



HERPES SIMPLEX IN HUMANS

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Presented by Harry Hazelwood, MD, MPH

Reproductive Health Research

WHO, Geneva

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Introduction

- The HSV-2 virus, often called, Genital Herpes, is a devastating virus which often causes widespread, disseminated recurrent illness in adults.
- HSV-2 is a cause of the Herpes Zoster Virus (HZV) which is also known as "Shingles".
- Post-Herpetic Neuralgia, a painful condition is also attributed to HSV-2.

Introduction (continued)

- Post-Herpetic Neuralgia is very painful and can be very debilitating and crippling
- Neonates are most-often affected with the HSV-2 virus by their passage through the vaginal birth canal-producing blindness, deafness, and stillbirth

Introduction (continued)

- To prevent this outcome, all women who are showing ACTIVE Herpes lesions are delivered routinely by Caesarean Section (C-section)

Introduction (continued)

- Recent advances in immunology and vaccinology have led to the creation of a novel vaccine which may make these heretofore risks and issues concerns of the past

Study Design and Methodology

- The Herpes Zoster Shingles study was conducted by the National Institutes of Health, VA system, and Merck Pharmaceuticals
38,546 healthy subjects >60 were enrolled in the study, and were randomized into two groups: one receiving the experimental Herpes Vaccine (Zostavax), and one group used as the Control group

Study Design and Methodology

- The group receiving the experimental vaccine received an attenuated Varicella Zoster Virus (VZV) with an antibody titer which was 14 x higher than that of the Varicella vaccine.

Primary efficacy endpoints used were the incidence of Shingles, the burden of illness (defined as Zoster incidence x intensity x duration), and the incidence of Post-Herpetic Neuralgia

Study Design and Methodology

- Monthly telephone follow-up calls were used to find cases and adverse events
- Median follow-up was done approximately every 3-years

Design and Methodology

- A one-hour long Herpes Virus Powerpoint tutorial on the Pathogenesis, Treatment-Modalities and rationale for vaccination was provided to both the Experimental vaccine group and the Control Group receiving Placebo
- This educational intervention provided both background on Herpes Simplex Viruses and also served as a Post-vaccination Assessment tool which enabled us to assess the intervention



The Educational Intervention

- The following Powerpoint Tutorial was used as an Education tool in order to provide an educational framework about the Epidemiology, Pathogenesis, Course of Disease, Treatment-Modalities, and the role of Vaccine in preventing Herpetic lesions and recurrent illness

HERPES VIRUSES

- **α -herpesvirinae: Neutrotrophic**
- Simplex virus human herpes virus 1, 2 (HSV-1, HSV-2) Varicello virus human herpes virus 3 (VZV)
- **B-herpesvirinae:**
- Cytomegalovirus human herpes virus 5
- 1 Roseolovirus human herpes virus 6, 7 (HHV HHV7).
- **γ -herpesvirinae: Lymphocryptovirus**
- human herpes virus 4 (EBV)
- Rhadino virus human herpes virus 8 (HHV-8)

HSV PATHOGENESIS IN CARTOON REPRESENTATION

- HSV Structure
- Receptor Binding
- RNA Transcription in Productive Infection
- DNA Replication
- Encapsulation and Nuclear Egress
- Release
- Latent Infection

HSV structure

- 1 Inner core viral genome double stranded linear DNA
- 2 Icosadeltahedral Capsid -162 capsomers of 5 diff. proteins
- 3 Tegument or Matrix – multiple viral proteins
- 4 Outer envelope with 10 glycoproteins-gB gC gD gE gG gH gI gK gL and 2 glycosylated proteins.

HSV 1 152,260 base pairs

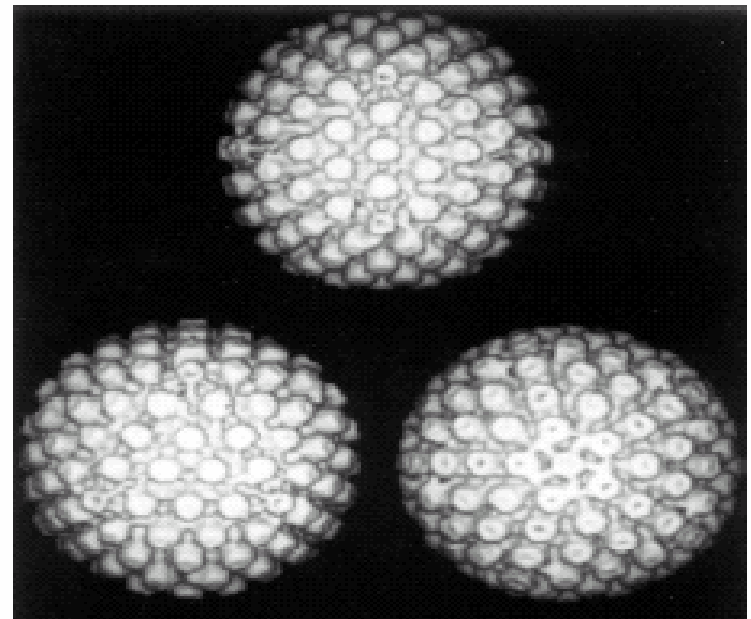
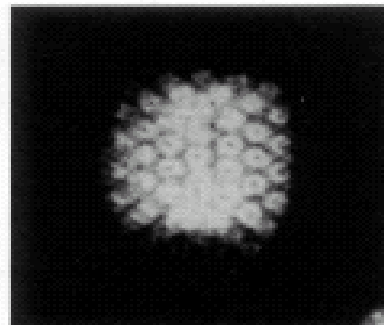
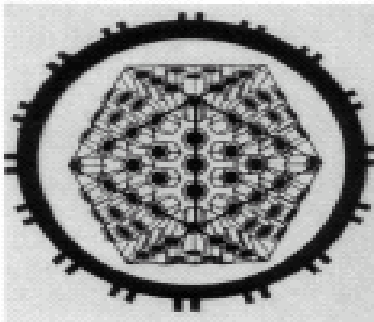
Open Reading Frames ORF

Latently associated transcripts

HSV 2 156,746 base pairs

90 in total

LAT

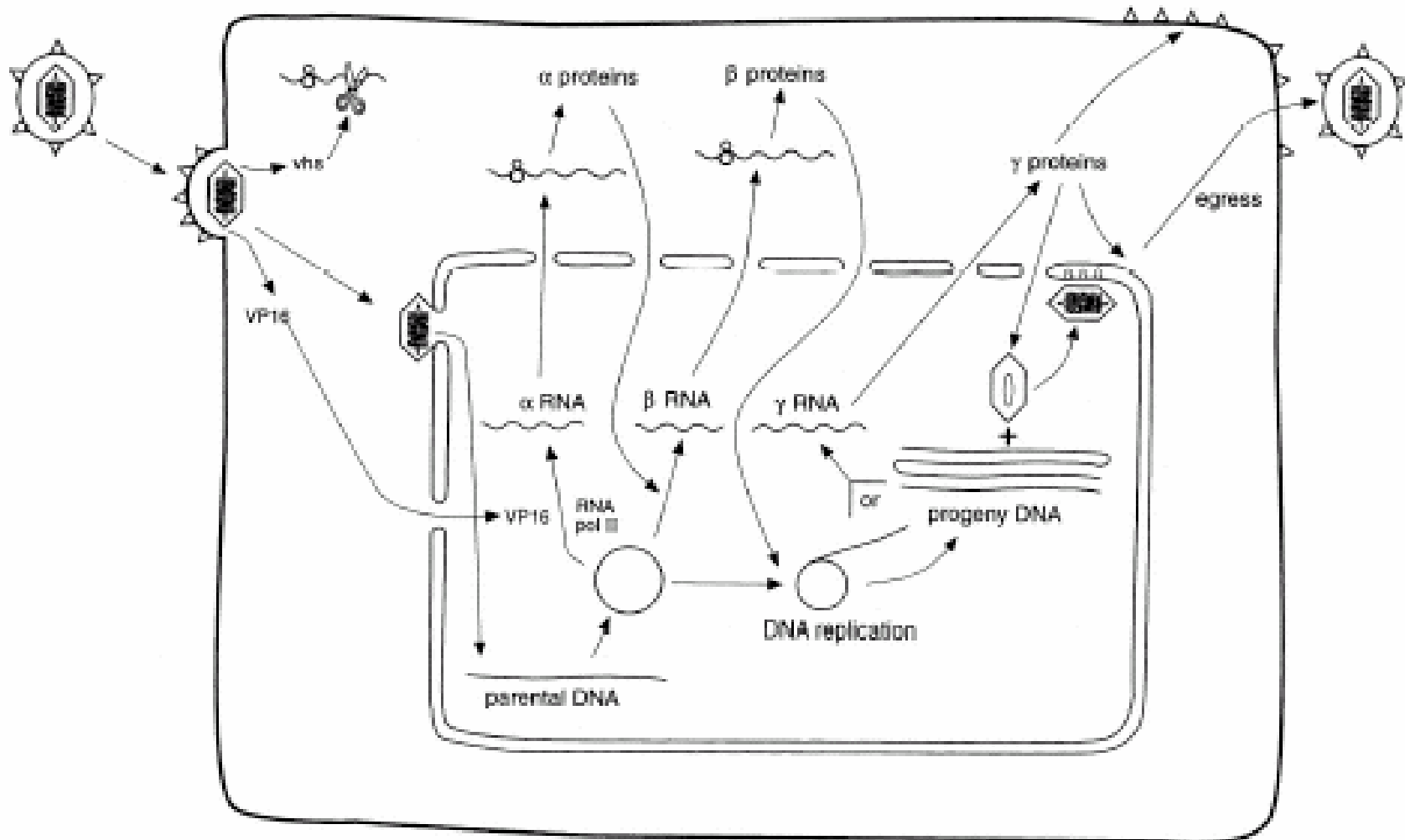


HSV STRUCTURE

HSV – Takes ~20 hrs from entry to exit

DNA REPLICATION

ENCAPSIDATION & EGRESS



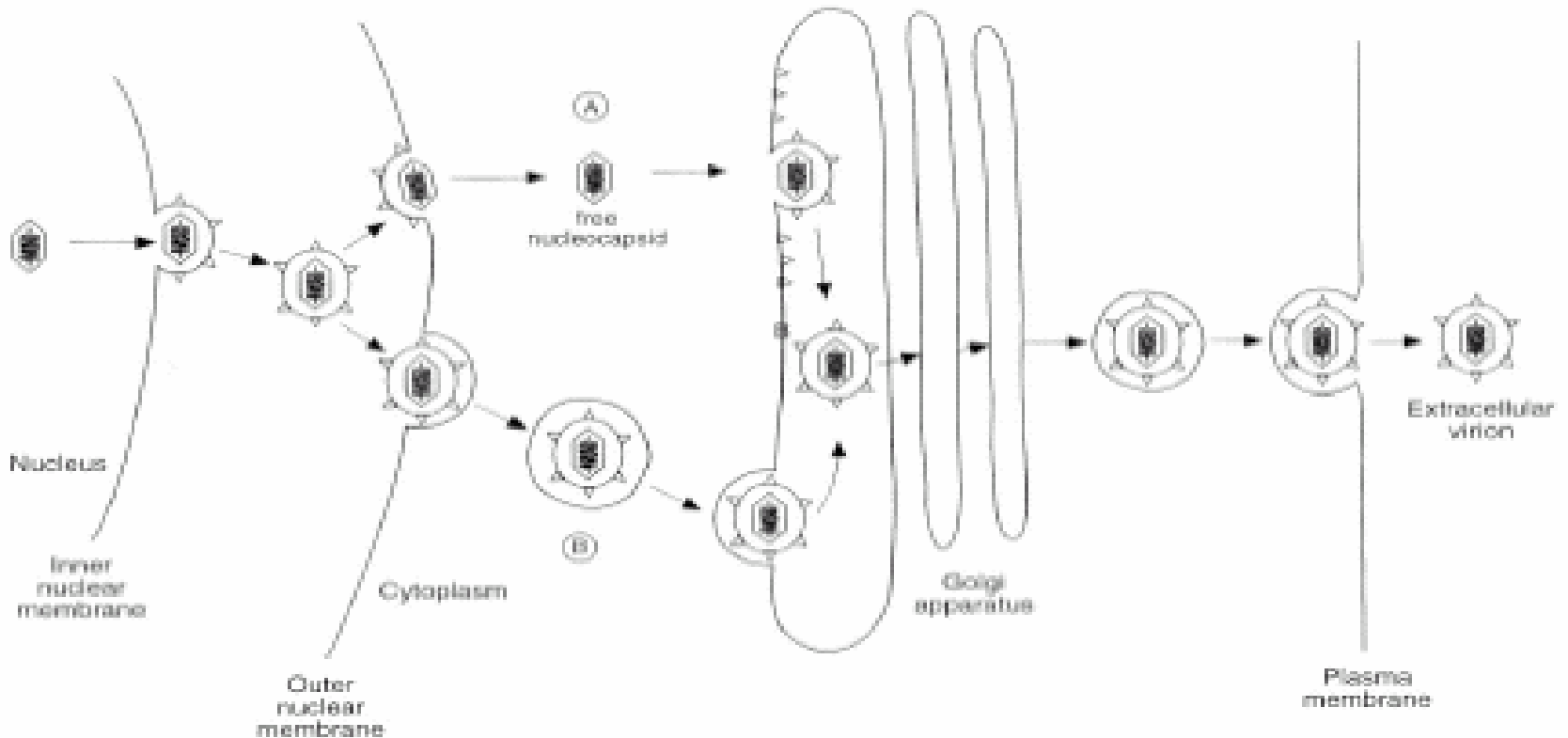
Capsulation and Release

1 Through Inner, Outer Nuclear membrane

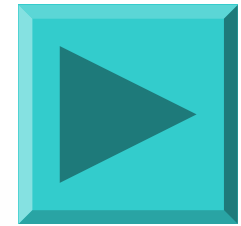
2 Cytoplasm and Golgi Apparatus & Plasma Membrane



RELEASE

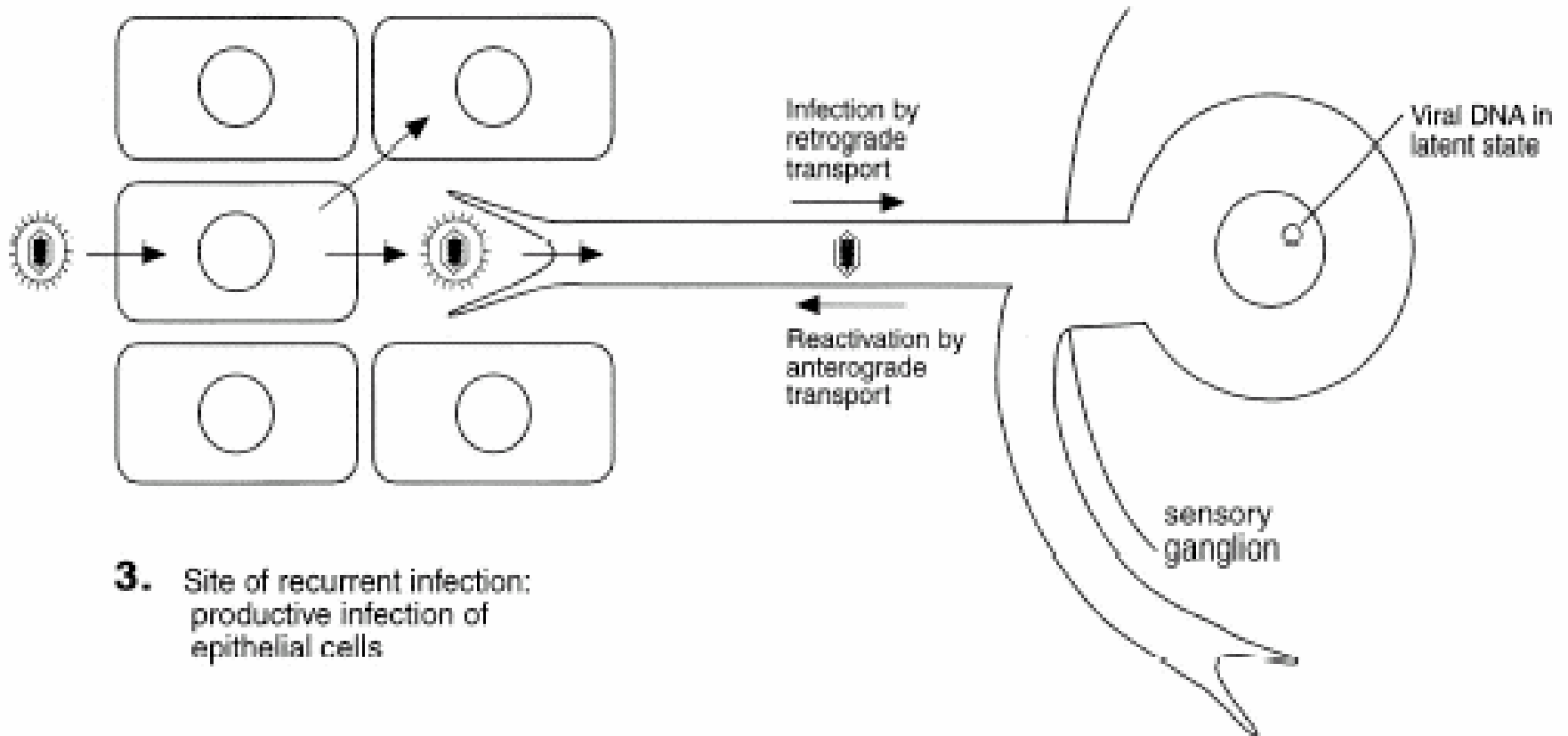


LATENCY

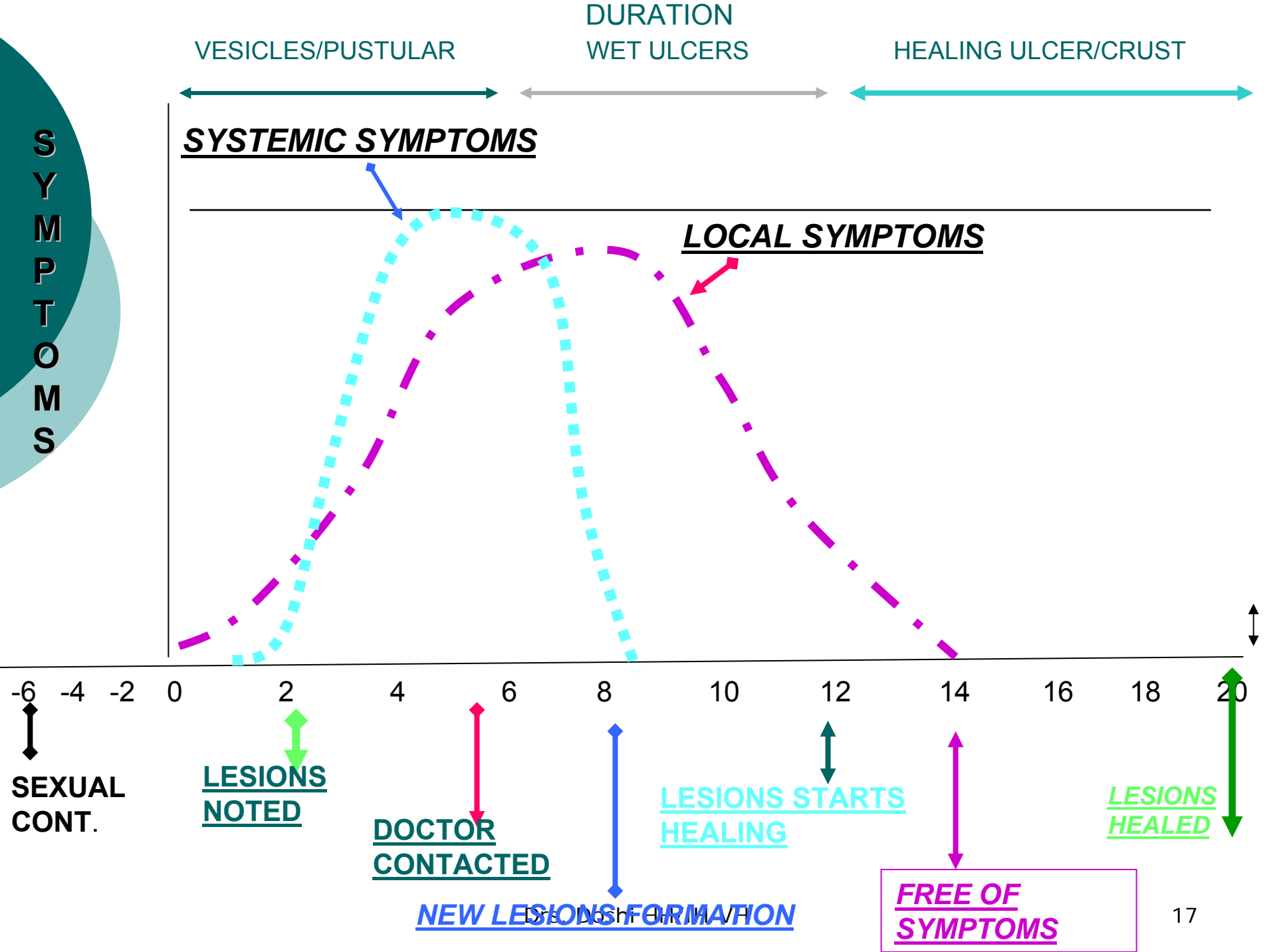


1. Primary site of infection:
productive infection of
epithelial cells

**2. Secondary site of infection
and site of latent infection:**
sensory neuron



3. Site of recurrent infection:
productive infection of
epithelial cells



1st Episode of 1st Primary HSV

○ LOCALLY:

○ In Males: :

- Pain, burning, tingling, grouped vesicles, ulcers
-

○ Lesions:

- **Grouped vesicles, sup. Ulcers on glans, prepuce or even shaft penis**

○ In Females:

- Severe vulvitis, vaginitis, dysuria, hematuria, discharge leading to retention

○ **Lesions:**

- **Inflammation of vulva- edematous, tender numerous sup. ulcers,**

% Sym & Signs of Primary HSV-2 Inf. In M & F

Males Females

	<u>Males</u>	<u>Females</u>
<u>% with Constitutional Symptoms</u>	39	68
<u>% with Meningitis Symptoms</u>	11	36
<u>% with local pain (duration)</u>	95(11)	99 (12)
<u>% with Dysuria</u>	44	83
<u>% with urethral / vag. discharge (days)</u>	27(6)	85(13)
<u>% with local tender lymphadenopathy (days)</u>	80(9)	81(14)
<u>Mean area of lesions per sq. mm</u>	427	550
<u>Mean duration of viral shedding from lesions</u>	10.5	11.8
<u>% with HSV isolated from urethra</u>	28	76
<u>% with HSV isolation from cervix (days)</u>	88	(11.4)
<u>Mean duration lesions days</u>	16.5	19.7

HSV - RECURRENCE

- 50-70% recurrence are asymptomatic, the main transmitters. Patient either unaware or not worried
- Women may have mild itch of vulva &/or discharge. Seen only at routine Pap Smear.
- In men, many – prodromal symptoms and recurrent trouble ulceration.
- Most men oblivion of recurrence.
- Rx: Episodic Acyclovir / Famciclovir / Valacyclovir
- SUPPRESSIVE: Can be given 6/12 – 1 year or more.
- Has been found to prevent transmission to unaffected partners. Acyclovir in dose of 800 mg BD or VALACYCLOVIR 500 – 1000 mg daily
- LOOK FOR OTHER SITES OF RECURRENCES

OTHER & NEW EMERGING CONDITIONS

1. Keratitis – in primary orofacial HSV-1 esp. in neonates
2. Herpetic Whitlow – periungual a painful infection
3. Herpetic Gladiatorum – sportsman in contact sports
4. Erythema Multiforme (strong precipitating factor)
5. Eczema Herpeticum (widespread cut. HSV in A.D.)
6. Pneumonia
7. Bell's Palsy* (presence of HSV 2 by PCR)
8. Mollaret's Meningitis* (recurrent aseptic mening.)
9. Alzheimer's Disease* (human ApoE4 gene allele)

HSV - Specific Laboratory Tests

as per 2002 CDC recommendation

- Genital Ulcer Swabs or vesicle fluid in viral transport medium for VIRUS ISOLATION, CULTURE or for PCR
- WRIGHT'S OR GIEMSA stain of ulcer scrapping for intra-nuclear inclusion or multi-nucleated giant cell
- Direct IF on smears
- Serology maybe useful in primary, surveillance, but not for recurrent infection
- MULTIPLEX PCR to detect HSV, &/or T.Pallidum and H.Ducreyi

	Virus Culture	Antigen IMF Tzanck Test	Antigen EIA	Nucleic Acid/PCR
Smears	Swabs/Scraps	Smear/tissue section	Swabs/Scrapings	Swabs/Scrapings
Sensitivity	High >90%	Low	80%	Highest
Specificity	High	High	High	Importance to have cross controls
Advantage	Allow virus typing using monoclonal testing	Inexpensive	Cost & Speed	High Sensitive, allows viral typing
Disadvantage	Labor-intensive, Expensive	Insensitive	Insensitive, No viral typing	Not available everywhere Expensive

Diagnosis

Mucocutaneous Lesion:

- Genital Lesions –
 - Syphilis, Chancroid and Other genital ulcerative conditions
- Oral Lesions –
 - Aphthous ulcers and Oral candidiasis esp., in AIDs patients
- Proctitis
 - GC, Chlamydia, other perianal ulcer conditions
- Esophagitis
 - C. albicans and CMV Esophagitis
- Encephalitis
 - Toxoplasmosis, Tuberculoma, Lymphoma, HIV encephalitis
 - Progressive Multifocal Leucoencephalitis, PML,
- Meningitis
 - TB, Aseptic and other Meningitis

MANAGEMENT

ANTIVIRALS:

- Acyclovir, is time proven. Started by the 3rd or 4th day for. 200 mg 5 hourly x 5 days OR
- Famciclovir 250 mg 8 hourly x 5 days OR
- Valaciclovir 500mg 12 hourly x 5 days
- In severe cases: IV 10 mg / Kg / 3 x daily
 - IV does not change the natural history of HSV
- SUPPORTIVE
 - Analgesics, Saline bathing of ulcers, Gargles for oral ulcers
- COMPLICATIONS:
 - Urine Retention – by suprapubic catheterization
- COUSELING:
- SPECIFIC CIRCUMSTANCES

DRUG RESISTANCE – ALTERNATIVE

- Deficiency of Thymidine Kinase activity, HSV resistance have emerged, esp., in HIV patients
- Forscarnet: Dose 40 – 60 mg /kg. x 3/day x 15/7
- Cidofovir: IV
- Topical 1% Trifluridine
- Topical Forcanet cram
- Cidofovir gel

HSV in Pregnancy - 1

- First Episode Primary – in line with her clinical condition
 - 1st & 2nd Trimester: **oral or IV acyclovir in standard doses. Acyclovir in last 4 weeks** followed by LSCS
 - 3rd Trimester: **LSCS for all**, as viral shedding is high esp., if acquired in last 8 weeks. **Acyclovir for both mother & child**
- Recurrent HSV – Viral cultures not reliable for prediction
 - Vaginal delivery possible if no active lesion. However, cover with acyclovir due to 1-3% chance. Monitor the baby.
 - LSCS does solve the problem. Discuss with patient
- HSV Lesions at onset of labour:
 - LSCS with coverage for both with Antivirals
- Prevention of acquisition of infections:
 - Screen at first ANC.
 - No sex if partner is HSV recurrence.
 - Use condoms. Oro-genital contact: PNC acquisition of HSV

HSV – Neonates & Infants --- 1

1. Incidence: 1/2000 - 1/5000 --- increasing
2. 50% affected infants born to women – asymptomatic delivery
3. Increased risk with primary vs. recurrent – 1-3%
4. 2/1000 mothers – asymptomatic - are culture positive

5. 50% risk: Infants born to women with primary (No antibodies against HSV 1 or 2) reasons for the increased risk – due to increased viral shedding ~ ~ 3 wks as compared to recurrent
6. Neonatal risk factors
 1. Rupture membranes for > 6 hrs
 2. Scalp electrodes
 3. Chorioamionitis & Cervicitis
 4. Vaginal Delivery

7. Antepartum culture not useful in risk assessment

HSV - Neonatal & Infants --- 2

- Disseminated HSV – most lethal- by 9-11th day – pneumonitis, hepatitis, intravascular coagulation with/out encephalitis, exanthema, &/or kerato-conjunctivitis
 - Mortality Without Rx 80% With Rx 57%
 - Survivors few – Neurological & other complications
- CNS: 70% mortality. 10% with Rxed- eventually die
 - Irritability, Seizures, Thermal Instability, Bulging fontanallae
- Ocular: Kerato-conj., Chorio-retinitis leading to ulcers, optic atrophy & blindness
- Oral: Mucosal ulcers & mucocelles
- Cutaneous: Typical clustered vesicles
- TREATMENT: BY PAEDIATRICIAN :
 - IV acyclovir 45 mg /Kg/ day x 14 days
 - Topical Trifluorothymidine
 - Outcome poor

HSV – in HIV patients

- IN HIV PATIENTS: Lesions are severe, protracted and all too often resistant to standard treatment of HSV
- If they fail to respond to standard dose increase to 800mg 5 hourly daily, repeat culture/PCR
- Trifluoridine locally 8 hourly
- IV foscarnet 50 mg /kg x 2 days
- Discuss with patient and partner about the asymptomatic shedding
- Counseling

TAKE HOME MESSAGE

1. **COUNSEL** AND TRY TO EDUCATE YOUR PATIENT
2. DO NOT SERMONISE
3. GENITAL HSV-1 IS ON THE RISE
4. **MONOGAMY** IS THE BEST POLICY
5. **CONDOMS** DO PREVENT TO CERTAIN EXTEND
6. **FDA HAS APPROVED** USE OF SUPPRESSIVE VALACYCLOLVIR AS A FORM OF PREVENTION OF HSV IN DISCORDANT PARTNERS

THANK YOU

Zoster: It's Now a Vaccine Preventable Disease

**Presented by Dr Harry Hazelwood
M.D., MPH**



Outline

- Clinical manifestations of zoster
- Epidemiology of zoster
- The pivotal zoster vaccine study
- Provisional recommendations regarding zoster vaccine

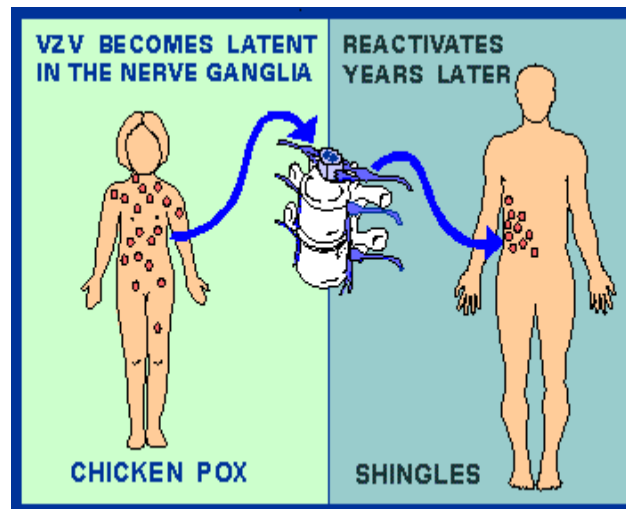
Clinical Manifestations of Zoster



Definition:

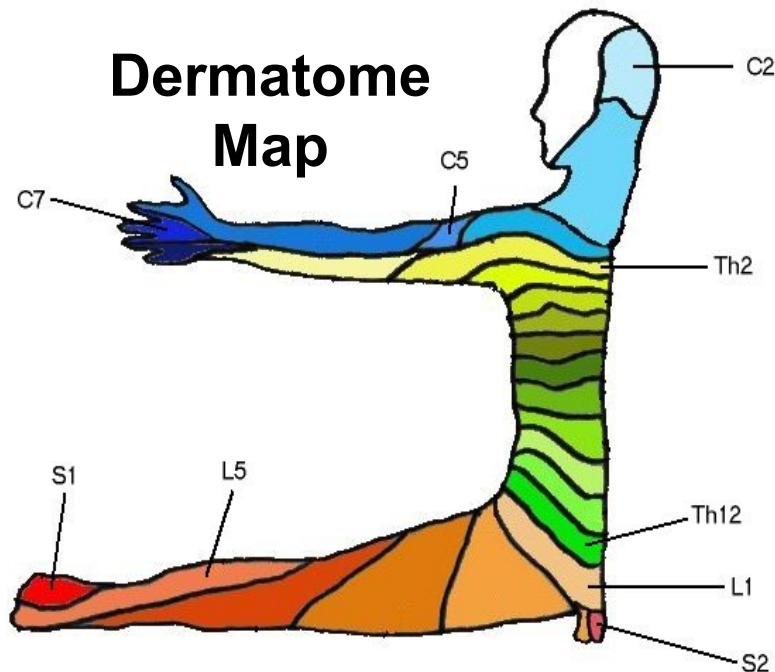
Zoster (herpes zoster, shingles): reactivation of varicella zoster virus (VZV), leading to crop of blisters in a dermatomal distribution

- Following initial infection (chickenpox), VZV establishes a permanent latent infection in dorsal root ganglia along neuraxis
- Years to decades later VZV reactivates
- VZV virions reappear & spread to skin through peripheral nerves



Primary Manifestations of Zoster

A vesicular rash in dermatomal pattern
(dermatome: an area of skin supplied by sensory nerve fibers coming from one nerve root)



Primary Manifestations of Zoster: Signs

Rash:

- Unilateral; 1-3 adjacent dermatomes (+/- few scattered lesions)
- Distribution in order of frequency: 1) thoracic > 2) lumbar, trigeminal, & cervical > 3) sacral, other cranial dermatomes
- Duration of rash
 - New lesions can arise over ~5-7 days
 - Evolve from erythematous maculopapules to vesicles +/- pustules
 - Crust forms over 7-12 days, with full resolution in ~5-25 days
- Occasional consequences of rash
 - Secondary infections
 - Scarring and changes in pigmentation
 - Can transmit VZV to susceptible children, causing chickenpox
 - Zoster perhaps 1/5th as contagious as chickenpox

Fever & regional adenopathy can occur

Classic Zoster Rashes: Thoracic, Lumbar Distribution



Classic Zoster Rashes: Cranial (Trigeminal) Distribution



Primary Manifestation of Zoster: Symptoms

Occasional headache, photophobia, malaise

Key symptom is pain

- Can be excruciating (e.g., like renal colic, childbirth)
- Described as aching, burning, stabbing, shock-like
- Continuous or paroxysmal
- Often associated with:
 - Altered or painful sensitivity to touch (paresthesia, dysesthesia)
 - Provoked by trivial stimuli like bed sheets or breeze (allodynia)
 - Exaggerated, prolonged response to pain (hyperesthesia)
 - Unbearable itching

Primary Manifestation of Zoster: Symptoms

- Zoster accompanied by pain prior to rash in ~84% of cases
 - Starts as abnormal skin sensation, itching or tingling
 - Precedes rash by 1-5 days but occasionally weeks or more
 - On occasion, rash never develops (zoster sine herpete)
 - Diagnostic dilemmas & work-ups (e.g., cardiac, gallbladder)
- Zoster accompanied by some degree of pain during rash in ~89% of patients

Complications of Zoster: Post Herpetic Neuralgia (PHN)

- Prolonged, sometimes incapacitating, pain after resolution of rash
 - Variable definitions of “prolonged” by clinicians and researchers
- May persist months or even years; some experience recurrence
- PHN prevention (antivirals +/- steroids): partial, inconsistent efficacy
- PHN treatment (multiple modalities): partial, inconsistent efficacy

Complications of Zoster: PHN

Impact on Quality of Life

- Comparable to congestive heart failure, diabetes, and depression.

Physical	Psychological
<ul style="list-style-type: none">○ Chronic fatigue○ Anorexia & weight loss○ Physical inactivity○ Insomnia	<ul style="list-style-type: none">○ Anxiety○ Difficulty concentrating○ Depression, suicidal ideation
Social	Functional
<ul style="list-style-type: none">○ Fewer social gatherings○ Change in social role	<ul style="list-style-type: none">○ Interferes with activities of daily living: dressing, bathing, eating, travel, cooking, shopping

Schmader KE. Clin Infect Dis 2001;32(10):1481-6

Complications of Zoster: Herpes Zoster Ophthalmicus (HZO)

- Involvement of ophthalmic division of trigeminal nerve
- ~ 15% of zoster cases
- Untreated, 50-70% develop acute ocular complications
- Can lead to chronic ocular complications, reduced vision, even blindness
- No known risk factors for HZO



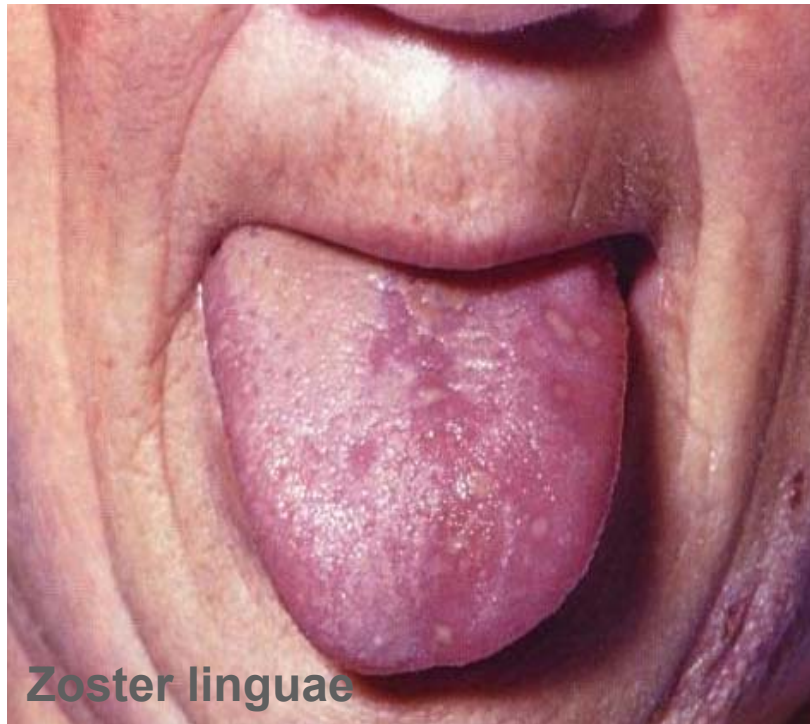
Courtesy of MN Oxman UCSD/San Diego VAMC.

Less Common Zoster Complications

Neurologic:

- Invasion by VZV of adjacent vascular or neurologic structures
 - Encephalitis, myelitis, optic neuritis, cranial / peripheral nerve palsies
 - Hearing impairment, vertigo, loss of taste sensation
 - Diaphragm paralysis, neurogenic bladder, colon pseudo-obstruction
- Oral:
 - Osteonecrosis of alveolar bone with exfoliation of teeth
 - Immunocompromised:
 - Above complications can have much more aggressive course
 - Dissemination: generalized rash +/- visceral involvement (pneumonia, encephalitis, hepatitis)
 - Complications coincident with rash or weeks to months later
 - Mortality rare in immunocompetent persons - deaths mostly occur among the immunocompromised

Epidemiology of Zoster



Zoster linguae

Epidemiology of Zoster in U.S.

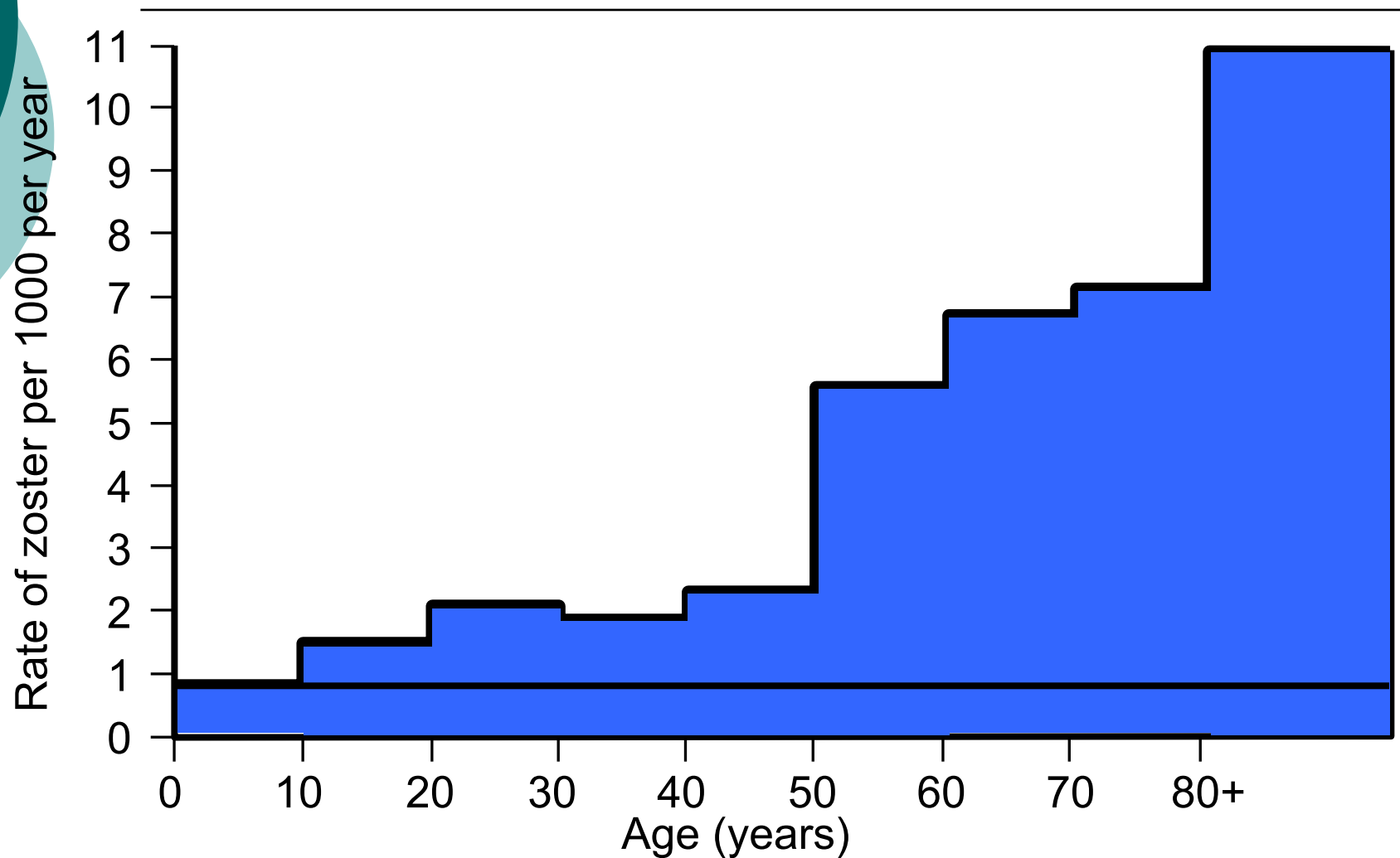
- Annual rate 3 to 4 per 1000 population per year (6 studies)
- ~1 million cases in the U.S. annually
- Rate appears to be increasing in recent decades
- Lifetime risk of developing zoster: about 30%
- Repeated episodes of zoster occur
 - Rate of repeats comparable to rates of first episode?

Risk Factors for Zoster

- Age (detailed in next slide)
 - Dominant factor influencing incidence in the population
- Immunosuppression
 - Less common but influential due to magnitude of risk, e.g.:
 - Following bone marrow transplant: 17-52%
 - Patients with hematological malignancies: 5-14%
 - HIV: risk increased 12-17 fold, and recurrences common

Risk Factors for Zoster: Age

Hope-Simpson, General Medical Practice, UK (1975)



Other Risk Factors for Zoster:

(inconsistent, unconfirmed or of lower magnitude)

Gender: most studies show risk ↑ in females

Race: risk in blacks less than half that in whites (U.K., U.S.)

From regions where varicella occurs at older ages: risk ↓
44%

- Local trauma: 30-day risk in affected area ↑ 12-fold
- Psychological stress: risk ↑ ~40% following stressful life events
- Pesticide exposure: risk ↑ 2-fold when living near disposal site
- Cigarette smoking: risk ↓ in one study, no effect in 2nd study
- Genetic: risk ↑ in certain haplotypes
- Early varicella (*in utero*, infancy): risk of pediatric zoster ↑
- Varicella exposure ("external boosting"): most studies show risk ↓

→ **However, we do not understand why some immunocompetent persons get zoster and others do not!!**

Epidemiology of PHN in U.S.

- Proportion of zoster patients that develop PHN:
 - 10% of zoster patients will have ≥ 90 days of pain
 - 18% of zoster patients will have ≥ 30 days of pain
- 100 to 200 thousand new PHN cases per year

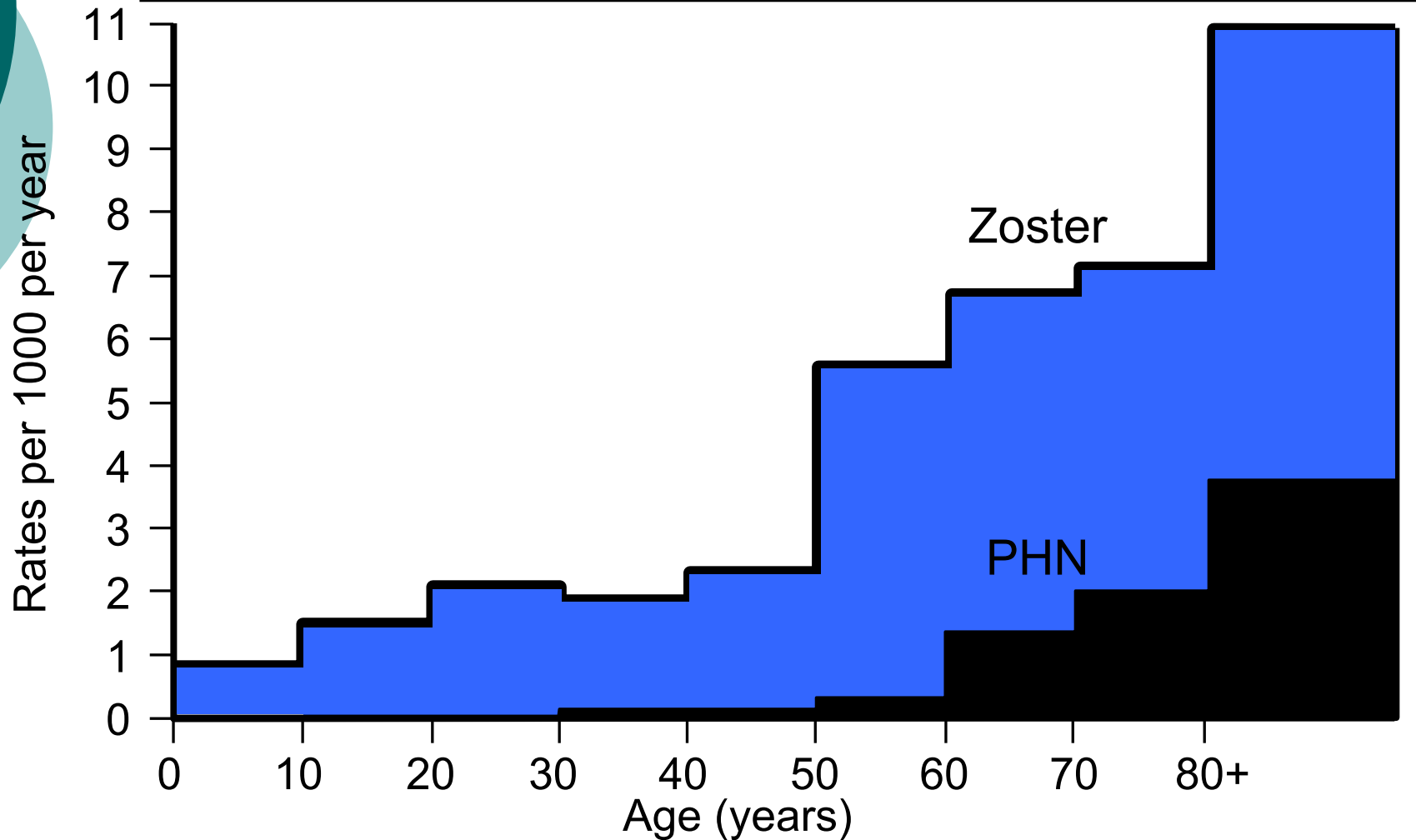
Risk Factors for PHN

Risk factors for PHN:

- Gender: risk may be greater among women with zoster
 - Dermatome: possibly increased following ophthalmic zoster
 - Immunosuppression is NOT strongly associated with PHN
- Of those with zoster, age is the key risk factor for developing PHN

Risk Factors for PHN (pain ≥ 30 days): Age

Hooper-Simpson, General Medical Practice, UK (1975)



Burden of Zoster in U.S. (Unpublished, Merck*)

- 12,000 to 19,000 hospitalizations
 - Average length of stay 5-7 days
- ~3 ambulatory visits per episode zoster
- >10 ambulatory visits per episode PHN (pain \geq 90 days)
- ~1/3 of zoster episodes involve \geq 1 visit to specialist
- Work loss per episode zoster: ~3-7 days

* Presented at ACIP, June 2006

The Shingles Prevention Study



The Shingles Prevention Study: Scientific Basis for a Vaccine

- Increased incidence in elderly & immunosuppressed
 - Both have decreases in VZV-specific cell mediated immunity
- Inactivated VZV reduces the burden of zoster in immunosuppressed
- High doses of live attenuated VZV vaccine stimulate cell mediated immunity in older adults
- Approach: use high-potency attenuated VZV to ameliorate or prevent zoster in VZV-infected individuals

The Shingles Prevention Study: Methods

- Double-blind, placebo-controlled, multicenter trial
- Collaborators: the VA system, the NIH, and Merck
- Enrolled 38,546 healthy subjects ≥ 60 years old
- Randomized: zoster vaccine vs. placebo
 - Attenuated VZV with titer $\geq 14X$ higher than varicella vaccine
- Primary efficacy endpoints:
 - Incidence of shingles
 - Burden of illness (BOI: zoster incidence X intensity X duration)
 - Incidence of PHN
- Monthly telephone follow-up to find cases and adverse events
- Median follow up about 3 years

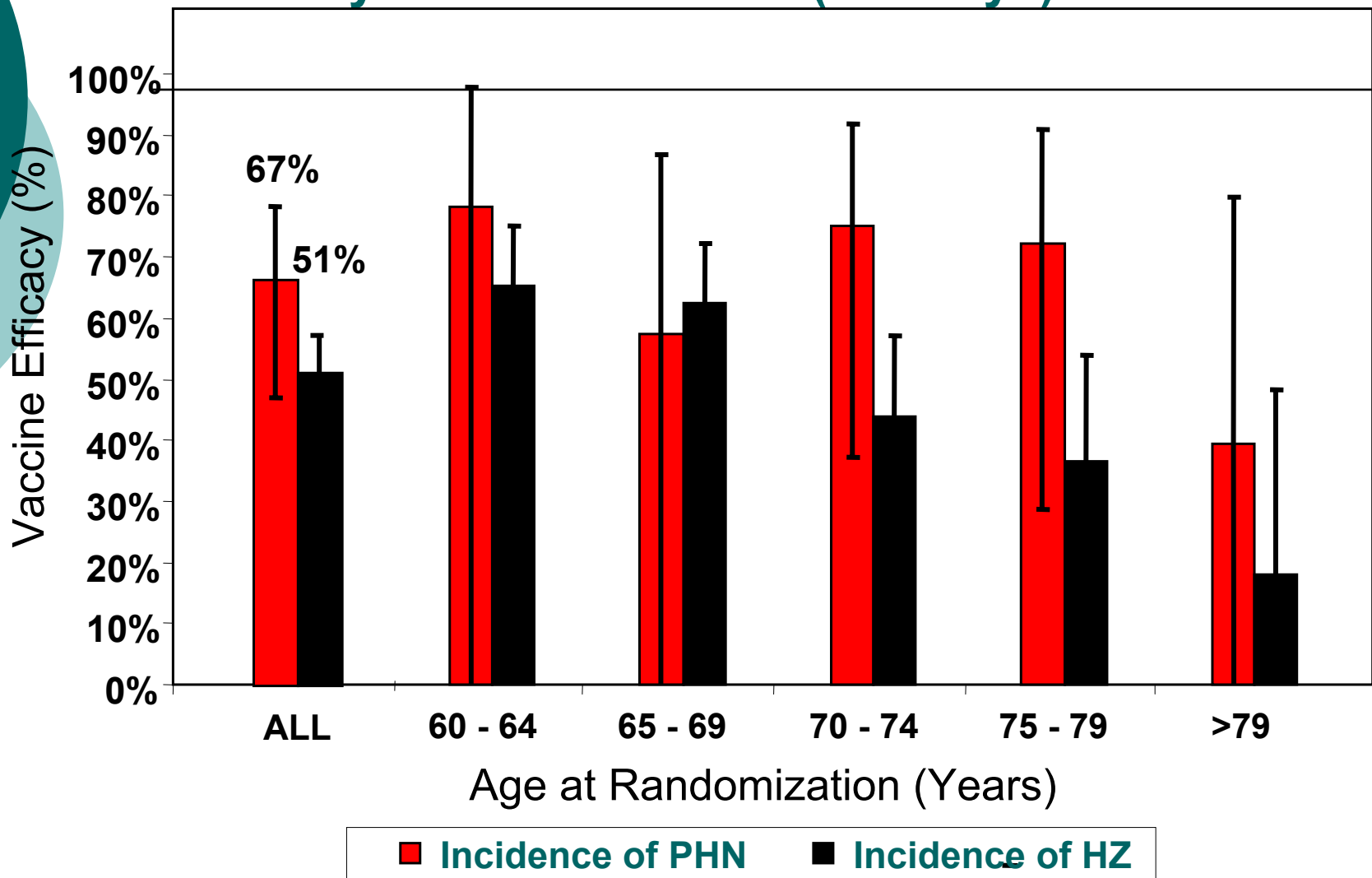


A Vaccine to Prevent Herpes Zoster and Postherpetic Neuralgia in Older Adults

M.N. Oxman, M.D., M.J. Levin, M.D., G.R. Johnson, M.S., K.E. Schmader, M.D., S.E. Straus, M.D., L.D. Gelb, M.D., R.D. Arbeit, M.D., M.S. Simberkoff, M.D., A.A. Gershon, M.D., L.E. Davis, M.D., A. Weinberg, M.D., K.D. Boardman, R.Ph., H.M. Williams, R.N., M.S.N., J. Hongyuan Zhang, Ph.D., P.N. Peduzzi, Ph.D., C.E. Beisel, Ph.D., V.A. Morrison, M.D., J.C. Guatelli, M.D., P.A. Brooks, M.D., C.A. Kauffman, M.D., C.T. Pachucki, M.D., K.M. Neuzil, M.D., M.P.H., R.F. Betts, M.D., P.F. Wright, M.D., M.R. Griffin, M.D., M.P.H., P. Brunell, M.D., N.E. Soto, M.D., A.R. Marques, M.D., S.K. Keay, M.D., Ph.D., R.P. Goodman, M.D., D.J. Cotton, M.D., M.P.H., J.W. Gnann, Jr., M.D., J. Loutit, M.D., M. Holodniy, M.D., W.A. Keitel, M.D., G.E. Crawford, M.D., S.-S. Yeh, M.D., Ph.D., Z. Lobo, M.D., J.F. Toney, M.D., R.N. Greenberg, M.D., P.M. Keller, Ph.D., R. Harbecke, Ph.D., A.R. Hayward, M.D., Ph.D., M.R. Irwin, M.D., T.C. Kyriakides, Ph.D., C.Y. Chan, M.D., I.S.F. Chan, Ph.D., W.W.B. Wang, Ph.D., P.W. Annunziato, M.D., J.L. Silber, M.D., for the Shingles Prevention Study Group

The Shingles Prevention Study: Results

Vaccine Efficacy for Zoster & PHN (≥ 90 days)



Vaccine Study Results

- The following slides summarize in tabular form the Results of the Herpes Virus Vaccine Efficacy clinical trials

The Shingles Prevention Study: Results

Vaccine Efficacy Versus PHN of Varying Duration

PHN Defined by Varying Duration (days)	Vaccine Efficacy VE_{PHN} (95% CI)
30	59% (47, 69)
60	60% (44, 73)
90	67% (48, 79)
120	69% (45, 83)
180	73% (42, 89)

Shingles Prevention Study: Results

Adverse Events

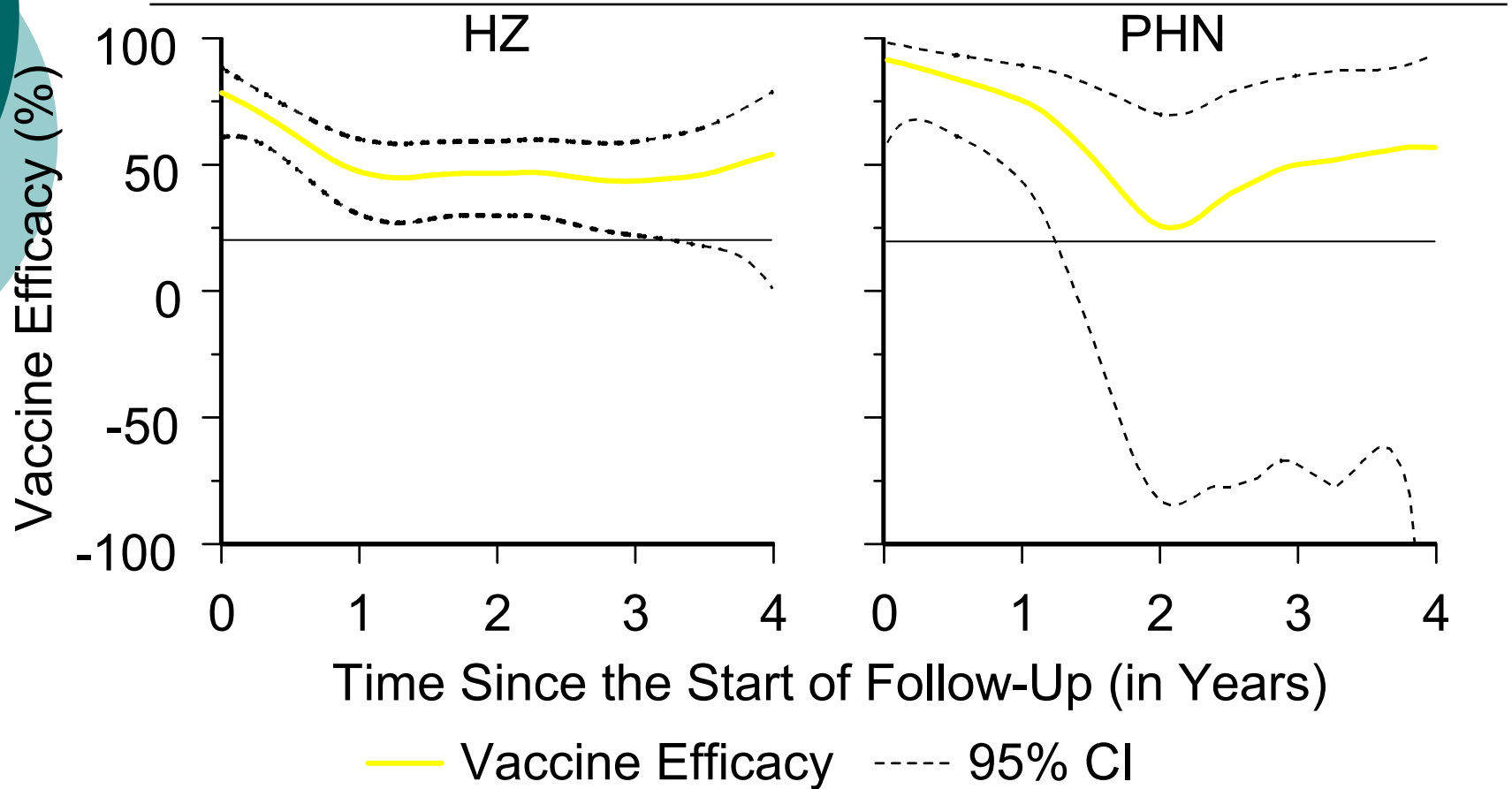
Appears to be safe:

- No pattern suggesting a causal link to serious adverse events
- Vaccine rashes did not occur in the trial
- Excess of mild reactions in vaccines:

	Zoster Vaccine N=3345	Placebo N=3271
Local injection-site reaction :	48%	17%

The Shingles Prevention Study: Results

Duration of Vaccine Efficacy



Provisional Recommendations Regarding Zoster Vaccine



FDA Licensure: May 2006

- Indicated for prevention of shingles in persons ≥ 60 years
- Not indicated for the treatment of shingles or PHN
- Contraindications:
 - History of anaphylaxis to vaccine components
 - Immunodeficiency and immunosuppression

Provisional ACIP Recommendations: October 2006

- A single dose of zoster vaccine recommended for adults ≥ 60 years of age whether or not they report a prior episode of zoster
- It is not necessary to assess a history of chickenpox
- Should be offered at the 1st clinical encounter
- Residents of chronic care facilities should be included in vaccination efforts as appropriate

Role of Varicella Exposure on Risk of Zoster

Evidence that varicella exposure (external boosting) can prevent zoster

- Biologically plausible
 - Risk ↓ 86% in persons with ≥ 5 exposures to varicella
 - Risk ↓ 25-30% in persons living and working with children (surrogate for varicella exposure)
 - Risk ↓ in pediatricians
 - Risk ↓ in leukemic children following household exposure
 - Results of zoster vaccine trial itself: external boosting effective
- Methodologic flaws in individual items but together these make a strong case varicella exposure can prevent zoster, at least in theory
 - If so, it is possible that reduced varicella circulation due to vaccine program could increase the incidence of zoster

Role of Varicella Exposure on Risk of Zoster

Unresolved issues: external boosting & impact of varicella program

External boosting may be sufficient to prevent zoster but is it necessary?

- VZV in ganglia may reactivate subclinically, boosting anti-VZV immunity
- Can such internal boosting compensate when external boosting declines?
- How much varicella exposure needed to be effective?
 - Thomas paper: 5 varicella exposures needed to see effect
 - How relevant is such a magnitude of exposure to general population?
- How prolonged is the effect?
- Does exposure protect the elderly at risk of zoster as well as the young?
- Might reduced exposure increase zoster incidence but shift it to the young?
 - Since PHN risk low in young, this could paradoxically reduce burden
 - Thus important to monitor PHN and pain indices as well as zoster itself
 - How to monitor pain duration and intensity???

Provisional ACIP Recommendations: October 2006

- Zoster vaccine must be kept at +5°F or colder, until reconstituted for injection - discard if excursions to warmer temperatures occur
- ACIP emphasizes safety monitoring & reporting of adverse events

Of note, zoster vaccine is 1st live vaccine specifically for the elderly; safety monitoring will be challenging because the high rate of background medical events in older persons.

Provisional ACIP Recommendations: October 2006

- Zoster vaccine is not recommended for sole purpose of preventing occupational transmission of VZV (e.g., healthcare workers)
- Zoster vaccine is contraindicated for immunosuppressed persons (high dose corticosteroids, chemotherapy, biological response modifiers, AIDS)



Thank You!!

...Questions??