VIROVÉ REAKTIVACE U KRITICKY NEMOCNÝCH

LÉČIT NEBO IGNOROVAT?

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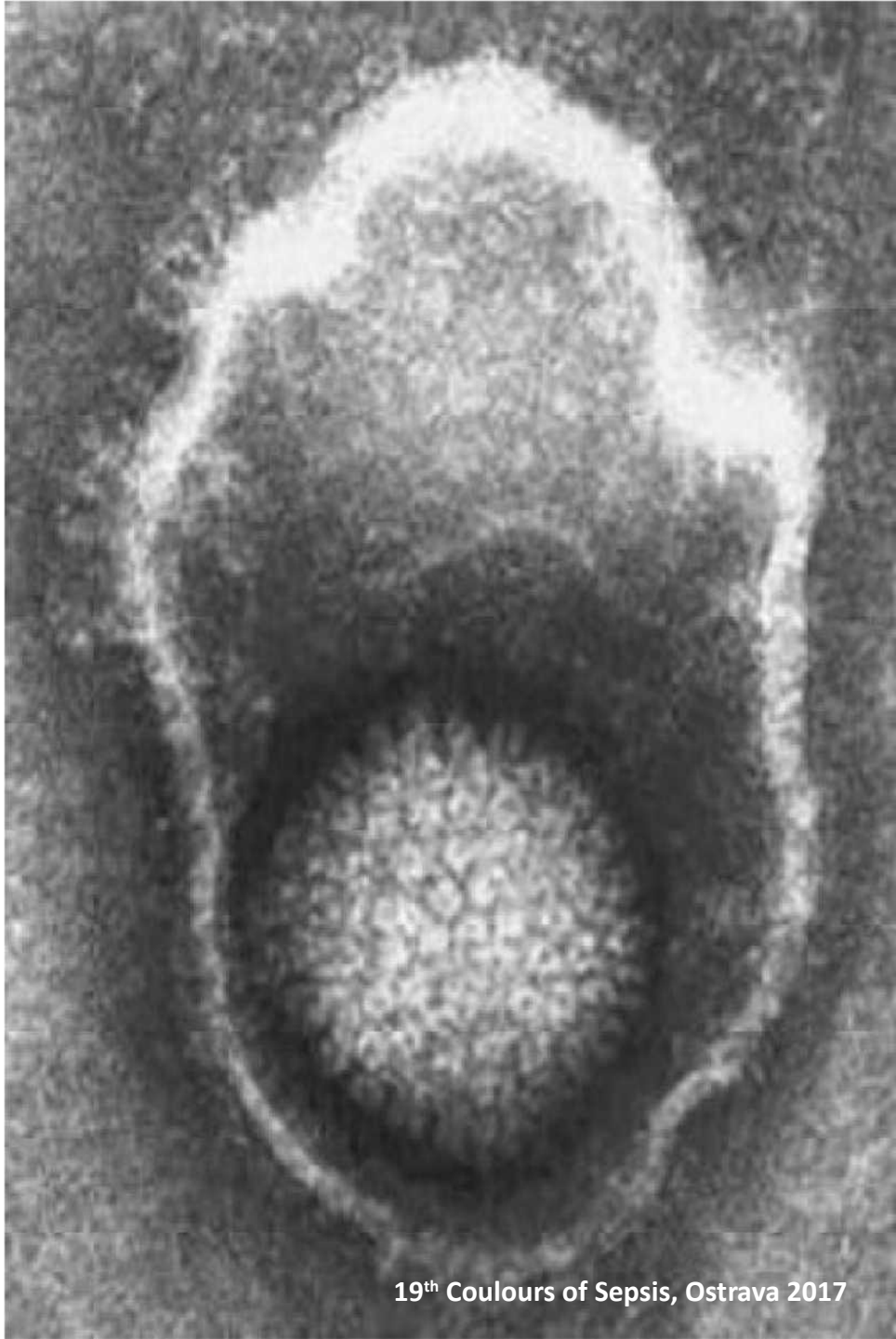

19th Coulours of Sepsis, Ostrava 2017

VIRY U KRITICKY NEMOCNÝCH

prostředí	endogenní*	exogenní**
komunitní	**HHV**	influenzavirus, parainfluenzavirus, adenoviry, rhinoviry, RSV, coronaviry, metapneumovirus, HHV (primoinfekce) aj.
nozokomiální	**HHV**	CMV (transfuze), influenza (epidemická), mimivirus, HHV (primoinfekce)

adaptováno dle: Chiche L et al. Curr Opin Infect Dis 2011

***dominantní postavení herpetických virů – endogenní infekce/reaktivace**

**pouze limitovaný význam u imunokompetentních nemocných

HERPETICKÉ VIRY (HHV): *TAXONOMIE*

- dsDNA viry
- 200-300kb: 150-200 genů

taxonomie	HHV	virus	cílová tkáň/buňky	latentní fáze
α-herpesvirinae	1	HSV1	mukóza/epitel	neurony
α-herpesvirinae	2	HSV2	mukóza/epitel	neurony
α-herpesvirinae	3	VZV	mukóza/epitel	neurony
γ-herpesvirinae	4	EBV	epitel/B-lymfocyty	B-lymfocyty
β-herpesvirinae	5	CMV	epitel/B-lymfocyty/monocyty	lymfocyty/monocyty/DC
β-herpesvirinae	6	HHV6	T-lymfocyty	T-lymfocyty
β-herpesvirinae	7	HHV7	T-lymfocyty	T-lymfocyty
γ-herpesvirinae	8	HHV8	endotel	?

Human Herpes Viruses: Biology, Therapy, and Immunoprophylaxis. Arvin A, Campadelli-Fiume G, Mocarski E et al. Cambridge University Press, 2007

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γ-herpesvirinae	4	EBV	epitel/B-lymfocyty	B-lymfocyty
β-herpesvirinae	5	CMV	epitel/B-lymfocyty/monocyty	lymfocyty/monocyty/DC
β-herpesvirinae	6	HHV6	T-lymfocyty	T-lymfocyty
β-herpesvirinae	7	HHV7	T-lymfocyty	T-lymfocyty
γ-herpesvirinae	8	HHV8	endotel	?

Human Herpes Viruses: Biology, Therapy, and Immunoprophylaxis. Arvin A, Campadelli-Fiume G, Mocarski E et al. Cambridge University Press, 2007

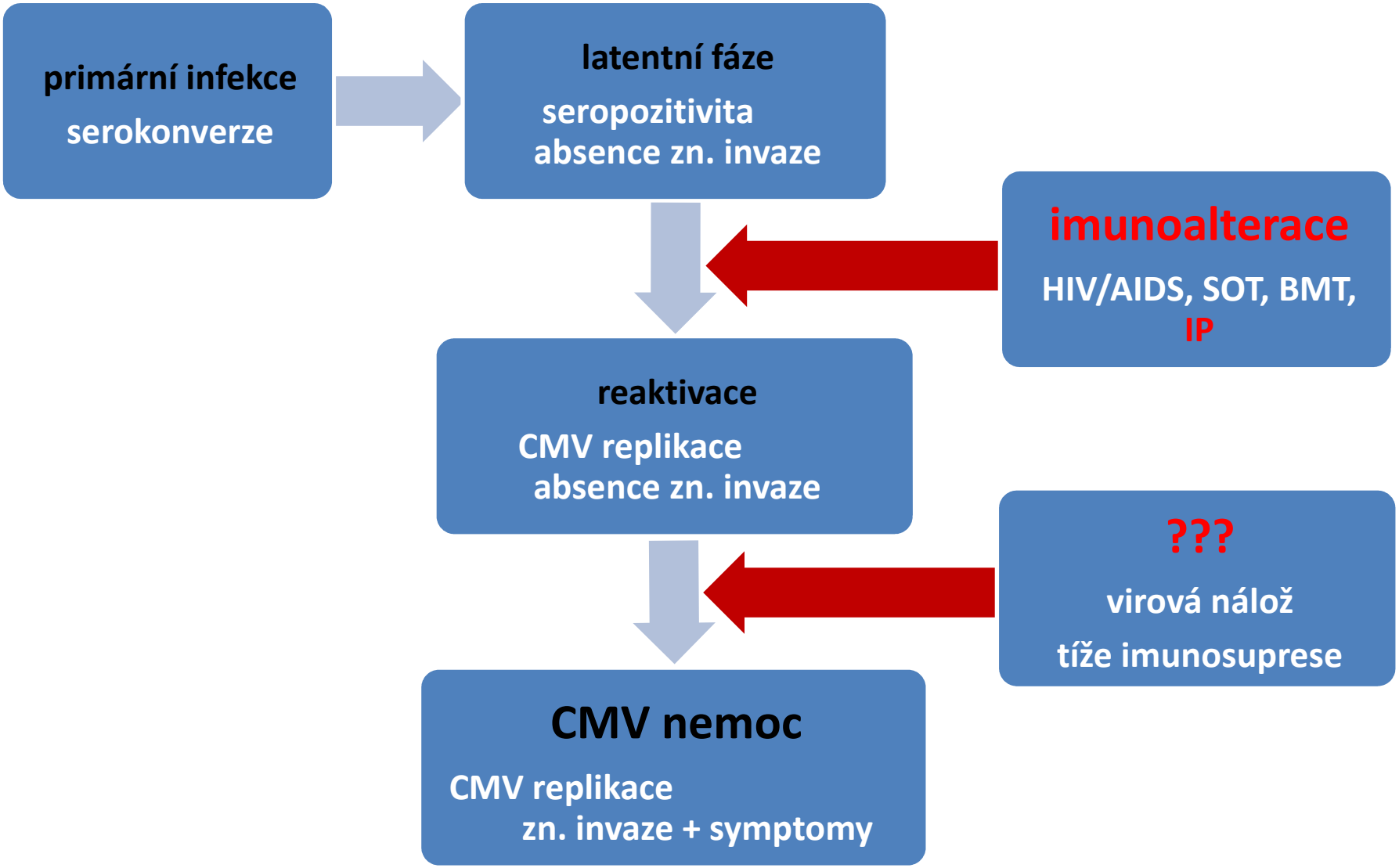
CYTOMEGALOVIRUS (CMV)

- ubikvitární
- **primární infekce** často zcela asymptomatická, self-limiting
- vertikální + horizontální přenos
- seroprevalence 30% - >90% (>věk; populace/etnikum): **anti-CMV IgG**

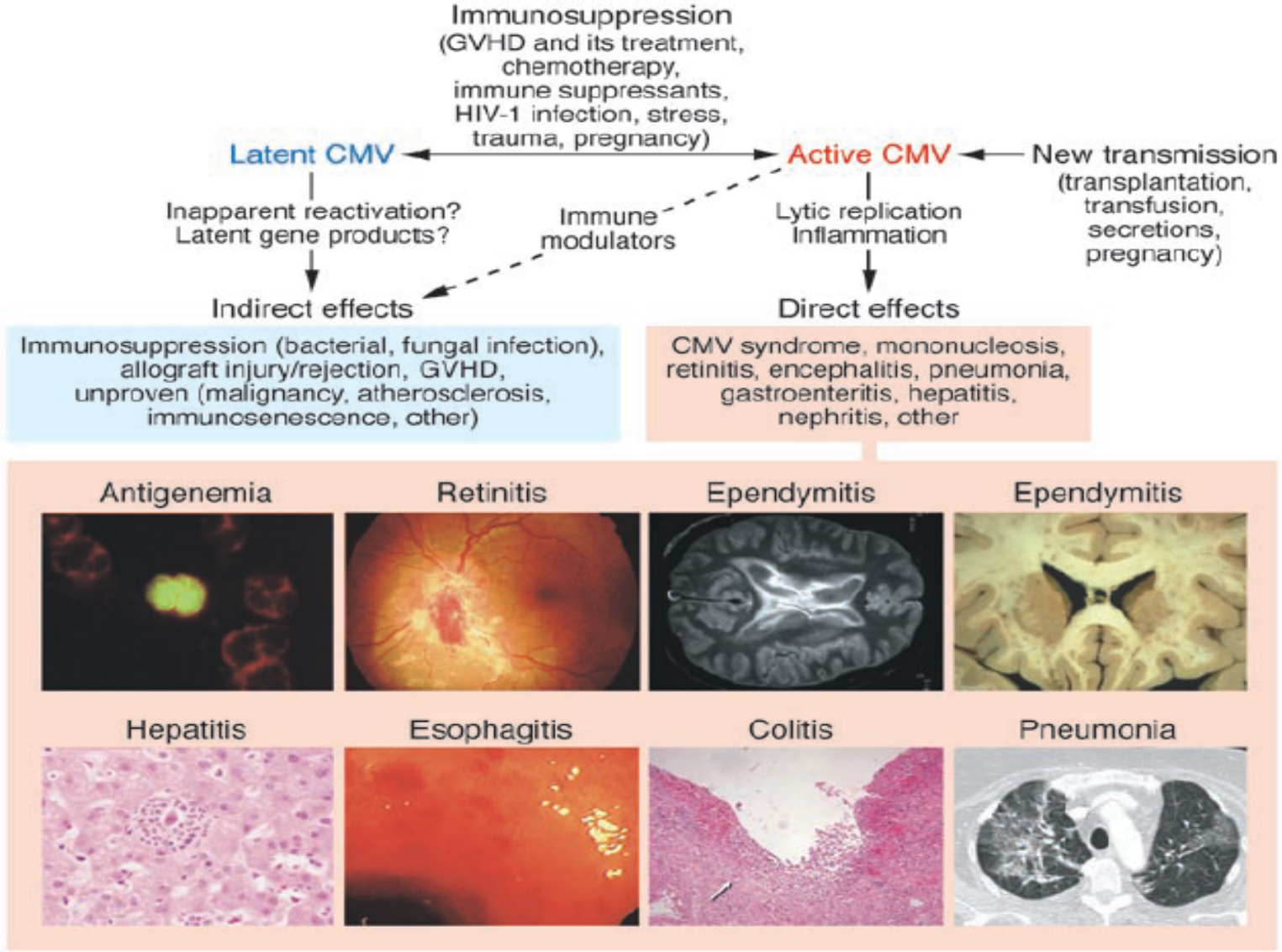
- **latentní fáze** (lymfocyty/monocyty/dendritické buňky)
- kontrola/prevence CMV reaktivace/nemoci = komplexní imunitní odpověď: **CMV specifické $CD8^+$ TC (>10% totTC), NKC; INFs, CKs**

Al-Omari A et al. Ann Intensive Care 2016
Gandhi MK et al. Lance Infect Dis 2004

CMV CYKLUS


primární infekce
serokonverze
latentní fáze
seropozitivita
absence zn. invaze
imunoalterace
HIV/AIDS, SOT, BMT,
IP
reaktivace
CMV replikace
absence zn. invaze
???
virová nálož
tíže imunosuprese
CMV nemoc
CMV replikace
zn. invaze + symptomy

CYTOMEGALOVIRUS (CMV)



Boeckh M et al. J Clin Invest 2011

CMV: IMUNOSUPRIMOVANÝ JEDINEC

CMV EXECUTIVE ~~ORDER~~ GUIDELINES

CMV: IMUNOSUPRIMOVANÝ JEDINEC

How I treat cytomegalovirus in hematopoietic cell transplant recipients

Michael Boeckh[1] and Per Ljungman[2]

[1]Vaccine and Infectious Disease Institute and Program in Infectious Diseases, Fred Hutchinson
Hematology, Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden

Cytomegalovirus (CMV) continues to cause major complications after hemato-poietic cell transplantation (HCT). Over the past decade, most centers have adopted preemptive antiviral treatment or prophylaxis strategies to prevent CMV disease. Both strategies are effec also have shortcomings with pi available drugs. Here, we review of CMV treatment and prevention recipients, including currently use and diagnostics, ways to optim

ELSEVIER

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

ASBMT American Society for Blood and Marrow Transplantation

Recent Advances in Cytomegalovirus: An Update on Pharmacologic and Cellular Therapies

Michael Boeckh [1], William J. Murphy [2], Karl S. Peggs [3,*]

Biol Blood Marrow Transplant 21 (2015) 24–29

Updated International Consensus Guidelines on the Management of Cytomegalovirus in Solid-Organ Transplantation

Camille N. Kotton,[1,8] Deepali Kumar,[2] Angela M. Caliendo,[3] Ander Sunwen Chou,[5] Lara Danziger-Isakov,[6] and Atul Humar,[7] on behalf of The Transplantation Society International CMV Consen

Keywords: Cytomegalovirus, CMV, Ganciclovir, Prevention, Prophylaxis, Resistance,

(*Transplantation* 2013;96: 333–360)

Published in final edited form as:

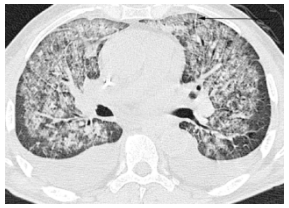
Pediatr Infect Dis J. 2013 November ; 32(0 2): i–KK4. doi:10.1097/01.inf.0000437856.09540.11.

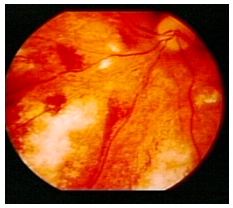
Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children:

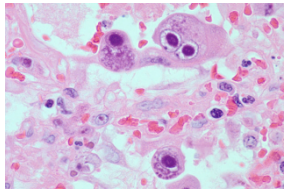
Recommendations from the National Institutes of Health, Centers for Disease Control and Prevention, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics

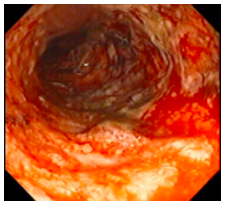
George K. Siberry, MD, MPH[1] [Executive Secretary], Mark J. Abzug, MD[2] [Co-Chair], Sharon Nachman, MD[3] [Co-Chair], Michael T. Brady, MD[4], Kenneth L. Dominguez, MD, MPH[5], Edward Handelsman, MD[1,§], Lynne M. Mofenson, MD[1], Steve Nesheim, MD[5], and the Panel on Opportunistic Infections in HIV-Exposed and HIV-Infected Children*

Cytomegalovirus (Last updated November 6, 2013; last reviewed November 6, 2013)

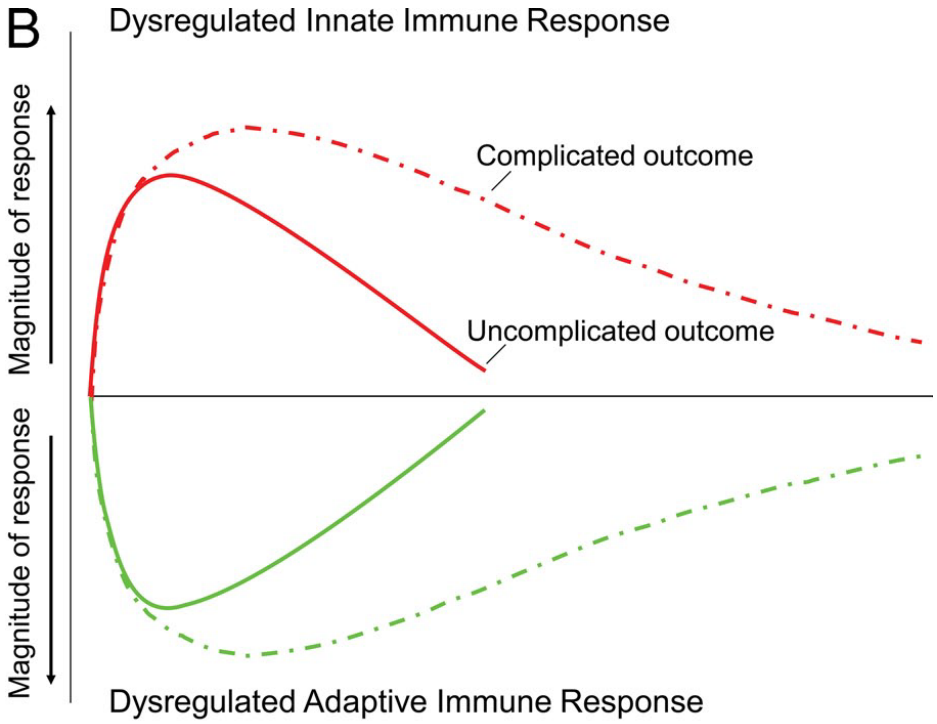




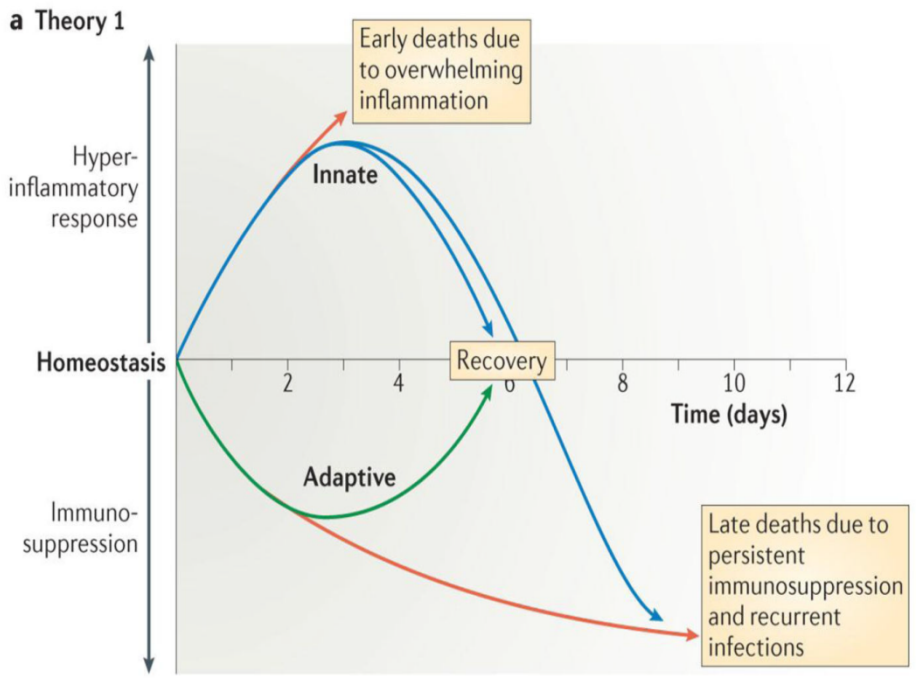




CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC



Xiao W et al. J Exp Med 2011

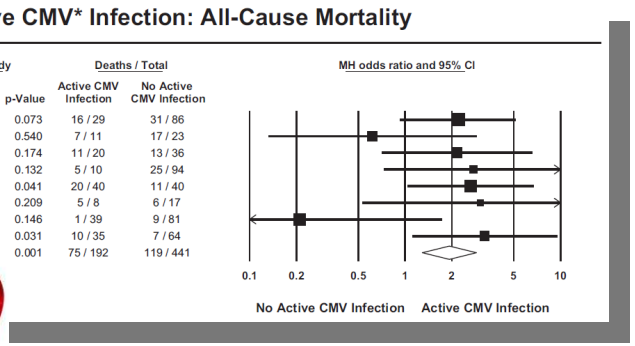


Hotchkiss R et al. Nat Rev Immunol 2013

CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

VÝZNAM

- ↑ ICU-LOS/HOSPITAL-LOS
- ↑ DÉLKA UPV
- ↑ INCIDENCE ORGÁNOVÝCH DYSFUNKCÍ
- ↑ FREKVENCE BAKTERIÁLNÍCH A MYKOTICKÝCH INFEKCÍ
- …
- ↑ MORTALITA



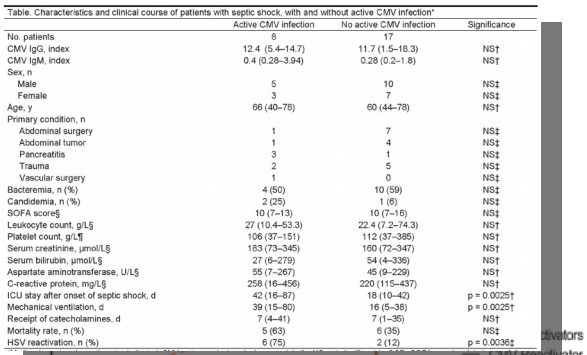
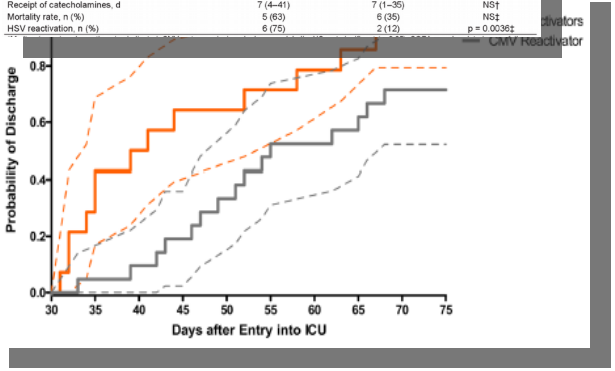


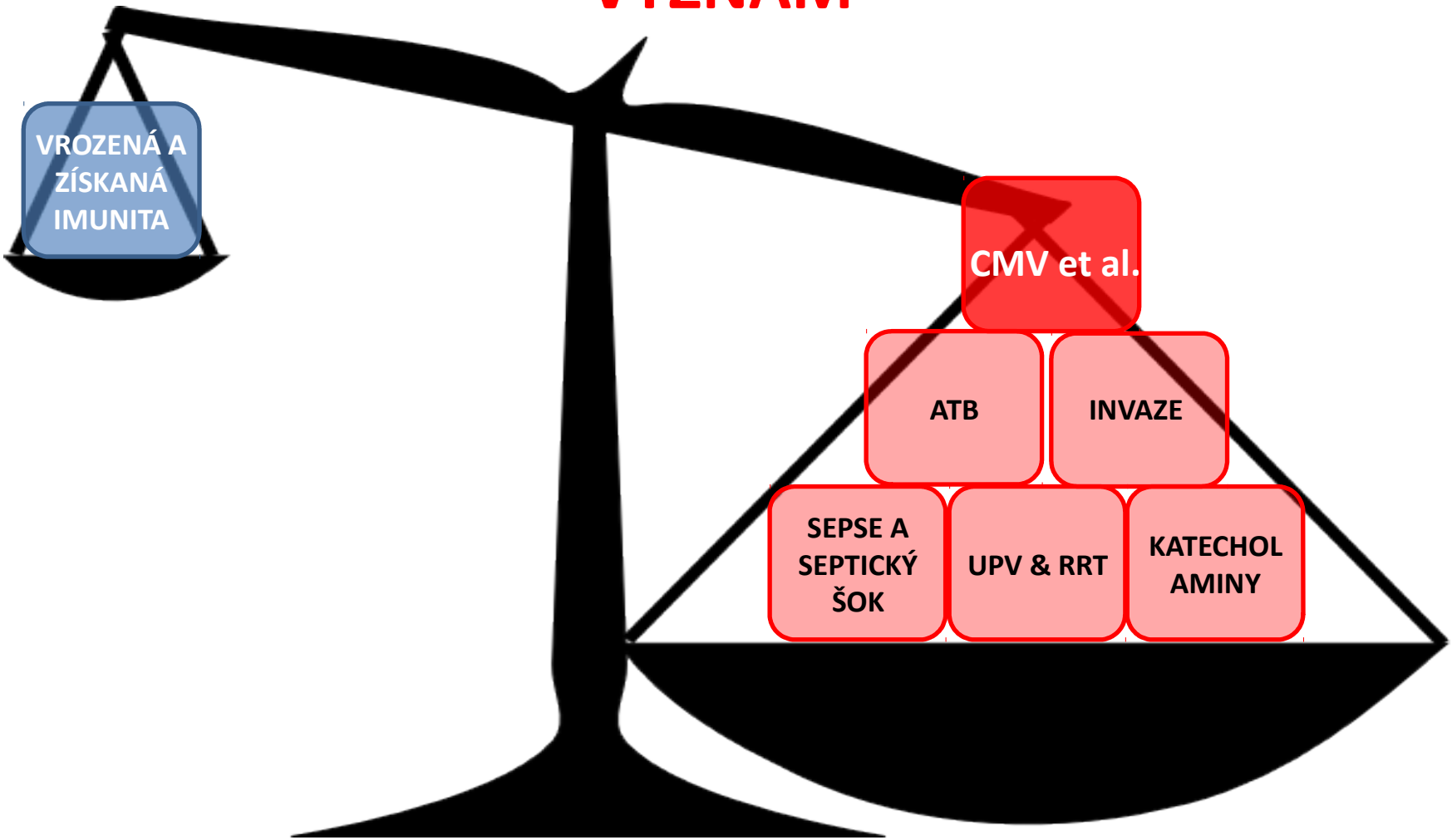
Table. Characteristics and clinical course of patients with septic shock, with and without active CMV infection*

	Active CMV infection	No active CMV infection	Significance
No. patients	8	17	
CMV IgG, index	12.4 (5.4–14.7)	11.7 (1.5–18.3)	NS†
CMV IgM, index	0.4 (0.28–3.94)	0.28 (0.2–1.8)	NS†
Sex, n			
Male	5	10	NS‡
Female	3	7	NS‡
Age, y	66 (40–78)	60 (44–78)	NS†
Primary condition, n			
Abdominal surgery	1	7	NS‡
Abdominal tumor	1	4	NS‡
Pancreatitis	3	1	NS‡
Trauma	2	5	NS‡
Vascular surgery	1	0	NS‡
Bacteremia, n (%)	4 (50)	10 (59)	NS‡
Candidemia, n (%)	2 (25)	1 (6)	NS‡
SOFA score§	10 (7–13)	10 (7–16)	NS‡
Leukocyte count, g/L§	27 (10.4–53.3)	22.4 (7.2–74.3)	NS†
Platelet count, g/L¶	106 (37–151)	112 (37–385)	NS†
Serum creatinine, μmol/L§	183 (73–345)	160 (72–347)	NS†
Serum bilirubin, μmol/L§	27 (6–279)	54 (4–336)	NS†
Aspartate aminotransferase, U/L§	55 (7–267)	45 (9–229)	NS†
C-reactive protein, mg/L§	258 (16–456)	220 (115–437)	NS†
ICU stay after onset of septic shock, d	42 (16–87)	18 (10–42)	p = 0.0025†
Mechanical ventilation, d	39 (15–80)	16 (5–36)	p = 0.0025†
Receipt of catecholamines, d	7 (4–41)	7 (1–35)	NS†
Mortality rate, n (%)	5 (63)	6 (35)	NS‡
HSV reactivation, n (%)	6 (75)	2 (12)	p = 0.0036‡



CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

VÝZNAM



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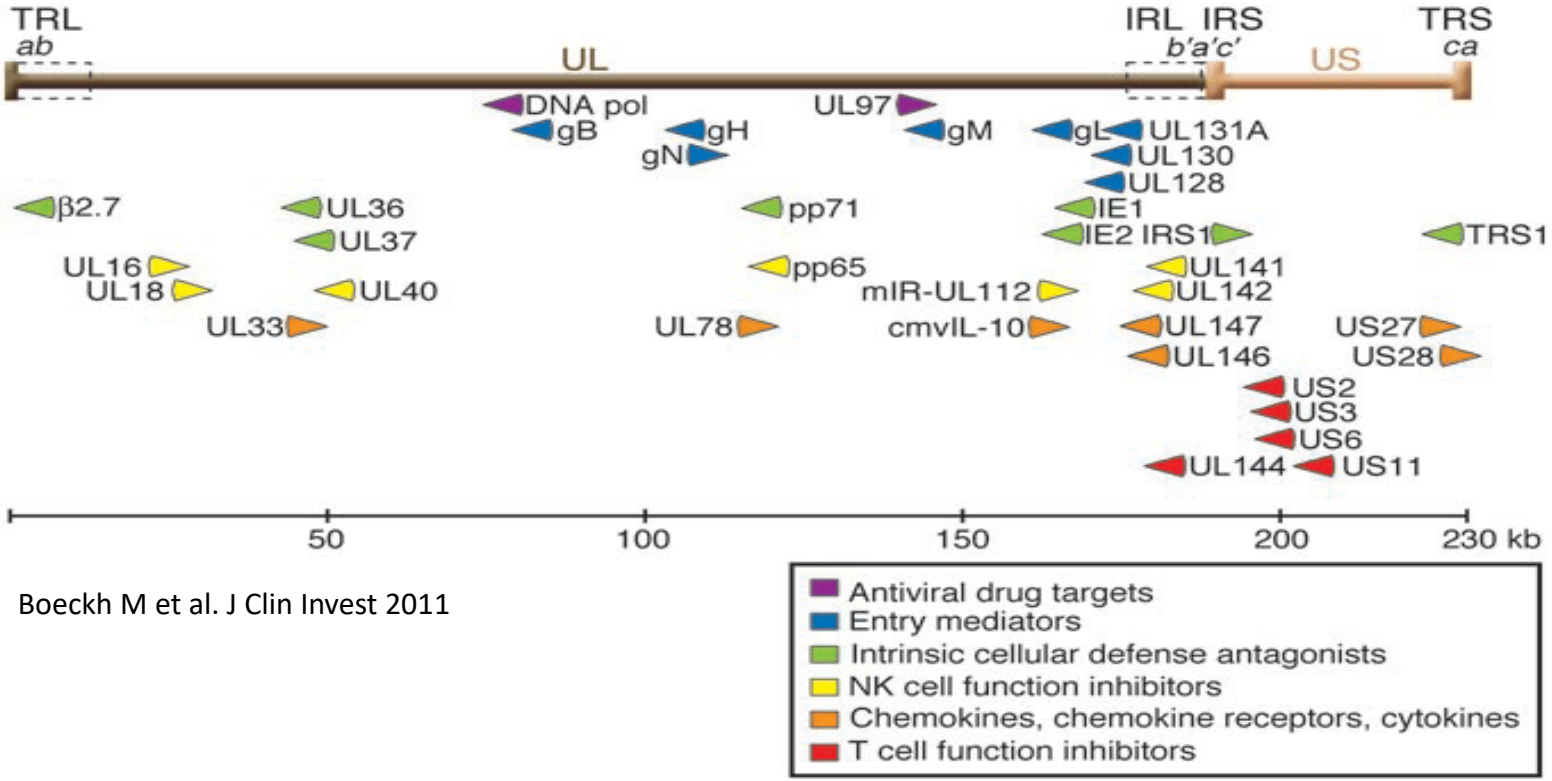
VÝZNAM



Boeckh M et al. J Clin Invest 2011

CMV INDUKOVANÁ/ASOCIOVANÁ IMUNOMODULACE

CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

VÝZNAM

CMV INDUKOVANÁ/ASOCIOVANÁ IMUNOMODULACE

- fylogeneticky ověřené mechanizmy invaze

- **indukce apoptózy imunokompetentních buněk**
- **modulace/inhibice funkcí DC a NKC**
- **produkce cytokinů (cmvIL-10), cytokinových receptorů**
- **inhibice exprese a modifikace funkce MHC**
- **permanentní stimulace imunitního systému…exhausce?**

- **marker stavu/kompetence imunitního systému**

- **asymptomatická replikace/subklinická reaktivace (sliny, moč)**

Boeckh M et al. J Clin Invest 2011
Slobedman B et al. J Virol 2009
Noda S et al. Blood 2006
Moss P. Curr Opin Immunol 2010
Beisser PS et al. Curr Top Microbiol Immunol 2008
Al-Omari A et al. Ann Intensive Care 2016

CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

VÝZNAM

CMV INDUKOVANÁ/ASOCIOVANÁ IMUNOMODULACE

IMUNOSUPRESE

↓ HLA expression
HLA class I homologue
↓ Antigen presentation
↓ T-cell proliferation
↓ Production of IL-2, INF-γ, PD-1
↑ Fc receptor expression
Fc receptor homologue
↑ Complement inhibitors
↓ Macrophage migration

POTENCIACE INFLAMACE

Translocation of NF-κB to nucleus
↑ TNF-α production
↑ smooth muscle cell proliferation
↑ Adhesion molecule expression
↑ IL-8 and chemokine secretion

Boeckh M et al. J Clin Invest 2011
Slobedman B et al. J Virol 2009
Noda S et al. Blood 2006
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CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

EPIDEMIOLOGIE

Active CMV* Infection - Overall ICU Rate

Study name	Event rate	Lower limit	Upper limit	Total
Domart Y 1990	0.25	0.18	0.34	29 / 115
Papazian L 1996	0.09	0.05	0.18	8 / 86
Stephan F 1996	0.02	0.00	0.26	1 / 24
Kutza A 1998	0.32	0.19	0.50	11 / 34
Cook CH 1998	0.08	0.05	0.14	12 / 142
Desachy A 2001	0.01	0.00	0.07	1 / 96
Heininger A 2001	0.36	0.24	0.49	20 / 56
Razonable R 2002	0.01	0.00	0.06	1 / 120
Cook C 2003	0.10	0.05	0.17	10 / 104
Jaber S 2005	0.17	0.13	0.22	40 / 237
von Muller L 2006	0.32	0.17	0.52	8 / 25
Limaye A 2008	0.33	0.25	0.41	39 / 120
Ziemann M 2008	0.35	0.27	0.45	35 / 99
	0.17	0.11	0.24	215 / 1258

Event rate and 95% CI

-0.50 -0.25 0.00 0.25 0.50

Rate of Active CMV Infection

incidence 17 – 36%

b Active CMV* Infection Rate by Diagnostic Method

Group by CMV Diagnostic Method	Study name	Event rate	Lower limit	Upper limit	Total
Viral Culture	Domart Y 1990	0.25	0.18	0.34	29 / 115
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Viral Culture	Cook C 2003	0.10	0.05	0.17	10 / 104
Viral Culture		0.12	0.06	0.22	59 / 447
Viral DNA or Antigen	Stephan F 1996	0.02	0.00	0.26	1 / 24
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Viral DNA or Antigen		0.20	0.13	0.31	156 / 811

Event rate and 95% CI

-0.50 -0.25 0.00 0.25 0.50

Rate of Active CMV Infection

Active CMV* Infection Rate: + CMV Serology and > 5 ICU Days

Group by CMV Diagnostic Method	Study name	Event rate	Lower limit	Upper limit	Total
Viral Culture	Domart Y 1990	0.36	0.19	0.58	8 / 22
Viral Culture	Cook C 2003	0.13	0.07	0.23	10 / 76
Viral Culture		0.22	0.07	0.51	18 / 98
Viral DNA or Antigen	Stephan F 1996	0.02	0.00	0.26	1 / 24
Viral DNA or Antigen	Kutza A 1998	0.32	0.19	0.50	11 / 34
Viral DNA or Antigen	Heininger A 2001	0.36	0.24	0.49	20 / 56
Viral DNA or Antigen	von Muller L 2006	0.32	0.17	0.52	8 / 25
Viral DNA or Antigen	Limaye A 2008	0.33	0.25	0.41	39 / 120
Viral DNA or Antigen	Ziemann M 2008	0.56	0.41	0.70	23 / 41
Viral DNA or Antigen		0.36	0.26	0.47	102 / 300

Event rate and 95% CI

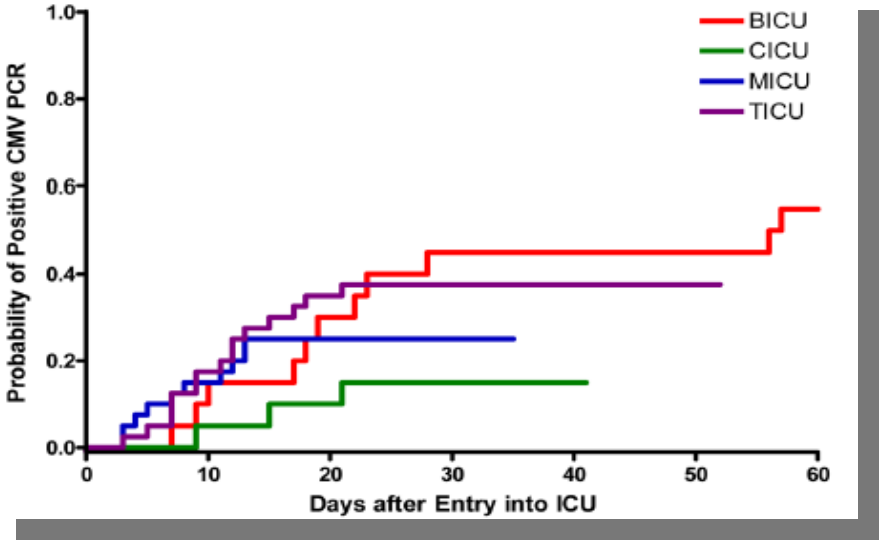
-0.50 -0.25 0.00 0.25 0.50

Rate of Active CMV Infection

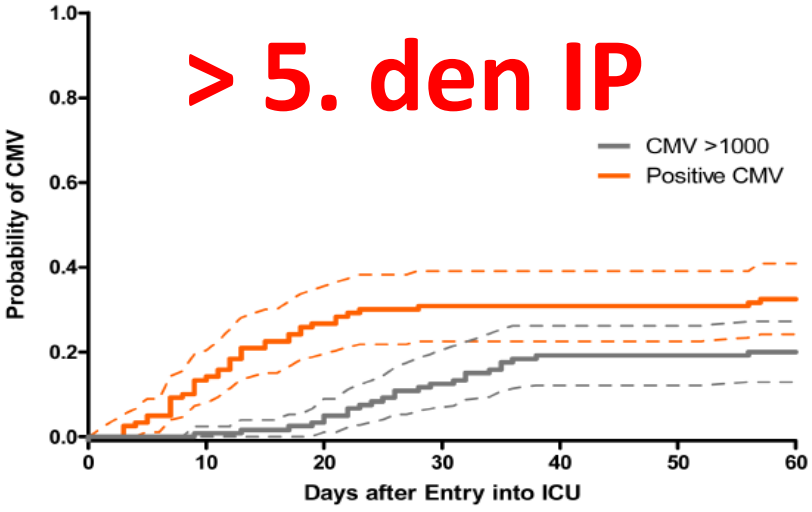
Kalil A. Crit Care 2011

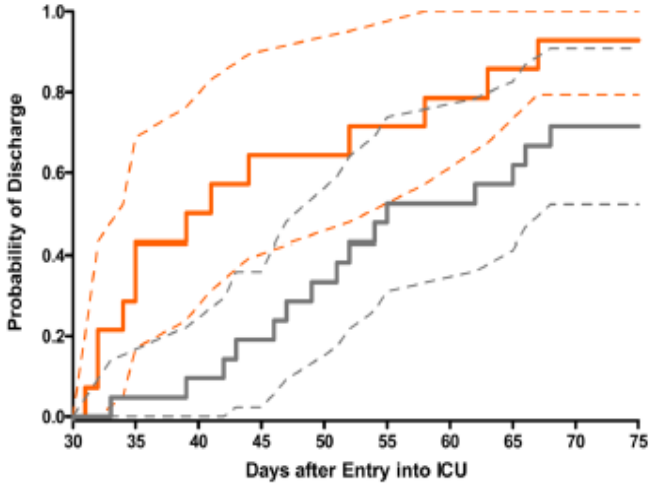
CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

EPIDEMIOLOGIE



> 5. den IP





JAMA. 2008 July 23; 300(4): 413–422. doi:10.1001/jama.300.4.413.

Cytomegalovirus Reactivation in Critically-Ill Immunocompetent Patients

Ajit P. Limaye, M.D.[1,2], Katharine A. Kirby, M.Sc.[6,7], Gordon D. Rubenfeld, M.D.[2], Wendy M. Leisenring, Sc.D.[3,6,7], Eileen M. Bulger, M.D.[4], Margaret J. Neff, M.D.[2], Nicole S. Gibran, M.D.[4], Meei-Li Huang, Ph.D.[1,5,7], Tracy K. Santo, B.Sc.[1], Lawrence Corey, M.D.[1,2,5,7], and Michael Boeckh, M.D.[2,5,7]

CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

RIZIKOVÉ FAKTORY

silná asociace	imunokompromitace	Florescu DS. Infect Disord Drug Targets 2011
	UPV	Limaye AP. JAMA 2008; Osawa R. Crit Care 2009
	sepse	Osawa R. Crit Care 2009; Kalil A. Crit Care 2011
slabá asociace	kortikosteroidy	Cook CH. Crit Care Med 2003
	krevní deriváty/transfuze	Cook CH. Crit Care Med 2003; Jaber S. Chest 2005; Limaye AP. JAMA 2008
	stres	Prosch S. Virology 2000
žádná asociace	věk (& pohlaví)	Osawa R. Crit Care 2009
	aktivní malignita	Heininger A. Crit Care Med 2001; Jaber S. Chest 2005; Ziemann M. Crit Care Med 2008
	tíže onemocnění (skore)	Domart Y. Chest 1990; Kutza A. Clin Infect Dis 1998; Heininger A. Crit Care Med 2001; Cook CH. Crit Care Med 2003; Jaber S. Chest 2005; von Muller L. Emerg Infect Dis 2006; Limaye AP. JAMA 2008

CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

KLINICKÁ MANIFESTACE

CMV reaktivace/replikace vs. CMV nemoc

- **nespecifické symptomy & víceorgánové postižení (≈10%)** (Heininger A. Crit Care Med 2001)

- **GIT:** hepatitida, gastroenteritida, kolitida
- **CNS:** meningo-/encefalo-/myelitida
- **hematol. systém:** hemolytická anémie, trombocytopenie, neutropenie, DIC, trombotické komplikace/PE
- **plíce:** pneumonie/pneumonitida – **raritně?**
- **srdce:** myokarditida - raritně

CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

KLINICKÁ MANIFESTACE

Intensive Care Med (2016) 42:333–341
DOI 10.1007/s00134-015-4071-z

ORIGINAL

David S. Y. Ong
Cristian Spitoni
Peter M. C. Klein Klouwenberg
Frans M. Verduyn Lunel
Jos F. Frencken
Marcus J. Schultz
Tom van der Poll
Jozef Kesecioglu
Marc J. M. Bonten
Olaf L. Cremer

Cytomegalovirus reactivation and mortality in patients with acute respiratory distress syndrome

27%

Table 1 Characteristics of ARDS patients by CMV reactivation status

	Reactivation (n = 74)	Non-reactivation (n = 197)	p value
Patient characteristics			
Age (years)	64 (56–74)	64 (54–72)	0.50
Male gender	44 (59)	120 (61)	0.83
Non-European descent	13 (18)	27 (14)	0.42
Prior ICU admission during hospital stay	16 (22)	24 (12)	0.05
Surgical reason for admission	22 (30)	73 (37)	0.26
COPD	13 (18)	30 (15)	0.64
Congestive heart failure	2 (3)	9 (5)	0.49
Diabetes mellitus	14 (19)	26 (13)	0.24
Cancer	9 (12)	28 (14)	0.66
Renal insufficiency	12 (16)	11 (6)	<0.01

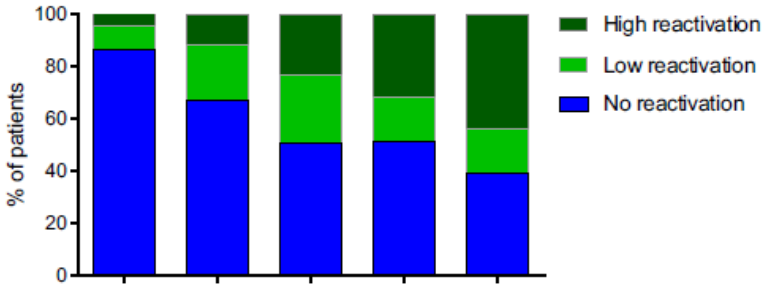


Table 2 Crude clinical outcomes of ARDS patients by CMV reactivation status

	Reactivation	Non-reactivation	p value
Death on ventilator before day 30[a]	23/74 (31)	29/197 (15)	<0.01
Death in ICU[b]	26/76 (34)	32/195 (16)	<0.01
Death by day 90[b]	35/76 (46)	55/195 (28)	<0.01
Duration of mechanical ventilation (days)	15 (10–26)	8 (6–12)	<0.01
Length of stay in ICU (days)	16 (11–28)	9 (7–14)	<0.01

CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

DIAGNOSTIKA

Diagnostic method	Advantages	Disadvantages
Anti-CMV immunoglobulins	Might be used for screening for latent CMV infection	Low sensitivity and specificity for active infection
CMV PCR assays	High sensitivity and specificity and considered gold standard, quick easy to perform, gives information of viral load, can be used for wide variety of samples	Better to be performed on whole blood, qualitative might be so sensitive and detect "innocent viral shedding" quantitative might be superior
CMV antigen assays	Quick and easy to perform, has comparable sensitivity and specificity to PCR	Might be inferior to PCR in case of leukopenia
Viral culture	Highly specific, can be performed on wide variety of samples	Time-consuming, low sensitivity
Histopathology	Highly specific, confirm CMV disease and pathogenicity and invasiveness	Invasive, low sensitivity, liable to sampling error, needs skilled pathologist and so operator dependent

Al-Omari A et al. Ann Intensive Care 2016

QR-PCR CMV – DNAemie = zlatý stadard
…kopie DNA/ml resp. IU/ml

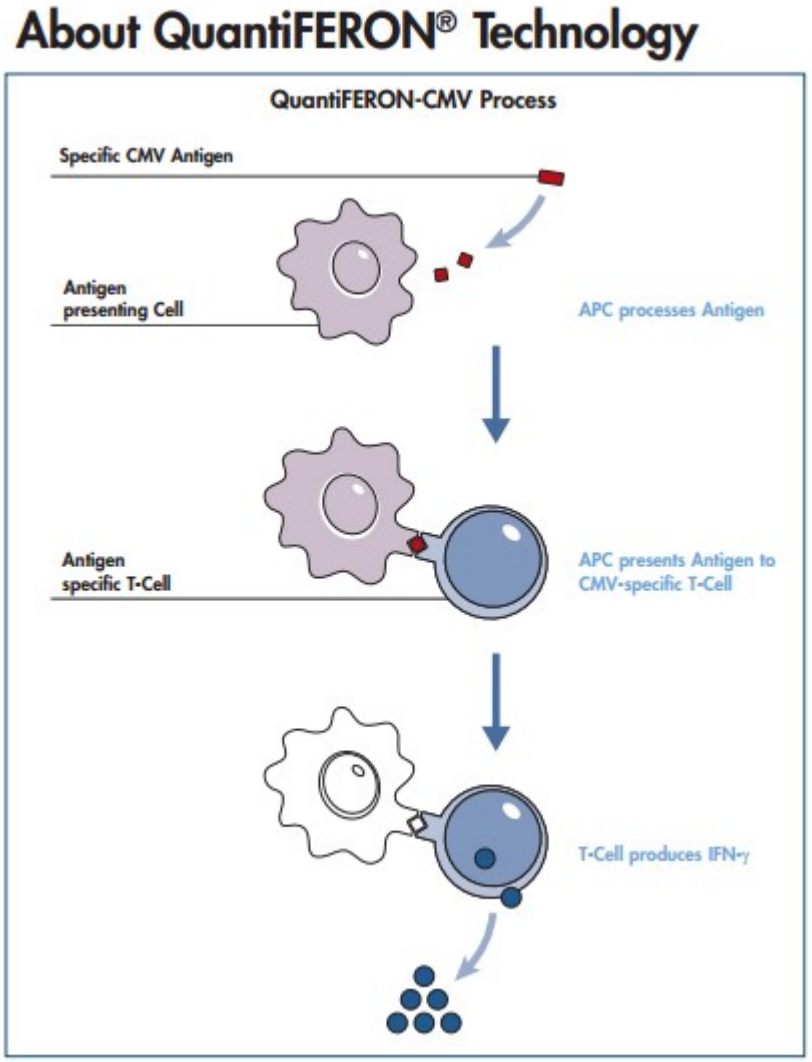
whole blood PCR CMV vs. BAL PCR CMV vs. histology

CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

DIAGNOSTIKA

INF-γ CD8⁺ TC assay (QuantiFERON© – CMV)

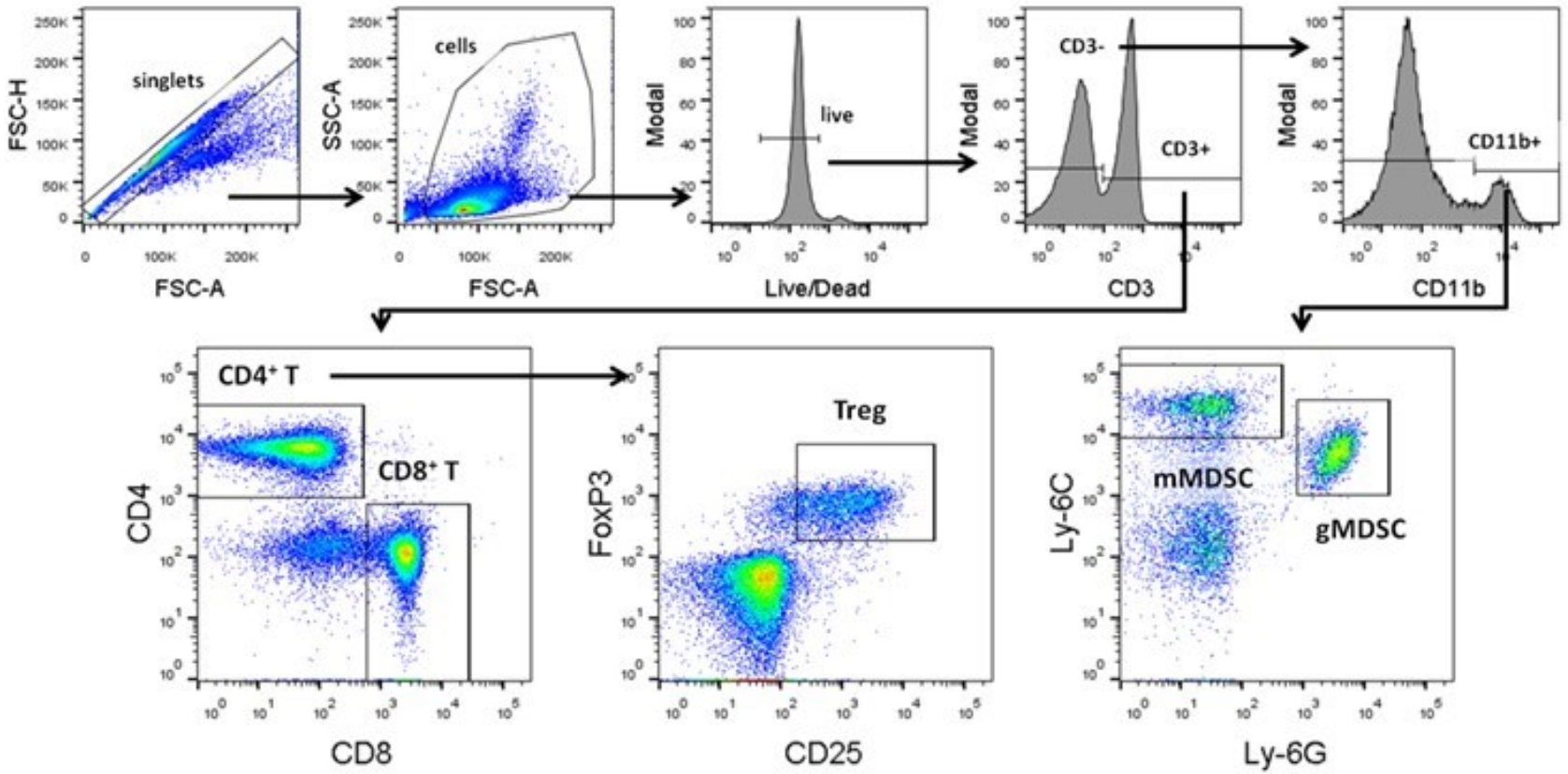
- ↑↑ NPV
- screeningový test



Castón JJ et al. Intensive Care Med 2016

CMV: KRITICKY NEMOCNÝ
„IMUNOKOMPETENTNÍ“ JEDINEC
DIAGNOSTIKA

flowcytometrický imunoscreening: CD4+, CD8+, CD4+/CD8+ ratio, NKC atd.



CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

LÉČBA

CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

LÉČBA

Agent	Mechanism of action	Common side effects
Ganciclovir	Competitively inhibits the binding of deoxyguanosine triphosphate to DNA polymerase resulting in inhibition of viral DNA synthesis	Thrombocytopenia, leukopenia, increased creatinine, fever, vomiting, diarrhea
Valganciclovir	Converted to ganciclovir in the body, much higher bioavailability of ganciclovir compared to oral ganciclovir	As ganciclovir
Foscarnet	Non-competitive inhibitor of many viral RNA and DNA polymerases	Electrolyte abnormalities, fever, vomiting, diarrhea, anemia, granulocytopenia, renal insufficiency, cardiotoxicity, central nervous system toxicity, hepatic toxicity
Cidofovir	Suppresses CMV replication by selective inhibition of viral DNA synthesis	Fever, alopecia, rash, ocular, renal, and gastrointestinal toxicity, cough, dyspnea

Al-Omari A et al. Ann Intensive Care 2016

Fomivirsin	HIV	Randomized trial	124	Treatment[C]	Injections only
Leflunomide	HCT, SOT	Uncontrolled case series	105	Salvage treatment	Hepatotoxicity; hematotoxicity; immunosuppression; increased fetal death or teratogenic effects[A]
Investigational					
Maribavir	HCT, SOT	Not effective at low doses; phase III trials ongoing	101, 102	Prophylaxis; salvage treatment[D]	Full spectrum unknown to date; taste disturbance
CMX001[F]	HCT	Phase II trials ongoing	99	Prophylaxis; treatment	Full spectrum unknown to date
AIC246	HCT	Phase II trials ongoing	100	Prophylaxis	Full spectrum unknown to date

Boeckh M et al. J Clin Invest 2011

CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

LÉČBA

(**PREVENTIVNÍ/PROFYLAKTICKÁ LÉČBA:** high-risk pacienti (SOP, BMT, IS atd.))

PREEMPTIVNÍ LÉČBA: signif. zn. virové replikace + klinická situace

CÍLENÁ LÉČBA: sign. zn. virové replikace + klinická situace + orgánové postižení

CMV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

LÉČBA

seropozitivita
(anti-CMV IgG)

long-term ICU pacient (>1w)
non-resolving systémová infekce/pneumonie
nozokomiální infekce
non-resolving/progredující orgánové postižení

CMV DNAemie
(whole blood QR-PCR)

BAL viral load
(QR-PCR)

INF-γ CD8⁺ TC assay
(QuantiFERON©–CMV)

signif. viral load/CMV-DNA resp. dynamika
(???kopie(IU)/ml)

pozitivní
(inhibice INF-γ)

léčba: preemptivní resp. cílená (orgánové poškození)
+ kontrola DNAemie/viral load á 1w

HSV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

- HSV-1 seroprevalence 50-70%

- ↓ incidence v IP (vs. CMV): 3% vs. 30% ARDS pts. (Papazian L. Crit Care Med 2007)
  2-30% (Simmons-Smit AM et al. Clin Microbiol Infect 2006)

- HSV tracheobronchitida
- HSV pneumonia (HSV reaktivace v hypofaryngu + aspirace do DCD)
- (Bruynseels P et al. Lancet 2003; Luyt C et al. Am J Resp Crit Care Med 2007)

- mortalita 0% - >50% (Simmons-Smit AM et al. Clin Microbiol Infect 2006)

- whole blood PCR HSV
- BAL PCR HSV

- aciclovir/valaciclovir

„HSV-1 viral loads in respiratory symptoms are a symptom of a clinically poor condition rather than a cause of it!“
(Scheithauser S et al., Infection 2010)

EBV: KRITICKY NEMOCNÝ „IMUNOKOMPETENTNÍ“ JEDINEC

- seroprevalence >95%: anti-EBV IgG
- chronická aktivní EBV infekce asoc. s **lymfoproliferativním onemocněním a hemofagocytární lymfohistiocytózou**

- **synergie EBV + CMV (+ HSV)**; současná reaktivace
- CMV modulace imunitní odpovědi na EBV
- periodická reaktivace EBV

(Arcenas R et al. BMC Microbiol 2002; Manes R et al. J Infect Dis 1997; Aalto SM J Med Virol 1998; Khan N et al. J Immunol 2004)

- EBV reaktivace/replikace = marker imunoalterace

- asociace s LOS, délkou UPV…morbiditou/mortalitou (Libert N et al. Biomed J 2015)

- whole blood PCR EBV
- BAL PCR EBV

- **léčba?**
- aciclovir; aciclovir + ganciclovir; ganciclovir + foscarnet (Rafailidis PI et al. J Clin Virol 2010)

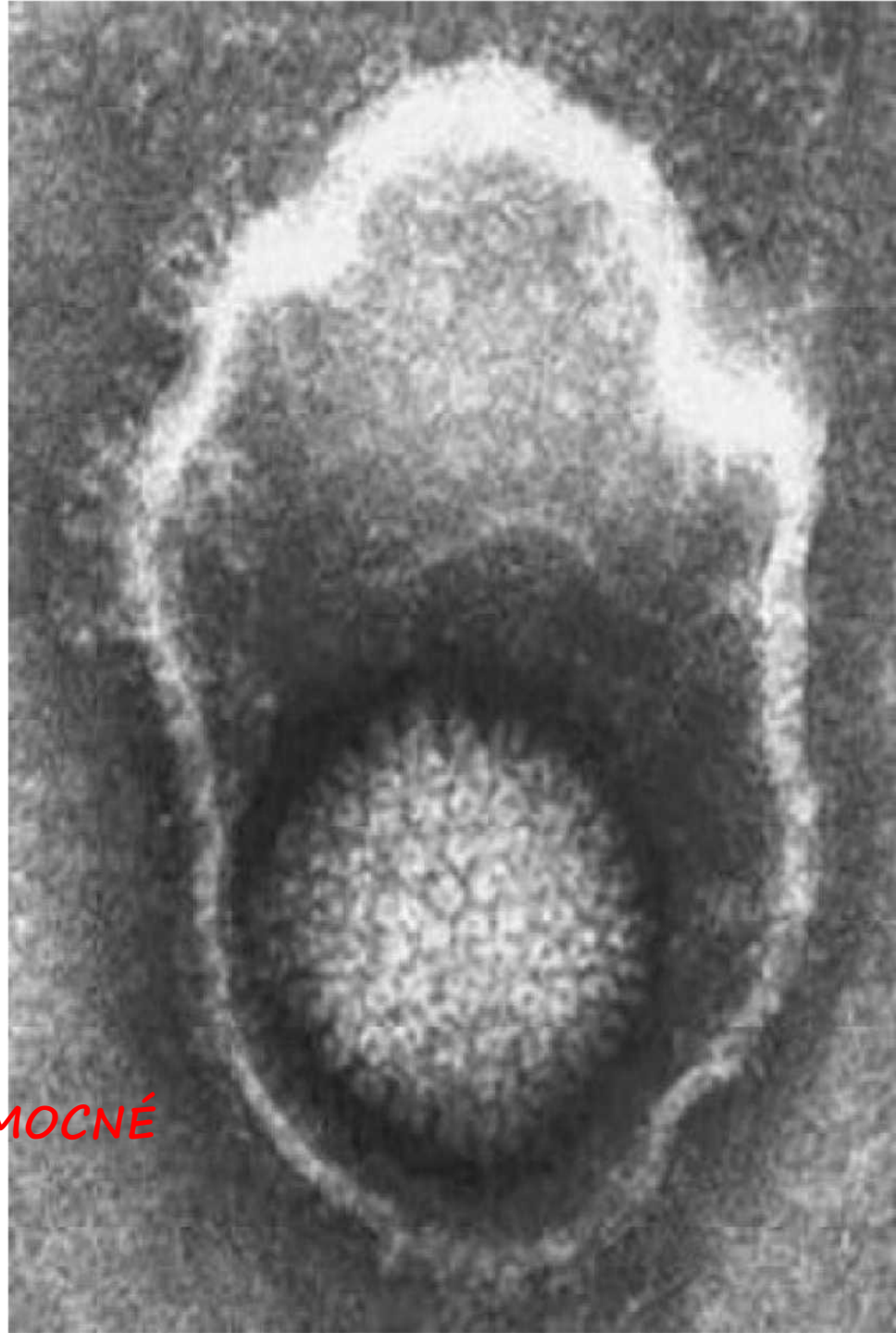
VIROVÉ REAKTIVACE U KRITICKY NEMOCNÝCH

- **frekventní problém vybrané skupiny nemocných v IP**
- **marker imunoalterace + potentní imunomodulace/imunosuprese**

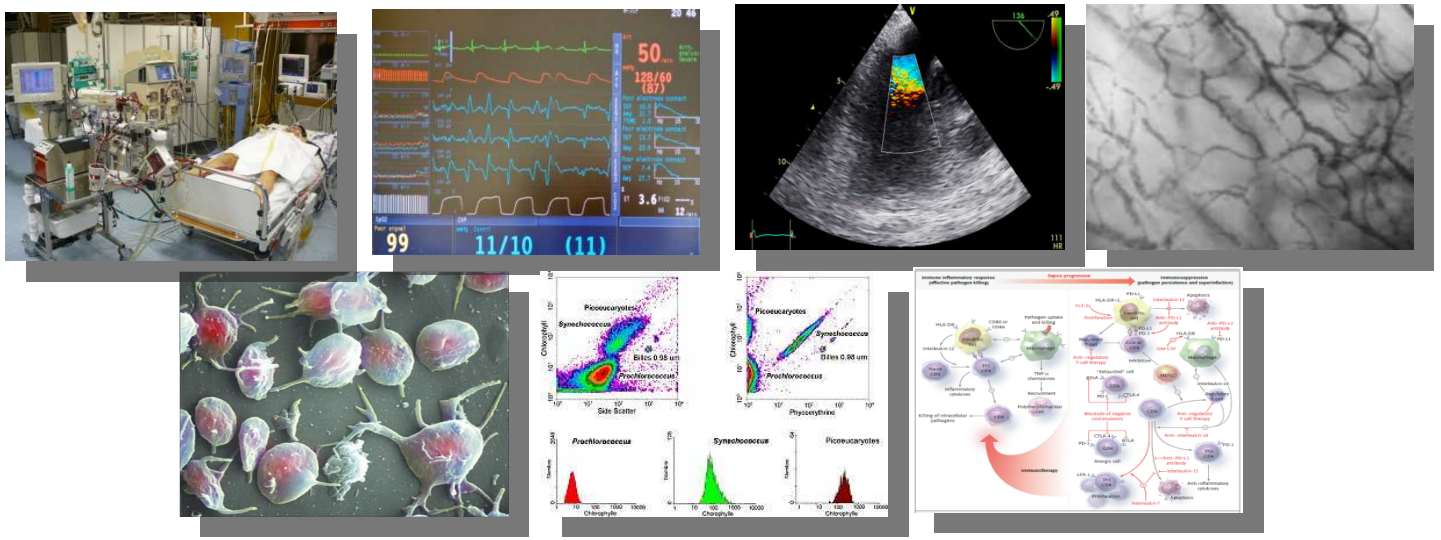
1. DIAGNOSTIKOVAT

2. LÉČIT NEBO ~~IGNOROVAT~~?

VYBRANÉ (RIZIKOVÉ) NEMOCNÉ



DĚKUJI ZA POZORNOST…



Podpora: Program rozvoje vědních oborů Univerzity Karlovy (PRVOUK – projekt P36); MZ ČR – RVO (Fakultní nemocnice Plzeň – FNPl, 00669806); CZ.1.05/2.1.00/03.0076 Evropský fond pro regionální rozvoj (Biomedicínské centrum LF Plzeň, Univerzita Karlova)