



Principle of Transplant Infectious Disease

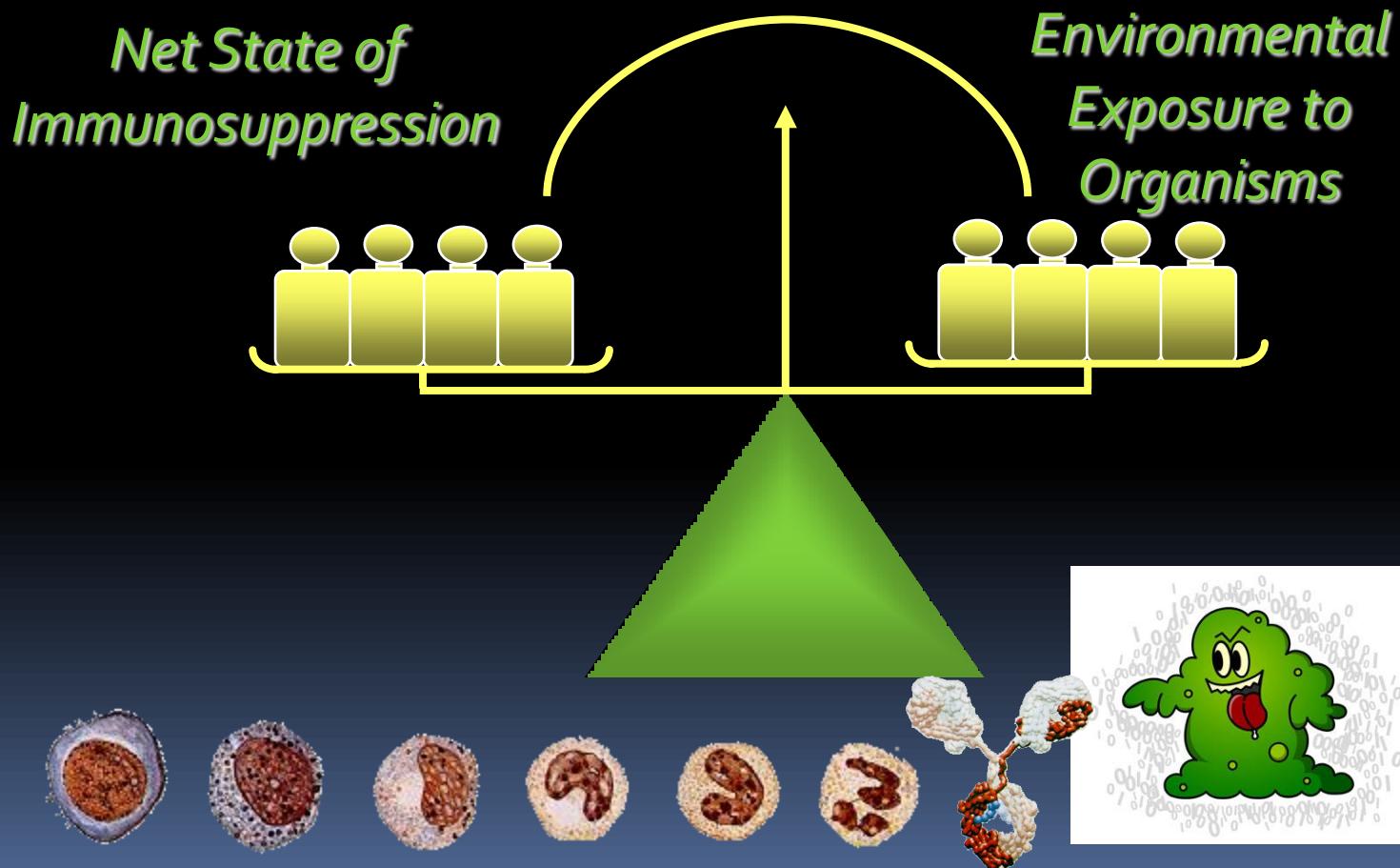
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Mahidol University**



Outlines

- Concept of infection in solid organ transplant population
 - Immunosuppressive therapy and infection
- Transplant infectious disease in Thailand
 - Perspective of the burden of the infections based on the western theory
- Principle in the diagnosis, prevention and treatment

Overall Risk of Infection



The chance of being infected and severity of Infection after Transplantation

- **Change of risk over time**
 - Environmental exposure
 - Related to post transplant complications
- **Host factors**
 - Degree of immunosuppression
 - Underlying comorbidities
- **Diminished clinical symptoms**
- **No accurate assay to measure risk of infection**

Modified from Chow J. et al, Clinical Infectious Diseases 2009; 49:1550–6, Rubin RH, Clinical Approach to Infections in Compromised Host 2002

Net State of Immunosuppression

Determined by;

1. The dose, duration, and temporal sequence of immunosuppressive drugs (ie, the total exposure to immunosuppression)
 - High-dose corticosteroid therapy for rejection
 - Antilymphocyte antibodies (induction/rejection)
 - Cytoreductive effects, eg. neutropenia

Net State of Immunosuppression

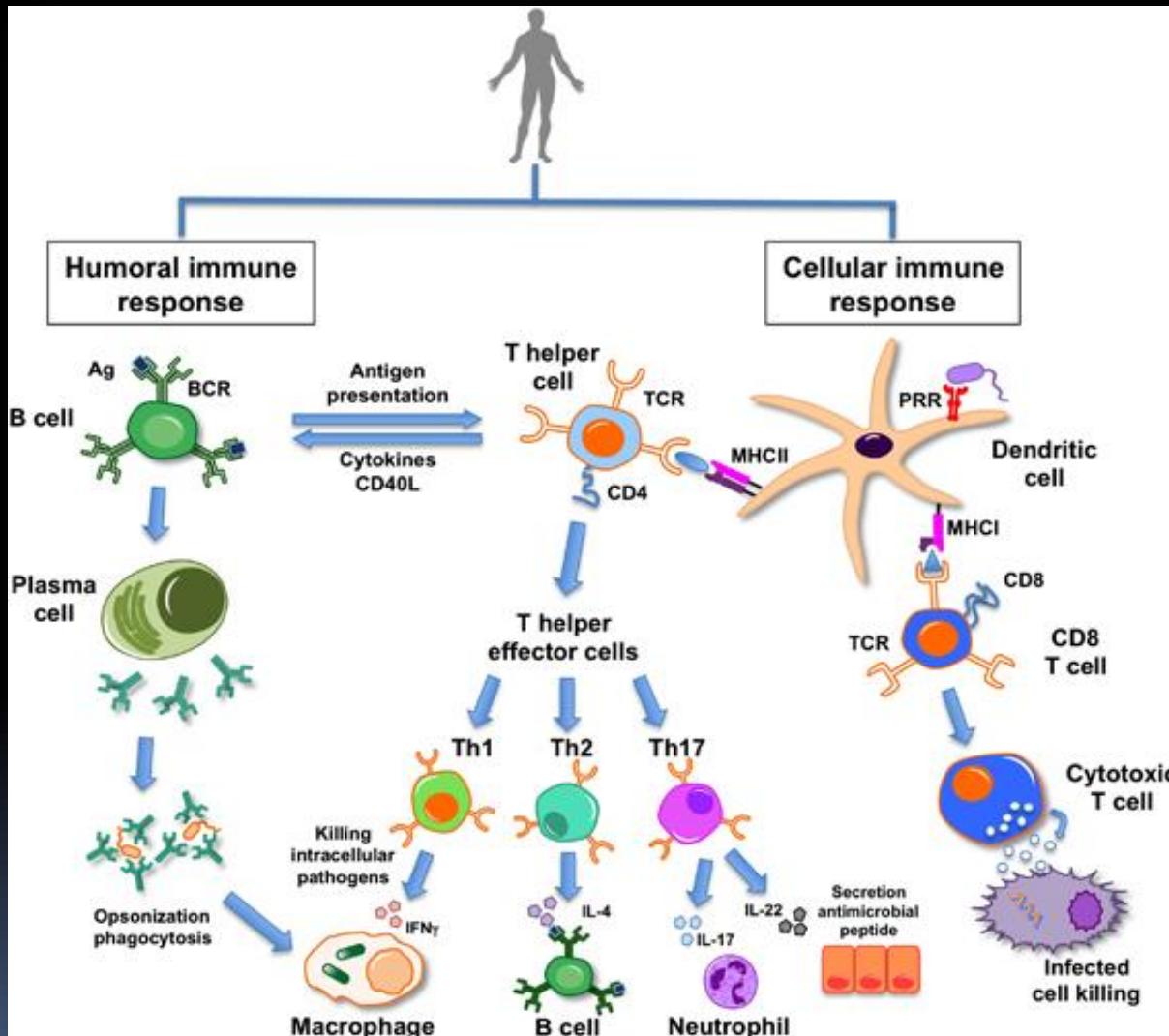
2. The underlying disease and comorbid conditions
3. Foreign bodies, injuries to the primary mucocutaneous barrier to infection (ex; lines), devitalized tissues, hematomas, effusions, and adhesions
4. Neutropenia and metabolic problems such as protein-calorie malnutrition, uremia, and perhaps hyperglycemia
5. Infections with immunomodulating viruses [CMV, EBV, human herpesvirus 6, hepatitis B

Viruses associated with immunosuppression

- CMV most common, but also HCV, HHV-6
- Induction of systemic immune suppression
- Infection can cause allograft injury
- Viruses may cause rejection which may necessitate increased immunosuppressive therapy

Major Immunological Pathway and the Significant in Transplant Related Infection

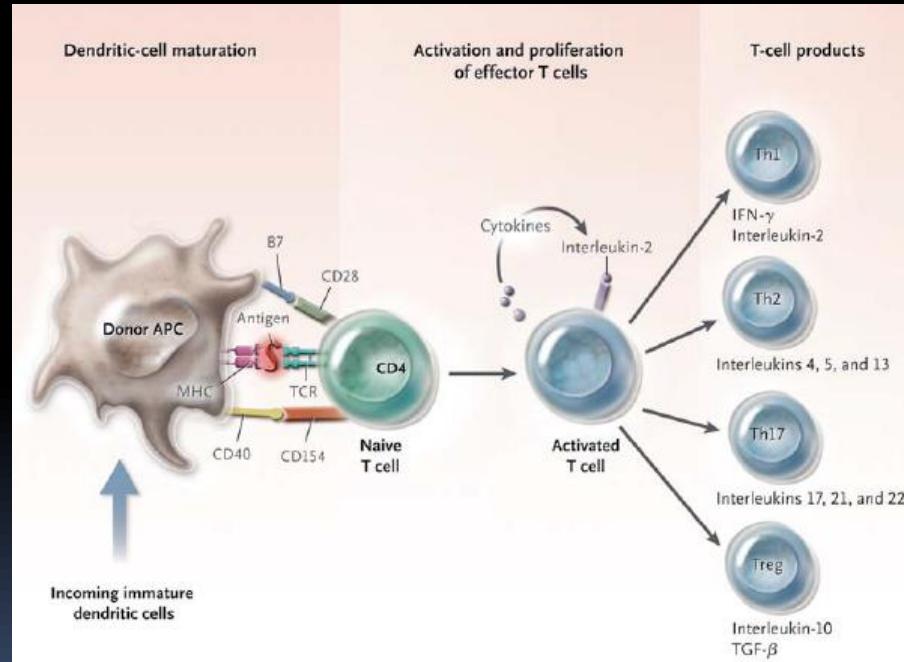
Human Immune Response to Infections



Pathway of Alloimmune response

Alloimmune responses involve both naive and memory lymphocytes

T-CELL-MEDIATED REJECTION



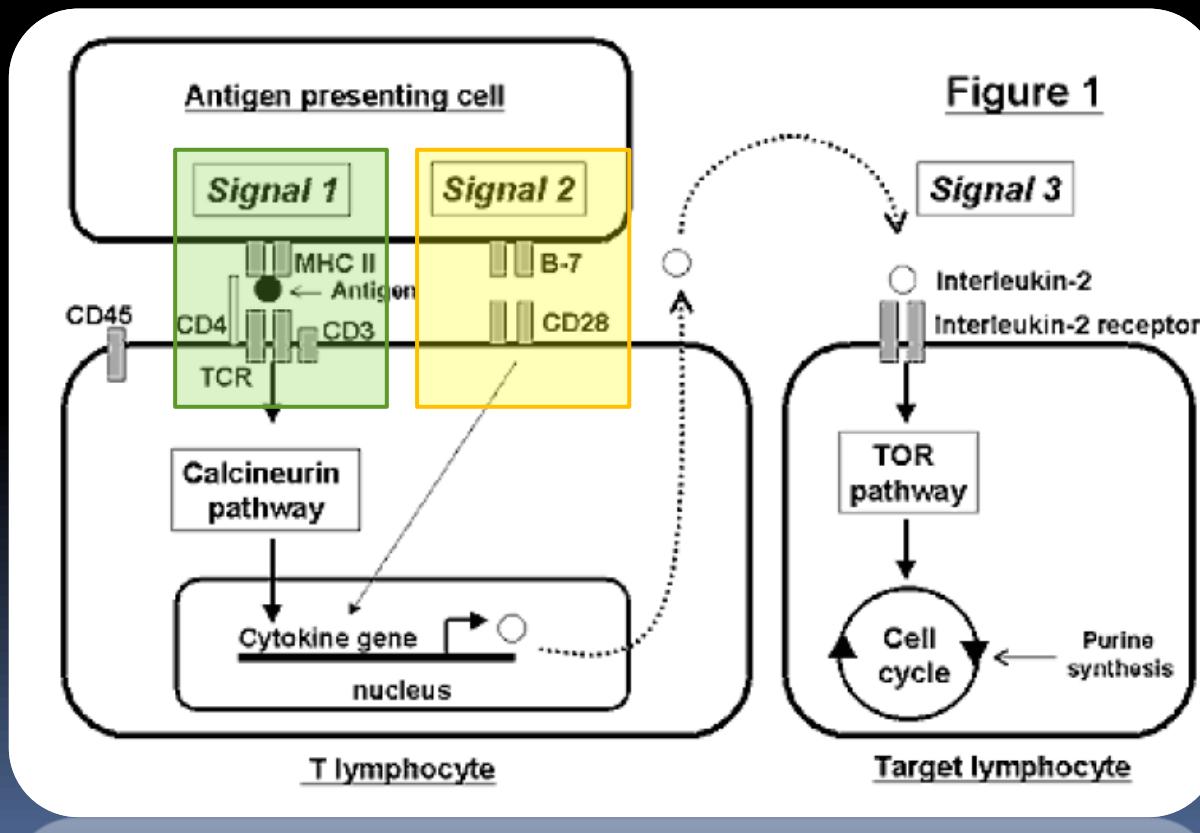
Nankivell BJ et al., N Engl J Med 2010;363:1451-62

- Dendritic cells of donor and host origin become activated and move to T-cell areas of secondary lymphoid organs
- There, antigen-bearing dendritic cells engage alloantigen-reactive naive T cells and central memory T cells that re-circulate between lymphoid compartments
- Within days the immune response generates the agents of allograft rejection, effector T cells and alloantibody

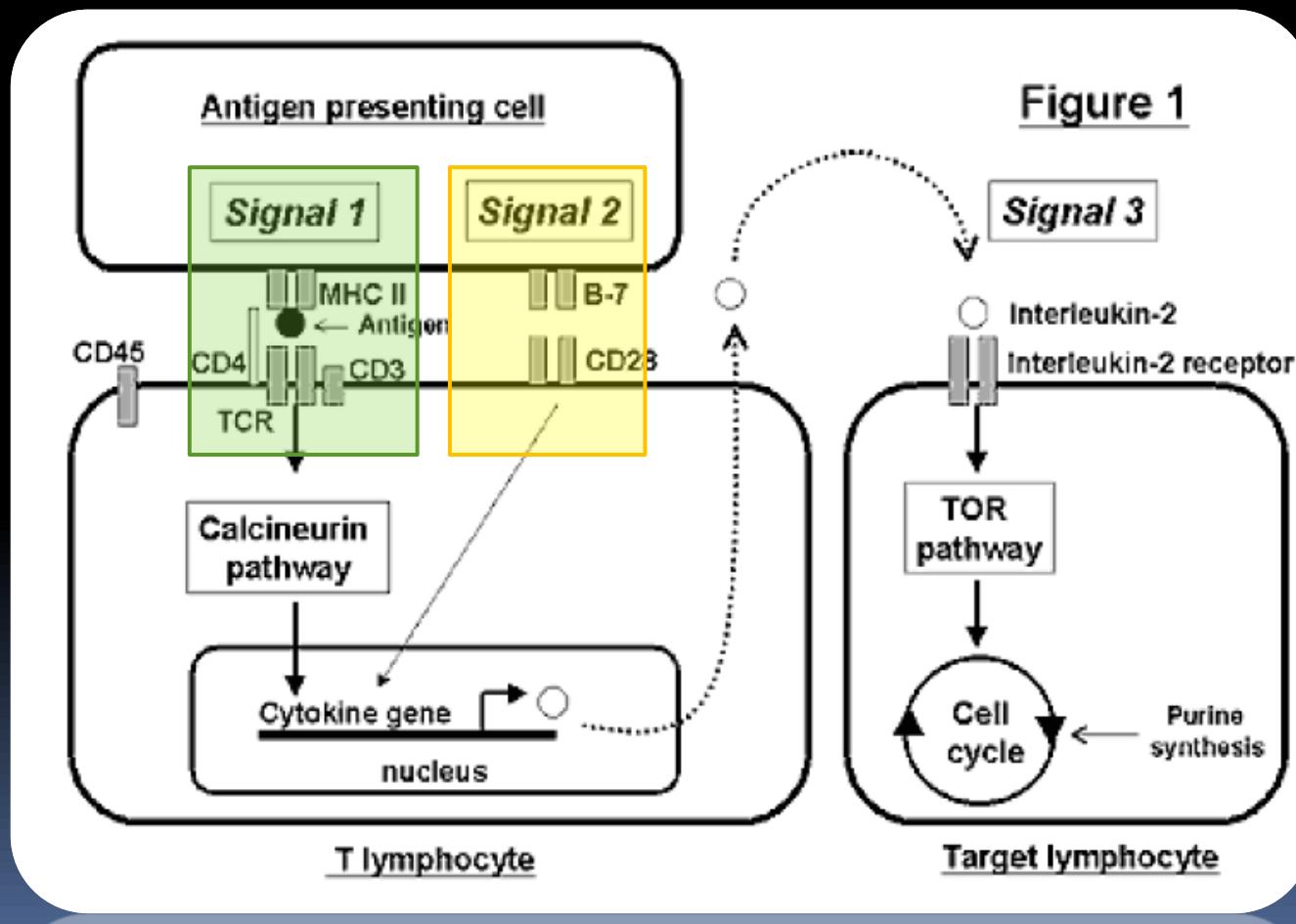
Halloran PF, N Engl J Med 2004;351:2715-29

The 3-signal model of T cell activation

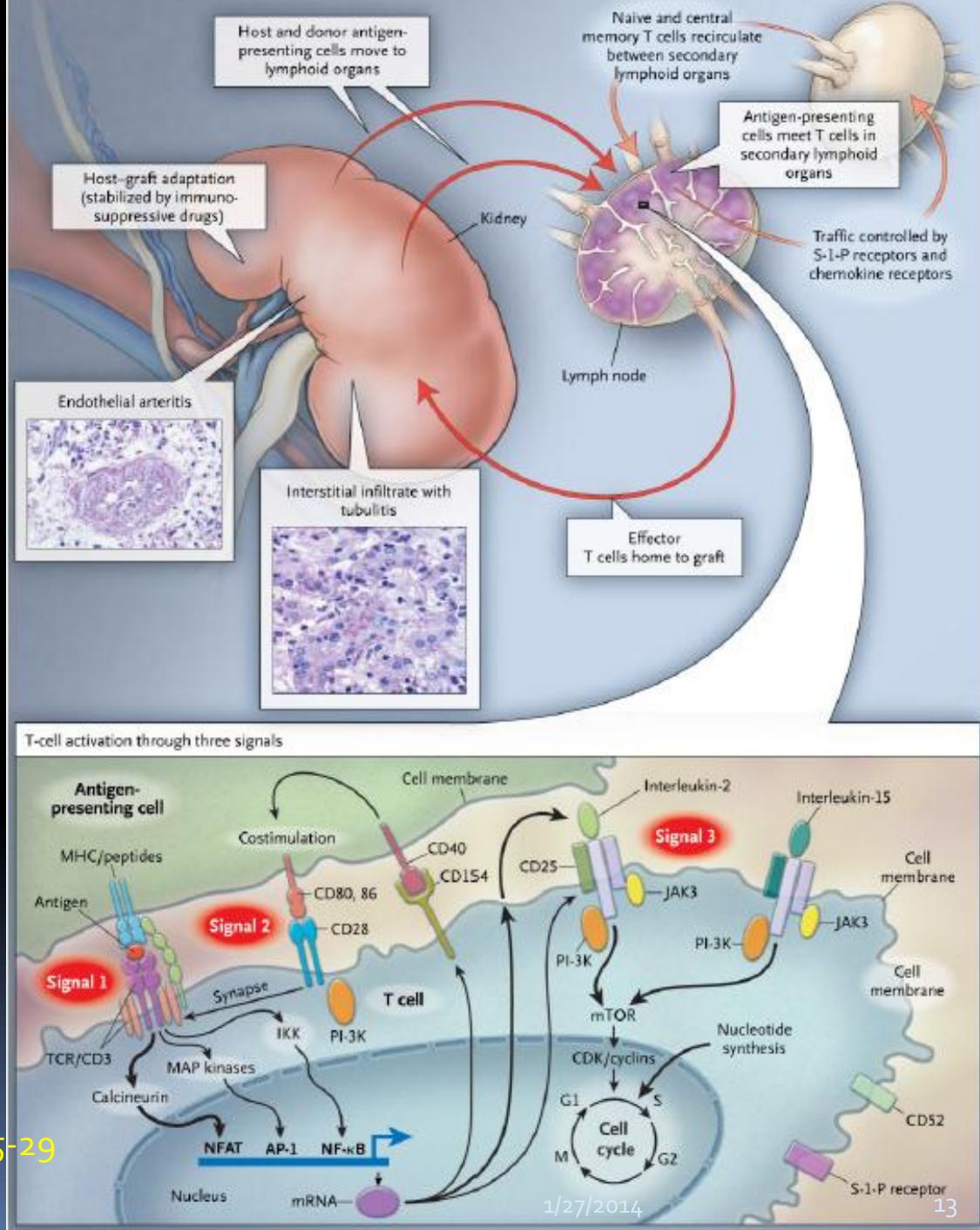
1. An antigen on the surface of dendritic cells that triggers T cells with cognate T-cell receptors constitutes “signal 1,” transduced through the CD3 complex
2. Dendritic cells provide **costimulation**, or “signal 2,” delivered when CD80 and CD86 on the surface of dendritic cells engage CD28 on T cells



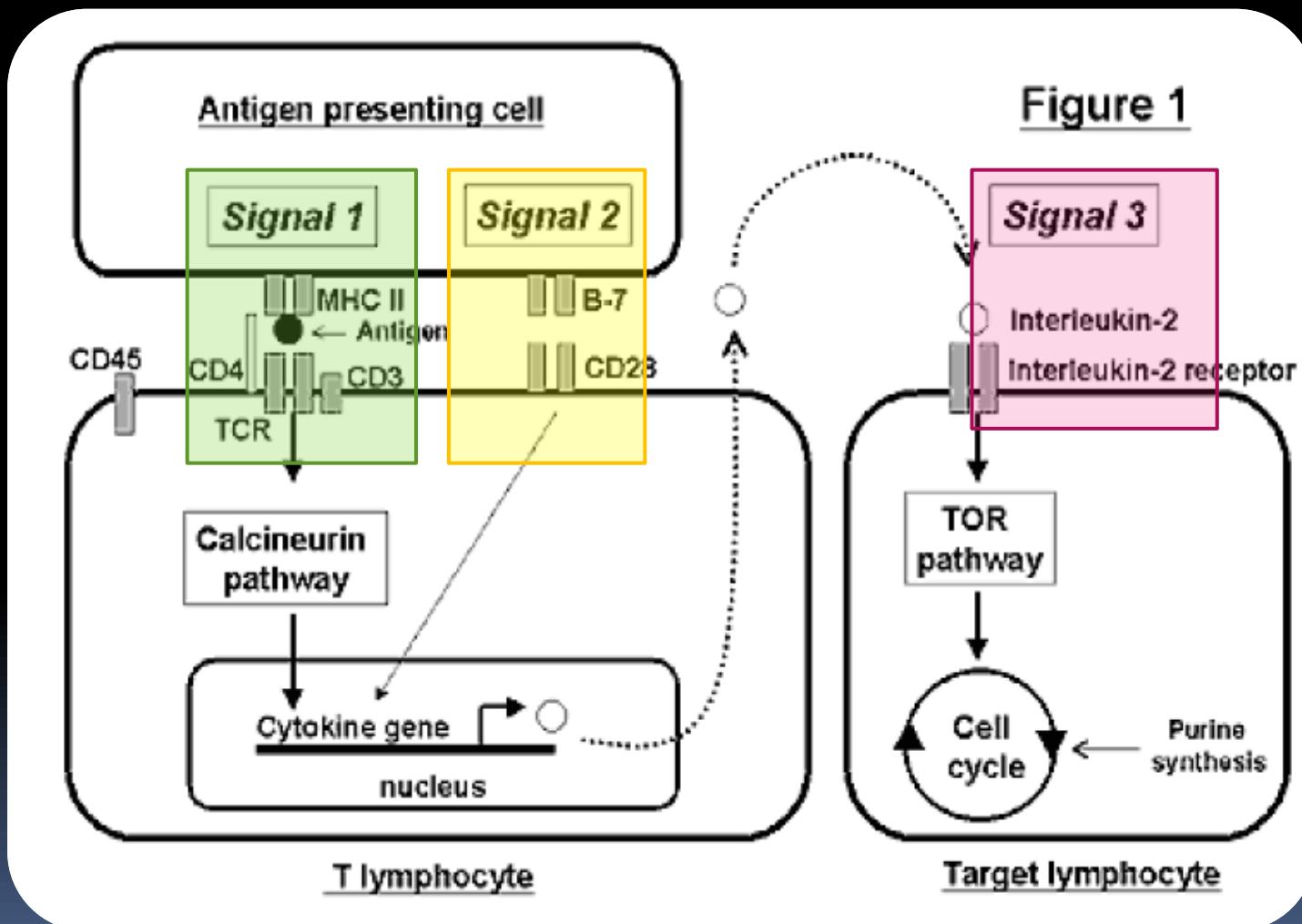
Signals 1 and 2 activate 3 signal transduction pathways:
the calcium–calcineurin pathway, the RAS–mitogen-activated protein (MAP) kinase pathway, and the nuclear factor *kB* pathway



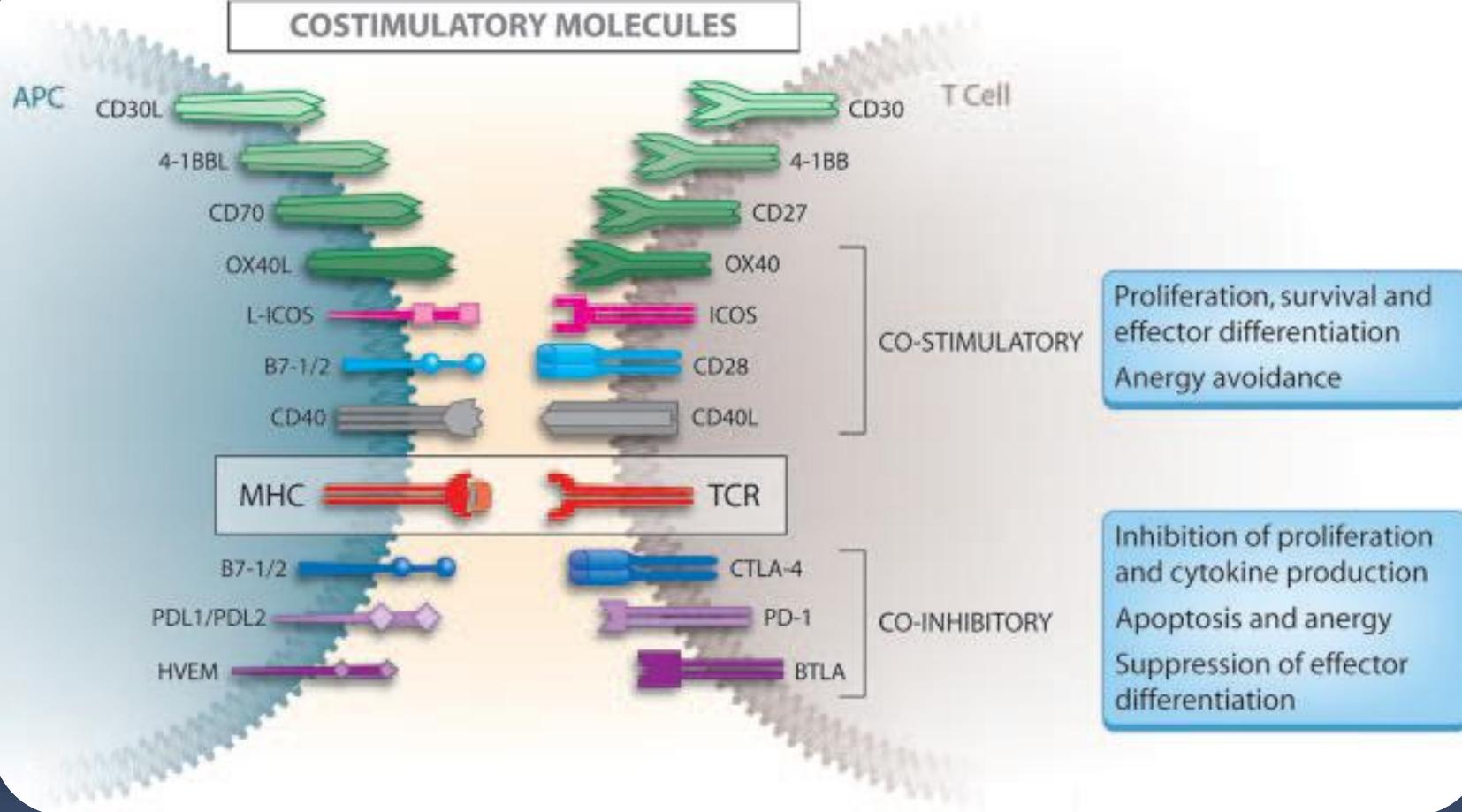
Steps in T-Cell–Mediated Rejection



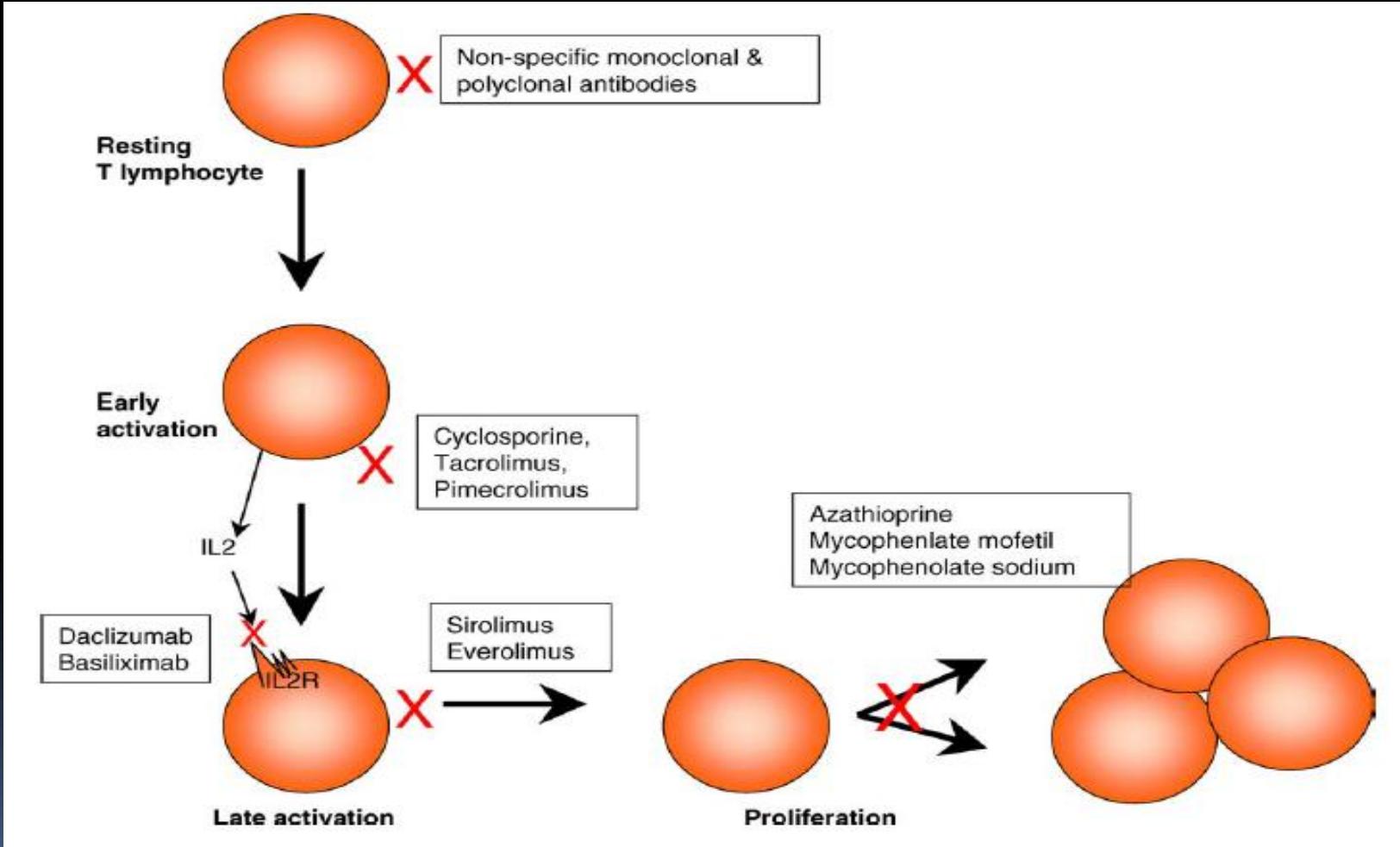
Interleukin-2 and other cytokines (e.g., interleukin-15) activate the “target of rapamycin” pathway to provide “signal 3”



The Novel Co-stimulatory Molecules

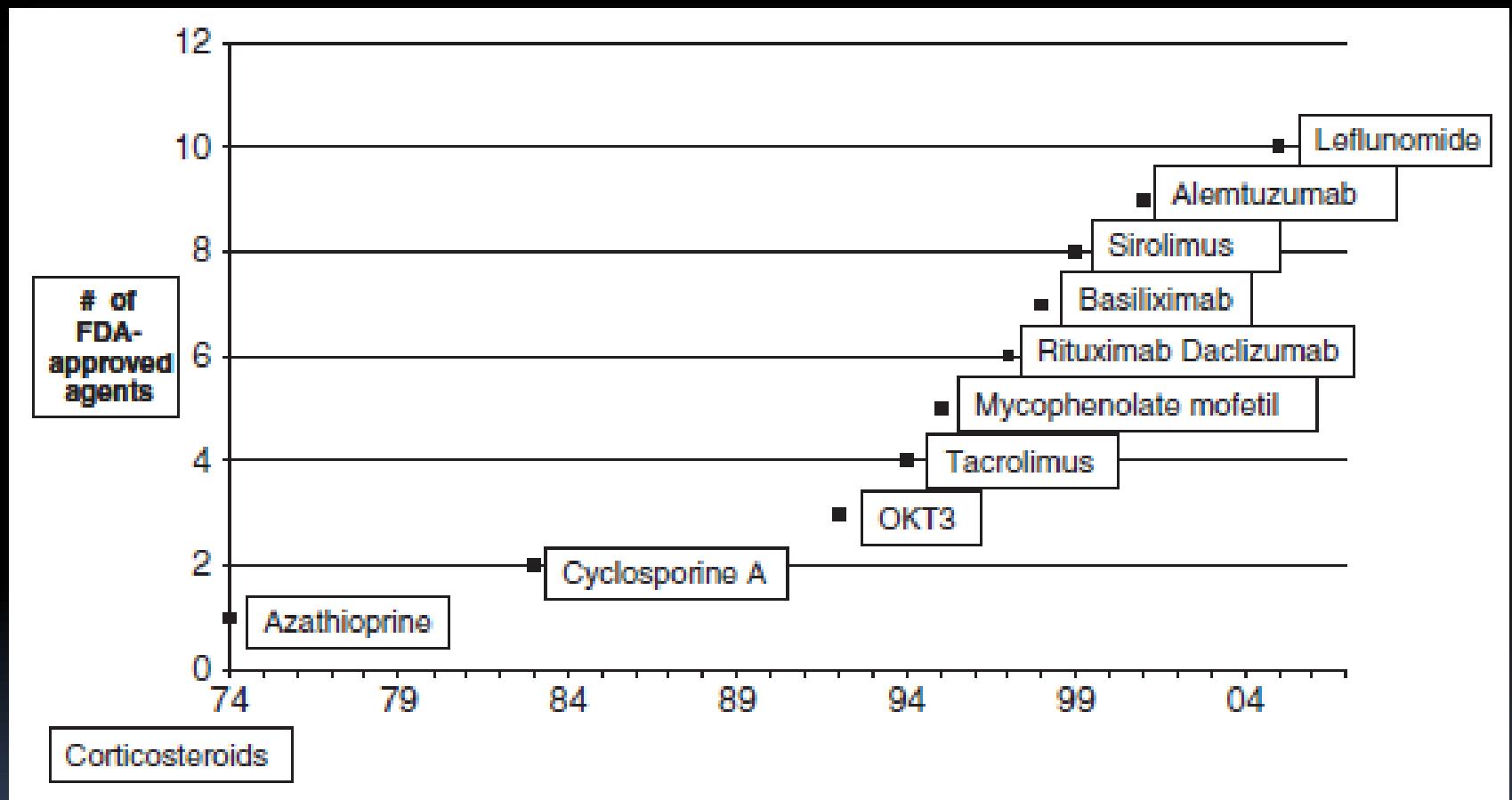


Schematic sites of action of common immunosuppressants



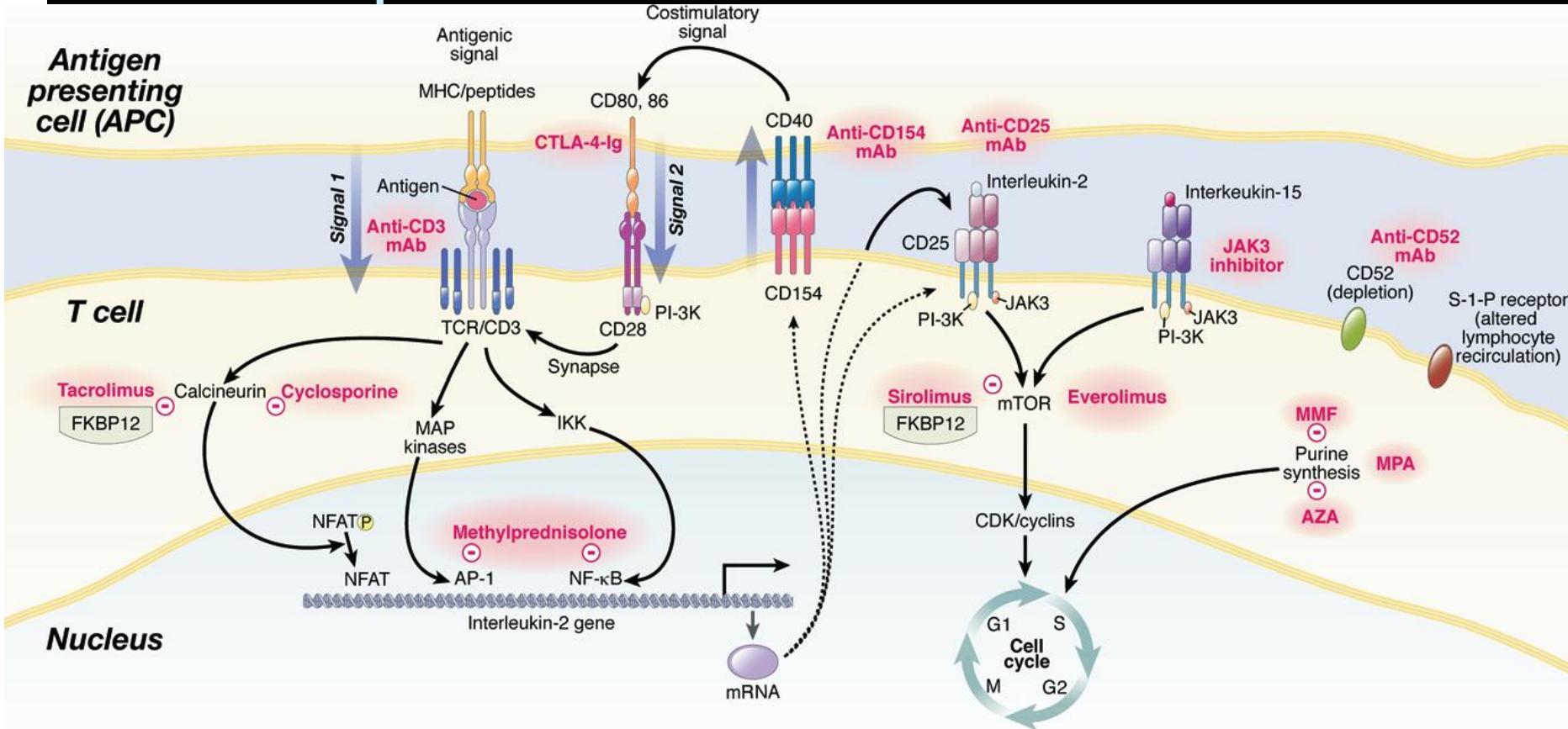
Taylor AL, et al. Crit Rev Oncol Hematol. 2005 ;56(1):23-46

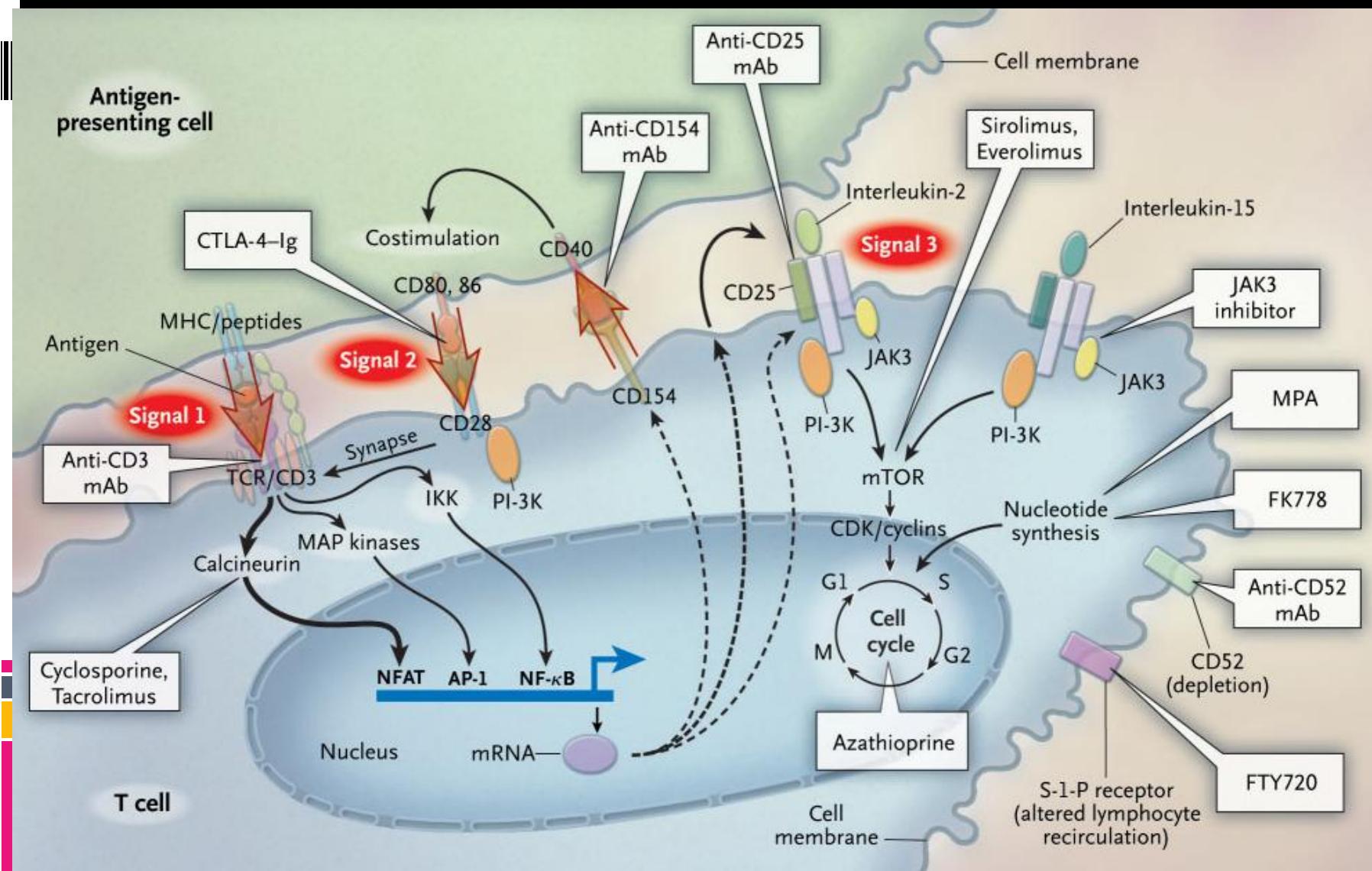
Timeline of US Food and Drug Administration (FDA)-approved agents used for immunosuppression in transplantation



Mueller NJ, Transpl Infect Dis 2008;10:379-84

Immunosuppressive Agents in Transplantation and Site of

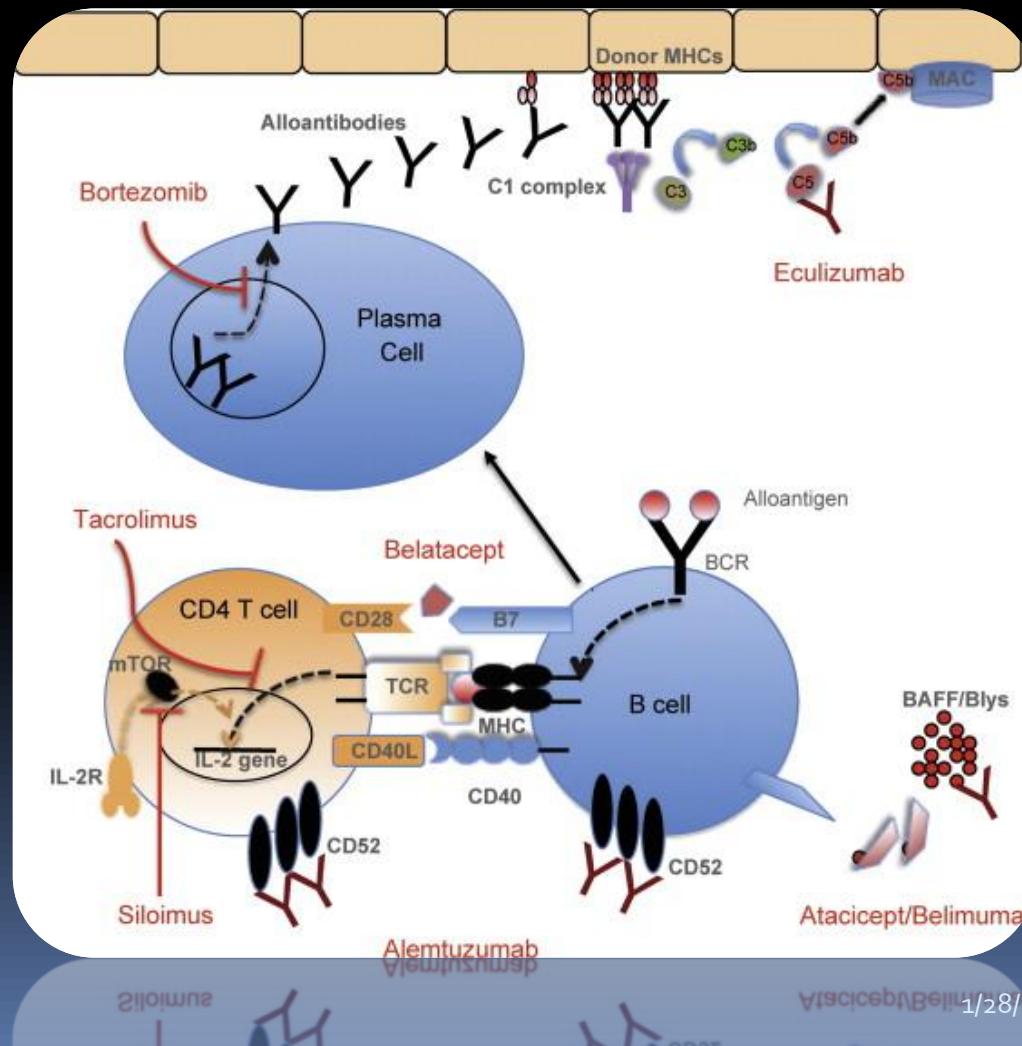




Halloran PF, N Engl J Med 2004;351:2715-29

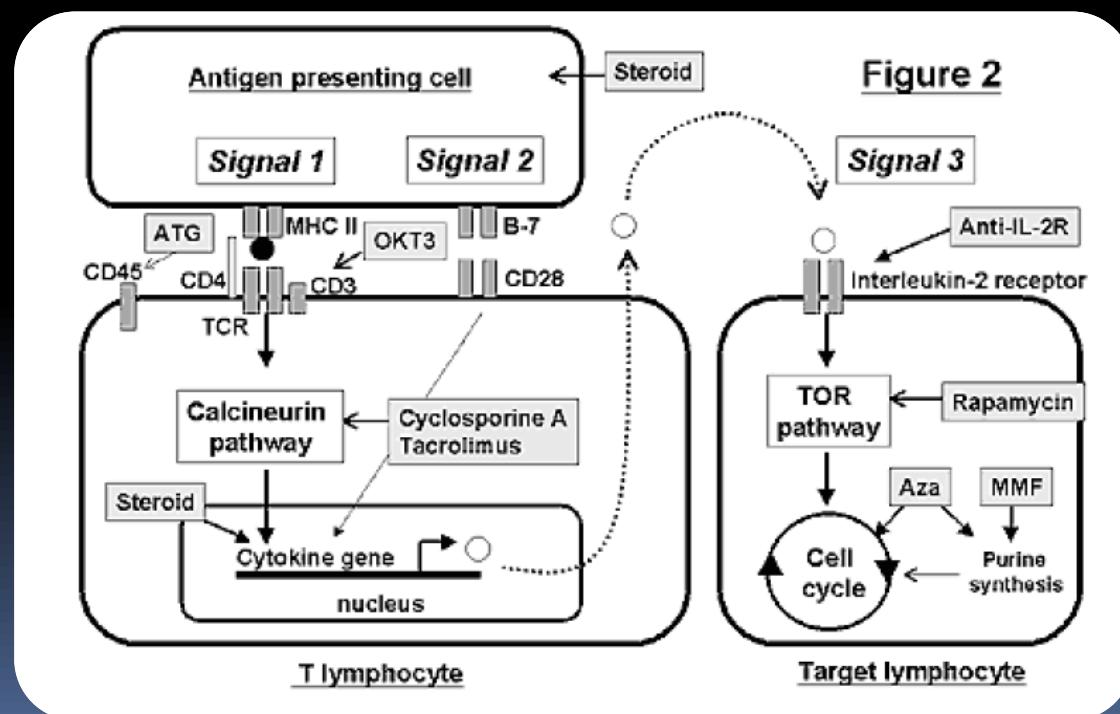
B cell Activation and Allo-Antibody: an emerging model of Antibody-Mediated Rejection Therapy

Kwun J et al, Seminar in Immunology 2012;24: 96-108



Immunosuppressive Agent	Target	Outcome
Cyclosporin A, FK506	Calcineurin	Inhibit calcineurin phosphatase activity, preventing dephosphorylation of NFAT and IL-2 transcription ¹⁰⁵
Rapamycin	mTOR	Inhibits growth factor signaling, blocks cell-cycle transition and cell survival (reviewed by Saunders et al. ¹⁰⁶).
Mycophenolate mofetil, azathioprine	Purine synthesis	Inhibit proliferation of T and B lymphocytes ^{107,108}
Glucocorticoids	Gene transcription	Inhibits NF-κB nuclear translocation and production of proinflammatory cytokines ^{109,110}
Anti-CD25 mAb Campath-1	CD25 CD52	Saturates IL-2 receptor and prevents T cell activation ^{111,112} Depletes mature peripheral lymphocytes, monocytes, natural killer cells, and subset of granulocytes ^{113–117}
ATG, ALS	T cells	Broad lymphocyte depletion and immunomodulatory activities (reviewed by Mohty ¹¹⁸)

^aALS, antilymphocyte serum; ATG, anti-thymocyte globulin; mTOR, mammalian target of rapamycin; NFAT, nuclear factor of activated cells.



Impact of newer immunosuppressive therapy

- Depends on their immunobiology effect
 - Affected pathway
 - Duration of immunological dysfunction
- Determine by their net effect> particular drug
- Enhance by immunomodulating viruses



Transplant Infectious Disease in Thailand: Theory into practice

Risk of the Infection and the Clinical Presentations

- Diminished clinical symptoms frequently diminished, or atypical
- Change of risk over time
 - Environmental exposure
 - Immunosuppression
- No accurate assay to measure risk of infection

Significant of Pathogen

- True pathogens: influenza, anthrax
- Sometime pathogens: Group A streptococcus
- Non Pathogen: *Pneumocystis jirovecii*, environmental bacteria



Opportunistic infection

Number of compromised host are increasing. How do we recognize infection?

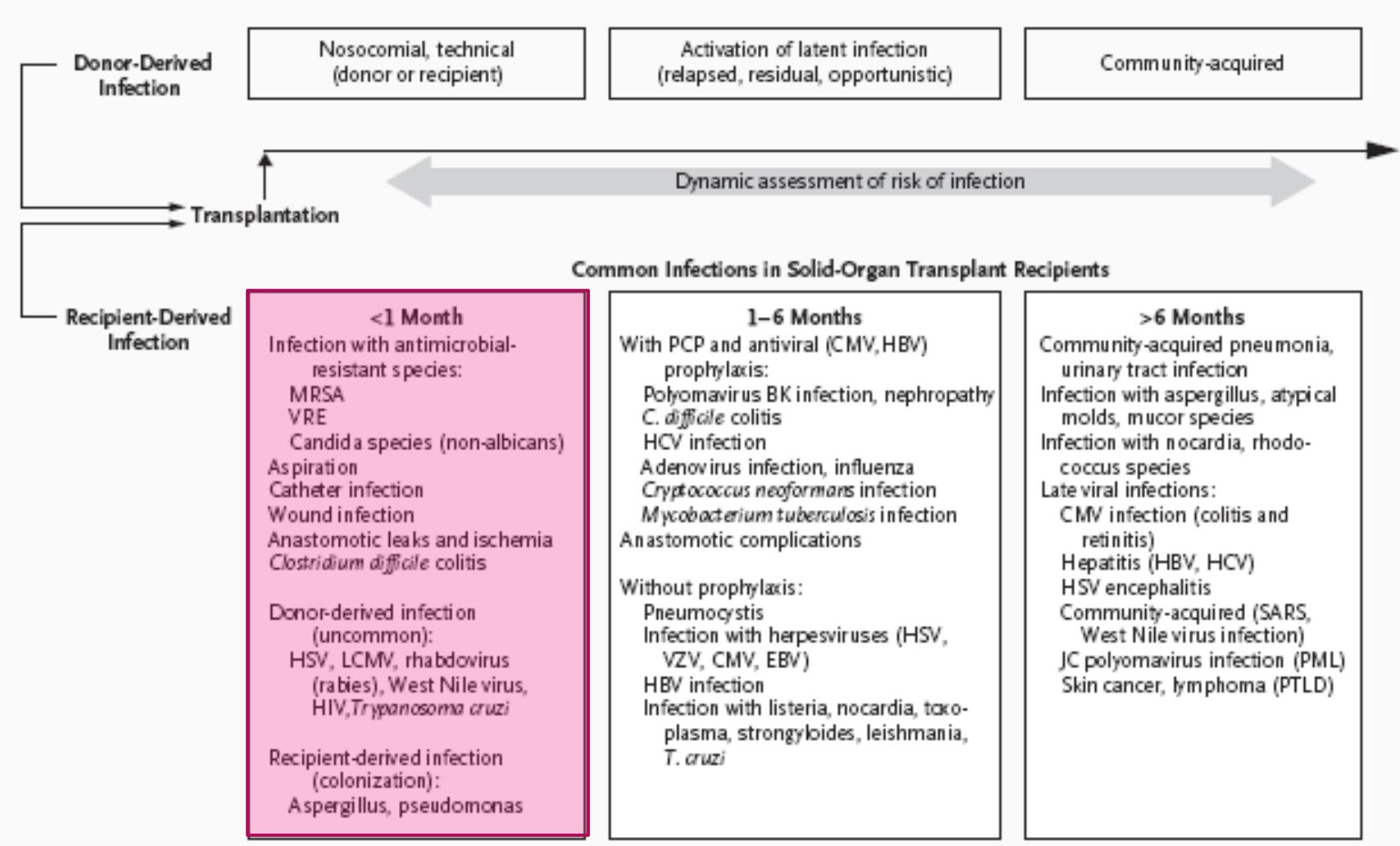
Scenarios

1. Opportunistic infection from unusual or less clinically significant pathogen
2. Severe infection from non-clinical significant pathogen or pathogen known for mild infection
3. Infection with unusual clinical presentation
4. Chronic infection that doesn't respond to treatment (excluding resistant pathogen and presumptive treatment)
5. Infection with unknown cause

Challenging Aspect of Transplant ID in Thailand

- Tropical country: climatic difference----difference in the epidemiology of infection (both past infection of D and R)
- Self belief and substandard hygienic practice--prone to infection and contagiousness
- Endemic of uncontrolled contagious disease; ex: TB, and multi-drug resistant organism
- Realtime and accurate laboratory diagnosis

Timing of Infections in SOT



Case#1: A 45 year-old man

- ESRD, S/P DDKT
- 5 days post transplantation, became febrile

CBC

- WBC 17,700
(N96, L3, M1, Eo)
- Hb 9 /Hct 26.9
- Plt 172,000

Urine analysis (31/1/09)

- Spgr 1.020
- Protein 4+
- WBC >20
- RBC >100
- Urine Gram stain - Gram negative bacilli
- (-) fluid drainage Gram stain

Blood and urine culture (29/1/09)

Chryseobacterium(Flavobacterium) meningosepticum (MDR)

Penicillin		Cefo/Sulb		Chloramphenicol
Ampicillin	R	Imipenem	R	Trimetho/Sulfa S
Oxacillin		Meropenem	R	Tetracycline
Amox/Clav	I	Ertapenem	R	Metronidazole
Pip/Tazo	S	Norfloxacin		Vancomycin
Cephalothin	R	Ofloxacin	S	Teicoplanin
Cefuroxime	R	Levofloxacin		Fosfomycin
Cefoxitin	S	Ciprofloxacin	S	Fusidic Acid
Cefoperazone	S	Gentamicin	R	Colistin
Cefotaxime	I	Amikacin	R	Tigecycline
Ceftazidime	R	Netilmicin	R	Linezolid
Ceftriaxone	I	Clindamycin		Amphi/Sulb
Cefepime	S	Erythromycin		Clarithromycin

Drainage c/s (31/1/09)

Chryseobacterium(Flavobacterium) meningosepticum (MDR)

Penicillin		Cefo/Sulb		Chloramphenicol
Ampicillin	R	Imipenem	R	Trimetho/Sulfa S
Oxacillin		Meropenem	R	Tetracycline
Amox/Clav	I	Ertapenem	R	Metronidazole
Pip/Tazo		Norfloxacin		Vancomycin
Cephalothin	R	Ofloxacin	S	Teicoplanin
Cefuroxime	R	Levofloxacin		Fosfomycin
Cefoxitin	S	Ciprofloxacin	I	Fusidic Acid
Cefoperazone	S	Gentamicin	R	Colistin
Cefotaxime	S	Amikacin	R	Tigecycline
Ceftazidime	R	Netilmicin	R	Linezolid
Ceftriaxone	R	Clindamycin		Ampi/Sulb
Cefepime		Erythromycin		Clarithromycin

Case follow up

- Subsequently noted graft tenderness on examination. MRI of transplanted kidneys showed infected perinephric collection and fluid collection in renal pelvis
- **Final diagnosis: infected urinoma**



Key Finding of this Case

- Infection from unusual or less clinically significant pathogen
 - Identified organism from blood or sterile site
 - Hospital setting (early onset after transplantation): environmental contamination?
 - Symptomatic

“Transplant recipients could have severe infection from non-clinical significant pathogen or pathogen known for mild infection”

Chryseobacterium meningosepticum

- Gram negative rod shaped bacteria
- Widely distributed in nature
 - eg. freshwater, saltwater, or soil
- not a human micro-flora

Table 1 Gram-negative bacteria species isolated from tap water, treated water and dialysate samples

Organism	No. of isolates			
	Tap water	Treated water	Dialysate	Total
<i>Pseudomonas aeruginosa</i>	7	8	17	32
<i>Chryseobacterium meningosepticum</i>	6	7	8	21
<i>Stenotrophomonas maltophilia</i>	5	4	10	19
<i>Escherichia coli</i>	1	2	15	18
<i>Enterobacter cloacae</i>	0	3	8	11
<i>Acinetobacter baumannii</i>	1	1	5	7
<i>Proteus mirabilis</i>	0	1	5	6
<i>Alcaligenes xylosoxidans.</i>	1	1	3	5
<i>Pseudomonas putida</i>	0	2	2	4
<i>Serratia liquefaciens</i>	0	0	4	4
<i>Moraxella osloensis</i>	1	0	2	3
<i>Burkholderia cepacia</i>	0	0	2	2
<i>Pseudomonas stutzeri</i>	0	0	2	2
<i>Serratia plymuthica</i>	0	1	1	2
Other Gram-negative bacteria*	2	1	2	5
Total	24	31	86	141

*Gram-negative bacteria with one isolate (*Acinetobacter lwoffii*, *Agrobacterium radiobacter*, *Alcaligenes faecalis*, *Citrobacter diversus*, *Rahnella aquatilis*).

Chryseobacterium Meningosepticum: An Emerging Pathogen Among Immunocompromised Adults: Report of 6 Cases and Literature Review

Bloch, Karen C.; Nadarajah, Rohan; Jacobs, Richard : Medicine (Baltimore), Volume 76(1).January 1997.30-41

Journal of Hospital Infection (2001) 47: 188–192
doi:10.1053/jhin.2000.0908, available online at <http://www.idealibrary.com> on IDEAL®



Chryseobacterium (Flavobacterium) meningosepticum outbreak associated with colonization of water taps in a neonatal intensive care unit

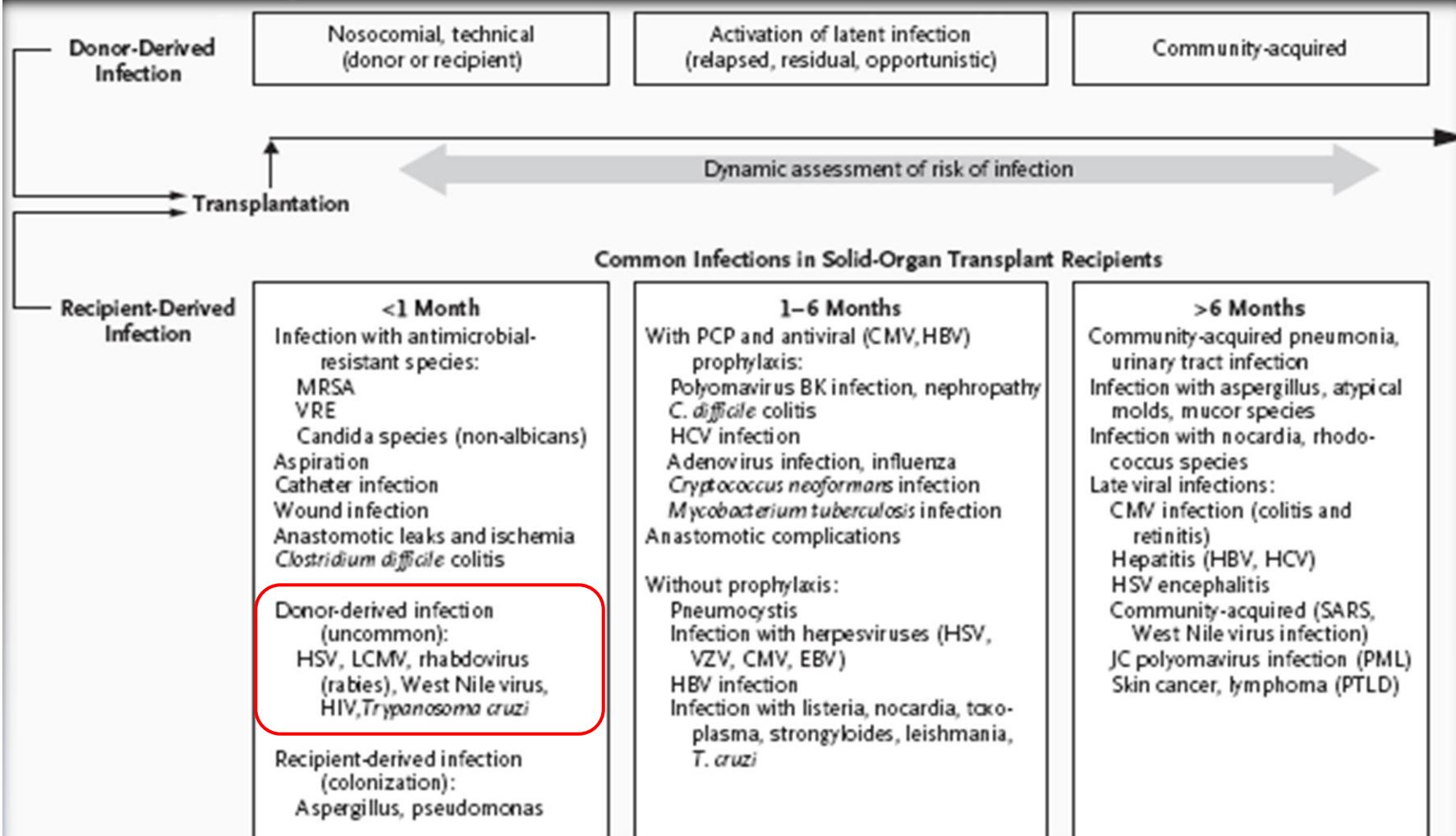
S. N. Hoque, J. Graham, M. E. Kaufmann* and S. Tabaqchali

The Department of Medical Microbiology, St Bartholomew's and the Royal London School of Medicine and Dentistry, Whitechapel, and *The Laboratory of Hospital Infection, Central Public Health Laboratory, 61 Colindale Avenue, London, NW9 5HT, UK

Infections in the First Month After Transplantation

1. Active infections
 - From allograft (usually bacteremia or candidemia) and commonly seed the allograft, especially at anastomoses
 - From recipient
2. Pulmonary infections (aspirational and postsurgical)
3. Infections in devitalized tissues or undrained fluid collections at a high risk for microbial seeding
4. C. difficile colitis

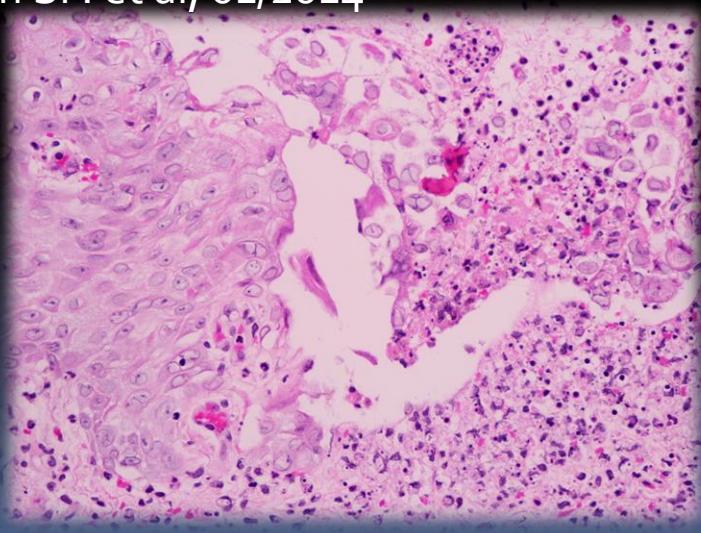
“Type of Infection is based on timing



Case #2: A 16 year-old man

- Congenital biliary atresia, S/P orthotopic liver transplantation
- Post transplantation course was complicated with anastomosis leakage, post surgical bacterial infection and enterococcus BSI
- Remained febrile despite systemic antibiotic
- Developed rising of the liver function test, esp. ALT up to 300

Disseminated HSV-2 infection



Watcharananan SP. et al, 01/2014

Case continued

- (-) Pre transplant HSV IgG
- Test not routinely performed in Thailand as pre-transplant screening

Standard Screening Tests for Organ Donors

- HIV antibody
- **HBV serology, including HBsAg, HBV core antibody and surface antibody**, and hepatitis delta virus antigen and/or antibody in HBsAg-positive donors
- HCV antibody
- **Nontreponemal** and treponemal testing (RPR + TPHA or TPPA or FTA antibodies)
- HTLV-I/II) antibody (less common currently given assay performance)
- Toxoplasma antibody (notably in cardiac donors)
- **Cytomegalovirus antibody**
- EBV antibody panel (EBV capsid antigen, with or without early antigen and nuclear antigen antibody levels)
- Herpes simplex virus antibody
- Varicella zoster virus antibody
- Blood and urine cultures

**Titles with bold are test that is currently suggested by
The Thai Red Cross Society**

Grossi PA, Fishman JA et al; AST ID Community of Practice. Donor derived infections in solid organ transplant recipients. Am J Transplant 2009; 9(Suppl 4):S19–26

Frequently utilized serologic tests for screening of donor and recipient

Tests Commonly Obtained in Both Donor and Recipient

- Human immunodeficiency virus (HIV) antibody
- Human T-cell lymphotropic virus (HTLV)-I/II antibody
- HSV (herpes simplex) IgG antibody (at some centers)
- Cytomegalovirus (CMV) IgG antibody
- Hepatitis C (HCV) antibody
- Hepatitis B (HBV) surface antigen (HBsAg)
- Hepatitis B core antibody (HBcAb IgM and IgG, or total core)
- Hepatitis B surface antibody (HBsAb) at some centers
- Rapid plasma reagin (RPR)
- Toxoplasma antibody (especially in heart recipients)
- Epstein-Barr virus (EBV) antibody (EBV VCA IgG, IgM)
- Varicella-zoster virus (VZV) antibody

Other Screening Measures for Infectious Diseases

- PPD or interferon gamma release assay (IGRA) for latent TB infection in recipients and living donors
- Strongyloides serology (for recipients from endemic areas)
- Coccidioides serology (for recipients from endemic areas)
- Trypanosoma cruzi serology (for donors and recipients from endemic areas)
- Serologies for tetanus, diphtheria, measles, mumps and pneumococcal titers as an aid to pretransplant immunization (at some centers)

Optional Screening Measures

- West Nile virus serology or NAAT
- HHV-8 serology (KSHV)
- Nucleic acid amplification testing (NAAT) for HIV, HCV, HBV, particularly in donors with high-risk social histories

Fischer SA et al and the AST Infectious Disease Community of Practice, *American Journal of Transplantation* 2009; 9 (Suppl 4): S7-S18

Prevalence of Pretransplant Infections among South East Asian Kidney Transplant Recipients



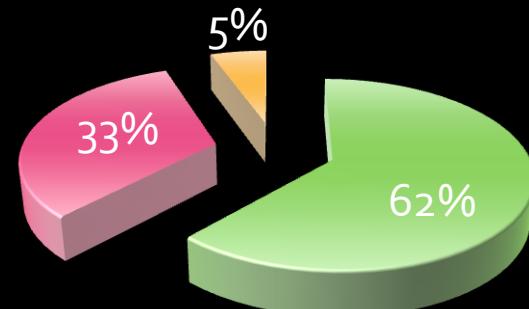
Siriorn P. Watcharananan¹, Kanjai Pipatpannawong², and Viroon Mavichak²

¹Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, ²Praram 9 Hospital, Bangkok, Thailand

- A total of 181 South East Asian KT recipients were studied prospectively for the evidence of pretransplant latent infections during January 2006 and December 2011
- Serological testing for viruses (HIV, HBV, HCV, CMV, VZV, HSV, EBV), strongyloides and syphilis, were performed

Racial Distribution of Study Cohort

■ Thais ■ Myanmars ■ Cambodians



Watcharananan SP et al, The Transplantation 2012

The Rate and Type of Latent Infections Pre-transplantation

Figure 1 Comparison in the Recipients' Hepatitis Profile

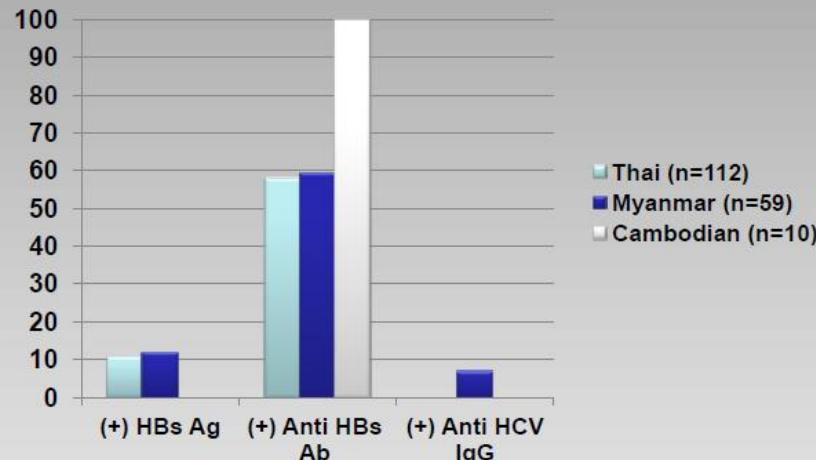
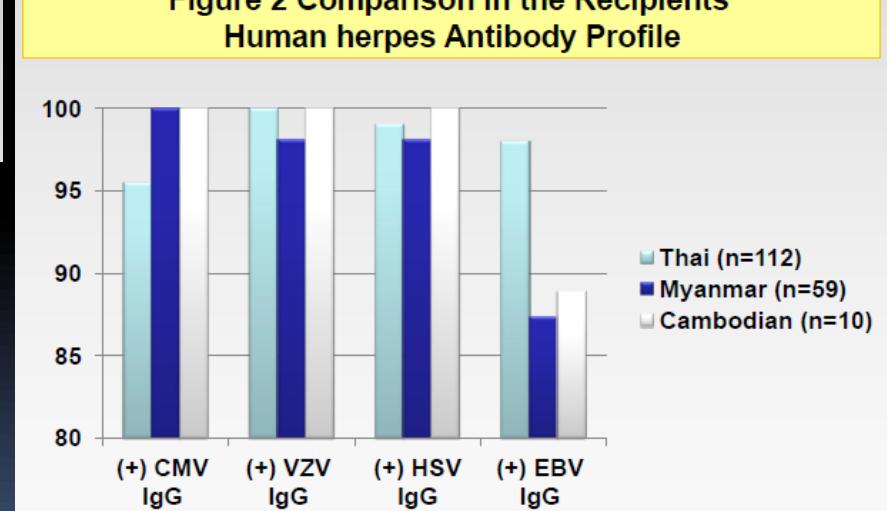


Figure 2 Comparison in the Recipients' Human herpes Antibody Profile



Definition of “DDI”

Infection that occurs by transmission of infectious pathogen through transplantation of human tissue/organs

Classification system for determining likelihood of the transmission event being donor-derived

Definition	Criteria	Definition	Criteria
Proven	All of the following conditions must be met: <ul style="list-style-type: none">• Suspected transmission event• Laboratory evidence of the suspected organism or malignancy in a recipient• Laboratory evidence of the same organism or malignancy in other recipients• Laboratory evidence of the same organism or malignancy in the donor• If there is pretransplant laboratory evidence, it must indicate that the same recipient was negative for this organism prior to transplantation	Possible	Suspected transmission event and Laboratory evidence of the suspected organism or malignancy in a single recipient or No evidence of transmission in the setting of active prophylaxis or treatment for the infection or Data that strongly suggests but does not prove a transmission event
Probable	Both of the following two conditions must be met: <ul style="list-style-type: none">• Suspected transmission event and• Laboratory evidence of the suspected organism or malignancy in a recipient <i>And at least one of the following criteria must also be met:</i> <ul style="list-style-type: none">• Laboratory evidence of the same organism or malignancy in other recipients;• Laboratory evidence of the same organism or malignancy in the donor; If there is pretransplant laboratory evidence, it must indicate that the same recipient was negative for this organism prior to transplantation	Excluded	Suspected transmission event and <i>at least one of the following conditions is met:</i> <ul style="list-style-type: none">• There is clear evidence for an alternative reason for the event• Lack of infection with the same organism in any other recipients, from the same donor, given appropriate testing• Laboratory evidence that the recipient had infection with this organism or malignancy prior to transplantation
		Confirmed	Any case that is classified as proven, probable or possible.

Ison MG et al, American Journal of Transplantation
2009; 9: 1929–1935

Comparison in the Incidence of Donor-Derived Infection

Organ Transplantation

- >70 000 organs, 100 000 corneas, and 2 million human tissue allografts are implanted worldwide each year
- Available data suggest that unexpected transmission events occur in <1% of solid organ recipients

Blood Transfusion

- Transmission of bacteria occurs in 1/10 000 to 1/500 000 units
- Transmission of hepatitis C virus (HCV) or human immunodeficiency virus (HIV) occur in <1/2–3 million units

An Update on Donor-Derived Disease Transmission in Organ Transplantation

M. G. Ison^{a,*} and M. A. Nalesnik^b

Table 3: Potential donor-derived infectious diseases transmissions reported to the OPTN, 2005–2009

Disease	# of donor reports ¹	# of recipients with confirmed transmission ²	# of DDD-attributable recipient deaths ³
Virus ⁴	86	31	8
Bacteria ⁵	38	26	7
Fungus ⁶	30	26	8
Mycobacteria ⁷	26	10	2
Parasitic ⁸	21	13	4
Total infections	201	106	29

¹Each report reflects a single donor but may involve multiple recipients.

²Number of recipients with a confirmed infectious disease transmission—transmission classified by DTAC as either proven, probable or possible.

³Number of recipients with a confirmed infectious diseases transmission that died directly as the result of the transmitted infection.

⁴Reported viruses: Adenovirus (2), Hepatitis B virus (13), Hepatitis C virus (25), herpes simplex, human immunodeficiency virus (HIV, 15), human T-lymphotrophic virus (HTLV, 3), influenza (3), LCMV, parainfluenza (PIV)-3, parvovirus B19 (3), rabies, West Nile virus (14). Confirmed viral transmissions: HCV, HIV, LCMV, parvovirus B19 and West Nile virus (there are previous reports of documented influenza and rabies transmissions not included in this report).

Note: Several viral transmission reports (esp HBV, HCV, HIV and HTLV) represent false positive testing (mostly NAT) that was subsequently documented to be nonreproducible and not associated with documented disease transmission. See text for further discussion.

⁵Reported bacteria: *Acinetobacter* (2), *Brucella Enterococcus* (including VRE), *Ehrlichia* spp (2), *E. coli*, Gram Positive Bacteria, *Klebsiella* (2), legionella, listeria, Lyme disease, nocardia, *Pseudomonas* (4), Rocky Mountain Spotted Fever, *Serratia* (2), *S. aureus* (MRSA 2), *Streptococcus* spp, Syphilis (5) *Veillonella*; bacterial meningitis and bacterial emboli.

⁶Reported fungi: *Aspergillus* spp (4), *Candida* spp (5), *Coccidioides immitis* (6), *Cryptococcus neoformans* (5), *Histoplasma capsulatum* (6), zygomycetes (5). Although not all cases were associated with confirmed transmission, each of the listed pathogen has been confirmed to have been transmitted through organ donation.

⁷Reported mycobacteria: Tuberculosis (22), Non-TB mycobacteria (4): All confirmed mycobacterial transmissions have involved *M. tuberculosis*; no mycobacteria other than tuberculosis (MOTT) have been associated with a confirmed transmission to date.

⁸Reported parasites: Babesia (2), *Balmuthia mandrillaris*, Chagas (*Trypanosoma cruzi*, 9), *Naegleria fowleri*, schistosomiasis (3), strongyloides (5). Confirmed parasitic transmissions: Babesia, *Balmuthia*, Chagas, schistosomiasis and strongyloides.

Clinical Presentation of DDI

“The manifestations vary with the type of graft and the nature of the host”

Localized disease

- Infected urinoma
- Perinephric hematoma/abscess
- Fungal ball
- Infected aneurysm
- Anastomotic rupture

Multi-organ involvement

- Fever
- Pancytopenia
- Hepatitis
- Colitis
- Multiple symptoms without clear explanation; ex joint pain

Infections 1 to 6 Months After Transplantation

1. Residual infections from the first month
2. Immunomodulating viruses [particularly CMV but also EBV, herpes simplex virus (HSV), human herpesvirus 6, HBV, HCV, and BK virus]
3. Opportunistic infections due to *Pneumocystis carinii*, *Aspergillus*, and *L. monocytogenes*

Case #3: 54 year-old man from Nakorn Prathom, ESRD S/P LRKT

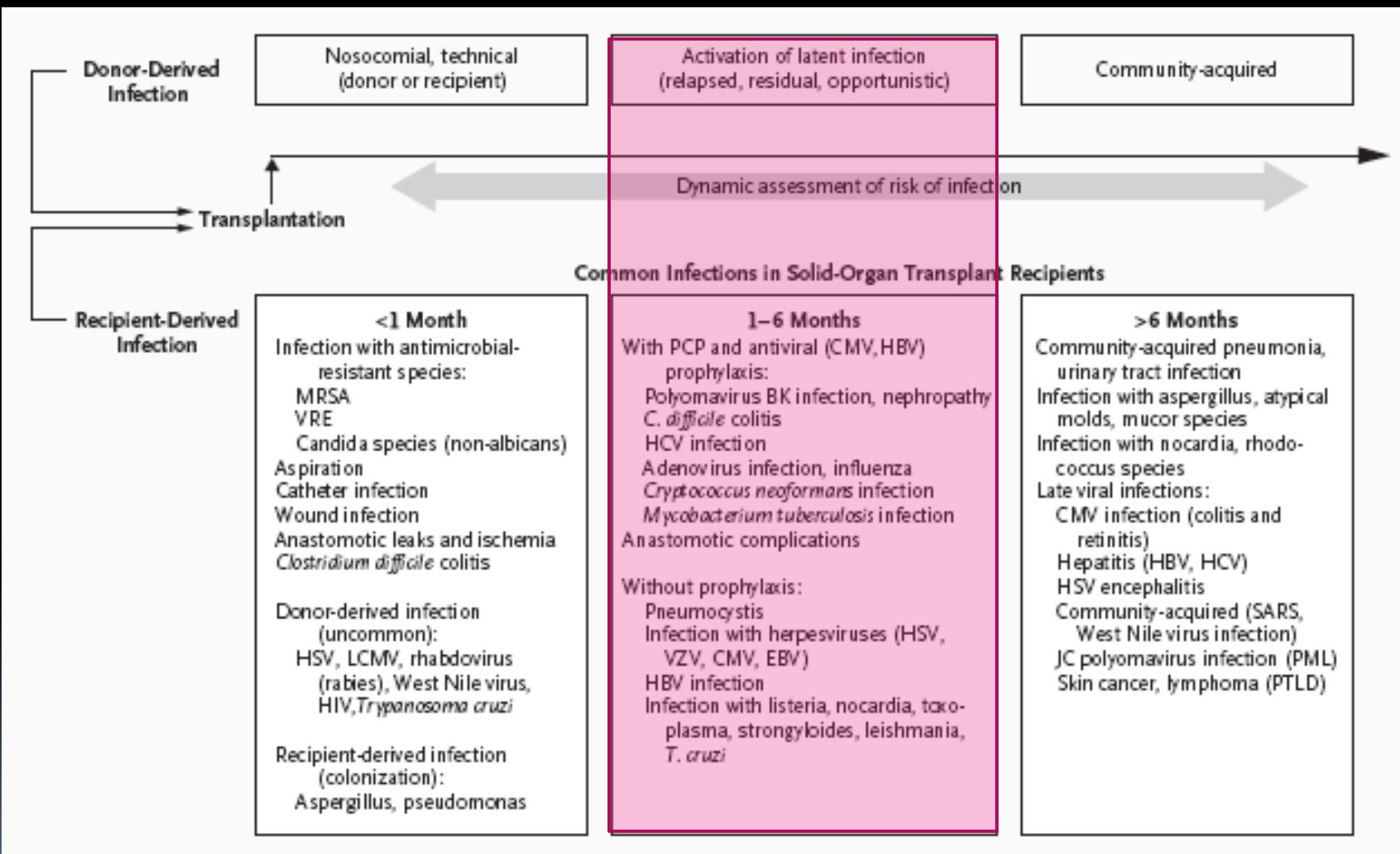
- Received anti-thymocyte globulin induction
- Uneventful operation and post-operative period
- Discharged home with tacrolimus/MMF/prednisolone
- Should an Infectious Disease consult be obtained as part of the care?

Case continued

- 1 month post KT, admitted with acute diarrhea and pancytopenia
- No fever, looked well otherwise
- 3 days after admission, noted the following findings on examination



Timing of Infections in SOT



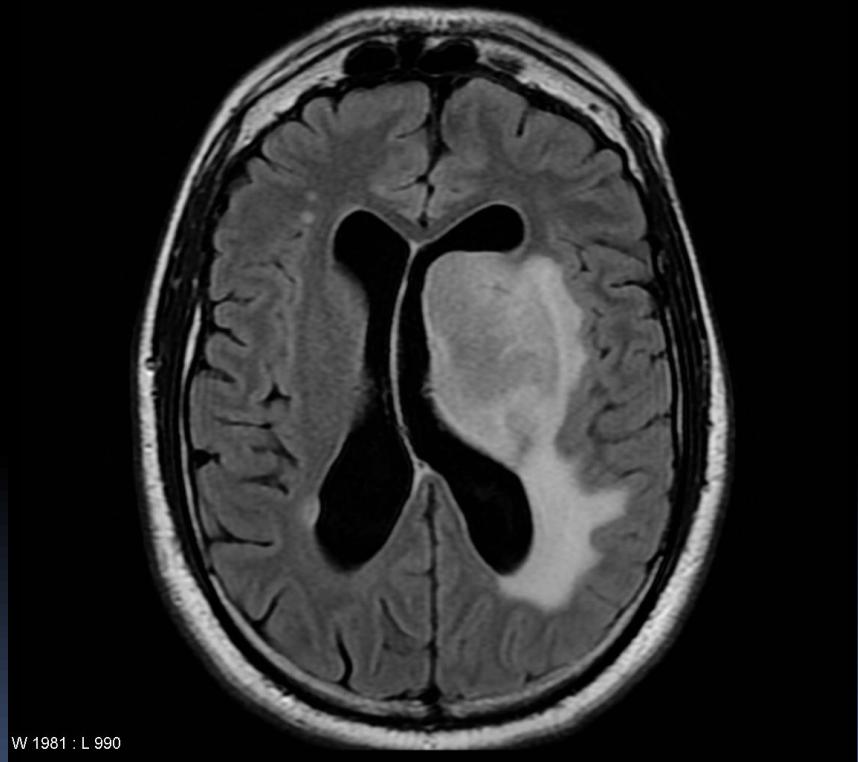
Case continued

- Final diagnosis: disseminated cryptococcosis (skin biopsy, serum/CSF cryptococcal Antigen)
- Retrospective review of the chart noted an unattended small LUL pulmonary nodule pre transplantation
- Few months into the treatment of the fungal disease, he complained of the progressive onset of headache

Case continued:

- Presumptively diagnosed with post transplant lymphoproliferative disorder
- Brain biopsy not possible due to severe brain edema, midline shift and impending brain herniation
- Responded to CNS radiation, dexamethasone and rituximab therapy
- Course of the treatment complicated by Invasive pulmonary aspergillosis
-

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W 1981 : L 990

Infections More Than 6 Months After Transplantation to 12 Months After Transplantation: 3 Categories of Patients

1. Community-acquired infections (respiratory viruses, pneumococcal pneumonia, and urinary tract infections) for those with good allograft function. Opportunistic infections occur only with particularly intense environmental exposures (eg, nocardiosis or aspergillosis)
2. Chronic and/or progressive viral infections with HBV, HCV, CMV, EBV, and papillomavirus.
 - direct effects (ie, the impact is generally greatest on the transplanted organ)
 - malignancies (eg, hepatocellular carcinoma after HBV or HCV, lymphoma due to EBV, squamous cell cancer due to papillomavirus, and Kaposi's sarcoma due to human herpesvirus 8/Kaposi's sarcoma-associated herpesvirus)
 - secondary effects of viral infection (graft rejection and a susceptibility to opportunistic infections)

Infections More Than 6 Months After Transplantation to 12 Months After Transplantation: 3 Categories of Patients

3. Recurrent or chronic rejection with less than satisfactory allograft function and generally with high-dose immunosuppression.
- Susceptible to opportunistic pathogens such as *P. carinii*, *L. monocytogenes*, *Nocardia asteroides*, *Cryptococcus neoformans*, and *Aspergillus* species.
- may benefit from lifelong prophylaxis

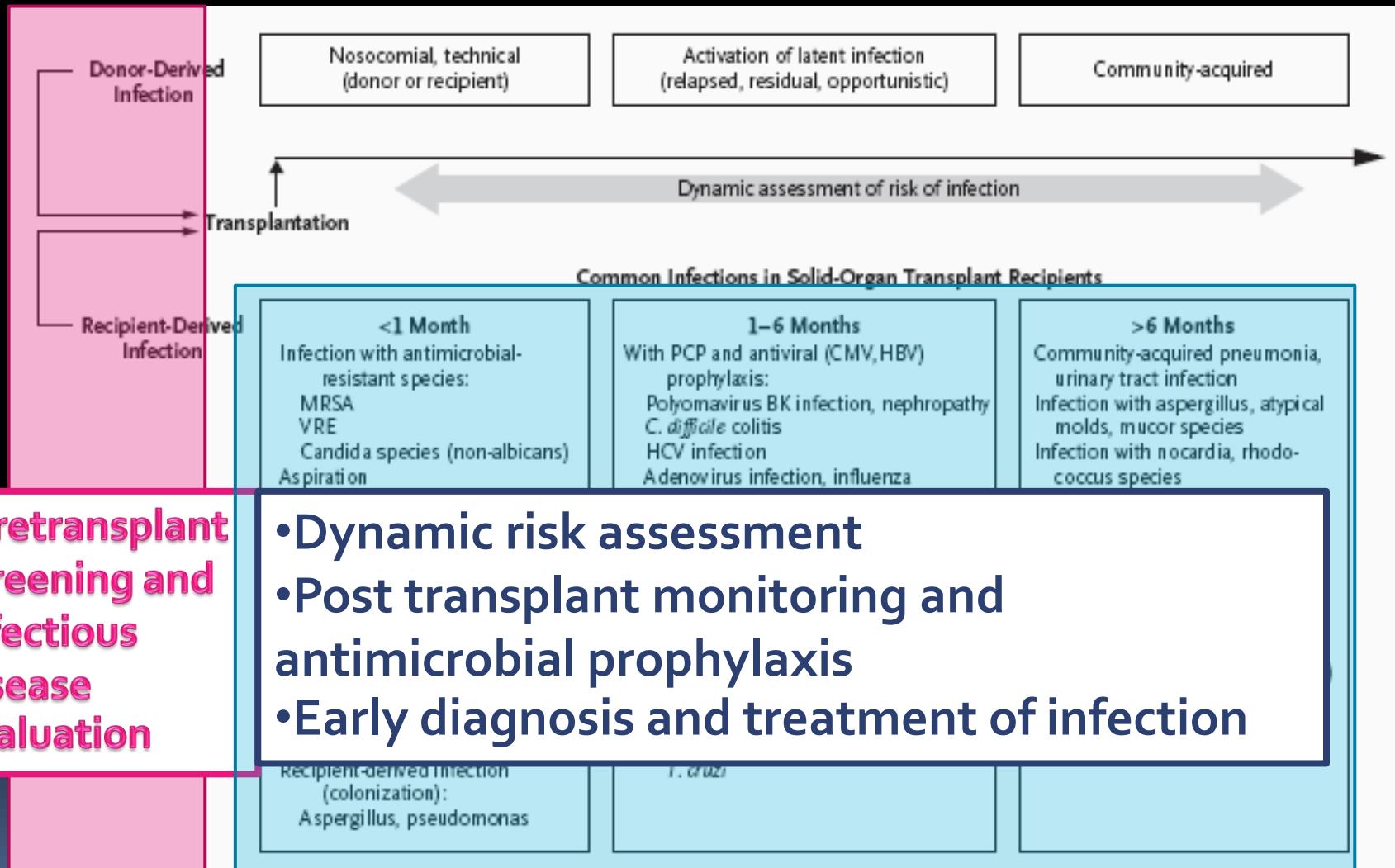
Burden of Infection in solid organ transplant population

- Still a significant cause of morbidity and death
- Infection leads to;
 - direct infectious disease consequences of microbial invasion
 - Indirect consequences of local and systemic cytokine, growth factor, and chemokine release in response to microbial invasion

Treatment of Transplant Related Infections

“The most important principles of patient treatment are prevention, early diagnosis, and specific therapy”

Timing of Infections in SOT



Key points

Infection within first month: treat the cause adequately

- Antimicrobial prophylaxis can only delay the occurrence of infections in these circumstances. Each technical or anatomical problem must be corrected in conjunction with antimicrobial therapy to prevent the selection of resistant microbes