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**Economics and Prevention
of Herpes Zoster**

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ECONOMICS AND PREVENTION OF HERPES ZOSTER

Target Audience

This monograph is intended for medical directors, physician executives, nurse case managers and other healthcare professionals interested in herpes zoster.

This activity is supported by an educational grant from Merck & Co.

Statement of Need

Herpes zoster affects millions of older adults annually and causes significant suffering from acute and chronic pain. Herpes zoster is caused by the reactivation of varicella-zoster virus along nerve tracts in the setting of age, disease, and medication-related decline in cellular immunity. Virus-induced neuronal destruction and inflammation cause the pain, interference with activities of daily living, and reduced quality of life. Optimal treatment of herpes zoster requires early antiviral therapy and pain management. For post-herpetic neuralgia, evidence-based pharmacotherapy can reduce but not eliminate pain burden. The zoster vaccine is effective in reducing pain burden and preventing herpes zoster and post-herpetic neuralgia in older adults.

With an aging population, the costs and related quality of life for patients are huge impacts on our society. The benefit of available vaccinations to patients and managed care can provide a higher quality of life and has potential cost savings.

Learning Objectives

- Review the epidemiology of herpes zoster
- Identify patients at risk for herpes zoster
- Recognize complications of herpes zoster
- Discuss costs and benefits of vaccination in an aging population

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The National Association of Managed Care Physicians (NAMCP) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education to physicians.

NAMCP designates this activity for a maximum of 1 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

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Author

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Disclosure

Dr. Briggs has no financial relationships that result in a real or potential conflict of interest.

NAMCP planning committee members have no financial relationships that result in a real or potential conflict of interest.

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To receive continuing education credits for this activity, participants must read the monograph, complete the post test and submit an activity evaluation. A passing score of 70% must be achieved on the post test. Certificates of credit will be sent to the address on the evaluation form within six weeks of receipt.

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Release and Expiration Dates

The release date of this activity is November 1, 2007. CME/CEU Credit is available through November 1, 2008. Post tests postmarked after November 1, 2008 will not be considered for continuing education credits.

Economics and Prevention of Herpes Zoster

Summary

Herpes zoster affects millions of older adults annually and causes significant suffering from acute and chronic pain. Herpes zoster is caused by the reactivation of varicella-zoster virus along nerve tracts in the setting of age, disease, and medication-related decline in cellular immunity. Virus-induced neuronal destruction and inflammation cause pain, interference with activities of daily living, and reduced quality of life. Optimal treatment of herpes zoster requires early antiviral therapy and pain management. For post-herpetic neuralgia, evidence-based pharmacotherapy can reduce but not eliminate pain burden. The zoster vaccine is effective in reducing pain burden and preventing herpes zoster and post-herpetic neuralgia in older adults.

HERPES ZOSTER, OR SHINGLES, IS CAUSED by the same virus that causes chickenpox—varicella-zoster.¹ After an episode of chickenpox, the virus remains dormant in the body. Herpes zoster occurs as a result of the virus re-emerging after many years. Many individuals, particularly those born before 1995 when widespread chickenpox vaccination began, have been infected with this virus.

Herpes zoster is an acute, localized infection with varicella-zoster virus, which causes a painful, blistering rash.¹ After a varicella infection, the virus migrates along sensory nerve fibers to the satellite cells of dorsal root ganglia of the spinal cord where it becomes dormant. This dormancy may be permanent, or the virus may become reactivated by conditions of decreased cellular immunity.

When it is reactivated, it spreads out along a nerve tract, first causing pain or a burning sensation (prodrome). The typical blistering rash (Exhibit 1) usually appears within 2–3 days of pain onset. Lesions usually appear along a single dermatome (the body area served by a single spinal nerve) and are on only one side of the body. The trunk is most often affected with a rectangular belt of rash from the spine around one side of the chest to the sternum. The pain and rash may also appear on the neck or face, particularly along the three branches of the trigeminal nerve. This nerve innervates the forehead, mid-face, and lower face. Lesions in the mouth or eye can occur with trigeminal nerve involvement.

Although zoster usually appears along one dermatome, widespread outbreaks can occur. It is uncommon for a patient to develop herpes zoster more than once, suggesting that the first reactivation of varicel-

la-zoster virus usually provides future immunologic protection.² Widespread or recurrent outbreaks may indicate an underlying problem with the immune system such as leukemia, Hodgkin's disease and other cancers, atopic dermatitis, human immunodeficiency virus (HIV) infection, or acquired immunodeficiency syndrome (AIDS).³

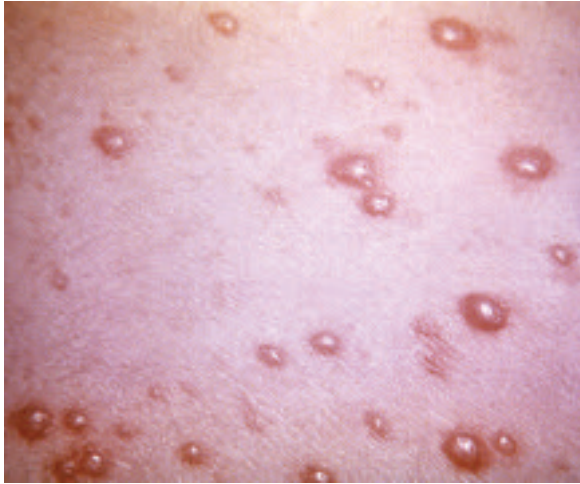
Prevalence

The disorder is common, with about 1 million cases in the U.S. per year.³ In adults of all ages, 1.2 to 4.8 cases per 1000 persons occur yearly.⁴ In adults 60 years of age and older, prevalence rates of 7.2 to 11.8 cases per 1000 persons per year have been reported.^{5–7} The rate in older adults may be even higher than this.

In 2004, the Centers for Disease Control conducted a national random-digit dial telephone survey of older adults (65) to obtain information on self-reported herpes zoster, demographic characteristics, and exposure to children with chickenpox in the past decade.⁸ In this survey, the incidence rate of self-reported zoster was 19 per 1,000 persons per year. In the surveyed population, previous exposure to children with chickenpox did not protect against zoster. Seven percent of adults 65 years of age and older reported an exposure to children with chickenpox in the past decade. The authors concluded that the incidence of zoster among individuals 65 and older in the U.S. might be higher than previously described in the literature.

The lifetime risk of herpes zoster is estimated at 10–30 percent.^{3,9} Fifty percent of individuals living until 85 years of age will ultimately develop herpes zoster.¹⁰

Exhibit 1: Typical Rash of Herpes Zoster



Risk Factors for Herpes Zoster

The cause of virus reactivation is usually unknown, but seems to be linked to aging, stress, or an impaired immune system. The most prominent risk factors are cellular immunosuppression and age. Patients with HIV, hematological malignancies, organ and tissue transplant patients who are undergoing immunosuppressive therapy, and patients receiving other immunosuppressive treatments such as chemotherapy, radiation therapy, and high dose corticosteroids are at high risk for developing this condition.^{4,5} The incidence of herpes zoster increases sharply with advancing age, roughly doubling in each decade past the age of 50 years (Exhibit 2).⁶ Herpes zoster is uncommon in persons less than 15 years old. In one study, patients more than 55 years of age accounted

for more than 30 percent of herpes zoster cases despite representing only 8 percent of the study population.⁷ In this same study, children less than 14 years old represented only 5 percent of herpes zoster cases.⁷ As the baby boom generation ages and life expectancy increases, the absolute number of herpes zoster cases will likely increase.^{4,5}

Race may influence susceptibility to herpes zoster. Blacks are one-fourth as likely as whites to develop this condition.¹¹ In one survey, Caucasian individuals were 3.5 times more likely to report shingles than Hispanic individuals.⁸

Consequences of Herpes Zoster

The common complications of herpes zoster include acute neuralgia, post-herpetic neuralgia, ocular complications of ophthalmic zoster, scarring, and bacterial superinfection.³ Less common complications include cutaneous dissemination, herpes gangrenosum, pneumonitis, hepatitis, encephalitis, motor neuropathies, myelitis, and hemiparesis secondary to granulomatous CNS vasculitis.^{1,3,5}

Acute herpes zoster causes significant morbidity. In a prospective study of herpes zoster pain and its relationship to physical, role, social, and emotional functioning, 72 percent of patients 50 years and older reported a pain burden.⁹ Greater pain burden was associated with poorer physical functioning, increased emotional distress, and decreased role and social functioning. Forty-two percent of patients reported that acute zoster pain was “horrible” or “excruciating”. This pain had interfered “quite a bit” or “extremely” with physical (14.6 percent), role (21.8 percent), and social functioning (26.3 percent) of the patients surveyed. Acute herpes zoster causes a

Exhibit 2: Incidence of Herpes Zoster

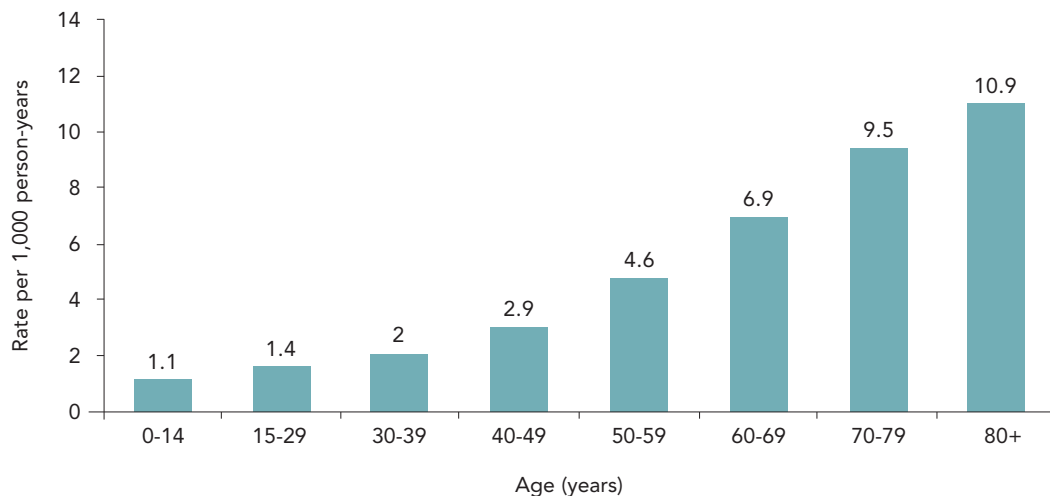
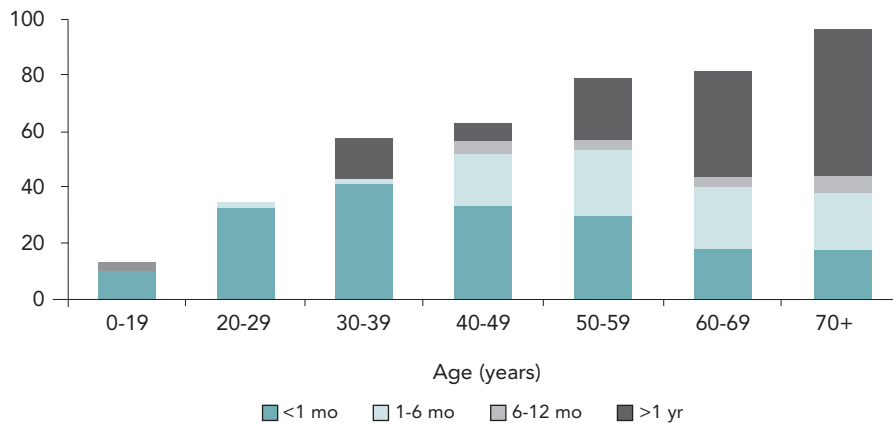


Exhibit 3: Prevalence of Post-herpetic Neuralgia and Duration of Pain



change in quality of life similar to or greater than many chronic diseases such as diabetes.^{12,13} In a large case series, insomnia (25 percent) and feeling helpless and depressed (20 percent) were common problems related to herpes zoster pain.¹³

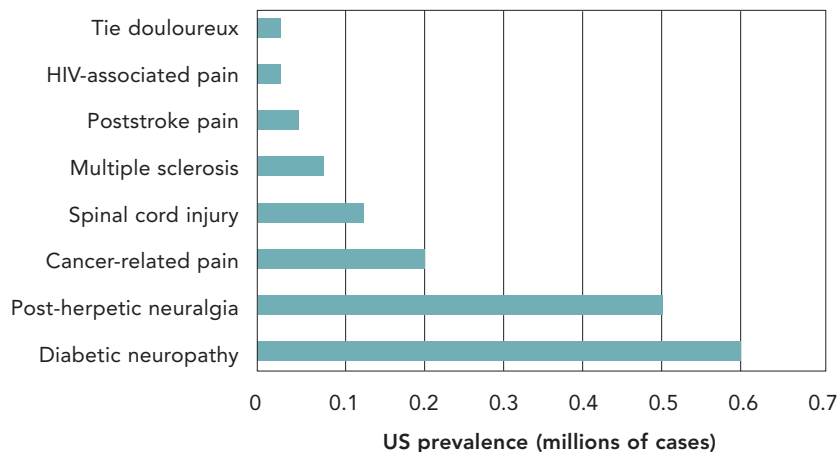
Herpes zoster may be complicated by post-herpetic neuralgia. This is persistence of pain greater than 90 days after rash resolution in the area where the outbreak occurred.¹⁴ This pain can be severe enough to be incapacitating and may last from months to years following the initial episode. The pain may be constant, intermittent, and/or stimulus-evoked such as allodynia. Allodynia is severe pain after a non-painful stimulus such as clothing touching the skin or wind on the face. Many patients also experience distracting tingling and severe itching, which has been called postherpetic itch. Sensory loss, which can cause functional problems such as difficulty walking, can also occur. Though the pathophysiology of post-

herpetic neuralgia is unclear, studies suggest peripheral and central demyelination, as well as neuronal destruction, are involved.

Increasing age is the most powerful risk factor for development of post-herpetic neuralgia.¹⁵ As illustrated in Exhibit 3, the prevalence of post-herpetic neuralgia and the duration of pain associated with this condition increase with increasing age.¹⁴ Other risk factors for post-herpetic neuralgia include severity of the acute pain, severity of the acute rash, presence of a painful prodrome, and female gender.¹⁶

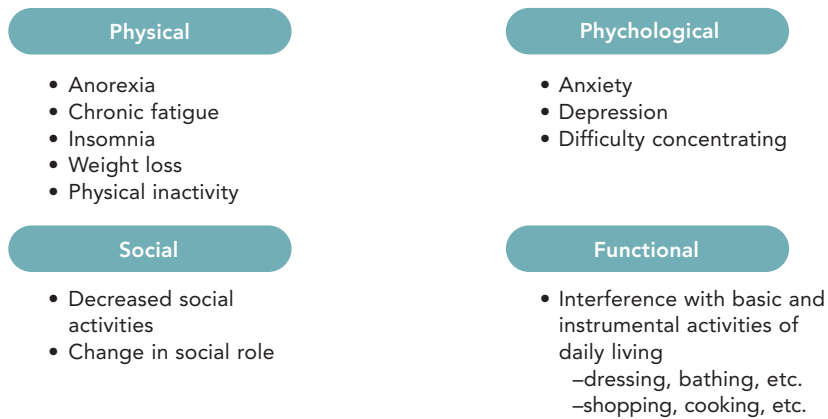
Post-herpetic neuralgia is a common source of neuropathic pain in the U.S. (Exhibit 4).¹⁷ It also causes significant decreases in quality of life.^{18,19} In one pain clinic, 59 percent of post-herpetic neuralgia patients were prevented from pursuing their usual activities for up to 16 years, with the average being 1.4 years.²⁰ Post-herpetic neuralgia has significant effects on the lives of older patients and impacts

Figure 4: Sources of Neuropathic Pain



Reference 16

Figure 5: Impact of Post-herpetic Neuralgia on Quality of Life in Older Adults



Reference 21

physical, social, functional, and psychological aspects of life (Exhibit 5).²¹

About 15 percent of zoster cases involve the ophthalmic division of the trigeminal nerve.²² Keratitis, conjunctivitis, scleritis, iritis, anterior uveitis, and retinitis can occur. Without antiviral therapy, 50-70 percent of patients with ophthalmic herpes zoster develop ocular complications.²³ This can result in chronic ocular complications and reduced vision, even blindness. Another consequence of trigeminal nerve involvement is Ramsay Hunt syndrome with facial paralysis, hearing loss, loss of taste in half of the tongue, and skin lesions around the ear and ear canal.¹

Another potential consequence of herpes zoster is transmission of the varicella-zoster virus to the non-immune. If an adult or child is exposed to the herpes zoster virus and has not had chickenpox or received the chickenpox vaccine, a severe case of chickenpox may develop. Household transmission rates have been noted to be approximately 15 percent.²⁴

Treatment of Herpes Zoster

The treatment of herpes zoster has three major objectives: (1) treatment of the acute viral infection, (2) treatment of the acute pain, and (3) prevention of post-herpetic neuralgia.² Antiviral agents, oral corticosteroids, and adjunctive individualized pain-management modalities are used to achieve these objectives.

Herpes zoster is usually treated with orally administered antivirals—acyclovir (Zovirax®), famciclovir (Famvir®), and valacyclovir (Valtrex®). Antiviral agents have been shown to decrease the duration of herpes zoster rash and the severity of pain associated with the rash.²⁵ However, these benefits have been demonstrated only in patients who received antiviral agents within 72 hours after the onset of a rash.² Antiviral agents may be somewhat beneficial as long as new lesions are actively being formed, but they are unlikely to be helpful after lesions have crusted. The effectiveness of antiviral agents in preventing post-herpetic neuralgia is more controver-

Figure 6: Estimates of Herpes Zoster Patients Over 50 with Pain after Rash Onset

| Days After Rash Onset | Percentage of Patients with Pain | |
|-----------------------|----------------------------------|-----------|
| | Placebo | Antiviral |
| 30 | 68 | 49-57 |
| 60 | 60 | 50 |
| 90 | 55 | 25-35 |
| 120 | 46 | 29 |
| 150 | 42 | 26 |
| 180 | 40 | 15-26 |

Data from major antiviral trials. References: 34-37

sial. Numerous studies evaluating this issue have been conducted, but the results have been variable. Based on the findings of multiple studies, acyclovir appears to produce a moderate reduction in the development of post-herpetic neuralgia.²⁶ Valacyclovir and famciclovir appear to be at least as effective as acyclovir.²⁷⁻³³ Unfortunately, even when treated with antivirals, a significant portion of patients develop post-herpetic neuralgia (Exhibit 6).³⁴⁻³⁷ Fifteen to 35 percent of patients will still have pain greater than 90 days after rash onset.

Orally administered corticosteroids are commonly used in the treatment of herpes zoster, even though clinical trials have shown variable results. Prednisone used in conjunction with acyclovir has been shown to reduce the pain associated with herpes zoster.³⁸ The likely mechanism involves decreasing the degree of neuritis caused by active infection and, possibly, decreasing residual damage to affected nerves.² Corticosteroids do not appear to be effective in preventing post-herpetic neuralgia.³⁸⁻⁴¹ Additionally, corticosteroids can cause significant adverse effects in the very elderly and their use in older adults for this indication is not routinely recommended.⁴²

The pain associated with herpes zoster ranges from mild to excruciating. Patients with mild to moderate pain may respond to over-the-counter analgesics. Patients with more severe pain may require the addition of a narcotic medication. When analgesics are used, with or without a narcotic, a regular dosing schedule results in better pain control and less anxiety than “as-needed” dosing.^{2,42} Capsaicin cream (Zostrix[®]), topical lidocaine patches, topical anti-inflammatory agents, and nerve blocks also have been used with some success to manage the acute pain of herpes zoster.

Treatment of Post-Herpetic Neuralgia

Multiple medications reduce the pain associated with post-herpetic neuralgia. These include tricyclic antidepressants, gabapentin (Neurontin[®]), pregabalin (Lyrica[®]), opioids, topical lidocaine, and capsaicin. Evidence-based pharmacotherapy would suggest that nortriptyline, desipramine, pregabalin, and gabapentin are the agents with the best evidence for efficacy.^{2,43-47} For intractable pain, nerve blocks, intrathecal corticosteroids, and surgeries also have been tried.

Although various therapies may help reduce pain, they have been associated with disappointing results with up to 50 percent of patients failing to receive acceptable pain relief.⁴⁶ Therefore, it is likely that the most effective future “treatment” for post-herpetic will be prevention of varicella-zoster infection through mass immunization against varicella and herpes zoster.

Herpes Zoster Vaccination

Herpes zoster vaccine (Zostavax[®]) is the first vaccine approved for the prevention of herpes zoster.⁴⁸ The FDA approved the vaccine in May 2006 for adults aged 60 years or older. This vaccine contains live, attenuated varicella-zoster virus in an amount that is approximately 14 times greater than that found in the varicella virus vaccine (Varivax[®]) indicated for chickenpox prevention.⁴⁹

A physiologic decline in varicella-zoster virus cell-mediated immunity occurs as people with prior infection age. Cell-mediated immunity is restored on administration of live-attenuated varicella vaccine. Various studies report serum anti-virus antibody concentrations and production of interferon-gamma were increased following vaccination.⁵⁰

The efficacy of the herpes zoster vaccine was demonstrated in the Shingles Prevention Study.^{51,52} This study enrolled 38,546 adults 60 years of age or older who had no history of herpes zoster in a randomized, double-blind, placebo-controlled trial of the vaccine. Subjects received either a single dose of zoster vaccine (n=19,270) or placebo (n=19,276). Subjects in this study were under surveillance for herpes zoster a median of 3.12 years.

Results of the Shingles Prevention Study demonstrated that in older individuals, administration of zoster vaccine reduces the burden of illness associated with herpes zoster by 61.1 percent, the frequency of herpes zoster pain and discomfort by 51.3 percent, and the frequency of post-herpetic neuralgia by 66.5 percent.⁵¹ The herpes zoster vaccine decreased the occurrence of herpes zoster by approximately 50 percent, with 3.3 percent of unvaccinated persons developing herpes zoster compared with 1.6 percent of vaccinated persons.⁵¹ Vaccination prevented post-herpetic neuralgia in 66.5 percent of persons receiving the vaccine, although the absolute number of cases occurring were small (approximately 0.4 percent of unvaccinated persons versus 0.14 percent of vaccinated persons).⁵² Vaccine efficacy for the prevention of herpes zoster was highest for those subjects 60-69 years of age and declined with increasing age.⁴⁸ The efficacy decreased to 18 percent for persons 80 years and older, although this small benefit may be particularly important because the oldest group is probably the most vulnerable to herpes zoster and its sequelae.⁵³

The Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP) recently recommended universal vaccination for those 60 years of age and older, including those who have experienced previous episodes of herpes zoster.⁵⁴ Although the vaccine has not been studied in persons with a history of herpes zoster, the ACIP voted to recommend its use in such patients, thus

making screening for eligible patients simpler. This vaccine has not been studied in persons younger than 60 years. The duration of protective effects of herpes zoster vaccine has not been determined; current studies show that protection lasts at least four years.^{48,52}

Vaccine Safety

The overall safety of herpes zoster vaccine has been demonstrated in studies involving >20,000 vaccine administrations.^{51,55} There appears to be no increased risk of varicella-like or zoster-like rashes with this vaccine. Two cases of varicella-like rashes that contained the virus strain included in the vaccine have been reported, so the potential for such reactions cannot be ruled out.⁵²

The vaccine was safe in the Shingles Prevention Study population, with little differentiation from the safety profile of placebo other than an increased risk for reactions at the injection site. Approximately one third of patients receiving the vaccine will experience erythema, pain, or tenderness at the injection site.⁴⁸ Rates of serious adverse events, systemic adverse events, hospitalization, and death were low and similar to those observed in the group that received placebo.⁵⁶ Overall, adverse events reported in clinical trials of zoster vaccine live were classified as mild.^{51,55}

Herpes zoster vaccine should not be used in patients who are immunosuppressed, including those with HIV or taking immunosuppressive doses of corticosteroids. No instances involving the transmission of herpes zoster virus to close contacts of vaccine recipients occurred in clinical trials. However, based on experience with the varicella virus vaccine, such episodes may be possible.

Concerns

Some practitioners have questioned why the already approved lower potency varicella vaccine given to children could not be used to prevent herpes zoster. A higher potency vaccine may be necessary to boost the immune response in older patients sufficiently to prevent zoster.² There are no data to suggest that the licensed varicella vaccine would be efficacious in protecting older adults from herpes zoster or post-herpetic neuralgia.

Exposure to varicella zoster virus through close contact with people with chickenpox has been suggested to boost immunity in adults, reducing the risk of herpes zoster. Since the introduction of the varicella immunization program in the U.S. in 1995, varicella incidence has decreased substantially.⁵⁷ Based on the CDC phone survey discussed earlier, the potential contribution of exposure to chickenpox as a mechanism for maintaining cell-mediated immunity against zoster may

be limited to a small percentage of the population.⁸ Vaccination against zoster may represent the best means of boosting cellular immunity.

It is unknown if widespread varicella vaccination in childhood will impact rates of herpes zoster, because the varicella vaccine is a live viral strain that becomes dormant in the dorsal root similar to wild-type varicella. Additionally, though rare and usually reported thus far in immunocompromised hosts, the childhood vaccine strain of the virus can recur as zoster later in life.⁵⁸ Multiple studies and surveillance data demonstrate no consistent trends in herpes zoster incidence in the United States since implementation of the varicella vaccination program in 1995.⁵⁹

Economic Issues

Herpes zoster is costly to treat in terms of both medical and societal costs. To analyze the cost of treating acute herpes zoster from a payer perspective, Insinga and colleagues utilized data from a healthcare claims database.⁶⁰ The acute phase of herpes zoster was estimated to result in an average additional 1.7 physician and hospital outpatient visits, 0.05 emergency room visits, 0.03 inpatient hospital admissions, 2.1 prescriptions filled, and \$431 in healthcare costs per patient. The average estimated incremental costs per patient with acute disease increased with age, ranging from \$258 among patients aged 19 years and younger to \$805 among those older than 80. The numbers of additional outpatient visits, inpatient admissions, prescriptions filled for pain medications and coded complications were also substantially higher among older with acute herpes zoster. Another cost analysis of acute herpes zoster found medical costs were highest in those aged over 65 and societal costs highest in those under 65 years.⁶¹

Development of post-herpetic neuralgia also adds significantly to the cost of treating herpes zoster. In a retrospective cohort analysis of Medicare, commercial insurance, and Medicaid claims databases, healthcare costs associated with post-herpetic neuralgia were substantially greater than those associated with herpes zoster pain that resolved within 30 days.⁶² Based on United Kingdom data, the lifetime costs of treating post-herpetic neuralgia have been estimated to be between 4.8 million and 17.9 million British pounds.²⁰

Since the target age group for this vaccine is greater than 60 years old, a discussion of Medicare vaccine coverage is important. Currently Medicare Part B does not cover the herpes zoster vaccine. Part B does cover influenza, pneumococcal, and hepatitis B vaccination and covers the administration of other vaccines covered by Part D plans. Medicare Part D allows for compensation of all non-Part B vaccines

through its contracted prescription drug plan (PDP) sponsors.⁶³ To facilitate greater access to Part D vaccines, CMS has directed that starting in 2008 all Part D plans' formularies must contain all commercially available vaccines (unless excluded due to available reimbursement under Part B).⁶⁴ The Tax Relief and Health Care Act of 2006 mandated coverage for administration of Part D vaccines under Medicare Part B in 2007. However, this same law mandated that payment for the administration of Part D vaccines be covered under Part D in 2008 and beyond. It is unclear at this point how physicians will bill and receive payment from Part D prescription drug plans for the administration of Part D vaccines after 2007.⁶⁵

Because of the possibility for use in a broad population (more than 49 million U.S. adults are ≥ 60 years of age) and higher cost than most other vaccines used in the adult population, cost-effectiveness evaluations of the herpes zoster vaccine have been performed.⁶⁶⁻⁶⁸ At the time two of the published cost analyses were performed, the vaccine was not commercially available; therefore, actual cost was not yet known. The vaccine costs approximately \$183 (average wholesale cost) plus administration costs (average Medicare reimbursement of \$19.33).^{65,69} Additionally, these cost analyses have used data from the Shingles Protection Study and epidemiologic studies of prevalence and morbidity. Because the vaccine is new, prospective cost data have not yet been published.

Hornberger and colleagues used a decision theoretical model to assess the extent to which clinical and cost variables influence the cost-effectiveness of vaccination for preventing herpes zoster in immunocompetent older adults from a U.S. societal perspective.⁶⁶ They used published herpes zoster rates and vaccine effectiveness from the Shingles Protection Study. By reducing incidence and severity of herpes zoster, vaccination can increase quality-adjusted survival by 0.6 days compared with no vaccination. Vaccination costs less than \$100,000 per quality-adjusted life-year (QALY) gained when 1) the unit cost of vaccination is less than \$200, 2) the age at vaccination is less than 70 years, and 3) the duration of vaccine efficacy is more than 30 years. As noted previously, the duration of vaccine efficacy is not known at this time. Sensitivity analysis found that vaccination would be more cost-effective in "younger" older adults (age 60 to 64 years) than in "older" older adults (age $>$ or $= 80$ years). Longer life expectancy and a higher level of vaccine efficacy offset a lower risk for herpes zoster in the younger group. Other factors influencing cost-effectiveness included quality-of-life adjustments for acute zoster, unit cost of the vaccine, risk for herpes zoster, and duration of vaccine efficacy. These authors concluded that using

the zoster virus vaccination to prevent herpes zoster in older adults would increase QALYs compared with no vaccination. They also noted that resolution of uncertainties about the average quality-of-life effects of acute zoster and the duration of vaccine efficacy are needed to better determine the cost-effectiveness of zoster vaccination in older adults. An editorial accompanying this analysis noted that several variables such as the value of averted pain are not known with certainty and were not included or were estimated.⁵³ This analysis used a human capital approach to place a monetary value on time spent at less than full health. By only valuing work productivity time, the authors did not capture the value of leisure time, which is so important in the target population that is mostly retired.⁵³

Rothberg and colleagues constructed a cost-effectiveness model, based on the Shingles Prevention Study, to compare varicella zoster vaccination with usual care for healthy adults aged >60 years.⁶⁷ Outcomes included cost in 2005 U.S. dollars and quality-adjusted life expectancy. In this analysis, compared with usual care, vaccination increased quality-adjusted life expectancy by 0.0007-0.0024 quality-adjusted life years per person, depending on the age at vaccination and gender. These increases came almost exclusively as a result of prevention of acute pain associated with herpes zoster and post-herpetic neuralgia. Vaccination also increased costs by \$94-\$135 per person, compared with no vaccination. The incremental cost-effectiveness ranged from \$44,000 per quality-adjusted life year saved for a 70-year-old woman to \$191,000 per quality-adjusted life year saved for an 80-year-old man. For the sensitivity analysis, the decision was most sensitive to vaccine cost. Other variables related to the vaccine (duration, efficacy, and adverse effects), post-herpetic neuralgia (incidence, duration, and utility), herpes zoster (incidence and severity), and the discount rate all affected the cost-effectiveness ratio by greater than 20 percent. The authors concluded that the cost-effectiveness of the varicella zoster vaccine varies substantially with patient age and often exceeds \$100,000 per quality-adjusted life year saved and that age should be considered in vaccine recommendations.

Utilizing published data on epidemiology of herpes zoster and post-herpetic neuralgia in the United Kingdom, the potential cost-effectiveness of vaccination was assessed in another publication.⁶⁸ These authors estimated a loss of 20,000 quality adjusted life years annually in England and Wales from herpes zoster and 17,400 due to post-herpetic neuralgia and a cost of treating herpes zoster-associated disease at 47.6 million pounds annually. They concluded that since both the health and economic burden are high,

vaccination of the elderly is expected to be cost-effective under most scenarios, the attractiveness of immunization increasing with age due to the increased burden of disease in the very elderly.

Overall, about 60 patients will need to receive the vaccine to prevent one additional case of herpes zoster over the next three years.⁷⁰ Roughly 360 patients will need to be treated to prevent one additional case of post-herpetic neuralgia.⁷⁰

Conclusion

Herpes zoster has significant impact on the older population in terms of pain and reduced quality of life. Vaccination decreases the incidence of herpes zoster and post-herpetic neuralgia. Despite unresolved questions about cost-effectiveness and duration of efficacy, the herpes zoster vaccine is an effective vaccine that has been recommended by ACIP for patients who are 60 years or older. This vaccine may lead to substantial reductions in morbidity from herpes zoster and post-herpetic neuralgia. **JMCM**

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CONTINUING EDUCATION INSTRUCTIONS

To receive continuing education credits for this activity, participants must read the monograph, complete the post test and submit an activity evaluation. A passing score of 70% must be achieved on the post test. Certificates of credit will be sent to the address on the evaluation form within six weeks of receipt.

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The release date of this activity is November 1, 2007. CME/CEU Credit is available through November 1, 2008. Post tests postmarked after November 1, 2008 will not be considered for continuing education credits.

1. Herpes Zoster is a common disorder, with about 1 million cases per year.
 - a. True
 - b. False
2. Virus induced neuronal destruction and inflammation cause
 - a. Reduced quality of life
 - b. Pain
 - c. Interference with daily activities
 - d. All of the above
3. It is suggested that the first reactivation of varicella-zoster virus provides future immunologic protection.
 - a. True
 - b. False
4. The risk of developing herpes zoster increases with age resulting in at least a 50% chance of development for patients living to age 85.
 - a. True
 - b. False
5. High risk patients include:
 - a. HIV patients
 - b. Patients with hematological malignancies
 - c. Organ and tissue transplant patients
 - d. Patients on high dose corticosteroids
 - e. Radiation and chemotherapy patients
 - f. All of the above
6. Common complications include
 - a. Hepatitis
 - b. Myelitis
 - c. Acute Neuralgia
 - d. Post-herpetic neuralgia
 - e. Scarring
 - f. Bacterial superinfection
 - g. C, D, E, F
 - h. A, B, D, E, F
7. In a prospective study of pain and its relationship to physical, role, social and emotional function, 82% of patients 50 and older reported a pain burden.
 - a. True
 - b. False
8. Other common problems related to herpes zoster pain were insomnia and depression.
 - a. True
 - b. False
9. Acute herpes zoster causes a change in quality of life similar or greater than many chronic diseases such as diabetes.
 - a. True
 - b. False
10. The objective of treatment is
 - a. Prevention of post-herpetic neuralgia
 - b. Management of acute pain
 - c. Treatment of acute viral infection
 - d. All of the above
11. If administered 72 hours after the onset of rash, antivirals have shown to decrease the duration and pain severity of the rash.
 - a. True
 - b. False
12. Successful management of acute pain can be accomplished with
 - a. Nerve blocks
 - b. Topical lidocaine patches
 - c. Capsaicin cream
 - d. Topical anti-inflammatory agents
 - e. All of the above
13. Evidence-based pharmacotherapy suggests the following have the best evidence for efficacy in treatment post-herpetic neuralgia
 - a. Gabapentin
 - b. Topical Lidacaine
 - c. Nortriptyline
 - d. Desipramine
 - e. Pregabalin
 - f. All of the above
 - g. A, C, D, E
14. The Shingles Prevention Study demonstrated when the zoster vaccine was administered, the burden of illness decreased, frequency of post-herpetic neuralgia decreased and frequency of pain and discomfort decreased.
 - a. True
 - b. False
15. Economic results in the acute phase result in 2.1 filled prescriptions and 1.7 physician/hospital visits and \$431 in healthcare costs per patient.
 - a. True
 - b. False

16. A retrospective review of Medicaid, Medicare and commercial insurance claims showed a substantially greater cost associated with post-herpetic neuralgia than pain that was resolved within 30 days.

- a. True
- b. False

17. With up to 50% of patients failing to receive acceptable pain relief, it is likely the most effective "treatment" is prevention of varicella-zoster infection.

- a. True
- b. False

18. Fifteen to 35 percent of patients still have pain more than 90 days after rash onset.

- a. True
- b. False

19. The CDC's Advisory Committee on Immunization Practices has recommended universal vaccination of those 60 years and older including those with previous episode of herpes zoster.

- a. True
- b. False

20. Despite unresolved questions on cost-effectiveness and duration of efficacy, when administered to patients 60 years and older, the vaccine decreases the incidence of and may lead to reductions in morbidity from herpes zoster and post-herpetic neuralgia.

- a. True
- b. False

ANSWER SHEET

There is only one correct answer per question.

Circle your answer clearly.

- | | |
|---|--|
| <p>1. a b</p> <p>2. a b c d</p> <p>3. a b</p> <p>4. a b</p> <p>5. a b c d e f</p> <p>6. a b c d e f g h</p> <p>7. a b</p> <p>8. a b</p> <p>9. a b</p> | <p>10. a b c d</p> <p>11. a b</p> <p>12. a b c d e</p> <p>13. a b c d e f g</p> <p>14. a b</p> <p>15. a b</p> <p>16. a b</p> <p>17. a b</p> <p>18. a b</p> <p>19. a b</p> <p>20. a b</p> |
|---|--|

EVALUATION

Please rank the following

(1=strongly disagree, 4=strongly agree)

1. As a result of my participation I am better able to:

- | | | | | |
|--|---|---|---|---|
| <input type="checkbox"/> Review the epidemiology of herpes zoster | 1 | 2 | 3 | 4 |
| <input type="checkbox"/> Identify patients at risk for herpes zoster | 1 | 2 | 3 | 4 |
| <input type="checkbox"/> Recognize complications of herpes zoster | 1 | 2 | 3 | 4 |
| <input type="checkbox"/> Discuss costs and benefits of vaccination | 1 | 2 | 3 | 4 |

2. The content was:

- | | | | | |
|---|---|---|---|---|
| <input type="checkbox"/> Current and relevant | 1 | 2 | 3 | 4 |
| <input type="checkbox"/> Well-organized and effectively written | 1 | 2 | 3 | 4 |
| <input type="checkbox"/> Free of commercial bias | 1 | 2 | 3 | 4 |
| <input type="checkbox"/> Useful in improving patient care | 1 | 2 | 3 | 4 |

3. This method of learning is very beneficial to me.

1 2 3 4

4. As a result I will change my behavior/practice patterns by:

- Implementing ACIP recommendations for vaccination
- Educating providers on herpes zoster and prevention for appropriate population

Educating members who are at high risk about herpes zoster and prevention

I will not change

5. What other topics are of interest to you?

Continuing education implies quality improvement/change in behavior. As part of our quality improvement process, NAMCP will contact you six months from your post test submission to determine the impact of this activity on practice patterns.

First Name _____

Last Name _____

MD DO RN Other

Title _____

Company _____

Mailing Address _____

Phone: _____

Fax: _____

E-mail _____

Send my certificate by:

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