Workshop On Infections in Transplant Recipients: Prevention, Control and Management

Difficult to Treat Infections in Paediatric HSCT Recipients: Local Experience

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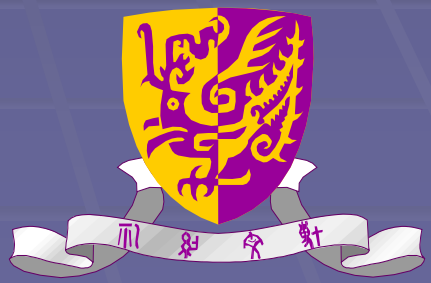
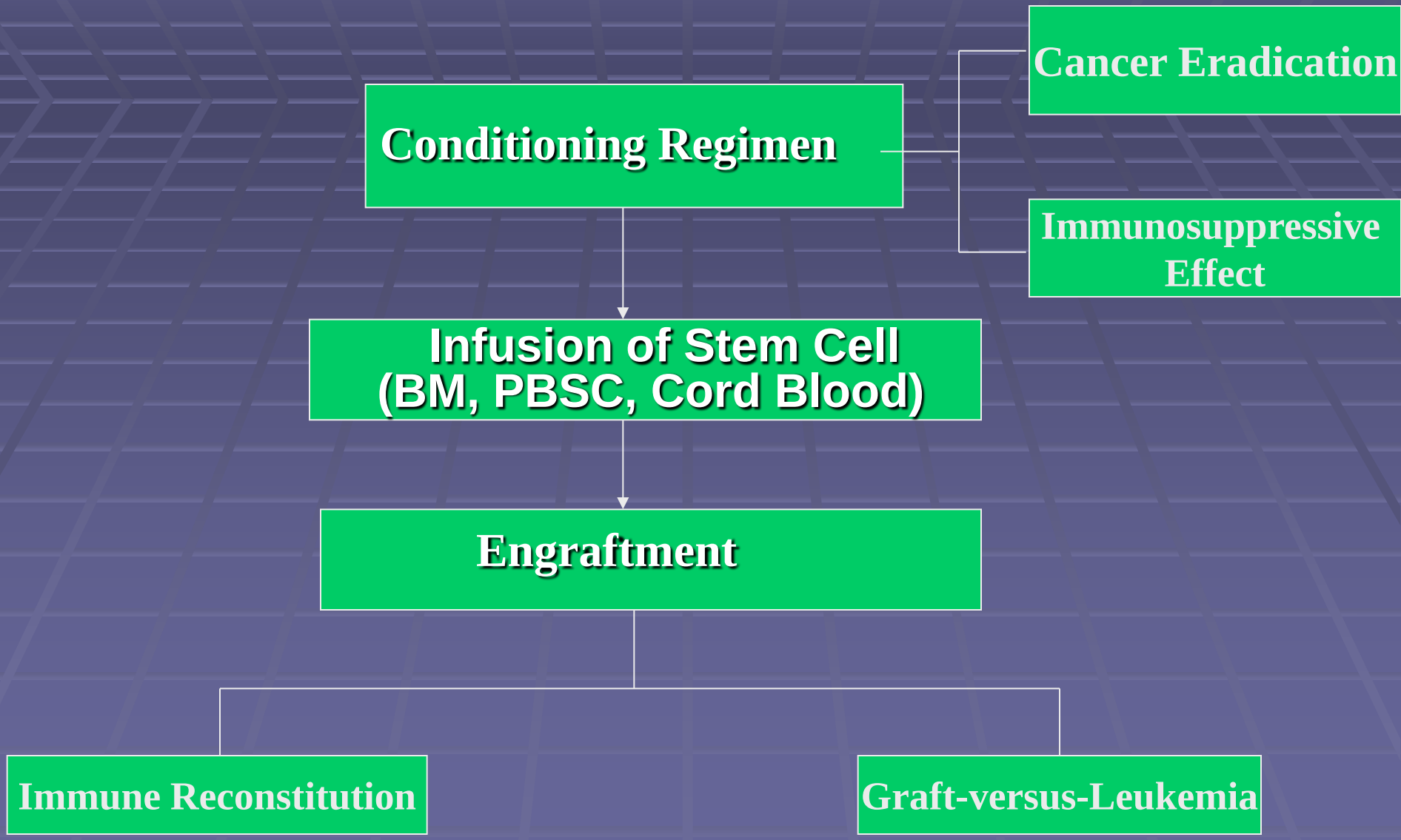
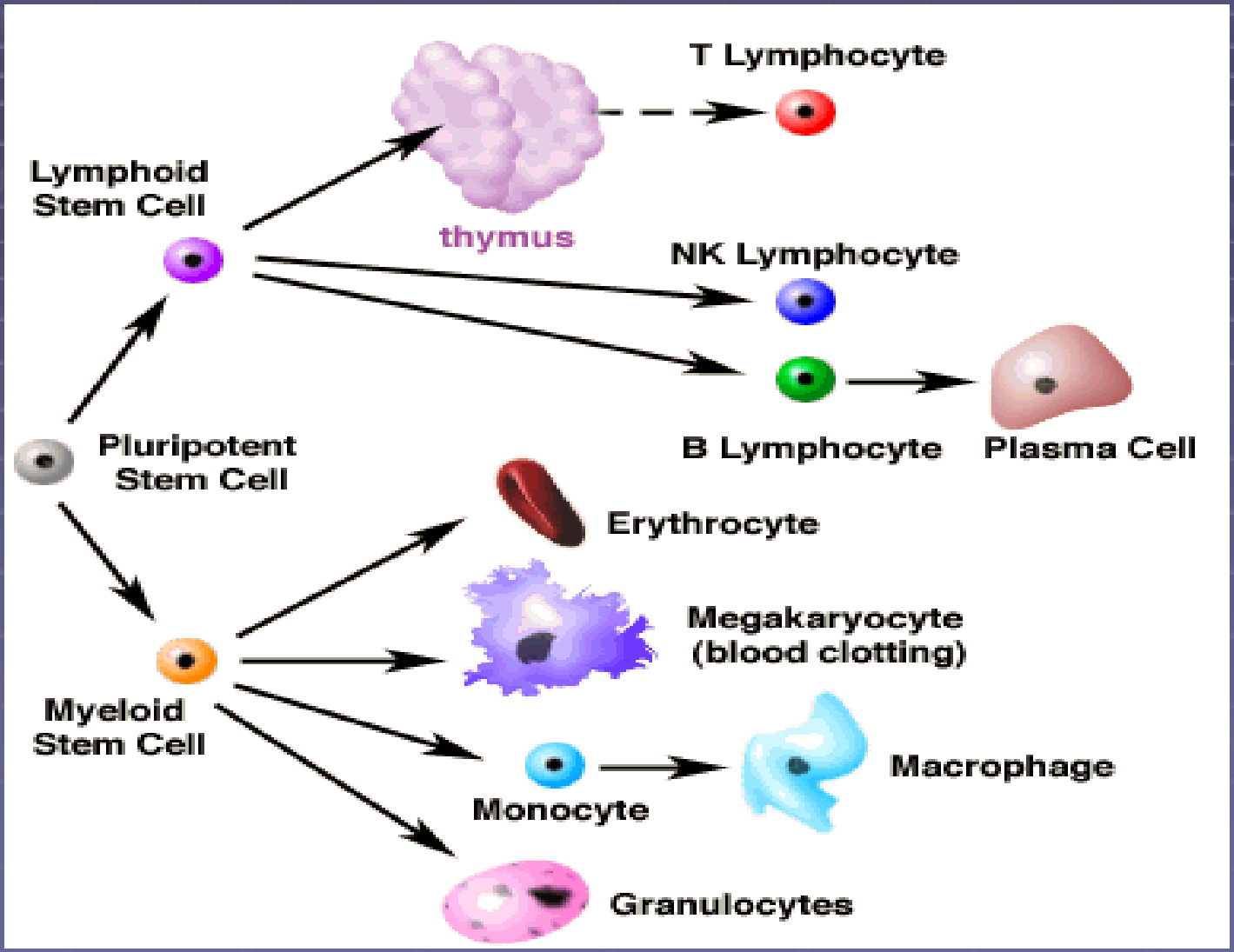


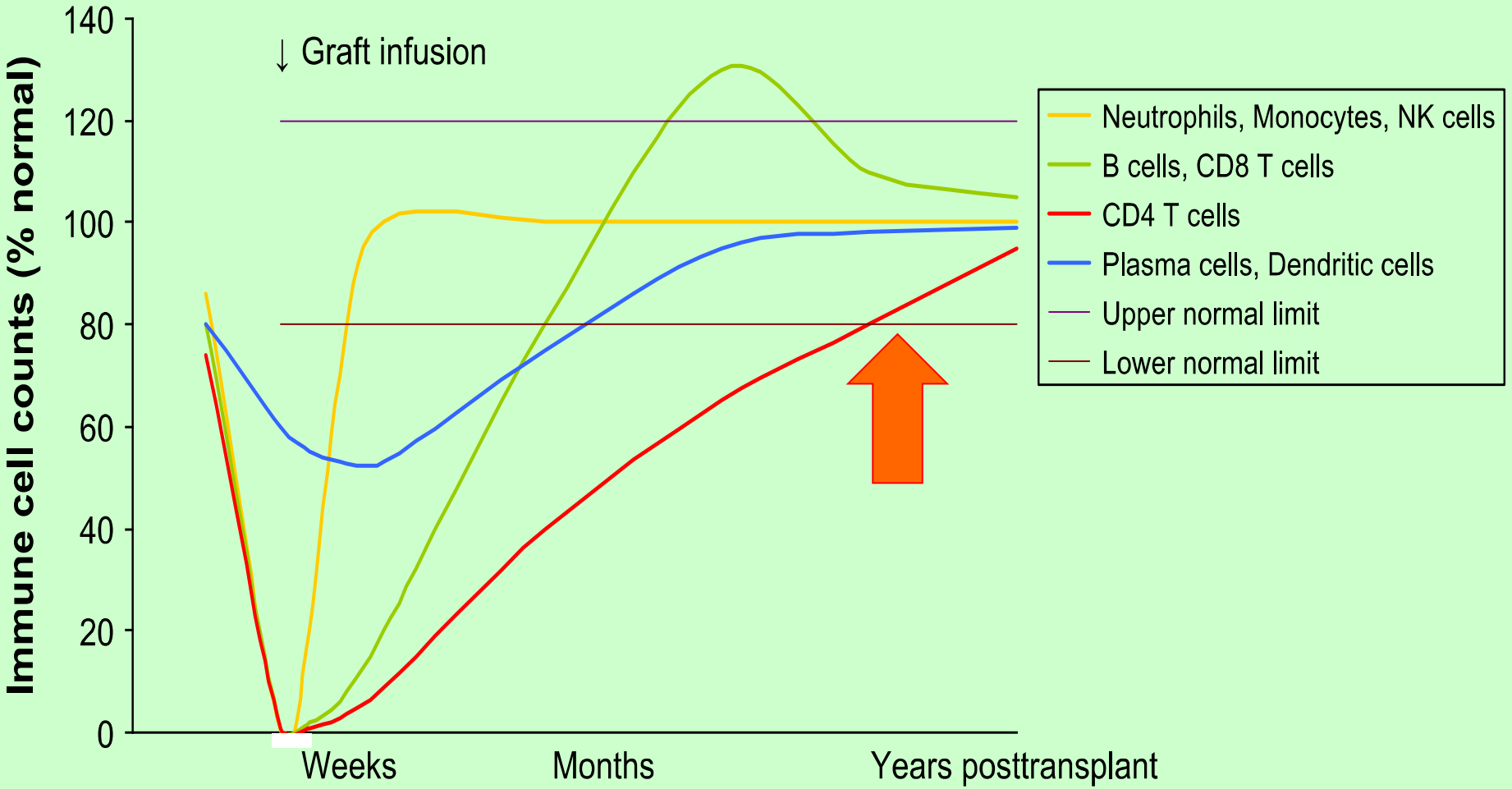
Outline of HSCT



Recovery of Immune System after HSCT



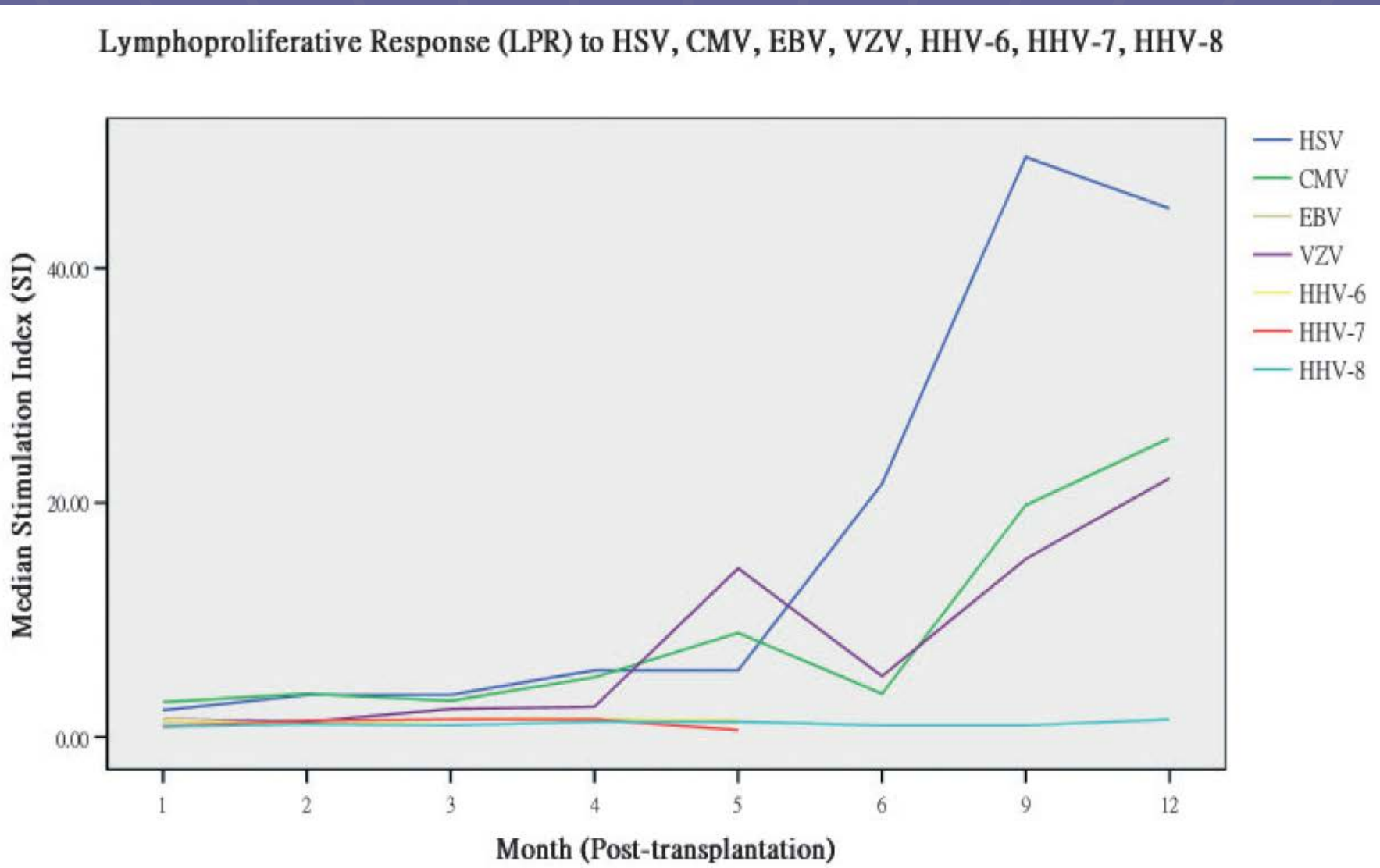
http://www.ismaaustralia.com/wp-content/uploads/2010/10/immune.bmp



Tomblyn et al. Biol Blood Marrow Transplant 2009 15:1143-1238

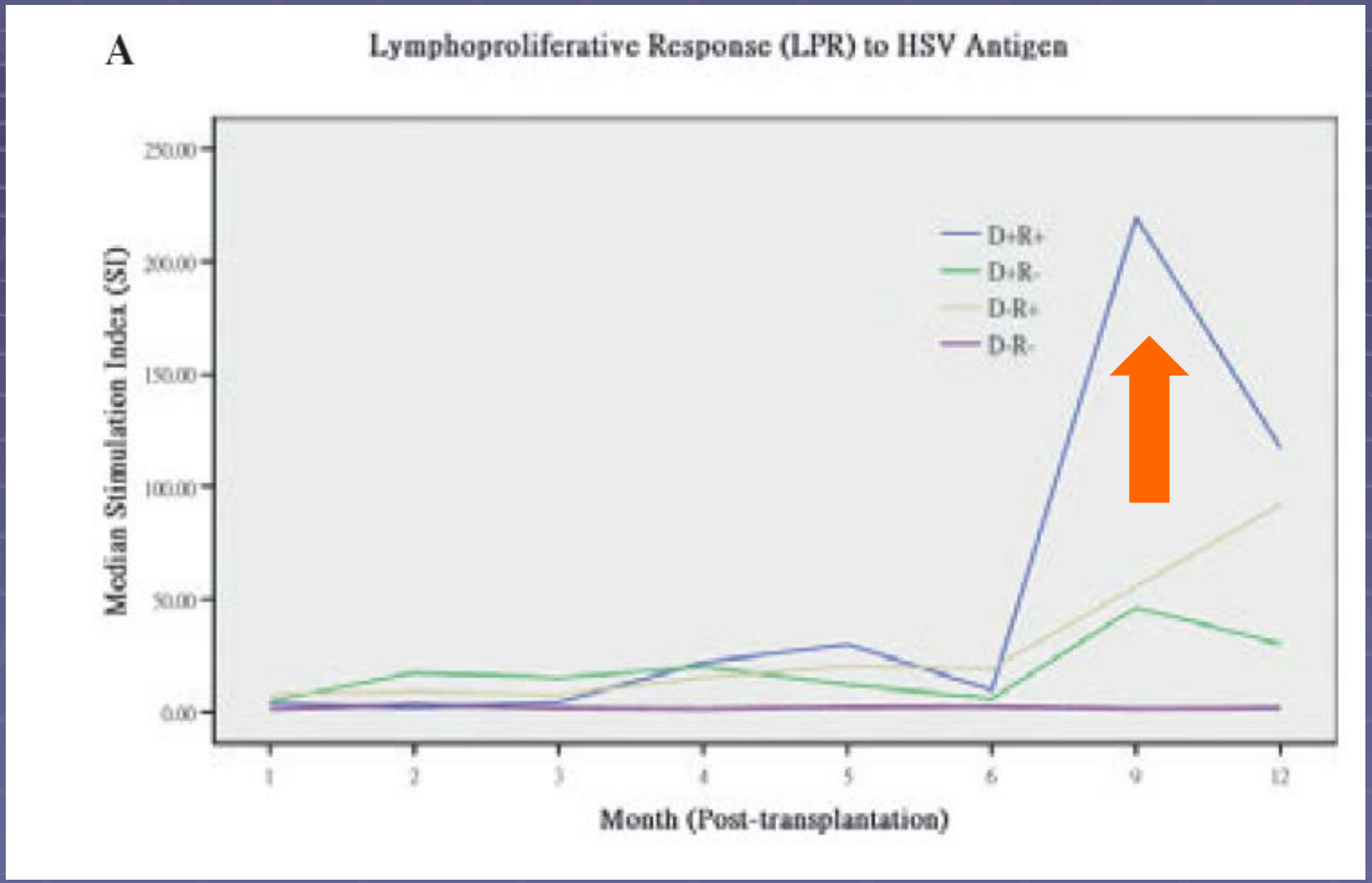
Lymphoproliferative Response to Herpes Viruses In Pediatric Allogeneic Stem Cell Transplant Recipients

Cheng et al. Pediatr Transplant 2010;14:761-769.

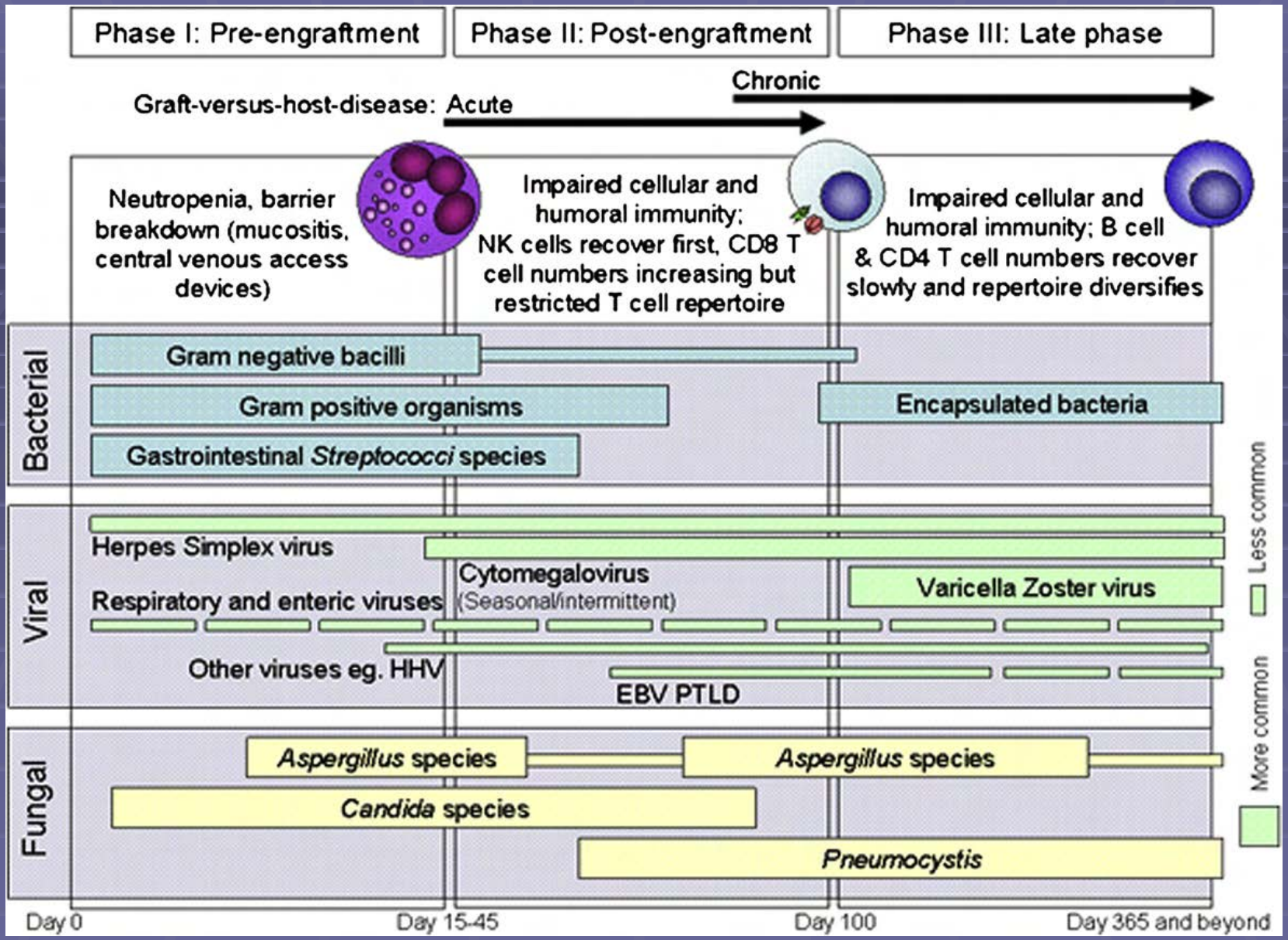


Lymphoproliferative responses to HSV, CMV, EBV, VZV, HHV-6, -7, and -8.

Cheng et al. Pediatr Transplant 2010;14:761-769.



Cheng et al. Pediatr Transplant 2010;14:761-769.



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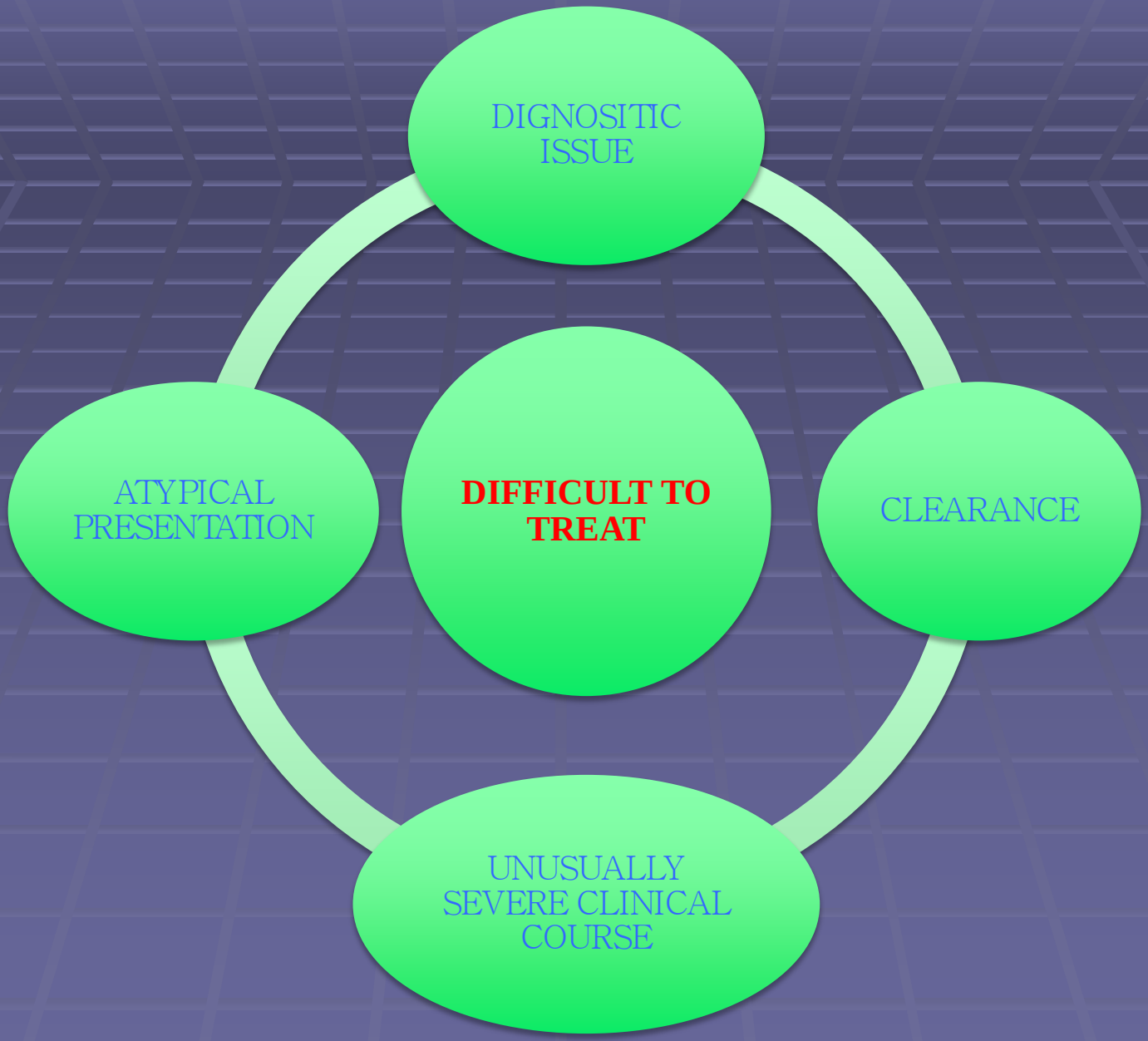
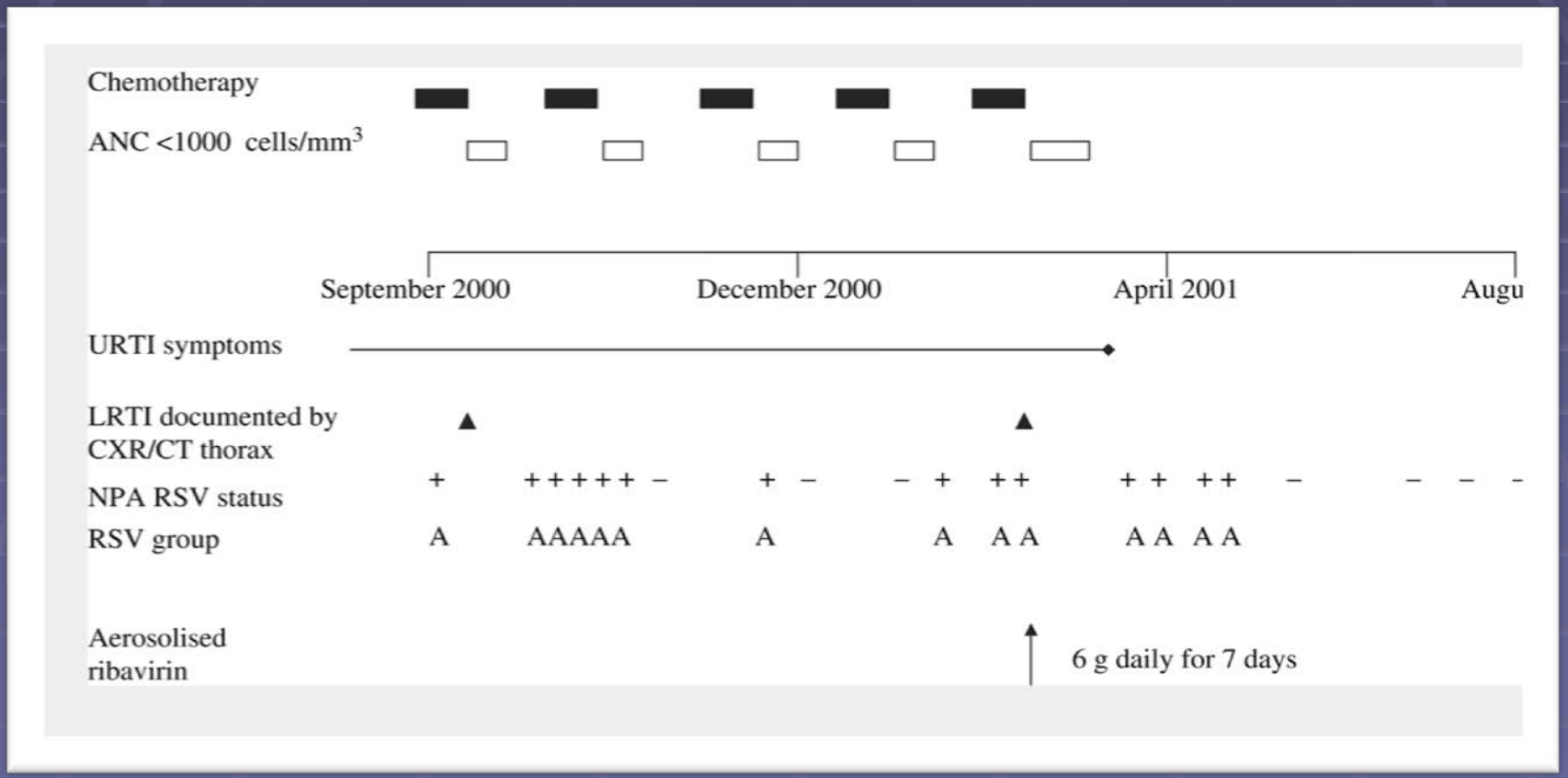

DIGNOSITIC ISSUE
ATYPICAL PRESENTATION
DIFFICULT TO TREAT
CLEARANCE
UNUSUALLY SEVERE CLINICAL COURSE

Diagnosis

- Serology
  - Due to impaired humoral immune response, they do not usually mount a specific antibody response to infection
  - Pitfall in interpretation
  - Loss of humoral immunity in paediatric oncology patients after chemotherapy
    - Hepatitis B (pretreatment : 70% vs 18 months post-treatment: 40%)
    - Cheng et al 2010.
- Direct detection of virus / antigens
  - By immunofluorescence or molecular-based methods
- Communications with microbiologists / virologists

Prolonged Shedding

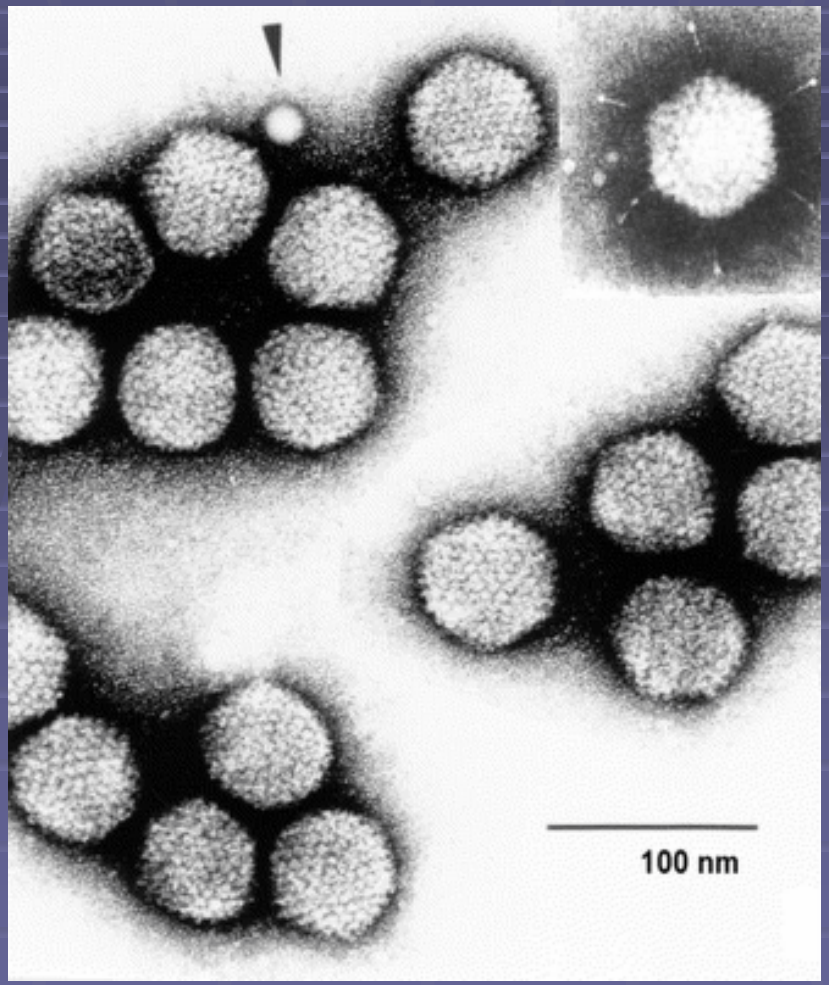
Prolonged RSV shedding during whole treatment period



Cheng FWT et al J Hosp Infect 2008

Prolonged Shedding

- Isolation based on symptoms
- Isolation based on surveillance results
  - Viral shedding has been reported to 4 months for influenza, 9 months for RSV or even up to 2 years for adenovirus
- Impact of isolation facilities and in clinic setting
  - 30% of bed should be attributed for isolation facilities
- ASBMT guideline did not have a clear recommendation on strategies of screening

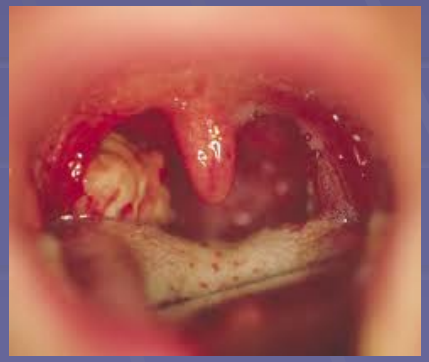

100 nm

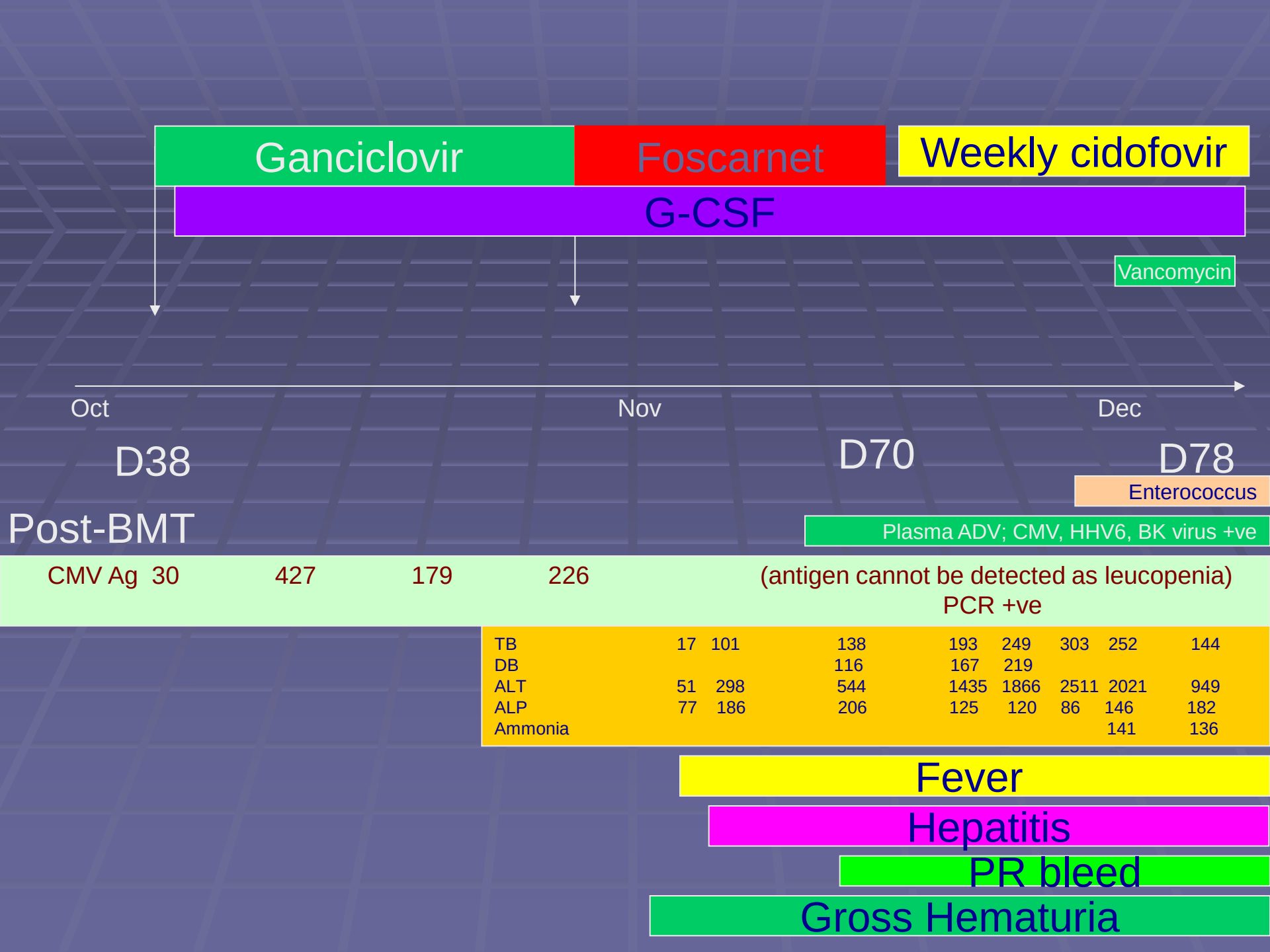
History

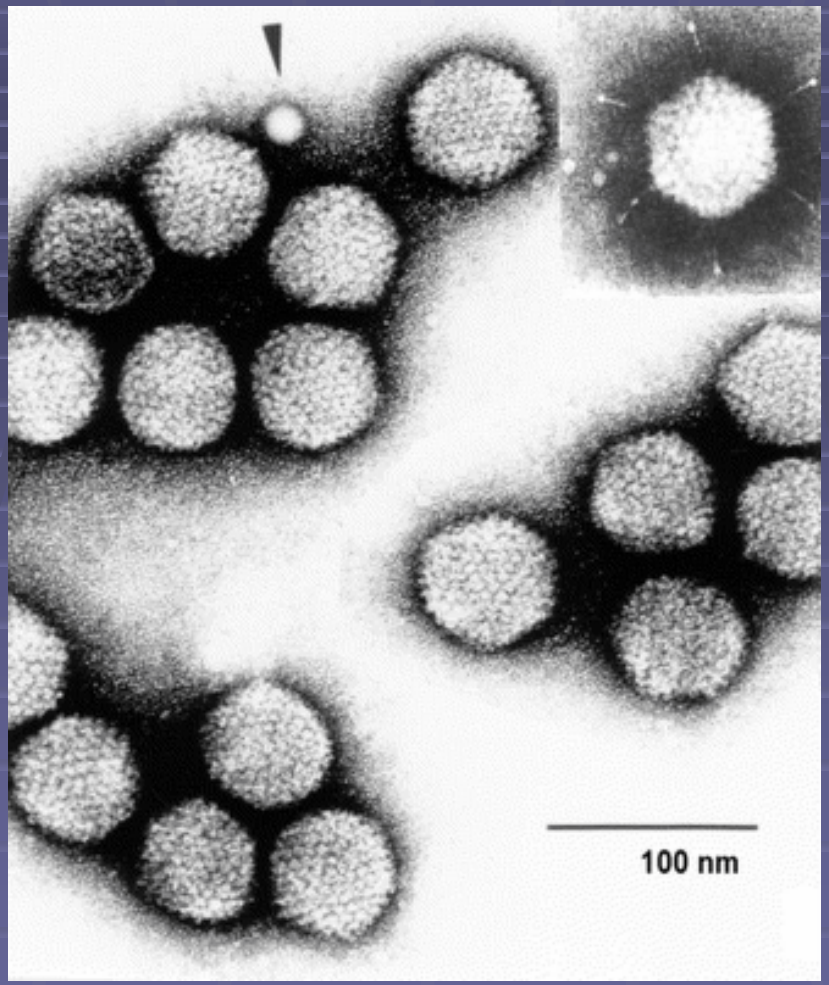
- F/10 years
- Acute myeloid leukaemia (AML) with myelodysplastic changes (MDS) diagnosed at 9 years old
- Matched unrelated bone marrow transplant was done at 7 months after diagnosis with Busulphan/Cyclophosphamide/Melphalan as conditioning
- Engrafted on day 16
- Complicated by transient CMV antigenaemia and skin graft-versus-host disease (GVHD) and settled subsequently

Relapse

- 5-month after transplant, she developed fever and ulcers at tonsillar region.
- Punch biopsy showed myeloid leukaemic infiltrate and bone marrow study confirmed relapse of AML; chimerism: 96.5% recipient cells
- 2 courses of reinduction chemotherapy (FLAG) were given,
- Followed by haploidentical CD3/CD19 depleted PBSC transplantation on 21-9-2011 (11 month after 1st transplant) from father




Ganciclovir
Foscarnet
Weekly cidofovir
G-CSF
Vancomycin
Oct
Nov
Dec
D38
D70
D78
Enterococcus
Post-BMT
Plasma ADV; CMV, HHV6, BK virus +ve
CMV Ag 30 427 179 226
(antigen cannot be detected as leucopenia)
PCR +ve
TB 17 101 138 193 249 303 252 144
DB 116 167 219
ALT 51 298 544 1435 1866 2511 2021 949
ALP 77 186 206 125 120 86 146 182
Ammonia 141 136
Fever
Hepatitis
PR bleed
Gross Hematuria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Adenovirus Infection

- A non-enveloped double-strand DNA virus
  - Sized from 65-80 nm
- 52 recognized serotypes divided into 7 subgroups (A to G)
  - Respiratory tract infections
  - Keratoconjunctivitis
  - Gastroenteritis
- Disease occurred mainly in children, 5-10% febrile illnesses in children
- As non-enveloped virus, adenovirus is highly resistant to physical and chemical agents.
- Remain infectious at room temperature for prolonged period (up to 3 weeks)
- This is stable at acidic pH and is resistant to gastric and biliary secretion that allow the virus to replicate to high viral load in GI tract
- Sodium hypochlorite (500 ppm) for 10 minutes or 70% alcohol for at least 1 minute can inactivate them

Adenovirus in Paediatric HSCT Patients

- Retrospective review of 26 children from 1998 – 2002 (before the introduction of regular weekly surveillance)
- 42% of children (n=11) had evidence of adenovirus infection by PCR
- Recipient of T-cell depleted transplant was associated with significant higher incidence of adenovirus infection
- 2 children died of adenovirus infection within 2 weeks after transplantation and both had very low lymphocyte count. Both had T-cell depleted graft.
- 8 children with evidence of adenovirus found retrospectively did not receive antiviral therapy
- Risk factors: T-cell depletion; lymphopenia; early post-transplant period

Walls T, et al. Clin Infect Dis.2005;40:1244-1249.

	ML	LCY	LA
Primary Disease	AML/MDS	Infant ALL (high risk)	AML CR2
Age at diagnosis (Years)	10	0.45	17
Age at Transplant (Years)	1st transplant: 10 2nd transplant: 11	0.83 (10 months)	1st transplant: 16 2nd transplant: 17
Type of Transplant	1st transplant: MUD 2nd transplant: Haplo-ID (father)	1st transplant: DUCBT=> non-engraftment 2nd: Haplo-ID (father)	1st transplant: MUD PBSC 2nd tranasplant: Haplo-ID (father)
T-cell Depletion	1st transplant: ATG 2nd transplant: ex-vivo + in-vivo	1st transplant: ATG 2nd transplant: ex-vivo + in-vivo	1st transplant: unknown 2nd transplant: ex-vivo + in-vivo
Presentation	Fever, liver derangement, GI bleed	Fever, liver derangement	Diarrhea
Diagnosis of ADV	PCR in Blood/Stool	PCR in Blood/ Isolation in Stool	PCR in Blood Isolation in Stool
Reactivation of other viruses	CMV, BK virus	CMV, HHV-6	CMV
WBC and LYM count at Diagnosis of ADV	WBC <0.1 LYM 100%	WBC 0.1 LYM: 0	WBC 1.4 LYM 0.1
Time from Transplant (Months)	2.5 months	1 month from 1st transplant	2 months from 2nd transplant
Treatment	Cidofovir	Treated with GCV and FOS (for CMV, HHV-6)	Treated with GCV and FOS
Other Treatment-related complications	Hemorrhagic cystitis	1st transplant: non-engraftment 2nd transplant: VOD	Pneumonia with cavitating lesion in lungs (? fungal>)
Outcome	Died of Disseminated ADV Infection	Died of Liver failure (VOD +/- ADV)	Died of multiple organ failure (lung, kidney, liver, BM)

Treatment of ADV in Transplant Setting

- Antiviral Agent
  - Cidofovir
- Approach of using Antiviral Agents
  - Treatment of ADV diseases
  - Pre-emptive approach
- Cellular Therapy
  - Specific cytotoxic T-cell therapy
  - Un-manipulated donor leukocyte infusion

Cidofovir in ADV Infection

- Clearance of ADV in about 56-71% in different case series
  - Vandercam B, et al. Clin Infect Dis 1999;29:948-949.
  - Bordigoni P et al. Clin Infect Dis 2001;32:1290-1297.

- 15% developed severe nephrotoxicity
  - Vandercam B, et al. Clin Infect Dis 1999;29:948-949.
  - Bordigoni P et al. Clin Infect Dis 2001;32:1290-1297.

Management of ADV in Post-Transplant Setting

- Routine monitoring with pre-emptive treatment with CDV
  - Is it useful in preventing this fatal complication?

Monitoring of ADV and Pre-emptive Treatment

- Mortality of ADV infection is closely associated with increasing and high levels of ADV DNA (>10,000 copies / ml) in peripheral blood with a median time of 3 weeks between first detection of ADV DNA in blood and onset of symptoms.
  - Echavarria M, et al. Lancet 2001;358:384-385
  - Schilham MW, et al. Clin Infect Dis 2002;35:526-532.

- 81% of asymptomatic patients resolved the infection when cidofovir was given as pre-emptive therapy
  - Ljungman P, et al. Bone Marrow Transplant 2003;1:481-486.

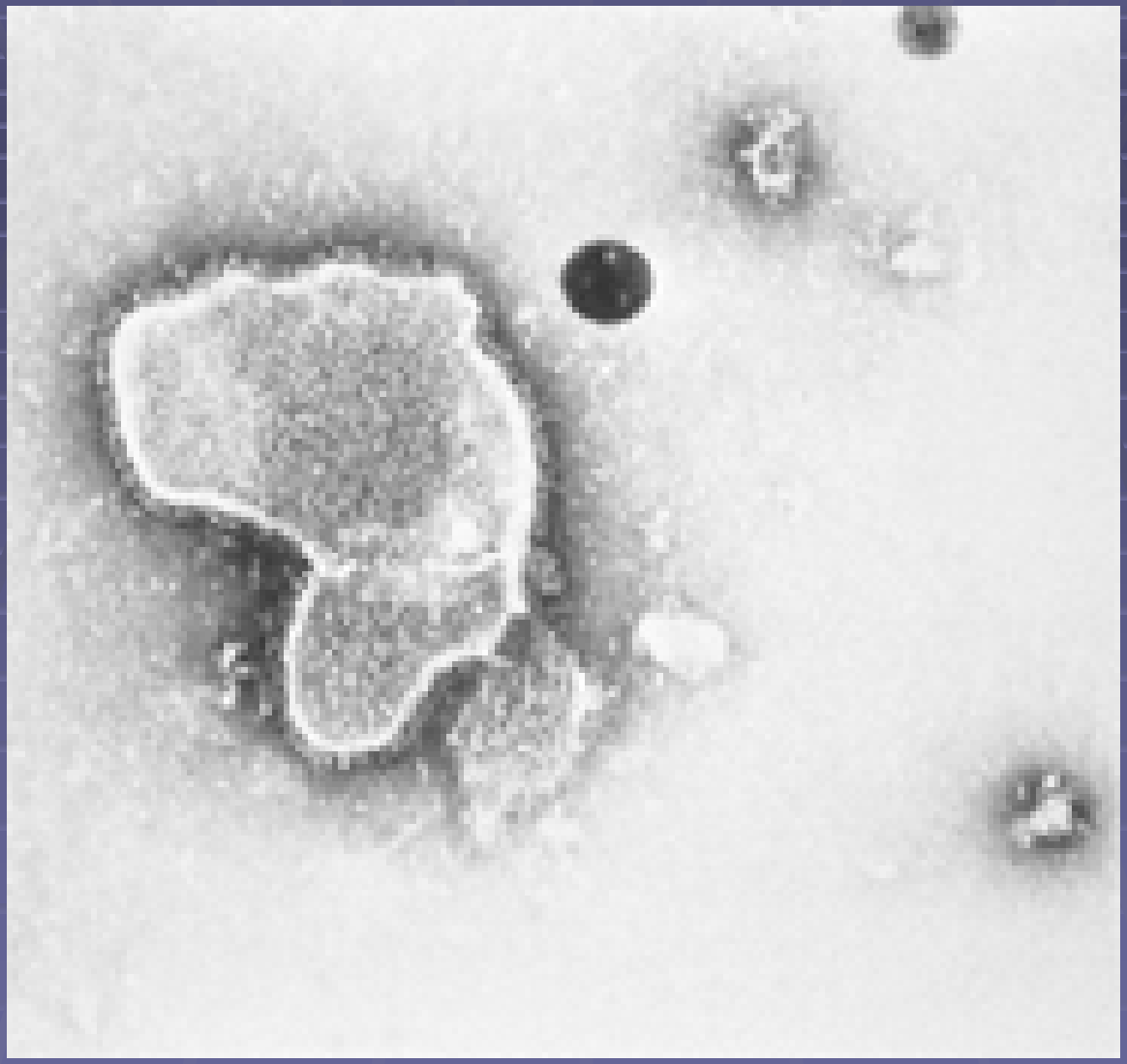
Pre-Emptive Use of Cidofovir

- Weekly surveillance in blood and stell with pre-emptive CDV at a first detection of ADV in post-transplant period has been attributed to marked reduction in ADV related complication and survival.
  - Yusuf U, et al. Transplantation 2006;81:1398-1404.

Recommendations of CIBMTR

- For patients at highest risk, weekly monitoring for active adenovirus infection by quantitative PCR for either the first 6 months after HSCT or the duration of severe immunosuppression/lymphopenia could be considered
  - Lion T,et al. Blood. 2003;102:1114-1120.
  - Tomblyn M et al. Biol Blood Marrow Transplant 2009;15:1143-1238.

- The available data suggest that cidofovir could be used as preemptive antiviral therapy of adenoviral disease in selected high-risk HCT patients. A reduction of DNA load has been shown, but the evidence of its efficacy in preventing mortality in HCT patients is inconsistent
  - Tomblyn M et al. Biol Blood Marrow Transplant 2009;15:1143-1238.
  - Neofytos D, et al. Biol Blood Marrow Transplant 2007;13:74-81.



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Respiratory Syncytial Virus (RSV)

- Virus: Single-stranded RNA virus
- Main concern in oncology patients: progression from URT to LRT

Virus	Incidence of infection (%)	Progression from URI to pneumonia (%)	Time from URI to pneumonia (median, d)	Proportion of pneumonia without URI (%)	Pulmonary copathogens in cases with pneumonia (%)	Overall mortality at 1 month after diagnosis of pneumonia (%)
RSV	1·8–6*	40	7	20–50	2·5–33	45
Parainfluenza virus 3	4–7	18–44	7	31	53	35–37
Influenzaviruses A and B	1·3–2·6†	18	11	18	50	25–28

M Boechk. Br J Hematology.2008;143:455-467.

Respiratory Syncytial Virus (RSV)

- Median time to progression: 7 days
- Risk factors
  - Younger age group (< 2 years)
  - Lymphopenia
    - Nichols WG, et al. Biol Blood Marrow Transplantation.2001;7(suppl):11S-15S.
  - ? Role of asymptomatic shedding
    - Peck AJ, et al. Blood.2007;110:1681-1688.
  - Role of prolonged symptomatic shedding
    - Cheng, et al. J Hosp Infect.2008;70:383-385.
- Overall mortality 8.6%

RSV Pneumonia in Paediatric Oncology Patients

- Factors to affect outcome of RSV pneumonia
  - Degree of immunosuppression
    - Uniformly fatal in highly immunosuppressed HSCT patients
      - Harrington, et al. 1992.
    - Presence of co-pathogens
    - ? Timing of starting therapy
      - Whimbey, et al 1995.
- Treatment modalities for RSV pneumonia
  - Aerosolized ribavirin 6 grams/day (Q8H or continuous)
    - Technically difficult
    - 20 mg/ml for 18 hours via aerosol generators via face mask inside a tent to prevent environmental contamination
  - In severe cases, IV ribavirin can be an option
  -

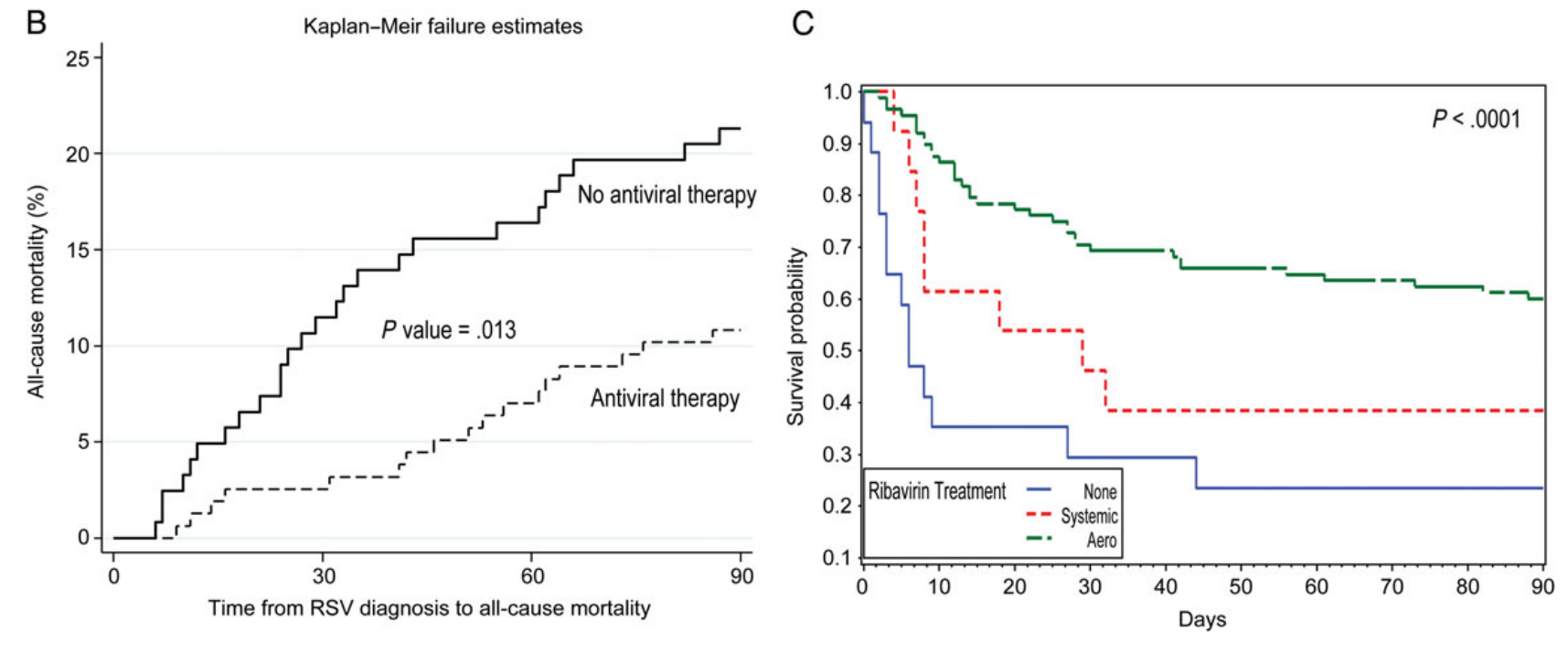
Recent Studies on RSV in HSCT Patients

- Impact of Aerosolized Ribavirin on Mortality of 280 Allogeneic HSCT Recipients with RSV Infections
  - Shah DP, et al. Journal of Antimicrobial Chemotherapy 2013

RSV in HSCT

- Retrospective review (1996-2009)
- Adult patients (n=280), laboratory-confirmed RSV infection
- 80 (29%) developed LRTI within 19 days (median 1 day, range 0-19 days)
- 44 (16%) died within 90 days (median 26 days, range 1-82 days) from RSV diagnosis
- Aerosolized ribavirin-based treatment at URTI stage was the single significant factor in reducing risk of RSV-related mortality, all-cause mortality and RSV LRTI

RSV in HSCT



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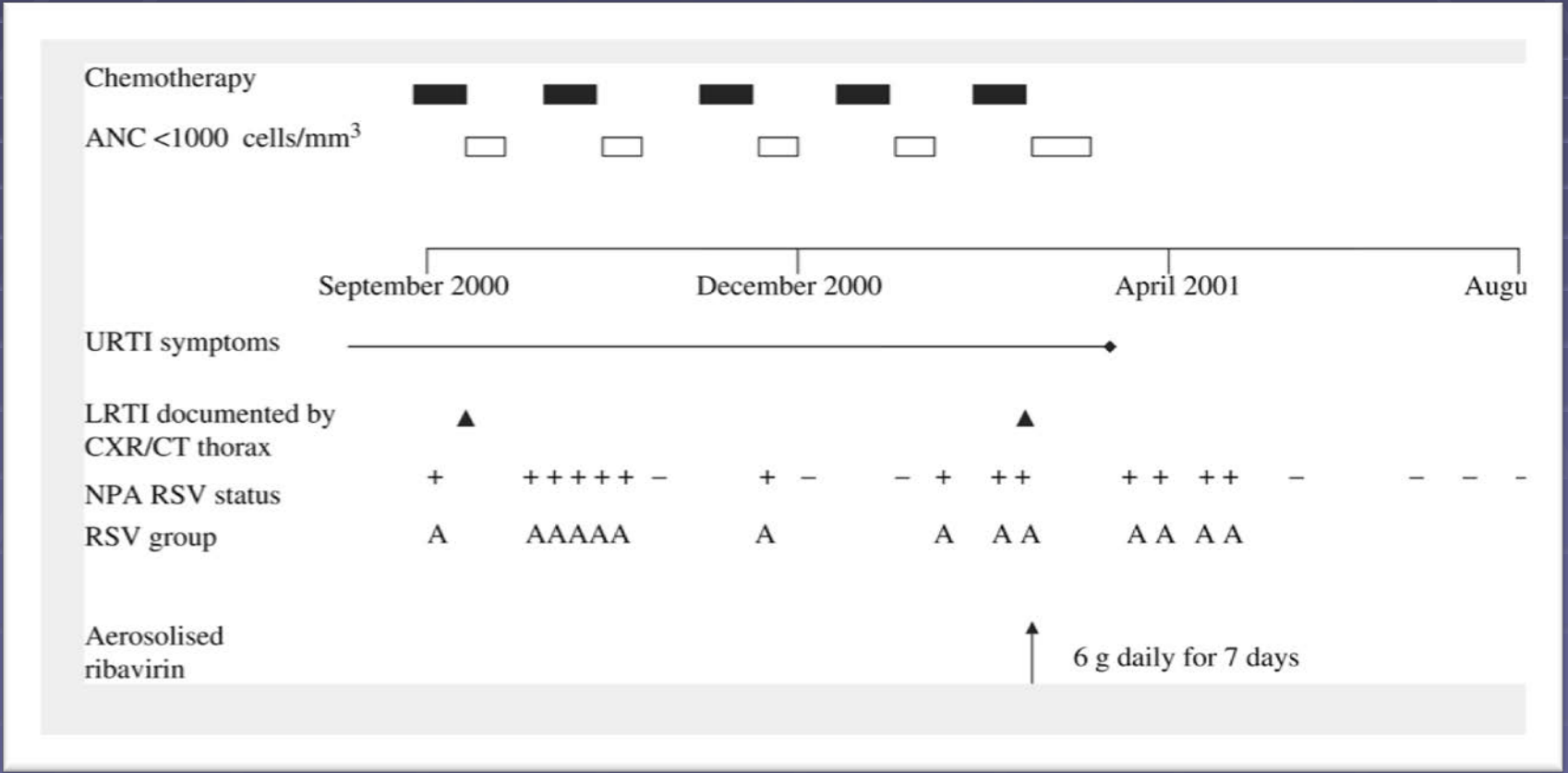
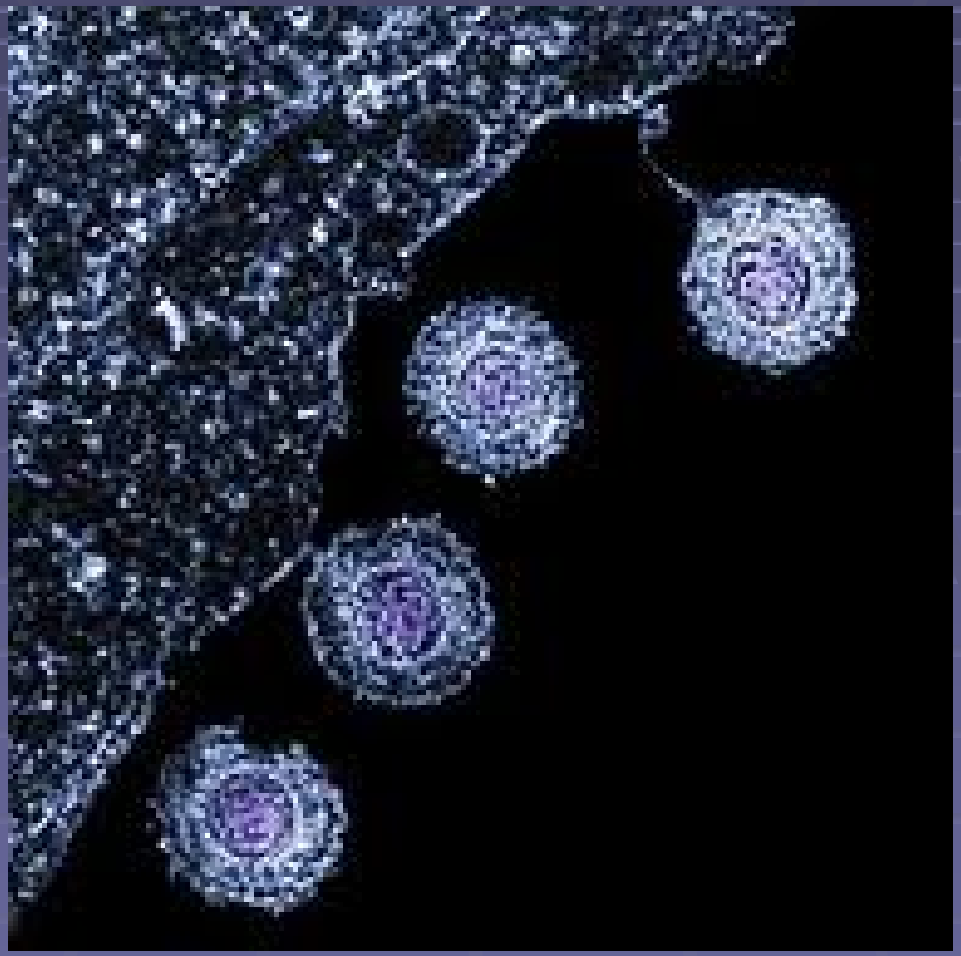
Chemaly RF et al. Clin Infect Dis 2014;59(S5):S344-351.

Prolonged RSV Shedding

Prolonged RSV shedding during whole treatment period



Cheng FWT et al J Hosp Infect 2008



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Our Patient

- 5 years old girl
- Juvenile myelomonocytic leukaemia (JMML) diagnosed in Dec 2013 at age of 4
- Transformed to acute myeloid leukaemia (AML) in April 2014
- Received single unit cord blood transplantation

Our Patient

- 5/6 HLA matched, Single unit unrelated cord blood transplantation
- Conditioning: cyclophosphamide, bulsulfex, melphalan, ATG
- GVHD prophylaxis: Cyclosporin A from day -1
- Infection prophylaxis:
  - Fluconazole
  - Ganciclovir from day -7 to day -1
  - Acyclovir from day 0 to day 21
  - Septrin prophylaxis after stable engraftment
  - CMV pp65 / EBV monitoring weekly

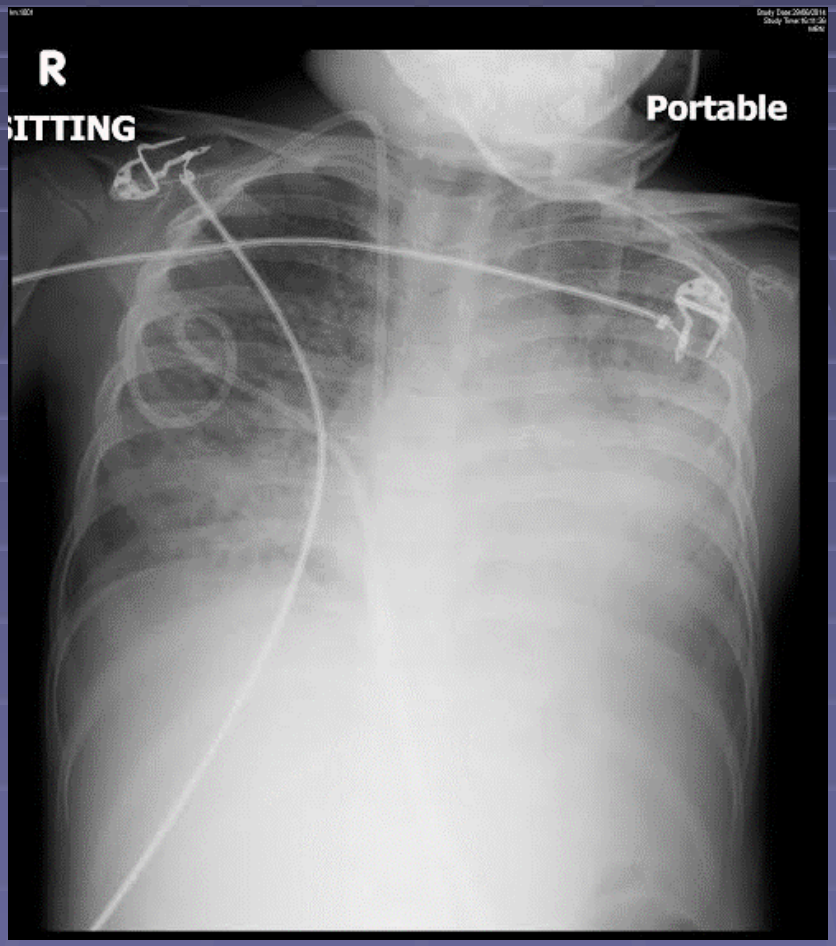
Post-Transplant Day 19

- Convulsion
  - Developed generalized tonic clonic convulsion
  - Aborted by midazolam
  - Electrolytes/Glucose normal; Calcium Low → Corrected
  - CT brain: no SOL/acute haemorrhage
  - CSF: WBC 1, RBC 184, gram stain −ve; protein, CSF/plasma glucose normal

Multi-organ deterioration

- Pneumonia / Pneumonitis / Heart failure
  - Progressive tachypnea RR 60/min
  - Increase O2 requirement to 100% oxygen via non-breathing mask
  - Chest examination showed basal crepitations
  - CVS: apex displaced to 1cm lateral to left MCL; Liver 6cm
  - CXR: bilateral haziness
  - LFT: raised ALT and bilirubin (hepatitis picture)
- Transferred to PICU for possible ventilatory support

CXR: Diffuse lung infiltrates, cardiomegaly



29/6/2014

Progress in PICU

- Respiratory – Pneumonia/pneumonitis
  - Put on BIPAP, oxygen requirement up to FiO2 0.6

- Cardiac – Myocarditis/Heart failure
  - BP gradually drops despite hydralazine taken off
  - ECG: Sinus rhythm, Tachycardia 155/min, generalized low voltage, no acute ST changes. TWI over V3-V6.
  - Echocardiogram: impaired left ventricular function (LVEF 43.2%, LEFS 21.3%)
  - Troponin T: 83.3; Creatinine kinase normal

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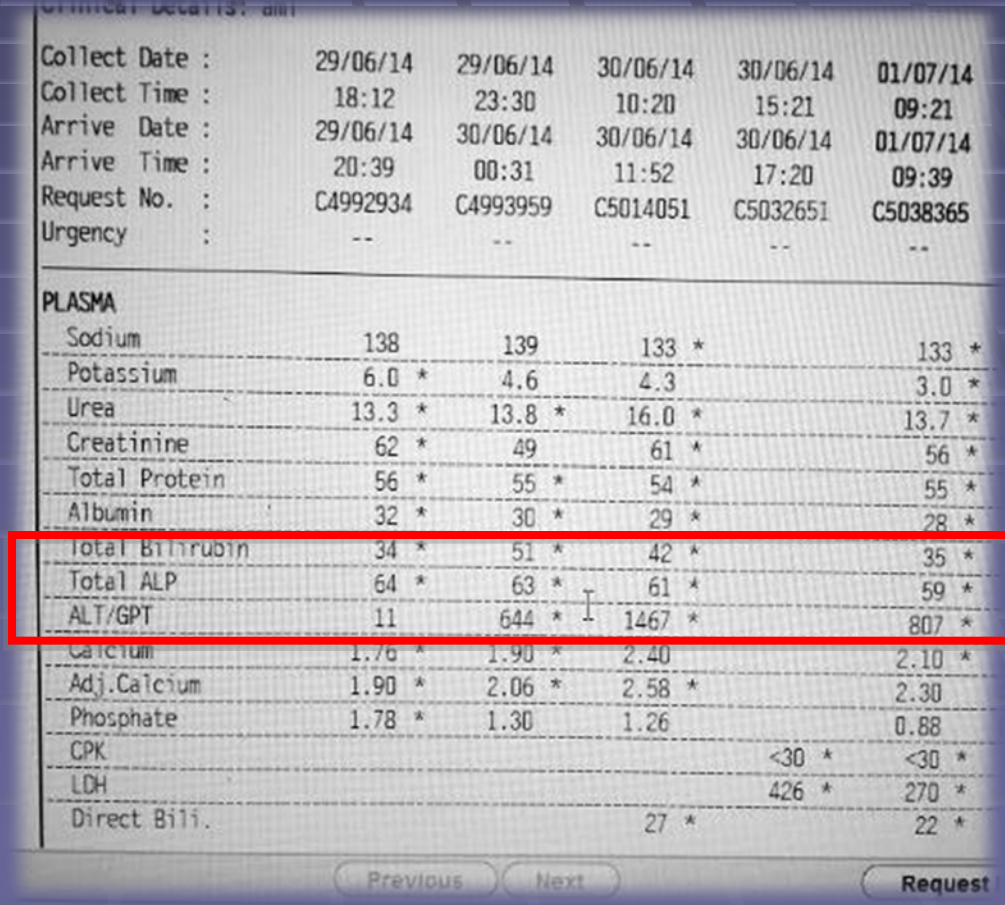
rgency :	--	--	--	--	--
ardiac Troponin (cTn)					
Plasma hsTnT	79.7 *	83.8 *	76.8 *	60.7 *	49.9 *

Progress in PICU

- Neurological: Encephalitis
  - Neuro observation stable
  - No further seizure noted
  - Sleep disturbance
  - Subtle change of behaviour

- Hepatitis
  - Liver function derangement:
  - ALT up to 1467
  - Bilirubin 51



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Collect Time :	18:12	23:30	10:20	15:21	09:21
Arrive Date :	29/06/14	30/06/14	30/06/14	30/06/14	01/07/14
Arrive Time :	20:39	00:31	11:52	17:20	09:39
Request No. :	C4992934	C4993959	C5014051	C5032651	C5038365
Urgency :	--	--	--	--	--
PLASMA					
Sodium	138	139	133 *		133 *
Potassium	6.0 *	4.6	4.3		3.0 *
Urea	13.3 *	13.8 *	16.0 *		13.7 *
Creatinine	62 *	49	61 *		56 *
Total Protein	56 *	55 *	54 *		55 *
Albumin	32 *	30 *	29 *		28 *
Total Bilirubin	34 *	51 *	42 *		35 *
Total ALP	64 *	63 *	61 *		59 *
ALT/GPT	11	644 *	1467 *		807 *
Calcium	1.76 *	1.90 *	2.40		2.10 *
Adj.Calcium	1.90 *	2.06 *	2.58 *		2.30
Phosphate	1.78 *	1.30	1.26		0.88
CPK				<30 *	<30 *
LDH				426 *	270 *
Direct Bili.			27 *		22 *

Previous Next Request

Investigation results

- Blood
  - CRP highest up to 45.1
  - Bacterial/Fungal Culture: -ve
  - HHV-6 PCR +ve (retrospective, from 1 week before seizure)
- CSF
  - Bacterial Culture -ve
  - Herpes/Enterovirus/Varicella/CMV -ve
  - HHV 6 PCR +ve

Human Herpes Virus 6

- HHV-6 has 2 variants (A & B)
- Only HHV-6B has definitely linked with disease
  - Exanthem subsitum (Roseola infantum)
- Majority of patients acquired this at childhood

Human Herpes Virus 6

- Prospectively study of a cohort of 277 children from birth till 24 months
- Saliva test weekly for HHV-6 DNA PCR
- By 12 months => 40% infected; By 24 months=> 77% infected
- Peak age of acquisition 9-21 months
- 93% had symptoms
  - Fever, fussiness, diarrhea, rash

Zerr DM, et al. N Engl J Med.2005;352:768-776.

Human Herpes Virus 6

Figure 1. Cumulative Incidence of Primary HHV-6 Infection.

The midpoint between the last negative salivary test for HHV-6 DNA and the first positive test served as the time of acquisition.

Zerr DM, et al. N Engl J Med.2005;352:768-776.

Presentation of HHV-6 in HSCT

- In HSCT setting, it causes disease in 2-4 weeks after HSCT.
  - Aysmptomatic reactivation
  - Fever, macular rash
  - Interstitial pneumonitis
  - Hepatitis, colitis, pancreatitis
  - BM suppression
    - Delayed engraftment
    - Presence of HHV-6DNA in blood and exclusion of other possible causes
  - Encephalitis
    - Mostly in mismatched related or unrelated SCT
    - CNS signs and symptoms
    - Abnormal imaging or EEG change
    - Detection of HHV-6 DNA in CSF
    - Initial CSF biochemistry may be normal or near normal

Presentation of HHV-6 in HSCT

- Any symptoms and signs from organ in question
  - Tests on tissue are required to establish evidence of HHV-6 replication and consequent pathology
  - Possible techniques
    - In-situ hybridization
    - Immunohistochemistry
    - PCR for HHV-6 DNA is not recommended on tissue samples
- Treatment of choice
  - Foscarnet
  - Ganciclovir

Ljungman P, et al. Bone Marrow Transplantation.2008;42:227-240.

Presentation of HHV-6 in HSCT

Patient	Day of onset (post-transplant)	Peripheral blood count	Immunosuppressants	CSA trough level (μg/L)	Presentations	CSF cell counts and biochemistry	Treatment	Outcome
1	21	Hb 8.9 WBC 3.0 ANC 2.0 LYM 0.3 PLT 26.0	MP + CSA	235	Abnormal behavior; Seizure; Hyponatremia;	Traumatic tap	Ganciclovir 3 wk	Alive; Epilepsy; Now 8 yr post-transplant
2	20	Hb 9.7 WBC 0.3 ANC 0.2 LYM 0.1 PLT 88.0	MP + CSA	190	Depressed conscious level; Sleep disturbance; Euphoria, Generalized seizure	WBC 1/mm^3; RBC 3/mm^3; Total protein 0.24 g/L	Foscarnet 2 wk (treatment terminated because of renal impairment)	Died on day 38 (non-engraftment, refractory seizure, pneumonia, gastrointestinal bleeding)
3	19	Hb 9.0 WBC 0.2 ANC 0.1 LYM 0.0 PLT 30.0	MP + CSA	217	Fever; Headache; Hypertension; Abnormal behavior; Hyponatremia; Seizure	WBC 1/mm^3; RBC 2/mm^3; Total protein 0.15 g/L	Foscarnet 2 wk + ganciclovir 2 wk	Progression of clinical symptoms despite on foscarnet and ganciclovir. Died on day 61 (intracranial hypertension)
4	18	Hb 7.0 WBC 1.4 ANC 0.8 LYM 0.0 PLT 3.0	MP + CSA	163	Fever; Focal seizure; Loss of memory; Abnormal behavior; Hypertension	WBC 2/mm^3; RBC 5/mm^3; Total protein 0.23 g/L	Ganciclovir 2 wk + foscarnet 3 wk	Alive; Refractory epilepsy; Developmental delay

Presentation of HHV-6 in HSCT

HHV-6 encephalitis in pediatric unrelated umbilical cord transplantation: A role for ganciclovir prophylaxis?

Cheng FWT, Lee V, Leung WK, Chan PKS, Leung TF, Shing MK, Li CK. HHV-6 encephalitis in pediatric unrelated umbilical cord transplantation: A role for ganciclovir prophylaxis?
Pediatr Transplantation 2010: 14: 483–487. © 2009 John Wiley & Sons A/S.

Abstract: The role of ganciclovir as HHV-6 prophylaxis in unrelated HSCT setting remains controversial. We performed an eight-yr retro-

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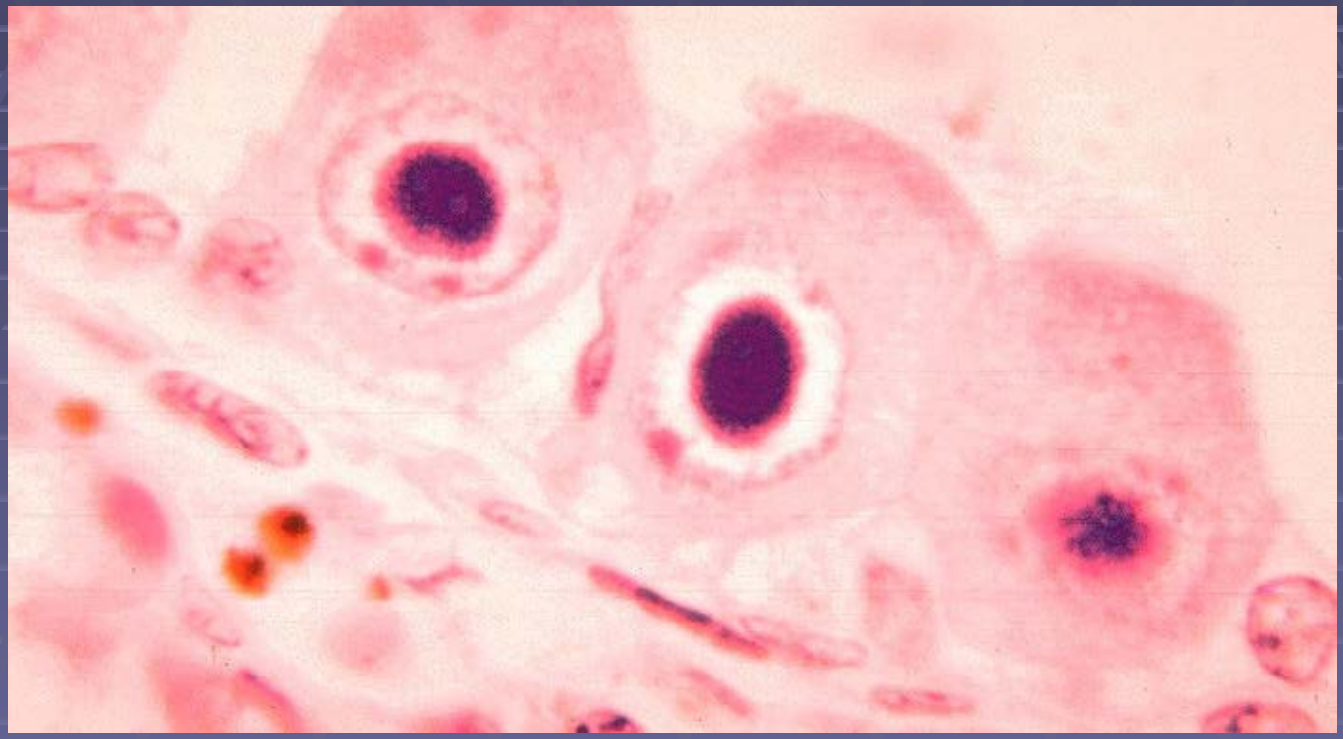

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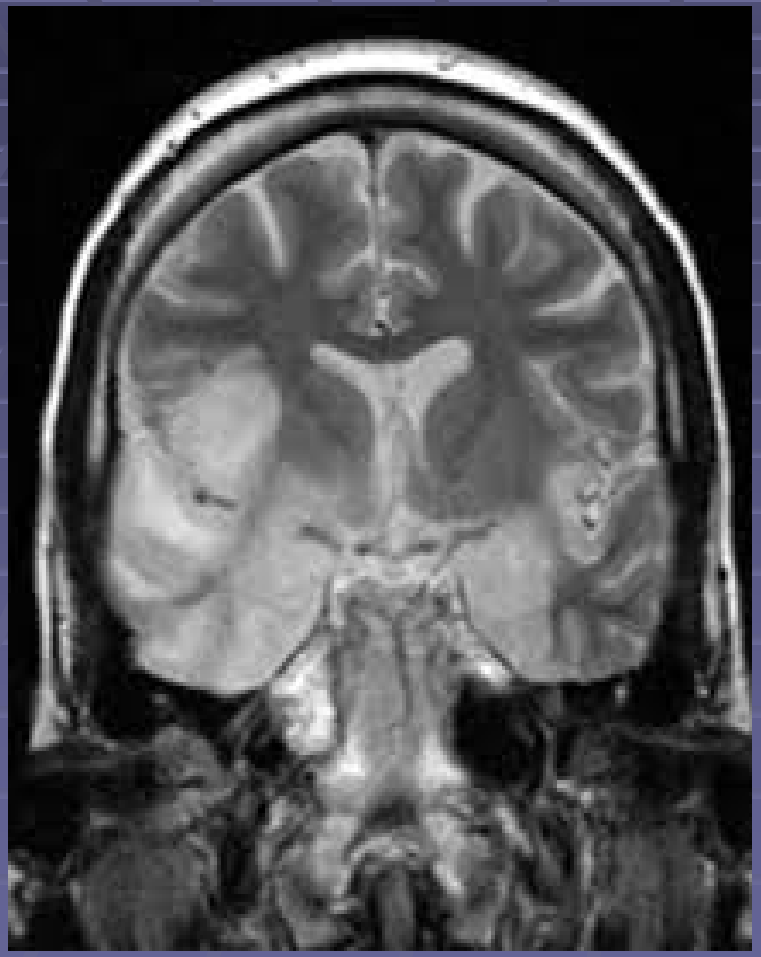

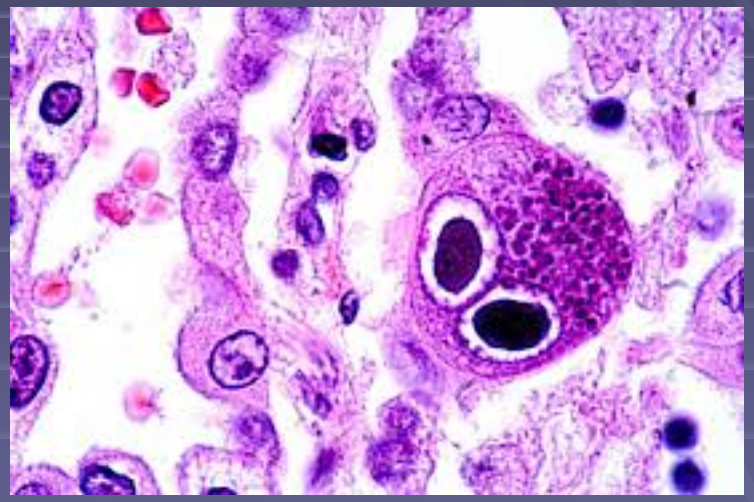

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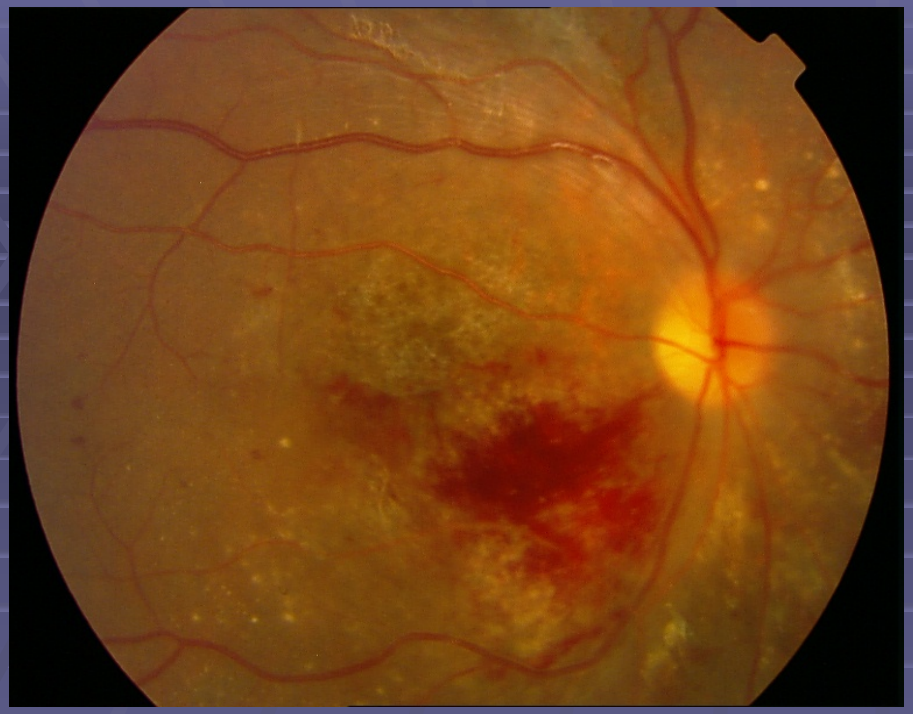
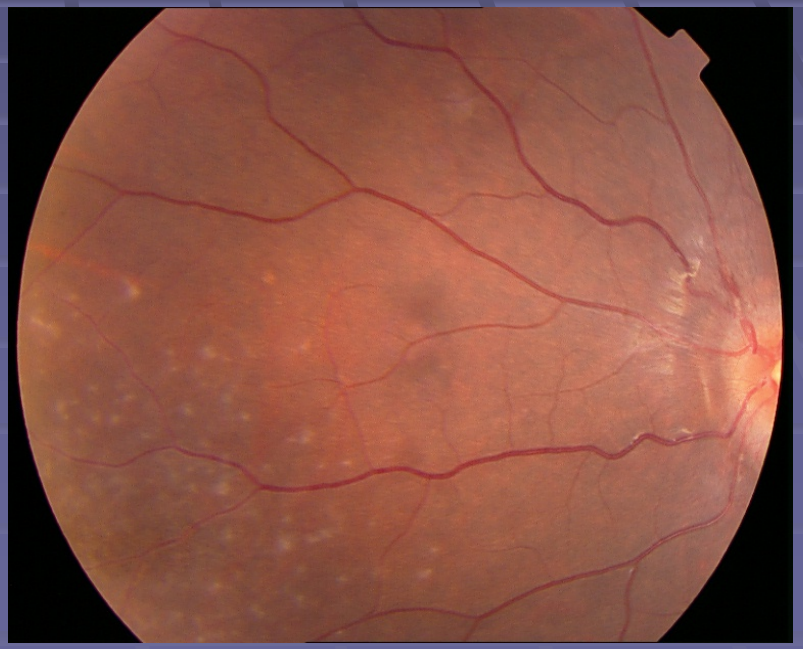
Journal of Pediatric Hematology and Oncology

Intact Survival of Refractory CMV Limbic Encephalitis in a Patient with Severe Aplastic Anemia after Unrelated Bone Marrow Transplantation

Manuscript Draft

Tam YS, Cheng FWT, et al. J Ped Hematol Oncol 2011

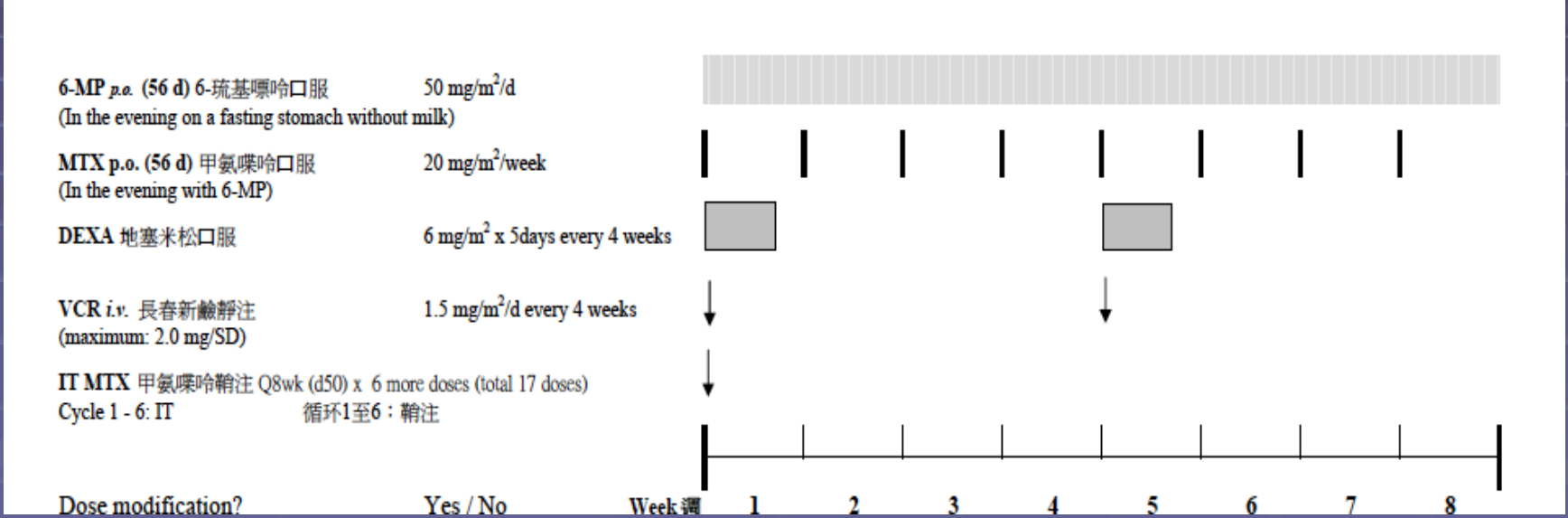




Background

- Cytomegalovirus (CMV) retinitis is a vision-threatening opportunistic infection in immunocompromised patients.
- It is mostly reported in patients with Acquired Immune Deficiency Syndrome (AIDS).
- It is seldomly reported in paediatric patients who were receiving chemotherapy with mild to moderate intensity, namely maintenance chemotherapy for acute lymphoblastic leukemia.

Maintenance Therapy For ALL



CMV Retinitis

- Retrospective case review in paediatric oncology patients (non-HSCT patients)
- Review period: Jan 2007 to Dec 2011,
- Case records of diagnosis of CMV retinitis were retrieved (non-HSCT patients)

CMV Retinits

- Definition of CMV retinitis
  - Based on the clinical findings seen on a dilated eye examination performed by opthalmologist

    +
  - Evidence of CMV reactivation
    - CMV pp65 Ag/PCR positivity in peripheral blood or
    - CMV PCR positivity by vitreous tapping

      +
  - Rule out other causes of visual symptoms
    - Namely leukemic infiltrates…..

Results

- Two cases of CMV retinitis developed in paediatric oncology patients were identified

Patient 1

- F/14 years
- Acute lymphoblastic leukaemia
- CR after induction and put on maintenance therapy (6-mercaptopurine and methotrexate)
- Developed persistent lymphopenia despite dosage of chemotherapy was adjusted
  - (lymphocyte <0.3, according to protocol)
- Her lymphocyte count remained at 0.2-0.6 x 10^9/L during maintenance therapy

History

- At 7 months of maintenance therapy, she developed persistent fever but no definite visual symptoms……

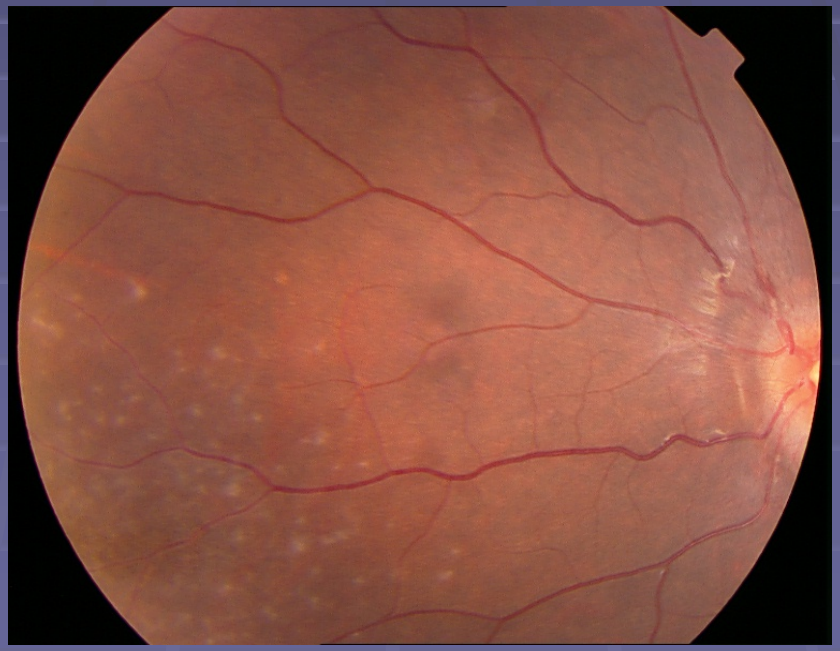


Photo from Dr Vesta Chan, PWH

History (Patient 2)

- M/6 years
- High risk ALL presented with fever and limping gait
- Achieved CR 1 after induction therapy
- Put on maintenance therapy
- Developed bilateral blurring of vision 3.5 months from initiation of maintenance therapy
- Lymphocyte count was 0.3-0.7x 10^9/L for 2 weeks before onset of symptoms

History (Patient 2)

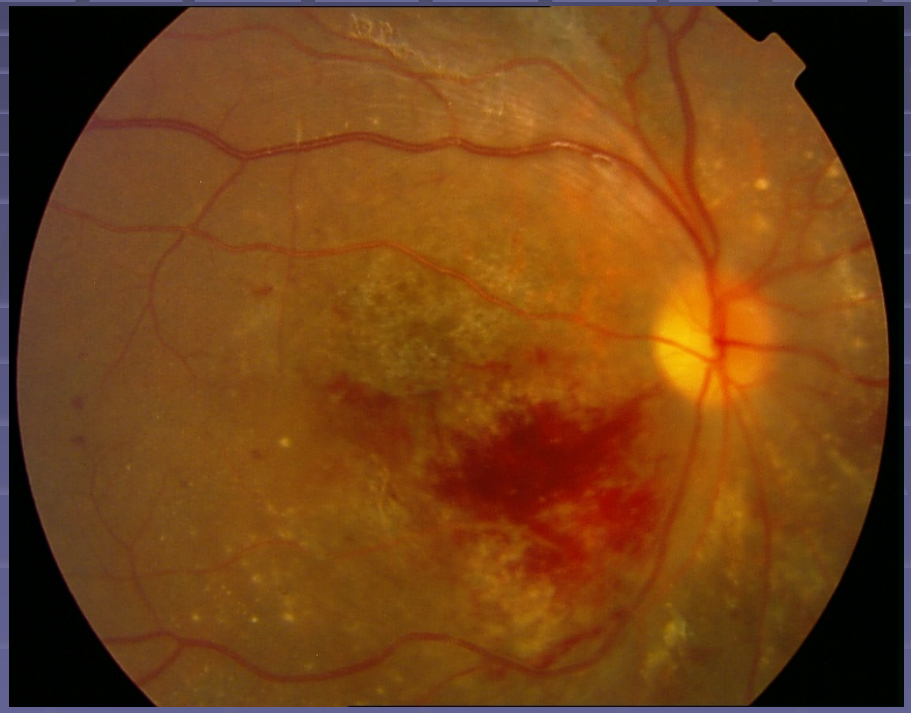


Photo from Dr Vesta Chan, PWH

Investigations

- Patient 1
  - Pre-treatment CMV IgG positive
  - Peripheral blood showed CMV Ag presented in 871 cells out of 200,000 leukocytes
  - Retinography was compatible with early CMV retinitis
- Patient 2
  - Pre-treatment CMV IgG positive
  - Bilateral vitreous tapping showed CMV PCR positive
  - Peripheral blood showed CMV Ag presented in 40 cells out of 200,000 leukocytes

Diagnosis

- CMV retinitis can be presented in maintenance therapy setting

Treatment

- Patient 1
  - 5 weeks of ganciclovir + 6 more weeks of oral valganciclor till CMV retinitis resolved
- Patient 2
  - 7 weeks of ganciclovir treatment till CMV retinitis resolved

Outcome

- Patient 1
  - Maintenance chemotherapy resumed and completed after suspension for 3 weeks
  - At 18 months after diagnosis of CMV retinitis (8 months after stopping treatment), she developed relapse of ALL
  - Currently in CR 2 status after re-induction chemotherapy

Outcome

- Patient 2
  - Chemotherapy was suspended for 3 weeks
  - 10 weeks after CMV retinitis, he developed relapse of leukemia
  - Put on re-induction chemotherapy
  - Refractory disease
  - Died of refractory leukemia

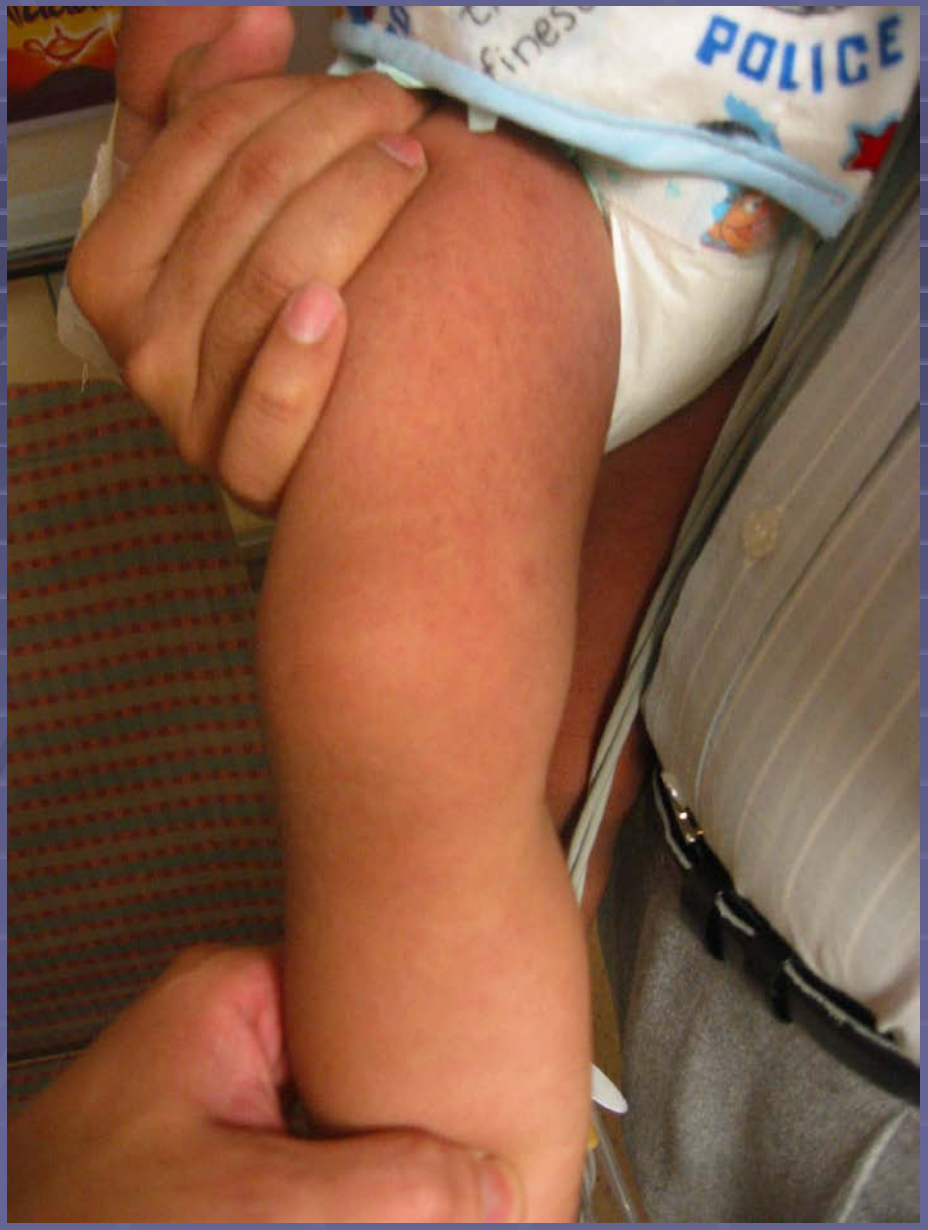
Discussion

- In our 2 cases, they had persistent "mild" lymphopenia in the range of 0.3-0.5x10^9/L
- Controversies
  - Whether ALC <0.5x10^9/L is a "better" cut-off to adjust chemotherapy since CMV retinitis is a severe vision-threatening condition
  - Impact of leukemia disease control for loosening the dose defining criteria

Discussion

- 2 patient developed relapse of leukemia after CMV retinitis (18 months and 10 weeks)
  - Co-incidence or related?
    - Early subtle change of bone marrow or immune function before relapse => CMV retinitis developed in a mild lymphopenic setting?
    - CMV retinitis => suspension of chemotherapy => relapse
    - Or just co-incidence


What else?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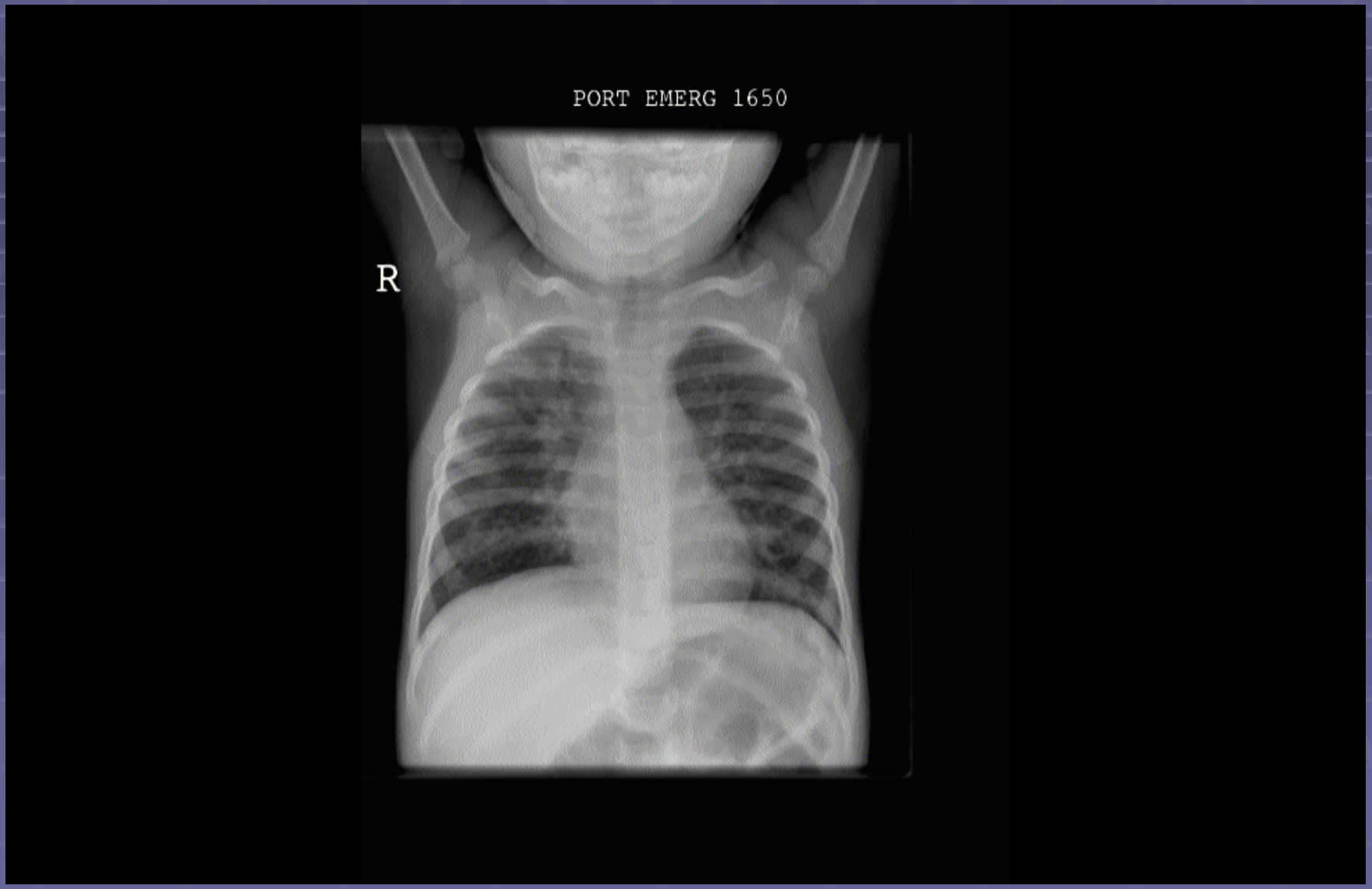
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Measles

- Enveloped RNA virus
- Human is the only natural host
- One of the most highly communicable infectious diseases
  - Droplet, contact and airborne precautions
- Incubation period
  - 8-12 days
  - The average interval between appearance of rash in index case and subsequent cases is 14 days (range 7-21 days)
- Diagnosis
  - IgM
  - Isolation of measles virus
  - Measles RNA from urine, blood, nasopharyngeal specimens

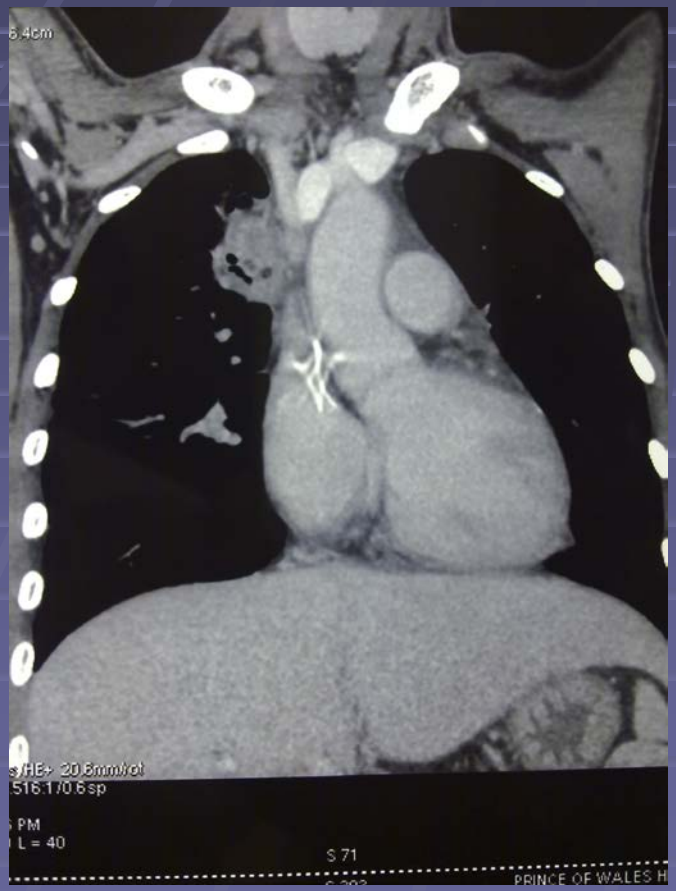
Georgescu G, et al. Expert Opin Biol Ther.2009;9:139-147.

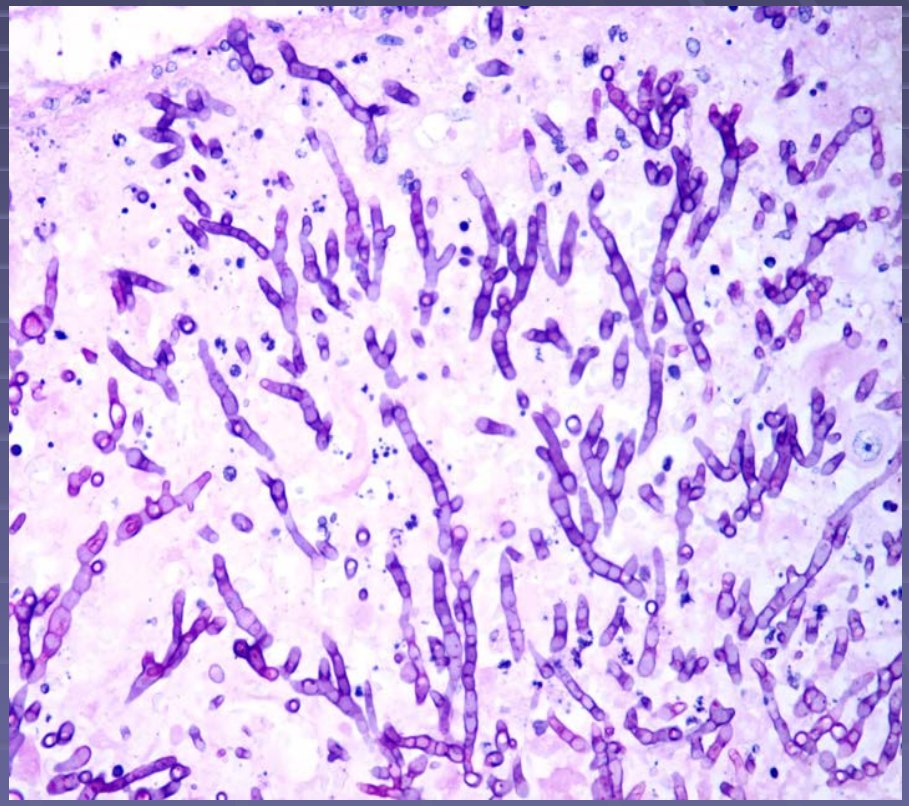
Measles

- Treatment
  - No specific antiviral therapy
  - Vitamin A
    - WHO recommends vitamin A for all children with acute measles, regardless of their country of residence. Administer once daily for 2 days

- Pitfall
  - Rash in immunocompromised patients may NOT be apparent
  - Presented as complications
  - High index of suspicions

Immune Recovery is the Key





Slide from Prof KF To, CUHK

Take Home Messages

- Beware of prolonged shedding of viruses in immunocompromised patients
  - RSV ……
  - Implications of infection control policy
- Atypical presentation of common viral infection
  - Unapparent rash in measles infections in immunocompromised patients
  - CMV / HHV 6/….
- Unusually severe clinical course
  - Adenovirus….

Take Home Messages

- Maintain an effective communication channel with Microbiologists / Virologists is ALWAYS the KEY to SUCCESS

Acknowledgements

Virology Laboratory, CUHK

- Prof Paul Chan and his team

Public Health Laboratory Services Branch, CHP

Thank You !