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Infections Associated With Group Childcare

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On average, 12.5 million (61%) of the 20.4 million children in the United States who are younger than 5 years of age were enrolled in a regular childcare arrangement during the spring of 2011.1 Group childcare settings can increase the frequency of certain infectious diseases and amplify outbreaks of illness (Table 3.1). Aggregation of young children potentiates transmission of organisms that can produce disease in other children, adult care providers, parents, and community contacts. Children newly entered into group childcare are at especially high risk of enteric and respiratory tract infections. However, mothers whose children were enrolled in group childcare before 2.5 years of age reported their children had less frequent respiratory and gastrointestinal tract infections and episodes of otitis media during elementary school years.² A longitudinal repeated-event analysis of 3963 newborns followed for 8 years found that children who were enrolled in childcare at <2 years of age had more episodes of wheezing in the first years of life; however, among those children without older siblings, wheezing episodes and steroid use between ages 4 and 8 years were reduced compared with children who were not enrolled in childcare at an early age. Overall, early childcare was not found to be protective against asthma symptoms, airway hyperresponsiveness, or allergic sensitization when children were assessed at 8 years of age.³ An increase in antibiotic use as an attempt to facilitate earlier return to care enhances the potential for emergence of resistant organisms, thus resulting in an increased economic burden to individual persons and society.⁴⁻⁶ Despite the challenges of frequent respiratory and gastrointestinal illness exacerbations among children enrolled in group childcare, these arrangements facilitate opportunities for socialization and enable primary caregivers to be employed outside the home.

CHILDCARE SETTINGS

Quantifying the number of children participating in each type of childcare setting is challenging because of different ascertainment methods used in several data sources. Types of facilities can be classified by size of enrollment, age of enrollees, and environmental characteristics of the facility. Grouping of children by age varies by setting, but in organized care facilities children usually are separated into the following groups: infants (6 weeks through 12 months), toddlers (13 through 35 months), preschoolers (36 months through 59 months), and school-aged children

(5 through 12 years). These designations have relevance to infectious disease epidemiology as well as regulation and monitoring. Most nonrelative care provided in an organized care facility is subject to state licensing and regulation, whereas care by a relative in a child's or provider's home is usually not subject to state regulations and monitoring.

The United States Census Bureau conducts the Survey of Income and Program Participation (SIPP), which collects information about childcare arrangements for children <15 years of age. In 2011, 51% of children <5 years of age with working mothers were cared for by a relative, 33% were in organized care including center-based care or family childcare homes, 27% had multiple arrangements, and 11% did not have a regular childcare arrangement, with some survey respondents selecting more than 1 option.1

EPIDEMIOLOGY AND ETIOLOGY OF INFECTIONS

Although most infectious organisms can be associated with outbreaks in settings that do not involve childcare, many agents have the propensity to propagate in childcare settings (see Table 3.1.)

Enteric Infections

Enteric viruses are the predominant cause of diarrheal syndromes among children in group childcare.7 Outbreaks of diarrhea occur at a rate of approximately 3 per year per childcare center and are associated most frequently with organisms that cause infection after ingestion of a low inoculum. These organisms generally are transmitted from person to person and include rotavirus, norovirus, sapovirus, astrovirus, enteric adenovirus, Giardia intestinalis, Cryptosporidium, Shigella spp., Escherichia coli O157:H7, other Shiga toxin-producing E. coli (STEC), E. coli O114, and enteropathogenic E. coli. These fecal coliforms and enteric viruses contaminate the environment with greater frequency during outbreaks of diarrhea. In a prospective study of acute gastroenteritis in childcare centers, viruses isolated from the stool of children with diarrhea also were detected on environmental surfaces in 45% of outbreaks.8 The inoculum associated with diarrhea, the attack rates, and the frequency of asymptomatic excretion of organisms for common enteric infections in childcare settings are shown in Table 3.2. Reported attack rates depend on several factors, including methods used for organism detection.

TABLE 3.1 Association of Infectious Diseases With Group Childcare Settings					
Disease or Infection	Risk Factors and Association With Outbreaks				
Enteric Viral	Close person-to-person contact, fecal-oral contact, suboptimal hand hygiene and food preparation practices				
Rotaviruses, enteric adenoviruses, astroviruses, noroviruses, hepatitis A virus (HAV) Bacterial	Commonly associated with outbreaks; HAV and rotavirus vaccine preventable				
Shigella spp., Escherichia coli O157:H7	Commonly associated with outbreaks				
Campylobacter spp., Salmonella spp., Clostridium difficile Parasitic	Less commonly associated with outbreaks				
Giardia intestinalis	Commonly associated with outbreaks				
Cryptosporidium parvum					
Respiratory tract (acute upper and lower respiratory tract infections and invasive disease) Bacterial	Aerosolization and respiratory droplets, person-to-person contact, suboptimal hand hygiene				
Haemophilus influenzae type b (Hib)	Few outbreaks; vaccine preventable				
Streptococcus pneumoniae	Few outbreaks; vaccine preventable; invasive S. pneumoniae caused by serotypes not in vaccine				
Group A streptococcus	Few outbreaks and low risk of secondary cases				
Neisseria meningitidis	Few outbreaks; some serogroups vaccine preventable				
Bordetella pertussis	Increasingly associated with outbreaks in childcare centers and schools; vaccine preventable				
Mycobacterium tuberculosis Kingella kingae	Occasional outbreaks, usually as a result of contact with an infectious adult care provider Outbreaks rare; oropharynx usual habitat; usually manifest as arthritis and osteomyelitis				
Viral					
Rhinoviruses, parainfluenza, influenza, respiratory syncytial virus (RSV), respiratory adenoviruses, influenza, metapneumoviruses, bocavirus	Disease usually caused by same organisms circulating in the community; influenza vaccine preventable in children ≥6 months of age				
Multiple organ systems					
Cytomegalovirus	Prevalent; asymptomatic excretion with transmission from children to providers				
Parvovirus B19	Outbreaks reported; risk to susceptible pregnant women and immunocompromised				
Varicella-zoster virus (VZV)	Outbreaks in childcare centers occur; vaccine preventable in children ≥12 months of age; zoster lesions present low risk of infection				
Herpes simplex virus (HSV)	Low risk of transmission from active lesions and oral secretions				
Hepatitis B virus	Rarely occurs in childcare centers; vaccine preventable				
Hepatitis C virus	No documented cases of transmission in the childcare setting				
Human immunodeficiency virus (HIV)	No documented cases of transmission in the childcare setting				
Skin Staphylococcal and streptococcal impetigo	Close person-to-person contact Transmission increased by close person-to-person contact with lesions; outbreaks less likely with decreased incidence of varicella infections; methicillin-resistant <i>Staphylococcus aureus</i> (MRSA) infection common				
Scabies	Outbreaks in group childcare reported				
Pediculosis	Common in children attending group childcare				
Ringworm	Tinea corporis and tinea capitis outbreaks associated with childcare				
Conjunctiva	Outbreaks in group childcare reported with both bacterial and viral causes				

TABLE 3.2 Outpleaks of Diamiea by organism					
Organism	Inoculum Required to Cause Diarrhea in Adult Volunteers	Attack Rate in Enrollees (%)	Secondary Attack Rate in Family Members (%)	Asymptomatic Excretion in Enrollees	
Rotavirus	18–1000 virions	50	15–80	Common	
Enteric adenovirus	Unknown	40	Unknown	Common	
Astrovirus	Unknown	50–90	Unknown	Common	
Calicivirus	Unknown	50	Unknown	Common	
Giardia intestinalis	10 ¹⁻² cysts	17–54	15–50	Common	
Cryptosporidium	132 oocysts	33–74	25–60	Common	
Shigella	10 ¹⁻²	33–73	25–50	Uncommon	
<i>Escherichia coli</i> 0157:H7 0114:NM 0111:K58	10 ⁸	29, 34 67 56, 94	Unknown Unknown Unknown	Uncommon Uncommon Uncommon	
Clostridium difficile	Unknown	32	Unknown	Common	

Organisms generally associated with foodborne outbreaks, including *Salmonella* spp. and *Campylobacter jejuni*, are infrequently associated with diarrhea in the childcare setting. However, reports of childcare outbreaks of diarrhea in association with ingestion of fried rice contaminated with *Bacillus cereus*,⁹ and of norovirus infection in association with frozen strawberries,¹⁰ highlight the issue that foodborne outbreaks can occur in the childcare setting, especially when food is prepared and served at the childcare center.

Spread of diarrheal pathogens from index cases in the childcare setting to family members has been reported for many enteropathogens (see Table 3.2), with secondary attack rates ranging from 15% to 80%. During outbreaks of diarrhea in childcare centers, asymptomatic excretion of enteropathogens is frequent (see Table 3.2). In a longitudinal study of serial stool samples collected from 82 children <2 years of age in a childcare center, enzyme immunoassay revealed that 21 of 27 (78%) children from whom *G. intestinalis* was detected and 19 of 37 (51%) children from whom rotavirus was detected were asymptomatic.¹¹ A point-prevalence evaluation of 230 asymptomatic preschool children attending childcare in southwest Wales and inner London demonstrated a 1.3% fecal colonization rate with both *Cryptosporidium* and *Giardia* spp.¹² The role that asymptomatic excretion of enteropathogens plays in spread of disease is unknown.

Acute infectious diarrhea is 2 to 3 times more common in children enrolled in out-of-home childcare than in age-matched children cared for at home.^{13–15} Approximately 20% of outpatient visits for acute diarrheal illness among children younger than 3 years of age are attributable to childcare attendance.¹³ In addition, the incidence of diarrheal illness is threefold higher among children during their first month in out-of-home childcare compared with children cared for at home.^{13,16,17}

Diarrhea occurs 17 times more frequently in diapered children than in toilet-trained children.¹⁷ Higher attack rates among diapered children may represent exposure of a younger, nonimmune cohort. In contrast, in a multicommunity group childcare outbreak of *Shigella sonnei*, the highest attack rates were noted in rooms where both toilet-trained and diapered children were co-mingled (14%) compared with rooms with toilet-trained children only (9%) and rooms with diapered children only (5%), despite comparable availability of sinks and toilets.¹⁸ The likely reason for this finding was that the toilet-trained children were acquiring continence, and the diarrhea resulting from their shigellosis made them incontinent. Investigators in North Carolina demonstrated that adherence to proper diapering and hand hygiene practices and use of dedicated food preparation equipment decreased the incidence of diarrheal illness among children and staff in out-of-home childcare centers.¹⁹

Enteric Viral Infections

Rotavirus. In the prerotavirus vaccine era, rotaviruses were the most common cause of significant symptomatic diarrhea in children <2 years of age. Person-to-person transmission by the fecal-oral route predisposes nonimmune infants and young children and their childcare providers to rotavirus infection. Because rotavirus can be isolated from human stools for approximately 21 days after illness onset and rotavirus RNA can be detected on toys and surfaces in childcare centers, this organism has been associated with outbreaks of diarrhea in the childcare setting.²⁰

Primary prevention of rotavirus in all settings is accomplished with the completion of an oral rotavirus vaccine series. The universal uptake of rotavirus immunization in the US has changed the epidemiology of rotavirus infections and has resulted in a greatly reduced burden of disease and consequently fewer childcare-associated outbreaks.²¹ Pediatric rotavirus immunization has also provided indirect protection to adults, with a decline in peak prevalence by nearly 50% in 1 study.²² Rotavirus-immunized childcare enrollees can therefore provide indirect protection to rotavirus-nonimmune childcare providers, thus reducing opportunities for person-to-person transmission.

Norovirus. In the postrotavirus vaccine era, norovirus has become the leading cause of acute gastroenteritis in young children. A population-based surveillance study of children younger than 5 years of age with acute gastroenteritis who presented for medical care in 3 counties surrounding Nashville, Tennessee, Cincinnati, Ohio, and Rochester, New York in 2009 and 2010 detected norovirus in 278 (21%) of 1295 stool specimens, compared with rotavirus in 152 (12%).²³

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Several features of norovirus facilitate its spread, including the low inoculum required for transmission (approximately 18 to 1000 virions), asymptomatic shedding that can precede and extend beyond symptom duration (in up to 30% of infections), tolerance to a wide range of temperatures that facilitates persistence on environmental surfaces, and strain-specific immunity.²⁴ Outbreaks can occur in a variety of settings including childcare centers, long-term care facilities, hospitals, restaurants, and cruise ships. Two epidemiologic studies of norovirus gastroenteritis in Germany and Japan found that genogroup GII strains predominated in outbreaks associated with childcare facilities while these strains were circulating in the community.^{25,26}

Hepatitis A Virus. Hepatitis A virus (HAV) infections usually are mild or asymptomatic in children, and outbreaks in childcare centers generally are not recognized until illness becomes apparent in older children or adults. The first outbreak of HAV infection in a childcare center was reported in 1973 in North Carolina,²⁷ with subsequent outbreaks recognized throughout the US.²⁸ Before routine immunization of children with hepatitis A vaccines in the US, approximately 15% of HAV infections were estimated to be associated with childcare centers. Uptake of universal hepatitis A immunization in children has correlated with a decreasing proportion of outbreaks among children in childcare and elementary school settings, as well as among adults who have contact with children enrolled in childcare centers.^{29,30}

Peak viral titers in stool and greatest infectivity with hepatitis A occur during the 2 weeks before onset of symptoms. HAV infections are transmitted in the childcare setting by the fecal-oral route and occur more frequently in settings that include diapered children. The mainstays of prevention of HAV infection include maintenance of personal hygiene, hand hygiene, disinfecting procedures, and immunization.

The US Centers for Disease Control and Prevention (CDC) recommend hepatitis A vaccine for all children beginning at 1 year of age, with the 2 doses administered 6 to 18 months apart.³¹ Administration of hepatitis A vaccine to unimmunized, immunocompetent people 12 months through 40 years of age also is recommended for postexposure prophylaxis (PEP).32,33 The CDC advises that vaccine PEP be administered to all previously unvaccinated staff and attendees of childcare centers or homes when 1 or more HAV infections are identified in children or employees or when an HAV infection is recognized in 2 or more households of center attendees. In centers that provide care only to toilet-trained children, PEP need be administered only to unimmunized classroom contacts of the index child. If an HAV infection is identified in 3 or more households, PEP should be considered for members of households with diapered children attending the childcare center.³⁴ Standard immune globulin (IG) is no longer recommended for HAV PEP in the US in most situations. Despite the decline in the incidence of HAV, continued education, training, and monitoring of staff regarding appropriate hygienic practices are essential components of any prevention plan.

Enteric Bacterial Infections

Escherichia coli. Bacterial pathogens that have the potential to cause severe systemic infections, including E. coli O157:H7 and other Shiga toxin-producing E. coli (STEC) strains, have been associated with fecaloral transmission in group childcare settings. An epidemiologic study of non-O157 STEC outbreaks in the US found that 15 (39%) occurred through person-to-person transmission, with 13 (87%) of those occurring in childcare centers.³⁵ In an outbreak of E. coli O157:H7 infection in a childcare center in Bronx, New York, 11 of 45 attendees tested positive for E. coli O157:H7 by stool culture or Shiga-like toxin assay.³⁶ The original source of the outbreak was not determined; however, multiple sanitary violations were identified, including improper disinfection of diaper changing tables, lack of sanitary distribution of food, and inadequate exclusion of attendees who had diarrheal illnesses. After 2 cases of STEC were identified at a childcare center in Norway, an outbreak investigation found 9 additional cases among the 91 children enrolled and 1 case among the 41 employees; no evidence of common exposures was found, and person-to-person transmission was determined to be likely. Three of the persons with cases were asymptomatic, a finding that raises important questions regarding the utility of exclusion policies and screening of asymptomatic contacts.⁴

Shigella sonnei. S. sonnei causes periodic multicommunity outbreaks in group childcare settings. Childcare attendance and age <60 months

were associated with illness in a community outbreak of S. sonnei among traditionally observant Jewish children in New York City in 2000. Multiple illnesses in a single household were determined to result from intrahousehold secondary transmission. A multicommunity outbreak of more than 1600 culture-confirmed cases in the greater metropolitan area of Cincinnati, Ohio in 2001 had an overall mean attack rate of 10% among childcare center enrollees. The highest attack rates occurred among newly or incompletely toilet-trained enrollees, and the lowest attack rates were noted among diapered children. The attack rate was 6% among staff members. Secondary transmission was facilitated by poor hygiene practices, including inaccessible handwashing supplies and incomplete diaper disposal practices, as well as through recreational activities involving water.¹⁸ A prolonged multistate increase of shigellosis caused by organisms with similar biochemical and genetic profiles occurred in the South and mid-Atlantic areas in 2001 to 2003. A substantial proportion of infections was associated with group childcare.³⁹ In 2005, 639 cases of multidrug-resistant S. sonnei were reported in northwest Missouri. A case-control investigation of 39 licensed childcare centers demonstrated that centers with ≥ 1 sink or a diapering station in each room were less likely to have cases, thus reinforcing the importance of environmental design and hygiene in reducing the propagation of shigellosis in childcare centers.⁴⁰ An observational study following a shigellosis outbreak in St. Louis, Missouri examined the utility of requiring a second negative convalescent stool culture among those excluded from work or childcare. Of the 172 people who submitted at least 2 follow-up cultures, the probability that S. sonnei was isolated from a second culture after being isolated from a first culture was 7%. All (100%) of the second cultures from people who had a first negative follow-up culture result were without growth of S. sonnei, a finding suggesting that a single negative convalescent culture result is sufficient to document clearance.4

Respiratory Tract Infections

Organisms responsible for respiratory tract infections in childcare settings are similar to organisms that circulate in the community and include respiratory syncytial virus (RSV), parainfluenza viruses, adenovirus, rhinovirus, coronavirus, influenza viruses, human metapneumovirus, bocavirus, parvovirus B19, and *Streptococcus pneumoniae*.

Children <2 years of age who are attending childcare centers have an increased number of upper and lower respiratory tract infections, including acute otitis media and pneumonia, compared with agematched children cared for at home. Approximately 10% to 17% of respiratory tract infections in US children <5 years of age are attributable to childcare attendance.^{42,43} A prospective cohort study found that 89% of disease episodes among children attending a childcare center are respiratory tract infections.⁴⁴ Another prospective cohort study following 119 childcare attendees through 24 months of age demonstrated a mean annual incidence of 4.2 respiratory tract infections per child during the first year of childcare enrollment and 1.2 per child during the second year of childcare enrollment. One or more viruses were detected by real-time reverse transcriptase polymerase chain reaction (real-time RT-PCR) from two thirds of the children with respiratory tract infections.⁴⁵ Molecular-based diagnostics have increased the yield of virus detection in children with respiratory tract infections. An epidemiologic study of childcare attendees with new-onset respiratory illness detected at least 1 virus in 84% and multiple viruses in 46% of cases using PCR. Children with multiple viruses detected at the onset of illness were less likely to have fever (odds ratio [OR] 0.6; 95% confidence interval [CI], 0.4–0.9) but more likely to have symptoms lasting >7 days (OR 1.9; 95%) CI, 1.2-3.14).

A national registry-based study of Danish children from birth to 5 years of age revealed that the first 6 months of enrollment in group childcare among children enrolled at ≤ 1 year of age were associated with a 69% higher incidence of hospitalizations for acute respiratory tract infections compared with age-matched children in home care. The incidence of hospitalization decreased after 6 months of group childcare enrollment and was comparable to that of children in home care after >12 months of enrollment.⁴⁷ A prospective study comparing children enrolled in childcare in the first year of life with those who were not found that childcare attendees had more episodes of physician-diagnosed upper respiratory tract infections and acute otitis media in their first year

of life. Additionally, although the 2 groups had similar rates of illness over the entire 6-year study period, childcare attendees had increased visits to their general practitioner and an increased risk of specialist referral.⁴⁸

The risk of acute otitis media is increased among children enrolled in childcare, especially those <2 years of age. In 1 study, the incidence of otitis media was 1.5 times higher among children enrolled in childcare compared with children in home care.⁴³ Acute otitis media is the most common reason for antibiotic use in children <3 years of age in the childcare setting. Childcare attendance has been associated with increased risk of recurrent acute otitis media (>6 episodes in 1 year) and chronic otitis media with effusion persisting for more than 6 months. After controlling for the total size of the childcare group for children younger than 12 months of age, the previously established relationship between attending out-of-home childcare and frequent ear infections was reduced from an OR of 3.2 (95% CI, 1.5–6.7) to and OR of 1.34 (not significant; P = 0.60).⁴⁹ Because acute otitis media usually is diagnosed empirically, the relative contribution of bacterial versus viral causes is largely unknown.

Handwashing decreases the frequency of acute respiratory tract infections in childcare.^{50,51} A randomized controlled trial that included training childcare staff regarding handwashing, transmission modes of infection, and aseptic techniques related to nose wiping demonstrated a significant reduction in upper respiratory tract infections among enrollees <24 months of age.⁵⁰ A study to assess the potential role of clothing as a source of transmission of human rhinovirus found that teachers' clothing is unlikely to facilitate the transmission of rhinovirus in childcare settings. Symptomatic teachers are more likely to have rhinovirus in their nasal mucus and on clothing.⁵² Because most infectious agents are communicable for a few days before and after symptoms, exclusion of children and teachers based on upper respiratory tract symptoms is unlikely to decrease transmission, and the continued practice of respiratory and hand hygiene is likely to be more effective in preventing spread.

Respiratory Viral Infections

Influenza Virus. Rates of seasonal influenza are highest among children <2 years of age and older adults, and rates of complications are greatest among children of all ages with predisposing or underlying medical conditions. Among preschool-aged children with influenza virus infections, hospitalization rates range from 100 to 500 per 100,000 children, with the highest hospitalization rates among children from <1 year of age.⁵³ Influenza viruses are spread from person to person primarily through large respiratory tract droplets, either directly or by secondary contact with objects that are contaminated with infectious droplets. Children shed virus for several days before the onset of clinical symptoms and are contagious for >10 days following symptom onset. Transmission of infections can be increased by close contact among children who are not able to contain their secretions.

Annual vaccination of all people ≥ 6 months old is the primary method of preventing seasonal influenza infections.⁵⁴ A randomized controlled trial conducted during the 1996 to 1997 influenza season in 10 childcare centers in San Diego, California found that vaccinating children against influenza reduced influenza-related illness among their household contacts.⁵⁵⁻⁵⁷ In addition to preventing respiratory tract illness, influenza vaccine prevents acute otitis media among children attending childcare, as shown by several studies.^{50,51,58,59}

Routine use of intranasal influenza vaccine among healthy children can be cost effective and can be maximized by using group-based vaccination approaches. A prospective study of intranasal influenza vaccine in healthy children 15 through 71 months of age demonstrated clinical and economic efficacy when vaccination efforts were focused on children in group childcare settings.⁶⁰ Vaccinating children has been associated with indirect protection of older people as well.^{60,61}

Mandatory influenza vaccination before childcare attendance can increase immunization coverage and consequently decrease infection. In 2010, Connecticut became the second state, after New Jersey, to require all children 6 to 59 months of age in licensed childcare programs to receive at least 1 dose of seasonal influenza vaccine annually.⁶² Seasonal influenza vaccination rates among children 6 to 59 months of age in Connecticut increased from 68% in 2009 to 2010 to 84% in 2012 to 2013. Connecticut also was compared with the 10 other sites participating in the CDC Emerging Infections Program, none of which had an influenza vaccine mandate for childcare centers at the time. Between the 2007

to 2008 and the 2012 to 2013 seasons, Connecticut had the highest percentage of decrease in influenza-associated hospitalization rates; 9 of 10 sites without mandated influenza immunization for childcare attendees reported increasing influenza-associated hospitalization rates over this time period.

Childcare center closure as a strategy to prevent and monitor community spread of influenza was considered during the 2009 H1N1 influenza pandemic. Extrapolating to school-aged children, 58% of families of 402 students in Perth, Australia who were affected by pandemic-related school closures reported a substantial disruption of daily schedules. Almost one half of the parents had work absences, and 35% made alternative childcare arrangements. Children affected by the school closures were more likely to report out-of-home activities during the school closure period. Fewer than one half (47%) of the parent respondents believed that the school closures were an effective response in reducing the potential for community transmission.⁶³

Respiratory Syncytial Virus. RSV is among the most common causes of serious lower respiratory tract infections in young children, with an estimated 55,000 to 125,000 related hospitalizations and 200 to 500 RSV-related deaths annually in the US.⁶⁴ Attack rates as high as 98% have been reported after first exposure among children at risk for infection, with frequent reinfection (65% to 75%) on reexposure to RSV in the 2 years after initial exposure.⁶⁵

A prospective cohort study of children 4 weeks to 30 months of age who were attending full-time childcare detected RSV by RT-PCR from 59 (11%) of the children with respiratory illnesses and multiple viruses in 42 (71%) of the patients with RSV. This study also found longer duration of symptoms and increased frequency of healthcare visits in RSV-positive children compared with RSV-negative children. Additionally, 2 clusters of RSV infection resulted in 50% of enrolled children infected within 6 days of the index case in each room. When molecular sequencing was performed in 1 cluster, the same strain of RSV was isolated in 5 (38%) of 13 illness episodes, a finding suggesting rapid child-to-child transmission.⁶⁶

Respiratory Bacterial Infections

Pertussis. Infections caused by *Bordetella pertussis* in the US have increased dramatically since 2000; 7867 cases were reported in 2000, 27,550 cases in 2010, and 28,660 cases in 2014.^{67,68} Several pertussis epidemics have occurred since 2000, including outbreaks in Washington State in 2012 and in California in 2014.^{69,70} These outbreaks have been attributed to inadequate vaccine coverage and waning immunity related to universal use of acellular pertussis vaccines.

Incompletely immunized infants often experience severe clinical disease from pertussis. In many group childcare settings, adolescents and adults with mild to moderate illnesses can be the source cases of pertussis. An outbreak of pertussis occurring in a childcare center in northern Israel with 88% immunization coverage resulted in B. pertussis detected by a positive culture or PCR result in all unvaccinated children and in 7% of vaccinated children.⁷¹ In 2005, the CDC recommended that postpartum women and other contacts of newborn infants receive tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) vaccine to protect infants from pertussis exposure, a strategy known as cocooning.⁷² In 2011, the CDC recommended that unvaccinated pregnant women receive a dose of Tdap to protect infants by transplacental maternal antibody transfer.73 In 2012, the CDC expanded this recommendation to administration of Tdap immunization during the third trimester of every pregnancy.⁷⁴ Childcare providers of any age with routine contact with infants <12 months of age should receive a single dose of Tdap.7

Tuberculosis. An adult or adolescent often is the index case for *Mycobacterium tuberculosis* infections in a group childcare setting; child-to-child transmission occurs infrequently. An outbreak of tuberculosis (TB) associated with a private-home childcare facility in San Francisco, California occurred between 2002 and 2004. Of 11 outbreak cases, 9 (82%) occurred in children <7 years of age; all these children had extensive contact through childcare in a private home, where the adult index patient spent considerable time. Isolates from 4 of the pediatric patients and 2 of the adult patients had identical molecular patterns. Additionally, 36 children and adult contacts had latent TB infection.⁷⁵ In an outbreak of TB following prolonged contact with a provider with cavitary

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disease in a childcare center in Sweden, 17 children had radiographic evidence of pulmonary disease; 1 child had miliary disease, and 17 had latent TB infection.⁷⁶ These outbreaks demonstrate that detection and contact investigations in childcare centers are paramount in reducing TB infection.

Group A Streptococcus. Outbreaks of group A Streptococcus (GAS) infection among children and adult staff in childcare settings have been reported. In a study of prevalence of GAS conducted in a childcare center after a fatal case of invasive GAS disease, 25% of 258 children and 8% of 25 providers had GAS isolated from throat culture. Risk of carriage was increased in children who shared a room with the index case (OR, 2.7; 95% CI, 0.8–9.4).⁷⁷ Perianal GAS infection and infection associated with varicella also have been reported.^{78,79} A clone of GAS (*emm* type 4) was responsible for a community outbreak of streptococcal toxic shock syndrome among children attending a childcare center in northern Spain. In this situation, the outbreak-associated strains were not isolated from pharyngotonsillar swabs of staff, childcare, or household contacts of the colonized and infected children.⁸⁰

Invasive Bacterial Infections

Haemophilus influenzae Type b. Studies conducted before routine use of *Haemophilus influenzae* type b (Hib) conjugate vaccine in the US showed that the risk of developing primary invasive Hib infection was higher among children attending childcare centers than in children cared for at home, independent of other possible risk factors. Incorporation of Hib conjugate vaccines into the routine immunization schedule of children in the US dramatically reduced the frequency of invasive Hib disease. Oropharyngeal carriage of *H. influenzae* non-type b was associated with childcare attendance exceeding 15 hours per week in an epidemiologic study in Minnesota from 2008 to 2009.⁸¹ Despite its rising prevalence in other settings, nontypable *H. influenzae* has not been associated with childcare outbreaks.

Neisseria meningitidis. Risk of disease caused by *Neisseria meningitidis* can be increased in group childcare settings. Using space-time cluster analysis of invasive infections during 9 years of surveillance from 1993 to 2001 in the Netherlands, researchers noted that clustering beyond chance occurred at a rate of 3% and concluded that this rate was likely the result of direct transmission. Childcare center attendance was reported as the likely exposure for 8 of 40 (20%) clusters, thus accounting for 13 of 82 (16%) cases of invasive disease with multiple serosubtypes.⁸² For children 2 through 10 years of age, routine immunization with meningococcal conjugate vaccine is recommended only for those children at continued increased risk of invasive disease, a risk that does not include out-of-home childcare.⁸³

Streptococcus pneumoniae. Incorporation of heptavalent (7-valent) pneumococcal conjugate vaccine (PCV7) into the routine childhood immunization schedule in the US in 2000 resulted in dramatic reductions of both the frequency of invasive pneumococcal disease and the frequency of PCV7-containing serotypes.⁸⁴ Universal uptake of PCV7 also was associated with a decline in national rates of outpatient visits for acute otitis media in children <2 years old.⁸⁵ Serotype 19A was among the replacement serotypes associated with invasive disease in many communities,⁸⁶ as well as in childcare.⁸⁷ In 2010, introduction of a 13-valent pneumococcal conjugate vaccine (PCV13) replaced PCV7,⁸⁸ thus resulting in further declines in invasive pneumococcal disease among all age groups⁸⁹; vigilance for possible serotype replacement is ongoing.

Before the introduction of the PCVs, the risks of invasive pneumococcal disease, *S. pneumoniae* nasopharyngeal carriage, and carriage of antibiotic-resistant *S. pneumoniae* were increased in children attending childcare. This observation has not been fully explored in the postvaccine era. However, a French study of nasopharyngeal carriage of *S. pneumoniae* in childcare attendees found stable carriage rates, a decrease in all vaccine serotypes except 19A, and decreased antibiotic resistance from 1999 to 2012.⁹⁰ Secondary spread of *S. pneumoniae* in the childcare setting has been reported, but the risk has not been characterized.

Kingella kingae. Kingella kingae colonizes the oropharynx and respiratory tracts of young children and has been associated with invasive disease. Multiple childcare-associated outbreaks of *K. kingae* have been reported, primarily involving osteoarticular infections; endocarditis also has been described.⁹¹⁻⁹⁵

Invasive Viral Infections

Echovirus. During an outbreak of echovirus 30 infection in children and care providers in a childcare center, and in exposed parents, infection occurred in 75% of children and 60% of adults; aseptic meningitis was more frequent in infected adults (12 in 65; 18%) than in children (2 in 79; 3%).⁶ A retrospective cohort study of echovirus infections in 4 childcare centers in Germany revealed that 42% of childcare attendees, 13% of their household contacts, 5% of childcare center employees, and 2% of employees' household contacts were ill over a 31-day period. Thirteen percent (12 of 92) of childcare attendees had meningitis. This outbreak likely began among children enrolled in group childcare, with secondary cases occurring among their household contacts.⁹⁷ An association with childcare also was noted in an outbreak of echovirus 18 meningitis that occurred in a rural Missouri community with an attack rate of 1 per 1000 people; contact with childcare was noted as the most common risk factor among ill people.⁹⁸

Parvovirus B19. Parvovirus B19, the agent of erythema infectiosum (fifth disease), can cause arthropathy, transient aplastic crisis, persistent anemia in immunocompromised hosts, and nonimmune fetal hydrops. It spreads through contact with respiratory or oropharyngeal secretions. Serologic evidence of past infection has been reported to be 30% to 60% in adults, 15% to 60% in school-aged children, and 2% to 15% in preschool-aged children.⁹⁹ The virus is endemic among young children and has caused outbreaks of disease in the childcare setting.^{100,101} In an outbreak during which more than 571 school and childcare personnel were tested serologically, the highest attack rate (31%) occurred among childcare staff members revealed a seroprevalence of parvovirus B19 immunoglobulin G antibodies of 70%. Seropositivity was associated with age and, among staff members <40 years of age, with length of group childcare contact.¹⁰²

A concern exists that a previously nonimmune pregnant childcare provider could be exposed and infected during her childcare responsibilities, thus resulting in transplacental transmission leading to fetal hydrops. Estimates of the risk of fetal loss when a pregnant woman of unknown antibody status is exposed are 3% for fetal death after household exposure and 2% after occupational exposure in a school.¹⁰³ The American Academy of Pediatrics does not recommend exclusion of pregnant women from the workplace when erythema infectiosum is occurring. This recommendation is based on low rates of adverse effects on the fetus and high community prevalence of parvovirus B19 infection. Routine infection control practices, including hand hygiene and proper disposal of used facial tissues, are recommended to prevent transmission.¹⁰⁴

Cytomegalovirus. Young childcare attendees shed cytomegalovirus (CMV) intermittently in their saliva and urine after acquisition, and they often transmit virus to other children and adults with whom they have close daily interaction. Transmission is thought to occur through direct person-to-person contact and from contaminated toys, hands of childcare providers, or classroom surfaces. Prevalence studies have shown that 10% to 70% of children <3 years of age (peak, 13 through 24 months) in childcare are shedding CMV in their urine or saliva.¹⁰⁵⁻¹⁰⁷ Nonimmune childcare providers and mothers acquire CMV at annual rates of 8% to 20% while caring for CMV-infected children. In comparison, acquisition rates of 1% to 3% were noted among nonimmune childcare providers and mothers caring for CMV-uninfected children.¹⁰⁸⁻¹¹⁰ Given that care providers of young children are at increased risk of acquiring CMV, women of childbearing age should be educated about the risks of acquiring CMV, potential effects on the fetus, and methods to prevent transmission including hand hygiene after changing diapers or contact with saliva.1

Bloodborne Viral Pathogens

Concern about the potential for spread of bloodborne organisms in the childcare setting has focused on transmission of hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV). Universal immunization of infants with HBV vaccine in 1991 has reduced to negligible the potential for horizontal HBV transmission in the childcare setting. Because the highest concentrations of HBV in infected people are found in blood and blood-containing body fluids, the most common and efficient routes of transmission are through percutaneous blood exposure, by sexual exposure, and perinatally. However, high levels of HBV DNA have been detected in the saliva of hepatitis B e antigen (HBeAg)–positive children, a finding suggesting that exposure to saliva could be a means of horizontal transmission.¹¹² Thus, if a known hepatitis B surface antigen (HBsAg) carrier bites and breaks the skin of a hepatitis B–unimmunized child, hepatitis B immune globulin and the HBV vaccine series should be administered to the hepatitis B–unimmunized child.¹¹³ The transmission risk of HCV infection in childcare settings is unknown. The general risk of HCV infection from percutaneous exposure to infected blood is estimated to be 10 times greater than that of HIV but less than that of HBV. Rates for percutaneous exposure to HCV-containing saliva are unknown.

No cases of HIV infection are known to have resulted from transmission of the virus in out-of-home childcare. The risk of transmission of HIV by percutaneous body fluid exposure, such as biting, is low. Complete evaluation of the source and extent of exposure should be undertaken to assess the possible risk of HIV transmission and the need for PEP.¹¹³

Precautions for prevention of HBV, HCV, and HIV infections should be directed toward preventing transfer of blood or secretions from person to person. Childcare providers should be educated about modes of transmission of bloodborne diseases and their prevention, and each center should have written policies for managing illnesses and common injuries, such as bite wounds.¹¹⁴ Standard precautions for handling blood and blood-containing body fluids should be practiced in all childcare settings. Children known to be infected with HIV or HCV or children who are HBsAg carriers should be included in childcare activities. Decisions regarding attendance at childcare and the optimal childcare environment for these children should be made jointly by the child's physician and parents after considering the risks and benefits.

Skin Lesions

The magnitude of skin infections or infestations and the rates of occurrence in children in group childcare compared with rates in age-matched children not in group childcare are not known. The most frequently recognized non–vaccine-preventable conditions are impetigo or cellulitis caused by *Staphylococcus aureus* or GAS, pediculosis, and scabies. Other conditions with skin manifestations that occur in childcare attendees include molluscum contagiosum, head lice, ringworm, herpes simplex virus (HSV) infection, and varicella.

Molluscum Contagiosum. Molluscum contagiosum is a benign, superficial infection of the skin caused by a poxvirus. It is manifest by the presence of small, 2- to 5-mm painless skin-colored papules with central umbilication and typically resolves spontaneously within 6 to 12 months. The virus is spread by direct contact or by fomites, and humans are the only source. Infectivity is low, but outbreaks have been reported. Keeping skin lesions covered can help to prevent transmission.

Varicella-Zoster Virus. Since 2006, the CDC has recommended a 2-dose varicella-zoster virus (VZV) vaccination program for children, with the first dose administered at 12 through 15 months and a second dose at 4 through 6 years of age.¹¹⁵ Children entering childcare or starting school should be required to have age-appropriate VZV vaccination status or other evidence of immunity to chickenpox.¹¹⁶ As of January 2015, 47 states required VZV vaccination for childcare and school attendance; 1 state (Montana) requires vaccination only for childcare attendance, and 2 states (South Dakota and Ohio) require vaccination only for school attendance.¹¹⁷ Unimmunized children in childcare settings are susceptible to VZV infection; most reported cases occur in children <10 years of age. Universal VZV immunization has reduced cases of clinical disease among children in group childcare.¹¹⁵ However, several outbreaks of chickenpox have been reported among childcare attendees in the postvaccine era, often in the setting of inadequate vaccination coverage.^{115,118–122}

Herpes Simplex Virus. Clusters of primary HSV infections occur in children in childcare, and these infections most frequently manifest as gingivostomatitis. In a study conducted in a childcare center, restriction endonuclease analysis of HSV DNA revealed that a single strain of HSV-1 had been transmitted among children.¹²³ A longitudinal study of 115 childcare attendees followed from early infancy found that 37% of children had evidence of HSV-1 infection by 5 years of age based on virus isolation or seroconversion, or both. The highest incidence of infection occurred among children 1 to 2 years of age.¹²⁴ Children with

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Methicillin-Resistant Staphylococcus aureus. The emergence of community-acquired methicillin-resistant S. aureus (MRSA) and its predisposition for people in crowded conditions where sharing of fomites and skin-to-skin contact occurs make childcare exposure a potential risk factor. A molecular epidemiologic study of MRSA prevalence among 104 children, 32 employees, and 17 household contacts of attendees affiliated with a university medical center's childcare facility in Texas noted an overall 7% colonization rate with MRSA. Molecular typing revealed closely related, mostly community-associated isolates from 1 employee (3%), 6 (35%) family members, and 4 (2%) environmental samples. Macrolide antibiotics and asthma medications were associated with MRSA colonization.¹²⁵ An epidemiologic study of 1163 children attending 24 childcare centers in North Carolina and Virginia found that 18% were colonized with S. aureus and 1% with MRSA; genotyping did not indicate classroom transmission in the 2 centers that had multiple children who were colonized with the bacterium.¹²⁶ A draining wound is a reason for exclusion of a child from a childcare setting; MRSA colonization is not.

Scabies. Scabies is caused by a hypersensitivity reaction to the adult female mite of *Sarcoptes scabiei* subspecies *hominis*, which burrows in the upper epidermis of the skin. This infestation manifests as a pruritic, erythematous papular eruption, especially in skinfolds. Transmission occurs through prolonged close contact. Children with scabies should be excluded from childcare or school until treatment is completed, and household contacts of infected children should also be treated to prevent reinfection.¹²⁷ Prophylactic treatment for childcare providers and other contacts who have had prolonged skin-to-skin contact with an infected child should also be considered because symptoms can take 4 to 6 weeks to develop in persons who have not had a previous infection. Additionally, because transmission of crusted scabies—characterized by widespread, hyperkeratotic crusted lesions—can occur after minimal contact, treatment of all close contacts of patients with such cases is recommended.

Pediculosis. Head lice are cosmetically unappealing, but they do not transmit disease. The incidence of pediculosis capitis (head lice) among children in childcare facilities was 0.02 per 100 child-weeks in Seattle¹²⁸ and 0.03 per child-year in San Diego.¹²⁹ Because head lice are transmitted by direct head-to-head contact, childcare centers with shared sleeping areas can facilitate transmission. Treatment of infested children and their contacts with pediculicides can be considered as control measures.¹³⁰

Tinea Capitis. An outbreak of tinea capitis and tinea corporis secondary to *Trichophyton tonsurans* was reported at a childcare center in the United Kingdom, with infection of 12 children and 7 staff members over a 12-month period. Control of the outbreak was accomplished through use of oral antifungal agents and antifungal shampoo, exclusion of persons with cases for a short period, removal of shared items from the center, and enhanced decontamination of fomites.¹³¹

VACCINE-PREVENTABLE DISEASES

In the US, children should be immunized against the following 16 diseases or pathogens, unless medical contraindications exist: diphtheria, tetanus, pertussis, Hib, poliomyelitis, measles, mumps, rubella, varicella, *S. pneumoniae*, HBV, HAV, influenza, rotavirus, human papillomavirus, and meningococcal disease.^{31,132} Immunization of children and childcare providers should be a priority because high rates of immunization benefit children in childcare settings and their care providers. Laws requiring age-appropriate immunizations of children attending licensed childcare programs exist in almost all states. As of January 2015, vaccine mandates for HBV were active in 41 (82%) states, for HAV in 20 (40%) states, for pneumococcus in 38 (76%) states, for varicella in 48 (96%) states, and for influenza in 4 (8%) states.¹³³ In a study of exemptions to immunizations, children 3 through 5 years of age with immunization exemptions were 66 times more likely to acquire measles and 17 times more likely to acquire pertussis than were age-matched immunized children.¹³⁴

INFECTIONS ASSOCIATED WITH ANIMALS

Animal exposure has been associated with sporadic zoonotic infections as well as outbreaks, injuries, and allergies, most notably in children <5

years of age. The increased prevalence of infections in this age group likely reflects compromised hand hygiene resulting in transmission of pathogens from animal to child. Animal interaction can occur in locations where childcare is provided, with a resident pet or visiting animal, or in public venues where children visit, including petting zoos, aquariums, county fairs, parks, carnivals, circuses, or farms. Guidelines to reduce opportunities for transmission and infection have been developed to prevent disease transmission in many of these settings.¹² Inadequate hand hygiene, suboptimal supervision of children's activities following animal contact, and hand-to-mouth activities following animal contact are risk factors for infection. Organisms that have been associated with close contact with animals include E. coli O157:H7, Shiga toxin-producing E. coli (STEC), Salmonella enterica serotype Typhimurium, Cryptosporidium parvum, C. jejuni, and G. intestinalis. In addition to enteric infections, animal exposure can result in transmission of ectoparasites and endoparasites, M. tuberculosis in certain settings, and local or systemic infections as a consequence of bites, scratches, stings, and other injuries.

Contact with animals within the childcare environment should occur only where control measures are established to reduce the risk of injuries and disease. Supervision of children during animal contact, strict hand hygiene after direct animal contact or contact with animal products or environment, designation of areas for animal contact that are separate from areas in which food or drink are consumed, and disinfection and cleaning of all animal areas should be observed. Amphibians, reptiles, and weasels (ferrets and mink) should be housed in cages and not handled by children. Wild or exotic animals, nonhuman primates, mammals with a high risk of transmitting rabies, wolf-dog hybrids, aggressive wild or domestic animals, stray animals, venomous or toxin-producing spiders, insects, reptiles, and amphibians should not be permitted in the group childcare setting.^{137,138}

INFECTIOUS DISEASES IN ADULTS

Parents of children who attend a childcare facility and people who provide care to these children have an increased risk of acquiring infections such as CMV, parvovirus B19, HAV, and infectious diarrhea. A retrospective cohort study of children 12 to 60 months of age attending childcare in and around Quebec City, Canada found that transmission of acute gastroenteritis and acute respiratory illness from children to their parents occurred in about 1 in every 3 episodes of infection.¹³⁹ During outbreaks of diarrhea in childcare centers, 40% of childcare providers developed diarrhea.¹⁷ During a multicommunity outbreak of shigellosis, the overall median attack rate among employed staff members of childcare centers was 6%, with a range of 0% to 17%.18 In outbreaks of group A Streptococcus and echovirus 30 infection in childcare centers, adult providers and parents were affected.⁹⁶ Similar prevalence rates of pneumococcal colonization (5% among adult employees of childcare centers with child contact and 5% among nonclinical employees at a tertiary care center) were noted in a study performed in 2003 in Galveston, Texas; these data suggest that childcare providers are not at an increased risk for pneumococcal colonization in the universal PCV era.140 Compared with nonproviders, childcare providers have a significantly higher annual risk of at least 1 infectious disease and loss of workdays as a result of infectious disease.¹⁴¹ Childcare providers should receive all immunizations routinely recommended for adults.142

ECONOMIC IMPACT OF GROUP CHILDCARE ILLNESS

The economic burden of illness associated with group childcare was estimated at \$1.8 billion annually adjusted to 2015 US dollars.^{143,144} Precise estimates of illness burden and methods for evaluating the effectiveness of infection control interventions are limited by the multiple challenges associated with performing such assessments.¹⁴⁵ Attributing an outbreak to group childcare is challenging; although these settings can promote transmission of infection, childcare attendees and staff members interact with household contacts external to the childcare arrangement, thus facilitating secondary spread. A prospective evaluation of 208 families with at least 1 childcare enrollee that was conducted from November 2000 to May 2001 in the Boston area documented 2072 viral illnesses over 105,352 person-days. Among the 834 subjects, 1683 upper respiratory tract infections and 389 gastrointestinal tract illnesses were reported during the study period, with a total mean cost of \$49 per respiratory tract infection and \$56 per gastrointestinal illness. Decreased parental productivity during missed days of work to care for a child who had to be withdrawn from childcare accounted for a significant proportion of the nonmedical cost.¹⁴³ Another prospective study of 381 children attending childcare centers in Sydney, Australia in 2010 found that the mean cost of an influenza-like illness was AU\$626 (95% CI, AU\$484–768); independent drivers of cost were both parents being employed and longer duration of illness.¹⁴⁶

PREVENTION

Specific standards should be established for hand hygiene, maintenance of current immunization records of children and providers, exclusion policies, environmental cleaning, and appropriate handling of food and medication. In studies in which improved infection control measures were implemented and monitored, both upper respiratory tract illness and diarrhea were reduced in childcare centers that received infection control interventions.^{50,147} Because asymptomatic excretion and potential for transmission precede the onset of clinical symptoms in many childcare-associated infectious diseases, strategies that involve prevention are most efficacious.

Educational sessions on health topics by healthcare professionals were found to have the most impact in simultaneous surveys of licensed childcare center directors, parents, and health providers in Boston.¹⁴⁸ A prospective observational study of a convenience sample of 134 childcare centers in Pennsylvania noted that suburban, nonprofit, parent-funded centers had improved health and safety practices compared with centers that were located in urban areas, received their funding through state subsidies, or were designated as for profit.¹⁴⁹

Local health authorities should be notified about cases of communicable diseases involving children or care providers in the childcare setting. The American Academy of Pediatrics Healthy Child Care America Child Care & Health Partnership sets standards regarding quality early education and childcare.¹⁵⁰ Additional resources include information about group childcare infection rates,¹⁵¹ as well as guidance for preparation of childcare programs for pandemic response.¹⁵² Infection prevention, including reinforcement of meticulous personal hygiene, maintenance of immunization status, and efforts to reduce environmental contamination, ensures that both childcare attendees and childcare providers reduce opportunities for exposure and transmission. Controlling clusters and outbreaks of infectious diseases in the childcare setting can involve approaches that include cohorting of functional but symptomatic children and providers to minimize exclusion and economic loss. Provider and parental familiarity with guidelines and policies developed in collaboration with public health authorities and pediatric infectious disease physicians aids in the implementation of best practices.

All references are available online at www.expertconsult.com.

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