Welcome to the second newsletter of the Global Pertussis Initiative (GPI). This newsletter is an extension of our main goals – including raising awareness about pertussis as an important and preventable disease, improving understanding of the increasing incidence of reported pertussis, and sharing the most recent information and opinions among our members. Herein you will find summaries of current research, theories, and practice that apply to pertussis prevention and management strategies.

Content (Please use the links below to jump to a section of interest):
- NEWS FROM THE GPI
- NEWS FROM THE WEB
- NEWS FROM THE PUBLISHED LITERATURE
- NEWS FROM RECENT CONFERENCES
- UPCOMING EVENTS

Should you have any ideas for items you would like to see included in our updates, please send an e-mail to GPISecretariat@parexel.com. As this initiative has been developed with you in mind, your suggestions on additional content will be greatly appreciated.

Best,

Stanley A. Plotkin, MD
**NEWS FROM THE GPI**

**Update on GPI activities**

Ongoing GPI publications

The GPI currently have 2 publications in development

1. The cocooning strategy (including maternal immunization)
2. The global epidemiology of pertussis: from 2000 to today (including suggestions for improved surveillance programs)

**We’d like to hear from you...**

Do you have a research project, ongoing or planned, that may be of interest to other GPI members? Have you been selected to present at an upcoming meeting? Is there anything else you would like to share with the group? If so, please e-mail GPISecretariat@parexel.com and we’ll add your news to the next update.

Perhaps you wish to ask for input or an opinion from the GPI. Again, do please get in touch. Additionally, should you have any further thoughts on potential GPI publications, please let us know at GPISecretariat@parexel.com.

**Get involved...**

Do you have a paper, abstract, or presentation that you would like to see in the next issue? Would you like to provide your expertise on a piece? If so, please email GPISecretariat@parexel.com.

**Upcoming GPI Activities**

**GPI Global Summit Meeting, 2014**

The next GPI Global summit meeting is in its initial planning stages. Further details will be disseminated in due course.

**GPI Website – Coming Soon!**

We are pleased to announce the upcoming launch of the GPI Website for members. This is a place for you to come and browse the document library, see what the GPI is planning, and search for other GPI members in the member directory. You can also use the website to share ideas and discuss topics for inclusion in future GPI activities and review outcomes of previous activities. In the future, we may be using this portal for web-meeting access and to host a bi-annual member survey poll. Look for an e-mail in the coming weeks with a link to the GPI Website!

**NEWS FROM THE WEB**

**The European Centre for Disease Prevention and Control (ECDC) report increase of pertussis in Czech Republic**

In a recent Communicable Disease Threats Report (Week 40, 29 September – 5 October) the ECDC noted that the number of cases of whooping cough in the Czech Republic has increased during 2013, and according to the National Health Institute (EAA) this is the second highest incidence of the disease in the last 10 years. By contrast, the overall number of laboratory-confirmed cases in England has been declining since November 2012, aside from a slight seasonal increase in July 2013 and persistently high incidence in individuals aged ≥15 years. The greatest reduction of pertussis rates was observed in infants below 3 months of age. This is largely due to the maternal immunization program that started October 1, 2012. The ECDC concluded its European update by stating that no indications of major ongoing outbreaks were detected during September 2013 through the media or available surveillance sources.

CDC reports an overall decrease in pertussis rates nationwide in the US...

Although the states of Texas and North Carolina are experiencing an increase in the number of pertussis cases, according to the CDC this trend is not being replicated nationwide. The Centers for Disease Control and Prevention (CDC) reported that as of August 2013, there were 14,270 cases, which is notably lower than the 32,680 cases reported for the same time in 2012.


... However, pertussis outbreaks reported in several US states

In Texas, as of early September, the pertussis outbreak is looking as though it will be the worst reported in 50 years. As of October 7, there have been 2652 pertussis cases in the state reported to the CDC this year and 2 infants have died, both of whom were too young to be vaccinated. Given the severity of the outbreak, the Texas Department of State Health Services issued a public health alert ([http://www.dshs.state.tx.us/news/releases/Pertussis-HealthAlert-090313.aspx](http://www.dshs.state.tx.us/news/releases/Pertussis-HealthAlert-090313.aspx)) in which it recommended that all Texans be vaccinated against pertussis. The antibiotics recommended for treatment and post-exposure prophylaxis includes azithromycin, erythromycin, clarithromycin, and trimethoprim. The agency’s biweekly updates are available at: [http://www.dshs.state.tx.us/idcu/disease/pertussis/](http://www.dshs.state.tx.us/idcu/disease/pertussis/)


In response to a recent outbreak in North Carolina, the Department of Health and Human Services (DHHS) is offering free pertussis vaccines to individuals of all ages in 3 counties (ie, those with the highest number of cases). As of August 14, 326 cases of pertussis were reported in the state this year, with 50 cases occurring in infants. The first infant death attributable to pertussis in 2013 was reported on September 27. The child was 3 weeks old; too young to begin vaccination, which may only be initiated from 2 months of age. The DHHS therefore emphasized the importance of vaccination for anyone who lives with or will be around an infant to prevent transmitting the disease.


The Public Health Department of Washtenaw County in Michigan recently reported that there were over 151 cases of pertussis diagnosed to date, representing the highest number since the 2010 outbreak. The majority of cases occurred in those aged 10 to 14 years.


Links to the Pertussis Vaccines Working Group presentations at the CDC’s Advisory Committee for Immunization Practices (ACIP) meeting in June 2013

The ACIP meeting occurred on October 23-24, 2013, where respected speakers from around the world presented on the issue of pertussis. Topics included the status of pertussis circulation in the United States and the effectiveness of the Tdap vaccine in treatment, the safety and immunogenicity of Tdap revaccination, cost-effectiveness of a second dose of Tdap, conclusions from the ACIP working group, and maternal immunization and cocooning strategies.

Link to the slide presentations: [http://www.cdc.gov/vaccines/acip/meetings/slides-jun-2013.html](http://www.cdc.gov/vaccines/acip/meetings/slides-jun-2013.html)
NEWS FROM THE PUBLISHED LITERATURE

Study suggests that the 2010 pertussis outbreak in California may have been related to nonmedical vaccine exemptions

During 2010, there was a pertussis outbreak in California that was associated with more than 9000 infections. The outbreak represented the largest single year increase since 1947. Although this resurgence has been widely attributed to waning immunity of the acellular vaccine, the role of vaccine refusal had not been previously explored in the published literature. Therefore, the aim of this study was to determine if there was a link between the high rate of pertussis that occurred during the outbreak and nonmedical exemptions (NMEs).

California records of NMEs for children entering kindergarten between 2005 and 2010 and pertussis cases with onset in 2010 were analyzed to determine if NMEs increased in that period and to investigate respective clustering (spatially and/or temporally) for NMEs and pertussis cases.

The analysis revealed that there were 39 statistically significant clusters with high numbers of individuals who voluntarily were not vaccinated. In addition, there were 2 significant clusters of pertussis cases. Individuals in the NME clusters were 2.5 times more likely to also be in a pertussis cluster. Furthermore, more cases occurred within, as compared with outside, exemptions clusters and the association remained significant for demographic factors. Thus NMEs may have been a contributing factor to the pertussis outbreak.


Undervaccination in very young children is strongly associated with pertussis

Undervaccination is an increasing trend that potentially places children and their communities at an increased risk for serious infectious diseases.

A matched-case control study was used to examine the association between undervaccination and pertussis in children aged 3 to 36 months. Using data for 8 managed care organizations from the Vaccine Safety Datalink between 2004 and 2010, 72 patients with confirmed cases of pertussis were matched to 288 randomly selected controls (4 each). The number of DtaP (diphtheria, tetanus toxoids, and acellular pertussis vaccine) doses that were missed or delayed was calculated.

Results showed that more children with pertussis had missed or had delayed vaccine (47.22% vs 22.22% for control) and that children undervaccinated for 3 or 4 doses of DtaP were significantly more likely to be diagnosed with pertussis than those who had been age-appropriately vaccinated. It is hoped that these findings may persuade parents of the risks associated with delaying or missing DtaP doses in the vaccination schedule.


Recent study conducted in maternity ward finds that although parental knowledge of pertussis is lacking, parental acceptance of vaccine is high

Parental immunization (cocooning) is a potentially effective strategy to protect newborns against pertussis. However, the effectiveness of this approach relies on the active involvement of those who are in close contact with these infants. Therefore, to evaluate the potential of a cocooning-based approach, this study assessed vaccine coverage rates and baseline knowledge regarding pertussis and vaccine recommendations in postpartum parents in a maternity ward in Canada.

Results showed that baseline knowledge on infant disease severity and adult vaccine recommendations were poor. Indeed, only 6% of women were considered protected. However, when vaccination against pertussis was offered, the majority of the parents accepted (46.9% of mothers and 60.5% of fathers). Therefore, although many parents are unaware of the importance of cocooning to protect their infants, when vaccination is offered within the maternity ward, the majority of parents will participate. This supports the use of a simple and cost-effective approach to promoting cocooning and increasing vaccine uptake.
Novel postpartum pertussis vaccination strategy which increased coverage in parents of newborns likewise changed the vaccination practices of maternity ward doctors

In 2008, a postpartum vaccination strategy was introduced in the maternity ward of the Angers University Hospital, France to increase coverage of parents of newborns. As a result, a vaccine coverage rate of 69% among mothers and 63% among fathers was achieved. The study described in this paper researched the impact of this strategy on the vaccination practices of general practitioners (GPs) in the county for which Angers is the main specialist maternity ward, through the use of an anonymous survey.

Data revealed that 97.8% of the respondents were familiar with the vaccination recommendations and further, 97.6% revealed that they had disseminated this information to their patients. Furthermore, almost all of the GPs who replied approved of the strategy and the majority of them said they had changed their information and vaccination practices since 2008. In conclusion, the majority of the maternity ward doctors were well informed about the protocol and this led to better patient education and increased coverage.


Link: http://www.ncbi.nlm.nih.gov/pubmed/23973244

Re-analysis of published data reveals that the whole-cell vaccine may not be associated with a reduced risk of pertussis relative to acellular vaccines

The results from a recently published study (Witt MA et al. Clin Infect Dis. 2013;56(9):1248-1254) suggested that the durability of the immune response was strengthened when 1 or more whole-cell vaccines were included in the vaccination schedule. Re-analysis of these data by André et al, allowed estimation of the pertussis attack rate per 100,000, which was then compared across age groups in subjects vaccinated with either whole-cell or acellular vaccines. Results showed that regardless of age, individuals receiving the whole-cell vaccine did not have a reduced risk of pertussis when compared with recipients of the acellular vaccine.

Reference: André P, Johnson DR, Greenberg DP, Decker MD. Reduced risk of pertussis in whole-cell compared to acellular vaccine recipients is not supported when data are stratified by age. Clin Infect Dis. 2013 Sep 5. [Epub ahead of print]

Link: http://www.ncbi.nlm.nih.gov/pubmed/23956165


Link: http://www.ncbi.nlm.nih.gov/pubmed/23487373

Reply to André et al
http://cid.oxfordjournals.org/content/early/2013/09/05/cid.cit554.extract

Effectiveness of pertussis vaccines for adolescents and adults: case-control study.

This case-control study assessed the effectiveness of reduced acellular pertussis (Tdap) vaccines in individuals aged 11 years and older from Kaiser Permanente Northern California. All such cases from January 2006 to December 2011 that had been confirmed by polymerase chain reaction (PCR) (n = 668) were compared for Tdap vaccination status against 2 control groups: individuals testing negative for pertussis by PCR (n = 10,098) and closely matched people from the same general population (n = 21,599). A significantly lower Tdap vaccination rate of 24.0% was reported for PCR positive cases versus 31.9% in PCR negative controls. Similarly, an estimate of the effectiveness of Tdap vaccination against pertussis, adjusted for demographic factors, was found to be 53.0% in the comparison with PCR controls and 64.0% in the comparison with Kaiser Permanente Northern California controls. In conclusion, Tdap vaccination was moderately effective at preventing PCR confirmed pertussis among adolescents and adults.


**Bordetella pertussis** infection induces a mucosal IL-17 response and long-lived immune memory cells in nonhuman primates.

Despite near universal vaccine coverage, the bacterial pathogen **Bordetella pertussis** has re-emerged as a major public health concern. A baboon (Papio anubis) model of pertussis was recently developed that provides an excellent model of human pertussis. Using this model, this study characterized the immune response to pertussis by measuring cytokines in the nasopharyngeal mucosa of infected baboons.

The investigators observed mucosal expression of interleukin-17 (IL-17), IL-6, IL-23, and several cytokines and chemokines that are orchestrated by IL-17 immune responses. In addition, substantial populations of circulating **B. pertussis**-specific Th17 and Th1 cells were found in convalescent animals >2 years postinfection. This is consistent with a role in immunological memory to pertussis. Collectively, these data shed important light on the innate and adaptive immune responses to pertussis in a primate infection model.


**NEWS FROM RECENT CONFERENCES**

**10th International Symposium on Bordetella, September 8–11, 2013**

*Abstract book is not available to the public*

**Dissection of the Bordetella pertussis Memory T Cell Responses in 9 to 12 Year-Old Children Vaccinated With Whole Cell or Acellular Vaccines.** Smits K, Pottier G, Smet J, et al. O5

A complex, yet not completely unraveled, combination of antibodies and T-cell responses directed against multiple components of **Bordetella pertussis** confers protection against disease. To better understand vaccine-induced protection and its potential failure in light of recent whooping cough resurgence, this study evaluated quantity as well as quality of memory T-cell immune responses after vaccination.

A technique based on flow cytometry was used to detect proliferation, cytokine expression, and phenotype of antigen specific cells.

It was demonstrated that **B. pertussis**-specific memory T cells are detectable several years after vaccination, as evaluated in 9- to 12-year-old children with a median of 4 years elapsed from the last booster vaccine. Furthermore, dissecting the cellular immune response revealed that whole-cell pertussis vaccination compared favorably to acellular vaccination in terms of cytokine production, although the cohorts in this study were relatively small, hampering definite conclusions. Phenotyping of the responding cells showed that the majority of antigen-specific cells, whether defined by proliferation or cytokine production, were CD45RA CCRT effector memory T cells.

These results support the immunological findings of recent epidemiological studies indicating that the choice of infant vaccination influences protection in the long run, with whole-cell vaccinated adolescents more protected than those given acellular pertussis vaccines.


During the last quarter of 2011, the expected seasonal reduction in laboratory-confirmed pertussis cases did not occur. Instead, the number of confirmed cases continued to increase, reaching an unusually high monthly peak in October 2012. This generated a total of 9747 confirmed cases for 2012, almost 10 times higher than 2011 (1119 cases) and the previous peak in 2008 (903 cases).

Subsequently, the estimated 2012 disease incidence was 17.35 per 100,000 (compared with 1.99 per 100,000 in 2011).

The increase in laboratory confirmations has largely been due to serological testing of those aged 15 years and over (82% of all confirmations in 2012). However, the number of confirmations was higher than in 2011 for all age groups. Incidence was highest in those aged <3 month olds (240 per 100,000).

As part of national surveillance, the investigators for this study received and analyzed 120 **B. pertussis** isolates during 2012. The results showed that the **B. pertussis** population was almost identical to the previous peak in 2008. 68% of isolates were MLV-27, 100% were ftxA(1), 93% were prn(2), and 98% were ptxP(3). The only noticeable difference occurred in fimbrial serotypes: 58%:40% Fim3:Fim2 in 2012 vs 96%:2% ratio in 2008. Over 95% isolates expressed solely Fim3 between 2002 and 2009. However, this
percentage has been slowly decreasing since 2010. Whether this observation is linked to the recent rise in cases or to changes in vaccination policy in the last decade remains to be determined.

Prevalence and Molecular Characterization of Pertactin-deficient Bordetella pertussis in the US. Pawloski L, Queenan AM, Cassiday P, et al. O10

Pertussis has made a striking resurgence in the US, returning to record numbers of reported cases last observed in the 1950s. Circulating isolates differ from isolates used to formulate pertussis vaccines. Bordetella pertussis isolates lacking pertactin expression have been observed worldwide, including in the US in 2013. Screening of 1300 isolates from outbreak and surveillance studies (the 2012 Washington pertussis outbreak, US isolates from routine surveillance between 2010–2012, the 2010 California pertussis outbreak, and historical isolates collected from 1935–2009) by conventional PCR, and later by Western blot and prn sequencing analyses, ultimately identified 293 pertactin-deficient isolates. Of these pertactin-deficient strains, 276 were identified as having an IS481 in the prn gene (prnIS481-positive). A single prnIS481-positive isolate was found in 1994, with the next detected in 2010. Pertactin-deficient isolates increased substantially to over 50% in 2012. Sequence analysis of pertactin-deficient isolates revealed various types of mutations in the prn gene, including 2 deletions, single nucleotide substitutions resulting in a stop codon, an inversion in the promoter, and single nucleotide insertions resulting in frame shift mutations. The majority of the mutant types were prn2 alleles. CDC013 was a predominant pulsed-field gel electrophoresis (PFGE) profile in the pertactin-positive isolates, but was found in only 5% of the pertactin-deficient isolates. Interestingly, PFGE profiles CDC002 and CDC237 represented 58% of the identified pertactin-deficient isolates from 2010 to present. These results indicate that there has been a recent, dramatic increase in pertactin-deficient B. pertussis isolates throughout the US.


Due to a pertussis upsurge since 1996, anacellular preschool booster was introduced in 2001 and anacellular vaccine (ACV) replaced the whole-cell vaccine (WCV) in infancy in 2005. This study aimed to measure the impact of these interventions in the light of a large outbreak in 2012. Notifications in the periods 1996–2001 (WCV, pre-booster), 2002–2004 (WCV, post-booster), 2005–2011 (ACV, post-booster) and 2012 were analyzed. The “screening” method was used to calculate vaccine-effectiveness (VE) using notification and coverage data. The overall mean incidence rate (IR) of notifications per 100,000 increased from 30 (1996–2001) to 35 (2002–2004), 38 (2005–2011) and 82 (2012). Mean VE in 1 to 3-year olds increased from 31% (1996–2004) to 83% (2005–2011) and 93% (2012). In the cohorts targeted for the booster vaccination, VE decreased from 82% to 52% in 5- and 9-year-olds, respectively.

These findings demonstrate that changes in the vaccination program have lowered IRs in targeted cohorts and the protective effect of the preschool booster wanes within 5 years. Conversely, IR in those aged >9-years was shown to have increased over time. Consequently, infants too young to be vaccinated, show little benefit of the measures taken, probably due to the increased circulation of pertussis in adolescents and adults. It is therefore of great importance that new vaccination strategies be considered to prevent pertussis in these infants.

Additional abstracts of interest:


Molecular Characterization of Bordetella pertussis Isolates Without Expression of Vaccine Antigen Pertactin in Finland. Barkoff AM, Mertsola J, He Q. P3


Emergence of Pertactin Deficient Bordetella pertussis in Australia Is Due to Independent Events. Lam C, Octavia S, Ricafort L, et al. P11
**Bordetella pertussis Seroprevalence in Belgian Adults 20-40 Years Old, Anno 2012.** Huygen K, Rodeghiero C, Govaerts D, , et al. P65

**Survey on Household Contacts of Infants Under 3 Months of Age During a National Pertussis Outbreak in England and Wales.** Kara E, Armithalingam G, Campbell H, et al. P68


**Comparison of Immune Responses in Pregnant and Age-matched Non-pregnant Women Following a Booster Dose of Pertussis Containing Vaccine.** Huygen K, Leuridan E, Rodeghiero C, et al. P88

**Adverse Events Following Immunization (AEFI) With Tdap in Pregnant Women in Vietnam and Belgium.** Leuridan E, Hoang TTH, Maertens K, et al. P91

**Implications of Maternal Pertussis Immunization: Multiple Vaccines for Recurrent Pregnancies in a Three-Year Period.** Schlaudecker E, Langdon G, Black S. P102

**IDWeek 2013, October 2–6, 2013**

All IDWeek 2013 abstracts can be obtained at [https://idsa.confex.com/idsa/2013/webprogram/](https://idsa.confex.com/idsa/2013/webprogram/)


A sixth dose of pertussis-containing vaccine, tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap), was recommended in 2005 for adults and adolescents, with preferred administration at 11-12 years. In 2012, Washington State declared a pertussis epidemic with a record 4921 cases reported. Despite high vaccine coverage with Tdap, an unexpectedly high disease incidence was observed in adolescents 13–14 years of age – the first birth cohorts to be vaccinated exclusively with acellular pertussis vaccines – suggesting early waning of immunity. A matched case-control study was conducted in Washington State to assess Tdap vaccine effectiveness (VE) and duration of protection among adolescents 11–14 years of age. Pertussis cases reported in countries with >50 cases from January 1 to June 30, 2012 were included. Cases were identified using Washington State surveillance definitions. Three controls were matched by healthcare provider and birth year to each case. Vaccination history was obtained through medical records, the state immunization registry and parent interviews. A total of 472 cases and 1362 controls were included in the analysis. Tdap vaccination status was verified in 94% of these subjects. Excluding those not verified, 77% of cases and 88% of controls received Tdap. VE within 1 year of Tdap vaccination was 75%. At ≥2 years post-vaccination, VE declined to 41%. This is the first study to estimate Tdap VE and duration of protection among adolescents who would have been vaccinated solely with acellular pertussis vaccines, and preliminary results indicate that Tdap VE is modest and wanes substantially with time. In summary, although current Tdap vaccines may not fully control pertussis in the United States, vaccination remains the best way to protect individuals against disease.

Additional abstracts of interest:

**Factors Associated with “Cocooning” Newborn Infants to Prevent Influenza and Pertussis.** O’Leary S, Pyrzanowski J, McCauley S, et al. P147

**High Rate of Vaccine Failure After Administration of Acellular Pertussis Vaccine Pre- and Post-Liver Transplantation in Children.** Ito K, Funaki T, Shoji K, et al. P573

**Effect of a Comprehensive Effort to Increase Pertussis Vaccination Among Direct-Care Healthcare Workers.** Knepper B, Burman W, Bisek M, Deyoung K, Price C. P148

**Provider Awareness and Altered Practice Following a 2011-2012 Bordetella pertussis Outbreak, New York City.** Arciuolo R, Rosen J, Zucker J. P940

## UPCOMING EVENTS

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<th>Meeting name, date, and venue</th>
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<td><strong>WSPID 2013:</strong> 8th Biennial World Congress of the World Society for Pediatric Infectious Diseases, November 19–22, 2013, Cape Town, South Africa</td>
<td>The conference will provide approximately 2000 specialists a world forum for sharing the latest knowledge and receiving updates on the treatment and prevention of pediatric infectious diseases. Website: <a href="http://www.wspid.com/">http://www.wspid.com/</a></td>
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<td><strong>ICID 2014:</strong> 16th Biennial International Congress on Infectious Diseases April 2–5, 2014, Cape Town, South Africa</td>
<td>The meeting will encompass all fields in infectious diseases with particular attention being paid to the major infectious causes of death. Website: <a href="http://www.isid.org/">http://www.isid.org/</a></td>
<td>December 2, 2013</td>
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<td><strong>24th Annual European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), May 10–13, 2014, Barcelona, Spain</strong></td>
<td>The program will focus on the latest developments in clinical microbiology and infectious diseases. This is the largest European microbiological meeting, attracting more than 7000 attendees a year. Website: <a href="http://www.eccmid.org/">http://www.eccmid.org/</a></td>
<td>December 10, 2013</td>
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<td><strong>114th Annual General Meeting of the American Society for Microbiology (ASM) May 17–20, 2014, Boston, USA</strong></td>
<td>ASM 2014 will include diverse perspectives and in-depth discussions on the current state and future direction of microbiology, and is the largest microbiological meeting, with 9000 attendees expected. Website: <a href="http://asm.org/asm2014">http://asm.org/asm2014</a></td>
<td>Website will open in November 2013</td>
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<td><strong>32nd Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID), May 6–10, 2014, Dublin, Ireland</strong></td>
<td>ESPID 2014 provides its 3000 attendees unparalleled access to the latest data and interpretation in the field of pediatric infectious diseases. Website: <a href="http://espid.kenes.com/scientific-information/abstract-submission">http://espid.kenes.com/scientific-information/abstract-submission</a></td>
<td>January 14, 2014</td>
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<td><strong>ICHS 2014:</strong> 18th Biennial International Symposium on Infections in the Immunocompromised Host June 15–17, 2014, Berlin, Germany</td>
<td>The scientific program will include plenary talks, symposia, roundtables, and poster and Meet the Expert sessions. A total of 300–400 delegates are expected to attend. Website: <a href="http://www.ichs.org/">http://www.ichs.org/</a></td>
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