Sepsis on early period after allogeneic haematopoietic stem cell transplantation

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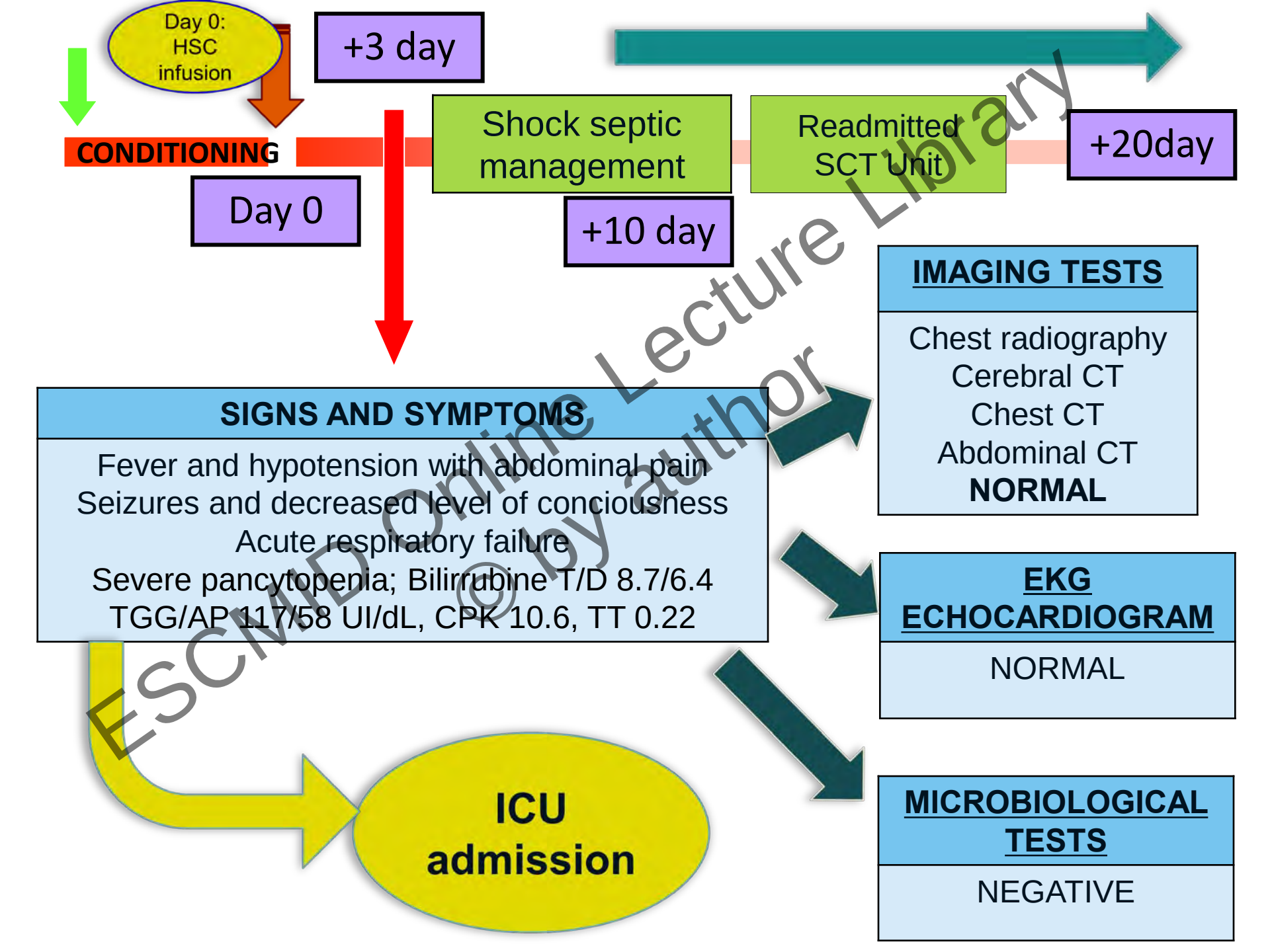
BACKGROUND (I)

- Ecuatorian 28-year old man
- Chronic Myeloid Leukemia (CML) in chronic phase (CP)
  - ✓ ressistant to Tirosine Kinase Inhibitors
- underwent allo-HSCT from *exvivo* expanded umbilical cord blood

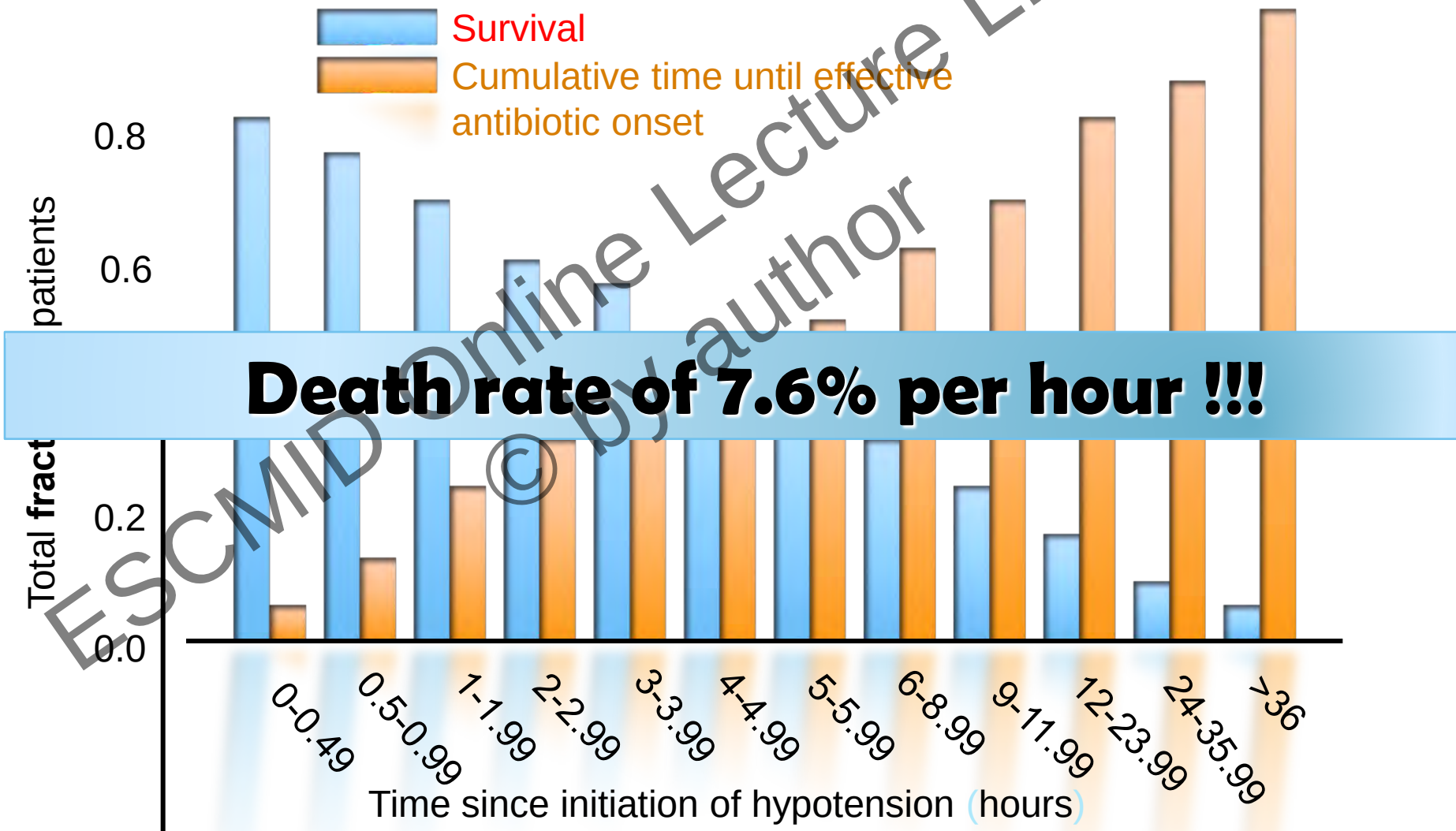
BACKGROUND (II)

PRE-TRANSPLANT SEROLOGIES	
PATIENT	IgG CMV IgG EBV IgG *T. gondii* } POSITIVES IgG *T. cruzi* IgG *Histoplasma* IgG *Strongiloides* } NEGATIVES
DONOR (CORD BLOOD UNIT)	IgG CMV POSITIVE IgG EBV IgG *T. gondii* } NEGATIVES

INFECTIOUS PROPHYLAXIS: ciprofloxacin, posaconazole, acyclovir and inhaled pentamidine



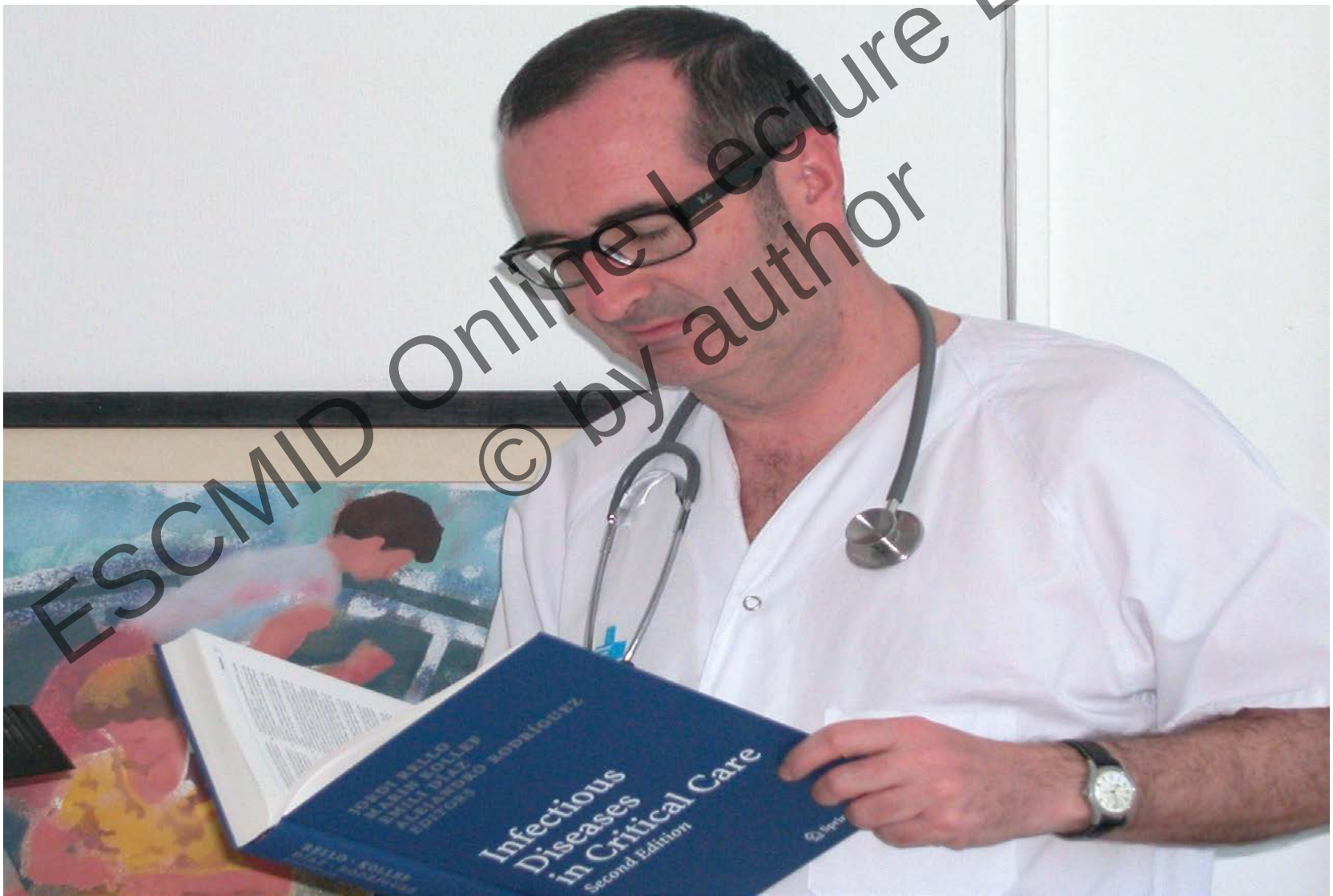
Septic shock, correct antibiotic initiation and mortality rate



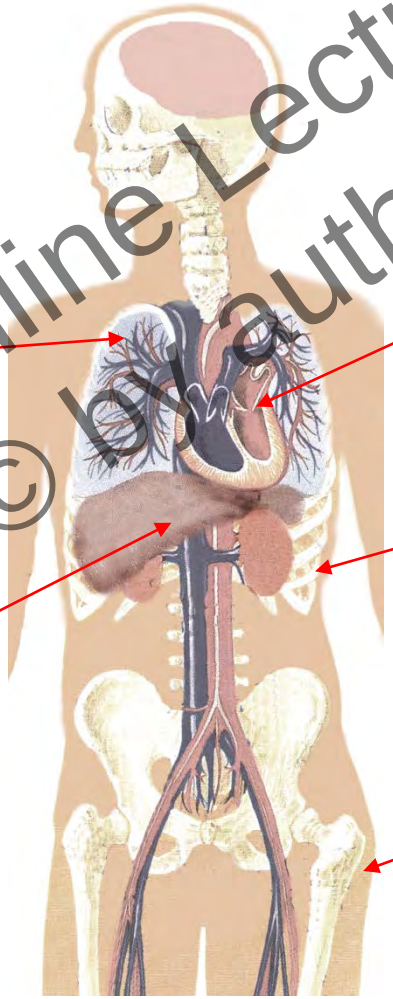
Death rate of 7.6% per hour !!!

Kumar A, et al. *Crit Care Med* 2006; 34:1589

How to re-evaluates patient's condition when antimicrobial therapy failed



Identifying severe sepsis and Septic shock



Cardiovascular:
PAS ≤ 90 or PAM ≤ 70
plus
Volume infussion
Or vasopressors for PAs≥90

Respiratory:

PaO2/FiO2 < 200.

PaO2/FiO2 < 250
If different from lung

Kidney:
Diuresis < 0,5 ml/Kg/h
1 h after resuscitation.

Metabolic:
pH< 7,30 or BE < - 5mEq
with lactate > 1,5

Hematologic:
Plat < 80.000mm^3 or
< 50% from last 72 hours

Hypotension, Fever, Hemoptysis

Severe acute respiratory insufficiency

EVOLUTION

ICU
re-admission

HEMOGRAM	BIOCHEMISTRY
Hb: 9 g/dL, L 0.3, Pl: 13x10^{9}/L	ALT: 338 UI/L, AST: 398 UI/L Bl T/D: 3.3/3.01 mg/dL
	MYOCARDIAL INJURY ENZYMES
	CK: 10.6, TT: 0.22

ECHOCARDIGRAM
Nodal tachycardal 150 bpm EFLV 80% No structurals lesions

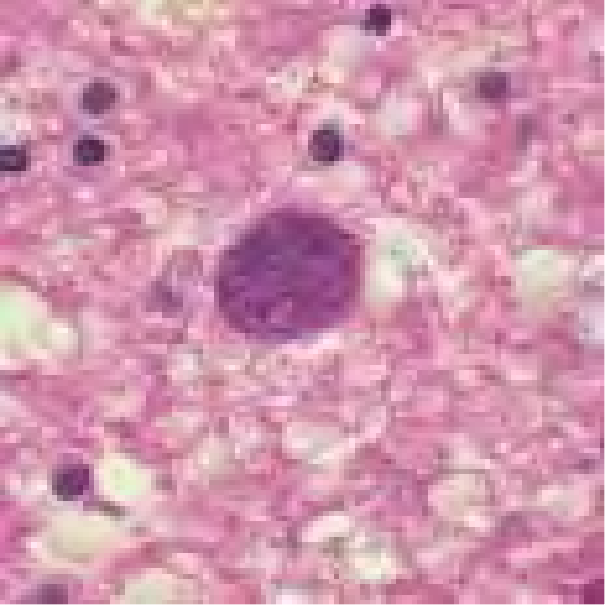
OTI
Broad spectrum antimycrobial

MICROBIOLOGICAL TESTS
NEGATIVES

Acidosis
Anuria
Impaired liver function
Vasoactive drugs

MOF
EXITUS

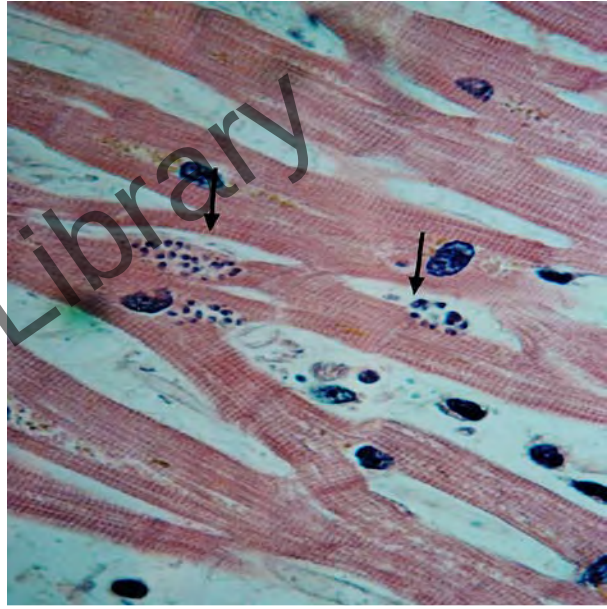
+22day



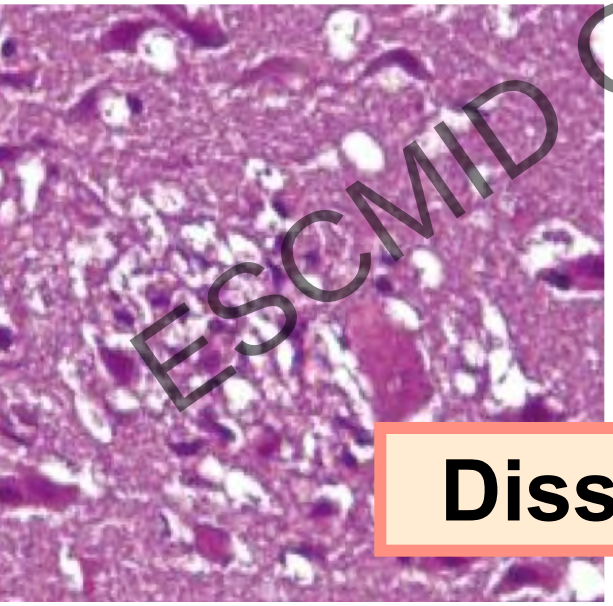
BRAIN

HISTOLOGICAL FINDINGS

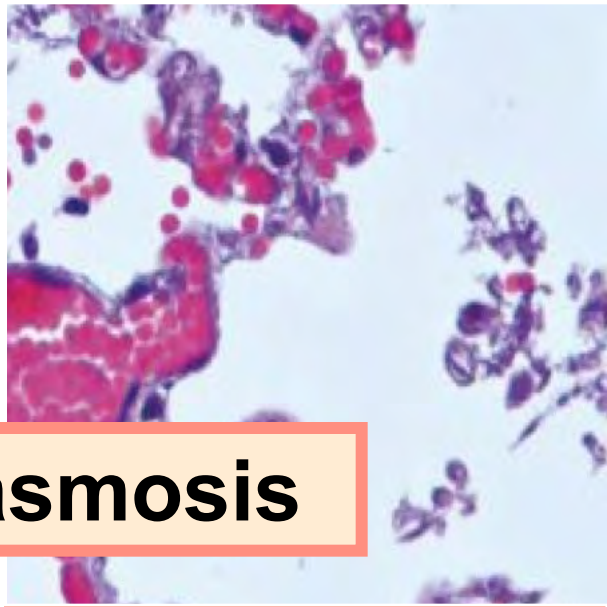
NECROPSY



MYOCARDIAL



LIVER



PULMONARY

Disseminated toxoplasmosis

Disseminated toxoplasmosis after HSCT

EPIDEMIOLOGY

- *T. gondii*: ubiquitous
- 70-96% seropositive of population
- Incidence of toxoplasmosis after HSCT: 0.3-5%
- Reactivation of latent infection
- Median onset after HSCT: 2 months
- Poor prognosis: 90% mortality

A Mele et al, BMT (2002) 691-698

CLINICAL

✓ **Primary infection**: usually in healthy individuals → assymptomatic and recognized serologically

✓ **Symptomatic infection**

1	Lymphatic form ≅ infectious mononucleosis
2	Chronic toxoplasmosis with retinochoroiditis
3	Acute fulminating disseminated infection
4	Single organ disease, usually encephalitis (pneumonitis, myocarditis, liver, nephritis)

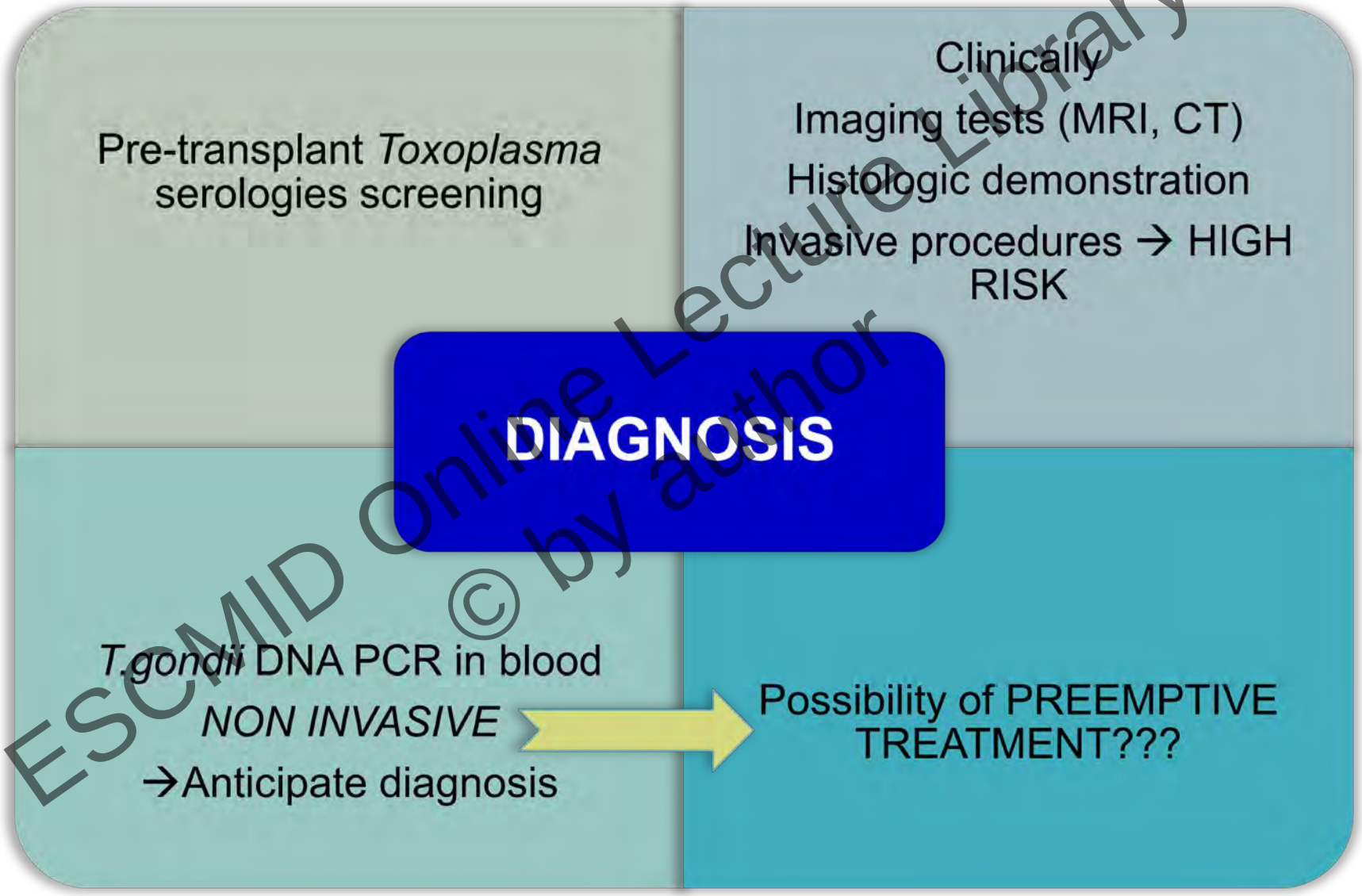
Martino R et al, Clin Infect Dis, 2000 Nov, 31(5): 1188-95

RISK FACTORS

SEROLOGIES	POSITIVE serostatus **recipient** for *Toxoplasma*
	NEGATIVE serostatus **recipient** with POSITIVE serostatus **donor**

UCBT, URDT, T cell depletion, immunosupressors, GVHD

IMPAIRED RECIPIENT IMMUNE RECONSTITUTION



Martino R et al, Clin Infect Dis, 2000 Nov, 31(5): 1188-95

- **PROPHYLAXIS in HSCT setting: TMP-SMX**

  -Recommended (for all seropositive recipients) but not standardized and limited supportive data after transplantation

  -High dosage schedule *vs.* low dosage schedule
  →high dosage more affective
  →adverse effects

  -Myelotoxicity → delayed of engraftment

- **Other prophylaxis alternatives**: pyrimetamine/sulphonamide, clindamycin or aerosilized pentamidine

  Less effectivity

Deourin F et al, Clin Infect Dis (2008) ; 14: 1089-1101

Summary

Severe and rare opportunistic infection after HSCT

Pre-transplant **Donor/Receptor serostatus**
→potencial risk evaluation

High mortality rates	Diagnosis often deferred
Main goal: diagnosis promptly	
Monitoring blood *Toxoplasma* PCR in high risk patients to start preemptive treatment	

SEVERE DIFFICULTIES IN DIAGNOSIS

THANK YOU

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