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# Recent Trends in the Study of Herpes Zoster Virus Causing Diseases and Cancer in Human

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**ABSTRACT**

Varicella zoster virus causes chickenpox and shingles (herpes zoster) in human. Some of the disease manifestations of herpes zoster are noted as post herpetic neuralgia, optic neuritis and encephalitis including cancer. Though, herpes zoster with the development of cancer in human has a murky relationship, recently it has been proved that herpes zoster develops a variety of cancer in human too. On the contrary, studies have also shown the patients with haematological or solid tumor cancer had a much higher risk of having herpes zoster than those with no cancer detection. The present paper is an attempt to discuss the researches done so far in the field of herpes zoster virus developing diseases and cancer in human.

***KEYWORDS:*** *Varicella zoster, chickenpox, Herpes zoster, Risk of cancer*

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## INTRODUCTION

One of the eight herpesviruses known to infect humans is Varicella zoster virus (VNV), herpes zoster or human alphaherpesvirus type 3. It usually causes chickenpox and shingles in children and geriatric persons respectively. Shingles is an outcome of reactivation of the virus hidden in the nerve cells (Mahale *et al.* 2015)[1]. But, how the virus survives in the body or subsequently reactivated is not yet fully known. In recent past, researches revealed that the appearance of shingles as a marker in elderly have been linked to the development of cancers in future (Buntix *et al.* 2005, Chiu *et al.* 2013, Cotton *et al.* 2013, Mahale *et al.* 2015 and Herbecke *et al.* 2020)[1-5]. The present paper deals with the study of Varicella zoster virus causing chickenpox, shingles and cancer in the human body.

### Clinical Presentation

Varicella zoster is a virus belonging to the subfamily Alfaherpesvirinae causing several human infections with various clinical manifestations. Varicella chickenpox infection as such is a mild disease and it recovers without any serious complications. But, sometimes bacterial parainfections may occur as pneumonia, bacteremia, sepsis and cerebellar ataxia in most of the infants and immunocompromised individuals. Herpes zoster or shingles is caused by the Varicella zoster virus, the same virus that causes chickenpox, but a little bit in a different way (Gilden *et al.* 2012)[6]. Furthermore, as VZV remains lifelong in the human body, shingles developed only after chickenpox. And, it all happens when the virus is reactivated usually in later half of life (Fawziah *et al.* 2020)[7]. Shingles is marked by the development of pink or red, itchy and painful maculopapular rashes with fluid filled skin on one side of the body. In addition, there are some internal shingles of eyes, lungs, nervous system and brain causing headaches, cough, fever, abdominal pain, optic neuritis, post herpetic neuralgia and encephalitis (Broucker *et al.* 2012, Mallick *et al.* 2016, Kennedy and Gershon 2018, Thomas *et al.* 2018 and Laura *et al.* 2020)[8-12]. Similarly, VZV has also been reported to cause fetal abnormalities during pregnancies (Ahn *et al.* 2016)[13].

### Oncology of the Virus

There are several reports that documented the role of shingles in the development of cancer in human. A kind of study says that patients with any kind of cancer diagnosed have usually been found to be associated with high risk of developing shingles. The patients suffering from solid tumor cancers of head and neck, brain, breast, lungs, prostate, kidney, bladder, stomach and ovarian or other organs of the body had a 30 to 40 % increased risk of developing shingles than people without cancer (Mina *et al.* 2012, Yu *et al.* 2012, Cotton *et al.* 2013, Laurel *et al.* 2013, Mahale *et al.* 2015, Qian *et al.* 2019 and Mikolaj *et al.* 2020)[1,4,14-18]. Similarly, the hematological blood or lymph cancer patients suffering from Hodgkin and non Hodgkin lymphoma and leukemia are also at substantially increased risk of developing herpes zoster (Laurel *et al.* 2013)[16]. While on the other hand the patients developing shingles have also been found to be associated with the development of cancer in future (Figure 1). It

produces several lymphoproliferative disorders, leukemia, necrotic skin lesions and breast tumors (Ferreira *et al.* 2008, Kurtaran *et al.* 2009, Gilden *et al.* 2012, Mina *et al.* 2012, Laurel *et al.* 2013 and Mikolaj *et al.* 2020)[6,14,16,18-20].

Varicella zoster virus is a medically important worldwide human herpesvirus whose infections are extremely common. Humans are the only reservoir of VZV causing diseases in human. This is composed of a double stranded D.N.A. enveloped in capsid (Depledge *et al.* 2018)[21]. VZV modulated neuronal and non neuronal cells via apoptosis (Baiker *et al.* 2004, Pugazhenthi *et al.* 2011 and Yu *et al.* 2013)[22-24]. It induces apoptosis in immune cells like T cells, B cells and monocytes (Steain *et al.* 2014, Sen and Arvin 2016 and Kennedy *et al.* 2019)[25-27]. Varicella zoster virus has got ability to modulate the function of these cells. It alters the transcriptional profile of apoptotic gene of neuronal cells (Konig *et al.* 2003, Pugazhenthi *et al.* 2009 and Brazeau *et al.* 2010)[28-30]. The inhibition of apoptosis is critical for maintenance, latency and reactivation of the virus (Hood *et al.* 2006 James *et al.* 2012 and Gerada *et al.* 2018)[31-33]. However, additional studies are still required to understand the exact mechanism of infection in human.

Summarizing all these facts as stated above in the light of recent researches done so far in the same field, in a nutshell the following facts may be derived as under:

- shingles is rarely developed in persons having latent herpes zoster virus in their sensory ganglia (Kenneth *et al.* 2013)[34].
- these viruses are usually reactivated as shingles in persons suffering from any type of cancer, immunocompromised or in chemotherapeutic patients (Mahale *et al.* 2015)[1].
- shingles have been hypothesized as a marker for cancer development and diagnosis in future (Buntix *et al.* 2005, Chiu *et al.* 2013, Cotton *et al.* 2013, Igler *et al.* 2013 and Nikhil *et al.* 2020)[2,3,4,35,36].

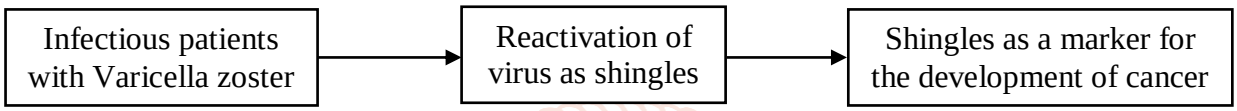


**Figure 1 A model proposed for the development of cancer caused by the herpes zoster virus**

## PREVENTION OF INFECTION

Chickenpox is highly contagious. The people who have neither been infected nor vaccinated with chickenpox earlier are at higher risk of developing the disease. The disease is more commonly spread through tiny droplets of saliva released into the air via talking, sneezing and coughing of the infected person. A good hygienic condition can only keep us away from infection. The vaccines are safe and effective measure in preventing the smallpox as well as shingles (Macartney *et al.* 2014 and Fawziah *et al.* 2020)[7,37].

## TREATMENT OF DISEASE

Currently, there are two FDA approved vaccines available for the prevention of these infections. Both of them are live attenuated Oka strain of VZV; Varivax, for the prevention of Varicella and Zostavax, for the prevention of Herpes zoster (Kristen & Messaoudi 2013 and Macartney *et al.* 2014)[37,38]. Similarly, the treatment with some antivirals like acyclovir (zovirax), valacyclovir (valtrex) and famcyclovir (famvir) are also available for the treatment of chickenpox and shingles. It can most effectively shorten the length and severity of the illness if treated within 24 hours after the onset of rashes (Wood *et al.* 1988, Arvin 2002, Wu *et al.* 2003 and Simpson and Lyseng 2006)[39-42].

## CONCLUSION

Varicella zoster is a virus causing chickenpox and shingles in human. After an initial infection Varicella zoster virus establishes lifelong latency in sensory ganglia and reactivates to produce cancer in the human body. But the link between shingles developing cancer in human is not enough to establish the fact. And, it appears that they are in a juvenile stage. Therefore, more researches are still required to prove the hypothesis proposed (Yu *et al.* 2012, Cotton *et al.* 2013, Qian *et al.* 2019 and Fawziah *et al.* 2020)[4,7,15,17].

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## CONFLICTS OF INTEREST

There are no conflicts of interest. The authors have approved the final version of the manuscript contributing equally.

## REFERENCES

[1] Mahale P., Elizabeth L. Y. and Eric A. E. (2015). Herpes zoster and risk of cancer in the elderly U.S. population. Cancer Epidemiology, Biomarkers & Prevention. 25 (1): 28-35.

[2] Buntinx F., Wachana R., Bartholomeeusen S., Sweldens K. and Geys H. (2005). Is herpes zoster a marker for occult or subsequent malignancy? Br. J. Gen. Pract. 55: 102-107.

[3] Chiu H. F., Chen B. K. and Yang C. Y. (2013). Herpes zoster and subsequent risk of cancer: a population-based study. J. Epidemiol. 23: 205-210.

[4] Cotton S. J., Belcher J., Rose P., Jagadeesan S. K. and Neal R. D. (2013). The risk of a subsequent cancer diagnosis after herpes zoster infection: primary care database study. British Journal of Cancer 108: 721-726.

[5] Herbecke R., Jensen N. J. and Depledge D. P. (2020). Recurrent herpes zoster in the shingles prevention study: are second episodes caused by the same Varicella zoster virus strain? Vaccine. 38(2) :150-157.

[6] Gilden D., Nagel M. A. and Cohrs R. J. (2012). Persistence of Varicella zoster virus DNA in saliva after herpes zoster. J. Infect Dis. 205 (7): 1178-1179.

[7] Fawziah M., Kamalpreet P., Bill H. and Nirma V. (2020). Risk factors for herpes zoster infection: A meta-analysis. Open forum Infectious diseases. 7 (1): 1-8.

[8] Broucker T. D., Mailles A., Chabrier S. and Morand P. and Stahl J. P. (2012). Acute Vericella zoster encephalitis without evidence of primary vasculopathy in a case series of 20 patients. Clinical Microbiology and Infection. 18 (8): 808-819.

[9] Mallick-Searle T., Snodgrass B. and Brant J.M. (2016). Postherpetic neuralgia: epidemiology, pathophysiology. J. Multidiscip. Healthc. 9: 447-454.

[10] Kennedy P. G. E. and Gershon A. A. (2018). Clinical features of Varicella zoster virus infection. Viruses. 10 (11): 609. doi.10.3390/v/10110609.

[11] Thomas S., Kaweh P. And Corinna T. (2018). Varicella zoster virus infections in neurological patients: a clinical study. BMC Infectious Diseases 18 (238): 1-11.

[12] Laura K. H., Kristoffer S. H., Jacob B., Lykke L., Christian B.(2020). Varicella zoster virus encephalitis in Denmark from 2015 to 2019 - A nationwide prospective cohort study. Clinical Infectious Diseases ciaa 185, http://doi.org/10.1093/cid/ciaa185.

[13] Ahn K. H., Park Y. J. and Hong S. C. (2016). Congenital Varicella syndrome: A systematic review. J. Obstet. Gynaecol. 36 (5): 563-566.

[14] Mina E., Ali Z., Mirsaed M., Reza G., Masood G. (2012). Detection of Varicella zoster in the benign and malignant breast tumors by polymerase chain reaction. Int. J. Mol. Clin. Microbiol. 2: 153-157.

[15] Yu-Ping Wang, Chia-Jen Liu, Yu-Wen Hu, Tzeng-Ji Chen, Yi-Tsung Lin and Chang-Phone Fung (2012). Risk of cancer among patients with herpes zoster infection: a population-based study. CMAJ 184 (15): 804-809.

[16] Laurel A. H., Gary T. R., Michael J. S., Barbara P. Y. and Trung N. T. (2013). The epidemiology of herpes zoster in patients with newly diagnosed cancer. Cancer Epidemiology, Biomarkers and Prevention. 22 (1): 82-90.

[17] Qian J., Anita E. H., karki S., Emily B., Kristine M., Lorraine C. and Bette L. (2019). Risk of herpes zoster prior to and following cancer diagnosis and treatment: A population-based prospective cohort study. The journal of Infectious diseases. 220: 4-11.

[18] Mikolaj W., Rafal B., Ewelina G. and Paulina N.R. (2020). Herpesviruses in head and neck cancers. Viruses. 12 (2): 172-182.

[19] Ferreira M,. Sanches M., Teixeira M., Guerra M. and selores M. (2008). Persistent Varicella as the initial manifestation of systemic lymphoma. Dermatol Online J. 14 (2): 24.

[20] Kurtaran B., Payolas S., Candevir A., Komur S. and Aksu HSZ. (2009). Disseminated herpes zoster infection in a patient with lymphoma. Turk. J. Med. Sci. 39 (3): 479-482.

[21] Depledge D. P., Sadoka T. and ouwendijk W.J.(2018). Molecular aspects of Varicella zoster virus latency. Viruses. 10 (7): 349-370.

[22] Baiker A., Fabel K., Cozzio A. and Sommer M. (2004). Varicella zoster virus infection of human neural cells *in vivo*. PNAS 101: 10792-10797.

[23] Pugazhenthi S., Nair S., Velmurugan K. and Cohrs R. J. (2011). Varicella zoster virus infection of differentiated human neural stem cells. J. Virol. 85: 6678-6686.

[24] Yu X., Seitz S., Pointon T., Bowlin J. L., Cohrs R. J. and Jonjic S. (2013). Varicella zoster virus infection of highly pure terminally differentiated human neurons. J. Neurovirol. 19: 75-81.

[25] Stein M., Sutherland J. P., Rodriguez M., Cunningham A. L. and Abendroth A. (2014). Analysis of T cell responses during active Varicella zoster virus reactivation in human ganglia. J. Virol. 88: 2704-2716.

[26] Sen N. and Arvin A. M. (2016). Dissecting the molecular mechanisms of the tropism of Varicella zoster virus for human T cells. J. Virol. 90: 3284-3287.

[27] Kennedy J. J., Steain M., Slobedman B. and Abendroth A. (2019). Infection and functional modulation of human monocytes and macrophages by Varicella zoster virus. J. Virol. 93:eo1887-18.

[28] Konig A., Homme C., Hauroder B., Dietrich A. and Wolff M. H. (2003). The Varicella zoster virus induces apoptosis *in vitro* in subpopulations of primary human peripheral blood mononuclear cells. Microb. Infect. 5: 879-889.

[29] Pugazhenthi S., Gilden D. H., Nair S., Macadoo A., Wellish M. and Brazeau E. (2009). Simian Varicella virus induces apoptosis in monkey kidney cells by the intrinsic pathway and involves down regulation of bcl-2 expression. J. Virol. 83: 9273-9282.

[30] Brazeau E., Mahalingam R., Gilden D., Wellish M. and Kaufer B. B. (2010), Varicella zoster virus induced apoptosis in MeWo cells is accompanied by down-regulation of Bcl-2 expression. J. Neurovirol. 16: 133-40.

[31] Hood C., Cunningham A. L., Slobedman B., Arvin A. M., sommer M. H. and Kinchington P. R. (2006). Varicella zoster virus ORF63 inhibits apoptosis of primary human neurons. J. Virol. 80: 1025-1031.

[32] James S. F., Mahalingam R. and Gilden D. (2012). Does apoptosis play a role in Varicella zoster virus latency and reactivation? Virus. 4:1509-1514.

[33] Gerada C., Stein M., Mc Sharry B. P., Slobedman B. and Abendroth A. (2018). Varicella zoster virus ORF63 protects human neuronal and Keratinocyte cell lines from apoptosis and changes its localization upon apoptosis induction. J. Virol. 92: e00338-e00318. doi:10.1128/JVI.0038-18.

[34] Kenneth R. C., Rebecca L. S., Frank J. and Igor I. (2013). Presentation and management of herpes zoster (shingles) in the geriatric population. 38 (4): 217-227.

[35] Iglar K., Kopp A. and Glazier R. H. (2013). Herpes zoster as a marker of underlying malignancy. Open Med. 7: 68-73.

[36] Nikhil K. M., Sharma M and Spinner R. J. (2020). Primary peripheral nerve tumors associated with nerv-

territory herpes zoster. Acta Neurochirurgica. 162; 1147-1151.

[37] Macartney K., Heywood A. and McIntyre P. (2014). Vaccines for post exposure prophylaxis against Varicella (chickenpox) in children and adults. Cochrane Database Sys. Rev. 6: CD001833.

[38] Kristen H and Messaoudi I. (2013). Animal models of Varicella zoster virus infection. Pathogens. 2 (2): 364-382.

[39] Wood M. J., Ogan P. H. and Mckendrick M. W. (1988). Efficacy of oral acyclovir treatment of acute herpes zoster. Am. J. Med. 85 (2A): 79-83.

[40] Arvin A. M. (2002). Antiviral therapy for Varicella and herpes zoster. Semin. Pediatr Infect Dis. 13: 12-21.

[41] Wu J. J. Brentijens M. H., Torres G., Yeung-Yue K., Lee P. and Tyring S. K. (2003). Valacyclovir in the treatment of herpes simplex, herpes zoster and other viral infections. J. Cutan Med Surg. 7 (5): 372-381.

[42] Simpson D. and Lyseng-Williamson K. A. (2006). Famciclovir: a review of its use in herpes zoster and genital and orolabial herpes. Drugs. 66 (18): 2397-2416.