

In Vitro and In Vivo Influenza-Inhibitory Effects of a Series of Polyoxometalates. R. W. Sidwell¹, J. H. Huffman¹, K. W. Bailey¹, A. Gessaman¹, M. J. Otto², C. Hill³ and R. F. Schinazi³. Inst. for Antiviral Res., Utah State Univ., Logan, UT 84322-5600¹; Avid Therapeutics, Inc., Philadelphia, PA 19104², and VA Medical Ctr./Emory Univ., Decatur, GA 30033³, USA.

A series of polyoxometalates were evaluated for their effects against influenza A (IV-A) and B (IV-B) viruses. Germanium or silicon-centered heteropolytungstates were particularly inhibitory to these viruses, the 50% effective concentrations (EC50) in vitro against IV-A (H1N1) and IV-B ranging from 0.025 to 0.2 µg/ml; against IV-A (H3N2), the EC50 concentrations were approximately 10-fold higher. These experiments used inhibition of viral cytopathic effect in MDCK cells, as determined microscopically and by neutral red uptake. Virus yield reduction studies indicated the EC90 concentrations to range from 0.2 to 3 µg/ml against these viruses. Fifty percent cytotoxic or cell inhibitory concentrations (IC50), determined by viable cell count using rapidly dividing cells, ranged from 17 to 189 µg/ml, indicating high selectivity indices for these compounds. Five of the most active polyoxometalates were studied against lethal IV-B infections in mice. Intraperitoneal treatments administered once daily for 5 days significantly prevented death and inhibited the usual decline in arterial oxygen saturation. Lung virus titers were lowered by these therapies only early in the virus infection. Dosages usually ranged from 2 to 20 mg/kg/day, and appeared well tolerated by the animals. [Supported by Contracts NO1-A1-15097, A1-35178, A1-32903 and the Veteran's Administration]

TREATMENT OF ATYPICAL HEMORRHAGIC FEVER WITH RENAL SYNDROME (KOREAN HEMORRHAGIC FEVER IN KOREA) WITH RIBAVIRIN: REPORT OF 10 CASES J. E. Smith*, J. W. Huggins**, J. D. Arthur**, B. J. Choi*, S. H. Yi*, R. S. Lofts**, C. Rossi**, M. P. Maninen*, M. J. Abele*, D. R. Hopenthal*, P. B. Kim*, M. R. Russo*, K. N. Chung*, G. E. Tomkins*, H. Kim* and D. Randall*. From the Departments of Pathology & Area Laboratory Services and Medicine, 121 General Hospital, Yongsan, Seoul, Korea. APO, AP 96205* and U.S. Army Medical Research Institute of Infectious Disease, Fort Detrick, MD**

Korean Hemorrhagic Fever (KHF) in Korea is clinically and serologically related to Epidemic Hemorrhagic Fever (EHF) in the People's Republic of China and to Nephropathia Epidemica (NE) in Europe. All of these diseases, collectively known as Hemorrhagic Fever with Renal Syndrome (HFRS) and caused by Hantaviruses, presents a geographic medical threat to deployed military personnel. Between 29 June 1994 and 30 November 1995 fourteen (14) patients with IgM ELISA Hantaan Positive HFRS (KHF) were admitted to the 121 General Hospital. Thirteen (13) patients, who are U.S. Army personnel, practiced maneuvers or worked in the same training area. There were 4 patients with mild disease, 8 patients with moderate disease and 2 patients with severe disease. One of the 14 patients had IgM ELISA Positive Hantaan serology and Vivax Malaria. One patient with severe disease died. All patients had atypical disease, both clinically and pathologically, to the classic presentation for HFRS (KHF) seen in Korea, China and Europe. Ten (10) of the 14 patients were treated with the Investigational New Drug for the treatment of HFRS, Ribavirin, under a Phase III clinical protocol. All patients who received Ribavirin, except for the one morbid on admission patient that died, skipped the hypotensive and oliguric phase of the disease and were discharged in 12 days or less. The only adverse side effect of Ribavirin was transient elevated amylase and lipase in 2 of the 7 patients tested. The clinical, laboratory and autopsy data from these cases will be presented.