

### 5.3 Further Reading

Buja LM. HHV-6 in Cardiovascular Pathology. Chapter 18 in Krueger GRF, Ablashi DV (eds.) Human Herpesvirus-6, 2nd. edition. Elsevier Science Publ, Amsterdam-London 2006

Fukae S, Ashizawa N, Morikawa S, Yano K. A fatal fulminant myocarditis with human herpesvirus-6 infection. Intern Med 39: 632-636, 2000

De Ona M, Melon S, Rodriguez JL, Sanmartin JC, Bernardo MJ. Association between human herpesvirus type 6 and type 7, and cytomegalovirus disease in heart transplant recipients. Transplant Proc 34: 75-76, 2002

## 6. RESPIRATORY SYSTEM

### 6.1 Introduction

Salivary glands and the respiratory system appear to constitute primary targets for HHV-6 infection and persistence, yet HHV-6 associated diseases in these tissues are rather rare in immunocompetent persons. A summary of HHV-6 associated disorders in the respiratory system is presented in **Table 3**. A comprehensive review of such diseases was recently prepared by Sebastian Schmidt and colleagues (2006).

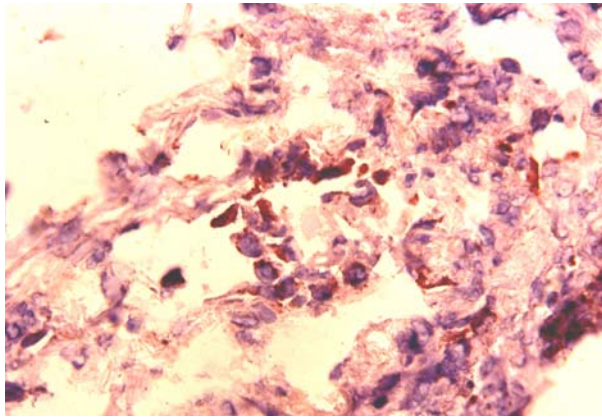
Pathologic Entity	Patient	Immune Status	HHV-6 Testing
Rhinopharyngitis	children	nl	serology
katarrheic tracheobronchitis	children	nl	serology
obstructive bronchiolitis	children	nl	serology
interstitial pneumonitis NIP	children, adults	nl, AIDS, post-transplant	serology, IHC, ISH, PCR
interstitial pneumonitis LIP	adults	AIDS	serology, IHC, ISH, PCR
dual infection pneumonitis	adult	immune deficient	serology, IHC, ISH, PCR

**Table 3:** Rare cases of respiratory diseases caused by HHV-6 infections. The first 3 entities in children may accompany exanthema subitum. Most other cases occur in some kind of immune deficiency including AIDS and transplant recipients. Dual infections in the latter patients consist of reactivated HHV-6 plus pneumocystis carinii, Legionella

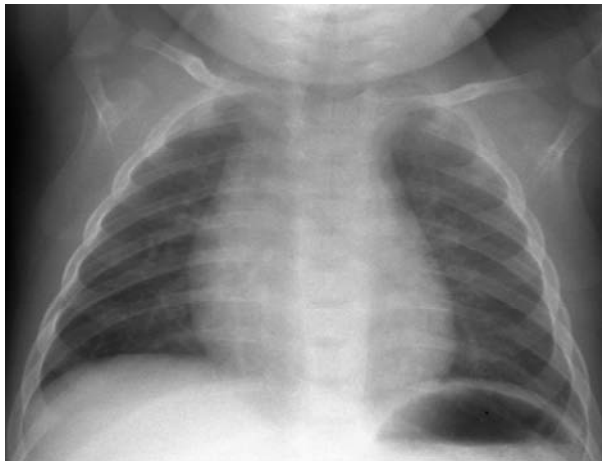
pneumophila, human cytomegalovirus or adenovirus infections. Abbreviations: nl = normal; IHC — immunohistochemistry (HHV-6 p41 antigen); ISH = in situ hybridization; PCR = polymerase chain reaction.

We have observed two patients with classical bronchioloalveolar cell carcinoma, in which tumor cells focally contained HHV-6 antigens (figure). Other adenocarcinomas, small cell carcinomas or squamous cell carcinomas were negative. The observation may further support the notion that pneumocytes or terminal bronchus cells are infectable by HHV-6, yet does not imply a causal relationship between tumor and HHV-6.

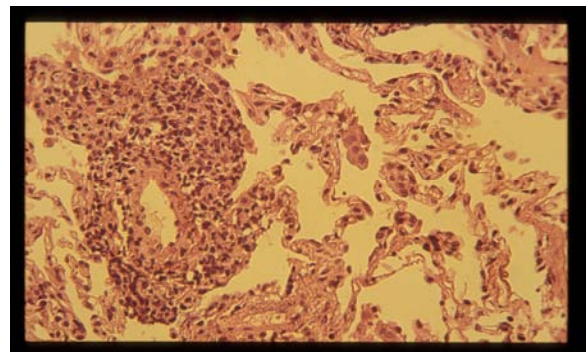
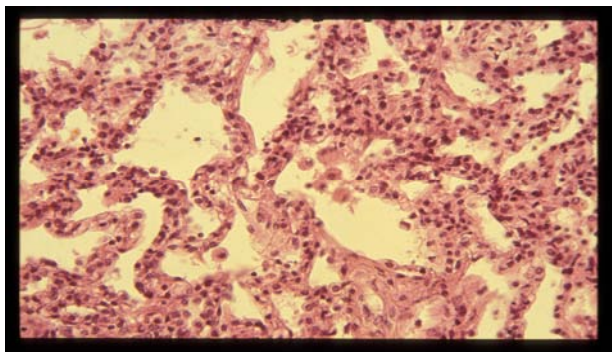
6.2 Figures



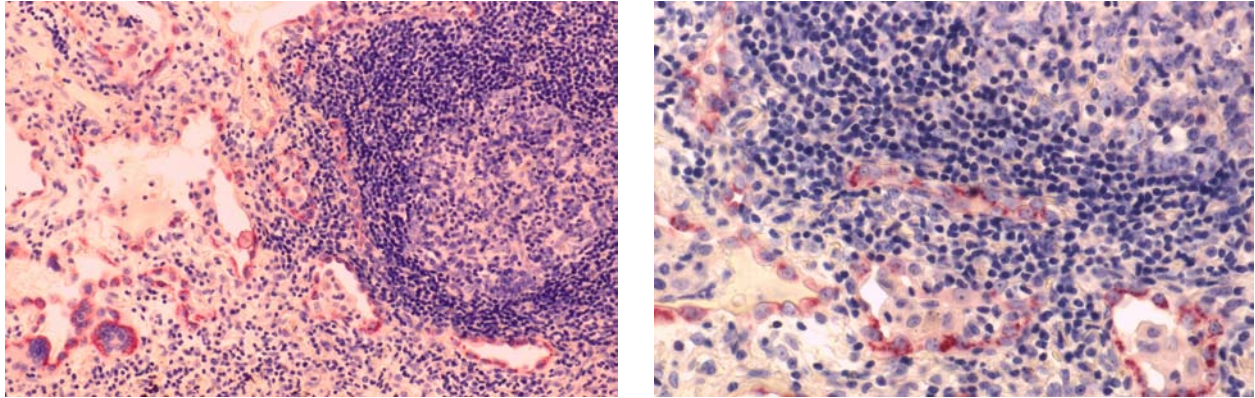
Immunohistochemistry for HHV-6 p41 on frozen section of lung biopsy



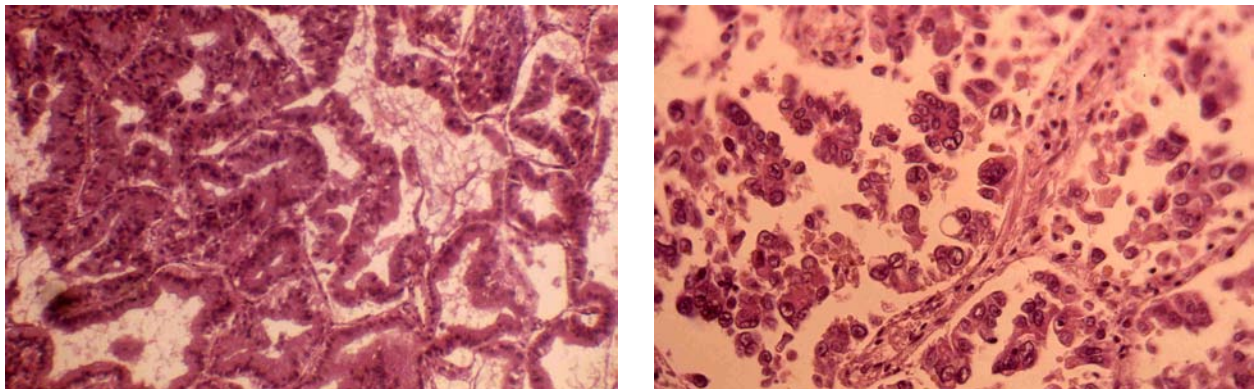
X-ray (left) and gross lung (right) of patient with interstitial pneumonia following bone marrow transplant and HHV-6 reactivation.



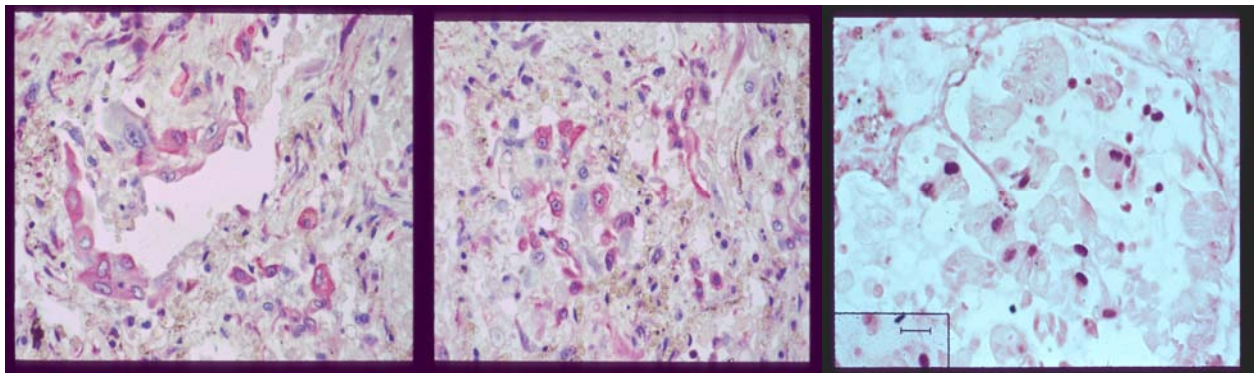
Non-specific interstitial pneumonitis (NSIP) following HHV-6 reactivation



Immunohistochemistry of HHV-6 positive cells (red) and lymphoid interstitial pneumonitis (LIP) in a patient with AIDS and HHV-6 reactivation.



Two cases of alveolar cell carcinoma of the lung in patients with HHV-6 reactivation



Immunohistochemistry (left & center) and in situ hybridization (right) for HHV-6 antigen and DNA (pZVH14) in atypical pneumocytes of alveolar cell carcinoma.

NOTE: replication of reactivated HHV-6 is probably supported by atypical pneumocytes rather than causing the cancer *per se*

### 6.3 Further Reading :

Schmidt SM, Wiersbitzky H, Wiersbitzky SKW. HHV-6 and the Respiratory System. Chapter 13 in Krueger GRF, Ablashi DV (eds.) Human Herpesvirus-6, 2nd. edition. Elsevier Science Publ, Amsterdam-London 2006

Krueger GR, Wassermann K, De Clerck LS, Stevens WJ, Bourgeois N, Ablashi DV, Josephs SF, Balachandran N. Latent herpesvirus-6 in salivary and bronchial glands. Lancet 336:1255-1256, 1990

Cone RW. Human herpesvirus 6 as a possible cause of pneumonias. Semin Respir Infect 10: 254-258, 1995

Nagate A, Ohyashiki JH, Kasuga I, Minemura K, Abe K, Yamamoto K, Ohyashiki K. Detection and quantification of human herpesvirus 6 genomes using bronchioloalveolar lavage fluid in immunocompromised patients with interstitial pneumonia. Int J Mol Med 8: 379-383,2001

Vuorinen T, Kotilainen P, Lautenschlager I, Kujari H, Krogerus L, Oksi J. Interstitial pneumonitis and coinfection of human herpesvirus 6 and pneumocystis carinii in a patient with hypogammaglobulinemia. J Clin Microbiol 42: 5415-5418, 2004