

Mary P. Fairchok MD^{1,2,6}, Wei-Ju Chen PhD^{1,6}, Deepika Mor^{1,6}, Christina M. Schofield MD², John C. Arnold MD³, Patrick J. Danaher MD⁴, Robert G. Deiss^{1,3,6}, Tahaniyat Lalani MD^{1,6,7}, Michael Rajnik MD⁵, Leslie Malone MS, MB(ASCP)CM⁸, Elena Grigorenko PhD⁸, Donald Stalons PhD⁸, Timothy H. Burgess MD MPH¹, Eugene V. Millar PhD^{1,6}, Christian L. Coles PhD^{1,6}

¹Infectious Disease Clinical Research Program, Department of Preventative Medicine and Biostatistics, Uniformed Services University of Health Sciences Bethesda, MD, USA; ²Madigan Army Medical Center, Fort Lewis WA; ³Naval Medical Center San Diego, CA; ⁴San Antonio Military Health System, San Antonio TX; ⁵Walter Reed National Military Medical Center, Washington DC; ⁶The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Bethesda ⁷Naval Medical Center, Portsmouth, VA, ⁸Diatherix Laboratories, Huntsville AL

Poster No.
1048

Background

- Parainfluenza virus (PIV) is a chief cause of croup.
- Less is known about the role of PIV in causing influenza-like illness (ILI) among healthy adults and children.
- We evaluated the rates and clinical characteristics of PIV compared to influenza (flu) infection in healthy subjects diagnosed with ILI.

Methods

- Dates:** From 2009-16, we enrolled otherwise healthy military personnel and beneficiaries into an observational, longitudinal study of influenza-like illness (ILI) at 5 military treatment facilities across the continental U.S.
- Eligibility:** Patients presenting for care <72h after the onset of ILI, defined as fever (temperature of 100.4° F or greater at the time of evaluation, or by self-report) and sore throat or one of the following respiratory symptoms: cough, sputum production, shortness of breath, or chest pain. Patients with underlying medical conditions were excluded.
- Procedures:** Clinical and demographic information, and a nasopharyngeal swab were collected at baseline (day 0). Participants returned on days 3±1, 7±2 and 28±7; a daily symptom diary was completed for the first seven days following ILI onset.
- Symptom presence and severity were recorded as: 0 (none); 1 (mild); 2 (moderate); and 3 (severe). Participants were trained by research personnel on the definitions of each score.
- Virus identification:** Swabs were tested for influenza by real-time reverse transcription polymerase chain reaction (rtRT-PCR) at the Naval Health Research Center (San Diego, CA). A target-enriched multiplex PCR (TEM-PCR) panel for adenovirus, Coxsackievirus/echovirus, bocavirus, coronavirus, human metapneumovirus, rhinovirus, influenza A/B, parainfluenza and respiratory syncytial virus was also performed by Diatherix Laboratories, LLC. (Huntsville, AL).
- Statistical analyses :** Performed using SAS (Version 9.3; SAS Institute, Cary, NC). The study was approved by the Infectious Disease Institutional Review Board of the Uniformed Services University of the Health Sciences (IDCRP-045).

Results-Demographics

- In comparison with influenza, PIV did not account for a large proportion of ILI in our population : **43/961 (4.7%)** were PIV+ versus **153/961 (15.9%) flu+**.
- Co-detections** occurred in **8/43 (18.6%)** of PIV+ subjects, but co-detected viruses did not show any specific pattern, with 5 different viruses found (rhinovirus, influenza A, RSV, Coxsackie/echovirus, HCoV).
- Sex, race, smoking status and BMI **did not** differ between PIV + and PIV - subjects with ILI
- There was **no difference** in the frequency of PIV detection according to the site nor year of enrollment
- Age < 5 years and presence of a child < 5 yrs of age in the household were more common in PIV+ subjects**
- On multivariable analysis, the presence of a child < 5y in the household remained associated with an increased risk of PIV detection (OR=2.58; 95%CI: 1.39, 4.80).
- When comparing detection of PIV to detection of influenza as the cause of ILI, the only demographic difference was that flu+ subjects were more often ≥5 years (p<0.001), and PIV+ subjects more often had a household member in daycare (p<0.001).

Characteristics	Among Patients tested by TEM-PCR		P-value
	PIV+ (N=43) N (%)	Influenza+ (N=153) N (%)	
Age (Years)			
0-4	19 (44.2)	8 (5.2)	<0.001
5-17	2 (4.7)	27 (17.6)	
18-44	20 (46.5)	98 (64.1)	
45-65	2 (4.7)	20 (13.1)	
Any HH member attending daycare			
Yes	16 (41)	21 (16.2)	<0.001
No	23 (59)	109 (83.8)	
Missing	4	23	

Results Symptomatology

- In comparing symptom profile and severity of 22 adults who had **PIV + ILI vs 118 with flu+ ILI**, we found **no differences** in:
 - The presence or severity of 20 symptoms**—although flu+ ILI adults tended to have higher reports of presence and severity of GI and systemic symptoms
 - The severity scores** for each of 5 categories (upper respiratory, lower respiratory, systemic, GI and composite symptom scores) at enrollment, nor on the first seven days of illness as recorded on the symptom diaries
 - The proportion of hospitalization and antibiotic use**
 - The durations of illness**

Comparison of severity measures between cases with parainfluenza and influenza virus. (FDR: false discovery rate adjusting for multiple comparison)

Clinical characteristics	Parainfluenza-Positive (N=22)	Flu-Positive (N=118)	Original P-value	P-value adjusted with FDR
Composite Score at enrollment	Med. (IQR)	Med. (IQR)		
Systemic	5 (4-8)	7 (5-10)	0.02	0.41
Upper resp.	6 (4-7)	4 (2-7)	0.19	0.65
Lower resp.	6 (3-7)	5 (3-7)	0.74	0.96
Total	16.5 (12-19)	17 (13-22)	0.56	0.88
Gastrointestinal	2 (1-3)	3 (2-5)	0.11	0.53

Conclusions

- This is one of few studies to detail the clinical characteristics of PIV presenting as ILI in healthy subjects.
- PIV did cause ILI in healthy adults and children, although it was a fourfold less cause of ILI in comparison to influenza
- The symptom profile of ILI associated with PIV was indistinguishable from that of influenza in adults
- ILI associated with PIV was also no more nor less severe than that caused by influenza
- Young children were at higher risk for having PIV associated ILI than adults and children over age 5 years
- Presence of young children in the household was also an independent risk factor for PIV associated ILI
- We demonstrated that PIV can present as ILI in both adults and children in addition to the typical presentation as croup in young children.

Acknowledgments

This project has been funded by the National Institute of Allergy and Infectious Diseases, National Institutes of Health (NIH), under Inter-Agency Agreement Y1-AI-5072 and the Department of the Navy under the Wounded, Ill, and Injured Program.

Disclaimer. The views expressed in this abstract are those of the authors and do not necessarily reflect the official policy or position of the Uniformed Services University of the Health Sciences, Henry M. Jackson Foundation, National Institutes of Health, Department of the Navy, Army, Department of Defense, nor the U.S. Government. This research has been approved by USUHS ID IRB.

The views expressed are those of the author(s) and do not reflect the official policy or position of the US Army Medical Department, Department of the Army, Department of Defense or the U.S. Government. The investigators have adhered to the policies for protection of human subjects as prescribed in 45CRF46.

Correspondence

Dr. Mary P Fairchok: mary.fairchok.ctr@mail.mil