Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Recent Singapore SARS case a laboratory accident

The recent case of severe acute respiratory syndrome (SARS) in Singapore was the result of a laboratory accident, so concludes an 11-member review panel led by Antony Della-Porta, Biosafety Expert for the WHO, in a report produced for the Ministry of Health in Singapore. Authorities in Singapore have continued surveillance for SARS since the last reported case in May 2003 and became alarmed when, at the end of August, a 27-year-old doctoral student at the Singapore General Hospital (SGH) developed symptoms consistent with SARS.

The student was working on West Nile virus samples at the BSL-3 laboratory, SGH 3·5 days before onset of illness, a time consistent with the SARS incubation period. Although no SARS work was being done that day, live SARS was definitely in the laboratory 2 days earlier. Stool and sputum samples tested for SARS coronavirus using reverse transcriptase polymerase chain reaction were positive and SARS infection was confirmed by the US Centers for Disease Control and Prevention. The frozen specimen that the student had worked on was positive for both the SARS coronavirus and West Nile virus, suggesting contamination.

The panel concluded that "inappropriate laboratory standards and a cross-contamination of West Nile virus samples with SARS coronavirus in the laboratory led to the infection of the doctoral student". Their investigation showed that because Department of Pathology BSL-2 laboratories were being renovated, mixed BSL-2/BSL-3 activities were in progress in the BSL-3 facility, which jeopardised good safety practices. Deficiencies were identified at other BSL-3 laboratories and the report recommends that BSL-3 work in Singapore cease until these have been addressed. "The report of the review panel indicates both structural and functional deficiencies in Singapore's BSL-3 facilities", comments Paul McKinney, Professor of Medicine and Public Health at the Center for the Deterrence of Biowarfare and Bioterrorism (University of Louisville, KY, USA). Of the two factors, practices are more important; BSL-3-level procedures should provide a sufficient margin of safety in handling the SARS virus. "There is a need for more precisely defined and internationally applicable standards to govern operations at such laboratories", he says. James Snyder, Professor of Microbiology at the same institute, agrees and stresses that "it is essential that laboratories in all countries achieve and maintain laboratory certification standards". Consideration should also be given to certification of personnel, which should involve periodic written and direct observation-based examinations, Snyder adds.

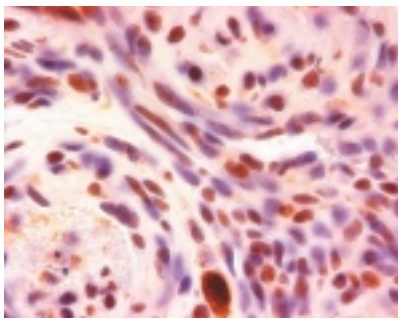
Kathryn Senior

HHV8 implicated in pulmonary hypertension

Human herpes virus 8 (HHV8), the virus thought to cause Kaposi's sarcoma, has been linked to primary pulmonary hypertension (PPH) *(N Engl J Med* 2003; **349:** 1113–21*)*.

Pulmonary hypertension arises in several diseases, all characterised by complex endothelial lesions that occlude the pulmonary blood vessels—a condition that frequently results in lung transplantation. Until now, HIV-1 was the only virus associated with PPH, since it occurs in AIDS patients. However, no trace of the virus has ever been seen in lung lesions.

"We thought HHV8 might be involved because HIV/AIDS patients often suffer severe PPH, because HIV patients are often infected with HHV8, because the virus was detected in two patients with HHV8-associated Castleman's disease with PPH, and because PPH patients show signs of infection: their inflammatory cytokine levels are up and their plexiform lesions contain both B and T cells", explains Norbert Voelkel (University of Colorado Health Sciences Center, Denver, CO, USA).



Carlyne Cool

Nuclear staining of cells in a PPH lesion

Voelkel's team took lung samples from 16 patients with PPH, and from 14 with secondary—ie, a complication of another disease—pulmonary hypertension (SPH), and tested for HHV8. Says team member Carlyne Cool, "We used an antibody to look for latency-associated nuclear antigen [LANA-1]—an HHV8 infection giveaway—and it turned up in the pulmonary vascular endothelial cells, the bronchoepithelial cells, lymphocytes, and macrophages of ten of the 16 PPH patients. However, neither the SPH patients nor the controls showed any sign of it". PCR also showed the ten positive patients to have the viral cyclin gene integrated into their DNA. "Moreover, under the microscope, the lung lesions had many histological similarities to Kaposi skin tumours, where we know you find HHV8", explains Cool.

But does HHV8 cause PPH? "Most people who develop angioproliferative pulmonary hypertension are genetically susceptible to it", explains Voelkel. "HHV8 may trigger the condition, but maybe the condition increases the risk of HHV8 infection."

Martin Blaser (New York University School of Medicine, NY, USA) remarked, "Implication of HHV8 extends the paradigm of persisting microbes inducing illness in a subset of infected patients, and further suggests that antiviral agents may one day have a role in therapy for PPH".

Adrian Burton