Chapter 39

DISEASES CONTROLLED PRIMARILY BY VACCINATION

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MEASLES

Introduction and Military Relevance

Measles (rubeola) has been called "the simplest of all infectious diseases."[1] It has a relatively distinct, homogeneous, and invariant etiology and pathogenesis. A high level of infectivity and relative lack of subclinical cases have contributed to its well-characterized epidemiology. It was first described in the 7th century but was not considered distinct from smallpox until 1629.[2] In 1758, attempts to prevent it through a process similar to variolization (application of smallpox crusts to susceptibles) was performed by Home and known as morbillization; it was mildly successful but never widely practiced.[3] The epidemiology of measles was elegantly described by Panum following an outbreak in the highly susceptible population of the Faroe Islands.[4] In the prevaccine era, most cases of measles in the United States occurred in children, although outbreaks in susceptible military recruits have been well documented.[5] A vaccine licensed in 1963 eventually resulted in a 99% decrease in measles cases in the United States, although there was a relative resurgence of cases in 1989 through 1991.[6] Elimination is currently a goal in the United States and elsewhere.[6,7]

Measles has been a constant presence during military deployments. During the Civil War, the case rate per 1,000 man-years was 32.2; during World War I, it was 26.1/1,000.[2] By World War II, the disease rate in the military had dropped to 4.7/1,000, and it was 0.9/1,000 during the Vietnam era. This pattern is similar to that seen with other contagious diseases and is thought to reflect a decreased number of susceptibles left in successive cohorts as travel and urbanization became more commonplace. In 1962, 98.8% of military recruits had measurable levels of antibody to measles.[8] Even with low population susceptibility rates, however, the virus circulates in large population clusters. Thus, military recruits experienced outbreaks before widespread vaccine use.[5] This was problematic for the involved installations and, because of the high mobility of these populations, for other posts and the surrounding civilian populations as well when servicemembers went home on leave. Transmission on posts extended to daycare centers and schools. In 1979 and the first half of 1980, about 9% of the reported measles cases in the United States were military cases.[9] Subsequent to the change in policy that mandated giving measles and rubella vaccine to recruits in 1980, cases were rare among the more than 750,000-member-strong active duty Army. In 1989, though, 12 confirmed and presumptive measles cases occurred among basic trainees at Fort Leonard Wood, Missouri, where immunization was delayed until the second week of basic training. Measles can also be a problem after training ends. For deployable military personnel, the risk of acquiring measles during worldwide deployments for humanitarian assistance missions remains high, particularly in Africa and Asia.

Description of the Pathogen

The causative agent of clinical measles is the measles virus, a member of the family *Paramyxovirida* and genus *Morbillivirus;* it is closely related to the viruses of canine distemper and rinderpest.[2] It is a spherical, single-stranded RNA virus. The only known reservoir is humans.

Epidemiology

Transmission

Measles is a ubiquitous, highly contagious, seasonal disease that affects nearly every person in a given population by the age of adolescence in the absence of immunzation programs. Infection at some point in life is the rule.[2] The virus is transmitted by airborne droplet spread, by direct contact with nasal or throat secretions of infected persons, and, less commonly, by fomites. Maximal dissemination of the virus occurs during the prodromal (or catarrhal) stage. In temperate climates, infections occur primarily in the late winter and early spring.[10] Measles is endemic in large urban areas, with epidemics occurring every second or third year. In smaller communities, outbreaks are more widely spread and severe. As demonstrated by Panum, island populations can remain free of infection for variable periods.[4] On reintroduction of the virus, epidemics of the disease strike all those not affected by the last wave. Thus, although transmission usually occurs among children, outbreaks in isolated communities include many older individuals, as was documented in the Faroe Islands. Overall, it is estimated that a herd immunity of greater than 95% may be needed to interrupt community transmission.[2] Immunization of 15-month-old children produces immunity in 95% to 98% of recipients; reimmunization may increase levels to 99%.[11]

Geographic Distribution

Measles is epidemic worldwide and is often a problem when people are displaced and congregated in settings such as refugee camps. Importations contribute to transmission in the United States.[6] Isolates currently circulating in the United States are similar to strains identified in Japan and Europe. Measles activity in the Western hemisphere is currently considered low, and elimination campaigns continue in the Americas.[7]

Incidence

Prior to vaccine use in the United States, epidemics affected largely children aged 5 to 9 years.[2] Average age at infection typically correlated with the age at which susceptible children increased their contacts outside the home. With the licensure of vaccine in 1963, cases declined from 450,000 per year to less than 50,000 per year in the United States by 1968.[12] The number of cases continued to decline, although small epidemics intervened in 1971 and 1977. During the late 1970s, elimination of measles was considered an achievable goal, with fewer than 5,000 cases documented through 1985. Measles resurged nationwide from 1989 to 1991, and incidence was highest among unvaccinated preschool-aged children.[13] An estimated 55,000 cases occurred during 1989 to 1990. In communities experiencing outbreaks, immunization of children at 12 months of age was conducted to protect them, with follow-up immunization at 15 to 18 months of age because of concern over the adequacy of resultant antibody levels in that age group. Additionally, immunization campaigns were conducted to increase awareness and coverage, and cases of measles once again declined. Between 1993 and 1995, an increasing proportion of cases were reported among older age groups, representing failure to vaccinate as well as vaccine failure.[6] Serosurveys conducted with US Army recruits in 1989 demonstrated overall that only 82.8% of the sample were seropositive by commercial enzyme immunosorbent assay.[14] Younger recruits were more likely to be seronegative, representing a cohort that may have missed both immunization and naturally acquired illness due to declining rates.

In 1995, 301 confirmed measles cases were reported, representing the lowest number in a single year since measles became reportable in 1912.[6] Although the number of cases is small, it provides evidence that the second dose of measles vaccine has not been uniformly implemented in all cohorts. Among the 96 cases who were not vaccinated, 56 were eligible for vaccine.

Worldwide, almost a million persons, mostly infants and young children, die annually from measles.[11] Poor nutrition and rapid loss of maternal antibody place infants at risk, and early exposure to the community and prolonged viral excretion result in infection. The case-fatality rates in developing countries are estimated to be 3% to 5% globally, but are commonly 10% to 30% in some localities.[1] In the spring of 2000, 2,961 cases of measles with three deaths and 68 hospitalizations occurred in the Netherlands. Although two-dose measles vaccines is recommended in the Netherlands, vaccine is not required for school attendance. The Netherlands has a large sub-population that refrains from vaccination on religious grounds. For this reason, measles epidemics occur in the Netherlands every 5 to 7 years.[15]

Pathogenesis and Clinical Findings

Measles is characterized by a prodromal fever, conjunctivitis, coryza, cough, and Koplik spots on the buccal mucosa.[10] A characteristic red, blotchy rash appears on the third to seventh day following exposure, beginning on the face, becoming generalized, lasting 4 to 7 days and sometimes ending in brawny desquamation.[1] Leukopenia is common. The incubation period from exposure to onset of fever is about 10 days, varying from 7 to 18 days; usually it is 14 days until the rash appears. Cases are infectious from the beginning of the prodromal period to 4 days after the appearance of the rash. The disease is more severe in infants and adults. Complications result from viral replication and bacterial superinfection and include otitis media, pneumonia, laryngotracheobronchitis (croup), diarrhea, and encephalitis. Subacute sclerosing panencephalitis develops very rarely (about 1 in 100,000 cases) several years after infection; over 50% of these cases have had measles diagnosed in the first 2 years of life.[10] Infection in pregnancy is not related to congenital malformations but has been associated with an increase in spontaneous abortions. The clinical course can be prolonged, severe, and fatal in the immunocompromised. The Immunization Practices Advisory Council's current recommendations include the immunization of those with human immunodeficiency virus to preclude the development of severe or potentially fatal naturally acquired measles.[16] In children who are borderline nourished, measles often precipitates acute kwashiorkor and exacerbates vitamin A deficiency, leading to blind-

ness. In malnourished children, measles may be associated with hemorrhagic rash, protein-losing enteropathy, otitis media, oral sores, dehydration, diarrhea, blindness, and severe skin infections.[10] Children with clinical or subclinical vitamin A deficiency are at particularly high risk.

Diagnostic Approaches

Compared with other exanthematous diseases, measles infections can be diagnosed clinically with relative accuracy. A case definition of rash, cough, and fever present at the onset of rash was demonstrated to have a sensitivity of 92% and a specificity of 57%.[17] Koplik spots are pathognomonic for measles, and a diagnosis of measles should not be made if cough is absent.[18] The differential diagnosis includes exanthem subitum (roseola infantum), in which the rash appears as the fever subsides; rubella; and enteroviral infections, which have less striking rashes and generally milder illness. Rickettsial infections may have cough, but headache is more prominent. Meningococcemia may have a similar rash but no cough or conjunctivitis. Scarlet fever has a rash that is confluent, textured, and most marked on the abdomen. Serological confirmation includes complement fixation, neutralization, and hemagglutination inhibition assays.[1] Enzyme-linked immunosorbent assays for measles IgG and IgM are widely available and convenient. Classic confirmation involves an increase in antibodies between acute and convalescent specimens. The use of IgM antibody assays allows for the diagnosis from the analysis of a single acute sample, if it is taken at least 2 days after the onset of rash.

Recommendations for Therapy and Control

Therapy is supportive. There is no specific treatment.

In the prevaccine era, approximately one birth cohort of 4 million persons was infected annually. In 1985 dollars, the estimated cost of these infections was $670 milllion.[19] The low number of cases of measles and shift in age distribution in the United States highlight the effectiveness and improved implementation of the Advisory Council's recommendations to provide the first dose of measles-mumps-rubella vaccine (MMR) at 12 to 15 months of age, with a second dose to address primary vaccine failure at either 4 to 6 or 11 to 12 years of age.[16] During outbreaks, observed attack rates in those who had received measles vaccine 15 years or more before reexposure have been approximately 5% or less.[1] During 1994 and 1995, coverage with measles vaccine was 89% among children aged 19 to 35 months, and an estimated 33% to 50% of school-aged children had received a second dose of MMR. Additionally, some states have mandated a prematriculation immunization requirement at colleges.[20]

As school requirements for second doses of MMR become the rule, the actual need for measles-rubella vaccine administration to recruits should diminish. As long as verification of vaccine status of recruits remains incomplete, however, it is a prudent practice. A second dose of MMR is recommended for health care workers and travelers. Furthermore, anyone vaccinated with a killed vaccine or a killed vaccine followed by a live vaccine within a 3-month period and anyone vaccinated between 1963 and 1967 with a vaccine of unknown type should be revaccinated.[1] Killed vaccine produced a short-lived immunity that was often associated with subsequent atypical measles—a milder but more prolonged illness.

About 5% to 15% of nonimmune vaccinees may develop malaise and fever up to 39.4°C within 5 to 12 days postimmunization and lasting 1 to 2 days but causing little disability.[10] Rash, coryza, mild cough, and Koplik spots may occasionally occur. Febrile seizures occur infrequently and without sequelae. Encephalitis and encephalopathy have been seen in approximately 1 to 3 cases per million doses distributed. The vaccine may be administered at the same time as other live vaccines and inactivated vaccines or toxoids. Contraindications include allergy to egg or neomycin, severe acute illness, and immunosuppression. Vaccination poses a theoretical risk to pregnant females, and vaccinees should be advised of the risk of fetal wastage if they become pregnant within 1 month of receiving monovalent measles vaccine or 3 months after receiving MMR.

In the event of an outbreak, vaccine given within 72 hours of exposure may provide protection.[9] If given after 72 hours, it may prolong the incubation period rather than prevent disease. Immune globulin may be given within 6 days of exposure for susceptible household members or other contacts for whom the risk is very high (eg, contacts under 1 year of age, pregnant women, immunocompromised persons) or for whom measles vaccine is contraindicated.[10] The dose is 0.25 mL/kg. For immunocompromised persons, the dose is 0.5 mL/kg up to 15 mL. Measles vaccine should be given 6 to 7 months later if there is no contraindication. Transmission to susceptible contacts often occurs before the diagnosis of the original case has been established. Isolation precautions to prevent spread, es-

pecially in hospitals or institutions that care for children, should be maintained from the seventh day after exposure until about 5 days after the rash has appeared. If vaccine is available, prompt use at the beginning of an epidemic is essential to limit spread; if vaccine supply is limited, priority should be given to young children for whom the risk is greatest. During community outbreaks, monovalent measles vaccine may be administered to 6- to 11-month olds.

Eradication of measles has been considered a fitting end to a disease confused with smallpox until 1629. Both diseases are dependent on humans for their propagation, need large human populations to sustain them, and elicit life-long immunity; neither leads to a chronic infectious state.[21] Measles vaccine has been used to reduce the incidence of the disease in the United States, Canada, Cuba, and some European countries. Elimination plans have been proposed many times, but the disease has not yet been eliminated from any large country.[11] The ineffectiveness of the vaccine for newborns and the high degree of contagion of the infection are the principal barriers to eradication of measles. The addition of "catch-up" campaigns to target all children aged 9 months to 14 years has recently been practiced in the Americas to increase coverage and, it was hoped, lead to elimination of measles by the year 2000.[7] During a 1996 meeting on global measles eradication, it was concluded that worldwide measles eradication is feasible using currently available vaccines and should be achievable worldwide within the next 10 to 15 years.[22]

[Coleen Weese]

RUBELLA

Introduction and Military Relevance

Rubella (or German measles) is a viral exantham that was recognized in the late 18th century but largely ignored until 1941, when it received dreaded notoriety because association had been made between it and congenital malformations.[23] The name German measles was popularized because German physicians distinguished it from measles, and the name rubella (little red) was given to it following an outbreak in India in 1841. Rubella is a mild febrile illness characterized by adenopathy of the head and neck, followed approximately a week later by a diffuse, punctate rash[10p435–440]; it is often indistinguishable from other mild viral exanthems. In unimmunized populations, it is largely a disease of children, who are often asymptomatic; the population of most concern is susceptible females of childbearing age. In 1941, an Australian ophthalmologist astutely observed an association between congenital cataracts and maternal rubella.[24] Rubella virus is now known to be a powerful teratogen when illness occurs during the first trimester of pregnancy, and congenital rubella syndrome (CRS) is distinguished by the classic triad of congenital cataract, heart defects, and deafness.[25] Other malformations may be seen as well. CRS patients, in addition to cataracts, congenital heart defects, and deafness, may also manifest encephalitis, microcephaly, mental retardation, autism, blindness, hepatosplenomegaly, and diabetes.[26] These cases of serious congenital disease provided the impetus to vaccine development and licensure.

Although rubella control aims primarily to prevent CRS, rubella outbreaks can disrupt military operations. In adulthood, rubella cases often occur in susceptible populations living in crowded quarters, such as university students and military personnel. Such cases represent a large proportion of the disease seen in the postvaccine era.[12p50] Serosurveys conducted among US Army recruits in 1989 demonstrated that only 85.2% had detectable rubella antibody.[14] Younger recruits were more likely to be seronegative, representing a cohort that may have missed both immunization and naturally acquired illness due to declining rates. Even with declining rates of rubella in the United States, however, susceptible recruits face risk from contact with multinational forces from countries whose immunization policies differ from the United States. In 1995, 120 German paratroopers arrived at Fort Bragg, North Carolina, to participate in a joint exercise.[27] German rubella policy immunizes only women of childbearing age. Several of the male paratroopers were incubating rubella when they arrived in the United States. Two days before the exercise, three succumbed to an illness consistent with rubella, and the entire German contingent was quarantined. Those without symptoms were given 2.0 mL of immune serum globulin to prevent further cases. Rubella IgM and IgG titers drawn on the contingent revealed that 10 of the 120 were nonimmune. Six of these became ill with rubella. Apart from the logistics of dealing with this outbreak, preventive medicine officials were faced with assessing the impact to the American troops and the wives and children who had contact with the German paratroopers. Recommendations to provide a second dose of rubella vaccine to school-age children (whether they are in kindergarten, 6th

grade, or high school) or adolescents, as well as the continued policy of providing measles and rubella vaccine to recruits, should reduce the risk to US citizens from imported rubella.[16]

Description of the Pathogen

The causative agent of rubella is a virus in the genus *Rubivirus* in the family *Togaviridae*. The virus is a cubical, medium-sized (70 mm), lipid-enveloped virus with an RNA genome.[25] Humans are the only reservoir.[10]

Epidemiology

Transmission

Infection of susceptible humans follows contact with the nasopharyngeal secretions of infected people. Although other togaviruses are arthropod-borne, there is no evidence that rubella can be transmitted that way.[23] Rubella is prevalent in the winter and spring. Although most childhood infections are asymptomatic and go largely unrecognized, infection tends to occur at young ages in countries with crowded living conditions or widespread daycare use. Age at infection roughly correlates with age when congregation of susceptibles occurs. Serologic surveys indicate that most Africans are immune by their 10th birthday.[28] In unimmunized countries where crowding is not prevalent, infection may occur during the school years or while at colleges or military camps. The introduction of rubella vaccination of recruits at Lackland Air Force base in 1979 resulted in a 95% reduction in rubella cases.[29] Even in highly immunized populations, however, outbreaks may occur in such settings because of either incomplete coverage or vaccine failure.[30] While rubella is not as infectious as measles, in a closed environment such as a recruit population, all susceptibles may be infected. Herd immunity was shown to be ineffective when rubella broke out in a company of military recruits. Most had antibodies due to vaccination or prior infection at the start of the epidemic, but 100% of those susceptible were infected.[31,32] Clinical rubella and subsequent CRS has been documented during reinfection of vaccinees and naturally immune individuals, although it is a rare event.[33–35] Infants with CRS may shed virus for months after birth.[10]

Geographic Distribution

Rubella occurs worldwide at endemic levels, except in remote or island populations where epidemics occur every 10 to 15 years. This contrasts with the US interval of 6 to 9 years between major epidemics noted in the prevaccine era.[23]

Incidence

The medical and socioeconomic importance of rubella lies in its ability to produce anomalies in the developing fetus. CRS occurs in up to 90% of infants born to women who acquired confirmed rubella during the first trimester of pregnancy; the risk of a single congenital defect falls to approximately 10% to 20% when infection is acquired in the 16th week, and defects are rare when the maternal infection occurs after the 20th week of gestation.[10] In susceptible populations, rates of CRS as high as 1% of pregnancies have been documented.[36] The last major epidemic of CRS occurred in the United States in 1964 and 1965.[37] During this epidemic, it was estimated that there were 12.5 million cases of rubella, many in pregnant women. Five thousand therapeutic abortions were performed, 6,250 spontaneous abortions occurred, and an additional 2,100 babies were stillborn. CRS occurred in 20,000 infants. Of those, 11,600 were born deaf, 3,580 blind, and 1,800 mentally retarded. The cost of this epidemic has been estimated at $1.5 billion.[36] Since the licensure of the vaccine in 1969, no major epidemic has occurred in the United States. The incidence of rubella dropped to less than 1 per 100,000 while the incidence of congenital rubella syndrome has fallen to less than 0.1 per 100,000 births. Rubella incidence increased five to six times from 1990 to 1991, primarily in teenagers and young adults, but then returned to previous levels. Just less than half of the cases of known age were in individuals aged 15 and older.[12]

Pathogenesis and Clinical Findings

Rubella enters the nasopharynx, where it replicates and spreads to the local lymph nodes. Secretory IgA induced by prior disease or vaccination can block mucosal replication.[25] The incubation period for rubella is 14 to 21 days; rash typically occurs 2 weeks following exposure.[22,25] Cases are infectious 1 week before and up to 4 days after onset of the rash. During the second week, viremia occurs in the blood and can be blocked by passively or actively acquired antibody.[25] At this time, low-grade fever, malaise, and mild conjunctivitis may be present. At the end of the incubation period, a maculopapular erythemetous rash appears on the face and neck and spreads downward, fading over the next 3 days. Viremia ends with the onset of the rash. Arthralgia and arthritis are commonly observed in adults, and

chronic arthritis has been reported. For unclear reasons, these complications are more common in women.[38,39]

Diagnostic Approaches

Field diagnosis of rubella is difficult and often inaccurate. Rash is not present in up to 50% of infections, and the other symptoms are relatively nonspecific.[27] The illness must be distinguished from measles, scarlet fever, mononucleosis, and other infectious exanthems and drug eruptions. Additionally, 10% to 85% of infections in various outbreaks have been inapparent.[26] Serologic confirmation of suspected cases should be sought, particularly in females of childbearing age. Such confirmation may be made by observing a 4-fold rise in titer between acute (within 7 to 10 days) and convalescent (2 to 3 weeks later) specimens via enzyme-linked immunosorbent assay, hemagglutinen inhibition, passive hemagglutination, or latex agglutination.[25] Rubella-specific IgM is quite reliable and obviates the need for multiple serum samples. Virus isolation is difficult and usually unnecessary.

Recommendations for Therapy and Control

Therapy is supportive; no definitive treatment exists.

As the goal of rubella control is the prevention of CRS, some countries have elected to immunize all adolescent girls without prescreening immune status. However, refusal rates of up to 15% in British women of childbearing years have been seen because of the concerns over the theoretical risk to the fetus.[40] It is a live virus vaccine, but no attributable increase in congenital defects in the offspring of 200 women immunized while pregnant was seen.[41] Reasonable precautions in a rubella immunization program include asking women of childbearing age if they may be pregnant and excluding those who may be, with the recommendation that those who receive vaccine not become pregnant for 3 months. Immune globulin has been used in an attempt to prevent CRS in exposed pregnant females; if any protection is incurred, however, it is incomplete at best.[42,43] The single indication for its use is a documented susceptible pregnant female who is exposed to the disease and would not consider abortion under any circumstances. The dose is 20 mL, given intramuscularly. Vaccine should not be given to anyone with an immunodeficiency or on immunosuppressive therapy, but measles-mumps-rubella vaccine (MMR) is recommended for persons with asymptomatic human immunodeficiency virus (HIV) infection and should be considered for those with symptomatic HIV infection.[10] All US military services recommend rubella immunization be given to recruits at accession.[44] The Department of Defense used to require screening of female recruits for susceptibility and pregnancy before vaccination. Susceptibility was included because of concerns about increased arthralgias and chronic rubella syndrome following vaccination in females. A 1991 Institute of Medicine report found evidence suggesting a causal association between rubella immunization and both chronic and acute arthritis.[45] The current regulation requires asking women about the possibility of pregnancy and deferring vaccine in those who are pregnant or who are unsure.[43]

The US strategy has been to immunize infants at 15 months and depend on herd immunity to protect pregnant women; postpartum vaccination is also advocated. However, rubella cases continued to occur in women of childbearing years. In 1989, the Advisory Council on Immunization Practices recommended a second dose of MMR be given to school-aged children or adolescents.[16] Until this regimen is fully implemented in successive cohorts, measles-rubella vaccination of recruits is prudent to prevent female service members and dependents from exposure and to prevent the disruption in training a rubella outbreak may cause. Other countries differ in age and sex targeted for immunization, so susceptible US service members could be exposed during multinational operations.

Mass immunization may be justified in an outbreak in a school or comparable population.[10] During an outbreak, isolation of cases to avoid contact with nonimmune pregnant women is advised; it is also recommended that contacts who may be pregnant should be tested serologically for susceptibility or early infection and advised accordingly.

[Coleen Weese]

MUMPS

Introduction and Military Relevance

Mumps is an acute communicable disease of children and young adults caused by a single strain of a paramyxovirus. The name may be related to an old English verb that means to grimace, grin, or mumble.[46] Mumps is a common cause of meningoencephalitis; other common manifestations and complications include orchitis, pancreatitis, mastitis, and oophoritis. Before widespread vaccination against mumps, the disease was associated with armies during times of mobilization. During World War I, mumps

was an important cause of days lost from active duty in the US Army. Average number of days lost from duty was 18, and hospitalization occurred at a rate of 55.8/1,000 recruits.[47] In 1940, the Surgeon General of the US Army stated that next to the venereal diseases, mumps was the most disabling of the acute infections among recruits.[48] During the prevaccine era, outbreaks were more common among recruits from rural areas, who generally had not been previously exposed. Following the widespread use of vaccine, mumps cases continued to occur frequently among Soviet recruits, and an outbreak occurred among US Army troops in 1986.[49] But increased awareness that has led to increased coverage of infants with the primary series, as well as recent recommendations to require a second dose of the measles-mumps-rubella vaccine (MMR) for adolescents or younger school-aged children, should reduce cases in these populations and the spread of disease to military populations.[44,50]

Description of the Pathogen

Mumps is caused by the mumps virus, a member of the family *Paramyxoviridae* and the genus *Paramyxovirus*; it is antigenically related to the parainfluenza viruses.[48] It is an enveloped, negative-strand RNA virus that contains six major structural proteins.

Epidemiology

Transmission

Mumps is acquired by the respiratory route, and the infection is frequently accompanied by viremia, which commonly leads to organ involvement, particularly of the salivary glands. It is transmitted by droplet spread and direct contact with the saliva of an infected person. The incubation period is roughly 18 days, with a range of 12 to 25 days.[10p353–355] Virus is secreted in saliva beginning 7 days before parotitis until 9 days after it began. Exposed individuals should be considered infectious from the 12th to the 25th day following exposure, with maximum infectivity occurring 48 hours before the onset of illness. Humans are the only reservoir.

Geographic Distribution

With the exception of very isolated island groups and remote villages, mumps occurs throughout the world. It is endemic within urban populations but of somewhat irregular incidence.[51] Mumps shows slight seasonality in temperate zones, with an increase in winter and spring.

Incidence

Before widespread vaccine use, mumps most commonly afflicted school-aged children, with the highest incidence reported in children 5 to 9 years of age.[46] During World War I, cases occurred predominately among men from rural areas.[47] In the prevaccine era, serosurveys of US Army recruits demonstrate a 47% to 76% seropositivity rate.[52,53] During World War II, reported rates were only 6.9/1,000 per year, and cases were largely among personnel from rural areas.[8] An outbreak of mumps occurred in 1943 at Camp McCoy, Wisconsin, and spread slowly. It ultimately involved 1,378 cases occurring over 30 weeks, and the highest attack rate for a single company in any given week was 2.5%. The post was divided into two roughly equal groups. The attack rate in one group was 74.4/1,000 per year, whereas in the second group it was only 15.4/1,000 per year, despite the fact that both groups had ample time to mingle at clubs, theaters, and other sites. The divergence in rate was partially attributed to the geographical makeup of the two cohorts.[54]

After the licensure of mumps vaccine in the United States in 1967 and the subsequent introduction of state immunization laws, the reported incidence of mumps decreased substantially. Cases dropped 98%, from the 1968 levels of approximately 100/100,000 to an all-time low of 1.2/100,000 in 1985.[50] A number of European countries initiated MMR vaccination programs in the 1970s and 1980s.[46] Cuba has nearly eliminated mumps since it began vaccinating preschool-aged children in 1988 and achieved coverage levels above 95%.[55] Policies for providing routine vaccination of young children recommended by the Immunization Practices Advisory Committee of the Public Health Service in 1977, targeting older populations at risk, and enacting school immunization laws have contributed to the decrease in mumps incidence in the United States. From 1988 to 1993, the incidence of mumps decreased further after the number of states with immunization laws increased and the two-dose vaccination schedule for measles using MMR was initiated. However, there was a relative resurgence of mumps in 1986 and 1987, with almost 20,000 cases reported during the 2-year period. From 1988 to 1993, most cases occurred in children 5 to 14 years of age (52%) and in persons older than 15 years of age (36%).[50] This trend reflected underimmunization of the cohort born from 1967 through 1977, a period when vaccine was not administered routinely to children and the risk for exposure to mumps was decreasing.

A serosurvey of US Army recruits in 1989 found an overall seropositivity rate to mumps of 86.4%,

with variation among recruits from urban, suburban, and rural backgrounds.[14] Persons from the western United States were more likely to be seronegative than others. Black, non-Hispanic recruits were more likely to be seropositive than other recruits.

The 1,692 cases of mumps reported for 1993 represents the lowest number of cases ever reported and a 99% decrease from 1968.[50] Although the incidence decreased in all age groups, the largest decrease (a greater than 50% reduction in incidence per 100,000 population) occurred in persons older than 10 years of age. Overall, the incidence of mumps was lowest in states that had comprehensive school immunization requirements and highest in states that did not.

Pathogenesis and Clinical Findings

Mumps virus is acquired through the respiratory tract with local replication there and in regional lymph nodes. Following an incubation period of 16 to 18 days, viremia occurs. At this stage, mumps most commonly presents as acute parotitis, which manifests itself as a unilateral or, more commonly, bilateral swelling of the parotid glands.[51] It may be preceded by several days of fever, headache, malaise, anorexia, and myalgia. Fever lasts from 1 to 6 days; parotid gland enlargement may last longer than 10 days. Mumps may be understood as a respiratory infection that is frequently accompanied by viremia, which commonly leads to organ involvement, particularly of the salivary glands.[46] Fifteen to twenty percent of mumps infections produce no symptoms (typically, these cases are adults), 30% to 40% of cases present with the typical parotitis (typically school-aged children), and up to 50% present as a respiratory infection (typically children under 5 years of age).[56,57] Serious complications may occur without evidence of parotitis, and some are more common in adults than children. Orchitis may occur in up to 20% to 30% of men who develop mumps.[58] Although testicular involvement can be bilateral in up to 30% of cases, sterility is thought to occur only rarely.[59] An increased risk of testicular cancer has been reported following mumps orchitis.[60] This is thought to be secondary to testicular atrophy following orchitis, as the mumps virus is not known to be oncogenic or transforming. Pancreatitis, usually mild, occurs in 4% of cases; an association with subsequent diabetes mellitus remains unproven.[61] Another concern is encephalitis, which is clinically indistinguishable from aseptic meningitis and occurs in 4% to 6% of cases.[56] Permanent sensorineural deafness may occur among children in about 1 in 15,000 cases.[62] Mastitis and oophoritis may occur in about 30% of women with mumps. An increase in fetal death has been reported among women with mumps in the first trimester of pregnancy, although no increase in fetal abnormalities has been demonstrated.[63] Arthropathy, arthralgias, and arthritis, occasionally chronic, have been reported, more commonly in adults.[64] Nephritis, common but clinically insignificant, and myocarditis, rare but occasionally catastrophic, are other manifestations.[46]

Diagnostic Approaches

The diagnosis of mumps is usually made clinically, based on the presence of parotitis. Other viral infections, such as coxsackie virus A and lymphocytic choriomeningitis infections, can cause parotitis, and the differential diagnosis also includes suppurative parotitis, recurrent parotitis, salivary calculus, lymphadenopathy, and lymphosarcoma. One third of sporadic cases seen by family practitioners in Canada could not be confirmed serologically as mumps.[61] Virus may be readily isolated from swabs of the opening of the Stenson duct or from saliva, urine, or cerebrospinal fluid during the first 5 days of illness.[46] Historically, serological assays, including complement fixation, neutralization, and hemagglutination inhibition, have been employed to diagnose mumps.[65] Currently, enzyme-linked immunosorbent assays for mumps IgG and IgM are widely available, and they are more sensitive and specific than previous tests. The use of IgM antibody assays allows for the diagnosis of mumps from the analysis of a single acute sample; cross reactions with other paramyxoviruses do not occur.

Recommendations for Therapy and Control

There is no specific treatment for mumps, and use of immune globulin in exposed susceptibles is not recommended.[46]

Incidence rates for mumps in the United States have declined substantially since the licensure and widespread use of mumps vaccine.[50] Mathematical models of the impact of mass vaccination on the incidence of mumps predict that 85% to 90% coverage of children by the age of 2 years would be required to eliminate mumps from the United States or Western Europe.[46] However, cases continue to occur due to failure to vaccinate and vaccine failure.[66]

The mumps vaccine efficacy in clinical trials ranges from 75% to 91%.[46] The vaccine may be administered singly, as part of MMR, or with additional vaccines without impairment of antibody response or increase in side effects. Adverse reactions to the vaccine have been infrequently reported and consist most frequently of fever and parotitis.

Transient rash, pruritis, and purpura have also been reported. The population most at risk for complications of the disease is adolescents and adults, so immunization of susceptibles before the onset of adolescence is important.

US Army and Air Force recruits are given measles and rubella boosters upon entry to active duty, but mumps vaccine is recommended only for high-risk occupational groups (eg, medical care providers). The US Navy and Marine Corps routinely immunize all recruits against mumps. But outbreaks have occurred among highly vaccinated populations. Risk to susceptible military personnel would be expected to be higher during deployment to areas with lower vaccine coverage and when they have close contact with endemic populations. An outbreak occurred among US Army troops stationed in South Korea in 1986.[48] During 1989 and 1990, a large outbreak occurred among students in a primary school and a secondary school.[67] Most of the troops and the students had been vaccinated, suggesting that vaccine failure, as well as the failure to vaccinate, might have contributed to the outbreaks.

The decline in cases of mumps in recent years has made routine immunization of recruits not cost effective. The cohort most at risk is the nonimmune group that missed both naturally occurring mumps and immunization in the 1970s; this group is less likely to be problematic for the military as time passes. Additionally, the Immunization Practices Advisory Committee's two-dose recommendation should eventually reach successive cohorts, further reducing the risk. Mumps continues to pose a small risk to military populations, but this risk is expected to decrease substantially in the future with continued attention to immunization of children and adolescents.[68]

[Coleen Weese]

VARICELLA

Introduction and Military Relevance

Varicella is the primary infection caused by varicella-zoster virus. Humans are the only natural host.[10p92–97,69] The virus is worldwide in distribution; 4 million cases of varicella, or chickenpox, occur each year in the United States.[70] Approximately 9,000 cases result in hospitalization, and as many as 100 deaths have been attributed to chickenpox each year.[70,71] Military environments, with their shared living quarters and close physical contact, facilitate transmission of the virus among susceptible individuals by the aerosol route (Figure 39-1). The disease thus affects training time and readiness; often infected recruits are hospitalized just to remove them from the crowded barracks during their illness. The licensed vaccine and antiviral agents for treatment provide new intervention strategies to reduce the impact of chickenpox on the military.

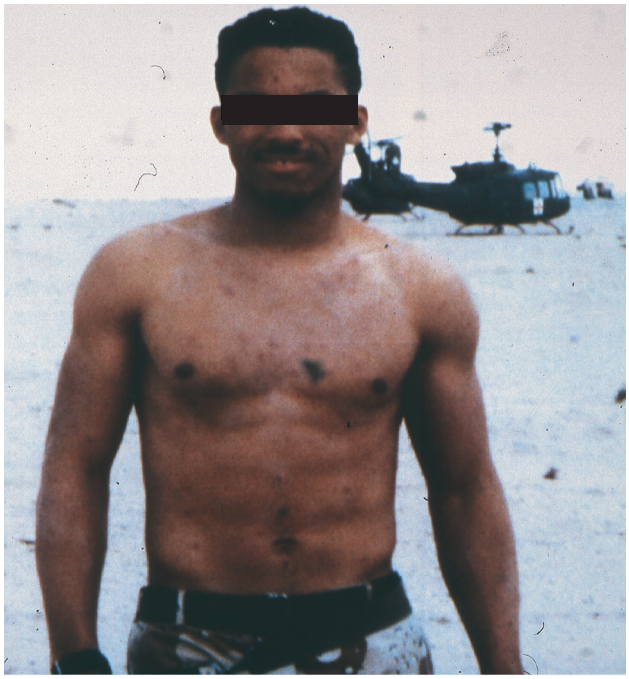

Fig. 39-1. Varicella infection in this new augmentee soldier to the 3d Armored Cavalry Regiment during Operation Desert Storm required him to be kept in an isolation tent and transported by ambulance until he was no longer infectious.
Photograph: Courtesy of Colonel Glenn Wasserman, Medical Corps, US Army.

Description of the Pathogen

Varicella is caused by varicella-zoster virus, a DNA virus also known as human herpesvirus 3. The virus is a member of the *Herpesvirus* group.

Epidemiology

Transmission

This generally benign disease of childhood is easily recognized because of its characteristic rash and is extremely contagious. Chickenpox is among the most highly communicable diseases in humans, with secondary attack rates from 70% to 90% in susceptible individuals.[10,72] Initial infection is usually symptomatic. Immunity lasts for life, but reactiva-

tion as herpes zoster can occur. Most civilian cases occur in children younger than 10 years of age.[69,72] Chickenpox is usually acquired by person-to-person contact via respiratory secretions, airborne spread, direct contact with zoster lesions, or freshly contaminated fomites. The lesions are infective until scabs have formed. The virus can also be transmitted in utero. Cases are most infectious 24 to 48 hours before the appearance of the rash and remain contagious for up to 5 days after the first vesicles appear. The average incubation period is 14 to 16 days but ranges from 10 to 20 days. Immuno-compromised patients may have a shorter incubation period and may remain communicable for longer than usual. The incubation period may be prolonged in those patients who received varicella-zoster immune globulin (VZIG).

Geographic Distribution

Chickenpox occurs in cycles of seasonal epidemics peaking in the winter and early spring in temperate zones but can occur worldwide. Infection is more common in adults in tropical climates than adults in temperate ones.

Incidence

In a sample of white, middle-class Americans, 100% were found to be immune by the age of 15, but in 810 young adults entering the US military from Puerto Rico, only 42% were seropositive.[73] The explanation for the later age of infection in tropical climates, such as Puerto Rico, the Philippines, and some Caribbean islands, is unclear but may include different population dynamics, climate, the relative heat-lability of the virus, or local protective environmental factors.[72,74]

Susceptibility to the virus among certain populations has been determined using the tools of molecular biology. National seronegativity rates in young adults in the United States have been estimated to be 6.7% from a large study of military recruits; the seronegativity rate for varicella in recruits was 8.2% by a commercial enzyme immunoassay.[75] Some protective cellular immunity may be present in persons with negative titers by enzyme immunoassay.[71] Nonwhite recruits and recruits from island nations or territories were more likely to be seronegative for varicella antibody.[75]

There was a substantial increase in the number of military hospitalizations for chickenpox from 1980 to 1988, but data from 1989 to 1995 show hospitalization rates have been declining.[74,76,77] In a review of military chickenpox admissions in the 1980s,[74] it was found that most of the persons hospitalized were new to the service. These younger service members were also more likely to be hospitalized than older personnel because otherwise they would be sent back to their barracks to recover. Soldiers with a home of record of the Caribbean islands, the Philippines, or Puerto Rico were at much increased odds of being hospitalized for varicella. An investigation done in the mid-1990s also found that those with foreign homes of record, who were junior in rank, and who were new to the service were at highest risk for hospitalization.[77]

The most common causes of death in children with chickenpox are septic complications and encephalitis, with the disease having a case fatality rate of 2 in 100,000.[10] The mortality for those 15 to 19 years old remains low at 1.3/100,000.[78] The case fatality rate in adults older than 20 years of age approaches 30/100,000, with death usually caused by varicella pneumonia.[10,78] Neonates, adults over the age of 20, the immunocompromised, persons with chronic cutaneous or pulmonary disorders, and those taking salicylates have a higher morbidity and mortality than children.

In the United States, chickenpox cases are selectively reportable and can be reported in groups instead of as individual cases. Significant underreporting is thought to occur. Notification of regional jurisdictions by local health departments can take as long as 1 year.[10] In the US Army, adult cases of varicella should be reported to the Army Medical Surveillance Activity for publication in the *Medical Surveillance Monthly Report*, published by the United States Army Center for Health Promotion and Preventive Medicine.

Pathogenesis and Clinical Findings

After varicella enters the body, the virus replicates in the oropharynx. The virus then invades local lymph nodes, blood, and viscera. After the 2- to 3-week incubation period, there is a secondary viremia and a vesicular rash that is pruritic and generalized. A single vesicular lesion scabs after 3 to 4 days as a result of host defense mechanisms.[10,79] The lesions tend to be of different ages, with all being scabbed usually by the sixth day. They are more likely to be located on covered areas of skin and in areas that are irritated. Mild fever and systemic symptoms can occur.

Complications include bacterial superinfection of the skin lesions, thrombocytopenia, arthritis, hepatitis, dehydration, encephalitis or meningitis, pneumonia, glomerulonephritis, and Reye syndrome.[69,72] Adults have an increased risk for complications of pneumonitis or encephalitis. In the immunocom-

promised, the course of illness can be complicated by continuing eruption of the rash, encephalitis, pancreatitis, hepatitis, and pneumonia.[69] The virus survives after the initial infection in a latent form in the dorsal root ganglia and can reactivate as shingles, typically years later under conditions of stress, trauma, malignancy, or immunosuppression.[72,79] Shingles is characterized by a unilateral vesicular eruption with a dermatomal distribution.[72] In fatal cases of varicella, intranuclear inclusions of the virus have been found in blood vessel endothelium and almost all organs of the body. In cases of encephalitis, perivenous demyelination in the brain has been described, as well as necrosis of nerve cells and meningitis.[28p801–803]

Congenitally acquired chickenpox is an uncommon syndrome consisting of skin scarring, muscle atrophy, extremity hypoplasia, low birth weight, and neurologic abnormalities. Infection of the mother in the first 16 weeks of gestation results in an estimated 2% incidence of fetal malformations.[10,72] While infection during pregnancy rarely leads to fetal death, deaths in utero can be from direct infection of the fetus with the virus or from fever and other maternal metabolic changes. Infection later in pregnancy results in fetal acquisition of protective maternal antibodies. However, maternal infection in the last 5 days of pregnancy can result in neonatal varicella, which is associated with a 30% case fatality rate.[72] With the administration of VZIG to these infants, the case fatality rate is drastically reduced, and in one uncontrolled study,[79] there were no fatalities. It does not appear that the disease is more severe in pregnant women than in other adults in the absence of pneumonia, and it is unclear whether or not it is more severe if complicated by pneumonia.

The clinical findings of varicella have some similarities to those of monkeypox and smallpox. The occurrence of monkeypox is increasing, and even though smallpox has been eradicated, it still exists as a potential biological warfare agent. Table 39-1 points out the salient differences between varicella and smallpox.

Diagnostic Approaches

Clinical diagnosis is based on the characteristic rash of varicella or dermatomal lesions of zoster. Other diagnostic options are available if necessary

TABLE 39-1

CLINICAL FEATURES OF VARICELLA AND SMALLPOX

Clinical Feature	Varicella	Smallpox
Onset	Progressive, moderate fever	Sudden, high fever; intense malaise (as in meningitis)
Rash	Appears on 2nd d, with continuing fever (in children the rash is often the first sign)	Appears on 3rd to 4th d, with transient fall of fever
	Begins on the trunk, where it will stay dense, but not on palms and soles	Begins on the face and extremities of the limbs, including palms and soles, where it will stay dense
	Macules become rapidly papular and produce clear vesicles that form crusts without going through the pustular stage	Macules require 4 to 6 d to transform into papules, vesicles, and pustules before producing scabs
	Successive crops appear during 4 to 5 d in the same area, which show lesions at different stages	Single crop only: all lesions are at the same stage in a given area
Vesicles	Soft, superficial, "tear-drop," not umbilicated	Hard, deep-seated, umbilicated; they transform into pustules with rise of fever and prostration
Crusts	Fall off rapidly, leaving temporary granular scabs	Healing is slow and leaves permanent pockmarks
Lethality	Exceptional	Case-fatality rate is 20% to 40% (Variola major)

Reprinted courtesy of the World Health Organization from Brés P. *Public Health Action in Emergencies Caused by Epidemics.* Geneva: World Health Organization; 1986.

but are not required in routine cases. The virus can be isolated from the lesions during the first 3 to 4 days. Visualizing multinucleated giant cells with intranuclear inclusions can be done using a method known as the Tzanck smear. These cells can also be visualized in herpes simplex lesions.[10,69] There are monoclonal antibodies available to diagnose the virus after immunofluorescent staining, this is a more accurate method than visualizing the giant cells.[10,14] Demonstration of viral DNA by polymerase chain reaction is also possible. Testing of acute and convalescent sera for the virus antibody (IgG and IgM) can be done using one of many available serologic tests, such the enzyme-linked immunosorbent assay (ELISA), but the tests may not be reliable in the immunocompromised. The commercial ELISA, which could be used to serologically screen populations before vaccination, has a reported sensitivity of 86.1% and specificity of 97.7%, as compared to the fluorescent antibody to membrane antigen assay (FAMA). The FAMA is a commonly used reference procedure that requires viral culture and considerable expertise to perform.[14,80]

Recommendations for Therapy and Control

No treatment is recommended for uncomplicated chickenpox in healthy children. In immunocompromised patients, treatment with intravenous acyclovir is preferred to vidarabine. Acyclovir is very effective in the immunocompromised if chickenpox is suspected; VZIG is not effective once disease is present. Oral acyclovir is recommended if the person is older than 12 years of age, has chronic cutaneous or pulmonary disorders, or is taking chronic salicylate therapy or steroids.[69] Acylovir is available for use in children, but studies have not clearly shown it has a significant effect on the rate of complications or absence from school.[70] It has been shown to be most beneficial if the drug is given within 24 hours of onset of the rash.[69,81] Because of the risk of Reye syndrome, salicylates should not be taken by individuals with varicella.

In 1995, a live attenuated vaccine for varicella was licensed in the United States. The vaccine has been shown to be safe, immunogenic, and efficacious. The most common side effects are pain and redness at the site of injection, rash, and fever.[82] Children older than 1 year of age may receive the vaccine subcutaneously in a single dose of 0.5 mL. Adolescents older than the age of 13 years and adults should receive two doses (0.5 mL each), 1 to 2 months apart.[10,83] The vaccine can be given simultaneously with MMR (measles-mumps-rubella), DTP (diphtheria-tetanus-pertussis), OPV (oral polio virus), and *Hemophilus influenzae* vaccines.[70] Postvaccine serology in healthy people is not necessary because the seroconversion rate is high.[82] The vaccine must be kept frozen. The vaccine should be reconstituted with diluent supplied with the vaccine and then discarded if not used within 30 minutes.[70]

The chickenpox vaccine protects very well (95%) against severe disease. Protection from infection and clinical disease is lower (70% to 80%).[71] Most breakthrough cases are mild.[82] Twenty-year follow-up studies of a similar vaccine in Japan show persistent immunity after vaccination, but it is difficult to assess whether that is purely from vaccine or is also from boosting due to exposure to circulating virus in the community.[71] Examination of infants and adolescents in the United States revealed that greater than 90% of subjects had measurable antibody 5 years after vaccination.[82] Definitive duration of protection and the need for a booster is not yet defined.

The vaccine should not be given to people who are allergic to gelatin or neomycin; who have untreated tuberculosis, blood dyscrasias, leukemia, lymphoma, febrile illnesses, or most immunodeficiency conditions; or who are pregnant.[70,83] Although there are no reported cases of Reye syndrome associated with the vaccine and concomitant aspirin use, it is recommended that salicylates not be taken for at least 6 weeks after vaccination. Compared to those who experience natural chickenpox, those that receive the vaccine may be less likely to get shingles. The Centers for Disease Control and Prevention, the Advisory Committee on Immunization Practices, and the American Academy of Pediatrics currently recommend that potential vaccinees who may be exposed to pregnant women and the immunocompromised still receive the vaccine.[70] There has been one case of potentially vaccine-associated symptomatic infection documented in a pregnant woman from her vaccinated and otherwise healthy child.[71,84] Although healthy people are very unlikely to transmit virus to susceptibles after vaccination, a very small risk does exist.[84] The risk of transmission after vaccination is higher if the vaccinee develops a rash,[70,84] so vacciness who develop a rash should be isolated from susceptible individuals.

The Advisory Committee on Immunization Practices does not recommend serologic testing to confirm lack of immunity because the vaccine can be administered safely to people who have had chickenpox infection in the past.[70,85] However, the estimated cost of the vaccine, $35 per dose in 1996, along with the cost of serologic testing must also

be considered.[70]

The vaccine is not being recommended for children less than 1 year of age.[10,83] All children 12 to 18 months of age should be routinely vaccinated. Persons between 18 months and 13 years of age who have not been previously vaccinated and lack a reliable history of varicella infection should receive one dose of vaccine. Selected populations of susceptible adults should be administered two doses of vaccine. These include health care workers, teachers, daycare employees, and others with potentially close and frequent contact with susceptible persons and the immunocompromised. Nonpregnant women who may become pregnant in the future should be also be vaccinated.[70] Manufacturers advise waiting at least 3 months before becoming pregnant after vaccination.[83]

According to the directive requirements for the Armed Forces Immunizations Program in November 1995, the Department of Defense policy is to administer the varicella vaccine to high-risk occupational groups and as directed by the applicable Surgeon General or Commandant, with the exception of the Marine Corps, which follows only the Commandant's recommendations.[44] The Navy and Air Force presently screen recruits using on-site rapid ELISA testing during inprocessing at basic training. Results are available within 24 hours and the 7.0% who are seronegative are vaccinated.[86] The Army is developing its policy toward screening recruits for varicella.

Relying on an individual's recall of clinical disease is one aspect of concern in varicella immunization policies. In one study, 95% of military recruits giving a history of varicella were seropositive.[75] The positive predictive value of a history of chickenpox may be lower in recruits who did not grow up in the United States. A study of US military recruits from Micronesia uncovered a positive predictive value of varicella history of only 81%.[87] A representative sample of Army basic trainees studied had a positive predictive value of 88%. Eighty-nine percent of those with a questionable history of varicella were also seropositive. Only 36% with a negative history of varicella were seronegative.[14]

Prevention other than vaccination includes keeping those who are infectious away from susceptible people, especially those at high risk in the hospital setting. The military should be especially concerned about close contact, such as in schools and military basic training. Exposed susceptibles, including health care workers, should be isolated from other susceptibles on the 8th to 21st days after the contact case develops the rash and to the 28th day if they received VZIG.[69,70] Children should be allowed to return to school or day care 6 days after the onset of their rash when all lesions are crusted over or covered, unless they are immunocompromised.[10,69] Active duty personnel and other adults should return to work according to these same guidelines.

Selected populations of exposed susceptible people need to be identified and offered VZIG. These include the immunocompromised, pregnant women, infants born to a mother who has onset of disease in the perinatal period, or premature infants (older than 28 weeks and no maternal history of varicella infection, younger than 28 weeks regardless of maternal history). VZIG should only be offered after considering the potential for significant exposure. The dose is 125 U intramuscularly for each 10 kg of body weight, with a maximum of 625 U (5 vials).[69] VZIG can prevent disease or lessen its severity if given within 96 hours of exposure, but it is not appropriate to use it as treatment once the disease has been established.

In the future, the maintenance of immunity and the need for future boosters after vaccination will become better defined. Postvaccination transmission also needs further investigation.[84] Vaccination programs should provide for those who were too old for the initial immunization campaign in children but escaped disease in childhood. The success of the immunization program in children will eventually affect the varicella seroprevalence of entering recruits and the cost-effectiveness of military vaccination strategies. Slow implementation of varicella immunization in children may for a time increase the susceptibility of incoming recruits as a result of reduced preaccession exposure. Future military policy should become more specific after incorporating economic considerations and continuing surveillance.

[Kathryn Clark]

PERTUSSIS

Introduction and Military Significance

Pertussis has been long, though erroneously, considered solely a disease of childhood. The availability of a vaccine since 1949 and the resultant 99% reduction in morbidity and mortality compared to the prevaccine era has removed pertussis from the consciousness of all but a small, specialized segment of the medical community. After the historic low of 1,010 cases reported in the United States in 1976, a

cyclic (every 3 to 4 years) resurgence of cases has been noted, with a high of 6,586 cases in 1993.[88] The renewed interest and research in pertussis has revealed that adult pertussis has been underdiagnosed as well as underreported. Many feel that adults with pertussis infection represent the most significant reservoir for ongoing transmission of disease, especially to susceptible infants and children, in whom the severity of illness is greater.

Although pertussis has not yet been implicated in outbreaks of respiratory illness among military populations, it may be that it simply has not been recognized as a cause. Waning immunity in the vaccine era appears to render many young adults susceptible again at the very age most begin military service, as the last booster dose of pertussis vaccine is given before the seventh birthday and vaccine-induced immunity is thought to be absent by 12 years after the last dose. Vaccination can be viewed as both boon and curse. While surely preventing many cases of serious disease and deaths among young children, widespread immunization has left so little natural infection in the community that there is little chance for adults to be "boosted" by exposure to natural cases. Approximately one fourth of the US adult population is thus thought to be susceptible to pertussis.[89] In the 1990s, especially with licensure of acellular pertussis vaccine for children for the last two booster doses, there has been renewed interest and research into re-immunization of adults.

The knowledge that pertussis occurs with some frequency in young adults, that it is a highly contagious respiratory disease, and that a significant proportion of military recruits are likely to be susceptible make it conceivable that large outbreaks of disease could occur among barracks contacts at basic training sites. Two studies in the 1990s are pertinent to the issue of military relevance of pertussis. One hundred thirty college students (the same age group as military recruits) with a cough illness of 6 or more days were enrolled in a study to examine the prevalence of pertussis.[90] Twenty-six percent had evidence of pertussis infection. Serology detected all but one of the infections, and no cultures were positive. In the second study,[91] antibody levels of US university students were compared to German military recruits. IgA levels to four different pertussis antigens ranged from 60% to 91% among all participants and did not differ between the Americans and Germans for any of the individual antigens. Since IgA titers are thought to reflect natural infection, the authors concluded that pertussis infections are common in this age group.

A second theoretical concern for the military regarding pertussis is related to the recent shift toward increased numbers of humanitarian assistance missions, in which US forces have close, prolonged contact with host populations. Since the incidence of pertussis is roughly three orders of magnitude greater in much of the world than it is in the United States (1 per 100 vs. 1 per 100,000), exposure to the host population increases the chance of infection in young service members. Alternatively, sporadic cases in those service members whose disease may be mild enough to preclude evacuation may result in transmission of disease to a relatively highly susceptible population in the host country.

Description of the Pathogen

The causative agent of pertussis is the Gram-negative bacillus, *Bordetella pertussis*. The organism produces several cellular products responsible for its virulence and for antigen presentation to the host immune system. Pertussis toxin is an important virulence factor, mediating the attachment of the bacterium to the respiratory epithelial cells. Filamentous hemaglutinin is the other major protein product also thought to mediate attachment of the organism to the respiratory epithelial cells.[92] Both of these protein products are believed to play a role in inducing immunity after natural infection and also represent the major components of the licensed acellular vaccine for children.[93]

Epidemiology

Transmission

Pertussis is transmitted readily by contact with respiratory secretions from an infected individual spread through airborne droplets.[10p375–379,92] Up to 90% of susceptible household contacts may become infected following close contact with an index case. Indirect transmission through fomites is considered unlikely.[92] The most susceptible age groups are (*a*) infants younger than 6 months of age who have not completed the three-dose primary immunization series and who do not have passive antibody protection from mothers whose vaccine-induced immunity has waned and (*b*) adolescents and adults whose immunity has waned and who may be exposed to infected family members or close contacts.

Geographic Distribution

Pertussis is a worldwide disease problem. Vaccination policies tend to be less stringent in some other developed nations than in the United States.

Pertussis vaccination is optional in Germany[91] and Italy,[94] and the vaccine was withdrawn in Sweden in 1979.[95] The schedule in Finland is different than in the United States, with four total doses recommended and the last booster at 2 years of age.[96]

Incidence

In 1986, the World Health Organization estimated that there are 60 million new cases of pertussis each year, causing about 600,000 deaths.[97] In the United States, the incidence of pertussis has generally increased since the historic low in 1976, with the greatest number of cases since then occurring in 1993. Pertussis continues to be largely a disease of infants and children, but the percentage of cases in persons aged 10 years or older has increased from 15.1% (1977 to 1979) to 18.9% (1980 to 1989) to 28% (1992 to 1994).[88,98] The rate of complications in the older age groups, however, is significantly lower than in infants and children. Specifically, there were proportionally fewer cases requiring hospitalization or developing pneumonia, seizures, or encephalopathies in those aged 10 years or older for the years 1992 to 1994.[88] All 32 deaths occurred in children younger than 10 years of age.

One study[99] has estimated that only 11.6% of pertussis cases in the United States are reported to the Centers for Disease Control and Prevention. Coupled with the fact that the illness in adolescents and adults is milder or atypical,[89,100] it is likely that cases in the older age groups are disproportionately underreported. Other studies,[101,102] which have attempted to prospectively diagnose pertussis in adults with a prolonged cough illness, suggest that pertussis may account for 21% to 26% of these illnesses.

Pathogenesis and Clinical Findings

The clinical syndrome of pertussis is variable, but illness severity is generally greatest in the very young. After an incubation period of 6 to 20 days, the first stage of illness, known as the catarrhal stage, arises with nonspecific nasal symptoms, low-grade fever, and mild cough. This stage corresponds to the period of greatest infectivity. After 1 to 2 weeks, the paroxysmal stage begins, with the characteristic symptoms of paroxysmal cough and inspiratory whoop (Figure 39-2). Especially in young children, the paroxysms of cough may be complicated by apnea, posttussive vomiting, and hypoxia-induced encephalopathy. Pneumonia is another complication and is highly correlated with death. Bronchopulmonary pathologic findings include damage to cilia, accumulation of secretions, and edema.[92] Adults are less likely to have paroxysms of cough or the classic whoop but are likely to present with a prolonged cough illness. Asymptomatic carriage is not a feature of this disease.

Diagnostic Approaches

Diagnosis is difficult, especially in adults. Culture of nasopharyngeal secretions has been the gold standard, but even in optimal circumstances only 80% of cultures are confirmatory.[92,103] The pertussis organism is fastidious and slow-growing, requires selective media, and must be obtained with a calcium alginate or Dacron swab. Previous immunization, use of antibiotics, or attempts to isolate the organism late in the illness all decrease the rate of recovery. Direct fluorescent antibody testing of nasopharyngeal secretions has been employed as a rapid means of diagnosis, but results have been mixed, with generally low sensitivity and specificity.[10,103] Serologic testing, using a variety of methodologies from agglutination to enzyme-linked immunosorbent assay and using either single elevated titers or paired (acute and convalescent) titers, has been employed.[92,103,104] Use of paired sera limits the applicability of the test to retrospective serosurveys in most cases. Further, because of the ubiquitous exposure to pertussis through im-

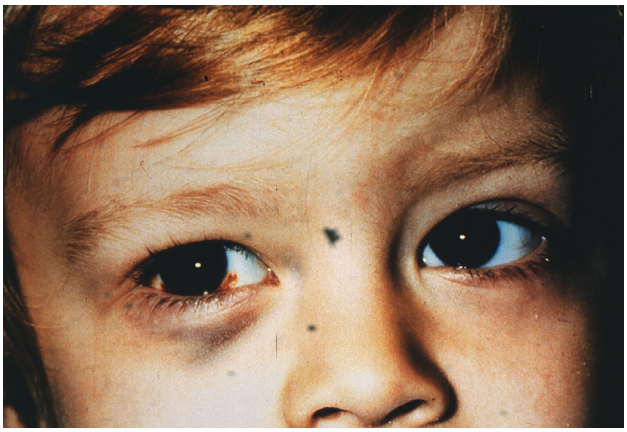

Fig. 39-2. Subconjunctival hemorrhage in pertussis occurs because the intrathoracic pressure rises sharply during violent paroxysms of coughing and leads to sudden surges in capillary pressure. In this child, the subconjunctival hemorrhage is accompanied by bleeding into the lower lid—a rarer complication. No permanent harm results, and these complications resolve rapidly.
Reprinted courtesy of Mosby-Wolfe Limited, London, UK from: Forbes CD, Jackson WF, eds. *Color Atlas and Text of Clinical Medicine*. 2nd ed. London: Mosby-Wolfe Limited; 1997: 55.

munization or natural infection, the ideal serologic test would be quantitative rather than registering the simple presence or absence of antibody. Researchers have developed a set of isotype-specific antibody responses to *B pertussis* antigens (ie, PT, FHA) for serodiagnosis of natural infection, but these are perhaps not practical except in reference laboratories.[104]

Diagnosis in a garrison environment can be accomplished with the aforementioned tools, subject to local resources. In the field or during wartime, though, reliance on clinical diagnosis is necessary because culture requires special media and direct fluorescent antibody requires special lab equipment that may not be available in forward-deployed hospital settings. It might be possible to use a single serum titer in the appropriate clinical scenario, if further study yields a quantitative titer that is judged positive and indicative of recent infection. The clinical case definition set forth by the Centers for Disease Control and Prevention consists of cough of at least 14 days' duration without other known etiology, accompanied by either paroxysms, inspiratory whoop, or posttussive vomiting.[105]

Recommendations for Therapy and Control

Erythromycin is the antimicrobial of choice for both treatment of individuals and for outbreak control. Individual patients should be treated with a 14-day course of erythromycin and are considered noninfectious after completion of 5 days of therapy. Only rarely is pertussis diagnosed early enough in the catarrhal phase to enable erythromycin to affect the clinical course; the goal of the antibiotic treatment is the eradication of the organism from the nasopharynx to interrupt transmission.[92] Close or household contacts who have not completed the vaccination series should receive a dose of vaccine as soon as possible after contact with the index case, and all contacts, regardless of age or immunization status, should receive 14 days of prophylaxis.[10]

Prevention of pertussis is accomplished in the United States by a vaccination series consisting of five doses: three primary doses at 2, 4, and 6 months of age and boosters at 12 to 18 months and at 4 to 6 years of age. Pertussis is usually combined with vaccines against tetanus and diphtheria, as diphtheria-tetanus-pertussis (DTP) or diphtheria-tetanus-acellular pertussis (DTaP). The use of acellular pertussis vaccine has been recommended for use in the booster doses since 1991,[106] but the Advisory Committee on Immunization Practices (ACIP) has broadened its recommendations for use of acellular pertussis for the primary doses as well as the booster doses for several products licensed by the Food and Drug Administration.[107,108] The ACIP does not recommend the use of pertussis vaccine beyond the seventh birthday,[10] despite the widely recognized problem of waning immunity.

Since the availability of acellular pertussis in 1991, there has been renewed interest in testing its safety and efficacy in adult populations. Long-term immunogenicity of acellular pertussis vaccine has still not been evaluated, but preliminary research shows that it is both safe and immunogenic in the near term when administered to adults.[93,109,110] Further study is likely to yield a recommendation for a tetanus-diphtheria-acellular pertussis (TdaP) booster for adults in the future.

Because of the potential for epidemic spread in a barracks setting or aboard ship and because of the shift in the role of the military in peacetime to humanitarian missions, it seems appropriate for military personnel, particularly new recruits, Special Forces units, and Civil Affairs units, to be immunized against pertussis when acellular pertussis becomes available for use in adults.

[David Goldman]

TETANUS

Introduction and Military Relevance

Tetanus, also known as lockjaw because of its propensity to cause painful, tonic spasms of the muscles, has been and will remain an important infection from a military perspective. In the military workplace, whether it be on the battlefield or the training ground, service members will sustain wounds, exposing them to the ubiquitous spores of tetanus. Tetanus spores live in soil for many years, so the risk is ongoing and permanent.

Even though there were very few recorded cases of tetanus during the Civil War, a doctor wrote, poignantly, "On account of exposure, many wounds were gangrenous when the patients reached the hospital. In these cases delay was fatal, and an operation almost equally so, as tetanus often followed speedily."[111p30] One of the historical figures who succumbed to lockjaw was General Gladden, who was with General Bragg's command in South Carolina. He had his left arm amputated after being hit by a musket ball. Refusing convalescence, he re-

joined the battle. In days, he required a second amputation, near the shoulder, but he still refused to give up command. He gave it up shortly thereafter, when he died of "lockjaw."[111]

In World War I, the case rate for tetanus was 0.16 per 1,000 wounded. The reason for the low incidence of tetanus was the universal and early administration of tetanus antitoxin as a form of passive immunization. Fifteen hundred units of tetanus antitoxin was given subcutaneously in all cases of wounds and injuries where there was the possibility of contamination with tetanus spores. A "T" was painted with iodine on the forehead of soldiers given the antitoxin at an aid station or at any point in front of the hospital station. Proof of the usefulness of antitoxin was evident in the experience of the British Army. In September 1914, their rate of tetanus was 8.6/1,000. After orders were issued to use the antitoxin, the rate fell to 1.4/1,000 by December 1914.[112p110–114]

In 1941, all US military personnel were immunized with tetanus toxoid.[113] During World War II, there were only 16 clinical tetanus cases, and only six of these died. After the toxoid was precipitated with alum or adsorbed onto aluminum salts, fewer doses were needed for effective immunization.[114]

Since the early 1990s, the US military has been increasingly involved in operations other than war, such as peacekeeping and provision of humanitarian assistance. These activities bring to bear issues in tetanus control that are especially pertinent in developing countries. Because tetanus spores are ubiquitous, it is not a matter of eliminating exposure but rather of limiting it. The issues are basic sanitation, appropriate wound care, aseptic technique during childbirth, and adequate immunization. There is precedent for military efforts in these areas. The US Army medical department made significant improvements in general sanitation measures while encamped in Cuba during the early part of the 20th century, which included decreasing the number of cases of tetanus resulting from unsanitary care of the umbilical cord in newborns.[115] Modern peacekeeping efforts provide a great opportunity to decrease the incidence of neonatal tetanus in developing countries by ensuring that pregnant women are vaccinated against tetanus.

Description of the Pathogen

Tetanus is caused by an exotoxin, called tetanospasmin, which is elaborated in wounds infected with *Clostridium tetani,* a Gram-positive, anaerobic bacillus.

Epidemiology

Transmission

The means of transmission is by introduction of tetanus spores into the body, typically through a puncture wound contaminated with soil or feces.[10p491–496] Cuts, burns, or contaminated illicit injectable drugs also create routes for infection to occur. The organism is harbored in the intestinal tract of humans, horses, and other animals. Tetanus is not communicable from person to person.

Geographic Distribution

Tetanus occurs worldwide; however, it is more prevalent in countries where immunization programs are lacking or there is difficulty in obtaining appropriate medical care. It is also found more frequently in densely populated areas with hot and damp climates where the soil is rich in fecal matter.[116]

Incidence

Almost all cases of tetanus in the United States occur in partially immunized or nonimmunized persons. Most cases occur in persons 60 years of age or older;[117] from 1989 to 1990, 58% of the 117 cases reported in the United States occurred in adults over the age of 60.[10] This is primarily due to waning immunity caused by declining antibody levels. The third national Health and Nutrition Examination Survey, a study of 10,618 people 6 years of age and older conducted from 1988 to 1991, showed that protective levels of tetanus antibody were found in 27.8% of those 70 years of age or older.[117] Lower rates of immunity were also seen in non-Hispanic blacks (68.1%) and Mexican-Americans (57.9%) in comparison to non-Hispanic whites (72.7%). A history of having served in the US military was associated with having protective levels of antibody, and male veterans had higher rates of immunity compared to female veterans. In fact, one of the risk factors for sustaining a tetanus infection for US citizens is a lack of military experience.[118] The following variables were all independent predictors of protective levels of tetanus antibody levels: male sex, non-Hispanic white race, US or Canadian birth, military service, and having some college education. Certain risk factors (ie, access to health care, poverty status, educational level of the head of the household) were not associated with immunity to tetanus.[117]

In spite of an effective vaccine, approximately 50,000 deaths from tetanus are reported per year worldwide.[118] In reality, there are many more deaths secondary to tetanus than are officially reported. Tetanus can be likened to a silent epidemic and may be the "most underreported lethal infection in the world."[119p191] After the advent of active immunization programs in the United States, the incidence declined, with 560 cases reported in 1947, 101 cases in 1974, and approximately 60 to 80 cases per year since the early 1980s.[118] These numbers reflect reported cases; underreporting of cases is also a problem in the United States. The case fatality rate varies, depending on patient age and length of incubation time. In general, the shorter the incubation period and the more extreme the age (ie, newborns, young children, the elderly), the higher the case fatality rate will be.

Pathogenesis and Clinical Findings

Once the tetanospasmin has entered the central nervous system, it binds to the ganglioside membranes of nerve synapses. This blocks release of the inhibitory transmitter from the nerve terminals, causing a generalized tonic spasticity. Spasms result from intensive afferent stimuli, which increases rigidity and causes simultaneous and excessive contraction of muscles and their antagonists.[116]

The average incubation period is 10 days, with a range from 1 day to several months, depending on the severity and location of the wound. When the period from injury to onset of symptoms is short, the illness will be more serious. Case fatality ranges from 10% to 90%. When symptoms occur within 2 or 3 days of injury, the mortality rate approaches 100%.[116] Occasionally, the presenting signs and symptoms may be nonspecific, but the most common presentation will include painful muscular contractions, especially of the masseter and neck muscles, and difficulty opening the jaw. Trismus, which may include a "risus sardonicus" or sardonic smile, may result in difficulty swallowing and irritability. Abdominal rigidity may be one of the first signs of tetanus in older children and adults. The rigidity can also occur around the site of the injury.[10] The posture of severe curving of the back upwards with the head and heels flat on the bed, or opisthotonus, is a result of tetanic spasm. Minor stimuli, such as noise or a breeze, may cause painful, tonic convulsions. Cyanosis and asphyxia may result when the respiratory muscles spasm.[120] These manifestations will increase in severity for 3 days and will remain stable for 5 to 7 days, after which spasms will occur less frequently until they disappear altogether.[116] Complications, including death, are the result of a combination of factors. These factors include the direct results of the toxin, such as laryngospasm, which leads to impaired respiration, hypoxia, and brain damage. Vigorous therapy and prolonged bed rest can result in secondary complications such as decubitus ulcers.

In a field setting, the first symptoms of tetanus may be quite subtle, consisting only of pain and tingling at the wound site, followed by spasticity of the nearby muscle groups.[120] This is referred to as a localized tetanus. Cephalic tetanus, which can involve all cranial nerves, is seen most commonly in children and is usually associated with a chronic otitis media.

Tetanus neonatorum, a form of tetanus that affects newborns as a result of nonsanitary medical or ritualistic perinatal practices, often presents as an inability to nurse. Stiffness, spasms, convulsions, or opisthotonus are subsequently noted. The average incubation period is about a week and mortality is high.

Diagnostic Approaches

Tetanus can be insidious to diagnose because a history of an injury may be lacking. Any scenario that allows for penetration of the skin and fosters an anaerobic environment is conducive to growth of tetanus spores. Burn victims and intravenous-injecting drug addicts are examples of particularly susceptible individuals.

There are no specific laboratory tests to diagnose tetanus. Laboratory confirmation is futile, as the organism is not usually recovered from the infection site, nor is there any appreciable antibody response.[10] About one third of patients may exhibit a granulocytosis, and various fluid and electrolyte disturbances may occur.[116] Tetanus is diagnosed strictly on clinical grounds when the signs and symptoms suggest it in an individual who has not been immunized or who has let his or her tetanus immunity lapse. Therefore, the treating physician must have a heightened sense of suspicion and make inquiries about tetanus immunization history.

Recommendations for Therapy and Control

The goals of therapy for tetanus are to neutralize the toxin, to remove the source of the toxin, and to provide supportive care.[118] Patients who recover from tetanus do not develop an immune response so they also require active immunization. In addi-

tion to wound cleaning, surgical debridement (when indicated), and prophylactic antibiotics (a 7-day course of penicillin), vaccine immunoprophylaxis is necessary to prevent tetanus. This will depend on the type of wound and the history of tetanus immunizations. Patients should be asked whether they have ever received tetanus immunization, and the wound site should be characterized as to whether it is clean and minor, severe, or contaminated. If the patient cannot recall or has had less than three doses of tetanus vaccine, he or she should be given tetanus vaccine (using a combined diphtheria-tetanus-pertussis vaccine, DTP), the amount of which will vary with the age of the patient. Children younger than 7 years old should receive DTP or DTaP (a formulation with acellular pertussis). Children older than 7 years and adults should receive Td (tetanus-diphtheria). Tetanus immune globulin (TIG) provides immediate neutralization of tetanospasmin and should be administered to patients with severe or dirty wounds who are unsure of their immunization status or those with a history of having had less than three doses of tetanus vaccine. When both TIG and toxoid are given, separate sites and syringes must be used. TIG is not necessary for patients who have had a full series of tetanus immunizations. Neither is it necessary to give a booster of tetanus vaccine to patients who have previously been fully immunized, except in certain situations. If a patient has sustained a minor, clean wound and it has been more than 10 years since the last dose of tetanus vaccine, he or she should receive a Td booster. If the wound is severe or dirty or both, and it has been more than 5 years since the last dose, a booster should be given[10] **(**Table 39-2**).**

Once tetanus is suspected, the patient should be admitted to an intensive care unit to ensure continuous monitoring capability and protection of the airway in the event of tetanus-induced laryngospasm. Aggressive therapy to inhibit generalized spasm and the treatment of autonomic instability is important.[118] Metronidazole or doxycycline can be given intravenously in large doses for 7 to 14 days. Parenteral penicillin G is an alternative treatment.[10,69p563–568,121] Tetanospasmin can be neutralized with TIG if the exotoxin has not already been fixed in the central nervous system. TIG will not ameliorate symptoms already present at the time tetanus is diagnosed.[116]

Military personnel will now usually see tetanus in the context of humanitarian assistance to non-US populations. Some of the simplest measures are also some of the most difficult to achieve in light of poverty, cultural behaviors, and lack of education. Individuals who cannot afford shoes are vulnerable to puncture wounds through their feet. The lack of control of pets and their excreta provides abundant opportunities for exposure to tetanus spores. Rituals involving abrasion or cutting provide easy access and introduction of the spores. Procedures used during childbirth, including attendance by untrained lay-midwives and use of unsterile instruments, foster tetanus infections in unimmunized pregnant women. In some cultures, mothers dress their babies' umbilical stumps with dust mixed with spider webs or dung, greatly increasing the risk for an ensuing tetanus infection unless the baby has transplacentally received passive tetanus antibody from its mother.[122]

TABLE 39-2

SUMMARY GUIDE TO TETANUS PROPHYLAXIS IN ROUTINE WOUND MANAGEMENT

History of Tetanus Immunization (doses)	Clean, Minor Wounds		All Other Wounds	
	Td*†	TIG	Td*	TIG
Uncertain or < 3	Yes	No	Yes	Yes
3 or more	No†	No	No‡	No

* For children less than 7 years old, DtaP or DTP (DT, if pertussis vaccine is contraindicated) is preferred to tetanus toxoid alone. For persons 7 years old or older, Td is preferred to tetanus toxoid alone.
† Yes, if more than 10 years since last dose.
‡ Yes, if more than 5 years since last dose. (More frequent boosters are not needed and can accentuate side effects.)
Reprinted with permission from: Chin J, ed. *Control of Communicable Diseases Manual*. 17th ed. Washington, DC: American Public Health Association; 2000: 496. Copyright 2000 by the American Public Health Association.
TIG: Tetanus immune globulin
Td: tetanus-diphtheria

The US military has played an active role in fostering immunization programs in developing countries. Preventing tetanus neonatorum and tetanus in postpartum women is a worthy focus. (Young, nonpregnant women can also be vaccinated against rubella at the same time as receiving tetanus vaccine.) However, targeting women attending prenatal clinics will not suffice. Strategy for preventing tetanus has to be aimed at the whole population and should be tailored according to the customs and needs of the countries supported. Since tetanus spores are ubiquitous, it is important to ensure universal vaccination with adsorbed tetanus toxoid by administering a basic series of the vaccine and giving booster doses every 10 years to ensure ongoing protection.[118] If resources are limited, an initial method may be to target school-aged children for vaccination. Later, when the girls become pregnant, they will transfer tetanus antibody transplacentally to the fetus, conferring protection against neonatal tetanus.

In the US military, tetanus toxoid is administered to all active duty personnel, recruits, and reserve components. They are vaccinated as they begin their military careers, receiving a primary series of Td toxoid if they lack a reliable history of prior immunization. If they have a history of receiving Td, they will still receive a booster dose upon entry to active duty and, ideally, every 10 years thereafter.[48] During soldier readiness processing (SRP) in the Army and its equivalent in the other services and especially for targeted deployments, screening of immunization records includes checking for the date of the last Td immunization. If this has not been given within the previous 10 years, the service member is given a booster. Excessive boosting may be associated with local and systemic reactions. Both military personnel and civilians should be educated about preventive measures: routine tetanus immunization, proper care of wounds, and tetanus immunization, if indicated, after receiving a tetanus-prone wound.

[Paula K. Underwood]

DIPHTHERIA

Introduction and Military Relevance

Diphtheria is an acute bacterial infection caused by *Corynebacterium diphtheriae*. The organism elaborates a toxin that produces a characteristic patch or patches of an adherent grayish membrane with surrounding inflammation, affecting the tonsils, pharynx, larynx, nose, and occasionally other mucous membranes or skin.[10p165–170] Diphtheria gets its name from the Greek word for tanned skin or leather, which describes the nature of the membrane that is almost pathognomonic for diphtheria. The organism is spread through the respiratory route and close personal contact. Military personnel are at greater risk of contracting diphtheria when they are in crowded conditions.

Diphtheria was not distinguished from scarlet fever during the Revolutionary War. It was also called "Throat Distemper, Angina Suffocativa, Bladder in the Throat, Cyanache Trachealis, Angina Maligna, Epidemical Eruptive Miliary Fever and Angina Ulcusculosa."[123] During the Civil War, diphtheria was one of the common diseases that affected all combatants.

In 1913, Schick introduced the skin test for immunity. However, disease control in the military did not involve using the Schick test on whole units and immunizing positive reactors because of the logistical burden that would have placed on time, materials, and workload. Instead, outbreaks were prevented by testing all known contacts of cases to identify carriers. The contacts were placed into group quarantine, which allowed for early detection and treatment with antitoxin of secondary cases.[112p74–83]

By World War I, the prevailing medical opinion dismissed diphtheria as a serious threat to military operations. Disease was usually sporadic among troops but could be epidemic if the conditions were favorable. Diphtheria was the 18th cause of death and the 28th cause of lost time during World War I in the Army, but it was often difficult to differentiate tracheitis and laryngitis caused by gassing from laryngeal diphtheria.[124] Adding to the confusion were laryngeal fibrino-purulent membranes, which formed in severely gassed patients and strongly resembled diphtheric membranes.

There were three documented epidemics of diphtheria during World War I. The disease was more common among enlisted white soldiers but had a higher case fatality rate among black soldiers. Crowding of troops in trains, transports, and billeting facilitated disease spread.[112] In 2 of the 42 divisions in the American Expeditionary Forces, diphtheria became a concern. Both divisions came from camps in the United States at sites with a high prevalence of diphtheria (the 32nd Division in Camp MacArthur, Texas, and the 35th Division in Camp Doniphan, Oklahoma). Carriers were the source of infection, and the crowded conditions allowed

propagation and transmission of the organism. Once the 35th Division was encamped in France, with 48 hours of close contact, a sharp increase in diphtheria admissions was noted. After troops were distributed in billets and dugouts in the Vosges Mountains, crowding decreased and the morbidity rate declined. Of 10,909 admissions for diphtheria, 2,439 complications and 107 deaths were reported. The case fatality rate for the US Army was 1.62%.[124]

During World War II, cutaneous diphtheria became a problem for military personnel in North Africa.[114] This type of indolent skin infection may act as a source of respiratory infection in others. It is more common in warmer climates.[125]

Description of the Organism

Diphtheria is caused by a Gram-positive, club-shaped bacillus. It was discovered by Kelbs in 1883, and Loeffler succeeded in growing the organism in culture in 1884.

All corynebacteria have the heat-stable O antigen. K antigens, which are heat-labile proteins in the cell wall, differ among strains of *C diphtheriae*, and these differences permit classification into a number of types. There are three morphologically different biotypes: gravis, intermedius, and mitis. There is no consistent correlation between clinical severity and specific biotype.

Epidemiology

Transmission

Humans are the reservoir. The means of transmission is person to person, from intimate physical contact with a case or an asymptomatic carrier. Because the infection can be subclinical, asymptomatic individuals can transmit the infection. There has been no clear proof of indirect transmission by airborne droplet nuclei, dust, or fomites. Cutaneous lesions are important in transmission. Also, there is evidence of outbreaks caused by contaminated milk and milk products.[125]

Geographic Distribution

In temperate climates, diphtheria occurs throughout the year but seasonal increases are seen in colder months, probably as a result of close contact indoors. In tropical and warm climates, cutaneous diphtheria is more common and is not related to the season.

In the late 1980s and continuing into the 1990s, diphtheria reemerged in all but one of the independent states of what was the Soviet Union. There is the potential for importation of cases into the United States from this region, given the ease of global travel. To date, no imported case has been reported; however, there have been imported cases in Europe.[126]

Incidence

In the past, diphtheria was a major cause of morbidity and mortality. Peaks in incidence were observed approximately every 10 years. In Massachusetts between 1860 and 1897, death rates ranged between 46 and 196 per 100,000 annually. The proportion of total deaths that were attributable to diphtheria annually ranged between 3% and 10% during the same period.[125] In the United States in 1900, more than half as many deaths were caused by diphtheria as were caused by cancer. With the introduction of diphtheria antitoxin in the early 1900s, a considerable fall in the death rate occurred, but the number of cases remained high. In 1921, more than 200,000 cases were reported, primarily among children.[127] There were only 28 cases reported in the United States between 1982 and 1991.[128]

During World War II, a major outbreak, which apparently originated in Germany, spread throughout Western Europe, and more than 1 million cases were eventually reported. Occasional widespread epidemics have occurred, notably in Austin and San Antonio, Texas, between 1967 and 1970.[125] In 1994 in the former Soviet Union, there were 47,802 cases and 1,746 deaths reported. Serological surveys for diphtheria antibodies reveal that 20% to 60% of US adults older than 20 years of age are susceptible.[126] US military recruits from Micronesia show a 39% seronegative rate for diphtheria.[87]

There has been a nearly complete disappearance of the disease in countries that have immunized widely. Ninety-six percent of school-aged children in the United States have received three or more doses of diphtheria and tetanus toxoids and pertussis vaccine.[127] A distinct and disturbing trend, though, seems to be an increasing serosusceptibility with advancing age. While diphtheria was once commonplace, it is now largely confined in the United States to adults over the age of 20 who have not obtained recommended boosting doses.[125]

Pathogenesis and Clinical Findings

Roux, one of Pasteur's assistants, and Yersin demonstrated in 1888 that the diphtheria bacillus produced a powerful toxin. Toxin production is

mediated by bacteriophages. When the bacteria are infected with the corynebacteriphage that contains the gene *tox*, toxin production will occur. The toxin is identical among all the strains. The diphtheria toxin is a polypeptide with a molecular weight of approximately 58,000. The toxin has two fragments: A and B. Fragment B penetrates the cell, and toxicity is due to the disruption of cellular protein synthesis by the A fragment of the toxin.[125] Antibodies directed against the B fragment protect against infection.

The incubation period is from 1 to 6 days. Early symptoms are mild and nonspecific. Fever, if present, does not usually exceed 38°C (101°F). The patient may complain of a sore throat, and the cervical lymph nodes may be enlarged, giving rise to the so-called "bull neck." There may be a serosanguinous nasal discharge. At first, the pharynx is suffused with blood on physical exam, but about 1 day after onset, small patches of exudate appear. Within 2 or 3 days, the patches spread, become confluent, and may form a membrane that covers the entire pharynx, including the tonsillar areas, soft palate, and uvula. The membrane will take on a grayish color and is thick and firmly adherent. Efforts to dislodge it usually result in bleeding. The patient will appear very ill and may have a rapid, thready pulse. If the patient is not treated, the membrane will begin to soften after a week and will eventually slough off. Other sites may become involved, including cutaneous, vaginal, aural, and conjunctival areas. Altogether, these sites account for 2% of cases and are secondary to nasopharyngeal infection.[125]

The impact of diphtheria is largely felt by its propensity to cause complications, especially in the nervous and cardiovascular systems. Severe complications typically fall into one of three categories: acute systemic toxicity, myocarditis, and peripheral neuritis. Only toxin-producing biotypes cause myocarditis and neuritis.[127] The major complications of laryngeal diphtheria are croup and respiratory obstruction.

Bacilli that are not infected by bacteriophages can also cause disease even though they do not produce the toxin. This condition is called avirulent diphteria, and it tends to be mild.[129]

Diagnostic Approaches

An adherent, grayish membrane in the throat of a patient who is acutely ill should suggest the diagnosis. The differential diagnosis would include bacterial and viral pharyngitis, Vincent's angina, oral syphilis, candidiasis, infectious mononucleosis, acute adult epiglottis, croup, and facial nerve palsies from neurological complications of Lyme disease.[10] Diphtheria most often appears as a membranous pharyngitis. A patient with a confluent pharyngeal exudate should be suspected of having diphtheria until proven otherwise. The onset is gradual, with a steady progression through hoarseness to stridor over a period of 2 to 3 days. Material for culture should be obtained with direct visualization and is best taken from the edge or beneath the edge of the membrane. Cutaneous diphtheria may appear as a sharply demarcated lesion with a pseudomembranous base at the site of a wound. Its appearance may not be distinctive, however, and the diagnosis can only be confirmed by positive culture.[127]

Recommendations for Therapy and Control

Treatment of diphtheria is a two-step process. The first step involves the administration of diphtheria equine antitoxin. The amount of toxin produced is in direct proportion to the size of the membrane. Depending on how extensive the local lesions are, the total recommended amount of antitoxin will vary between 20,000 and 100,000 U. A higher dose of antitoxin will also be required as the interval between onset of disease and initiation of treatment lengthens.[125]

The second step of treatment is to eliminate carriage of the organism in the pharynx or nose or on the skin. It is necessary to administer a course of either penicillin (intramuscular penicillin G benzathine 600,000 U for children younger than 6 years of age or 1.2 million U for patients 6 years and older) or erythromycin (7- to 10-day course at 40mg/kg per day for children and 1 g per day for adults). Treatment should continue until there are at least three consecutive negative cultures.

If a susceptible, unimmunized patient is exposed to diphtheria but is asymptomatic, the preferred course is to obtain a throat culture, begin immunization with diphtheria toxoid, and initiate prophylaxis with either a single dose of benzathine penicillin or oral erythromycin for 7 days. Patients should be kept under observation. If they cannot be observed, they should be given 5,000 to 10,000 U of antitoxin intramuscularly and started on a course of oral erythromycin (40 to 50 mg/kg per day for 7 days, maximum 2 g per day), or be given a single intramuscular dose of benathine penicillin G (600 U for children younger than 6 years of age and 1.2 million U for patients 6 years and older).[69p230–234]

Diphtheria is a reportable infection; case reports are obligatory in most states. Measures must be taken to avoid an epidemic. Patients with pharyngeal diphtheria must be kept in strict isolation, and those with cutaneous diphtheria require contact isolation. Two cultures from the throat and nose (taken not less than 24 hours apart and not less than 24 hours after finishing antimicrobial therapy), or from skin lesions for those with cutaneous disease, must be negative for diphtheria bacilli before the isolation precautions can be discontinued. All articles used by patients need to be thoroughly disinfected. All contacts need to be kept under surveillance for 7 days, and cultures of the nose and throat should be taken to rule out asymptomatic carriage of the organism. Regardless of their asymptomatic state and their immunization history, all contacts should be given a single dose of penicillin or a 7- to 10-day course of erythromycin. If contacts of cases are employed in occupations that involve handling food or working with children who may not be immunized, the contacts should be excluded from work until they are proven not to be carriers. If contacts have been immunized, they should receive a booster dose of diphtheria toxoid. If contacts have no history of immunization, a primary series should be started, using Td, DT, DTP, or DTP-Hib vaccine, depending on each contact's age.[10]

The cornerstone of prevention remains an active immunization program. It has its roots in the work of Theobald Smith in 1907. He noted that long-lasting immunity to diphtheria could be produced in guinea pigs by injection of mixtures of diphtheria toxin and antitoxin. The presence of antibodies to the toxin ensures clinical immunity. To provide protection against diphtheria, the toxin is rendered into a toxoid by using formaldehyde to destroy the enzymatic capabilities of the toxin while allowing it to retain its immunogenicity. This concept was demonstrated by Ramon in the 1920s.[125]

By the mid-1940s, diphtheria toxoid was combined with tetanus toxoid and pertussis vaccine in the now familiar diphtheria, tetanus, and pertussis vaccine combination, called DTP. Five doses are recommended for children at ages 2, 4, 6, 15, and 18 months and at school entry before the seventh birthday. It can be safely administered with other vaccines (eg, *H influenzae* type b vaccine; hepatitis B vaccine; live, attenuated measles-mumps-rubella vaccine) without loss of efficacy. DTP contains between 10 and 20 Lf (Loeffler units) per immunizing dose of 0.5 mL. The formulation for adults, Td, contains the same amount of tetanus toxoid as does DTP, but the amount of diphtheria toxoid is reduced to 2 Lf per dose. Seventy percent or more of a childhood population must be immune to diphtheria to prevent major community outbreaks.[125] Because of the concern about the proportion of susceptible adults, it is imperative that immunity to diphtheria be sustained by booster doses of Td every 10 years.

Service members' immunization records are screened before deployments and, when indicated, the personnel receive Td boosters every 10 years.[44] With the US military's ever increasing international role in operations other than war and recent joint training missions to places such as Ukraine, where diphtheria has become epidemic, it is imperative that vaccine status be vigilantly screened and personnel be appropriately immunized.

[Paula K. Underwood]

POLIO

Introduction and Military Relevance

Polio is an enterovirus, spread person to person through the fecal–oral route. At the most severe end of the clinical spectrum, it can cause a flaccid paralysis, respiratory failure, and death; most often, though, infection is mild or asymptomatic. It is difficult today to imagine the widespread terror that polio caused in the American public in the 1940s and 1950s. Anyone, including a future president of the United States, could be stricken with polio, and parents even kept their children from public swimming pools in fear of it. Although now it has been eradicated from the Western hemisphere, polio remains a problem throughout many developing countries, especially in India and sub-Saharan Africa. The World Health Organization's Global Poliomyelitis Eradication Initiative has reduced the number of reported cases of polio worldwide by more than 80% since the mid-1980s.[130] The goal, also ascribed to by Rotary International, the United Nations Children's Fund, and the Centers for Disease Control and Prevention, was to eradicate polio worldwide by the year 2000.[131] Certification of the complete interruption of indigenous transmission of wild polio virus is expected by 2005.[132]

Polio has not been considered an important disease in military forces primarily because 90% of the paralytic polio cases occur in persons younger than 20 years of age. During World War I, there were only 69 diagnosed cases.[112p110–114] But because of the seriousness of the disease, the probability that service

members will be deployed to endemic areas, the effectiveness of the preventive measures, and the worldwide effort to eradicate polio, polio vaccination remains an important component of military preventive medicine.

Description of the Pathogen

Polio is an enterovirus, an RNA virus belonging to the family *Picornaviridae*. There are three distinct serotypes: 1, 2, and 3.

Epidemiology

Transmission

Humans are the sole reservoir of polio, and no permanent carrier state is known. Polio is transmitted by the fecal-oral route but can also be spread by direct contact with nasal and throat discharges via respiratory particles—an oral-oral route. Polioviruses are transient inhabitants of the human alimentary tract and can be detected in the throat or lower intestine.[131] Although highly contagious, most infections are subclinical. The ratio of inapparent infections to overt cases is greater than 100:1 and can be as large a difference as 1,000:1.[133] Symptomless infected persons, as well as overt cases, can spread infection.

Paralytic polio tends to appear sporadically; usually there is no clear connection among cases. Even though a family has only one case of paralytic polio, the other family members may be infected. In fact, the prevalence of infection is highest among household contacts. The virus disseminates so rapidly that by the time the first case is recognized in a family, all the susceptible family members can already be infected.[134]

Geographic Distribution

Poliovirus infection occurs worldwide, but there are some differences in seasonal patterns. It occurs year-round in the tropics, while in temperate zones it is most common during the summer and fall. This helps explain the fear in the United States of contracting polio from swimming pools.

Incidence

The virus affects all age groups, but children are more susceptible than adults because of their lack of acquired immunity. The case fatality rate is variable, but it is 5% to 10% higher in the older population.[134] There are three major epidemiological phases of poliovirus infection: endemic, epidemic, and vaccine-era.

In an endemic state, polioviruses are commonly present. New susceptibles, usually infants, provide a constant supply of individuals to maintain the infection cycle. Women of childbearing age typically possess antibodies to all three serotypes of poliovirus, and their newborns benefit from temporary passive immunity. It is estimated that in developing countries there were 20,000 to 25,000 cases of paralytic polio in 1997.[135]

At the turn of the century in the United States (the prevaccine era), there were periodic epidemics of polio. This was largely a result of the improvement in household hygiene and community standards of sanitation. Infants and young children were not being exposed as early to the polioviruses. When they did encounter the viruses, they were older and more likely to experience paralysis. The likelihood of epidemics increased because the number of susceptibles increased as the delay until exposure lengthened. In 1916, 80% of cases were in children younger than 5 years of age. From 1953 to 1954, the annual number of paralytic cases in the United States was approximately 21,000. The peak age incidence had risen to 5 to 9 years. One third of cases and two thirds of deaths were in individuals older than 15.[134]

Paralytic poliomyelitis became a notifiable disease in the United States in 1951. Case ascertainment methods have not changed since 1958, when the Centers for Disease Control and Prevention (then known as the Communicable Disease Center) began classifying cases of paralytic poliomyelitis according to criteria known as the "best available paralytic poliomyelitis case count" or BAPPCC. This count included only cases of poliomyelitis that caused permanent paralysis. These criteria omitted cases caused by enteroviruses other than polioviruses. Since 1975, cases have been classified according to criteria known as the "epidemiological classification of paralytic poliomyelitis cases" (ECPPC). This classification describes cases as epidemic, endemic, imported, or occurring in immunodeficient individuals.[136]

In the vaccine-era, polio has become a rare disease in the United States. Administration of live oral polio vaccine (OPV) has halted epidemics in progress and has greatly reduced the incidence of polio. Poliovirus vaccines have decreased by 99.9% the annual number of reported cases of paralytic polio in the United States—from 21,269 in 1954 to 6 in 1991.[137]

Recruits in basic training have been immunized against polio since the introduction of an effective vaccine in 1955. A 1989 national serosurvey of US Army recruits showed that poliovirus seronegativity rates were similar across demographic subgroups. When looking at seronegativity by birth cohort, it was apparent that seronegativity to type 3 poliovirus has not clearly lessened.[14]

The wild type of polio was officially declared eradicated from the Americas on September 29, 1994, by the International Commission for the Certification of Poliomyelitis Eradication in the Americas. The last confirmed case occurred on August 21, 1991 in Peru.[138] The few cases that occur now in the United States are related to the polio vaccine. A study[139] of cases occurring from 1973 through 1984 in the United States revealed 138 cases of paralytic poliomyelitis, of which 105 (76%) were associated with receipt of OPV. Thirty five of the cases occurred in individuals who had received OPV, 50 in contacts of OPV recipients, 14 in previously undiagnosed immunodeficient individuals, and 6 in those with no history of either receipt of OPV or contact with recent OPV recipients and were assumed to have had community contact with an OPV recipient.

An approximation is made of the frequency of paralytic polio by estimating ratios of vaccine-associated cases to net doses of OPV distributed. The overall ratio was found to be one case per 2.4 million to 2.6 million doses distributed, including cases in immunodeficient patients and cases in persons without a history of having received a recent vaccine.[130,139] Annual numbers of cases have been reduced to as few as 3 per 100 million resident population. In immunologically normal recipients, the risk of paralysis following OPV is 1 case per 6.2 million doses. The risk to close contacts of OPV recipients is 1 case per 7.6 million doses.[130]

Pathogenesis and Clinical Findings

The virus enters the alimentary tract and multiplies locally. It then appears in the throat and the stools. The virus is excreted in stools for several weeks and is present in the pharynx 1 to 2 weeks after infection. Secondary spread occurs through the bloodstream and reaches other tissues, to include the lymph nodes, brown fat, and the central nervous system (CNS).[134] The invasion of the CNS occurs several days after the virus has entered the bloodstream. By this time, antibody has already been produced and is detectable.

The incubation period is 7 to 14 days, but can range from 3 to 18 days or longer. If present, the symptoms are nonspecific at first and can include fever, malaise, headache, drowsiness, constipation, sore throat, nausea, and vomiting. This constellation of symptoms can present in any combination. Two basic patterns of illness exist: (1) a minor or abortive type and (2) a major type, which can be either paralytic or nonparalytic. Only 1% of infections result in paralysis. The paralytic-type pattern is demonstrated after several symptomless days with a reappearance of symptoms, such as reoccurrence of fever, meningeal irritation, and paralysis, 5 to 10 days later.[140] Acute flaccid paralysis, characteristic of poliomyelitis, results when there is multiplication of the virus within the CNS with subsequent destruction of motor neurons. In children younger than 5 years old, paralysis of one leg is most commonly seen, but in patients 5 to 15 years of age, weakness of one arm or paraplegia is frequent. Quadriplegia is most common in adults. About 1% of cases develop aseptic meningitis.[10p398–405]

Even many years after infection, there can be a reoccurrence of problems. Twenty-five percent of individuals who had paralytic polio in the 1940s and 1950s have had a recrudescence of paralysis and muscle wasting by the 1990s. This is referred to as post-polio syndrome and has been reported only in people who were infected during the time when wild-type poliovirus was in circulation. Patients may experience an exacerbation of their already existing weakness, or they may go on to develop new weakness or paralysis.[130] The late effects may be associated with the changes of aging and further loss of anterior horn cells, the neurons that have been depleted by an earlier poliovirus infection.[141] Alternatively, there is evidence to suggest that poliovirus can persist in postpolio patients.[142]

Diagnostic Approaches

Enteroviruses, such as poliovirus, are exceedingly common. Other enteroviruses can be found in stools of patients with symptoms resembling all but the most severe paralytic manifestations of polio. Cultures of human or monkey cells are used to recover and identify the polioviruses. Throat or rectal swabs can be used. Stool cultures yield the greatest likelihood for positive identification of the virus, but they must be collected in a timely fashion to increase the likelihood of case confirmation.[130] The virus can be found in 80% of patients during the first 2 weeks of illness. It is very difficult to isolate the virus from the cerebrospinal fluid. Neutralizing antibodies, which should be assessed for each of the three

polio serotypes, are formed early; paired serum specimens show a 4-fold rise in antibody titer after 3 weeks. Cases must be clinically and epidemiologically compatible with poliomyelitis, must have resulted in paralysis, and must have a residual neurological deficit 60 days after onset of initial symptoms.[136] If a child or a young adult has any asymmetric flaccid limb paralysis or bulbar palsies without sensory loss during a febrile illness, this almost always is indicative of poliomyelitis. However, the diagnosis of polio cannot be reliably diagnosed solely on the basis of clinical presentation.[143] In reality, the only reliable method of diagnosing polio is by isolation of the virus from the stool. It is not possible to definitely distinguish polio and Guillain-Barré syndrome purely on the basis of clinical findings, because polio may have an atypical presentation.[144] Guillain-Barré may progress for up to 4 weeks, but polio usually manifests the maximum extent of paralysis within 4 days.[145] The differential diagnosis of paralytic polio also includes tick paralysis, insecticide poisoning, botulism, trichinosis, transverse myelitis, and various neuropathies.

Recommendations for Therapy and Control

Historically, quarantine was the only method of control. It was imposed for 3 weeks after the occurrence of the last diagnosed case. In 1940, Dunham's *Military Preventive Medicine*[112] noted that chemical prophylaxis (an olfactory mucosal spray of 0.5% picric acid and 0.5% sodium alum in 0.85% saline solution) was believed to be useful, but it was never proved to be effective in preventing polio.

The first polio vaccine, an inactivated polio vaccine (IPV) was developed by Jonas Salk following the successful propagation of poliovirus in tissue cultures by Enders, Weller, and Robbins. Use of IPV dramatically reduced cases of paralytic polio, from 21,269 cases in 1952 to 980 in 1961.[146] Later Albert Sabin and fellow researchers introduced the live OPV. It has been considered one of the safest vaccines in use. The first large-scale production of OPV took place in the Soviet Union, when a mass immunization campaign in 1959 and 1960 covered 77.5 million people. This resulted in a sharp decrease in incidence, from 10.6 per 100,000 in 1958 to 0.43 per 100,000 in 1963.[134] Routine use of live oral attenuated poliomyelitis vaccines was begun in many countries during the spring of 1960. OPV became a routine vaccine for childhood immunization.[147] At that time, monovalent vaccines were used, incorporating each serotype separately. The trivalent vaccine, with its mixture of three serotypes of attenuated polioviruses, replaced this methodology in 1965 and has become the standard. Live OPV prevents paralytic polio by inducing two distinct types of antibodies: a local secretory antibody at the primary sites of virus multiplication in the alimentary tract and a humoral antibody, which prevents virus from reaching and invading the CNS. Vaccination effectively interrupts secondary spread of the virus to the CNS by induction of antibodies. Persistence of protection is clearly demonstrated by the great reductions in cases of polio in all areas of the world where OPV is used.

In 1973, the World Health Organization (WHO) established a Consultative Group on Poliomyelitis, which serves as the custodian of Sabin's attenuated vaccine strains. There are 16 manufacturers of vaccine around the world; two use human diploid cells for growing their vaccine viruses and 14 use African green monkey kidney cells. In 1978, an enhanced-potency IPV was developed and found to be more immunogenic for both children and adults than the previous formulation of IPV.[130]

Because the risk of polio has been eradicated in the Americas, the only polio cases occurring within the United States since 1979 are those secondary to receipt of the oral polio vaccine. To reduce the amount of vaccine-associated paralytic poliomyelitis (VAPP), the Advisory Committee on Immunization Practices (ACIP) changed the recommendations for polio vaccine in 1997. The recommended schedule consisted of IPV given at 2 and 4 months, followed by OPV at 12 to 18 months and 4 to 6 years. With the progression of the global polio eradication campaign, the likelihood of importing poliovirus into the United States decreased substantially. Because the sequential schedule was well accepted without any concurrent decline in childhood immunization coverage, the ACIP made new recommendations in June 1999 to go to an all-IPV schedule. This, all children should receive IPV at 2, 4, and 6 to 18 months at 4 to 6 years. Sole use of IPV in vaccination against polio carries no risk of VAPP or secondary transmission of the vaccine virus.[133]

The Global Poliomyelitis Eradication Initiative relies heavily on the use of OPV, one of the limitations of which is the need to preserve the cold chain to ensure its potency. OPV requires storage at temperatures of below 0°C (32°F). It should also not be administered to immunocompromised individuals because of their increased risk for VAPP, though the WHO does recommend its use in infants infected with human immunodeficiency virus who are subject to polio exposure. OPV is contraindicated for use in households with immunodeficient individu-

als, because the vaccine virus is excreted in the stool for 6 to 8 weeks and can infect the immunocompromised person. IPV is a better choice for those individuals. Other key elements of effective eradication of wild poliovirus are case detection and immediate action to eliminate foci of persistent infection with "mopping up" techniques. This involves administration of OPV to children on a house-to-house basis, then repeating the task 4 to 6 weeks later. Any child under the age of 5 years who has an acute flaccid paralysis for which no cause can be identified or any child who has a paralytic illness at any age can be considered suspected cases of polio. The WHO recommends that OPV be given concurrently with vaccines against diphtheria, tetanus, and pertussis at 6, 10, and 14 weeks of age.[147] In polio-endemic countries, an additional dose at birth is recommended.[69p465–470] It has been noted that in tropical climates seroconversion following three doses of OPV was often lower than in temperate climates. Mass administration of OPV led to a dramatic reduction in the incidence of polio in Brazil during 1980 and showed the role National Immunization Days can play in polio eradication. In spite of failed individual seroconversion, the wild poliovirus can still be eliminated with mass immunization strategies.[147]

As long as polio exists elsewhere, there will always be the risk of importation of the wild-type virus into the United States. Therefore, it is crucial not to become complacent about immunization, the only effective defense against polio.[134] Population immunity can be maintained by vaccinating children early in their first year of life.[130] At least 440,000 cases of paralytic polio have been prevented annually by the use of live OPV, according to WHO estimates.[134]

Because military personnel deploy to and live in areas of the world where polio is endemic, their risk of exposure is a real one. It is and will remain imperative to assure high levels of immunity in service members. Persons who have had a primary series of OPV or IPV and who will be exposed to polio, as might happen on military deployments, may as adults receive another booster dose of either OPV or IPV. Adults who have not previously been vaccinated with OPV should receive the IPV series prior to travel. The need for additional booster doses of either OPV or IPV has not yet been established.[130]

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