

CDC Influenza Division

1918 Virus Research and Occupational Health Practices: A Perspective

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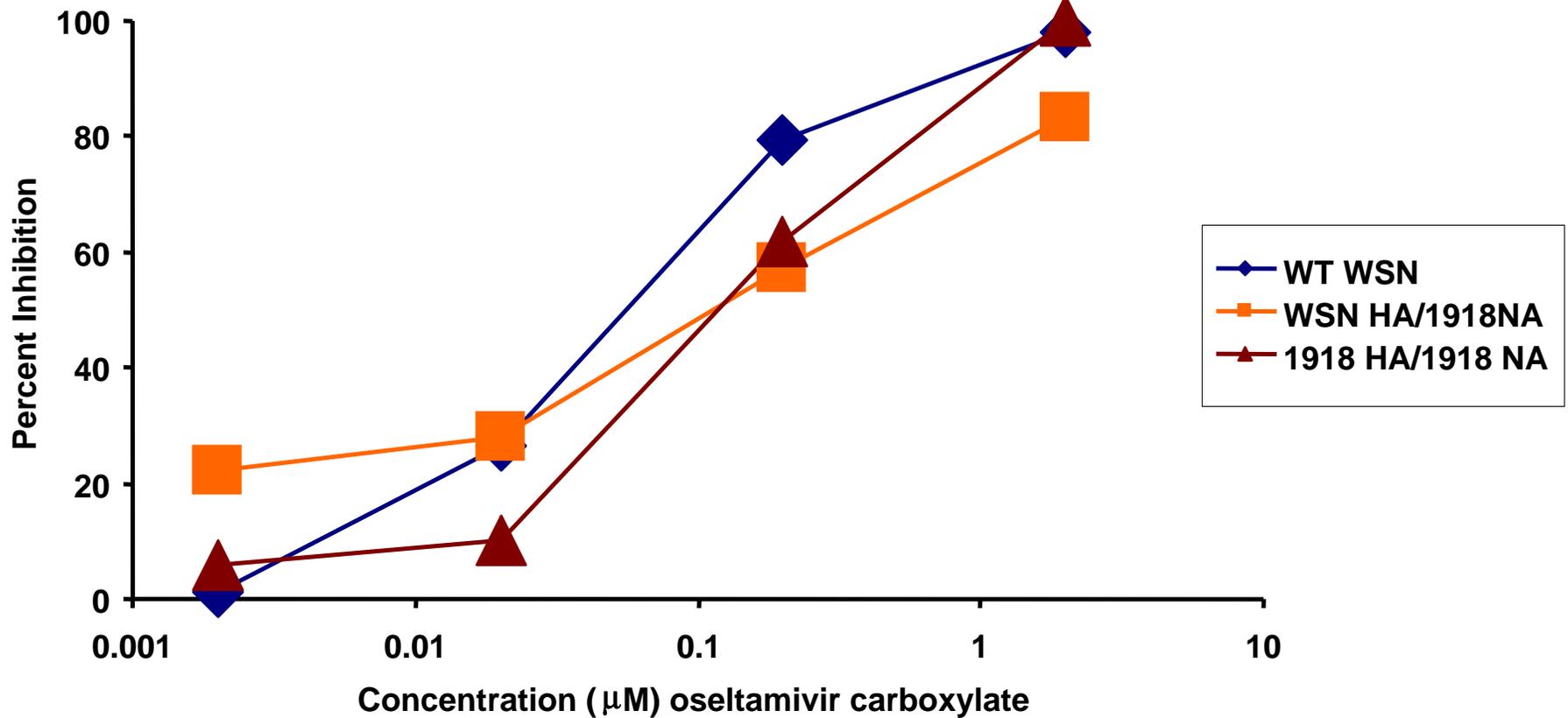


History of 1918 Virus Research at CDC - I

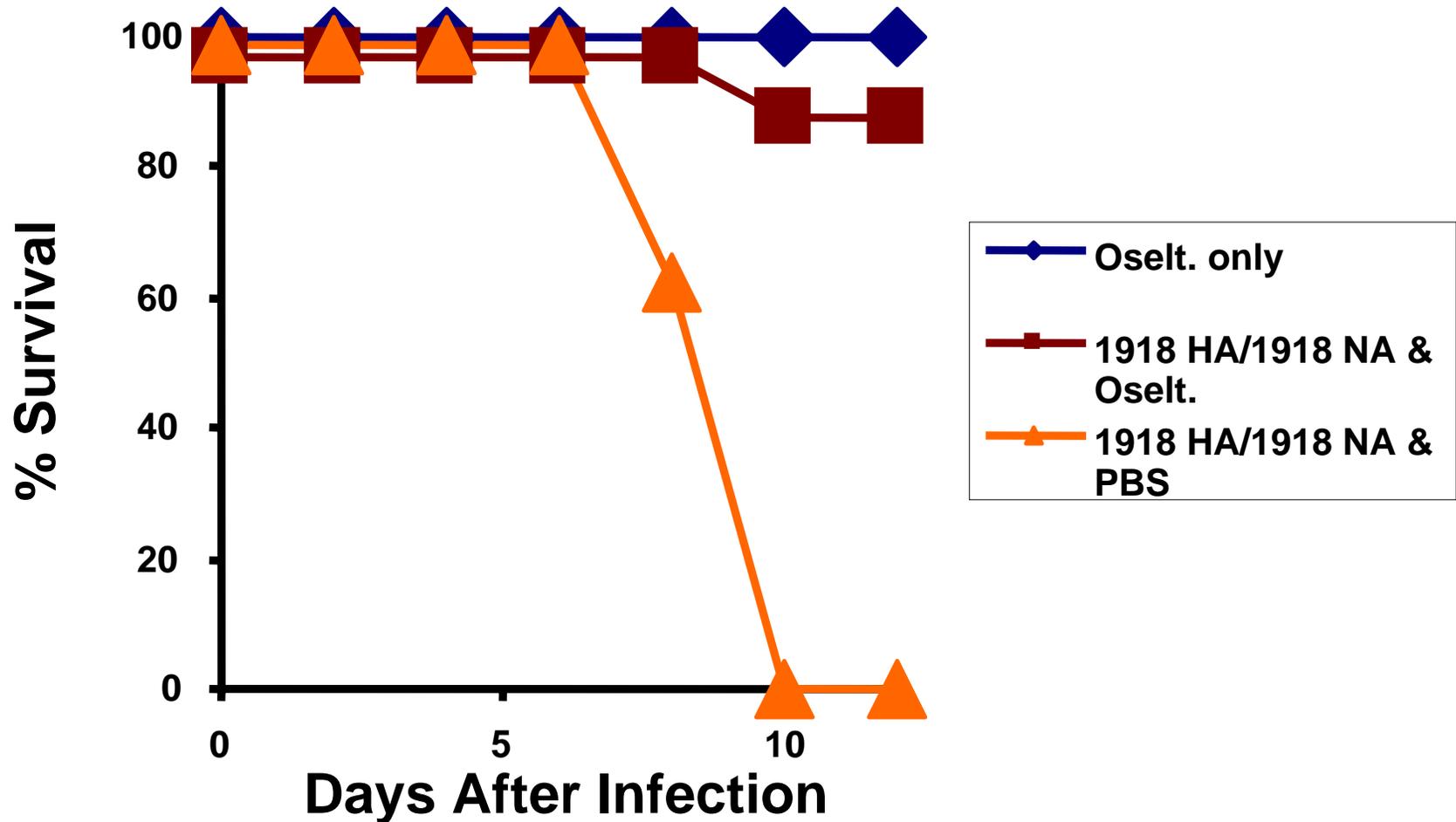
- **Prior to reconstruction of 1918 virus containing all 8 gene segments in 2005:**
 - **1918 gene sequence data indicated sensitivity to FDA licensed adamantane and NA inhibitor antiviral drugs**
 - **Extensive research on 1918 HANA and 1918 5 gene reassortants on a WSN backbone**
 - **Confirmed sensitivity of viruses containing relevant 1918 virus gene products**
 - **Provided data on partial cross-protection afforded by contemporary H1N1 virus vaccines in a murine model**
 - **Demonstrated a rise in HI antibody to Sw/Iowa/30 and 1918 recombinant virus in humans following vaccination with seasonal vaccine**
 - **Established virulence of viruses containing multiple 1918 virus genes in mice**



Inhibition of plaque formation by Oseltamivir carboxylate (GS4071)



Oseltamivir Protects Mice from a Lethal Challenge with 1918 HA/1918 NA Virus



Drug given (50 mg/kg of body weight) once daily for 6 days, beginning 24 h before intranasal infection with 10 LD₅₀ of virus

History of 1918 Virus Research at CDC-II

- Extensive risk assessment conducted by CDC Influenza Branch staff and the Office of the Chief Scientific Officer (CSO), CDC
- Goals were to provide protection of the individual worker, community, and CDC as a public health agency
 - Followed BMBL interim guidance for use of BSL-3 facilities, practices and procedures with enhancements for work with fully reconstructed 1918 virus
 - Defined specific occupational health and oversight requirements for work with fully reconstructed 1918 virus



CDC Occupational Health and Other Requirements for Work on Fully Reconstructed 1918 Virus

- Rigorous adherence to BSL-3 enhanced practices and procedures and:
 - Vaccination with seasonal trivalent inactivated influenza vaccine was *required*
 - Prophylaxis with Oseltamivir was *required*
 - Until a 1918 vaccine was developed
 - Daily temperature monitoring (later ILI) was *required*
 - Weekly reporting to the CDC CSO and others in chain of command on progress and any potential problems was *required*
 - Ongoing oversight and approval for progression of experiments was *required*
 - Detailed medical plan established in event of LAI
 - Developed real time RT-PCR primer set that could distinguish 1918 virus from contemporary H1N1 viruses

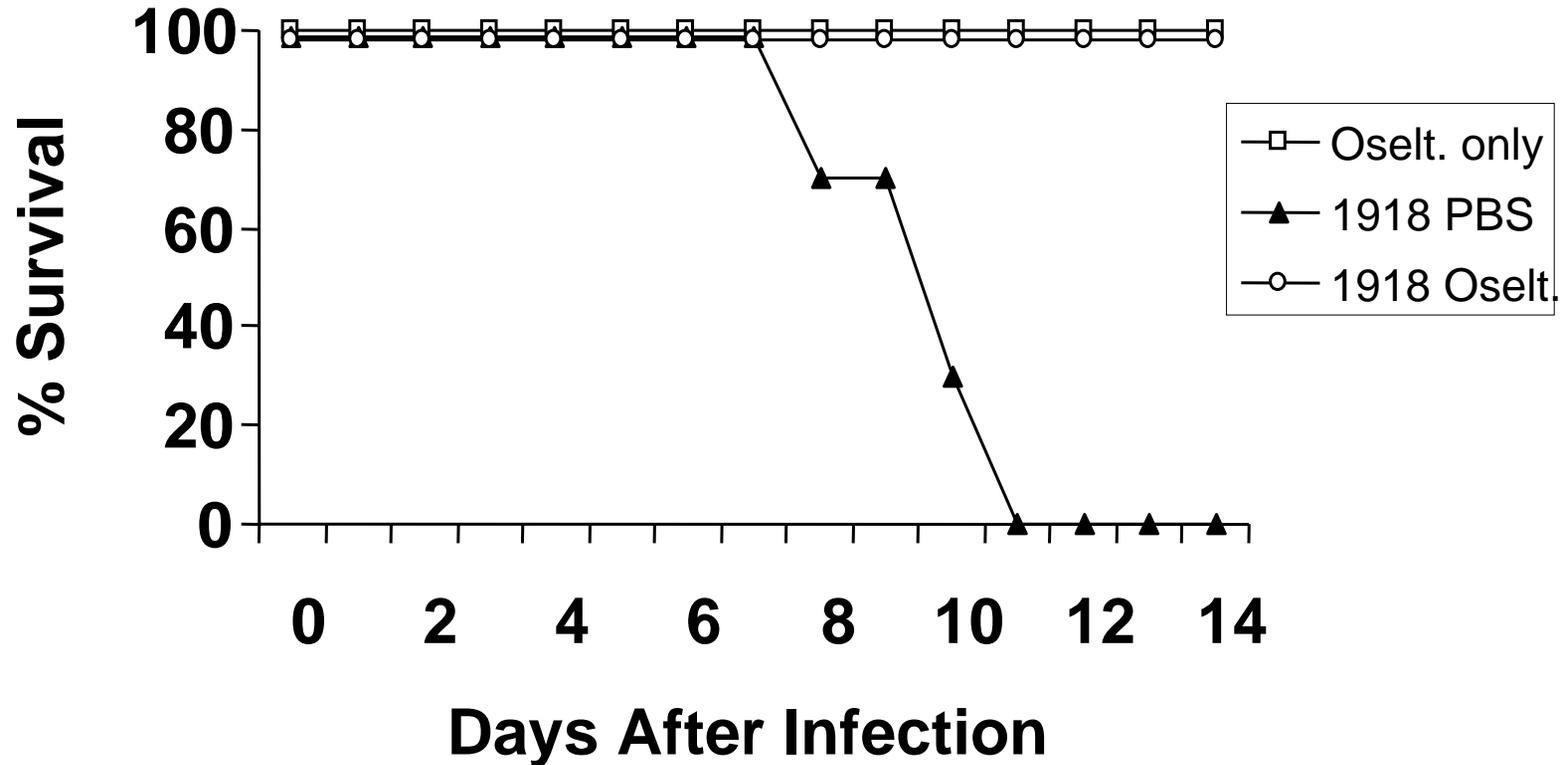


Influenza Division Early Experience with Worker Prophylaxis with Oseltamivir

- Work with fully reconstructed 1918 virus began in mid 2005
 - One worker conducted all studies
 - No animal husbandry technicians involved
 - Followed Oseltamivir (Tamiflu®) prophylaxis guidelines
 - One tablet (75 mg) daily starting one day before and for 7 days after laboratory work with virus
 - Longest single period on prophylaxis was 10 weeks
 - No adverse events noted
- In November, 2005 one additional experienced person worked with virus and was on prophylaxis for 8 weeks with no adverse events noted



Oseltamivir Protects Mice from a Lethal Challenge with all 8-gene 1918 Virus



Drug given (50 mg/kg of body weight) once daily for 6 days, beginning 24 h before intranasal infection with 10 LD₅₀ of virus

Influenza Division Experience with Oseltamivir Prophylaxis as of November, 2008

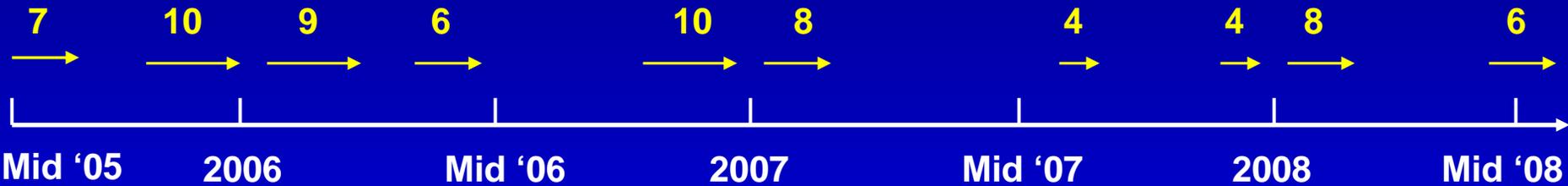
- A total of 7 trained individuals have worked with the fully reconstructed 1918 virus while on Oseltamivir prophylaxis
 - All had prior extensive (PhD level) virology and BSL-3 laboratory experience
 - All conducted self monitoring for ILI
 - 2 males, 5 females; 25-45 years of age
 - Longest time on prophylaxis was 12 weeks
 - 6 of 7 individuals have had repeated courses
 - Intervals between prophylaxis periods varied by nature and intensity of experimental work
 - Longest interval ~10 months
 - Shortest interval ~ 4 – 7 days
 - Adverse effects
 - Mild nausea, headache in one person
 - Daily “hot flash” and possible increase in no. headaches in one person

Three individuals on prophylaxis intermittently for over 2 years

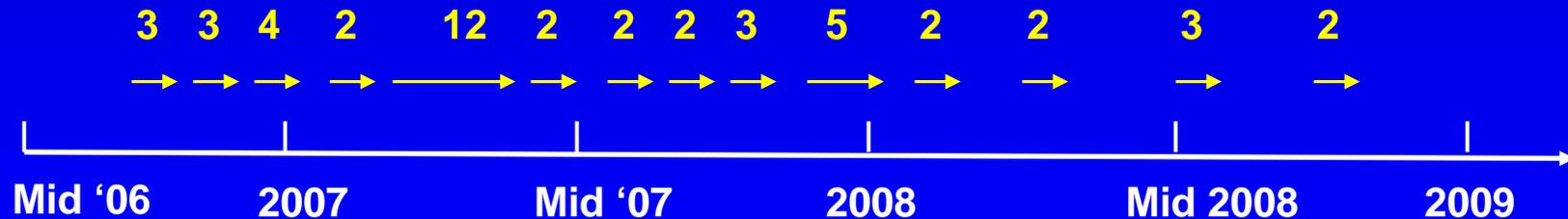


Overview of Extended Oseltamivir Prophylaxis in Two Workers

Worker A (duration in weeks)



Worker B



Current Status of Work with Fully Reconstructed 1918 Virus in the Influenza Division, CDC

- Three year track record of working safely with 8 gene 1918 virus
- Work with 1918 virus is ongoing on a voluntary basis
 - All work undertaken is conducted by Influenza Division staff only
 - All have PhD level training and expertise
- Oseltamivir prophylaxis is required of all individuals who chose to work with the 1918 virus
 - CDC Occupational Health and Safety Clinic continues to provides oversight in the safe use of prophylaxis
 - Medical surveillance program is in place
- Knowledge gained indicates that the fully reconstructed virus is unique among influenza viruses in its ability to cause severe and fatal disease and transmit efficiently by respiratory droplet spread among ferrets

