4-21-2017

Recurrence of Shingles in the Older Adult Population

Leeann Yang

Recurrence of Shingles in the Older Adult Population

Leeann Yang

University of North Dakota

NURS 997 Independent Study

April 12, 2017

Abstract

Shingles is an infection of the varicella zoster virus (VZV) and known as herpes zoster (HZ) with recurrence. Children who have been vaccinated with varicella seem to have a lower rate of HZ than individuals who were exposed to the wild-type VZV (Centers for Disease Control, 2016). At this time, 99.5% of the United States population over the age of 40 have been infected with the wild-type VZV (CDC, 2016). This may mean that recurrence will be increased in our aging population. Currently, the rate is highest amongst the older adults 60 years old and older (CDC, 2016). The incidence rate among this population is 10 cases per 1,000/year (CDC, 2016).

This report provides an overview of a patient who came into the office with a final diagnosis of shingles: at the age of 67 years old, without documentation of varicella vaccination, or having realized he had a rash. The clinician's ability to assess and formulate differential diagnosis is vital to correct diagnosis, treatment, and education. The importance of piecing together the classic signs of HZ along with comparing differential diagnoses, such as herpes simplex virus (HSV) is critical, as education and treatment between the two viruses will be varied.

Background

A white male presented to his primary care office with a chief complaint of back pain. He also stated he fell two or four days ago on ice. Because of this information, the student conducted a musculoskeletal exam to begin. Upon further investigation, he stated the pain to feel like hot pins and needles. The pain radiated to his right thigh originating from his right lower back. Looking at his chart this patient was 67 years old without a history of shingles vaccination. When his shirt was lifted, a classic vesicular rash was visualized on his right lower back, which he probably could not see himself.

Initially, the diagnosis was missed. Because of this incident, the student became interested in the topic of rate of recurrence of shingles. Investigating the recurrence rate led to studies with information on treatment options for patients with reactivation of VZV, known as herpes zoster (HZ). Studies that were reviewed showed no known rate of recurrence of VZV. To this date, the CDC does not have data on the rate of recurrence of VZV. To conclude, articles were examined until the most recent study was found to reveal that recurrence might, in fact, be more common than previous researchers may have believed.

Patient Case

History

The patient made a primary care appointment for chief complaint of back pain. Upon interview, the patient reported falling two or four days ago on ice. He denied using any assistive device and stated he lived alone. The patient was a sixty-seven year old Caucasian male residing in a private home. He denied any recurrent falls since the one mentioned during the interview. He denied other injuries such as bruising or history of skin ulcers but stated the pain in his back radiated to his right thigh. The patient could not pinpoint how far the pain radiated.

For pain control, the patient was taking Tylenol at home 325mg tablets (two at a time a couple times a day at most), which he also took for a history of bilateral knee arthritis. Other than arthritis the patient stated he has a history of reflux, which he uses Protonix 40mg daily. His pain was worse with activity which was reported to go up to a 7-8 on the 0-10 verbal pain scale. During the visit, the pain was rated at a 6 out of 10. The patient denied any history of back pain such as this, and when asked to characterize pain he stated, "hot pins and needles." The pain seemed to be constant but could become worse if laying down on his back or with activity. He also stated ice was attempted for relief but made the pain worse.

Looking over his immunization history there was influenza vaccine 2016 and Tdap in 2015. The patient did not currently drink alcohol, smoke, or use smokeless tobacco products. The patient denied any history of surgeries and family history of back problems. He denied any known allergies to medications or food. He also denied any past imaging of his back.

For the patient's review of systems, he denied any chest pain, palpitations, shortness or breath, or a current cough. The patient was asked if there were any abnormalities in his urination

including weak stream, nocturia, or difficulty with urination – all which were denied. The patient also denied any trouble with constipation, diarrhea, blood in stools, or abdominal pain. Regarding his musculoskeletal, the patient denied any gait imbalance, weakness, catching, locking, or giving way of his bilateral lower extremities. No paralysis, weakness, dizziness, changes in vision, or numbness/tingling to bilateral lower extremities was endorsed; although the patient did admit to pain in the low back radiating to right thigh.

Physical Exam and Treatment

The physical exam was conducted on musculoskeletal ability, as the correct diagnosis was missed. The shirt of the patient was not lifted, therefore his skin was not examined. In general, the patient was not in distress and responded to commands. His upper extremities which were exposed were appropriate in color, turgor, and did not present with lesions or rash. His head, ears, eyes, and throat showed: no matted lashes, masses, clear conjunctiva, normocephalic head, moist pink lips and mucosa, symmetrical eyes and ears. His neck was symmetrical without masses, and trachea midline. Respirations anterior and posterior were clear and unlabored. Cardiac rhythm auscultated for murmur, rub, gallops- all which were not present. S1 and S2 present. The abdomen was soft and nontender with audible bowel tones in all four quadrants. Neurologically, the patient was alert and oriented to self, place, situation, and time. There were no fleeting of ideas and he was able to hold a conversation with clear speech.

The focused back exam revealed tenderness with vertebral palpation. The patient was able to follow commands for forward flexion, hyperextension, bilateral lateral flexion with pain on the right side, and bilateral rotation with grimacing when rotating to the right side. Extremities revealed no trauma or cyanosis. Gait seemed to have been effected by right sided

pain with slight limping, but patient was able to get up and down exam table. Leg raise test not done due to patient stating too much pain when laying on his back. Radial pulses 2+.

Skin exam revealed a classic vesicular rash on the right low back consistent with shingles. Recommended treatment for this would include: antiviral, tramadol, appropriate use of ongoing Tylenol at home to not exceed daily limit of 4,000mg. Antivirals discussed were acyclovir or valacyclovir, which would depend on patients most recent labs, specifically his kidney function; but currently without a history of any baseline labs and no formal diagnosis of kidney disease or injury. The patient would be appropriate for either antiviral. Acyclovir at 800mg five times a day for 7 days, by mouth; or valacyclovir at 1000 mg every 8 hrs for 7 days, by mouth (Albrecht, Hirsch, & Mitty, 2017). Preference for valacyclovir would be given as frequency of dose is less and possibly for missed dose decreased (Albrecht, et al., 2017). Follow up for healing progression or pain continuation would be encouraged.

Education and Discussion

Education regarding transmission of disease would include: avoid contact with individuals who have not had chickenpox or without the varicella vaccine, especially pregnant women, premature babies, or any immunocompromised persons (CDC, 2016). The patient would also need to cover his rash and wash his hands frequently, and refrain from itching or scratching his rash as the fluid from the lesions can directly spread the virus (CDC, 2016). In addition to prescribed and OTC medications, the patient could try oatmeal baths, calamine lotion, or a wet compress to help soothe the skin (CDC, 2016). Of course, the shingles vaccine would need to be advised for future prevention unless the patient has had a severe reaction to neomycin or gelatin; patients who are immunocompromised, pregnant women, or anyone with a current acute illness with fever at 101.3 degrees Fahrenheit or higher (CDC, 2016). If the patient does not remember

receiving the vaccine or records cannot be found the patient is safe to get another dose, and even if the patient had shingles in the past they are appropriate for vaccination.

Because we did not have information on whether our patient was vaccinated in the past, nor did the patient recognize the signs and symptoms of the rash. This patient, in particular, would benefit from education in regards to possible recurrence, as the virus never leaves the body. If he does feel that he has exposed at-risk individuals prior to visiting the primary care office, he can also urge these individuals to notify their primary care provider.

Literature Review

The exam of the 67-year-old Caucasian male, who presented with a chief complaint of back pain led to a visualization of a vesicular rash. The rash was located on his right lower back characterized as "pins and needles." The process in which a diagnosis is made may be skewed by what we learn to be characteristic signs of one disease. The importance of processing differential diagnosis is to get down to an accurate conclusion. Ruling out possible outcomes assists in the critical thinking process. Naturally, after a diagnosis is made, the treatment and plan follow, but if the disease is one that may reoccur, healthcare practitioners should educate and understand preventative measures. The recurrence of varicella zoster virus (VZV) is a controversial topic within current literature. From this review, we uncover that misdiagnoses in the past have created a controversial topic over speculated rate of recurrence in VZV. We will explore the most common misdiagnosis discussed within literature, and best practice methods into how to differentiate a correct diagnosis. Further studies relating to recurrence bring up the importance of protecting individuals from recurrence. One way of doing this may be to further study the role vaccines play in HZ and what age is most appropriate for boosters. Finally, the current treatment method for HZ and the future science has in regards to new antiviral therapy will be discussed.

Often times during an assessment, healthcare practitioners may recognize characteristic rashes or symptoms that point towards a specific diagnosis. In our case, the visualized lesions follow the characteristic VZV presentation, following a dermatome within the basal layer of the skin (Kinchington, Guedon, & Hendricks, 2012). It is important to note there are also cases that do not present with any rash (Kinchington, et. al., 2012; Fox, Galetta, Mahalingam, Wellish, Forghani, & Gilden, 2001). Most of the controversy with recurrence is the differentiation between herpes simplex virus (HSV) and VZV. All three (HSV-1, HSV-2, VZV) viruses are acquired with a primary self-resolving infection of the skin or mucosa, which leads to latency and possible recurrence (Kinchington, et al., 2012). Not only are the viruses similar in presentation and latency but they share genes that encode similar functions on their host.

Differentiating between HSV and VZV should be understood, as there is controversy of misdiagnoses of recurrent VZV. As advanced testing emerges, such as polymerase esterase chain reaction (PCR), practitioners can now better determine HSV versus VZV outbreaks. Studies in the past (not using PCR but viral culturing) found 25% of outbreaks diagnosed as VZV were, in fact, HSV (Burkhart, 2002). Approximately one-fourth of herpetic eruptions diagnosed as VZV are confirmed to truly be HSV cases (Pierson, 2017). As a rule in dermatology, repetitive herpetic outbreaks are HSV infections until proven to be VZV (Burkhart, 2002). Within the immunocompetent patient population, there have been confirmed misdiagnosed recurrent VZV cases, which also create controversy of the real rate of recurrence (Chien, Andy, & Olerud, 2007). Sticking to the most up to date facts on differentiating one virus from the other will be critical in correct diagnosis, treatment, and prevention for our patients. Current laboratory diagnostics that can assist in differentiation include PCR, enzyme-linked immunosorbent assays, and immunofluorescence (Burkhart, 2002).

VZV is known to target the bodies immune system and establish a latency similar to HSV. The virus is transmitted through aerosol and inhalation. One difference is that VZV becomes dormant in multiple sensory neuronal nuclei, which gives the virus the ability to reoccur anywhere in the body (Kinchington, et al., 2012). While HSV lesions tend to affect one or few neurons and recur at the primary site of infection (Kinchington, et al., 2012). The area of the primary infection does not always foreshadow the recurrent location in HZ. Another variance between HSV and VZV is that recurrence rates increase with age whereas with HSV the recurrence rate drops with age (Kinchington, et al., 2012). Currently, the rate of recurrence of VZV and the mechanism behind how the virus maintains a latent state is unknown (Kinchington, et al.,2012). Due to the fact that VZV is much more reliant on host; current animal model mimicking viral recurrence is rare or nonexistent. Kinchington, et al. (2012) also state the extreme difficulty of reactivating human ganglia to study the recurrence of VZV.

Since we do know the recurrence rate correlates to immune system functioning, specifically the degradation of it, our older population will be at increased risk. HSV recurrence is triggered by both environmental and physiologic factors, VZV is not as closely linked to such triggers (Kinchington, et al., 2012). Our older individuals are at a higher risk for recurrence due to immune senescence. Although rash does not always present, 90% of patients with VZV suffer from pain which almost always involves neurological roots (Kinchington, et al., 2012).

Pain is another characteristic that differentiates VZV from HSV. Because pain can be a debilitating complication from VZV, the issue of recurrence should be worrisome for current healthcare professionals. The pain occurs during the active disease and the possibility of chronic postherpetic neuralgia (PHN) is also well known. PHN is pain that persists for 3 or more months after the VZV lesions crust (Tseng, Lewin, Hales, Sy, Harpaz, Bialek, et al., 2015). Kinchington,

et al. (2012) state that HZ patients develop PHN at a rate of more than 30%. The Centers for Disease Control (2016) states approximately 13% or more of individuals over the age of 60 to be at risk for PHN. This pain can lead to depression, insomnia, and decreased activity to name a few. In regards to developing PHN Tseng, et al. (2015) found that vaccination prior to VZV decreased rates of PHN in women.

Nakamura, et al (2016) found that Japanese patients age 50-79 years old had less severe pain associated with recurrent VZV versus primary VZV infection. Individuals 80 years old or older did not experience this less severe recurrence. This might be the case as cell-mediated immunity in the recurrent individuals were stronger in the 50-79-year-old population (Nakamura, et al., 2016). Not only is recurrent pain noted to be less severe, but also the lesion development was less severe in crusting, erythema, vesicles, pustules, erosions, ulcerations, and fusion of vesicles (Nakamura, et al., 2016). Depending on the age when the patient develops their primary VZV infection, the immune response will be varied. This means if a patient experiences primary VZV infection later in life the weaker the immune booster response will be. The implication of this information is that the older population is predisposed to a recurrence that is closer to their primary date of infection, along with similar pain and lesion to their primary experience. In this particular study, no difference was noted between genders or immunocompetent versus immunocompromised patients (Nakamura, et al., 2016).

Studies have proved the efficacy of the HZ vaccine to be 51.3% effective in preventing HZ in adults at 60 years old or older, but the protection wearing off with time (Levin, Schmader, Lei, Williams-Diaz, Zerbe, et al., 2016). Levin, et al. (2016) has confirmed that giving the zoster vaccine at an earlier age (particularly at age 60 years old), prior to 70 years old or older produces an increase in the cell immunity response. Although the vaccine's cell-mediated immunity

persists for 10 years or more, a booster has shown to enhance the immunity for older populations (Levin, et al., 2016). The question now is when to give the booster, as the age and primary infection date vary, this all plays a role in the longevity of the immune system's reaction to the vaccine. Levin, et al (2016) suggests further studies in order to investigate appropriate booster interval for immunization against HZ.

Currently, the Advisory Committee on Immunization Practices (ACIP) states that the zoster vaccine is most appropriate at the starting age of 60 years old. The United States Food and Drug Administration (FDA) has approved the vaccine for individuals 50 years old and older (CDC, 2016). There is no recommendation for a booster, but rather focusing on the appropriate age to administer the initial vaccine. The CDC (2016) states the efficacy of the zoster vaccine to be uncertain after the first 5 years. Current vaccination recommendations state to administer the shingles vaccine at age 60 years old, as this time is prime for highest risk of zoster and its complications.

Tseng, et al (2012) have confirmed this in their study showing a slightly higher trend to decrease VZV recurrence in individuals less than 70 years old when vaccinated; but they also mention the low recurrence rate overall in immunocompetent individuals and also raise the issue of possible vaccine shortage. Jumaan, et al. (2005) state that the rise in varicella vaccine for children has not been the reason for increased zoster virus incidence in adults. Therefore, the trend for increased incidence in VZV is still unknown, though currently we know it has been increasing prior to varicella vaccine in the United States (CDC, 2016).

In regards to current treatment, Albrecht et al. (2017) suggest antiviral therapy if onset has been 72 hours or less, in order to gain the maximum benefit. Patients that are immunocompromised should receive treatment no matter if the initial 72-hour onset has passed,

and for all individuals actively experiencing new lesions (even past 72-hour onset) are appropriate candidates for antiviral therapy (Albrecht, et al., 2017). The drug of choice depends on patients and their renal function, as acyclovir clears via the kidneys. The top choices for antiviral therapy are valacyclovir or famciclovir, as the doses are less frequent and the efficacy has been studied to be the same (Albrecht, et al. 2017). Additional therapies for symptoms related to pain include narcotics, NSAIDS, and/or Acetaminophen – depending on the pain rating. Bowsher (1997) studied the efficacy of using tricyclic antidepressants, particularly amitriptyline for treatment of neuritis or to prevent PHN, but without significant results as there were many limitations. Other more effective methods of treating acute herpes zoster pain are oxycodone, although constipation is a well-known side effect; but gabapentin proved not to be any greater than placebo (Dworkin et al., 2009). Lastly, some providers may choose to use corticosteroids to improve acute symptoms, but with patients who present with uncomplicated herpes zoster, the course does not seem to prevent PHN (Han, Zhang, Chen, Zhou, & Zhu, 2013).

Although some practitioners may believe that recurrence of VZV is rare, there is current evidence to show otherwise. This itself should warrant healthcare practitioners to include recurrent VZV as a differential when assessing patients with classic signs and symptoms. Yawn, Wollan, Kurland, St Sauver, & Saddier (2011) have found that recurrence is as common as primary VZV infection; but rare within the first 12-18 months after the primary HZ episode (Tseng, 2012). Hales, et al. (2016) revealed recurrent VZV patients were not as likely to seek healthcare unless pain was severe; suggesting that prior studies using healthcare data may have underestimated the recurrent rate of VZV. Women are also more likely to suffer from VZV

recurrence (Hales, Harpaz, & Bialek, 2016.) Currently, the treatment for recurrent VZV is the same as the primary infection (Albrecht, et al., 2017).

More studies are being conducted on the best antiviral treatment for herpes zoster. As viruses mutate and become resistant, newer drugs have been made. For example, valacyclovir which is approved for VZV treatment may be a better choice than the traditional acyclovir, a guanosine analog. This is the case because valacyclovir has an increased absorption and bioavailability (De, Hart, & Breuer, 2015). A newer drug has gone through phase 2 trial, called valacyclovir has been found to be noninferior to valacyclovir in treating herpes zoster (De, et. al., 2015). For patients who have passed the 72-hour mark and now have encrusted lesions the benefits of antiviral are minimal (Albercht, et al., 2017). The individuals who benefit most from antiviral therapy are patients older than 50 years old who have a history of pain lasting longer with their zoster; but overall the antiviral's are given to reduce severity of pain and increase the healing time of skin (Albrecht, et al., 2017). If secondary bacterial infections or complications in the eye occur then additional treatment therapy is to be added and antiviral therapy may be prolonged (Albercht, et al., 2017).

Returning to our initial 67-year-old male patient, his case is uncomplicated VZV, presenting classically with dermatomal vesicular rash and acute neuritis, PCR is unlikely needed to confirm diagnosis, although further investigation into past history could be useful for documentation to determine likelihood of HSV or if this current case is recurrent. Since he also presented before the 72-hour window, the patient was a good candidate for an antiviral, preferably valacyclovir. For prevention of recurrence, we would want to educate on receiving vaccination and keeping up with health maintenance as he ages. Managing ongoing co-morbidities will be key to keeping his immune system as healthy as possible. Healthcare

providers can additionally take time to educate patients if acute neuritis is felt (as it can precede the rash) they may make an appointment to be assessed for antiviral therapy early on, as to prevent PHN.

Learning Points

- The current and past rate of recurrent VZV is not known. There have been documented findings that have re-evaluated the research on VZV. These findings have concluded that previous studies have misdiagnosed VZV recurrence when the real infection was HSV.
- The most recent research shows that most individuals with recurrence do not seek healthcare, unless their pain is severe.
- So why should we care about herpes zoster recurrence? The answer is clear; as the older population continues to age and live longer the recurrence rate can also rise. Since we know that VZV rates increase with age and decline in immunity, our efforts to further prevent discomfort are valid, as pain can be debilitating.
- Further studies are needed in order to determine if boosters may assist in prevention, and in what age group that would be most effective.
- Overall, keeping recurrent VZV as a differential diagnosis in the back of our minds for patients most at risk: women, older age, immunocompromised patients; does not hurt our practice. If laboratory testing is needed, PCR is the most sensitive to distinguish between HSV.
- Vaccinating individuals at or after the age of 60 years old is best practice and gives the best preventative coverage.

References

Albrecht, M.A., Hirsch, M.S., & Mitty, J. (2017). UpToDate: Treatment of Herpes Zoster in the Immunocompetent Host. Retrieved from https://www.uptodate.com/contents/treatment-of-herpes-zoster-in-the-immunocompetent-host

Bowsher, D. (1997). The Effects of Pre-Emptive Treatment of Postherpetic Neuralgia with Amitriptyline: A Randomized, Double-Blind, Placebo-Controlled Trial. *Journal of Pain and System Management,* 13(6). 327-31.

Burkhart, C.N. (2002). Recurrent Herpes Zoster Revisited. *International Journal of Dermatology*, 41(8). 528. Doi: 10.1046/j.1365-4362.2002.15474.x

Centers for Disease Control. (2016). Shinges (Herpes Zoster): Clinical Overview. Retrieved from http://www.cdc.gov/shingles/hcp/clinical-overview.html

Center for Disease Control. (2016). Vaccines and Preventable Diseases: What Everyone Should Know about Shingles Vaccine. Retrieved from https://www.cdc.gov/vaccines/vpd/shingles/public/index.html

Chien, Andy J., & Olerud, J.E. (2007). Why do so many clinicians believe that recurrent zoster is common?. *Dermatology Online Journal*, 13(2). Retrieved from: http://escholarship.org/uc/item/91r2g01n

Dworkin, R.H., Barbano, R.L., Tyring, S.K., McDermott, M.P., Pennella-Vaughan, J., Bennett, G.J., Gnann, J.W., Irvine, C., Kamp, C., Kieburtz, K., Max, M.B., & Schmader, K.E. (2009). A Randomized, Placebo-Controlled Trial of Oxycodone and of Gabapentin for Acute Pain in Herpes Zoster. *Pain*, 142(3). 209-17. Doi: 10.1016/j.pain.2008.12.022

De, S., Hart, J.L., & Breuer, J. (2015). Herpes Simplex Virus and Varicella Zoster Virus: Recent Advances in Therapy. *Current Opinion In Infectious Diseases,* 28(6). 589-95. Doi: 10.1097/QCO.0000000000000211

Fox, R.J., Galetta, S.L., Mahalingam, R., Wellish, B.S., Forghani, B., & Gilden, D.H. (2001). Acute, Chronic, and Recurrent Varicella Zoster Virus Neuropathy Without Zoster Rash. *Neurology,* 57. 351-54. Doi: http://dx.doi.org.ezproxy.undmedlibrary.org/10.1212/WNL.57.2.351

Han, Y., Zhang, J., Chen, N., Zhou, M., & Zhu, C. (2013). Corticosteroids for Preventing Postherpetic Neuralgia. Cochrane Database System Review. Doi: 10.1002/14651858.CD005582.pub4

Hales, C.M., Harpaz, R., & Bialek, S.R. (2016). Self-Reported Herpes Zoster, Pain, and Health Care Seeking in the Health and Retirement Study: Implications for Interpretation of Health Care-Based Studies. *Annals of Epidemiology,* 26(6). 441-46. Doi: 10.1016/j.annepidem.2016.04.006

Jumaan, A.O., Yu, O., Jackson, L.A., Bohlke, K., Galil, K., & Seward, J.F. (2005). Incidence of Herpes Zoster, efor and After Varicella-Vaccination-Associated Decreases in the Incidence of Varicella, 1992-2002. *The Journal of Infectious Diseases,* 191(12). 2002-07. Doi: https//doi.org/10.1086/430325

Kinchington, P.R., Leger, A.S., Guedon, J.G., & Hendricks, R.L. (2012). Herpes Simplex Virus and Varicella Zoster Virus, The House Guests Who Never Leave. *Herpesviridae,* 3(5). Doi: 10.1186/2042-4280-3-5

Levin, M.J. Schmader, K.E., Lei, P., Williams-Diaz, A., Zerbe, B., Canniff, J., & Su, S. (2016). Cellular and Humoral Responses to a Second Dose of Herpes Zoster Vaccine

Administered 10 years After the First Dose Among Older Adults. *Journal of Infectious Diseases,* 213(1O. 14-22. Doi: 10.1093/infdis/jiv480

Nakamura, Y., Miyagawa, F., Okazaki, A., Okuno, Y., Mori, Y., Iso, H., Yamanishi, K., & Asada, H. (2016). Clinical and Immunologic Features of Recurrent Herpes Zoster (HZ). *American Academy of Dermatology,* 75(5). 950-56. Doi: http://dx.doi.ort/10.1016/j.jaad.2016.05.037

Pierson, J.C. (2017). Reluctance Regarding Recurrent Herpes Zoster. American Academy of Dermatology. Doi http://dz.doi.org/10.1016/j.jaad.2016.12.042

Tseng, H.F., Lewin, B., Hales, C.M., Sy, L.S., Harpaz, R., Bialek, S., Luo, Y., Jacobsend, S.J., Reddy, K., Huang, P., Zhang, J., Anand, S., Bauer, E.M., Chang, J., & Tartof. S.Y. (2015). Zoster Vaccine and the Risk of Postherpetic Neuralgia in Patients Who Developed Herpes Zoster Despite Having Received the Zoster Vaccine. *Journal of Infectious Disease,* 212. 1222-31. Doi:10.1093/infdis/jiv244

Tseng, H., Chi, M., Smith, N., Marcy, S., Sy, L., & Jacobsen, S. (2012). Herpes Zoster Vaccine and the Incidence of Recurrent Herpes Zoster in an Immunocompetent Elderly Population. *Journal of Infectious Diseases,* 206(2). 190-96.

Yawn, B., Wollan, P., Kurland, M., St Sauver, J., & Saddier, P. (2011). Herpes Zoster Recurrences More Frequent than Previously Reported. *Mayo clinic Proceedings,* 86(2). 88-93. Doi: 10.4065/mcp.2010.0618