recent changes in palivizumab use guidelines. Although we find these comments from Dr. Ambrose (an employee of AstraZeneca, the manufacturers of palivizumab) provocative, we believe that a few points should be clarified.

Related to the point of causality, it is well-known that an observational study cannot, by nature, prove causality. Therefore, we direct the reader back to the fact that a power analysis simply gives the reader a frame of reference regarding the size of our study and an estimated difference able to be detected, if indeed one existed. Our power analysis should not be interpreted as a presumed result. We are very transparent that our study was the first real-world experience published to describe the impact of implementing the nationally recognized 2014 American Academy of Pediatrics (AAP) palivizumab guideline.

Dr. Ambrose states that the newly excluded patients from the most recent palivizumab guideline represent a small number of total US children. We do not disagree with this claim; however, we propose that this group represents both a more clinically and financially significant change in palivizumab usage than Dr. Ambrose’s stated percentage may suggest. Moreover, the population of greater interest would be the relative percentage change of patients eligible for palivizumab in the US, not the percentage of total US children affected by individual guideline criteria. Our observed baseline dose rate of 21.7 doses per 1000 children <24 months represents an epidemiologically relevant rate for treatment in this population as a whole and would submit that our observed utilization decrease of nearly 50% represents a valid and valuable observation, especially when the numerical rate of respiratory syncytial virus (RSV) hospitalizations observed had changed only minimally (5.37–5.78/1000 children <24 months).

Dr. Ambrose cites a very dramatic number of RSV hospitalizations that the small percentage of children affected by these recent changes would need to incur to meet our specified level of statistical significance. We would direct Dr. Ambrose to the discussion portion of the article where this limitation is specifically addressed. The authors must also clarify the implausibility of recreating our study using only the birth cohort of children affected by this guideline change in a pre-post format. A study of that magnitude would require nearly every RSV hospitalization in the US for this affected group to be recorded. Additionally, in order for our observed difference of 0.41 hospitalizations per 1000 children to be due solely to the group affected by the guideline change, this would require an absolute increase of 53 hospitalizations per 1000 children, not 323. Our observed hospitalization rates are similar to or lower than previously recorded rates for both the general pediatric population and the rate for those affected by the guideline change for prematurity alone. Thus, the clinical significance of our observed small change would be debatable compared with the highly significant decrease in palivizumab utilization and associated costs.

We trust that the AAP acts only in the best interest of their patients, with intent to do no harm both medically and economically. The aim of this study was primarily to quantify the impact of the guideline update at our institution; hospitalization rates and palivizumab utilization were the clearest markers to demonstrate change, if any would be seen. Our study provides a valuable look at institutional-level guideline implementation, as the cost of palivizumab can be devastating to both health systems and families of patients, particularly when evidence is conflicting or does not exist to show that palivizumab immunoprophylaxis would change the clinical outcome. We feel our conclusions remain valid that the change in the guidelines did significantly reduce the use and thereby the cost of palivizumab treatment while not having a significant adverse impact on RSV hospitalization rate. The authors and our institution choose to support the ongoing work of the AAP who must help health systems provide both evidence-based and cost-effective care in the setting of our continued healthcare spending crisis.

Carlinha J. Grindeland, PharmD, BCPS
David D. Leedahl, PharmD, BCPS, BCCCP
Department of Pharmacy
Sanford Medical Center
Fargo, North Dakota

REFERENCES


© 2017 Wolters Kluwer Health, Inc. All rights reserved.
contrasting with group B in which 1 transient thrombopenia and 1 persistent neutropenia (<500/mm³) were observed. For this one, treatment was started at birth leading a neutropenia <500/mm³ at 2 months of life ruling therapeutic, then Fansidar* was reintroduced after with neutropenia reappearance leading to a definitive stopping of the treatment at 3 months of life.

In order to measure compliance of treatment, pharmacological tests were done in sera to determine pyrimethamine and sulfadoxine levels as described previously.6,7 Pyrimethamine and sulfadoxine assays in serum were possible in 78 children only from group B, 8 among these children had insufficient levels of drugs: a bad observance was reported in 2 children, 1 child had a reflux gastroesophageal, and posology was incorrect for 5 children. From these, the levels of drugs measured in serum were corrected after increase of therapeutic concentrations without adverse event.

So we are totally agree to the conclusion of this work and that sulfadoxine-pyrimethamine combination is well-tolerated even if the children are treated from birth.

Cathy Chemla, PharmD
Isabelle Villena, MD, PhD, for the Reims Toxoplasmosis Group
Laboratoire de Parasitologie-Mycologie Centre National de Référence Toxoplasmosis Centre Hospitalier et Universitaire de Reims UFR Médecine, SFR CAP-SANTE Université Reims Champagne Ardenne Reims, France

ACKNOWLEDGMENT
Members of Reims Toxoplasmosis Group are as follows: J.P. Bory, M.G. Tremque, and P. Unger from Gynecology-Obstetrics Department of C.H.U. Reims and Gynecology-Obstetrics Department of medical centers from Reims, France; C. Chemla, F. Foudriner, J.M. Pinon, and I. Villena from Laboratory of Parasitology C.H.U. Reims, France; G. Delebarre, C. Devulder, D. Dupouy, B. Leroux, A. Ninot, C. Sommer, and E. Tisserand from Paediatrics Department of C.H.U. Reims, CH Epernay, CH Troyes, Paediatrics Department of medical centers from Reims, France; J. Eutrope and E. Siadul, Child Psychiatry Department, C.H.U. Reims, France; M. Talmud from Laboratory of Ophthalmology Department, C.H.U. Reims, France; T. Tremque from Laboratory of Pharmacology, C.H.U. Reims, France.

REFERENCES

In Reply: Sulfadoxine–Pyrimethamine Combination in Congenital Toxoplasmosis

In Reply:

We would like to thank you for the opportunity to respond to the letter by Chemla et al.1 We believe that their results corroborate our study, thus highlighting the safety of sulfadoxine-pyrimethamine (Fansidar, Roche, Switzerland) use in children with congenital toxoplasmosis. We found it necessary to stress the fact that our study used a causality assessment method to evaluate the causal relationship between adverse effects and drug administration bringing new insights into neutropenia encountered in both cohorts.

Moreover, we believe that Fansidar remains a drug of choice for treatment of toxoplasmosis. Its safety combined with efficacy make it a suitable alternative for treatment of congenital toxoplasmosis, although the length of treatment remains to be determined.

Damien Dupont, PharmD
Hospices Civils de Lyon Institut de Parasitologie Mycologie Médicale Hôpital de la Croix-Rousse Lyon, France

Integrative Physiology of the Brain Arousal Systems Centre de Recherche en Neurosciences de Lyon

The authors have no funding or conflicts of interest to disclose.
Address for correspondence: Damien Dupont, PharmD; E-mail: damien.dupont@chu-lyon.fr.
Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.
ISSN: 0891-3668/16/363-348
DOI: 10.1097/INF.000000000001436

To the Editors:

Eponymous Signs of Meningitis—The Isaacs’ Sign

D r. Forgie1 has provided a timely description of the “classical” signs of bacterial meningitis, in a useful historical context. In 1993, our group at The Royal Alexandra Hospital for Children in Sydney, Australia, described torticollis as “an unusual and poorly recognized presenting symptom of bacterial meningitis.” Two pediatric patients, a 5-year-old boy and a 30-month-old boy were described, in whom “the diagnosis of bacterial meningitis was delayed because the significance of torticollis was unrecognized.” I propose that heretofore, this sign (torticollis with bacterial meningitis) be known as Isaacs’ Sign, in honor of the Sydney-based pediatric infectious diseases, David Isaacs, a coauthor of the 1993 description.

Edwin D. McIntosh, MBBS, MPH, LLM, PhD, FAFPHM, FRACP, FRCP&CH, FFPM, DRCOG, DCH, Dip Pharm Med
Faculty Education Office Imperial College London, United Kingdom

REFERENCES

The author has no funding or conflicts of interest to disclose.
Address for correspondence: Edwin D. McIntosh, MBBS, MPH, LLM, PhD, FAFPHM, FRACP, FRCP&CH, FFPM, DRCOG, DCH, Dip Pharm Med; E-mail: e.mcintosh@imperial.ac.uk
Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.
ISSN: 0891-3668/16/363-348
DOI: 10.1097/INF.000000000001437

Letters to the Editors

The Pediatric Infectious Disease Journal • Volume 36, Number 3, March 2017