Year-Round, Routine Testing of Multiple Body Site Specimens for Human Parechovirus in Young Febrile Infants

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Objectives To test our hypothesis that routine year-round testing of specimens from multiple body sites and genotyping of detected virus would describe seasonal changes, increase diagnostic yield, and provide a better definition of clinical manifestations of human parechovirus (PeV-A) infections in young febrile infants.

Study design PeV-A reverse-transcriptase polymerase chain reaction (RT-PCR) analysis was incorporated in routine evaluation of infants aged ≤60 days hospitalized at Nationwide Children's Hospital for fever and/or suspected sepsis-like syndrome beginning in July 2013. We reviewed electronic medical records of infants who tested positive for PeV-A between July 2013 and September 2016. Genotyping was performed with specific type 3 RT-PCR and sequencing.

Results Of 1475 infants evaluated, 130 (9%) tested positive for PeV-A in 1 or more sites: 100 (77%) in blood, 84 (65%) in a nonsterile site, and 53 (41%) in cerebrospinal fluid (CSF). Five infants (4%) were CSF-only positive, 31 (24%) were blood-only positive, and 20 (15%) were nonsterile site–only positive. PeV-A3 was the most common type (85%) and the only type detected in CSF. Although the majority (79%) of infections were diagnosed between July and December, PeV-A was detected year-round. The median age at detection was 29 days. Fever (96%), fussiness (75%), and lymphopenia (56%) were common. Among infants with PeV-A–positive CSF, 77% had no CSF pleocytosis. The median duration of hospitalization was 41 hours. Four infants had bacterial coinfections diagnosed within 24 hours of admission; 40 infants had viral coinfections.

Conclusions Although most frequent in summer and fall, PeV-A infections were encountered in every calendar month within the 3-year period of study. More than one-half of patients had PeV-A detected at more than 1 body site. Coinfections were common. PeV-A3 was the most common type identified and the only type detected in the CSF. *(J Pediatr 2021;229:216-22)*.

Human parechoviruses (PeV-A) are nonenveloped RNA viruses previously classified as enteroviruses.[1,2] PeV-A infections are associated with fever, sepsis, and meningitis in young infants.[1,2] Of the 19 known PeV-A types, types 1 and 3 commonly cause illness in young infants.[2-7] PeV-A3 has been associated with intensive care unit ICU admission, seizures, death, and poor neurodevelopmental outcomes.[5,8] Clinical manifestations of other PeV-A types are not well defined.[4,9,10]

PeV-A infections peak during summer and fall months but seasonality and overall epidemiology are incompletely understood.[2,3,9,11-14] It has been reported that testing blood in addition to cerebrospinal fluid (CSF) increases PeV-A detection,[15,16] but this has not been widely implemented. Combining PeV-A polymerase chain reaction (PCR) with enterovirus PCR, thereby testing for both viruses at the same time, has been described as helpful.[16,17] At our institution, in addition to routine herpes virus and enterovirus PCR testing, reverse-transcriptase PCR (RT-PCR) testing for PeV-A of blood, CSF, and nonsterile sites has been included in the standard evaluation of young infants (age ≤60 days) presenting with fever and possible sepsis since July 2013.

AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
CSF	Cerebrospinal fluid
C_t	Cycle threshold
IV	Intravenous
PeV-A	Human parechovirus
PICU	Pediatric intensive care unit
PCR	polymerase chain reaction
RT-PCR	Reverse-transcriptase polymerase chain reaction
UTI	Urinary tract infection

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The objectives of this study were to define the year-round epidemiology, clinical, and laboratory findings associated with PeV-A infections in infants aged ≤60 days and, when possible, to identify virus types associated with disease severity. We hypothesized that performing routine testing of specimens from multiple body sites at the time of initial encounter and genotyping the PeV-A detected will improve our understanding of clinical disease.

Methods

Electronic medical records of infants aged ≤60 days hospitalized between July 2013 and September 2016 for fever and/or possible sepsis and tested for PeV-A were identified. Of these, infants who had positive PeV-A RT-PCR from any clinical sample were included. All infants had bacterial cultures obtained. Laboratory records were accessed to determine whether samples were available for further testing.

To define seasonality, clinical, and laboratory findings, we collected demographic and seasonal information, including date, age, gestational age, sex, presenting symptoms and signs (eg, fever, rash, seizures, fussiness/irritability, diarrhea, cough, congestion), complete blood count and differential of white blood cells (WBCs); blood chemistry; imaging; additional viral testing for enterovirus, herpes simplex virus, and respiratory viruses; bacterial cultures from blood, urine, and CSF; antibiotic treatment and duration; types of samples that tested positive for PeV-A RT-PCR (CSF, blood, and nonsterile specimens from throat, rectum, skin, mouth, conjunctival swabs or "pooled specimens" combined any of the previous sites) and semiquantitative PeV-A loads; and clinical outcomes, including admission to a pediatric ICU (PICU), duration of hospitalization, and readmission within 7 days due to the same illness. During the study period, 2 different respiratory viral panel PCR assays were in use: single-plex PCR assays that detect 6 respiratory viruses (respiratory syncytial virus, influenza A/B, rhinovirus, adenovirus, human metapneumovirus, and parainfluenza) for July 2013-January 2014 and the FilmArray Respiratory Panel, which detects 20 respiratory pathogens (Biofire Defense, Salt Lake City, Utah) for February 2014-September 2016.

The Nationwide Children's Hospital Institutional Review Board approved this study (IRB15-01020). Informed consent was waived for the retrospective review.

PeV-A Detection and Typing

PeV-A was detected using a real time RT-PCR assay as described by Nix et al.[18] Semiquantitations of viral load data were analyzed and reported as cycle threshold (C_t) values, which represent the number of cycles required to detect a positive result.

PeV-A Genotyping Analysis

We first screened available samples for PeV-A3 using a PeV-A3–specific RT-PCR assay as described previously.[19] The samples with adequate RNA quantity and quality that tested negative for PeV-A3 were sequenced for the partial viral protein 1 region.[20] Sequence assembly was performed using Geneious software, Auckland, New Zealand (www.geneious.com). Partial viral protein 1 sequences were blasted, and genotypes were assigned as per GenBank.

Statistical Analyses

Continuous variables were recorded as mean ± SD or median (IQR) and analyzed using the *t* test or a nonparametric test according to data distribution. We analyzed categorical data using the Fisher exact test and computed correlations using the Spearman *r* for nonnormally distributed data. A *P* value of $< .05$ was considered statistically significant. Analyses were done with GraphPad Prism version 7.03 (GraphPad Software, La Jolla, California).

Results

Study Population

Between July 2013 and September 2016, 1475 infants aged ≤60 days were tested for PeV-A by RT-PCR. Patients came to medical attention predominantly because of fever and were well appearing or had a sepsis-like picture, respiratory distress, or concern for meningitis/central nervous system disease. Patients were admitted to rule out serious bacterial infection. Intravenous (IV) antibiotics and IV acyclovir were administered when appropriate. Of these patients, 130 (9%) tested positive for PeV-A: 100 from blood (77%), 53 from CSF (41%), and 84 from nonsterile site swabs (65%). In 83 infants (64%), PeV-A RT-PCR assays were performed on samples from all 3 sites. Five infants (4%) had only positive CSF samples, 31 (24%) had only positive blood samples, and 20 (15%) had only positive nonsterile site swabs (**Figure 1**).

Excluding 20 infants with only nonsterile site swabs positive, patient characteristics were median age 29 days (IQR, 18-39 days), 56% male, and median gestational age 39 weeks (IQR, 39-40 weeks). Symptoms were fever (96%), fussiness (75%), rash (29%), respiratory symptoms (cough, congestion, and rhinorrhea; 20%), diarrhea (12%), abdominal tenderness/distention (10%), and vomiting (6%). One patient (1%) had seizures (**Table I**; available at www.jpeds.com).

Using our institution's standardized laboratory reference values for age, median values of hemoglobin, platelets, and WBC count were within normal ranges. Fifty patients (46%) had leukopenia, 61 (56%) had lymphopenia, 11 (10%) had neutropenia, and 4 (4%) had thrombocytopenia. The median serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) values were within normal ranges. Twenty patients (18%) had an elevated AST level, and 10 (8%) had an elevated ALT level. The median creatinine level was 0.35 mg/dL (IQR, 0.3-0.42 mg/dL).

We analyzed the 20 infants who had only a nonsterile site positive for PeV-A separately, and the only significant differences were that these infants had a higher proportion of respiratory symptoms (65% vs 20%; $P < .01$) and were fussy less frequently (40% vs 75%; $P < .01$).

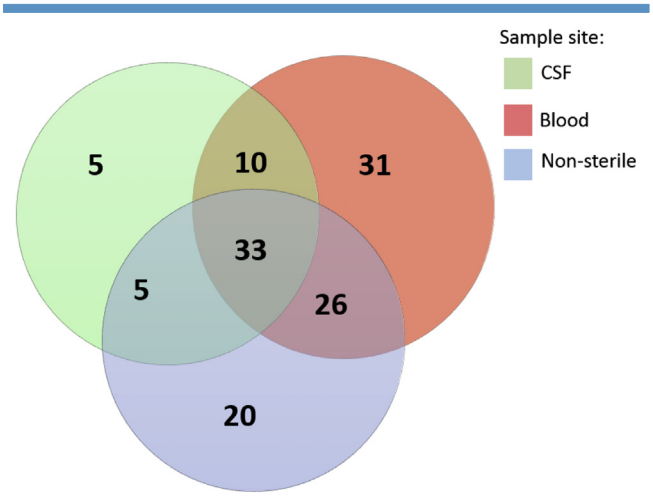

Figure 1. Venn diagram showing positive test results and overlap of various specimen types.

During the study period, 103 (79%) of positive PeV-A infants presented between July and December. However, from 2013 through 2015, most diagnoses were made between August and October, whereas in 2016, patients were identified as early as May, with a peak in July (**Figure 2**). Analysis of patients with sterile site positive results only, excluding those with nonsterile samples, showed a similar pattern (**Figure 3**; available at www.jpeds.com).

Among the 53 patients with PeV-A detected in CSF, the median CSF WBC count was 4 cells/μL (IQR, 1-10 cells/μL), median CSF protein level was 61 mg/dL (IQR, 44-85 mg/dL), and glucose 49 mg/dL (IQR, 44-55 mg/dL). All median values were within the normal ranges. Forty-one patients (77%) had no CSF pleocytosis (cutoff values from Kestenbaum et al[21]). Of these, 19 patients (46%) had peripheral blood leukopenia. The C_t values in CSF did not differ between infants with pleocytosis and those without pleocytosis ($P = .17$). During the study period, enterovirus infections were twice as common (289/1475; 20%).

Identification of Concomitant Infections

Forty-four patients (34%) with PeV-A detection had another agent identified by culture or by RT-PCR. Forty infants (25 with PeV-A in CSF or blood; 15 from nonsterile sites) had viral codetection. Two infants had bacteremia, and 2 had urinary tract infection (UTI). Coinfections were more common in the patients who had PeV-A detected only from nonsterile site swabs compared with patients with positive sterile site samples (85% [17 of 20] vs 25% [27 of 110]; $P < .01$).

Of the 25 infants with PeV-A in CSF or blood and viral codetection, 24 had detection of respiratory viruses (all from nonsterile body site swabs): 23 with rhinovirus/enterovirus and 1 each with adenovirus, human metapneumovirus, and parainfluenza type 1. One infant had enterovirus detected from a nasopharyngeal swab.

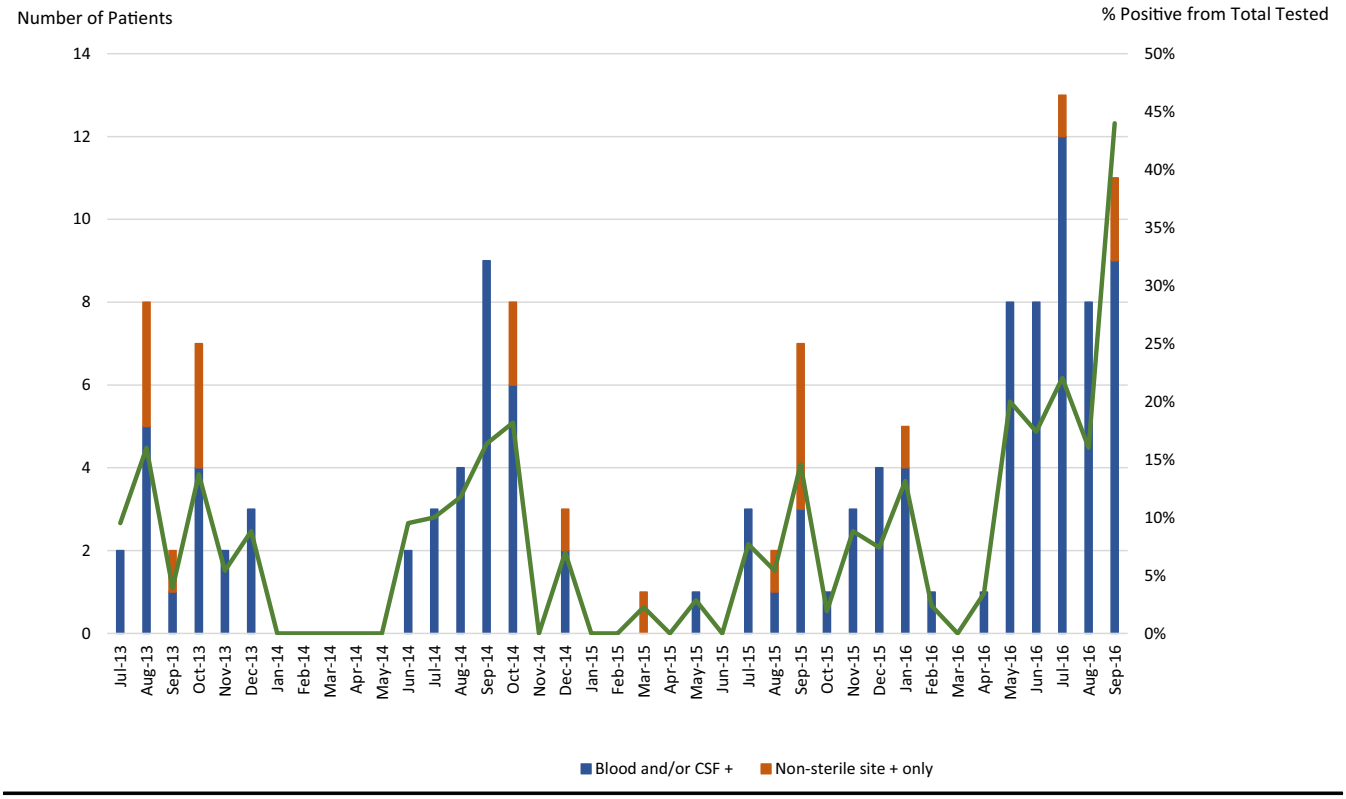

Figure 2. Monthly distribution of infants testing positive for PeV-A by RT-PCR assay for 2013-2016.

Of the 15 infants with PeV-A detected from nonsterile sites and viral codetection, 11 had rhinovirus/enterovirus detected in nasopharyngeal samples. Among all patients with codetection of respiratory viruses, 60% (22 of 38) had respiratory symptoms, whereas among the patients without codetection, 14% (13 of 92) had respiratory symptoms.

Four infants had serious bacterial infections; all bacterial cultures were positive within 24 hours of incubation. The first infant was a 28-day-old term-born male evaluated for fever whose blood culture was positive for *Streptococcus pneumoniae* at approximately 24 hours after inoculation. His CSF studies were normal, and CSF culture was sterile. His CSF was positive for PeV-A. A blood culture repeated before antibiotic therapy was sterile.

The second infant was a 33-day-old full-term male with a history of gastroesophageal reflux and tracheomalacia. He presented with respiratory distress, fever, and fussiness and was treated with ampicillin/sulbactam for possible aspiration pneumonia. Blood culture was positive at 14 hours of incubation for group B *Streptococcus*. His CSF culture was negative; only a pooled nonsterile specimen tested positive for PeV-A.

The third infant was a 13 day-old, full-term female. She was febrile and fussy, and a urine culture grew *Escherichia coli* (>100 000 CFU/mL) within 16 hours of incubation. Her CSF sample was obtained on day 9 of hospitalization after several attempts and while receiving IV antibiotics. The CSF had values of glucose 35 mg/dL, protein 74 mg/dL, 536 RBCs/μL, and 160 WBCs/μL (with 2% neutrophils and 98% lymphocytes). CSF and blood cultures were negative. She was treated for presumed *E coli* meningitis for 21 days. PeV-A virus was detected from an eye swab, and coronavirus was detected from a nasopharyngeal swab.

The fourth infant was a 42-day-old full-term female who had an *E coli* UTI identified within 16 hours of urine culture. All samples (CSF, blood, and nonsterile sites) tested positive for PeV-A. CSF values were glucose 49 mg/dL, protein 328 mg/dL, >6000 RBCs/μL, and 31 WBCs/μL.

PeV-A Load According to Anatomic Site and Disease Severity

Overall, the semiquantitative PeV-A loads, expressed as median C_t value, were lower (reflecting higher viral loads) in the blood (31.47; IQR, 27.7-34.76), followed by nonsterile sites (34.44; IQR, 32.17-37.31) and then CSF (36.81; IQR 34.49-39.31). Viral loads in blood, CSF, and nonsterile sites in patients admitted to the PICU were not significantly different from those in patients hospitalized in the medical units. Blood C_t values were weakly correlated with the duration of hospitalization (Spearman $r = -0.21$; $P = .039$).

Outcomes

Nine of the 130 infants with PeV-A infection (7%) required admission to the PICU, due to respiratory distress (n = 1), seizures (n = 1), low blood pressure and tachycardia (n = 3), and apnea/apparent life-threatening events (n = 2). Seven infants tested positive for PeV-A in CSF, and all had ≤8 CSF WBCs/μL. Five infants tested positive for PeV-A in blood, and 4 had positive RT-PCR results from a nonsterile site swab. None of the infants admitted to the PICU had bacterial coinfection identified, but 3 had rhinovirus/enterovirus detected in the respiratory tract.

The median duration of hospitalization for all admissions was 41 hours (IQR, 36.2-55.9 hours). The median duration of hospitalization for patients admitted to the PICU was 88 hours (IQR, 65-134 hours).

There were no deaths, and no infant had any complications of infection at the time of discharge. Two patients were readmitted within 7 days of discharge, 1 with parainfluenza virus and the other with adenovirus and respiratory syncytial virus infections.

PeV-A Genotyping

Of the 130 infants with PeV-A infection, 100 (77%) had samples available for genotyping (**Table II**; available at www.jpeds.com), and of these, 87 were PeV-A3. The remaining 13 genotypes included PeV-A1 in 5 infants, PeV-A4 in 6, PeV-A5 in 1, and PeV-A6 in 1. Because the non–PeV-A3 samples were a small proportion of the samples tested and of insufficient number to allow for a detailed comparison, type comparisons were done between PeV-A3 and non–PeV-A3 types (**Table III**).

All CSF-positive samples (n = 36) and the majority of blood samples were PeV-A3. Only 3 infants had PeV-A4 detected in blood. Genotypes 1, 5, and 6 were detected at nonsterile sites. Of the 5 infants admitted to the PICU with available samples, 4 had PeV-A3 (4 from CSF, 3 from blood, and 2 from nonsterile sites). One infant requiring PICU care presented with respiratory distress and had concomitant detection of rhinovirus/enterovirus in a respiratory sample and PeV-A1 detected from a nonsterile site.

PeV-A3 was detected year-round, whereas other PeV-A types were identified only during the second half of the year.

Among infants with samples available for genotyping, 26 had viral coinfections and 2 had bacterial coinfections. The infant with group B *Streptococcus* bacteremia had PeV-A type 6 identified from a nonsterile specimen, and 1 of the infants with *E coli* UTI had PeV-A type 3 detected in CSF, in blood, and on a nasopharyngeal swab.

Discussion

This retrospective study describes the routine, year-round application of RT-PCR analysis of specimens from multiple body sites for detection of PeV-A infections in young infants hospitalized for fever and/or a sepsis-like clinical picture. We found that PeV-A infections were detected year-round, peaked during late summer to early fall, and did not have a striking biennial pattern. In addition to fever and fussiness/irritability, infants commonly had rash, upper respiratory tract symptoms, diarrhea, and abdominal distention. Almost one-half of the infants had leukopenia and lymphopenia, 18% had elevated AST and ALT values, and a minority (7%) were admitted to the PICU. Coinfections were common (34%) and were possibly the cause of clinical

Table III. Patient demographics, presenting signs, symptoms, clinical outcomes, and laboratory values for patients with positive PeV-A RT-PCR according to type

Patient demographic, clinical, and laboratory features	PeV-A type 3 (N = 87)	PeV-A non–type 3 (N = 13)	*P* value
Demographic data			
Age, d, median (IQR)	29 (19-42)	30 (21-34)	.99
Male sex, n (%)	45 (52)	10 (77)	.13
Clinical findings			
Fever (≥38 °C), n (%)	86 (98)	10 (77)	<.01
T max (°C), median (IQR)	39 (37.1-40.1)	38.3 (37.3-39.8)	.01
Duration of fever, d, median (IQR)	2 (1-3)	1.5 (0.25-2.75)	.08
Fussiness/irritability, n (%)	74 (85)	3 (23)	<.01
Rash, n (%)	30 (35)	3 (23)	.53
Diarrhea, n (%)	13 (15)	2 (15)	.99
Respiratory symptoms, n (%)	11 (13)	10 (77)	<.01
Abdominal tenderness/distention, n (%)	11 (13)	0	.35
Vomiting, n (%)	7 (8)	0	.59
Inotropic support, n (%)	1	0	.99
Seizures, n (%)*	0	0	—
Outcomes			
Duration of antibiotics, d, median (IQR)	2 (2-2)	2 (1-2)	.08
Duration of hospitalization, h, median (IQR)	42 (37.2-56.3)	38.3 (35.8-58.2)	.61
PICU admission, n (%)	4 (5)	1 (7.7)	.51
No adverse events at discharge, n (%)	87 (100)	13 (100)	—
Readmission within 7 d due to same illness, n (%)	0	0	—
Laboratory values			
Hemoglobin, mg/dL, median (IQR)	11.6 (10.2-13)	11.6 (10.1-13.1)	.834
Platelets, $10^3/\mu$L, median (IQR)	289 (231-368)	293 (235-336)	.922
WBC count, $10^3/\mu$L, median (IQR)	5.3 (4.3-6.85)	8.2 (3.1-12.5)	.137
Leukopenia, n (%)	36 (41.3)	5 (38.5)	.99
Neutropenia, n (%)	6 (7)	2 (15.4)	.28
Lymphopenia, n (%)	47 (54)	4 (31)	.144
ALT >60 U/L, n (%)	9 (10)	9 (69)	<.01
AST>60 U/L, n (%)	17 (20)	1 (8)	.45
All coinfections (codetections), n (%)	17 (20)	11 (85)	<.01

Comparisons of median values were done with the Mann–Whitney *U* test; comparison of proportions, with the Fisher exact test. A *P* value of <.05 was considered statistically significant.
*One patient had seizures but did not have an available sample for genotyping.

symptomatology in several infants. Some patients with viral coinfections had manifestations more consistent with a respiratory virus. For infants without identified concurrent infections, routine testing was helpful not only to determine the etiology of fever, but also possibly to avoid unnecessary antimicrobial treatment and shorten hospital stay.

PeV-A type 3, the most prevalent type in the cohort, was the only PeV-A type identified in CSF samples and the most common type in infants needing PICU care. Notably, most patients with PeV-A in the CSF did not have CSF pleocytosis. Why PeV-A does not elicit a robust inflammatory response in the CSF is not clear, but one possibility is that young infants are diagnosed early in the course of illness at the onset of fever, as a similar observation has been documented with enteroviruses.[22]

Most of PeV-A testing has been performed during summer, and thus precise annual distribution or seasonality has not been established, and viral circulation during other times of the year may be underrecognized.[3,9,11,14] Data from our cohort demonstrate that PeV-A can be detected year-round, and thus testing should be considered throughout the year.[11] PeV testing varies among centers; some centers test only 1 compartment, such as CSF,[23,24] blood, or respiratory samples.[8,9,15,16,25] In our cohort, only 24% of patients who were PeV-A positive were diagnosed by PeV-A detection in blood, and only 15% were diagnosed by detection in a nonsterile site. By testing samples from multiple compartments, the diagnostic yield was increased.

PeV-A surveillance and typing data could aid the determination of patterns of circulation, spectrum of disease,[26-28] and potentially the prognosis for individual genotypes.[3,29] Similar to other studies, PeV type 3 was the most common circulating type in our study period.[8,10,30,31] In 2015, Renaud and Harrison showed that PeV type 3 causes seasonal outbreaks and that central nervous system disease, and that infections are associated with lack of CSF pleocytosis and leukopenia/lymphopenia.[10] Our analysis with a larger cohort confirms the association of PeV-A3 infection with a lack of CSF pleocytosis and with the findings of leukopenia/lymphopenia.

Mortality and sequelae are rare in PeV-A infections.[10] Unlike previous reports,[8,26,30,32-34] there were no deaths or complications in our cohort. Although we did not have long term follow up to measure the neurodevelopmental outcomes, patients recovered well at the time of discharge with overall low frequency of reported seizures and absence of disordered consciousness all suggesting a reassuring short-term outcome.

Coinfections in patients with PeV-A have not been well studied.[28,35-37] We detected coinfections in about one-third of our patients and in some infants these other pathogens were possibly the cause of clinical symptomatology. All bacterial infections in our cohort were identified within 24 hours

of hospitalization, and there was no interruption of antibiotic treatment due to detection of PeV-A. Coinfections were more common with PeV-A non–type 3 infections. Whether the presence of coinfections or codetections has any impact on PeV and/or bacterial infection is unclear and merits further exploration. The possibility of asymptomatic PeV-A carriage adds complexity to this knowledge deficit.

The nonsterile site results might not be as helpful in determining true disease, but may help understand the epidemiology of certain genotypes (types 1, 5, and 6). We were able to demonstrate that although these types circulated in our population, they were unlikely to cause viremia/severe disease.

Our retrospective study has some limitations. We did not follow and evaluate the long-term outcomes of patients for the reported study period. Our study lasted 3 years; a longer period of observation would allow better assessment of year-to-year variation. Nonetheless, by identifying a large number of infants, we have confirmed the value of testing multiple samples from different body sites and provided a better understanding of the seasonality of infection.

In conclusion, our present findings show that PeV-A is a common infection in young infants that can be detected year-round. A picture emerges of a brief, self-limited febrile illness with fussy behavior and sometimes rash as the prominent features and laboratory findings of leukopenia and lymphopenia. The neurologic manifestations, even in infants with RT-PCR–positive specimens from CSF, were mild and apparently self-limited in this cohort. Testing specimens from multiple body compartments increases the diagnostic yield. PeV-A3 was the most common type identified. ■

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50 Years Ago in *THE JOURNAL OF PEDIATRICS*

Does One Size Fit All? High-Value Care For Learning and Developmental Concerns

Kenny TJ, Clemmens RL. Medical and Psychological Correlates in Children with Learning Disabilities. J Pediatr 1971;78:273-77.

This article discusses the utility of neurologic and psychological evaluations, as well as the benefit of electroencephalography (EEG) in the assessment of 100 children. Children included in the study were referred to the central evaluation clinic at the University of Maryland Hospital for behavioral, learning, or developmental concerns suggesting possible minimal brain dysfunction (MBD), one of the previous lenses through which children who might now be identified as having attention-deficit/hyperactivity disorder were viewed. Most were referred via the school system or a physician. In their discussion, the authors advocate for a more thoughtful approach to evaluating children with suspected MBD. The learning problems that subjects most likely had were usually identifiable by school systems. The authors found little value added by comprehensive neurologic examinations and EEG. Their article mirrors discussions that continue today around high-value care.

High-value care emphasizes "restraint, stepwise decision-making, plans that avoid excess, and the incorporation of patient and family perspectives."[1] With this practice, a clinician must understand the benefits and costs of specific tests, procedures, or interventions, accurately identifying those with maximum benefit to her patient and minimal expenditure of resources. Like other pediatric specialties, developmental pediatrics has grappled with how to recommend the most cost-effective and vital tests and interventions for patients, especially in light of bottlenecks due to high demand for services and long waitlists. In the 1960s and 1970s, many children with MBD underwent EEG and neurologic evaluations that were often only minimally helpful in final diagnosis and management. Recent practice guidelines aimed at children with neurodevelopmental concerns have recommended widespread application of neuroimaging, genetic testing, and cardiovascular monitoring for stimulant medications, among other evaluations. Can we start to temper caution and a desire for thoroughness with stewardship of resources—or does one size have to fit all?

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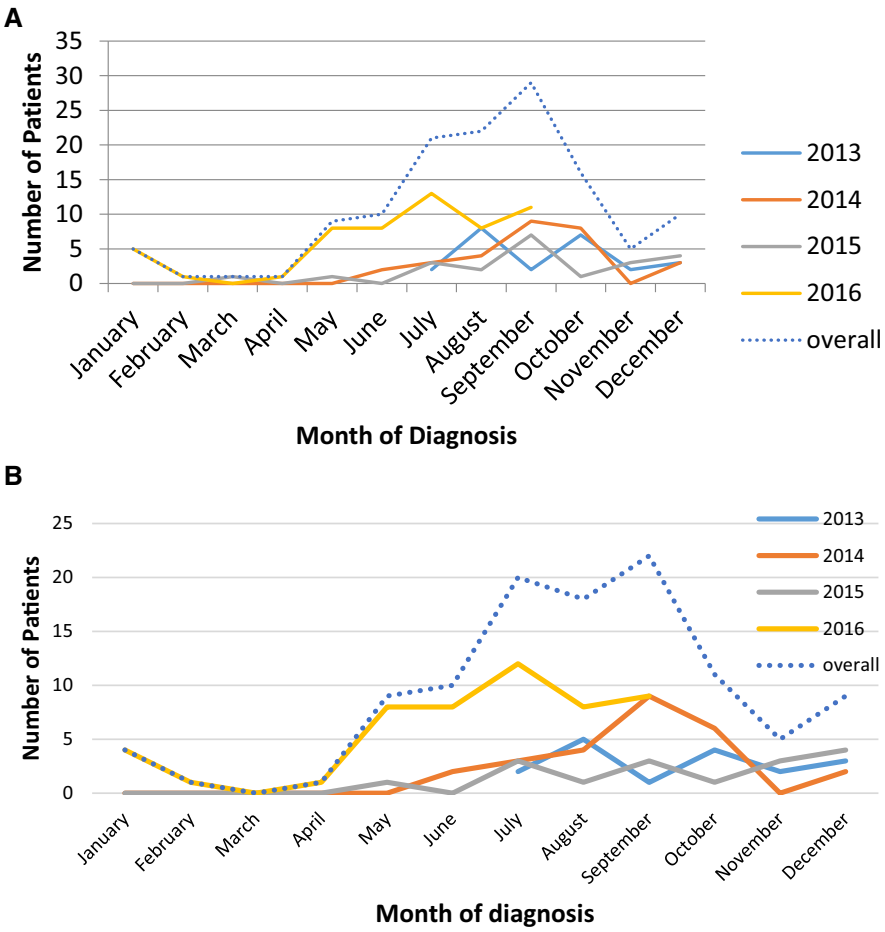

Figure 3. **A,** Monthly distribution of infants testing positive for PeV-A by RT-PCR assay for 2013-2016. **B,** Monthly distribution of infants testing positive for PeV-A by RT-PCR assay from sterile sites only for 2013-2016.

Table I. Demographic, clinical and laboratory features of patients with positive PeV-A result from blood and/or CSF and/or a nonsterile site, excluding patients with positive result only from a nonsterile site

Parameters	PeV-A$^+$ patients (N = 110)	Patients with coinfection, n (%)
Demographic data		
Age, d, median (IQR)	29 (19-39)	
Male sex, n (%)	62 (56)	
Clinical findings		
Fever (≥38 °C), n (%)	106 (96)	25 (24)
Tmax, °C, median (IQR)	39 (38.5-39.4)	
Duration of fever, d, median (IQR)	2 (1-3)	
Fussiness/irritability, n (%)	83 (75)	20 (24)
Rash, n (%)	32 (29)	6 (19)
Respiratory symptoms, n (%)	22 (20)	12 (55)
Diarrhea, n (%)	13 (12)	5 (39)
Abdominal tenderness/distention, n (%)	11 (10)	2 (18)
Vomiting, n (%)	7 (6)	2 (29)
Seizures, n (%)	1 (0.9)	1 (100)
Inotropic support, n (%)	1 (0.9)	0 (0)
Outcomes		
Duration of antibiotics, d, median (IQR)	2 (2-2)	
Duration of hospitalization, h, median (IQR)	41.4 (37-56.1)	
PICU admission, n (%)	8 (7)	
No adverse event at discharge, n (%)	110 (100)	
Readmission within 7 d due to same illness, n (%)	0	
Laboratory values		
Hemoglobin, mg/dL, median (IQR)	11.6 (10.5-13.2)	
Platelets, 10^3/uL, median (IQR)	289 (231-349)	
WBC count, 10^3/uL, median (IQR)	5.3 (4.2-7.2)	
Leukopenia, n (%)	50 (46)	
Neutropenia, n (%)	11 (10)	
Lymphopenia, n (%)	61 (56)	
ALT >60 U/L, n (%)	10 (9)	
AST>60 U/L, n (%)	20 (18)	

Table II. Number of each sample type tested, number positive, number genotyped, and number of each genotype

Parameter	Sample type		
	Blood	CSF	Nonsterile
Tested per site	120	109	107
Positive per site	100	53	84
Genotyped per site	72 (69 type 3, 3 type 4)	36 (all type 3)	64 (53 type 3, 5 type 1, 4 type 4, 1 type 5, 1 type 6)

N = 130 patients. PeV types are in parentheses.