Launch of
AdV Diagnostics Working Group

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Reviews in Medical Virology
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Management of adenovirus infection in patients after haematopoietic stem cell transplantation: state-of-the-art and real-life current approach

A position statement on behalf of the Infectious Diseases Working Party of the European Society of Blood and Marrow Transplantation

Hiwarkar P, Kosulin K, Cesaro S, Mikulska M, Styczynski J, Wynn R, Lion T

Diagnostic screening and monitoring in the allo-HSCT setting

PERIPHERAL BLOOD

HAdV monitoring in peripheral blood at least 1x/week
in pediatric patient (A II)/in adult patients (B III)

Monitoring of HAdV levels 2x/week
in patients testing positive for HAdV in peripheral blood (A II)

Monitoring of HAdV levels 1-2x/week
in patients with viremia undergoing antiviral treatment (A II)

Diagnostic screening and monitoring in the allo-HSCT setting

STOOL

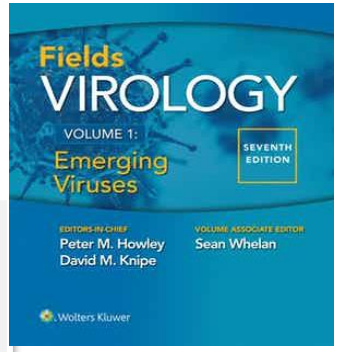
Screening for HAdV in stool specimens 1x/week
in pediatric patients (A II)/in adult patients, no recommendation

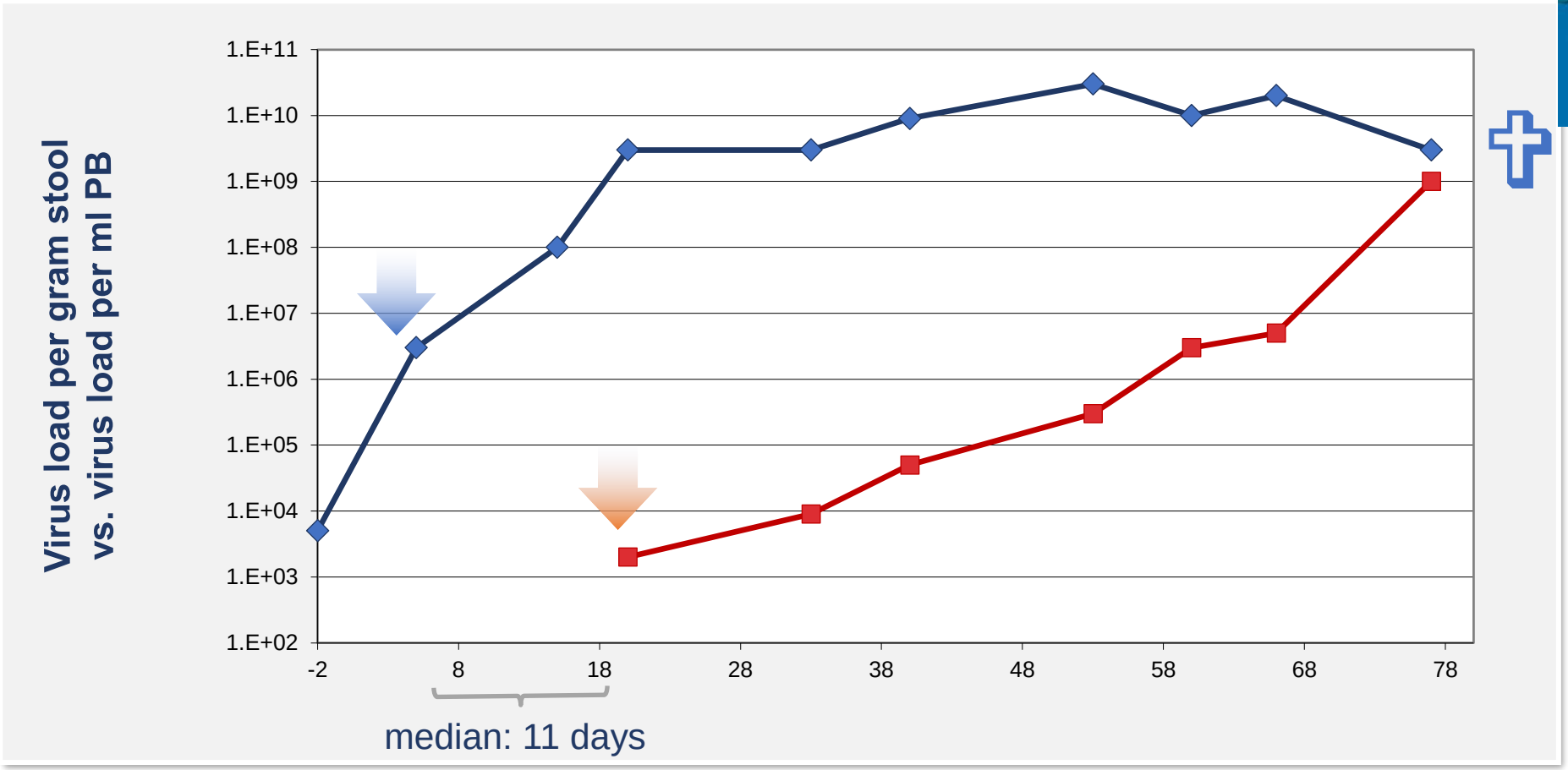
Monitoring of HAdV levels in stool 1-2x/week
in the presence of virus levels in stool above the critical threshold, in the absence of viremia, in pediatric patients receiving preemptive anti-HAdV treatment (A III)

Screening for HAdV shedding into the stool
on at least two different days 1-2 weeks prior to conditioning
in pediatric patients (B II)/in adult patients, no recommendation

Intestinal HAdV Infection and Virus Expansion Precede Viremia

Lion T, et al. *Leukemia.* 2010;24(4):706-714; Lion T. *Fields Virology, 7th Edition,* 2022





Confirmed by : Jeulin H, et al. *Clin Microbiol Infect.* 2011,17(11):1674-1680

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Recommendations for anti-adenoviral treatment

- Tapering of immunosuppression, whenever possible
- Preemptive antiviral therapy (Cidofovir: 1mg/kg 3x per week)

in the presence of

Viremia >1000 HAdV copies/µl (AII)
(in lymphopenic pts with circulating CD3+ T-cells < 25/µl)

HAdV positivity in stool with repidly rising levels above the critical threshold (BII)

Human Adenoviruses: a Steadily Growing Family

Double-stranded DNA-Virus **Genome size: ~36 kb**

7 species (subgenera): A-G	
Species	**Types (serotyping/computational analysis)**
A	12, 18, 31, 61
B	3, 7, 11, 14, 16, 21, 34, 35, 50, 55, 66, 68, 76-79. 106
C	1, 2, 5, 6, 57, 89, 104, 108
D	8-10, 13, 15, 17, 19, 20, 22-30, 32, 33, 36-39, 42-49, 51, 53, 54, 56, 58, 59, 60, 63, 64, 65, 67, 69-75, 80-88, 90-103, 105, 107, 109-113
E	4
F	40, 41
G	52

Most newly identified HAdV types resulted from homologous recombination events

intraspecies ⟷ interspecies recombination

Deghan S, et al. *Virology.* 2013;443:197-207; Lion T. *Clin Microbiol Rev.* 2014;27(3):441-462.97-207*; Lion T. Clin Microbiol Rev. 2014,27(3):441-62*

Comparative Study > J Clin Virol. 2016 Dec;85:31-36. doi: 10.1016/j.jcv.2016.10.021.
Epub 2016 Nov 1.

Comparison of different approaches to quantitative adenovirus detection in stool specimens of hematopoietic stem cell transplant recipients

K Kosulin [1], S Dworzak [1], A Lawitschka [2], S Matthes-Leodolter [2], T Lion [3]

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Conclusions: The differences in quantitative analysis of adenovirus copy numbers between the systems tested were primarily attributable to the DNA extraction method used, while the qPCR assays revealed a high level of concordance. Both systems showed adequate performance for detection and monitoring of adenoviral load in stool specimens.

ddPCR ? ⟷ Basis for harmonized diagnostics? ⟷ Internal standards?

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