ELSEVIER

Mucocutaneous Manifestations of Viral Diseases in Children

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There are numerous types of viruses that manifest themselves as dermatologic disorders in children. Some of these affect the skin alone, but many of them are associated with or are even harbingers of serious systemic disease. This contribution discusses the most common viral conditions to affect the skin, as well as some that are less well known. Current treatments and preventive measures for many of these diseases are also considered.

There are several groups of viruses that produce mucocutaneous lesions in children: herpesviruses, papovaviruses, poxviruses, picornaviruses, and retroviruses. In addition, there are various other viruses that can have cutaneous manifestations, such as human parvovirus B19, rubella, rubeola, and hepatitis B and C, among others.[1] Finally, there are other dermatological disorders and exanthems thought to be viral in nature but that have yet to demonstrate a particular viral etiology.

All herpesviruses may have manifestations dermatologic: herpes simplex viruses 1 and 2 (HSV-1 and HSV-2, respectively); varicella zoster virus (VZV); Epstein-Barr virus; cytomegalovirus (CMV); and human herpesviruses 6, 7, and 8 (HHV-6, HHV-7, and HHV-8, respectively). Human papillomavirus (HPV) is a papovavirus that may affect children, especially if they are immunocompromised. Poxviruses, such as molluscum contagiosum (MC), milker's nodules, and orf, can also present in the pediatric population. Coxsackieviruses are the most common picornavirus infections that cause skin disorders in children. Finally, HIV is a retrovirus well known to cause not only cutaneous but also severe systemic disease and death in children. Fortunately, many of these disorders have good treatments, which, when they are recognized early, can significantly reduce morbidity and mortality. Some may be prevented through immunization with licensed vaccines (Table 1),[2] and others are the subjects of experimental preventive and therapeutic vaccination. There is still need, however, for ongoing study of those for which no good treatment or vaccine exists.

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Herpesvirus Infections

HSV-1 and HSV-2

HSV-1 and HSV-2 are enveloped DNA viruses well known to cause mucocutaneous vesicular eruptions in adults and children. HSV-1 is most commonly associated with orofacial herpes, whereas HSV-2 primarily causes anogenital herpes. Herpes labialis is generally transmitted to children through contact with infected oral secretions by way of family members or friends, regardless of whether they have active lesions. For HSV-1 and HSV-2, asymptomatic viral shedding, or subclinical disease, can be a significant source of transmission. Primary HSV-1 infection in children is usually asymptomatic, but in 25-30% of affected children it manifests as herpetic gingivostomatitis.[3] After infection, there is a 2- to 12-day incubation period before clinical symptoms appear. Symptoms include oral ulcers, fever, and feeding difficulties, and many develop extraoral lesions as well. In a study in Israel of 36 children with primary infection, 85% had oral lesions as opposed to 72% with extraoral lesions. Many times these oral lesions are extensive or painful enough to cause difficulties in eating and drinking, leading to complications such as dehydration and the need for hospitalization for intravenous (IV) hydration.[3] In a Thai study of mucocutaneous manifestations in 91 HIV-positive children, HSV stomatitis lesions exhibited typical characteristics but were more likely to become chronic and ulcerative.[4] Treatment, especially if the patient is hospitalized, includes IV acyclovir at 750 mg/m^2 divided into three doses of 5 mg/kg every 8 hours for 5 to 10 days, although recent data have shown that oral acyclovir, given 200 mg every 4 hours, 5 times daily for 7 to 10 days, can shorten the duration of the episode and of viral shedding. It is important to note, however, that antiviral therapy should be started immediately upon onset of symptoms and no later than 72 hours thereafter. Oral acyclovir use in children <2 years old has not been completely studied. For recurrent herpes labialis, studies have shown that treatment with topical or oral acyclovir is largely ineffective. Prophyl-

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Table 1. Recommended Childhood Immunization Schedule (2) - January-December 2000

Vaccine	*Recommended Regimen*	*Comments*	*Special Considerations**
Hepatitis B (Hep B)	(Infants of HBsAg - mothers) 1st dose- birth to 2 months		If infant with HBsAg + mother, 1st dose at birth along with 0.5 mL hepatitis B immune globulin (HBIG), 2nd dose at 1–2 months, and 3rd dose at 6 months
	2nd dose- 1 to 4 months	At least 1 month after 1st dose	
	3rd dose- 6 to 18 months	At least 4 months after 1st, 2 months after 2nd dose, and not before 6 months of age	If infant with mother of unknown HBsAg status, Hep B should be given at birth, and mother's HBsAg status determined; if positive, HBIG should be given to infant ASAP (no later than 1 week of age)
	11–12 years (Previously unvaccinated)	1st dose at any time, 2nd dose 1 month later, 3rd dose 6 months later	
Diptheria, Tetanus Toxoids and Pertussis (DTaP)	1st dose- 2 months 2nd dose- 4 months 3rd dose- 6 months		
	4th dose- 15–18 months	4th dose can be as early as 12 mos if at least 6 months from 3rd dose and if unlikely for child to return at 15–18 months	
	5th dose- 4–6 years		
	Booster(Td)-11–12 years	Given if at least 5 years since last DTaP, DTP, or DT	
	Booster(routine, Td)	Given every 10 years	
Haemophilus influenzae type b (Hib)	1st dose- 2 months		DTaP/Hib combination should not be used for primary vaccination at 2, 4, and 6 months
	2nd dose- 4 months		
	3rd dose- 6 months		3rd dose unnecessary if Hib conjugate used
	4th dose- 12 to 15 months		
Poliovirus (IPV)	1st dose- 2 months		Routine vaccination should always use IPV (completely inactivated poliovirus vaccine)
	2nd dose- 4 months		
	3rd dose- 6 to 18 months		OPV only in special circumstances
	4th dose- 4 to 6 years		
Measles-Mumps-Rubella (MMR)	1st dose- 12 to 15 months		
	2nd dose- 4 to 6 years	2nd dose may be given anytime 4 or more weeks after first dose and should be completed by age 11 to 12 years	
Varicella Virus (Var)	One dose on or after 1st birthday	For children with no reliable history of chicken pox, as judged by a healthcare provider	Now recommended by AAP for post-exposure prophylaxis in susceptible children (given to household contacts within 3 days of appearance of the rash in the index case)
		If >13 years when first dose given, should have 2 doses 4 weeks apart	
Hepatitis A	24 months - 11 to 12 years		Only in certain states and regions

Abbreviations used: HBsAg - hepatitis B surface antigen; Td - tetanus and diphtheria toxoids; DTP - diphtheria and tetanus toxoids and pertussis vaccine; DT - diphtheria and tetanus toxoids; OPV - oral polio vaccine; AAP - American Academy of Pediatrics.

** For the latest recommendation on all these vaccines, consult the CDC on the internet at www.cdc.gov/mmwr/.*

actic oral acyclovir, however, reduced the frequency of outbreaks by 50–78% when used in doses from 400 to 1000 mg/day.[1]

With the incidence of herpes genitalis increasing worldwide, it is expected that the incidence in younger age groups will rise as well. Regardless of the mode of transmission to children, the recognition and treatment of the condition in children are important, as is the education of the children and parents in prevention of transmission. Primary genital herpes may appear as

soon as 2 to 8 days after infection but because of latency of the virus may not manifest until months to years later. The virus enters the nerve endings underlying the primary infection and travels to the dorsal root ganglia, where it remains dormant. It then may reactivate at any time but usually does so in response to a stimulus, such as immunosuppression, illness, skin trauma, menses, ultraviolet light exposure, or physical or emotional stress. Such reactivation prompts the virus to travel back down the efferent nerve to any of its branches, causing recurrences in the same nerve distribution, but sometimes at different sites from the primary infection. In children, as in adults, vesicular eruptions appear, sometimes accompanied by systemic symptoms such as fatigue, fever, body aches, and regional lymphadenopathy, which usually resolve within 7 days. Healing of lesions occurs over about 10 days to 2 weeks. Oral acyclovir (200 mg five times a day or 400 mg three times a day, each for 10 days) significantly reduces the duration of acute infection and lesion healing in adults, but newer antivirals such as valacyclovir (1000 mg twice a day for 10 days) and famciclovir (250 mg three times a day for 10 days), although not extensively studied in patients <18 years old, can also do so with the advantage of less frequent dosing, potentially increasing compliance in the pediatric population. For recurrent genital herpes, treatment regimens differ, depending on the severity of symptoms and frequency of outbreaks. Patients with less frequent or less severe outbreaks may benefit from oral acyclovir (200 mg five times daily or 400 mg three times a day), but valacyclovir (500 mg twice a day) and famciclovir (125 mg twice a day) offer more convenient dosing. In these patients, episodic therapy is helpful when initiated during prodromal symptoms or immediately at the first onset of lesions and is continued for 5 days. Patients with more frequent (six or more per year) outbreaks may benefit from suppressive or prophylactic therapy, in which medication is taken at least daily for months to years. Oral acyclovir (400 mg twice a day) has reduced the frequency or severity of recurrences in >95% of patients. Valacyclovir (500 mg once daily) prevented or delayed 85% of outbreaks, when compared with placebo, with 69% recurrence-free after 16 weeks (compared with 9.5% in the placebo group). Famciclovir, used in single daily doses of 500 mg, achieves less complete suppression than when a 250-mg, twice-daily regimen is used. A concise summary of the most current therapeutic recommendations is found in a review written by Trizna and Tyring in 1998.[1]

Although HSV-1 and HSV-2 create significant therapeutic and social issues in children, they produce much greater morbidity and mortality in the neonate. Neonatal herpesvirus infections occur in 1 of 3500 deliveries and are associated with a high mortality rate, especially when HSV-2 is involved. Most neonatal infections occur by contact with genital tract secretions infected with HSV-1 and/or HSV-2. Other routes of infection include transplacental transmission, intrauterine infection, ascending infection from prolonged rupture of membranes and, after delivery, through other nongenital contact. About 2% of susceptible women acquire HSV infection, with seroconversion during pregnancy. If the infection and seroconversion are acquired before labor, the outcome is less likely to be affected. Infection acquired around the time of delivery, however, is much more serious, because it is much more likely to be disseminated.[1] In a study by Forgren et al., neonatal HSV infection due to primary maternal infection had a short incubation period and was more likely to be disseminated; in contrast, neonatal herpes due to recurrent maternal disease tended to have a longer incubation period and tended to localize to the central nervous system.[1,4] Skin or mucosal lesions are present in >70% of cases, and in 10%, the disease remains localized to the skin. Pneumonia and encephalitis are other frequent complications; rarely, the central nervous system and liver may be involved in the absence of skin lesions, creating difficulty with diagnosis. The skin lesions usually appear in 2 days to 2 weeks but may be present at birth if infection occurred before delivery. Lesions are more likely on the scalp and face or perianal area (depending on presentation) if acquired during delivery. Oral lesions are also common. Diagnostic measures include Tzanck smear, viral culture, nucleic acid hybridization techniques, and use of monoclonal antibodies. Monoclonal antibody testing provides a rapid and precise diagnosis, unlike viral culture, which can be slow and is only 60–90% sensitive, and the Tzanck smear, which, though quick, is only positive in 60% of culture-positive cases. Rapid diagnosis is key for immediate initiation of treatment to reduce mortality. Acyclovir (IV, 10 to 30 mg/kg/day in three divided doses for 7 to 10 days) is recommended for rapid improvement and may be continued for up to 21 days for encephalitis. Adenine arabinoside (1.5 mg/kg/day for 10 to 14 days) has been used alternatively. Oral acyclovir (300 mg/m^2 twice or three times daily) can prevent cutaneous recurrences in neonates with solely mucocutaneous involvement.[1,5] Other manifestations of HSV include herpes keratitis and keratoconjuctivitis, eczema herpeticum, herpetic whitlow, and herpes gladiatorum.

VZV

VZV is another herpesvirus responsible for much morbidity and mortality. Varicella is a highly contagious disease that infects >90% of children before 10 years of age.[6] In most children, it is mild and self-limited but has been estimated to have caused 100 deaths per year in children before the institution of the varicella vaccination.[6] The exanthem appears after a 14- to 16-day incubation period. The onset is marked by

general symptoms, in addition to 'teardrop' vesicles on an erythematous base, with lesions being present in all stages of development at the same time in one area. The eruption usually starts on the trunk, face, and scalp and spreads centripetally. The infected person is considered to be infectious for 1 to 2 days before rash onset and for up to 7 days afterward. Lasting immunity is normally conferred. Treatment with acyclovir (20 mg/kg four times daily for 5 to 7 days) starting within 2 days of rash onset has reduced the maximum number of lesions, shortened the mean time to 50% healing, and decreased the proportion of patients with fever by the second day of treatment, with no change in the antibody response.[1] Those who are more likely to benefit from acyclovir therapy are children with household exposure (tends to be more severe than community-acquired), immunocompromised children, newborns up to 2 weeks, preterm infants, pregnant women, anyone with severe varicella, anyone with shingles (especially ophthalmic zoster), and children with serious cardiopulmonary disease or chronic skin disorders.[1] Acyclovir should be given IV to patients with severe disease, those at risk for dissemination, and children <2 years of age. The recommended oral doses of acyclovir for children are 20 mg/kg four times daily for 5 days (for children <40 kg) or 800 mg four times a day for 5 days (for those >40 kg). In any case, early treatment with acyclovir is important to prevent the development of more severe disease.

Vaccination against varicella is now available for routine childhood immunization. Clinical trials have shown varicella vaccine to be 70–90% effective for preventing varicella and 95–100% effective in preventing severe disease. 'Breakthrough' disease occurs in about 1–4% of vaccines per year but is usually mild and with low-grade or no fever.[6,7] The recommended age for vaccination is children between 12 and 18 months, and vaccination of older children who have not had varicella is also recommended. If not previously vaccinated, the vaccine should be given at 11 to 12 years, in two doses 1 month apart (because adolescents respond differently to vaccinations than children). The vaccine has been demonstrated to be safe and effective in 109 infants as young as 9 months old. Infants younger than 6 months are usually protected from varicella by circulating maternal antibodies, but the protective effect of these waning antibodies >6 months of age is variable. Further studies are planned to evaluate the safety and effectiveness in 6-month-old infants.[8]

Recently, varicella vaccine was recommended for postexposure prophylaxis within 72 hours of onset in children >12 months of age. This will have an important impact on outbreak control and in preventing moderate to severe disease. In a Philadelphia homeless shelter, varicella vaccine was given to 67 residents, 42 of whom were children <13 years of age. The vaccine was given within 36 hours of exposure. No cases of moderate to severe disease ensued, and the shelter was able to reopen to new admissions in 6 weeks, as opposed to 6 months (which occurred at another homeless shelter that used standard infection control measures and no postexposure prophylaxis).[6,9]

Other new recommendations include vaccination of children with altered humoral immunity but not those with deficient cellular immunity, including leukemia, lymphoma, bone marrow or lymphatic malignancies, and congenital T-cell abnormalities. Some children with HIV may be vaccinated if they are in CDC class I (CD4+ T-cell percentage of 25% or more) with mild or no signs or symptoms.[7]

Like herpes simplex, varicella (after the primary infection) establishes a state of latency in the dorsal root ganglia of the spinal cord. Shingles, or herpes zoster, is a result of reactivation of VZV. Although much more common in adults, shingles can rarely occur in children and is usually easily treated with acyclovir, valacyclovir, or famciclovir, depending on age. The incidence of herpes zoster in children varies from 0.2 per 1000 in children <5 years of age to 0.6 in 1000 in adolescents 15 to 19 years of age.[4] Zoster was present in 4.4% of 91 HIV-positive children observed in Thailand.[4] VZV can lead to postherpetic neuralgia, which is a significant cause of morbidity in adults but is rare in children. Acyclovir (800 mg five times a day within 72 hours of rash onset, used for 7 days) has been shown in adults to reduce the incidence of residual pain at 6 months by 46% and shorten the time to lesion crusting, healing, and complete cessation of pain; it also reduced the duration of new lesion formation, reduced the duration of viral shedding, and reduced the prevalence of VZV-associated abnormal sensations. Valacyclovir (1g three times a day) and famciclovir (500 mg three times a day) have yielded similar results in terms of reducing the duration of postherpetic neuralgia, when administered during the first 72 hours of onset.[10] Varicella vaccine has been shown to cause VZV in immunocompetent and immunocompromised patients from 25 to 722 days after vaccination. The rate of VZV after immunization, however, is reported to be 2.6 per 100,000 vaccine doses distributed, whereas the incidence of VZV after natural varicella infection in healthy children <20 years old was 68 per 100,000 person-years. However, one must make comparisons with caution, because the rates after natural infection are taken from populations monitored for a much longer period than those after immunization. Wild-type VZV, however, has been identified in cases of shingles after immunization, suggesting that VZV in immunized people may result from preceding natural infection.[7]

EBV

Epstein-Barr virus infection, or infectious mononucleosis, is common in teenagers. Its clinical signs and

symptoms are well known and described. Treatment is largely symptomatic.

CMV

CMV is the primary infectious cause of fetal abnormalities in the United States. Primary infection during pregnancy causes a mononucleosis-like illness and rarely causes a rash. Infection transmitted transplacentally, however, is far more serious, causing spontaneous abortions and serious fetal abnormalities. Congenital CMV infection is clinically evident only 10% of the time by way of jaundice, petechiae, or purpura.[1] Cidofovir, fomivirsen, ganciclovir, and foscarnet are all FDA-approved for life- and sight-threatening CMV infections in immunocompromised patients.[1] Vaccine studies are ongoing. CMV is frequently an opportunistic infection in HIV-positive children, especially those with CD4+ lymphocyte counts $<50/mm^3$. Not only can it involve the retina, central nervous system, and gastrointestinal tract, but it can also form large ulcers on the palate or pharynx, similar to aphthous ulcers, and mimic HIV-related periodontal disease.[4]

HHV-6 and HHV-7

HHV-6 and HHV-7 infections can be silent or can manifest as mild, febrile illnesses such as roseola (also known as exanthema subitum). In the laboratory, HHV-6 and HHV-7 infect activated CD4+ T cells preferentially, and HHV-6 can also infect neural, epithelial, or fibroblast cells. HHV-6 can be found in human salivary glands, lymph nodes, kidney, brain, macrophages, and monocytes; HHV-7, in salivary glands, macrophages, and monocytes. In fact, HHV-6 and HHV-7 establish latency in the salivary gland, in peripheral blood mononuclear cells, and possibly in the genital tract; during primary infection, HHV-6 and HHV-7 are in high concentrations in peripheral blood mononuclear cells. Most adults shed both viruses in the saliva. Transmission of HHV-6 infection to infants occurs early in life (after 6 months, when maternal immunity wanes), with 50–60% of children seroconverting by 12 months and almost all seropositive by 2 to 3 years of age. HHV-7 lags behind, with >90% prevalence by 6 to 10 years. Saliva is considered the major source of transmission. Most infections in healthy children are primary ones; immunocompromised patients and adults may develop disease due to reactivation of latent virus. HHV-6 is the principal etiologic agent of roseola, which classically includes a high fever (101 to 106°F), which remits abruptly and is followed by a maculopapular rash. HHV-6 has also been associated with fever (without classic roseola), febrile seizures, encephalitis, and infections in transplant patients. HHV-7 can also be responsible for 10–31% of roseola-like illnesses and febrile seizures and has been reported to have a strong relationship with pityriasis rosea (although data from another center are contradictory). No specific therapy is usually necessary for most children who develop roseola because it almost always resolves without sequelae. Ganciclovir, foscarnet, and cidofovir, however, inhibit these viruses in the laboratory and could be used to treat more serious infections.[11]

HHV-8

HHV-8 has shown to be associated with Kaposi's sarcoma. Its clinical manifestations in children are rare.

Human Papillomavirus Infections

HPV infections occur in children, but the epidemiology and natural history of the infection in children are debated. Studies in adults indicate that anogenital HPV infection is sexually transmitted; in children, although it is known that transmission can certainly be through sexual abuse, it is also possibly acquired perinatally, through inoculation from nongenital warts during diapering or bathing, and indirectly by contaminated fomites. Clinically apparent genital warts are rare in children. In a study that compared rates of virologically demonstrated genital HPV infection in abused and nonabused children, however, HPV prevalence was much higher than in controls (33% vs. 0%, respectively). Other studies detected HPV DNA in <5% of abused children. A recent study by Stevens-Simon et al[12] indicated that in sexually abused 5- to 12-year-old girls, subclinical HPV infection is common, whereas genital warts and HPV infections apparent by colposcopy are not. They demonstrated that 16% of abused and none of the nonabused girls had subclinical infection.

Most warts are treated through cytodestructive methods such as excision, cryotherapy, electrosurgery, and laser vaporization or by topical agents such as acetic acid, salicylic acid, and cantharidin. Other chemotherapeutics have been used, such as 5-fluorouracil, podophyllin, podophyllotoxin, and bleomycin. Retinoids and cimetidine have also been used with varying success. Many of these methods succeed in removing the wart; none of them address the virus present in remaining cells. Immunomodulatory and antiviral agents, however, are being developed and used to address the latent viral infection. Interferon-alfa is approved only for condyloma acuminata. Imiquimod is approved for condyloma as well and appears to be safe and effective in children.

HPV vaccines, antisense oligonucleotides, and cidofovir are currently undergoing study for use in HPV infections. Current recommendations are for frequent monitoring of HPV infections by anoscopy, Pap smear, and colposcopy in adults. These practices are not currently indicated in children, because of the fact that only a small percentage of abused children have evidence of HPV, because HPV infection is subclinical, and because

other possible modes of transmission create enough uncertainty that HPV cannot be considered an abuse-defining sexually-transmitted disease.[12]

Poxvirus Infections

MC is a DNA virus that forms whitish, waxy papules with a characteristic central umbilication. Transmission in children is usually through fomites or autoinoculation. MC has been known to resolve spontaneously in healthy hosts but can become disseminated in HIV-positive patients, indicating advanced disease.[1] Many treatments have been used in adults and children, with varying success: cryotherapy, electrodesiccation, curettage, cantharidin, keratolytic agents, topical tretinoin, and 5-fluorouracil. It can be difficult, however, to get children to submit to or continue painful treatments. To date, there are no FDA-approved antivirals for the treatment of MC. Two cases of successful treatment with 3% topical cidofovir, used twice daily for up to 6 weeks, however, were recently reported.[13] Neither patient had any evidence of recurrence at 6-month follow-up. Cidofovir has been shown to produce prolonged remission with other viruses. Cidofovir is a deoxycytidine monophosphate analogue that, when phosphorylated to its active form, inhibits viral DNA polymerase (thus why it works for many DNA viruses). It is FDA-approved for IV use in AIDS patients with CMV retinitis, with the risk of nephrotoxicity. Safety and efficacy in children are unknown, but topical cidofovir has been shown in small numbers of immunocompromised patients to clear advanced lesions, with only local irritation. Studies of topical use of cidofovir are ongoing. A recent case report describes a pair of siblings with multiple, recalcitrant MC who were treated with oral cimetidine (40 mg/kg/day divided into three doses) for 2 months; the girl (who also had atopic dermatitis) experienced complete resolution, whereas the boy (who did not have atopic dermatitis) showed minimal improvement.[14] These findings were consistent with other studies that demonstrate better results in atopic children. Cimetidine is thought to inhibit suppressor cell function and enhance cell-mediated immunity. Additional studies are necessary to demonstrate safety and efficacy in children. Topical imiquimod, an immune-response modifier approved for use in genital warts, has been used for treatment of MC in adults and appears to work well in children.

Cutaneous manifestations of other poxviruses include milker's nodules and orf. Milker's nodules are rare in children and are usually acquired from bovine udders infected with paravaccinia (pseudocowpox) virus. Orf (otherwise known as ecthyma contagiosum) is a parapox infection of goats and sheep, with a short incubation period. Both infections form single or multiple nodules on forearms or hands, are self-limiting, and heal in 6 to 10 weeks. Excision of the lesions can decrease healing time and minimize complications.[1]

Coxsackievirus Infections

Hand-foot-and-mouth disease is a coxsackievirus infection that occurs in adults and children but tends to be more severe in children and infants. It has a 3- to 6-day incubation period and is characterized by fever and a vesicular eruption, which is self-limited. Treatment is symptomatic.[1]

Other Viral Infections

In healthy children ages 3 to 12, parvovirus B19 (fifth disease, or erythema infectiosum) causes a rash with a characteristic 'slapped-cheek' appearance and a marbled pattern on the arms and thighs. It is only mildly contagious and only during the first stage when general symptoms are present without rash. Treatment is symptomatic.[1] Although rubeola, rubella, and hepatitis B and C can demonstrate cutaneous findings in children, they have become much less common because of effective vaccines. Effective treatment also exists for hepatitis B and C, in the form of interferon-alfa, ribavirin, and lamivudine.

Retrovirus Infections

In a Thai study of 91 HIV-positive children <13 years of age, mucocutaneous manifestations were seen in 51.6%. The most common finding in these patients was oral thrush (36.3%). Drug rashes were seen in 6.6%, pruritic papular eruption in 5.5%, herpes zoster in 4.4%, cutaneous candidiasis in 4.4%, Penicillium marneffei infections in 3.3%, and HSV stomatitis in 2.2%.[3] Other viral infections that have been seen in HIV-positive individuals include parvovirus B19, measles, and hepatitis B and C. Parvovirus B19 can cause an exanthem in patients with HIV but more importantly can cause a persistent and sometimes fatal aplastic anemia. Measles can exhibit atypical-appearing exanthems associated with encephalitis and pneumonitis in addition to its more characteristic eruption. HIV patients with concomitant hepatitis B or C infections can develop lichen planus, porphyria cutanea tarda, or leukocytoclastic vasculitis.[15] A case of Sweet's syndrome in a 3-month-old infant was found to be the initial presentation of HIV infection. It causes multiple, painful, erythematous or violaceous nodules or plaques, as well as fever, leukocytosis, and a dermal infiltrate of neutrophils. The etiology of Sweet's syndrome in unknown but is thought to be the result of a hypersensitivity reaction to a bacterial, viral, or tumor antigen.[16]

Conclusions

Although safe and effective treatments do exist for many viral diseases with cutaneous manifestations, many of these medications have not been tested in children. Fortunately, vaccines exist for many of the viral infections that involve the skin in the pediatric population, preventing much morbidity and mortality. It is fully evident, however, that ongoing research is necessary to find effective treatment or prophylaxis for many other viral diseases and to ensure they are safe to use in children.

References

1. Trizna Z, Tyring SK. Antiviral treatment of diseases in pediatric dermatology. Dermatol Clin 1998;16:539–52.
2. Recommended childhood immunization schedule: United States, January–December 2000. JAMA 2000;283:1561–2.
3. Amir J, Harel L, Smetana Z, Varsano I. The natural history of primary herpes simplex type 1 gingivostomatitis in children. Pediatr Dermatol 1999;16:259–63.
4. Wananukul S, Thisyakorn U. Mucocutaneous manifestations of HIV infection in 91 children born to HIV-seropositive women. Pediatr Dermatol 1999;16:359–63.
5. Dahr S, Dhar S. Disseminated neonatal herpes simplex: a rare entity. Pediatr Dermatol 2000;17:330–2.
6. Black S, Shinefield H, Ray P, et al. Postmarketing evaluation of the safety and effectiveness of varicella vaccine. Pediatr Infect Dis J 1999;18:1041–6.
7. American Academy of Pediatrics, Committee on Infectious Diseases. Varicella vaccine update. Pediatrics 2000;105:136–41.
8. Kanra G, Ceyhan M, Ozmert E. Postexposure varicella vaccination in nine-month-old children. Pediatr Infect Dis J 2000;19:1029–30.
9. Watson B, Seward J, Yang A, et al. Postexposure effectiveness of varicella vaccine. Pediatrics 2000;105:84–8.
10. Tyring SK, Beutner KR, Tucker B, et al. Antiviral therapy for herpes zoster: randomized, controlled clinical trial of valacyclovir and famciclovir therapy in immunocompetent patients 50 years and older. Arch Fam Med 2000;9: 863–9.
11. Leach CT. Human herpesvirus-6 and -7 infections in children: agents of roseola and other syndromes. Curr Opin Pediatr, 2000;12:269–74.
12. Stevens-Simon C, Nelligan D, Breese P, et al. The prevalence of genital human papillomavirus infections in abused and nonabused preadolescent girls. Pediatrics 2000;106:645–9.
13. Zabawski EJ, Jr, Cockerell CJ. Topical cidofovir for molluscum contagiosum in children. Pediatr Dermatol 1999; 16:414–5.
14. Yashar, SS, Shamiri B. Oral cimetidine treatment of molluscum contagiosum. Pediatr Dermatol 1999;16:493.
15. Yen-Moore A, Vander Straten M, Carrasco D, et al. Cutaneous viral infections in HIV-infected individuals. Clin Dermatol 2000;18:423–32.
16. Brady RC, Morris J, Connelly BL. Sweet's syndrome as an initial manifestation of pediatric human immunodeficiency virus infection. Pediatrics 1999;104:1142–4.

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