Shingles in Immunocompromised Patients: Infection Control Perspective

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Disclosure

- I have no actual or potential conflict of interest in relation to this presentation.

Outline

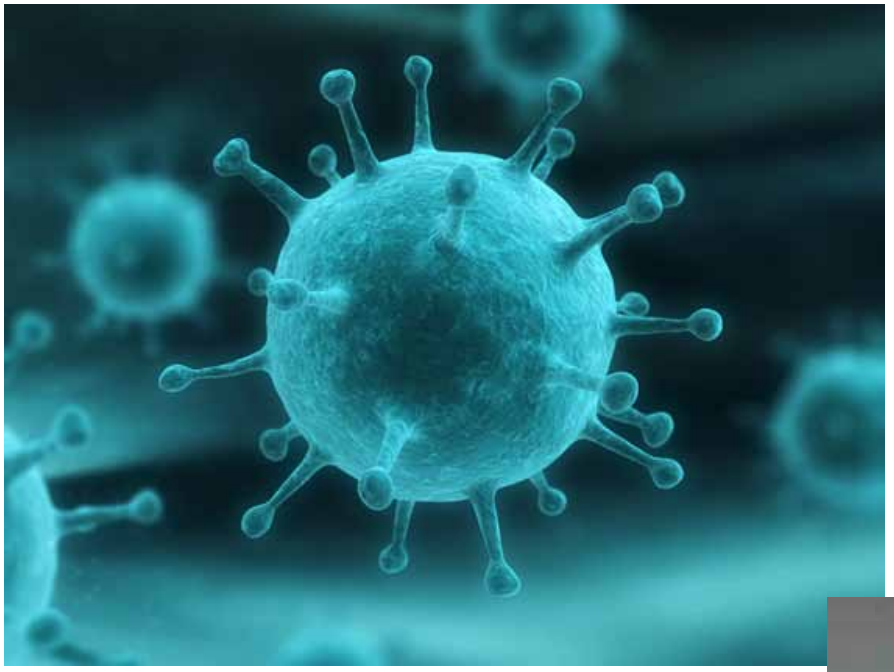
- Varicella zoster virus Infection

- Review of Herpes Zoster:
  - Transmission of VZV from HZ patients
  - Definition of Immunocompromised host
  - Impact of Varicella Vaccine on Incidence of HZ
  - Zoster vaccine

Background

Varicella zoster virus (VZV) causes 2 clinically distinct forms of disease:

1. Chickenpox: vesicular lesions in different stages of development on the face, trunk, and extremities
2. Herpes Zoster (Shingles):
   - reactivation of endogenous latent VZV infection within the sensory ganglia.
   - painful, unilateral vesicular eruption, which usually occurs in a restricted dermatomal distribution.



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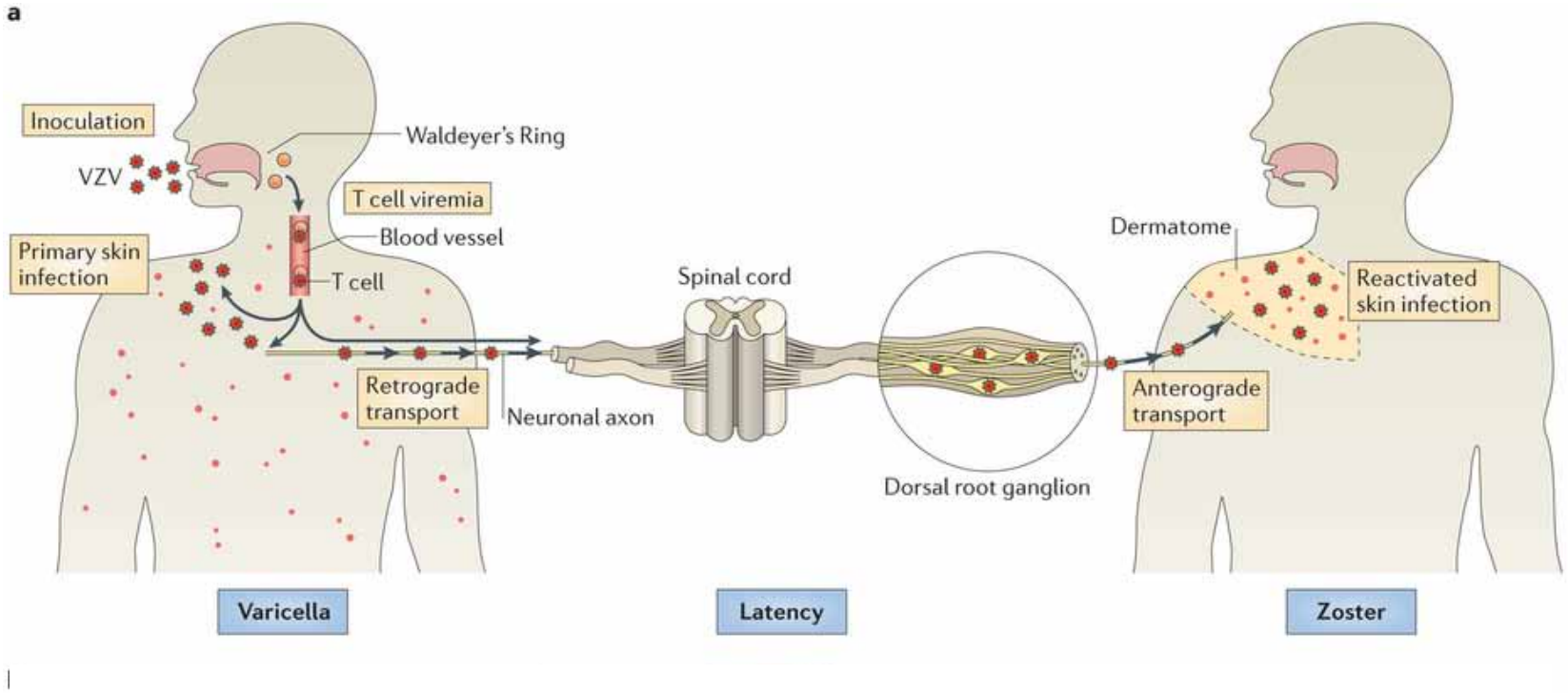
VZV

- Human is the only host
- Person-to-person transmission by airborne route
- Incubation period: 8-21 days

Pathogenesis



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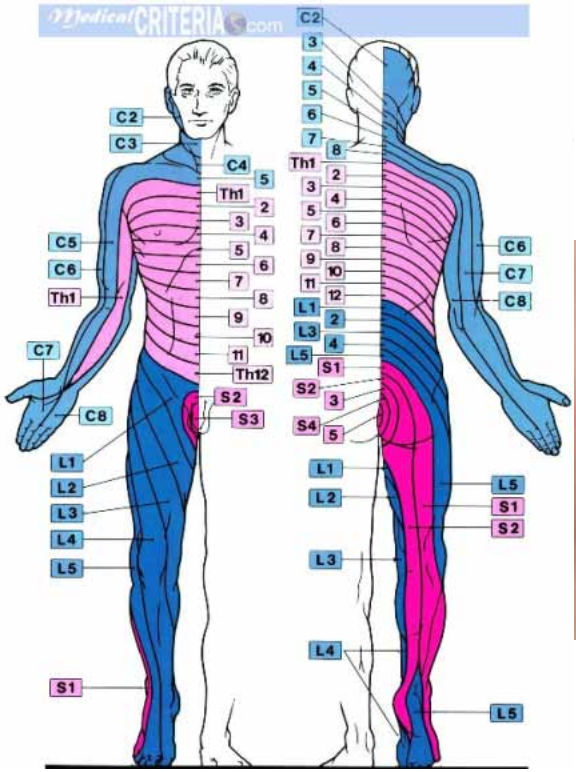
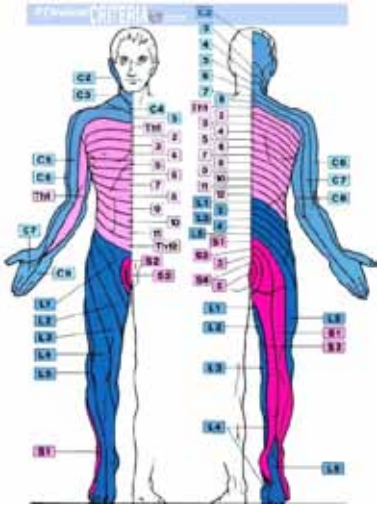
Herpes Zoster



Herpes Zoster

- Generally limited to one dermatome.
- Thoracic and lumbar dermatomes are the most commonly involved sites.
- ~20% have systemic symptoms, e.g. headache, fever, malaise, or fatigue



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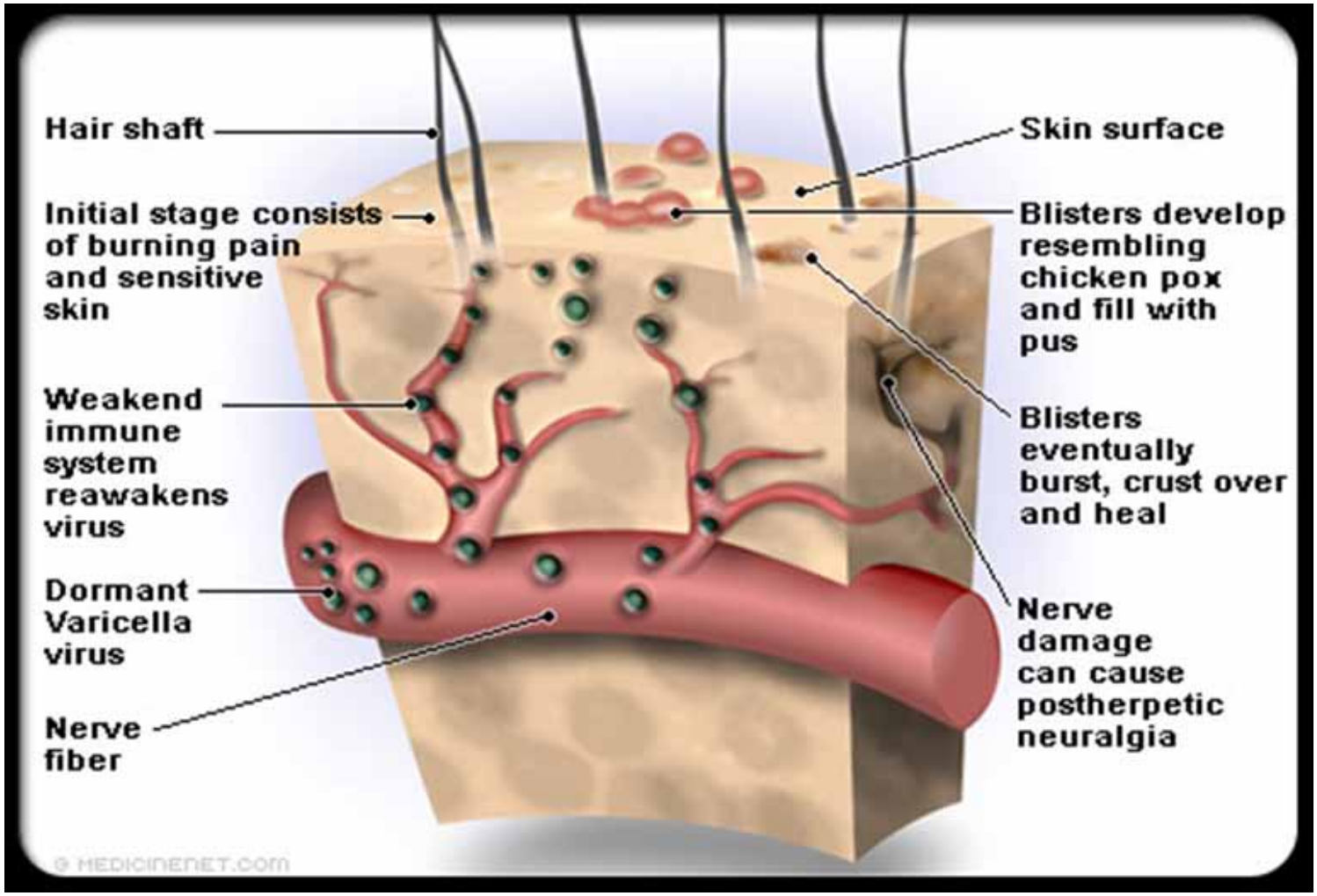
www.medicalnewstoday.com

Herpes Zoster

- Pain is the most common symptom of zoster; approximately 75% of patients have prodromal pain in the dermatome where the rash subsequently appears.
- Prodromal pain may be constant or intermittent and can precede the rash by days to weeks


Hair shaft
Initial stage consists of burning pain and sensitive skin
Weakend immune system reawakens virus
Dormant Varicella virus
Nerve fiber
Skin surface
Blisters develop resembling chicken pox and fill with pus
Blisters eventually burst, crust over and heal
Nerve damage can cause postherpetic neuralgia
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Herpes Zoster

- A more serious infection, such as zoster keratitis or zoster ophthalmicus, can result from involvement of the ophthalmic branch of the trigeminal cranial nerve

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Etymology

- **Herpesviridae** is derived from the Greek word *herpein* ("to creep"), referring to the latent, recurring infections typical of this group of viruses.
- ***Zoster*** comes from Greek *zōstēr*, meaning "belt" or "girdle", after the characteristic belt-like dermatomal rash.
- **Shingles**, derives from the Latin *cingulus*, a variant of Latin *cingulum* meaning "girdle"

Transmission of VZV from Patients with HZ

Transmission of VZV from Patients with HZ

- Patients are not infectious before vesicles appear.

- Patients are no longer infectious when the lesions have re-epithelized.

Transmission of VZV from Patients with HZ

- Airborne transmission from localized zoster has been documented
- Varicella-zoster virus DNA has been found to widely contaminate the rooms of patients with dermatomal zoster[1]

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1. Lopez AS et al. Transmission of a newly characterized strain of **varicella-zoster virus** from a patient with **herpes zoster** in a long-term-care facility, West Virginia, 2004. J Infect Dis. 2008 Mar 1;197(5):646-53.

J Infect Dis. 2004 Mar 15;189(6):1009-12. Epub 2004 Feb 27.

Detection of aerosolized varicella-zoster virus DNA in patients with localized herpes zoster.

Suzuki K[1], Yoshikawa T, Tomitaka A, Matsunaga K, Asano Y.

Author information

Abstract

We examined the excretion of varicella zoster virus (VZV) in hospitalized patients with herpes zoster localized to the thoracic region whose skin lesions were covered with either hydrocolloid dressing agents (hydrocolloid group) or conventional gauze bandages (gauze group). The presence of VZV DNA in swab samples from lesion coverings, the throat, and filters of air purifiers was examined by use of a sensitive polymerase chain reaction assay. For the hydrocolloid group, VZV was detected in none of the samples from lesion coverings or air purifier filters; for the gauze group, VZV DNA was detected in samples from gauze coverings and air purifier filters for all 6 patients. VZV DNA was detected less frequently in throat samples from patients in the hydrocolloid group than in those from patients in the gauze group. The results of the present study suggest that hydrocolloid dressing agents prevent excretion of aerosolized VZV DNA from skin lesions of patients with localized herpes zoster.

PMID: 14999603 [PubMed - indexed for MEDLINE] Free full text

Transmission of VZV from Patients with HZ

- VZV DNA was detected by PCR on the surface of dressings and in room air purifier filters of the gauze group, but none of the samples from the hydrocolloid group.

J Infect Dis. 2008 Mar 1;197(5):654-7. doi: 10.1086/527420.

Varicella-zoster virus in the saliva of patients with herpes zoster.

Mehta SK[1], Tyring SK, Gilden DH, Cohrs RJ, Leal MJ, Castro VA, Feiveson AH, Ott CM, Pierson DL.

Author information

Abstract

Fifty-four patients with herpes zoster were treated with valacyclovir. On treatment days 1, 8, and 15, pain was scored and saliva examined for varicella-zoster virus (VZV) DNA. VZV DNA was found in every patient the day treatment was started and later disappeared in 82%. There was a positive correlation between the presence of VZV DNA and pain and between VZV DNA copy number and pain ($P < .0005$). VZV DNA was present in 1 patient before rash and in 4 after pain resolved and was not present in any of 6 subjects with chronic pain or in 14 healthy subjects. Analysis of human saliva has potential usefulness in the diagnosis of neurological disease produced by VZV without rash.

Transmission of VZV from Patients with HZ

- 54 patients with zoster who were treated with valacyclovir.
- 20 control subjects
- VZV DNA was detected in saliva in all HZ patients on Day 1 of treatment.
- No VZV DNA was detected in 82% of patients by Day 15.

Transmission of VZV from Patients with HZ

- Analysis of human saliva has potential usefulness in the diagnosis of neurological disease produced by VZV without rash.

- Whether saliva is a vehicle of transmission, however, is not known.

Diagnosis of HZ

- Clinical!
- Atypical skin lesions in immunocompromised hosts.
- DDx: HSV reactivation
- Diagnostic techniques include:
  - DFA
  - PCR

Risk Factors

Risk Factors

- Age (>60 years old)
- Malignancy e.g. lymphoma, leukemia
- Bone Marrow and solid organ transplantation
- HIV with CD4 count < 200 cells/microL

Risk Factors

- Cancer chemotherapy
- Corticosteroid therapy (daily dose >=20 mg/day of prednisone or equivalent for >= 14 days
- Immuno-modulatory therapy e.g. rituximab or TNF-α inhibitors

Cell-mediated Immunity

- A decline in cell-mediated immunity to VZV is observed in the elderly population and immunosuppressed hosts.
- ~ 30-40 % of persons over the age of 55 years do not have any detectable varicella-zoster virus-specific cell responses[1].
- Zoster immunization is associated with a boost in VZV-specific cell immune responses.

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1. Weinberg A et al. Influence of age and nature of primary infection on varicella-**zoster** virus-specific cell-mediated immune responses. J Infect Dis. 2010 Apr 1;201(7):1024-30.

Cell-mediated Immunity

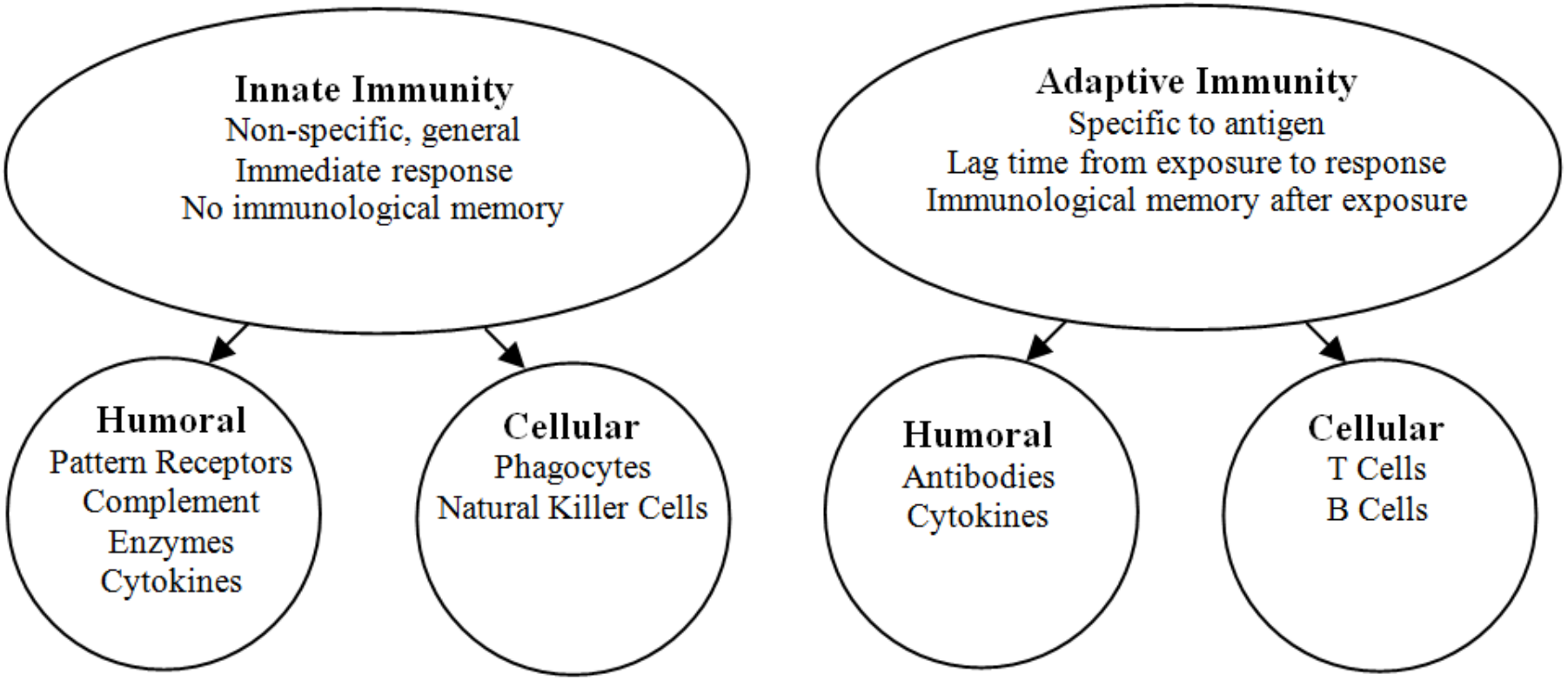
- Maintain latent VZV in a subclinical state in sensory ganglia.

- The magnitude of CMI responses at the onset of HZ correlates with the extent of diseases severity and risk of post-herpetic neuralgia.

Pathogens of concern

Intracellular pathogens:

- Herpesviridae, mainly herpes simplex, cytomegalovirus, **varicella zoster**
- *Listeria*
- Mycobacterium avium complex
- Salmonella species
- Pneumocystis jirovecii
- Toxoplasma
- Cryptosporidium
- Leishmania
- JC virus
- Cryptococcus neoformans



Role of ANC

- **Neutrophils** play important roles in the innate immune system.

- When neutrophils sense signals that an infection is present, they are the first cells to migrate to the site of the infection to begin killing the invading microbes.

- Severe neutropenia can lead to serious bacterial, and fungal infections.

Can we rely on ANC to define IC hosts at risk of VZV dissemination?

Epidemiology

- The average lifetime risk of herpes zoster (HZ) in developed countries is estimated to be ~ 30% and increases with increasing life expectancy[1].

- Incidence rate of HZ ranges from 1.2-3.4 per 1,000 person-years among younger healthy individuals, increasing to 3.9–11.8 per 1,000 person-years among those older than 65 years[2,3].

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1. Drolet M et al. (2010). The impact of herpes zoster and postherpetic neuralgia on health-related quality of life: a prospective study. CMAJ. 182(16):1731-6.
2. Dworkin RH et al. (2007)."Recommendations for the management of herpes zoster". *Clin. Infect. Dis*. 44 Suppl 1: S1–26.
3. Araújo LQ, Macintyre CR, Vujacich C (2007). "Epidemiology and burden of herpes zoster and post-herpetic neuralgia in Australia, Asia and South America". *Herpes* **14** (Suppl 2): 40A–44A.

Impact of Varicella vaccine on Incidence of HZ

www.adelaidenow.com.au

Impact of Varicella vaccine on Incidence of HZ

- Adults with latent VZV infection who are exposed intermittently to children with chickenpox receive an immune boost.
- This periodic boost to the immune system helps to prevent shingles in older adults.

Impact of Varicella vaccine on Incidence of HZ

- There is a concern that widespread varicella immunization in childhood may increase the incidence of HZ and may lead to an earlier age of onset of zoster reactivation in the general population

Impact of Varicella vaccine on Incidence of HZ

- The incidence of varicella decreased between 1995 and 2002 (from 2.63 cases to 0.92 cases/100 person-years), but the incidence of herpes zoster remained stable.

- A study from 1992 to 2010, the incidence of HZ increased 39 percent over this time period from 10.0 per 1000 person-years in 1992 to 13.9 per 1000 person-years in 2010. However, the widespread use of the varicella vaccine after 1996 did not appear to affect this increase.

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1. Jumaan AO et al. Incidence of herpes zoster, before and after varicella-vaccination-associated decreases in the incidence of varicella, 1992–2002. J Infect Dis 2005;191:2002-7
2. Hales CM et al. Examination of links between herpes zoster incidence and childhood varicella vaccination.Ann Intern Med. 2013 Dec 3;159(11):739-45.

Impact of Varicella vaccine on Incidence of HZ

- Other factors: aging of the population, changes in therapy for malignant and autoimmune diseases, and changes in chickenpox vaccination rates.

- However, a wide adoption of zoster vaccination could dramatically reduce the incidence rate of HZ.

Infection Prevention and Control Measures

webbertraining.com

Importance of IPAC Measures

- VZV is highly contagious
- Although a relatively benign disease, it may be associated with serious complications e.g. pneumonia
- Severe complications in immunocompromised patients
- Infection in pregnancy may lead to congenital varicella syndrome

Isolation Precautions

- Routine Practices/Contact Precautions:
  - Immunocompetent patients with dermatomal zoster

- Airborne and Contact Precautions:
  - Disseminated zoster
  - Immunocompromised patients with dermatomal zoster

Zoster Vaccine

Zoster Vaccine

- Live attenuated vaccine
- Approved for use in 50 years and older
- Reduces the incidence of HZ by ~51%
- Reduces the duration of pain and discomfort
- Incidence of post-herpetic neuralgia is reduced by ~67%

Summary

- Management of patients with herpes zoster infection depends on their immune status.
- A decline in VZV specific cell-mediated immune responses is the major precipitant for VZV reactivation and dissemination.
- ANC should not be used to define who is at risk of dissemination

QUESTIONS?