Infections in the Compromised Host

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Disclosures

- Consultant
  - Shionogi
  - MicroGenDx
- Many slides courtesy of Dr. David van Duin

Overview

- The immunocompromised host
- Testing in the immunocompromised host
- HIV/AIDS
- Autoimmune diseases/biologics
- Solid organ transplant
- Stem cell transplant
- Neutropenia
- Burn

General approach to ID

- Clinical history and physical exam
  - Be thorough
  - Get outside data
- Host
  - Is their immune system normal?
  - What parts of there immune system are abnormal?
- Environment
  - Travel/military service, employment, sick contacts, animal exposures, sexual contacts, hobbies

Who is the host?

- What parts of there immune system are abnormal?
  - Genetic mutations
  - Comorbidities
  - Immunomodulators, chemotherapy
  - Recent treatment for rejection/GVDH/disease flare
  - Prophylactic antimicrobials

Immunocompromising states

- Congenital/acquired immunodeficiency syndromes (CGD, HIV)
- Diabetes
- End-stage liver and kidney disease
- Autoimmune/rheumatologic diseases
- Solid organ transplantation
- Stem cell transplantation
- Malignancy, chemo, neutropenia
- Burns

Net state of immunosuppression

- Type, dose, and timing of immunosuppressive agents administered
- Nutritional, metabolic factors; renal dysfunction; age; comorbidities
- Breach of mucosal barriers (skin, gut); foreign bodies
- Neutropenia
- Lymphopenia
- Hypogammaglobulinemia

Making a diagnosis in immunocompromised hosts

- Clinical presentation
  - May be atypical
  - Fever or pain may be mild or absent
  - Lab changes may be subtle (ie, UA with few WBC in neutropenia)
- Imaging
  - Higher resolution imaging may be needed to detect subtle infection, particularly in the chest and sinuses

Making a diagnosis in immunocompromised hosts

- Serological tests may be unreliable
  - Antibody tests are less reliable after transplant or transfusions
  - Cross-reactivity, false-positives
- Biochemical/immunodiagnostic antigen tests
  - Not always sensitive enough (ie urine Legionella Ag)
  - Not always specific enough, cross-reactivity (ie urine Histoplasma Ag)

Making a diagnosis in immunocompromised hosts

- Molecular testing (NAA, NAT, NAAT, PCR)
  - Detects genetic material (DNA or RNA)
  - Blood, CSF, respiratory fluids, tissue biopsy, stool, urine
  - Can be quantitative (QNAT) for blood
  - Can be overly sensitive: does not always correlate with disease
  - Does not differentiate between live & dead organisms
- Histology & immunohistochemistry
  - More specific (preferred) for diagnosing tissue-invasive disease
  - “the gold standard” but not always realistic

Clinical pearls

- Reactivation of prior infection suggests a high net state of immunosuppression
  - #1 Reduce immunosuppression if possible
- Don't get the disease: When in doubt isolate
  - Infection Control Isolation Policies
  - Handwashing may be better for non-enveloped viruses (esp. enteric viruses) and spores (*Clostridium*)

Preventing reactivation of latent infections

- Who to screen
  - HIV
  - Cancer chemotherapy
  - Organ transplant
  - Screening protocols may differ among above groups
- Why screen
  - Early identification and treatment
  - Provide therapy to suppress infection

Preventing reactivation of latent infections

Viral

- Cytomegalovirus (CMV)
- Epstein-Barr (EBV)
- Hepatitis (HBV, HCV)
- Herpes simplex (HSV I & II)
- HIV
- Varicella-zoster (VZV)
- BK virus (GU disease)

Bacterial

- Syphilis
- Tuberculosis

Parasitic

- *Toxoplasma gondii*
- *Strongyloides*

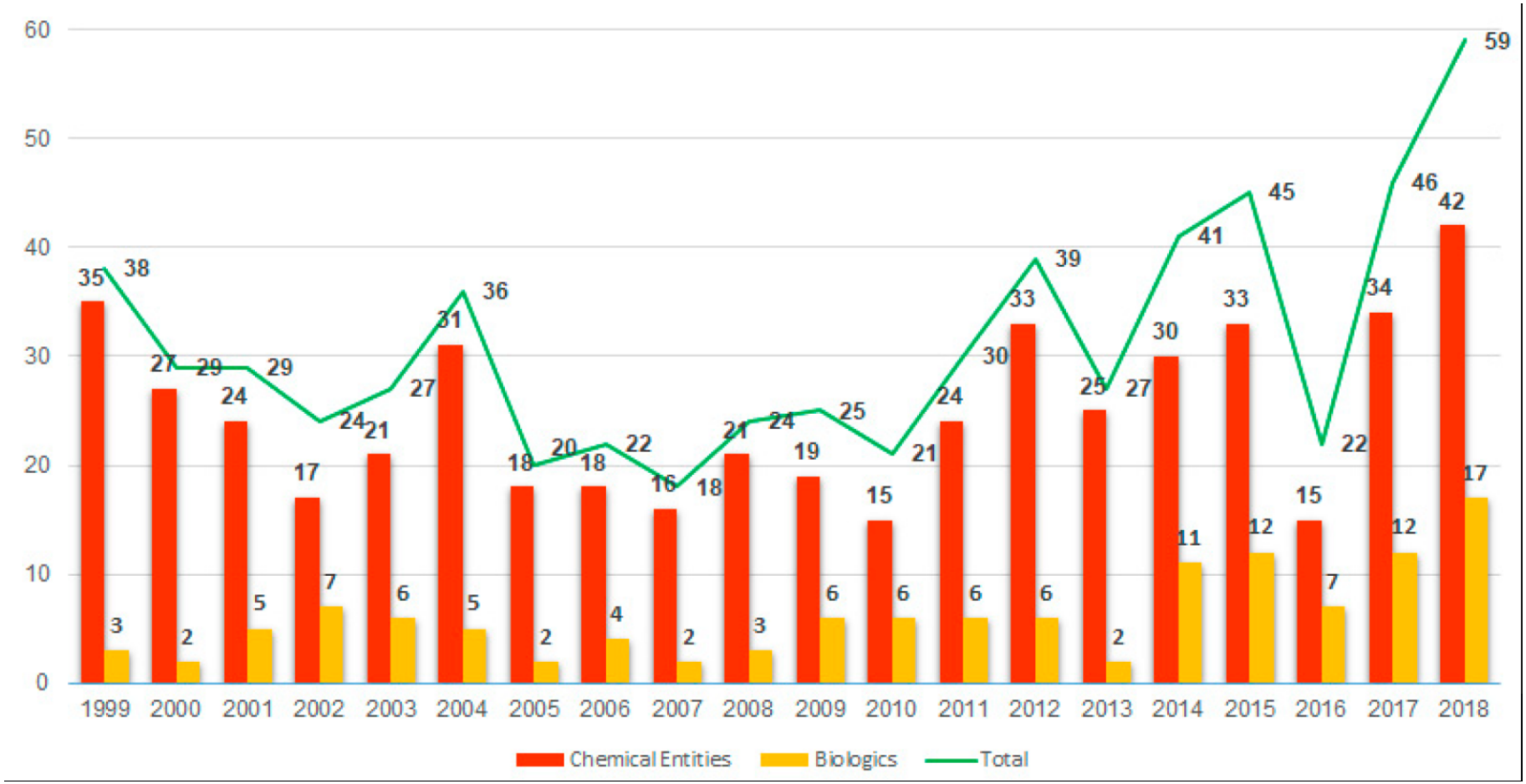
HIV opportunistic infections

CD4 count	Infections
Any	Kaposi sarcoma, pulmonary TB, VZV, bacterial pneumonia, lymphoma
<250	PJP, esophageal candidiasis, PML, HSV
<100	Cerebral toxoplasmosis, HIV encephalopathy, Cryptococcus, military TB
<50	CMV retinitis, atypical mycobacteriosis

Biologics

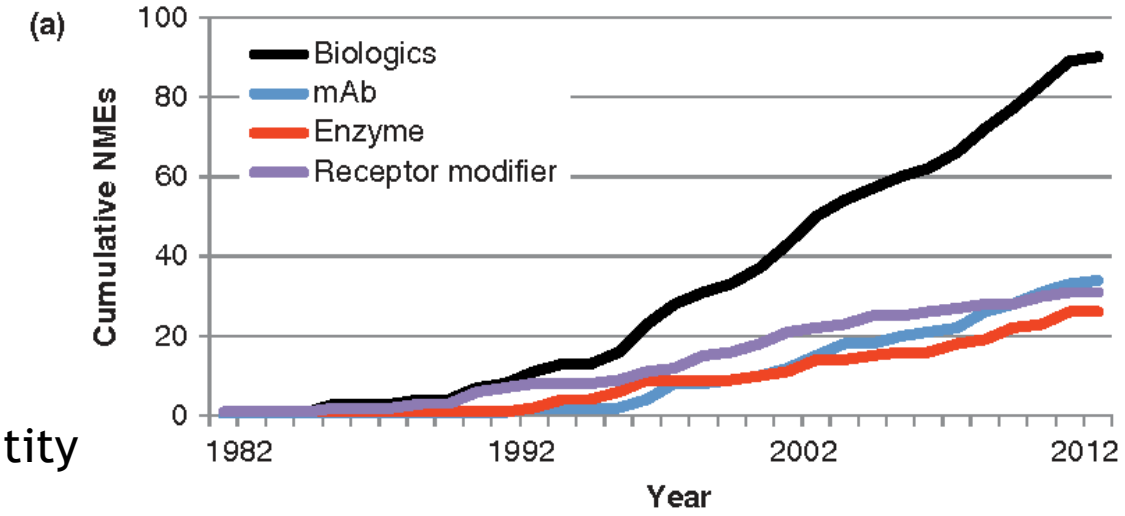
Figure 1

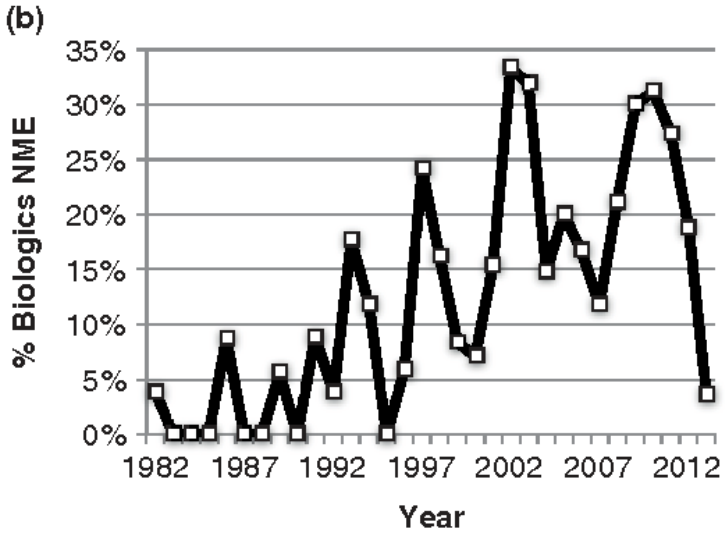
New chemical entities and biologics approved by the FDA in the last two decades

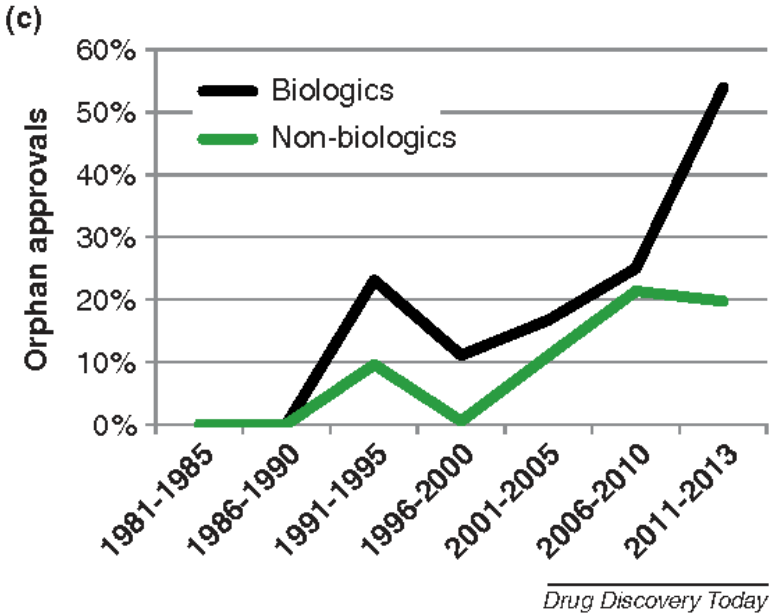


G. de la Torre B, Albericio F. *Molecules* 2019, *24*, 809.

NME = new molecular entity





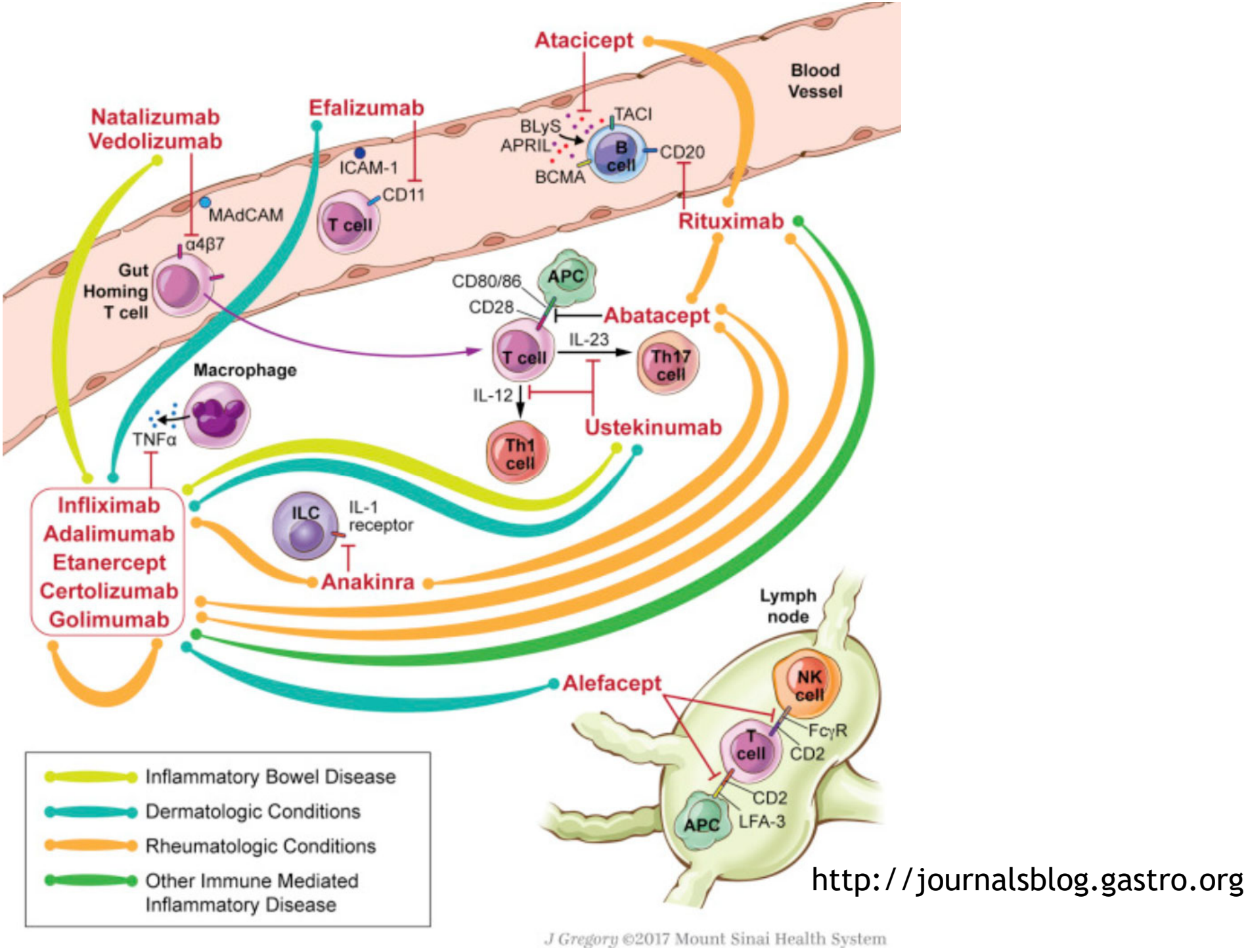


Drug Discov Today. 2015;20:393-8.

Biologics for inflammatory arthritis

Type	Name	Brand name	Biosimilar brand name
Tumour necrosis factor inhibitors (TNF-inhibitors)	Golimumab Certolizumab Etanercept Adalimumab Infliximab	Simponi Cimzia Enbrel Humira Remicade	 Brenzys Flixceli, Emisima, Inflectra, Jaximab, Remsima, Reflexis
Interleukin-6 inhibitor	Tocilizumab	Actemra	
Interleukin-1 inhibitor	Anakinra	Kineret	
Targeting B-lymphocytes (B-cells)	Rituximab	Mabthera	B-cells (a type of white blood cell)
Targeting T-lymphocytes (T-cells)	Abatacept	Orencia	T-cells (a type of white blood cell)

https://arthritisaustralia.com.au/things-to-consider-when-taking-a-biologic/



http://journalsblog.gastro.org

TNF-alpha inhibitor-associated infections

WARNING: SERIOUS INFECTIONS AND MALIGNANCY

See full prescribing information for complete boxed warning.

SERIOUS INFECTIONS (5.1, 6.1):

- **Increased risk of serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens.**
- **Discontinue HUMIRA if a patient develops a serious infection or sepsis during treatment.**
- **Perform test for latent TB; if positive, start treatment for TB prior to starting HUMIRA.**
- **Monitor all patients for active TB during treatment, even if initial latent TB test is negative.**

Tocilizumab-associated (anti-IL-6) infections

WARNING: RISK OF SERIOUS INFECTIONS

See full prescribing information for complete boxed warning.

- **Serious infections leading to hospitalization or death including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections have occurred in patients receiving ACTEMRA. (5.1)**
- **If a serious infection develops, interrupt ACTEMRA until the infection is controlled. (5.1)**
- **Perform test for latent TB; if positive, start treatment for TB prior to starting ACTEMRA. (5.1)**
- **Monitor all patients for active TB during treatment, even if initial latent TB test is negative. (5.1)**

Rituximab-associated (anti-CD20) infections

WARNING: FATAL INFUSION-RELATED REACTIONS, SEVERE MUCOCUTANEOUS REACTIONS, HEPATITIS B VIRUS REACTIVATION and PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

See full prescribing information for complete boxed warning.

- **Fatal infusion-related reactions within 24 hours of RITUXAN infusion; approximately 80% of fatal reactions occurred with first infusion. Monitor patients and discontinue RITUXAN infusion for severe reactions (5.1).**
- **Severe mucocutaneous reactions, some with fatal outcomes (5.2).**
- **Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death (5.3).**
- **Progressive multifocal leukoencephalopathy (PML) resulting in death (5.4).**

Biologics for multiple sclerosis

	Alemtuzumab (anti-CD52)	Interferon-beta 1a inhibitor
Infections	71%	53%
Serious infections	3% (appendicitis, gastroenteritis, PNA, HZV, tooth infection)	1%
Herpes viral infection	16%	3%
Cervical HPV	2%	
Active or latent TB	0.3%	
Acute acalculous cholecystitis	0.2%	0%
Other reported infections	Listeria, PJP, Nocardia, CMV, Aspergillus, dimorphic fungus	

http://products.sanofi.us/Lemtrada/Lemtrada.pdf

Eculizumab-associated infections (C5 - terminal complement inhibitor)

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

See full prescribing information for complete boxed warning

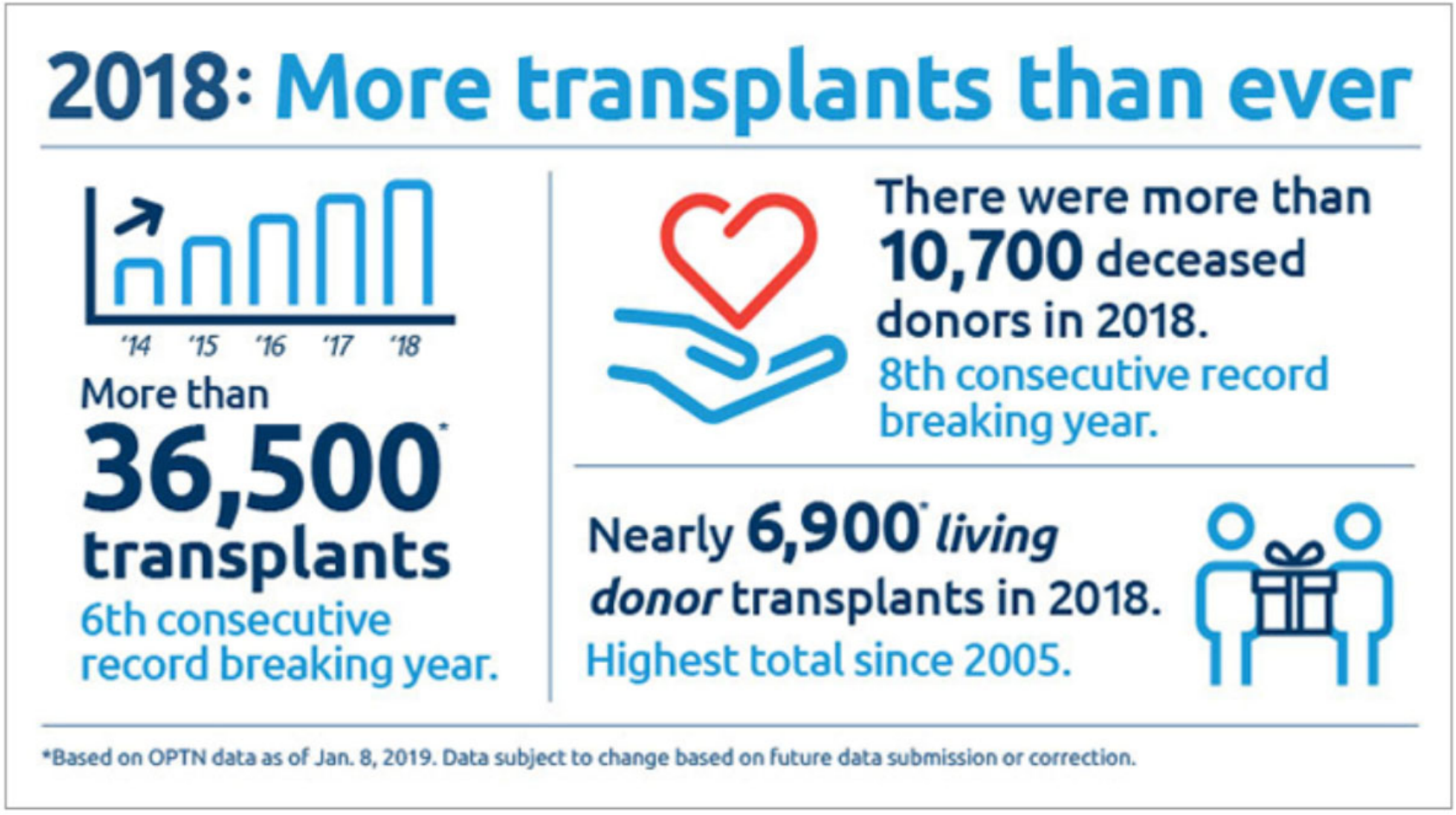
Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early (5.1).

- **Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies.**

- **Immunize patients with a meningococcal vaccine at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risks of developing a meningococcal infection. (See *Serious Meningococcal Infections* (5.1) for additional guidance on the management of the risk of meningococcal infection.)**

- **Monitor patients for early signs of meningococcal infections, and evaluate immediately if infection is suspected.**

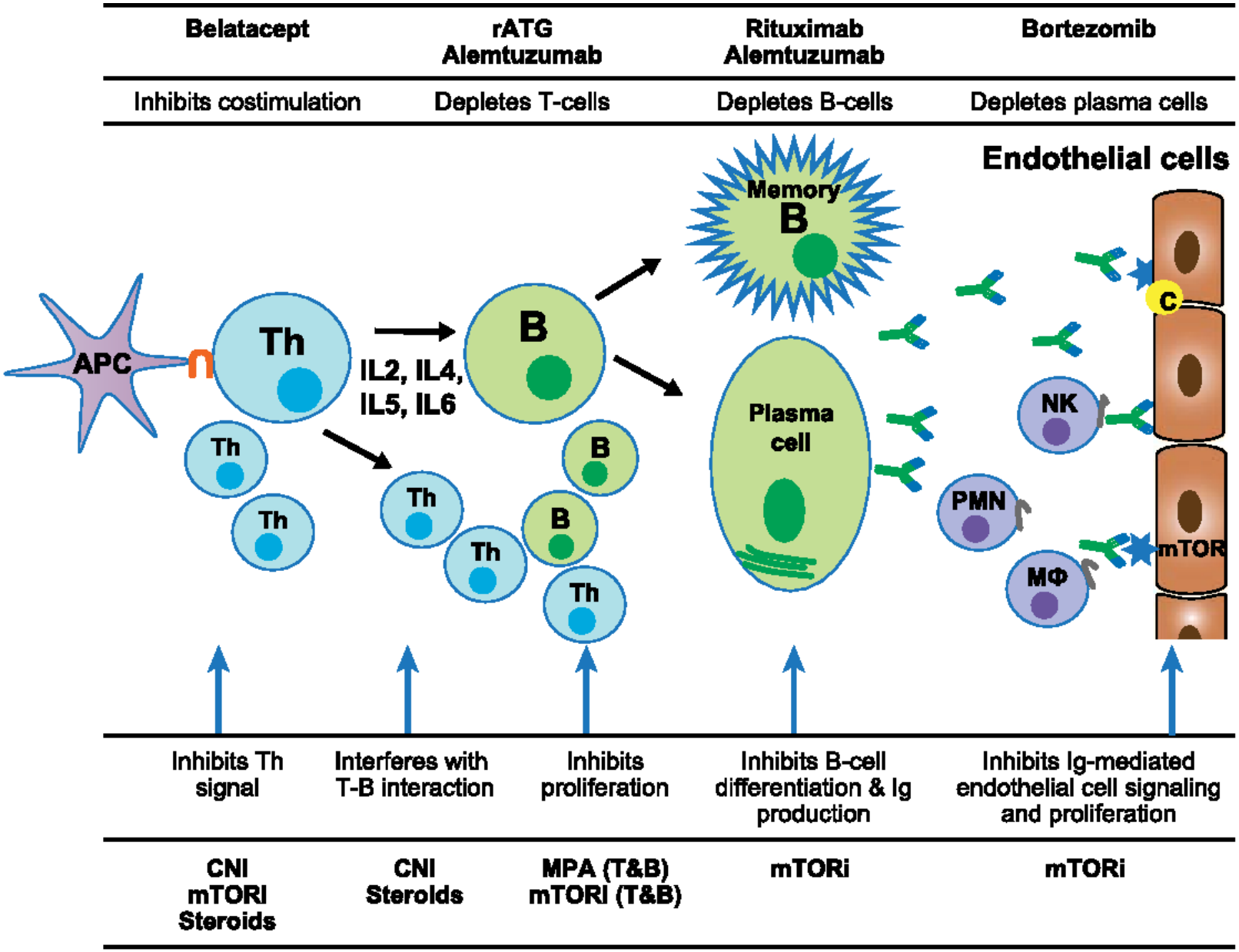
Solid organ transplant



Solid organ transplant

The Balance in Immunosuppression

UC Irvine Health



1. A schematic of the mode of action of key immunosuppressants. APC, antigen presenting cell; B, B-cell; C, complement

O'Leary et al.*Transplantation*. 2016: 100;39-53

Alemtuzumab

- Anti-CD52
- Profound and sustained T-, B- and NK cell depletion
- Use in induction and/or rejection treatment

Peleg et al. CID 2007;44:204

Table 2. Opportunistic infections (OIs) among the 547 organ transplant recipients who received ⩾1 dose of alemtuzumab from September 2002 through March 2004.

OI	No. (%) of OIs	Time to infection[a]	No. of OIs among transplant recipients receiving alemtuzumab[b]	
			Induction	Rejection
Any	62 (100)	84 (2–328)	16	46
Viral				
CMV disease	16 (26)	85 (7–254)	4	12
Pneumonitis	4	…	1	3
GI infection	8	…	1	7
Hepatitis	3	…	2	1
Febrile viral syndrome	1	…	0	1
EBV disease	3 (5)	95 (42–288)	2	1
PTLD	3		2	1
Febrile syndrome	0			
EBV-negative PTLD	2 (3)	24, 169[c]	0	2
HHV-6 infection	1 (2)	222	0	1
BK virus infection	12 (19)	134 (18–328)	5	7
Parvovirus infection	1 (2)	325	0	1
Fungal				
Esophageal candidiasis	12 (19)	51 (2–265)	1	11
Cryptococcal infection	2 (3)	54, 200[c]	2	0
Invasive aspergillosis	1 (2)	34	0	1
Mucormycosis	1 (2)	87	0	1
Scedosporium infection	2 (3)	57, 66[c]	0	2
Bacterial				
Nocardia	4 (6)	74 (54–96)	0	4
Mycobacteria	3 (5)	77 (63–323)	1	2
Tuberculosis	1		0	1
Nontuberculous	2		1	1
Parasitic				
Toxoplasmosis	1 (2)	59	0	1
Balamuthia mandrillaris	1 (2)	2	0	1

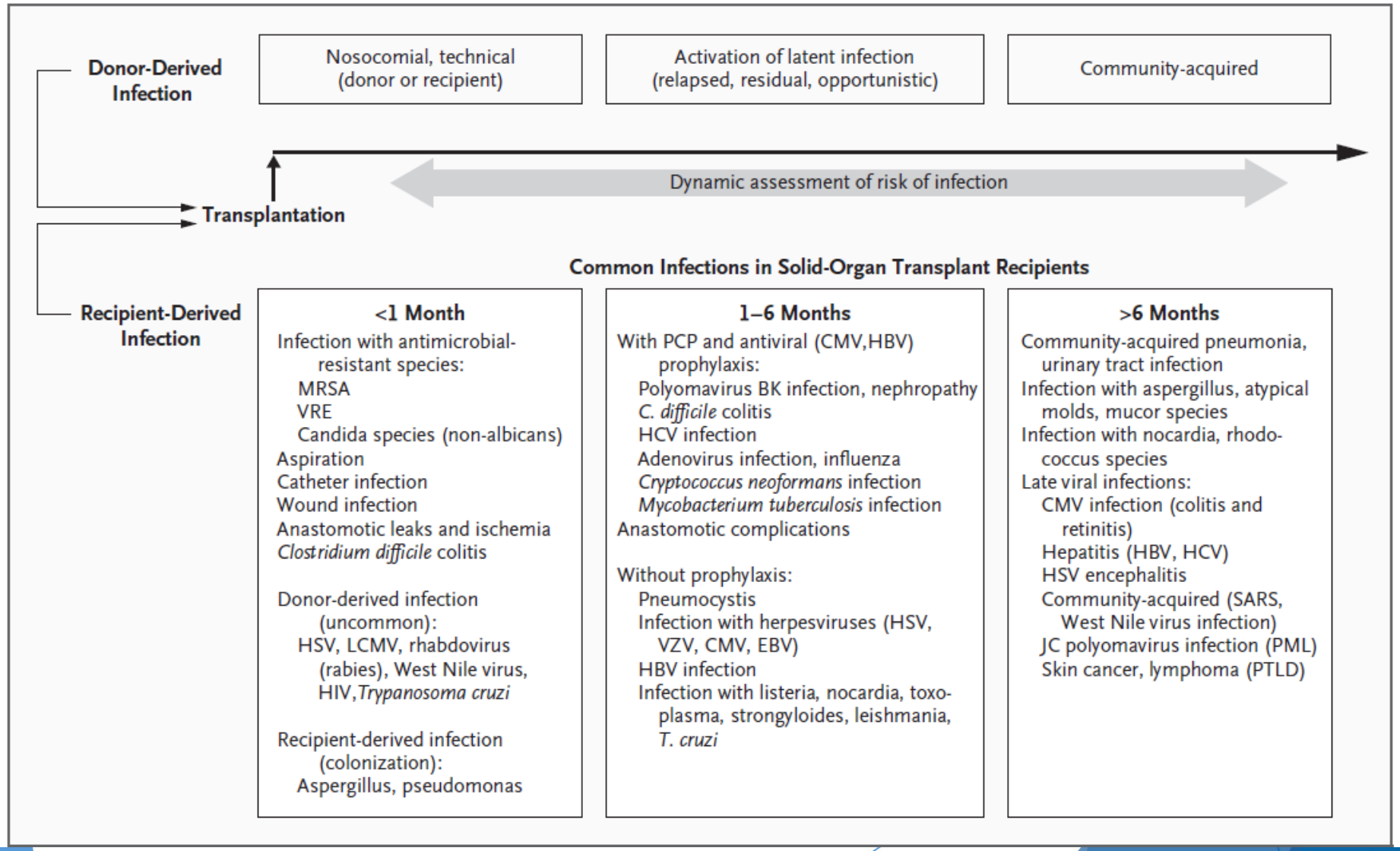
Increased OI risk when alemtuzumab used for rejection

Table 3. Characteristics of organ transplant recipients who received alemtuzumab, according to the development of an opportunistic infection (OI).

Characteristic	Recipients with an OI after receiving alemtuzumab (n = 56)	Recipients without an OI after receiving alemtuzumab (n = 491)	OR (95% CI)	P
Age, median (range)	51 (18–77)	51 (16–82)	…	.81
Sex, female	28 (50)	195 (40)	1.5 (0.9–2.6)	.14
Transplant received				
Kidney	16 (29)	235 (48)	0.4 (0.2–0.8)	.007
Liver	8 (14)	152 (31)	0.4 (0.2–0.8)	.01
Lung or heart/lung	12 (21)	44 (9)	2.8 (1.4–5.6)	.005
Pancreas or kidney/pancreas	6 (11)	44 (9)	1.2 (0.5–3.0)	.67
Intestinal or multivisceral	14 (25)	16 (3)	9.9 (4.5–21.7)	<.001
Previous transplant received	8 (14)	72 (15)	0.9 (0.4–2.1)	.9
Alemtuzumab received				
For induction therapy	16 (29)	338 (69)	0.2 (0.1–0.3)	<.001
For rejection therapy	40 (71)	153 (31)	5.5 (3.0–10.0)	<.001
Doses of alemtuzumab received, no. (range)	2 (1–5)	1 (1–5)	2.3 (1.7–3.1)	<.001
Received pulse methylprednisolone[a]	15 (27)	152 (31)	0.8 (0.4–1.5)	.5
Received >2 pulses of methylprednisolone[a]	10 (18)	49 (10)	2.0 (0.9–4.1)	.08
Received another lymphocyte-depleting antibody[b]	28 (50)	117 (24)	3.2 (1.8–5.6)	<.001

Peleg et al. CID 2007;44:204

Timeline of infectious risk (SOT)



Fishman. NEJM 2007;357:2601

Viral infections after SOT

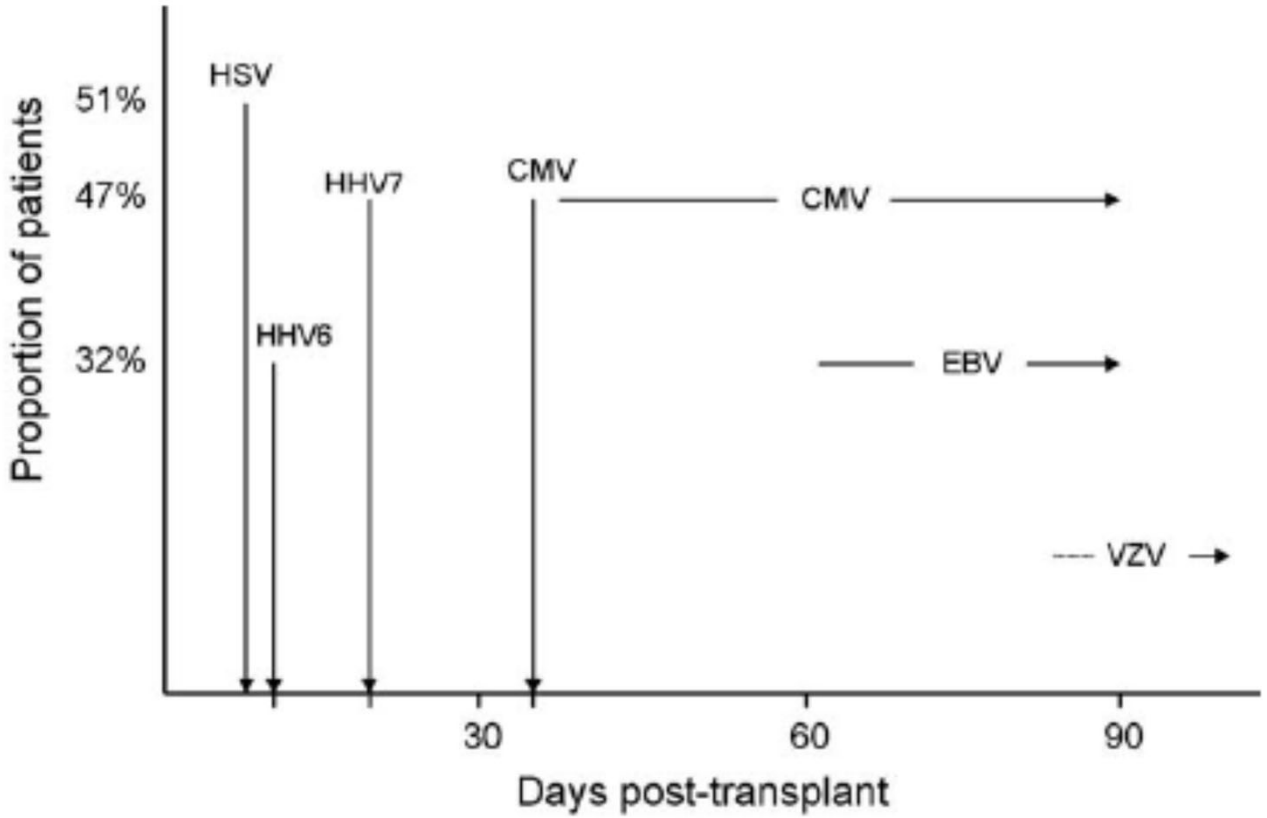


Fig. 2. Median time of detecting herpesviruses by polymerase chain reaction

Griffiths. Antiviral Res 2006;2-3:192

Risk for infection after SOT

- Exposures
  - Donor-derived
  - Recipient-derived
  - Nosocomial
  - Community

- “net state of immunosuppression”

Fishman. NEJM 2007;357:2601

Donor-derived infections

- Positive RPR/syphilis, *Streptococcus pneumoniae* bacteremia/meningitis
- Always think donor-derived infection for fever 1-3 months after transplant with no clear source
  - Was there anything unusual about the donor?
  - Who gave the history?
- Requires a high degree of suspicion
  - Report suspicions to the OPO – they can ask around to see how the other recipients are doing

Donor-derived infections

Table 1
Potential donor-derived infectious diseases transmissions reported to the OPTN, 2005–2009

Disease	Number of Donor Reports	Number of Recipients with Confirmed Transmission	Number of DDD-Attributable Recipient Deaths
Virus	86	31	8
Bacteria	38	26	7
Fungus	30	26	8
Mycobacteria	26	10	2
Parasite	21	13	4
Total infections	201	106	29

Chong et al. Inf Dis Clin N Am 2013;27:253

Recipient-derived infections

- Active, uncontrolled infection
  - LVAD associated bacteremia
  - Infection limited to organ to be explanted
- Colonization
- Recurrence of infectious indication for transplant
  - HCV
- Asymptomatic infection
  - Strongyloides
- Latent infection
  - TB
  - Herpes viruses (CMV, EBV, HSV, VZV)

Nosocomial infections

- Device-related
  - Line-associated blood stream infection
  - Catheter or stent associated UTI
  - Ventilator-associated pneumonia
- Surgery-related
  - Wound infection
  - Intra-abdominal abscess
- Multi-drug resistant organisms
- Outbreaks

MDR pathogens in SOT

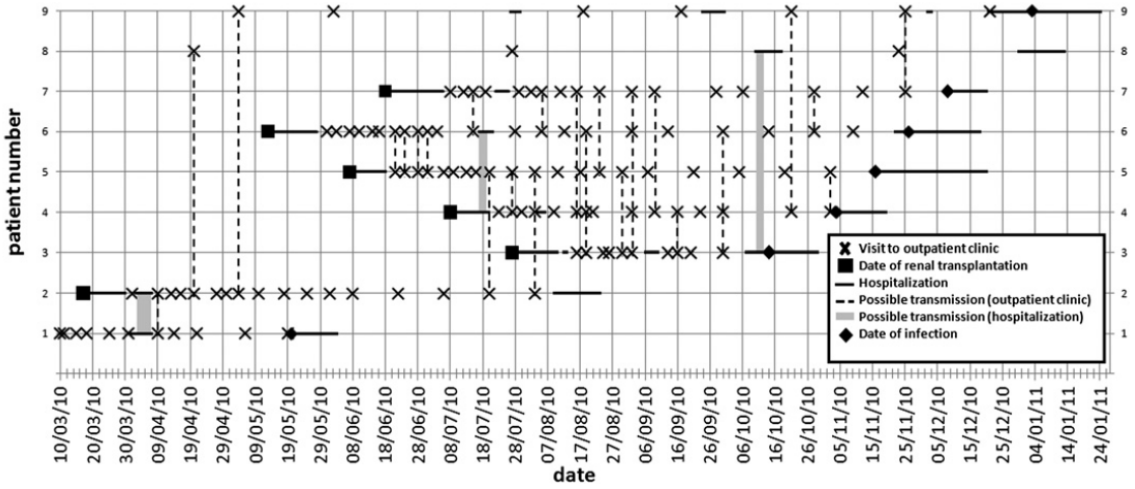
Table 2
Incidence and etiology of MDR pathogens among infectious episodes in patients with underlying transplant-treatable diseases

Disease/ Condition	Rate of MDR Pathogens Among Episodes of Infections/ Colonization	Main Isolated Pathogens	Comments/Notes
Liver cirrhosis[68,69,138]	25%–47%	MRSA 3%–7% ESBL-E 12%–15% CRE 3%–8% VRE 0%–7%	Major infections are spontaneous bacterial peritonitis, BSI, UTI, and pneumonia
End-stage renal disease[73,74]	12%–25%	MRSA 0%–14% VRE 2%–21% ESBL-E 12%–25%	Most of infections studied are hemodialysis catheter-related BSIs
Cystic fibrosis[76,139]	48%	MRSA 17%–36% MDR *Pseudomonas aeruginosa* 21%–52% ESBL-E 4%	Studies collected mostly culture (surveillance or diagnostic) samples rather than Infectious episodes

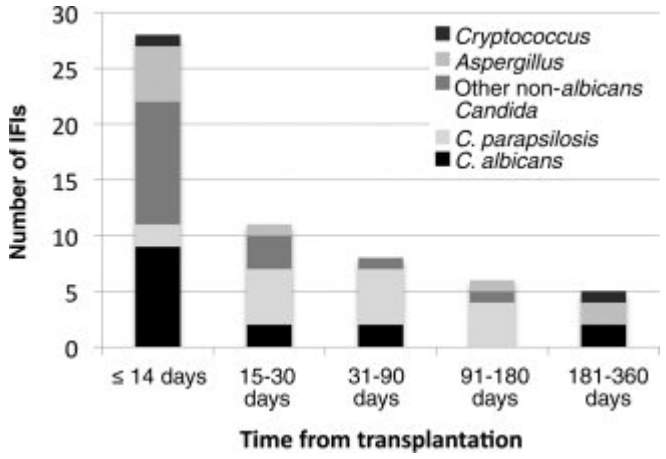
Abbreviations: BSI, bloodstream infection; CRE, carbapenem-resistant Enterobacteriaceae; ESBL-E, extended spectrum β-lactamase-producing Enterobacteriaceae; MDR, multidrug-resistant; MRSA, methicillin resistant *Staphylococcus aureus*; UTI, urinary tract infection; VRE, vancomycin-resistant Enterococci.

Barlotti et al. Infect Dis Clin N Am. 2018,32:551-580

Outbreaks



Pneumocystis in pediatric renal transplant recipients



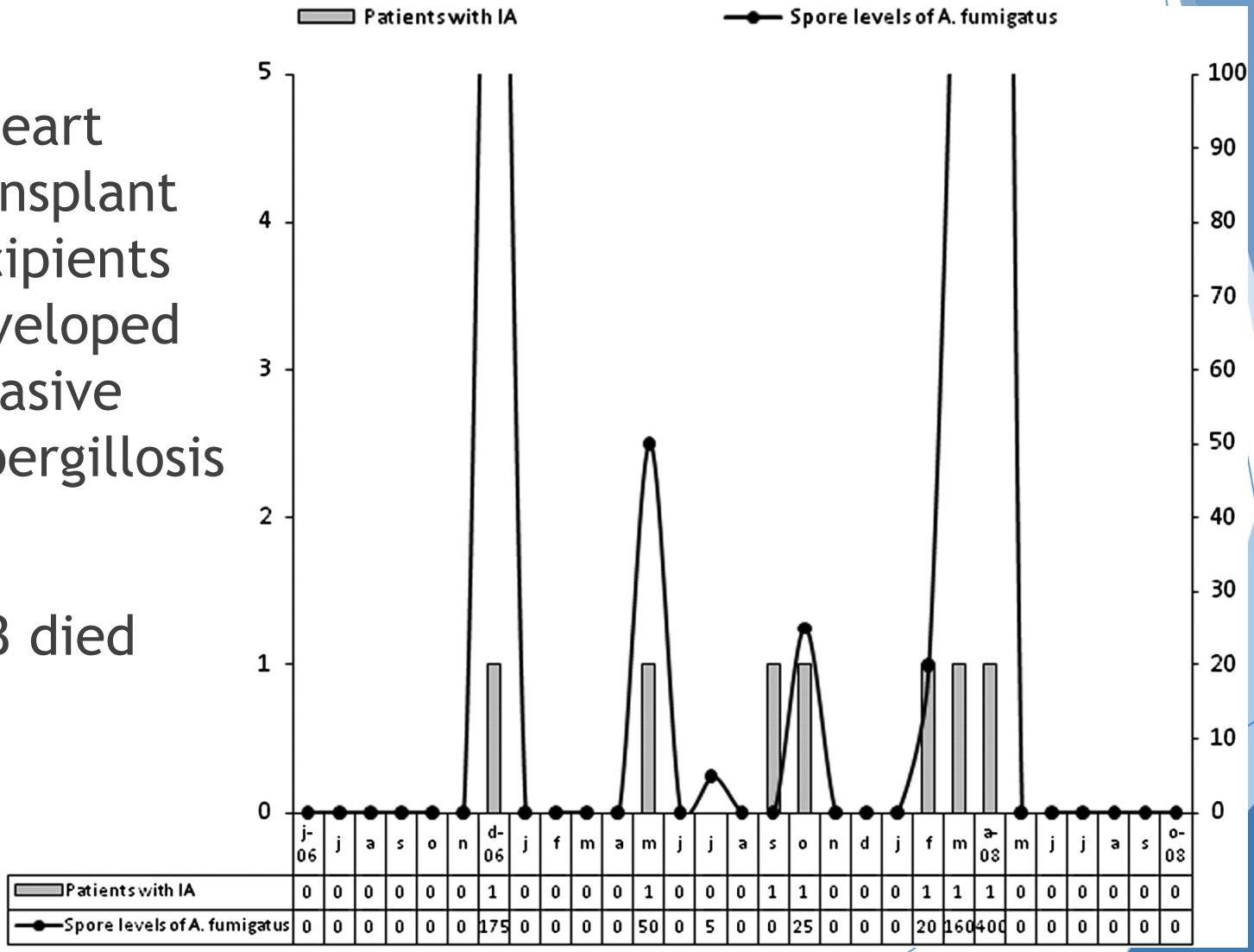
C. parapsilosis after liver transplantation

Raghuram et al. Liver Transplant 2012;18:1100
Brunot et al. Transplant Proc 2012;44:2818

Aspergillus in the cardiac ICU

3 heart transplant recipients developed invasive aspergillosis

2/3 died



Peláez T et al. Clin Infect Dis. 2012;54:e24-e31

Mold in the walls….

Community acquired infections

- Immunosuppression does not prevent common infections…
- Manifestations may be different
- Common pathogens include:
  - Respiratory viruses (influenza)
  - Skin flora (*S. aureus*, streptococci)
  - Enteric flora (GNR, enterococci)

Hematopoietic stem cell transplant

A. D'Souza et al. / Biol Blood Marrow Transplant 23 (2017) 1417–1421

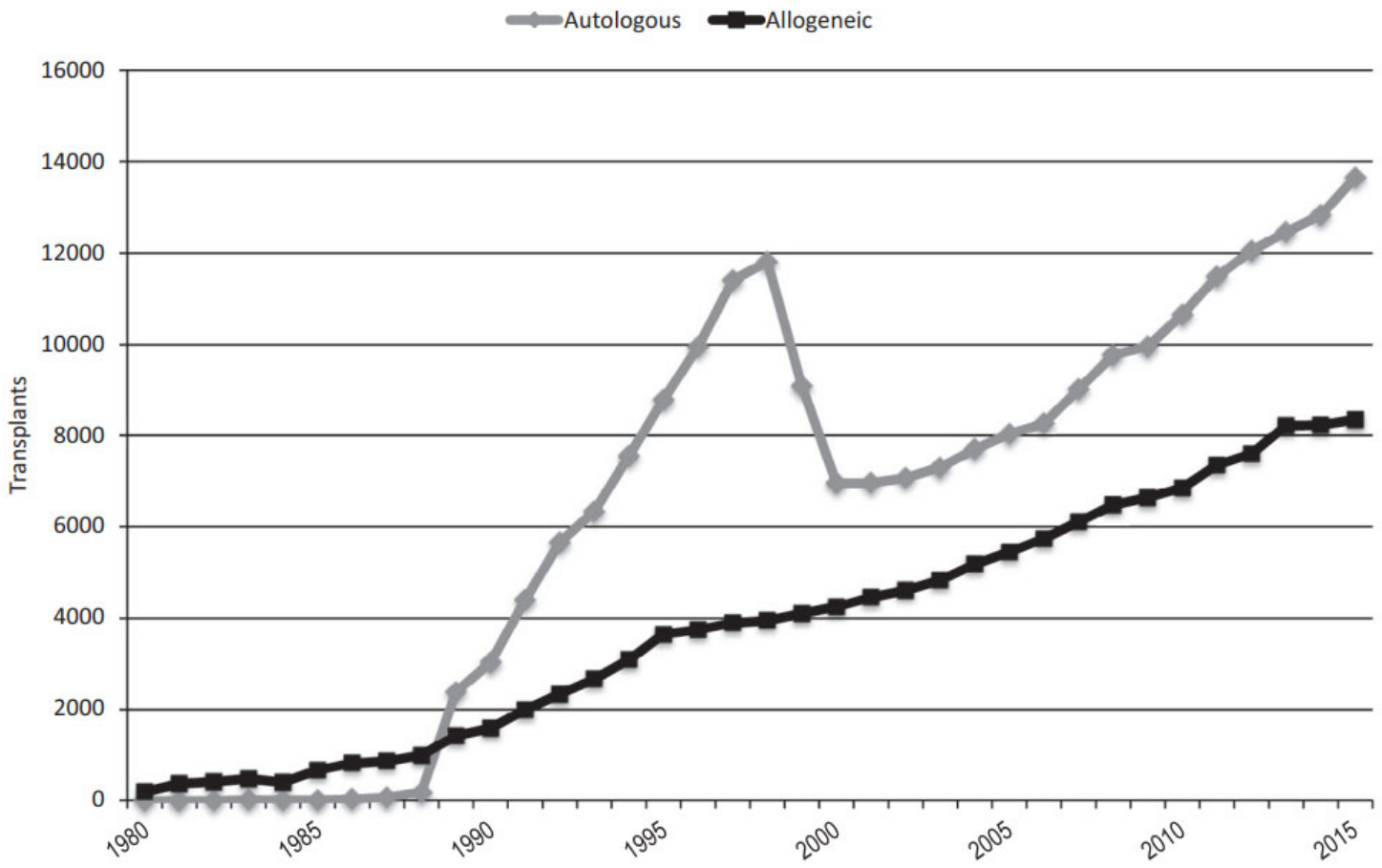
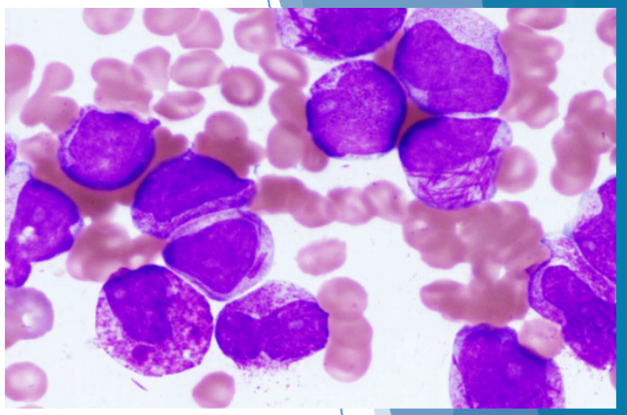


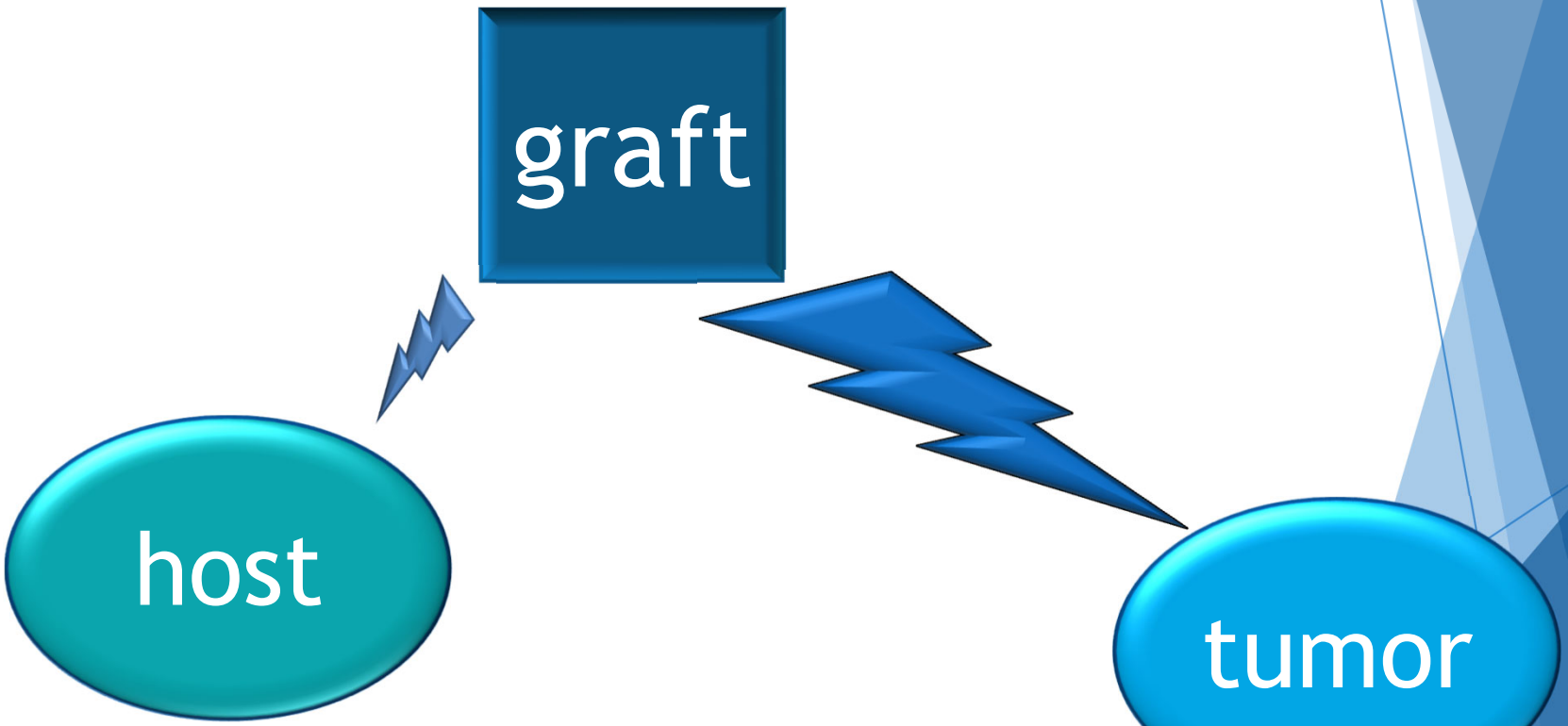
Figure 1. Estimated annual number of HCTs performed in the United States.

Indications for HSCT



- Hematologic malignancies
- Selected solid malignancies
- Acquired diseases
  - eg aplastic anemia, Paroxysmal nocturnal hemoglobinuria
- Congenital diseases
  - eg Immunodeficiency syndromes (e.g. SCID)

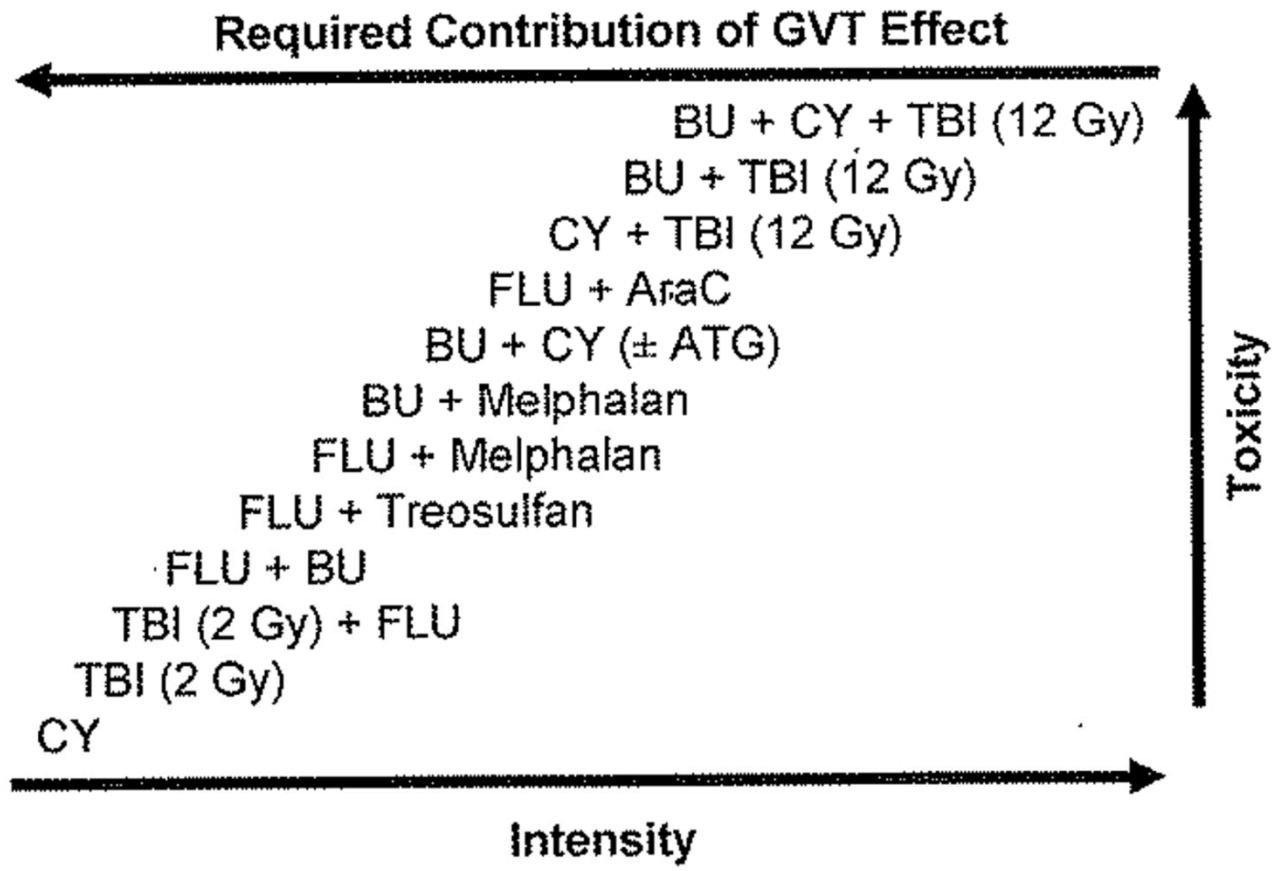
HSCT principles: maximizing graft vs tumor while minimizing graft vs host effects



Stem cell types

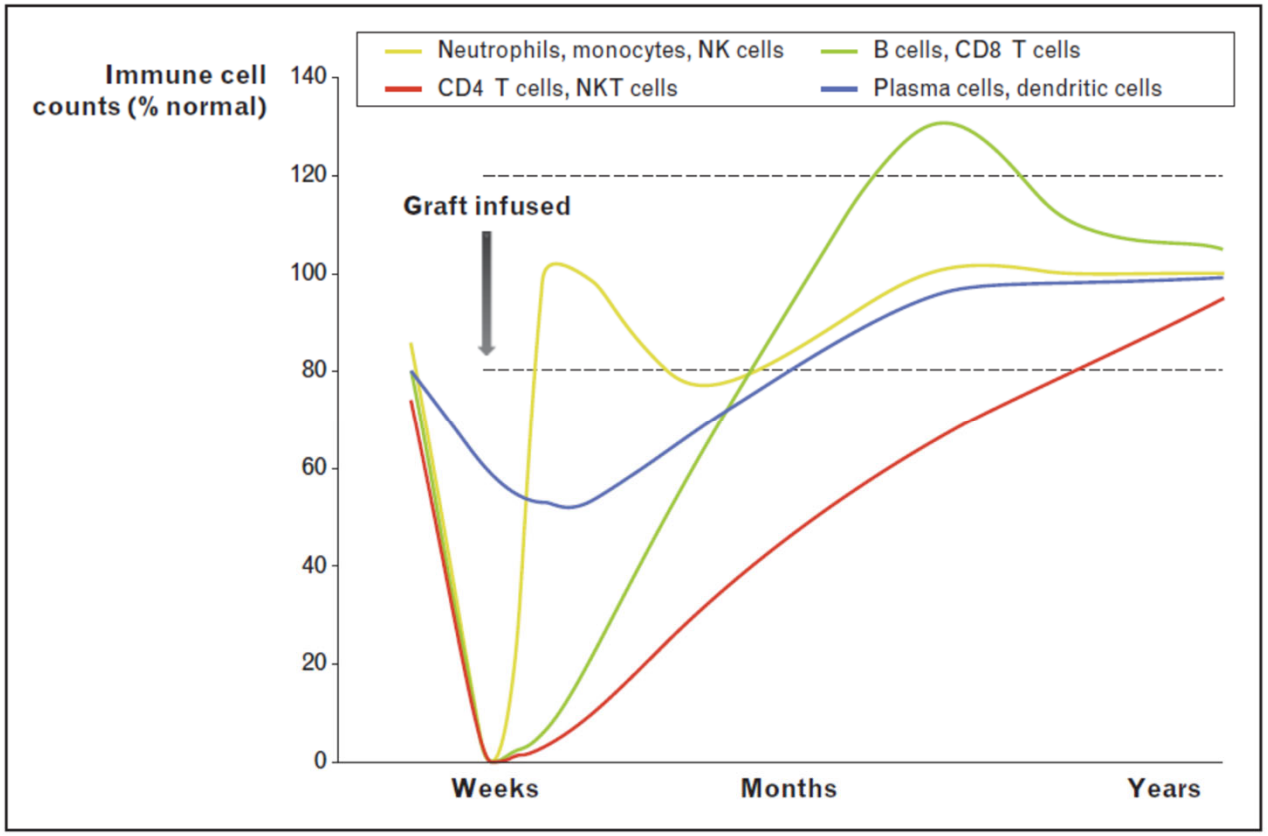
- Allogeneic vs. autologous
- Sources
  - Bone marrow
  - Mobilized peripheral blood stem cells
  - umbilical cord blood
  - (fetal liver cells)

Conditioning



Rezvani et al. in Transplant Infections 2009 Ed. Bowden et al.

Immune reconstitution after HSCT



--Neutrophils, monocytes, NK cells

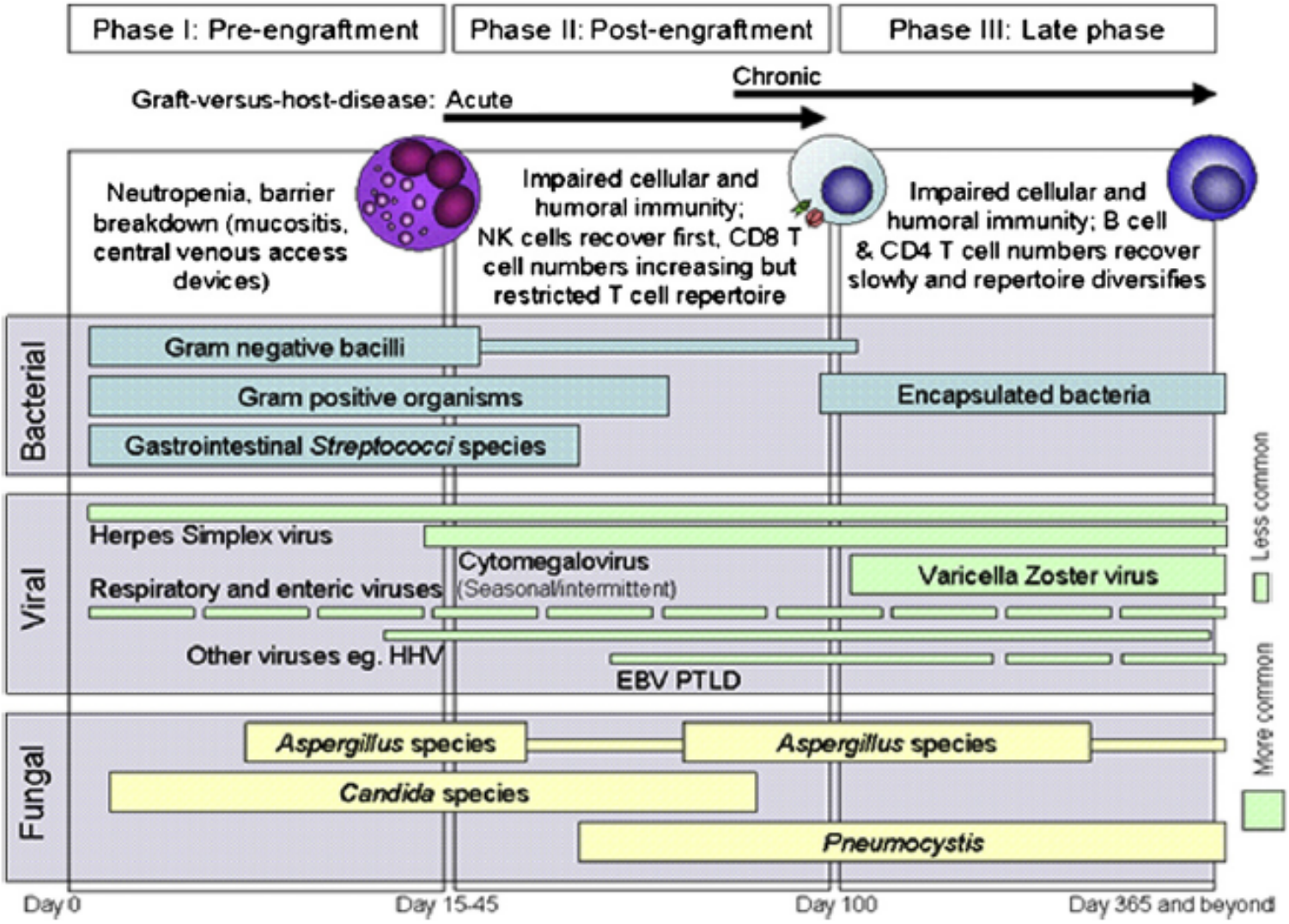
--CD4 T cells, NKT cells

--B cells, CD8 T cells

--Plasma cells, dendritic cells

Bosch et al. Curr Opin Hematol 2012;19:324

Timeline of infections



Tomblyn et al. Biol Blood Marrow Transplant 2009;15:1143

Infectious risk

	Higher risk	Lower risk
Transplant	allogeneic	autologous
Type of donor	Unrelated	related
HLA matching	HLA mismatch	HLA match
Stem cell source	Cord blood	Peripheral blood
Graft manipulation	T cell depletion	No manipulation
Conditioning regimen	Full intensity	Reduced intensity
immunosuppression	T cell depleting agents	Minimal IS
GVHD	Moderate-severe	None or mild

Wingard et al. Inf Dis Clin N Am 2010;24:257

Graft vs Host Disease

- GVHD requiring treatment in 40% of HLA-matched allo-HSCT recipients
- GVHD
  - Skin: pruritic maculopapular rash
  - GI tract: nausea, abd pain, diarrhea
  - Liver: cholestasis
- Graded based on extent of end-organ involvement
  - I mild
  - II moderate
  - III severe (~25% 5-year survival)
  - IV very severe (~5% 5 year survival)
- Steroids remain first line
  - Topical for skin and lung (inhaled)
  - Systemic for more severe disease and other target organs
- Calcineurin inhibitors may be used
- Steroid-refractory GVHD important concern

Ferrara et al. Lancet 2009;273:1550

Bacterial infections after HSCT

Table 2
Types of infections encountered at various times after HSCT

Type of Infectious Pathogen	Early Preengraftment (First 2–4 wk)	Early Postengraftment (Second and Third Month)	Late Postengraftment (After Second or Third Month)
Bacteria	Gram-negative bacteria (related to mucosal injury and neutropenia) Gram-positive bacteria (related to venous catheters) *Clostridium difficile* (related to neutropenia, antibiotics, antiacid medications)	Gram-positive bacteria (related to venous catheters) Gram-negative bacteria (related to enteric involvement of GVHD, venous catheters)	Encapsulated bacteria (related to poor opsonization with chronic GVHD) *Nocardia* (related to chronic GVHD)

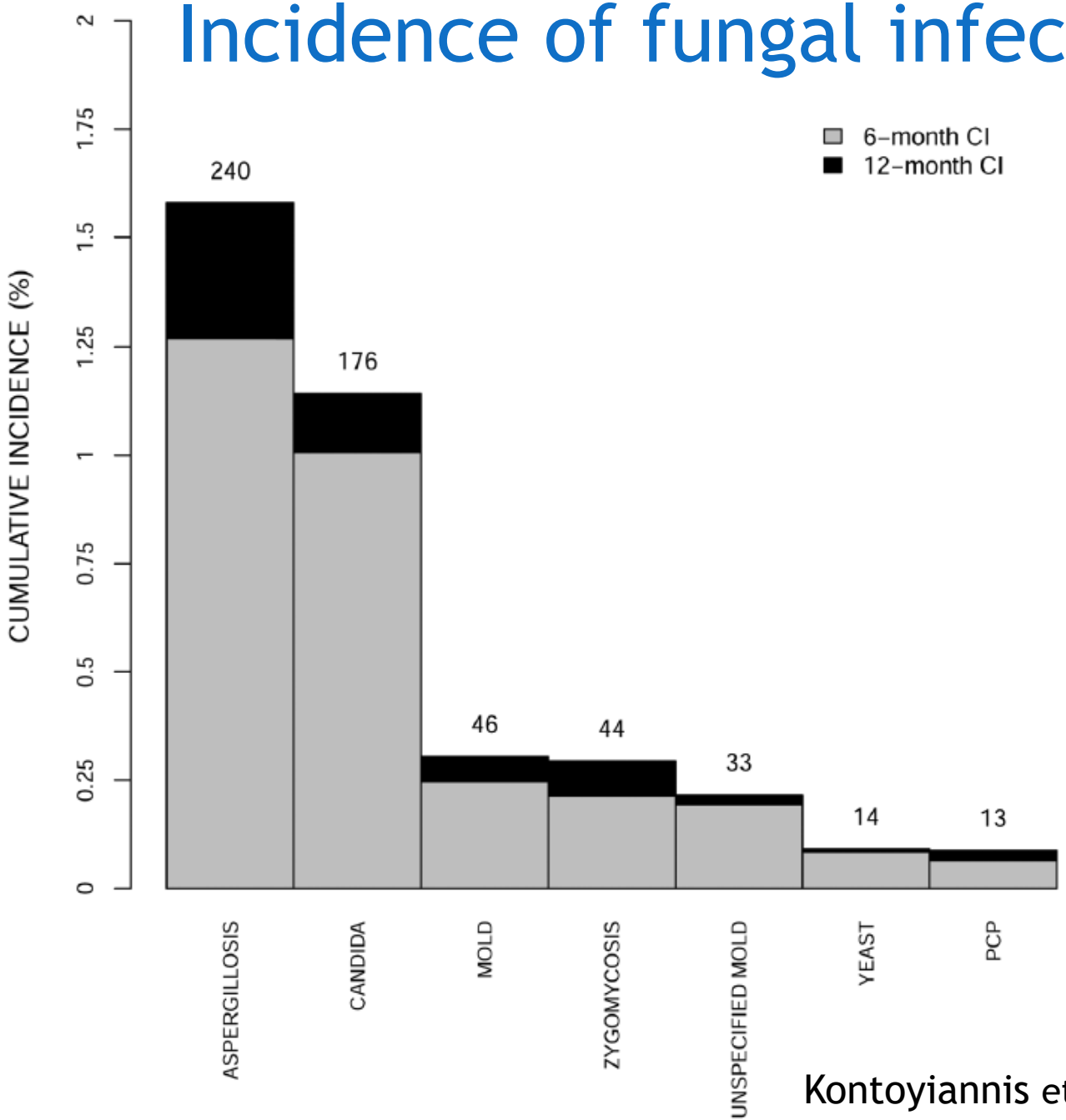
Wingard et al. Inf Dis Clin N Am 2010;24:257

Table 2
Types of infections encountered at various times after HSCT

Type of Infectious Pathogen	Early Preengraftment (First 2–4 wk)	Early Postengraftment (Second and Third Month)	Late Postengraftment (After Second or Third Month)	Time Independent
Fungi	*Candida* (related to mucosal injury and neutropenia)	*Aspergillus*, other molds and *Pneumocystis jirovecii* (related to GVHD)	*Aspergillus*, other molds and *P jirovecii* (related to GVHD)	
Herpesviruses	HSV	CMV (related to GVHD and impaired cellular immunity) EBV (in patients who have T-cell depleted grafts, receive ATG, or whose donor is mismatched)	CMV and VZV (related to GVHD and impaired cellular immunity and viral latency before transplant) EBV (in patients who have T-cell depleted grafts, receive ATG, or whose donor is mismatched)	
Other viruses		BK virus (related to GVHD and cyclophosphamide in conditioning regimen)		Respiratory viruses (temporally tracks with community outbreaks) Adenoviruses

Wingard et al. Inf Dis Clin N Am 2010;24:257

Incidence of fungal infections



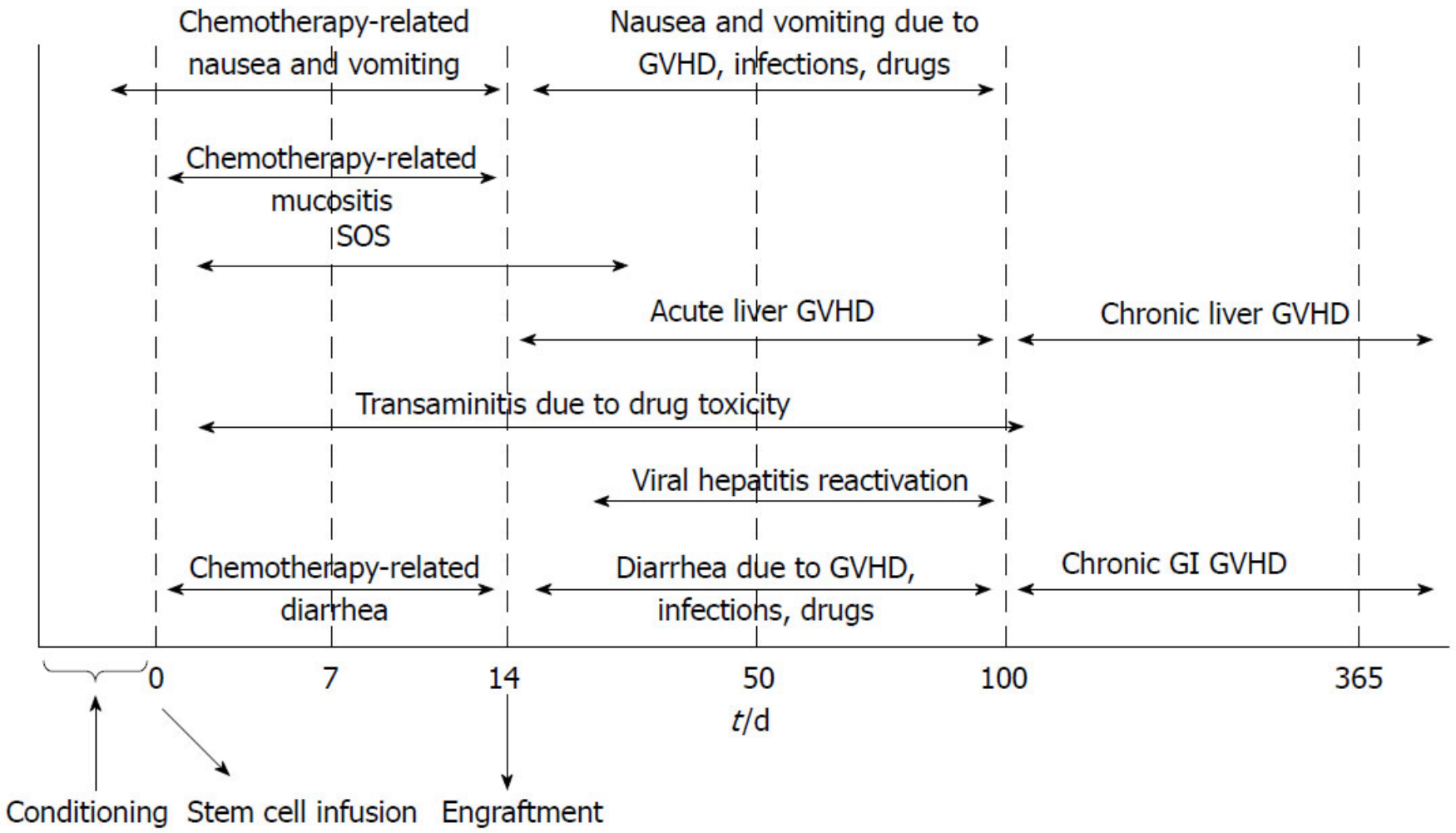
Kontoyiannis et al. CID 2010;50:1091

Pulmonary complications after HSCT

	Phase I Pre-engraftment (0-30 days)	Phase II Post-engraftment (30-100 days)	Phase III Late Phase > 100 days)
Host immune system defect	Neutropenia, mucositis, catheters and lines, acute GVHD	Impaired cellular immunity Acute GVHD	Impaired humoral and cellular immunity chronic GVHD
Infectious	gram - bacteria Gram + bacteria (Staph, Strept) Candida, other fungi Aspergillus HSV	*P. jiroveci* CMV Parainfluenza, RSV, influenza, adenovirus	Encapsulated bacteria Nocardia, mycobacteria Aspergillus HZV
Non-infectious	CHF ES VOD DAH IPS	BOOP	BO PTLPD

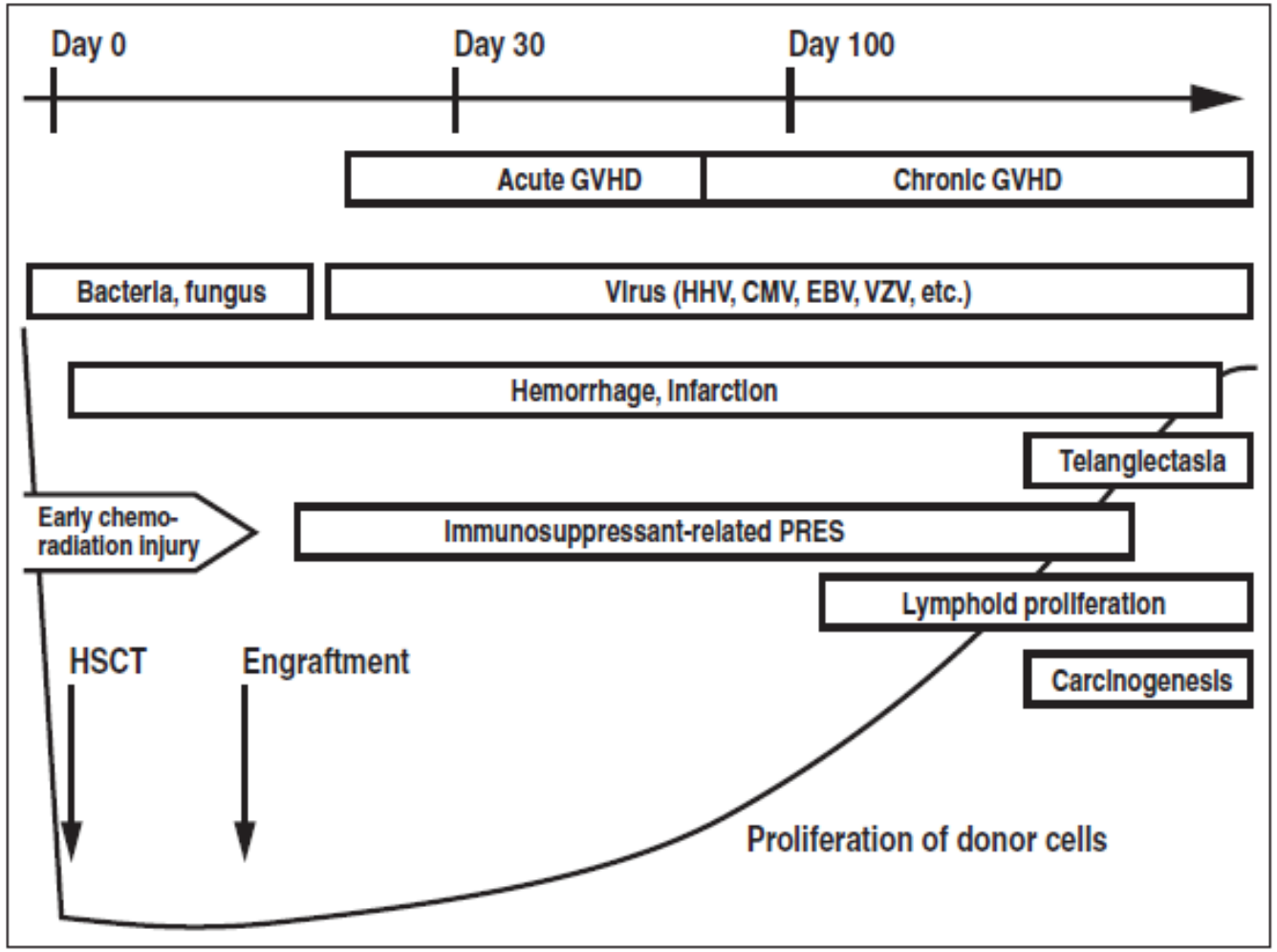
Rahman Safadi et al. Eur J Int Med 2009;20:268

GI complications



Tuncer et al. W J Gastroenterol 2012;18:1851

CNS complications after HSCT



Nishiguchi et al. AJR 2009;192:1003

Aspergillus outbreak in HSCT

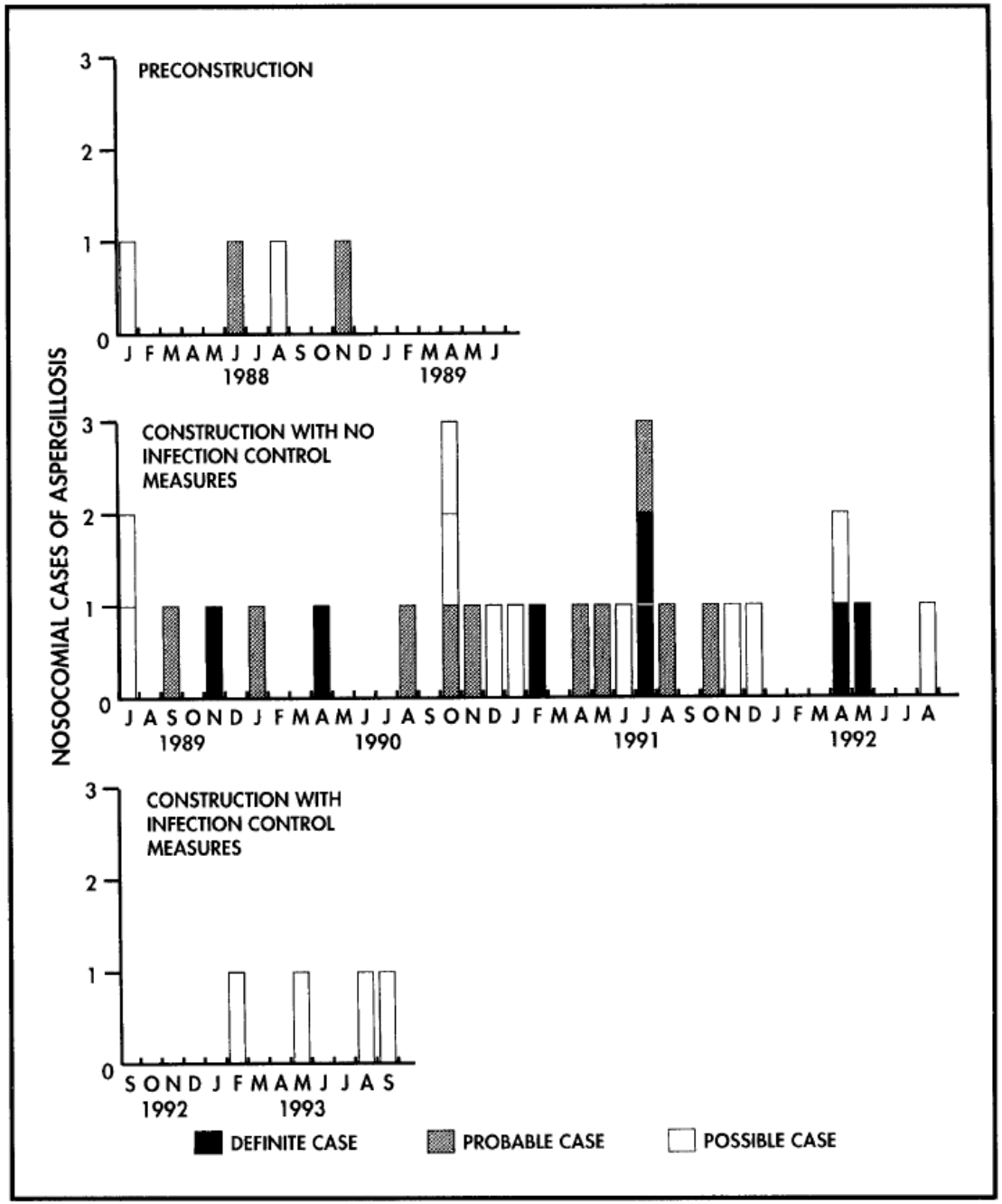


FIGURE. Nosocomial cases of aspergillosis in relation to construction.

Loo et al. ICHE 1996:360-36

Febrile neutropenia

- High risk
  - Prolonged (anticipated >7 days) and profound neutropenia (≤100 cells/mm^3)
  - "comorbid medical problems"
    - Hypotension
    - Pneumonia
    - New abdominal pain or new GI symptoms
    - Neurologic changes
    - Line infection
    - Severe mucositis
  - Hepatic or renal insufficiency

Freifeld et al. CID 2011;52:e56

MASCC score: less is worse

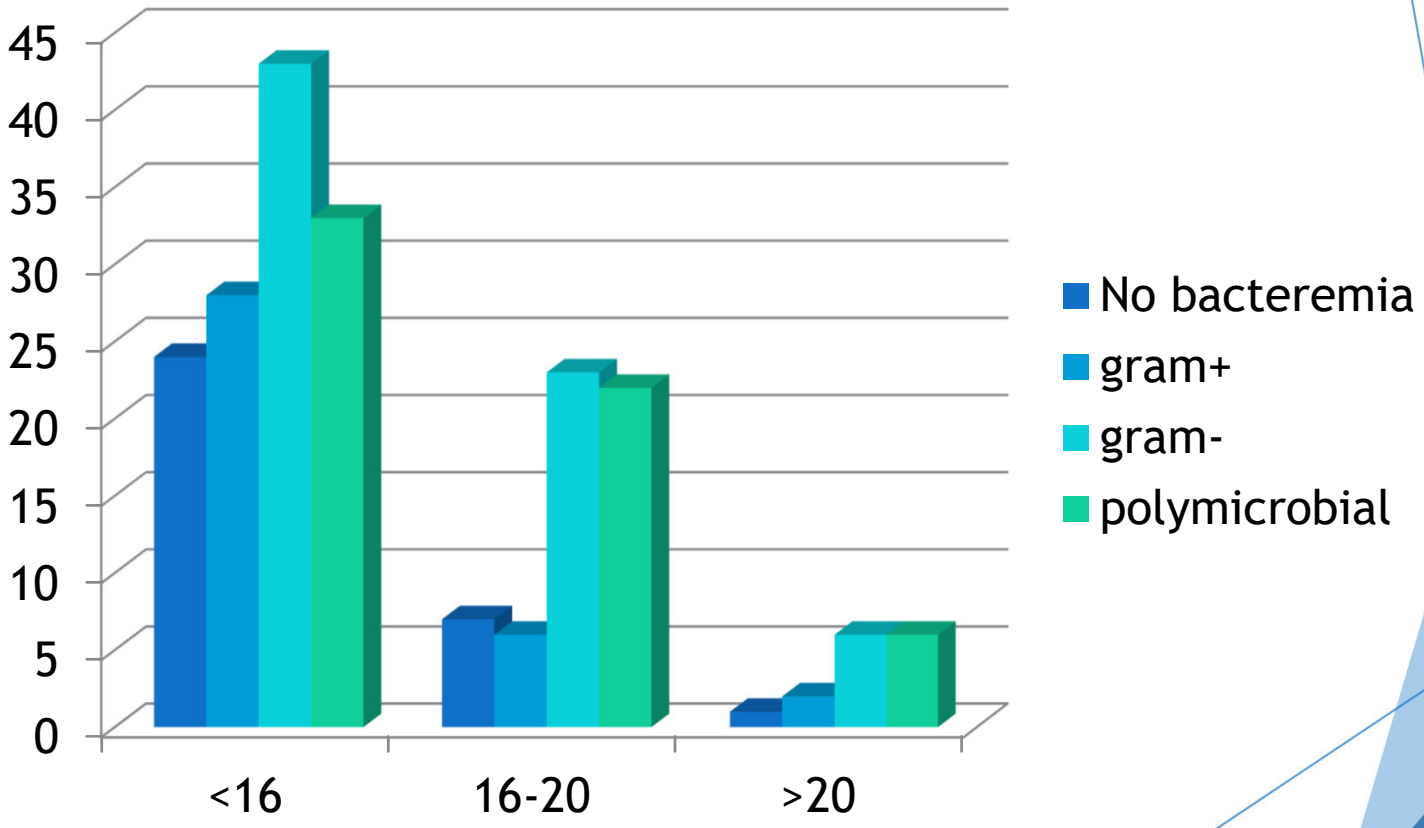
Multinational Association for Supportive Care in Cancer study

Characteristic	Weight
Burden of febrile neutropenia with no or mild symptoms[a]	5
No hypotension (systolic blood pressure >90 mmHg)	5
No chronic obstructive pulmonary disease[b]	4
Solid tumor or hematologic malignancy with no previous fungal infection[c]	4
No dehydration requiring parenteral fluids	3
Burden of febrile neutropenia with moderate symptoms[a]	3
Outpatient status	3
Age <60 years	2

- 26 maximum score -> lowest risk
- <21 considered high risk

Freifeld et al. CID 2011;52:e56

Mortality risk by MASCC score



Paesmans et al. Support Care Cancer 2011;19:1001

Risk determines initial treatment

Low risk patients…

- May be treated as outpatients
- May be considered for oral antibiotics
- Most commonly solid tumors

High risk patients…

- Require hospitalization
- Require initial IV antibiotics
- Most commonly HSCT preparation or acute leukemia induction chemotherapy
- CT chest +/- sinuses for fever >= 4 days

Freifeld et al. CID 2011;52:e56

Environmental precautions in febrile neutropenia, IDSA 2011

- General
  - Hand hygiene
  - Standard barrier precautions and infection specific precautions
  - HSCT recipients should be housed in private rooms. Allogeneic HSCT recipients should be housed in rooms with >12 air exchanges/h and HEPA filtration
  - Plants and dried or fresh flowers should be prohibited
  - Hospital work exclusion policies should be designed to encourage HCP to report their illnesses or exposures

Environmental precautions in febrile neutropenia, IDSA 2011

- Neutropenic diet
  - Consists of well cooked foods
  - Prepared luncheon meats should be avoided
  - Well cleaned, uncooked raw fruits and vegetables are acceptable, as are cooked foods brought from home or restaurants, provided that the freshness of ingredients and means of preparation can be confirmed

Environmental precautions in febrile neutropenia, IDSA 2011

- Patient skin and oral care
  - Patients should take daily showers or baths
  - Skin should be inspected daily
  - Gentle but thorough perineal care after bowel movement
  - Avoid rectal thermometers, enemas, suppositories, and rectal exams
  - Menstruating females should avoid tampons
  - Patients with ongoing mucositis should perform oral rinses 4-6 times per day with sterile water, normal saline, or sodium bicarbonate
  - Patients with brush their teeth ≥2 times/day with a soft regular toothbrush
  - Avoid fixed orthodontic appliances and space maintainers

Environmental precautions in febrile neutropenia, IDSA 2011

- Plants and animals
  - Avoid plants and dried or fresh flowers
  - Do not allow visitation by pets (including pet therapy)
- HCP personnel and visitors
  - Vaccination of HCP or visitors who are symptomatic with infections transmitted by air, droplet, and direct contact (e.g., VZV, infectious gastroenteritis, HSV lip lesions, URI) should not engage in patient care or visit patients unless appropriate barrier (e.g., mask and glove) protection is established
- Infection control surveillance
  - Do not routinely perform bacterial surveillance cultures of the environment, equipment, or devices

Engineering controls

- *Aspergillus* prevention
  - Filtered hospital air
  - Barrier protection during renovation or construction
  - Protective isolation (HEPA filtered) for hematopoietic stem cell transplants
  - Provide respiratory protection when patients must leave a protective environment

- *Legionella* prevention
  - Prohibit showers (use sponge baths)
  - Implement surveillance for *Legionella* cases
  - Monitor water supply: if *Legionella* present initiate decontamination (controversial)

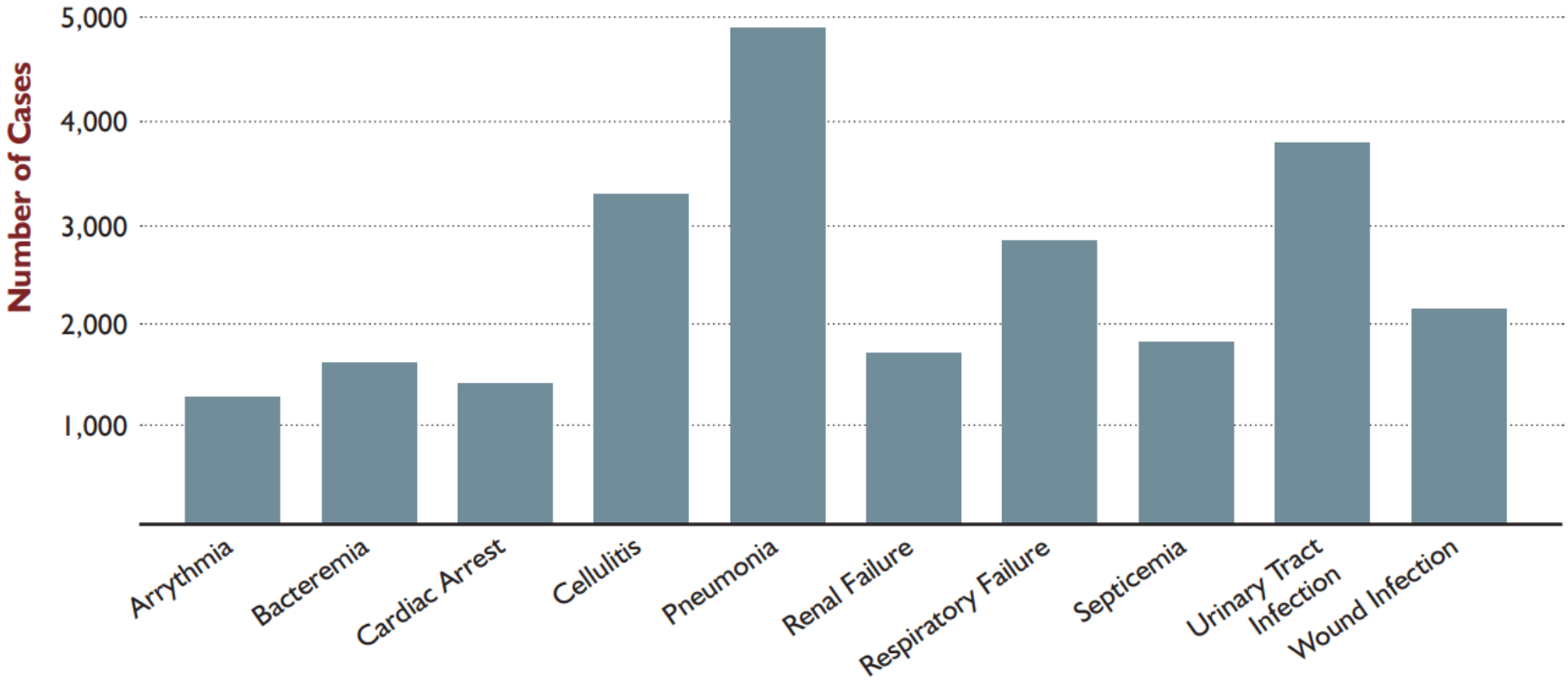
Procedures during construction & renovation

- Seal hospital construction areas behind impervious barriers
- Clean construction area daily (i.e., remove dust with HEPA vacuum)
- Assure that ventilation system does not transport dust from inside construction area to other locations
- Move immunocompromised patients from adjacent areas
- Thoroughly clean construction area prior to patient use
- Conduct surveillance for airborne fungal infections
- Assess airborne fungal levels adjacent to construction
- Avoid transporting construction material through patient areas
- Assess compliance with infection control guidelines

Infection in burns

COMPLICATIONS: FREQUENCY OF TOP TEN CLINICALLY RELEVANT COMPLICATIONS

Figure 17



Total N=219,505 (Excluding 2,014 cases from non ABA burn registry software centers)

6 of 10 are infectious complications!

2019 National Burn Repository Report of Data From 2009-2018
http://ameriburn.org/wp-content/uploads/2019/04/2019_aba_annual_report_website-content.pdf

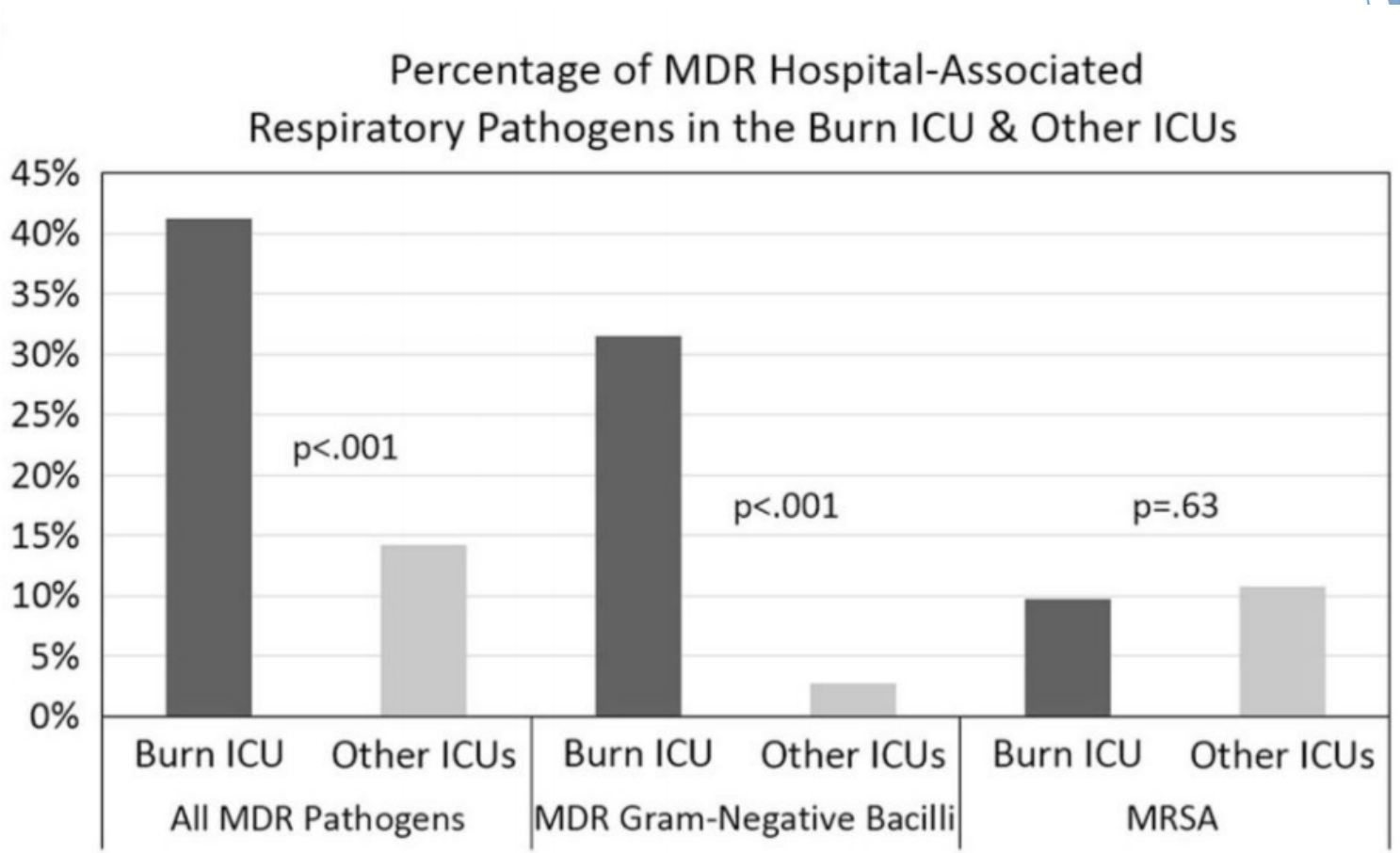
Nosocomial infection in burns

Table 3. Risk factors for development of NI

	Univariate Analysis			Multiple Analysis Model		
	Odds Ratio	95% CI	*P*	Odds Ratio	95% CI	*P*
Sex						
Male	1					
Female	1.02	0.69–1.49	.94			
Age	1.01	0.99–1.01	.163			
Underlying disease						
No	1					
Yes	1.61	0.96–2.69	.07			
Injury						
Scald	1					
Flame	3.48	2.32–5.22	<.001			
Electrical	1.58	0.87–2.87	.14			
Contact	1.38	0.57–3.37	.48			
%TBSA	1.05	1.04–1.06	<.001	1.05	1.04–1.06	<.001
ABSI*	1.44	1.33–1.56	<.001			
Admission day						
≤24 hr	1					
>24 hr	0.11	0.04–0.30	<.001			
Trauma						
No	1					
Yes	0.99	0.29–3.32	.98			
First excision day	1.14	1.10–1.18	<.001	1.13	1.09–1.17	<.001
Transfusion						
No	1					
Yes	5.01	3.29–7.63	<.001			

Alp et al. Burn Care Res 2012;379

Nosocomial infection in burns



- At UNC from 2008-2012, 32% of hospital-associated respiratory infections in the burn ICU were caused by MDR-GNB vs. 3% in all other ICUs

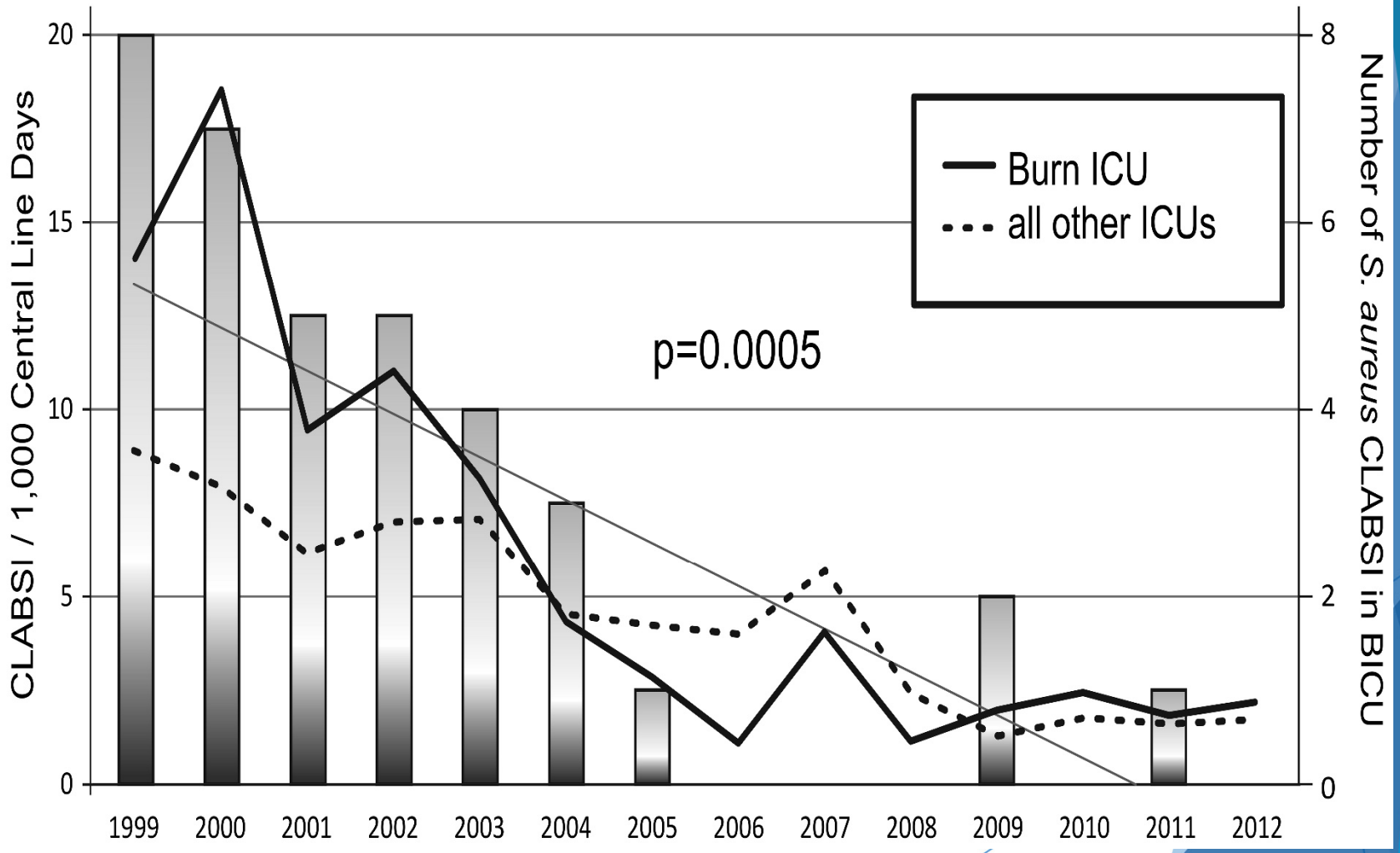
Lachiewicz A et al. *Infect Control Hosp Epidemiol* 2015;36:601

MDR-bacterial outbreaks in burn units

Study	Microorganism	Outbreak Duration	Patients Hospitalized, N	Cases, N (%)		
				Colonization	Infection	Total (Attack Rate)
Babík et al[13]	*Acinetobacter baumannii*	—	73	—	—	8 (10.96)
Bayat et al[11]	*A. baumannii*	12 mo	—	7 (54)	6 (46)	13
Herruzo et al[29]	*A. baumannii*	1 yr	72	—	—	21 (29)
Lyytikäinen et al[15]	*A. baumannii*	12 mo	—	—	—	21
Roberts et al[30]	*A. baumannii*	3 mo	—	1 (7)	14 (93)	15
Simor et al[19]	*A. baumannii*	16 mo	247	13 (42)	18 (58)	31 (12.55)
Fujioka et al[26]	*Alcaligenes xylosoxidans*	1 mo	—	—	2	2
Falk et al[37]	*Enterococcus faecium*	1 yr	—	17 (81)	4 (19)	21
Sanchez et al[24]	*Klebsiella pneumoniae*	10 mo	—	18 (69)	8 (31)	26
Douglas et al[31]	*Pseudomonas aeruginosa*	3 mo	30	—	4	4 (13.33)
Hsueh et al[32]	*P. aeruginosa*	2 mo	16	1 (25)	3 (75)	4 (25)
Tredget et al[16]	*P. aeruginosa*	2 yr	—	—	17	—
Saida et al[28]	*Providencia stuartii*	3 mo	—	—	17	17
Tsai et al[12]	*Stenotrophomona maltophilia*	9 yr	666	—	—	13 (1.95)
Edgar et al[20]	*Serratia marcescens*	1 mo	—	—	—	3
Boers et al[17]	MRSA	2½ yr	—	12 (71)	5 (29)	17
Dansby et al[27]	MRSA	7 yr	—	—	—	21.9/1000 PD
Embil et al[14]	MRSA	2 mo	126	11 (92)	1 (8)	12 (9.52)
Espersen et al[36]	MRSA	1 mo	23	—	10	10 (43.48)
Fuchs et al[10]	MRSA	8 mo	43	6 (75)	2 (25)	8 (18.60)
Hunt et al[21]	MRSA	8 yr	—	—	—	56
Lilly et al[22]	MRSA	2 yr	—	—	—	74
Meier et al[34]	MRSA	4 mo	—	6 (60)	4 (40)	10
Patel et al[23]	MRSA	1 mo	—	—	4	4
Rashid et al[9]	MRSA	5½ mo	176	15 (83)	3 (17)	18 (10.23)
Roberts et al[33]	MRSA	18 mo	1896	—	—	109 (5.75)
Rutala et al[35]	MRSA	—	—	—	—	66 (70)
Safdar et al[18]	MRSA	5 mo	—	7	5	12 (723/1000 PD)
Teare et al[25]	MRSA	16 mo	—	—	—	19

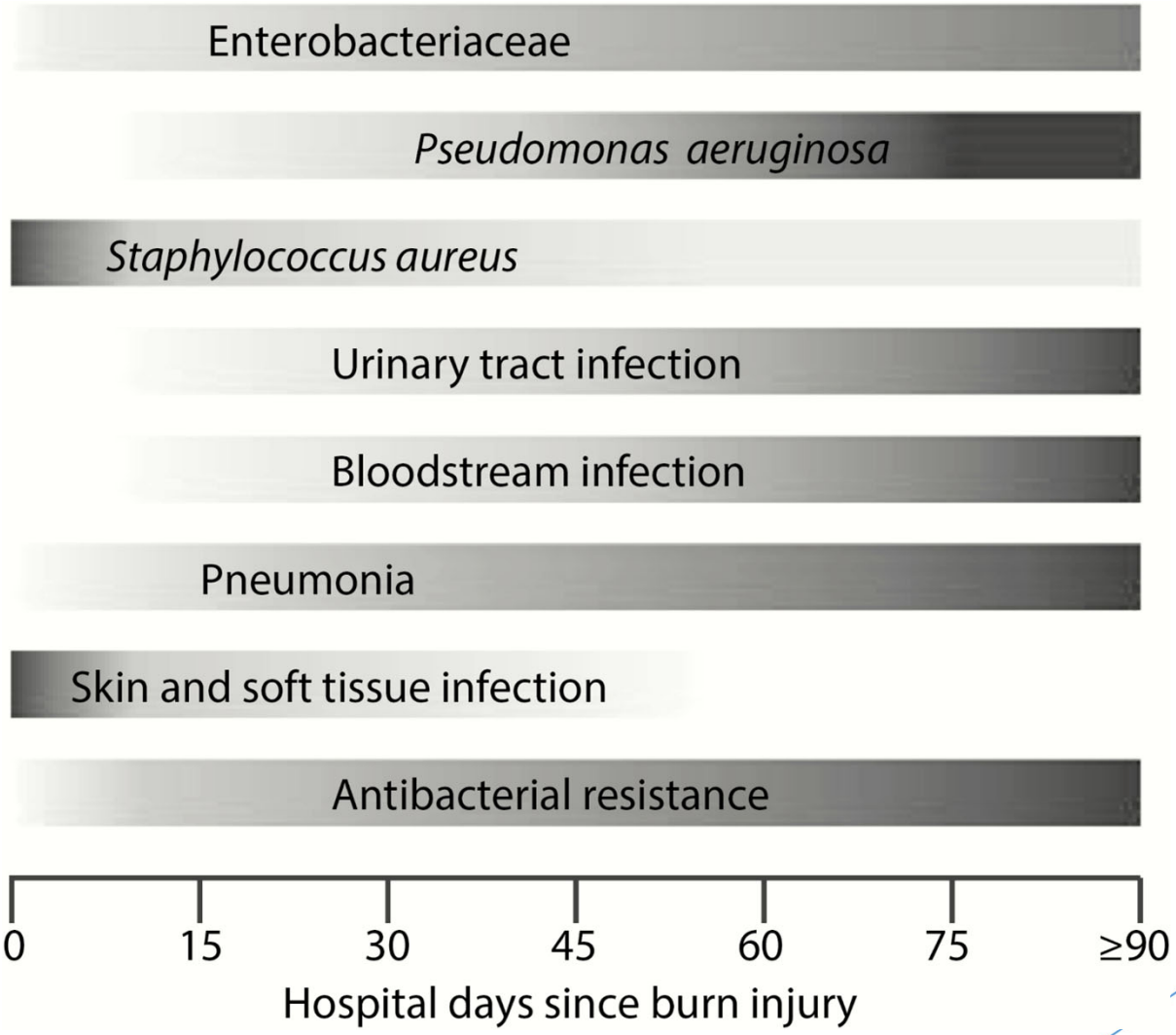
Girerd-Genessay et al. J Burn Care Res. 2016;37:172

Decline in the rate of BSI



van Duin et al. ICHE 2014;35:8;1066-68

Pathogens & infections in burn



Lachiewicz A et al. *Clin Infect Dis* 2017;65:2130-2136

Prevention of infection in burns

- Topical agents
- Systemic antimicrobial prophylaxis
- Wound care
- Universal isolation precautions
- Frequency of line changes

Interventions to decrease CLABSI rate at UNC

TABLE 1. Interventions to Reduce Central Line–Associated Bloodstream Infections (CLABSIs) at University of North Carolina Hospitals, 2000–2009

Year(s)		Intervention(s)
2000		Enhanced education of medical staff regarding central lines; addition of 2% chlorhexidine plus 70% isopropyl alcohol for skin preparation to central line kits
2001		Mandatory training for nurses on IV line site care and maintenance
2003	★	Central line changes over a guidewire every 3 days with use of a new site every 6 days becomes standard practice;[a] use of full body drape for line insertion and changes
2003–2005		Introduction of antibiotic-impregnated central venous catheters for all patients
2004		Enhanced nursing education on central line insertion and maintenance
2005		Customized catheter-insertion kits
2006	★	Universal glove and gown use for all patient encounters[a]
2007		Implementation of the Institute for Healthcare Improvement bundle to prevent CLABSI
2009		Use of chlorhexidine patch at insertion site

★ Specific to burn ICU

van Duin et al. ICHE 2014;35:8;1066-68

Questions?

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