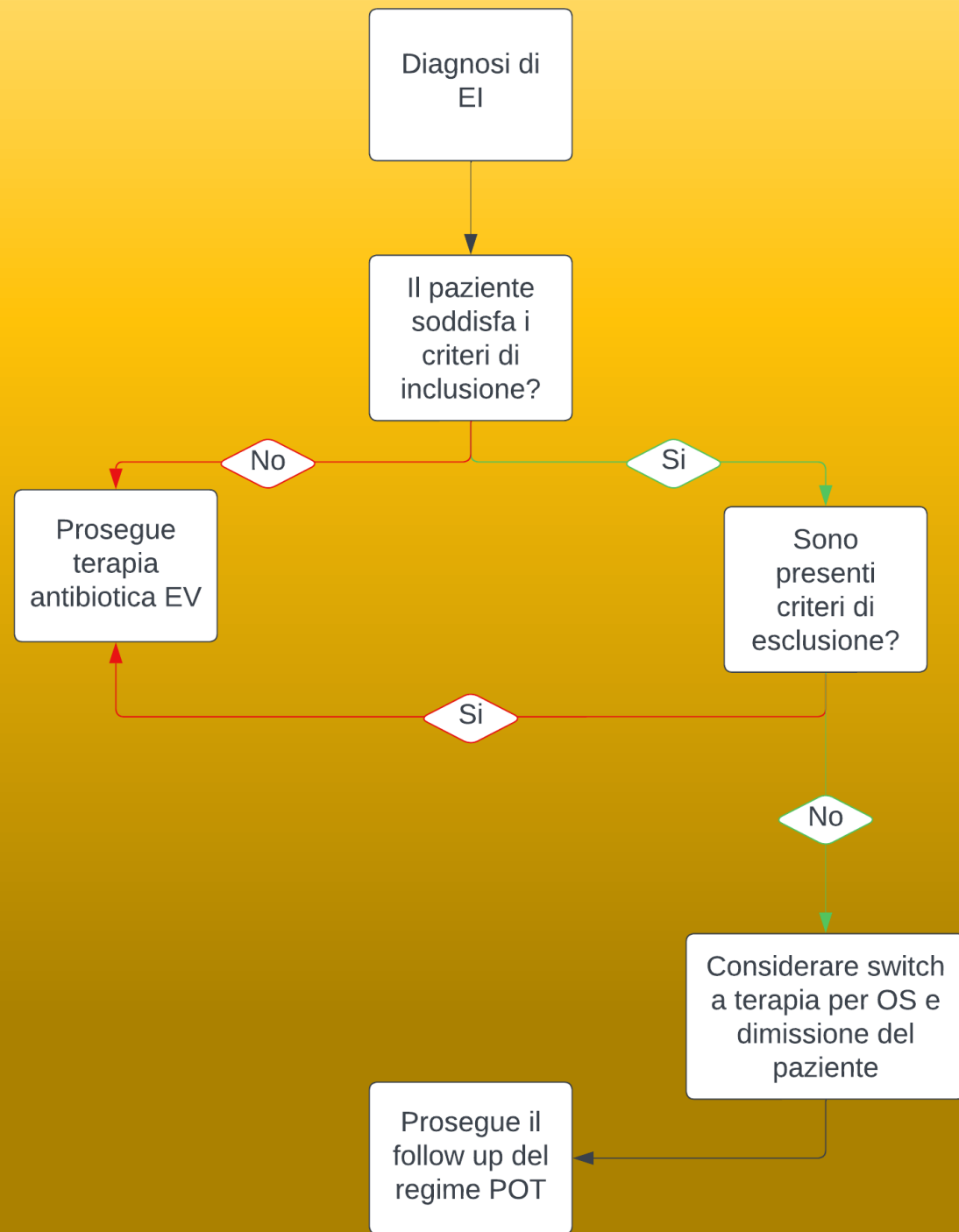
A black stethoscope is positioned diagonally across a white computer keyboard. The stethoscope's chest piece is on the left, and its two ear tubes extend towards the bottom right. The keyboard features standard white keys with black lettering, including letters like S, D, F, G, H, J, K, L, and function keys like 'option' and 'command'. The entire scene is set against a plain white background.

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Caratteristiche del paziente target

- Infezione causata da Streptococchi, Stafilococchi ed Enterococchi con adeguato profilo di sensibilità
- >10 giorni di terapia antibiotica endovenosa
- EC negative da almeno 5 giorni e negativizzazione entro 72h dall'introduzione di antibiotico EV
- Stabilità clinica (apiressia da 48h, PCR < 20 mg/L, PCT < 2 ug/mL, GB < 11000/uL, SOFA <2, MEWS < 3)
- Ecocardiografia di controllo 72h prima dello switch con assenza di segni di complicanze (es. ascesso)
- Possibilità di assumere terapia orale ed adeguato assorbimento intestinale



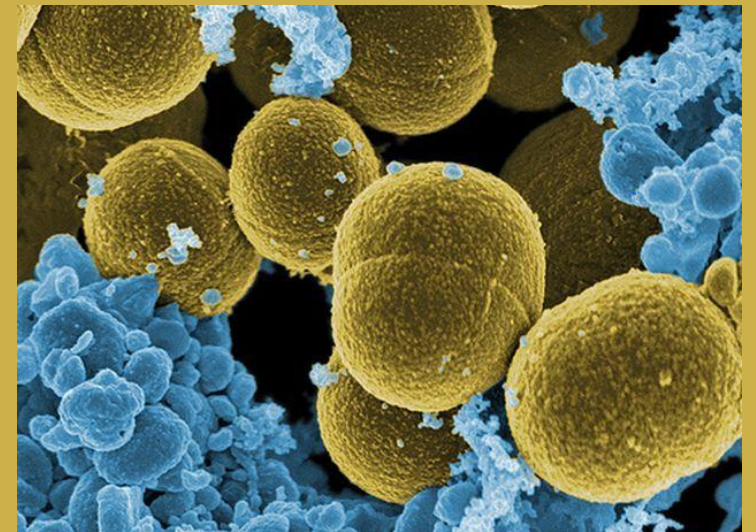
Terapia antibiotica orale proposta

MSSA e MRSA

I linea: linezolid 600 mg BID

II linea: levofloxacin 750 mg o
ciprofloxacin 750 mg BID +
rifampicin 600 mg BID

III linea:
trimetoprim/sulfametossazolo
800/160 mg BID



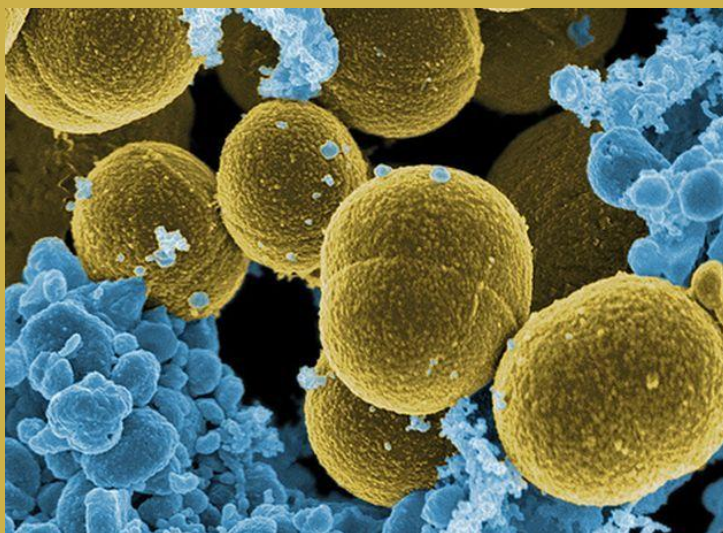
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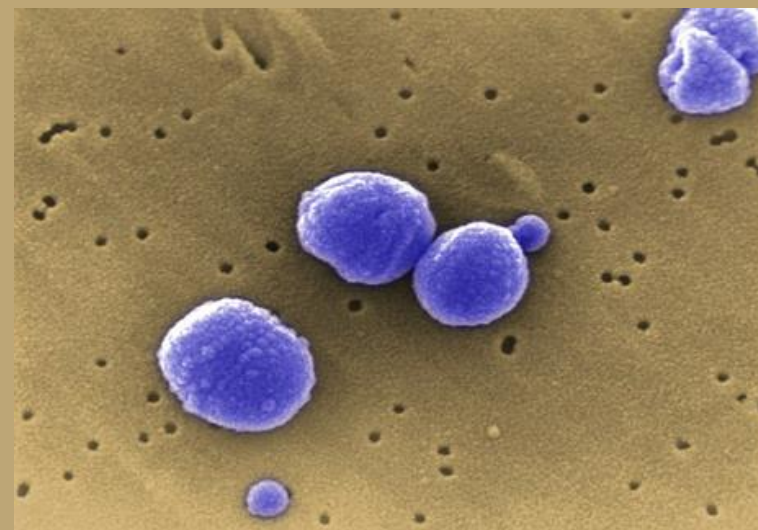
Streptococchi (MIC penicillina < 1)

I linea: amoxicillina/clavulanato 1 g
TID

II linea: linezolid 600 mg BID

Streptococchi (MIC penicillina > 1)

I linea: linezolid 600 mg BID

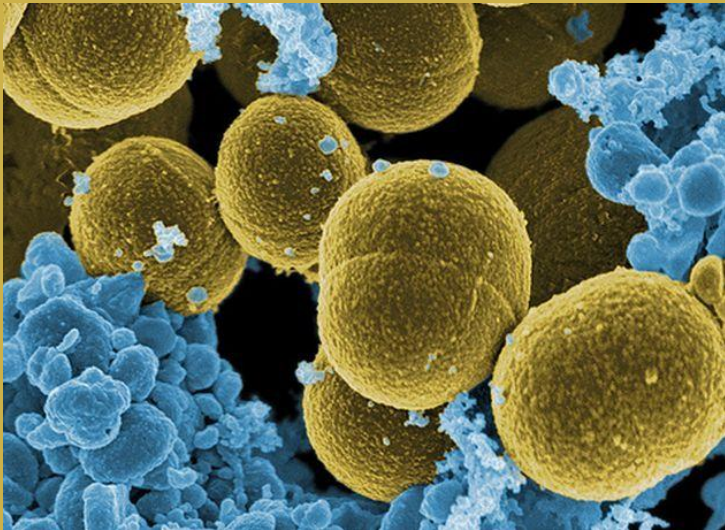


MSSA e MRSA

I linea: linezolid 600 mg BID

II linea: levofloxacin 750 mg o
ciprofloxacin 750 mg BID +
rifampicin 600 mg BID

III linea:
trimetoprim/sulfametossazolo
800/160 mg BID



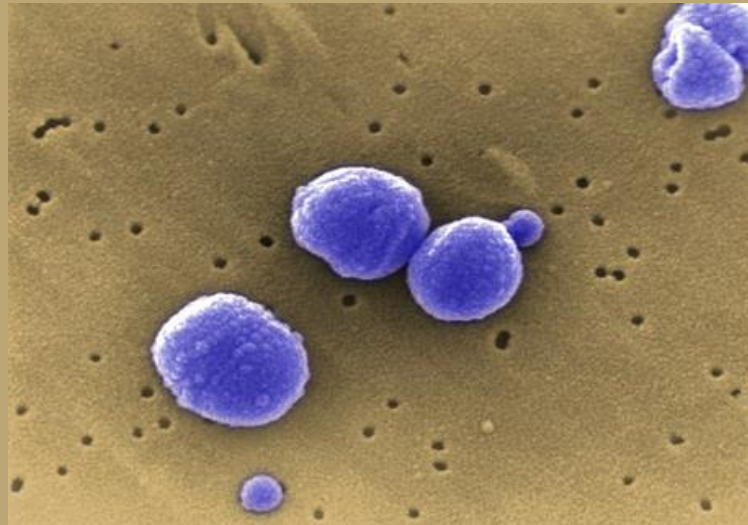
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II linea: linezolid 600 mg BID

Streptococchi (MIC penicillina > 1)

I linea: linezolid 600 mg BID



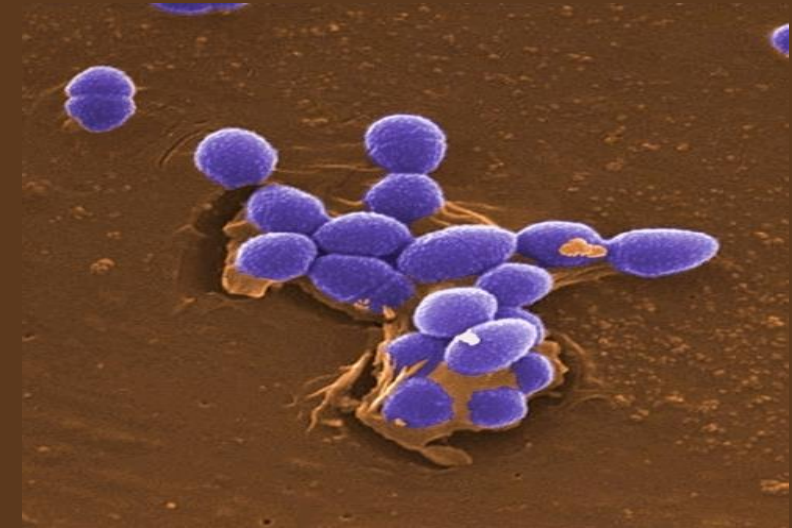
E. faecalis (MIC ampicillina < 4)

I linea: amoxicillina/clavulanato 1 g
TID

II linea: linezolid 600 mg BID

E. faecalis (MIC ampicillina > 4)

I linea: linezolid 600 mg BID



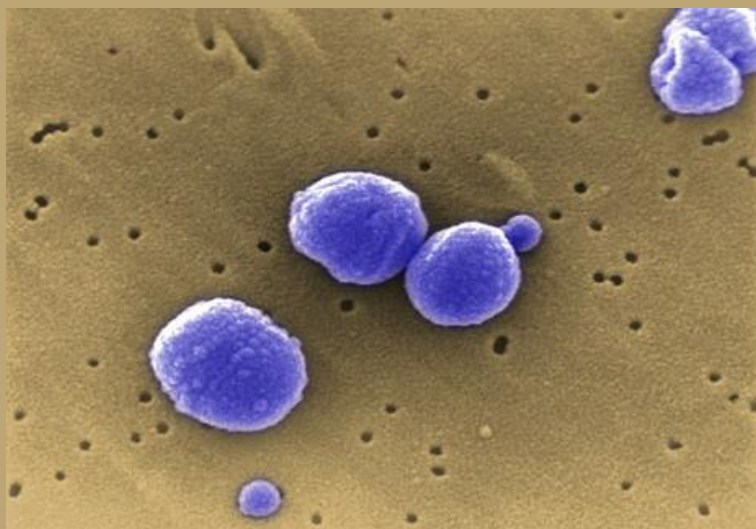
Streptococchi (MIC penicillina < 1) E. faecalis (MIC ampicillina < 4)

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I linea: linezolid 600 mg BID



I linea: amoxicillina/clavulanato 1 g
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II linea: linezolid 600 mg BID

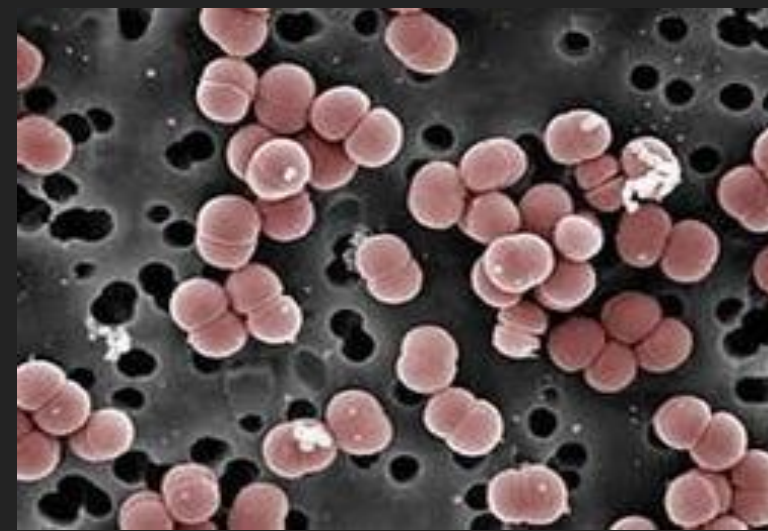
E. faecalis (MIC ampicillina > 4)

I linea: linezolid 600 mg BID



E. faecium

I linea: linezolid 600 mg BID



Follow-up POT

	DIAGNOSI	SWITCH	G7	G14
Consulenza infettivologica	✓	✓		
Ecocardiografia	✓	✓		
Esami ematici §	✓	✓	✓	✓
Dosaggio plasmatico dell'antibiotico (TDM) #			✓	
Visita infettivologica in telemedicina			✓	
Visita infettivologica ambulatoriale				✓

§Emocromo con formula, creatininemia, PCR, AST/ALT, bilirubina totale e frazionata, INR

#TDM per i seguenti antibiotici: linezolid, amoxicillina, levofloxacina/ciprofloxacina, rifampicina, trimetoprim/sulfametossazolo



Special thanks

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Dr.ssa F. Bai

Dr.ssa O. Viganò

