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)

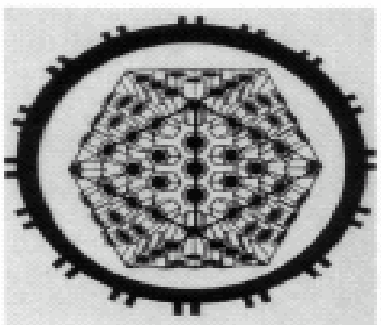
HSV PATHOGENESIS IN CARTOON REPRESENTATION

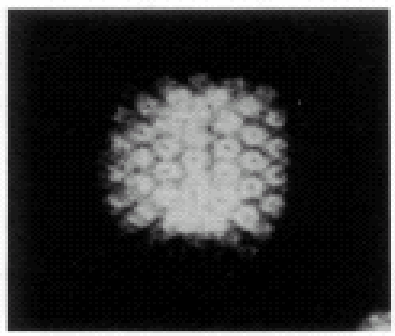
- HSV Structure
- Receptor Binding
- RNA Transcription in Productive Infection
- DNA Replication
- Encapsulation and Nuclear Egress
- Release
- Latent Infection

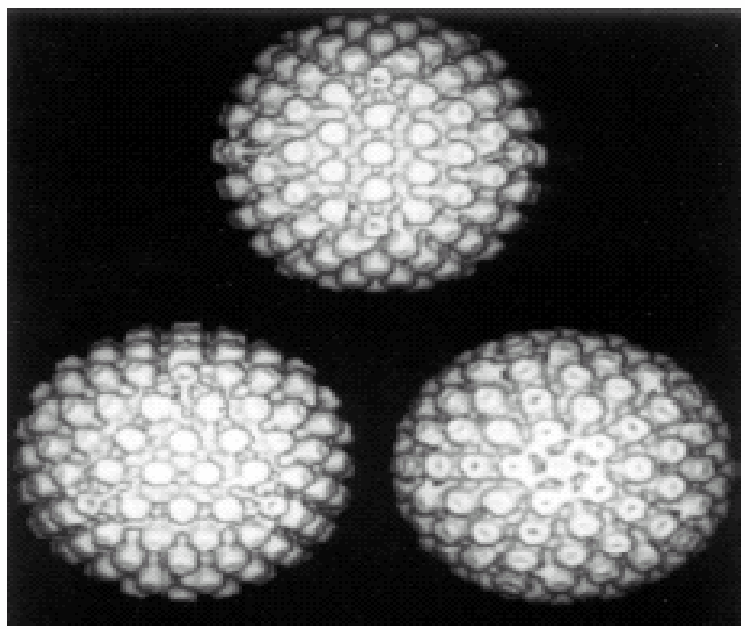
HSV structure

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 HSV 2 156,746 base pairs
Open Reading Frames ORF 90 in total
Latently associated transcripts LAT





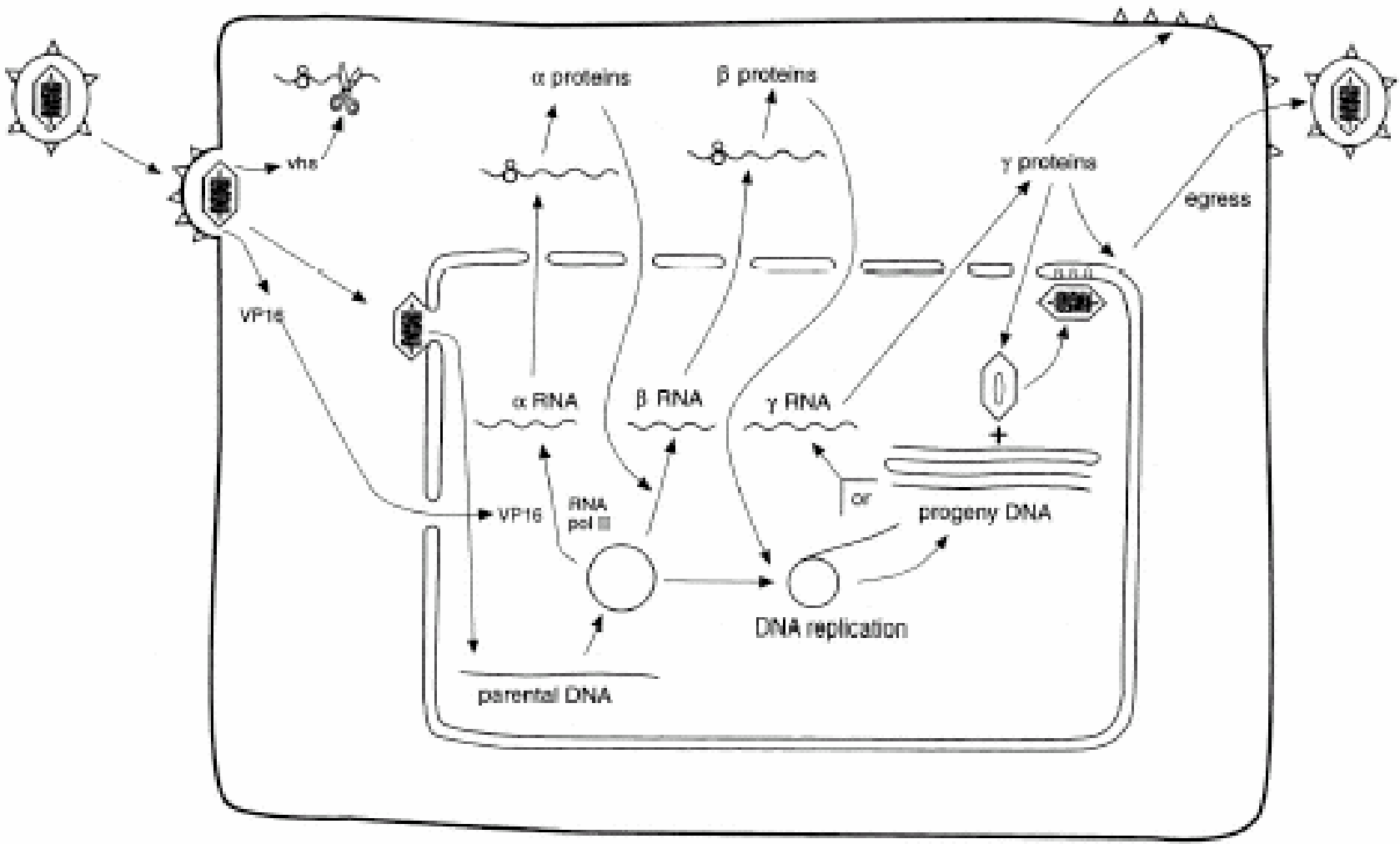


HSV STRUCTURE

HSV – Takes ~20 hrs from entry to exit

DNA REPLICATION

ENCAPSIDATION & EGRESS

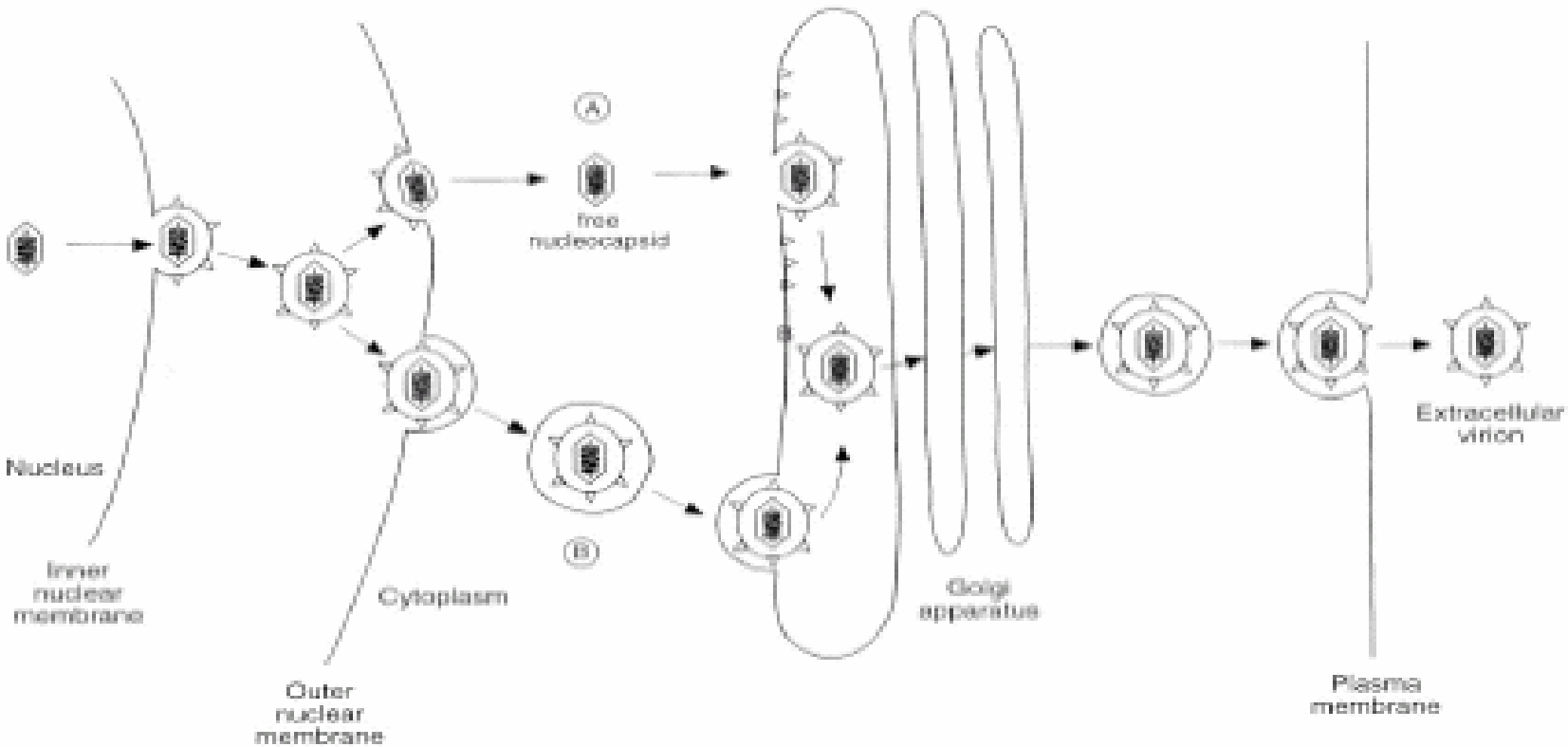


Capsulation and Release

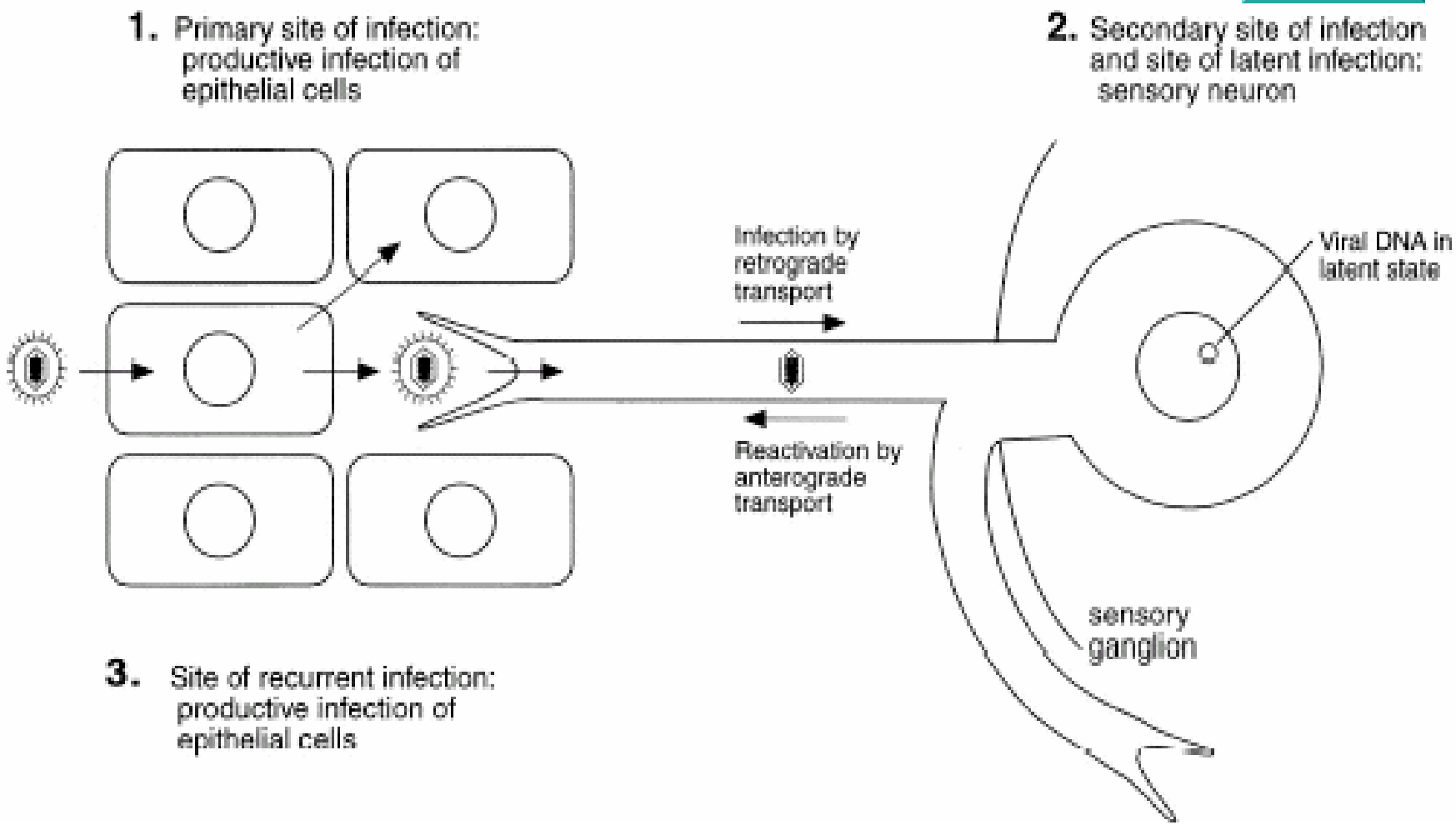
1 Through Inner, Outer Nuclear membrane

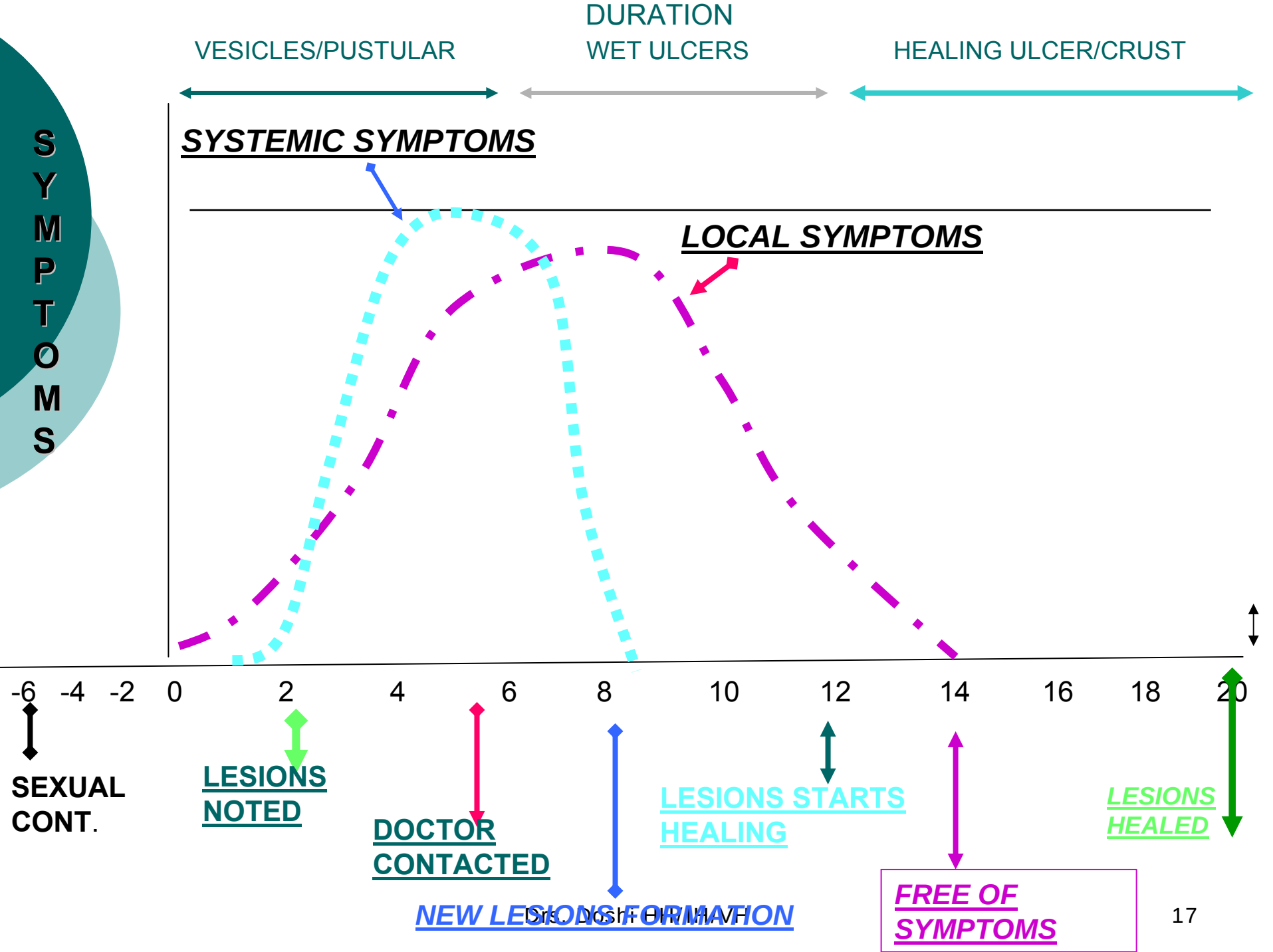
2 Cytoplasm and Golgi Apparatus & Plasma Membrane

RELEASE



LATENCY


1. Primary site of infection: productive infection of epithelial cells
2. Secondary site of infection and site of latent infection: sensory neuron
Infection by retrograde transport
Viral DNA in latent state
Reactivation by anterograde transport
sensory ganglion
3. Site of recurrent infection: productive infection of epithelial cells


DURATION
VESICLES/PUSTULAR
WET ULCERS
HEALING ULCER/CRUST
SYMPTOMS
SYSTEMIC SYMPTOMS
LOCAL SYMPTOMS
-6 -4 -2 0 2 4 6 8 10 12 14 16 18 20
SEXUAL CONT.
LESIONS NOTED
DOCTOR CONTACTED
NEW LESIONS FORMATION
LESIONS STARTS HEALING
FREE OF SYMPTOMS
LESIONS HEALED

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

HSV - RECURRENCE

- 50-7O% 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 / Valacylovir
- 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 VALACYLOVIR 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 – periungal 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 meng.)
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

Detection of HSV in lesions — *Burton et al.*

	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. albcans 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, examthema, &/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 frontanallae
- Ocular: Kerato-conj., Chorio-retinitis leading to ulcers, optic atrophy & blindness
- Oral: Mucosal ulcers & mucoceles
- Cutaneous: Typical clustered vesicles
- TREATMENT: BY PAEDIATRICIAN :
  - **IV acyclovir 45 mg /Kg/ day x 14 days**
  - **Topical Trifluorothymidine**
  - **Outcome poor**

HSV – in HIV patients

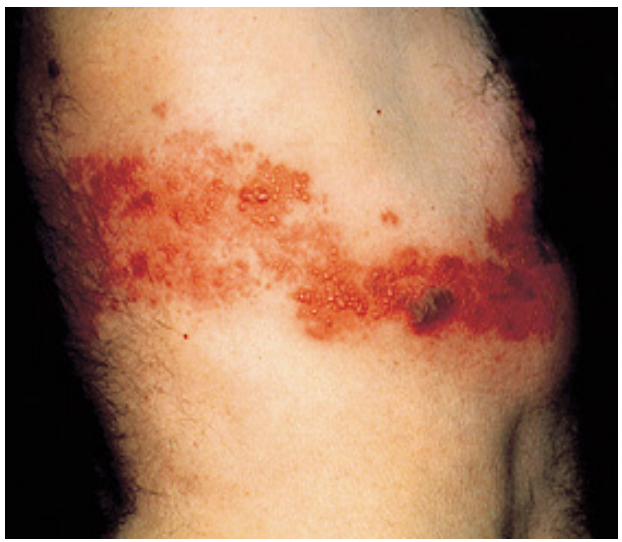
- IN HIV PATIENTS: Lesions are severe, protracted and all too often resistant to standard treatment of HSV
- If they fail to respond to standard dose increase to 800mg 5 hourly daily, repeat culture/PCR
- Trifluoridine locally 8 hourly
- IV foscarnet 50 mg /kg x 2 days
- Discuss with patient and partner 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 VALACYLORVIR AS A FORM OF PREVENTION OF HSV IN DISCORDANT PARTNERS

Zoster: It's Now a Vaccine Preventable Disease

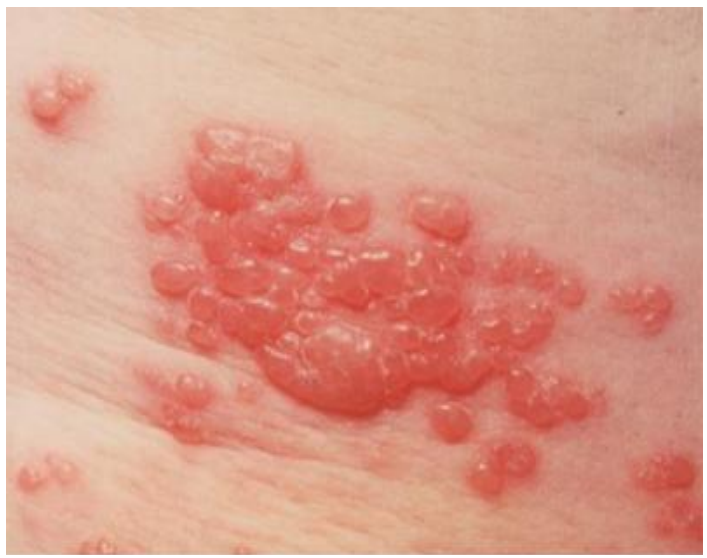
Presented by Dr Harry Hazelwood M.D., MPH



Outline

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

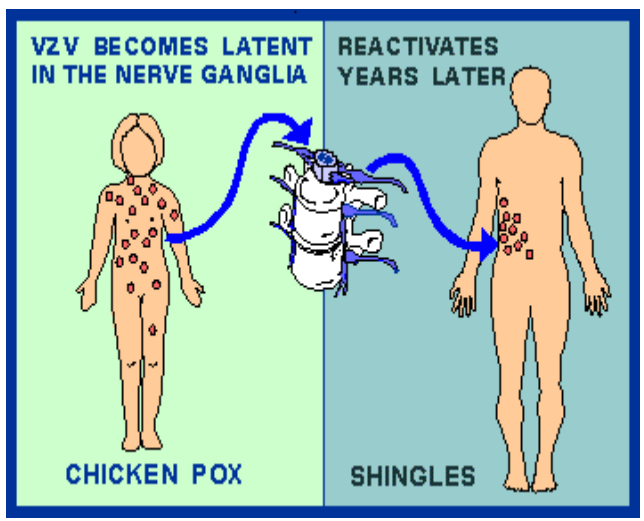
Clinical Manifestations of Zoster



Definition:

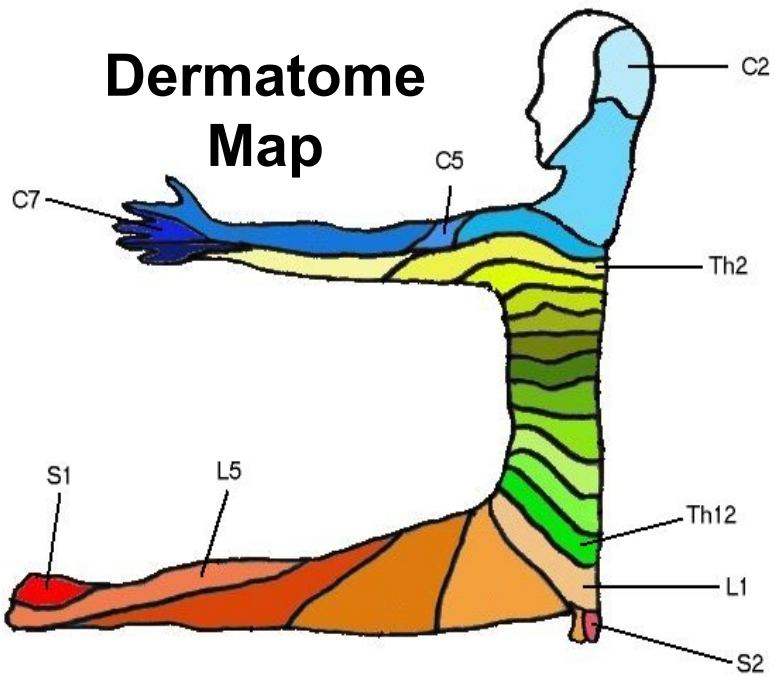
Zoster (herpes zoster, shingles): reactivation of varicella zoster virus (VZV), leading to crop of blisters in a dermatomal distribution

- 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)



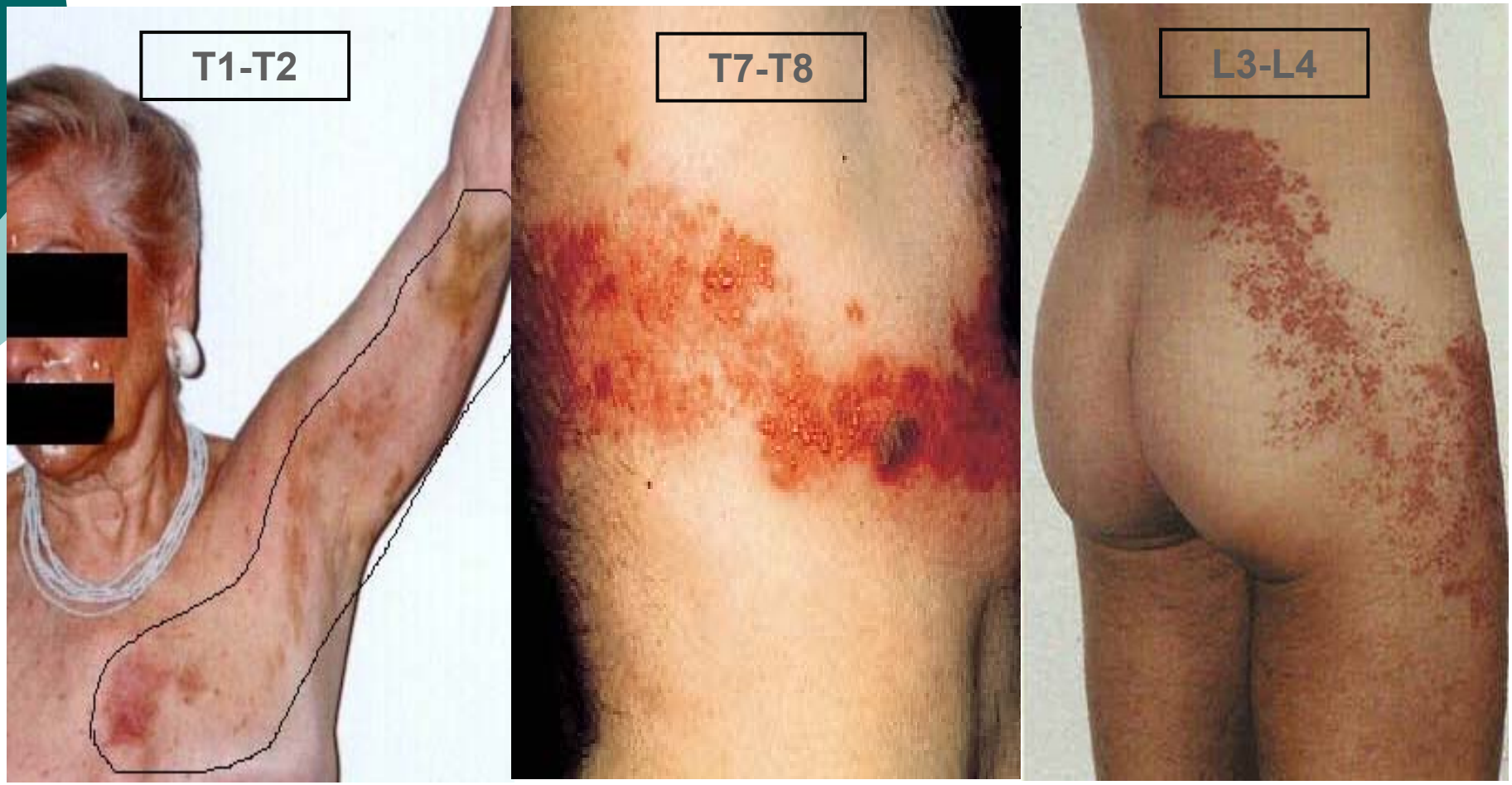
Primary Manifestations of Zoster: Signs

Rash:

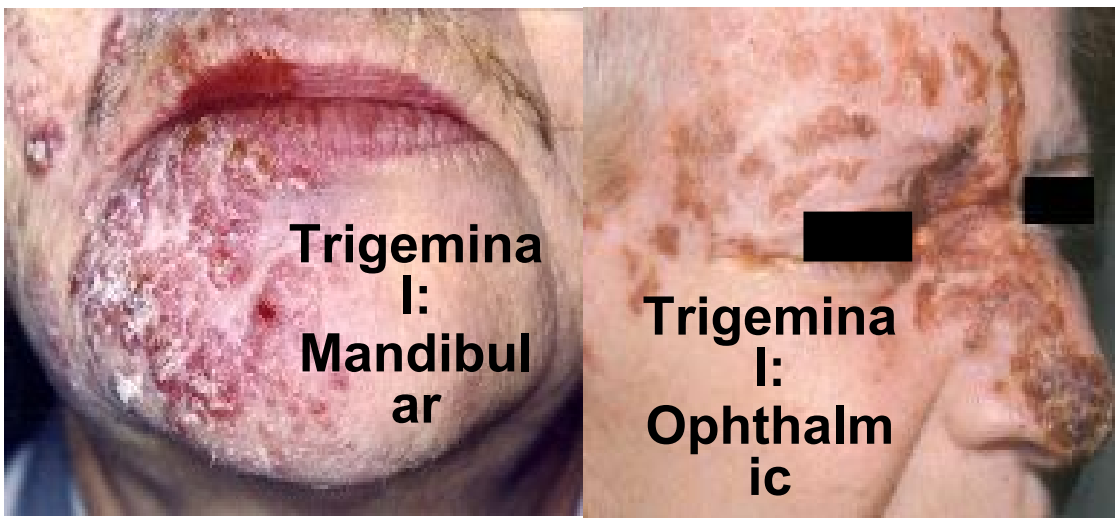
- Unilateral; 1-3 adjacent dermatomes (+/- few scattered lesions)
- Distribution in order of frequency: 1) thoracic > 2) lumbar, trigeminal, & cervical > 3) sacral, other cranial dermatomes
- Duration of rash
  - New lesions can arise over ~5-7 days
  - Evolve from erythematous maculopapules to vesicles +/- 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

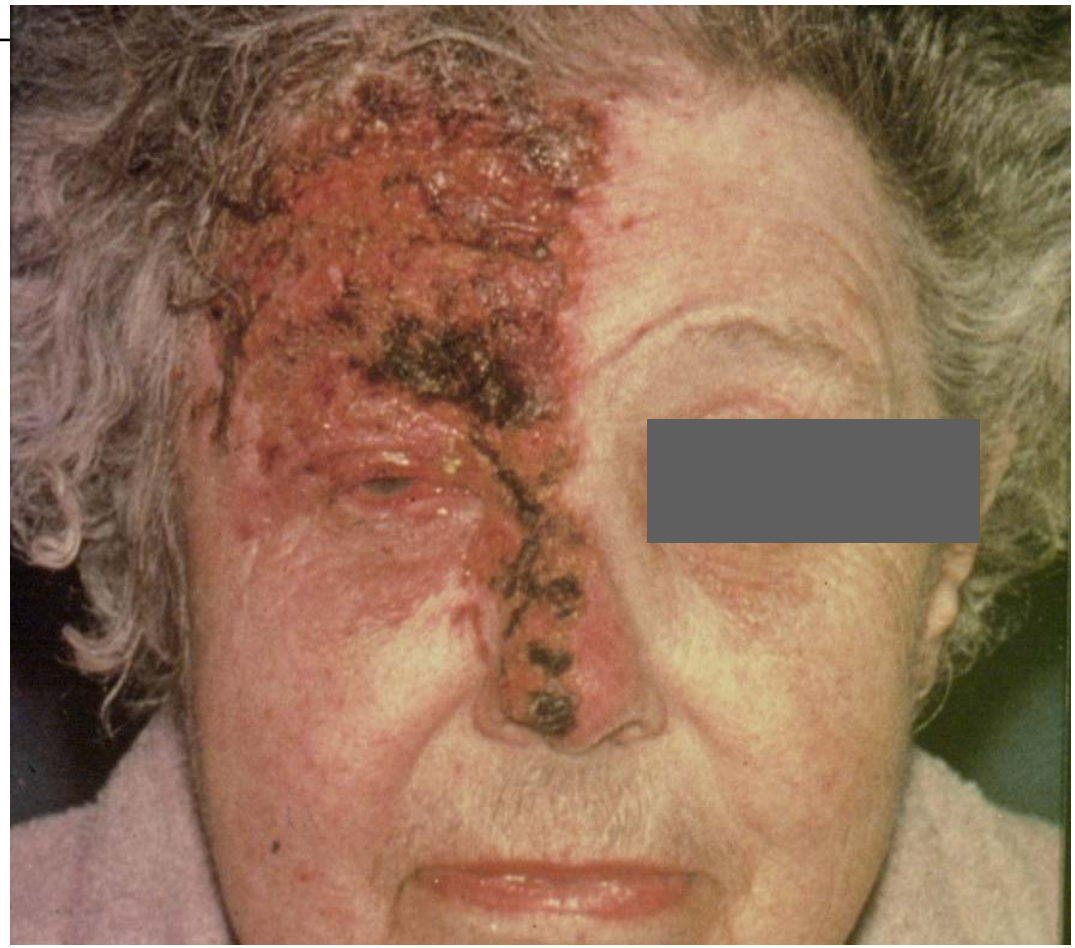
- Comparable to congestive heart failure, diabetes, and depression.

Physical	Psychological
○ Chronic fatigue ○ Anorexia & weight loss ○ Physical inactivity ○ Insomnia	○ Anxiety ○ Difficulty concentrating ○ Depression, suicidal ideation
Social	**Functional**
○ Fewer social gatherings ○ Change in social role	○ Interferes with activities of daily living: dressing, bathing, eating, travel, cooking, shopping

Schmader KE. Clin Infect Dis2001;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

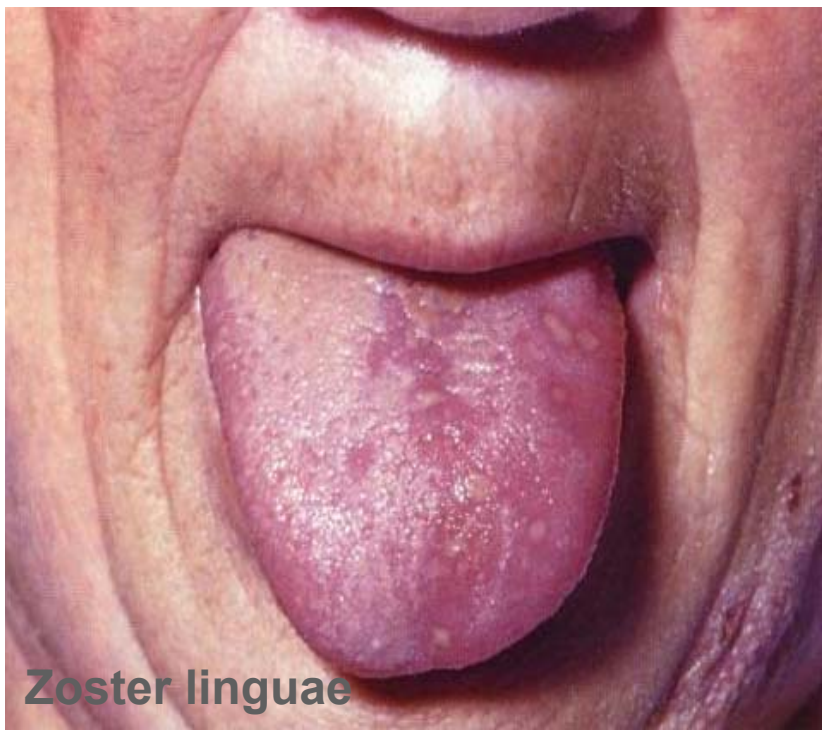


Courtesy of MN Oxman UCSD/San Diego VAMC.

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 agressive 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



Epidemiology of Zoster in U.S.

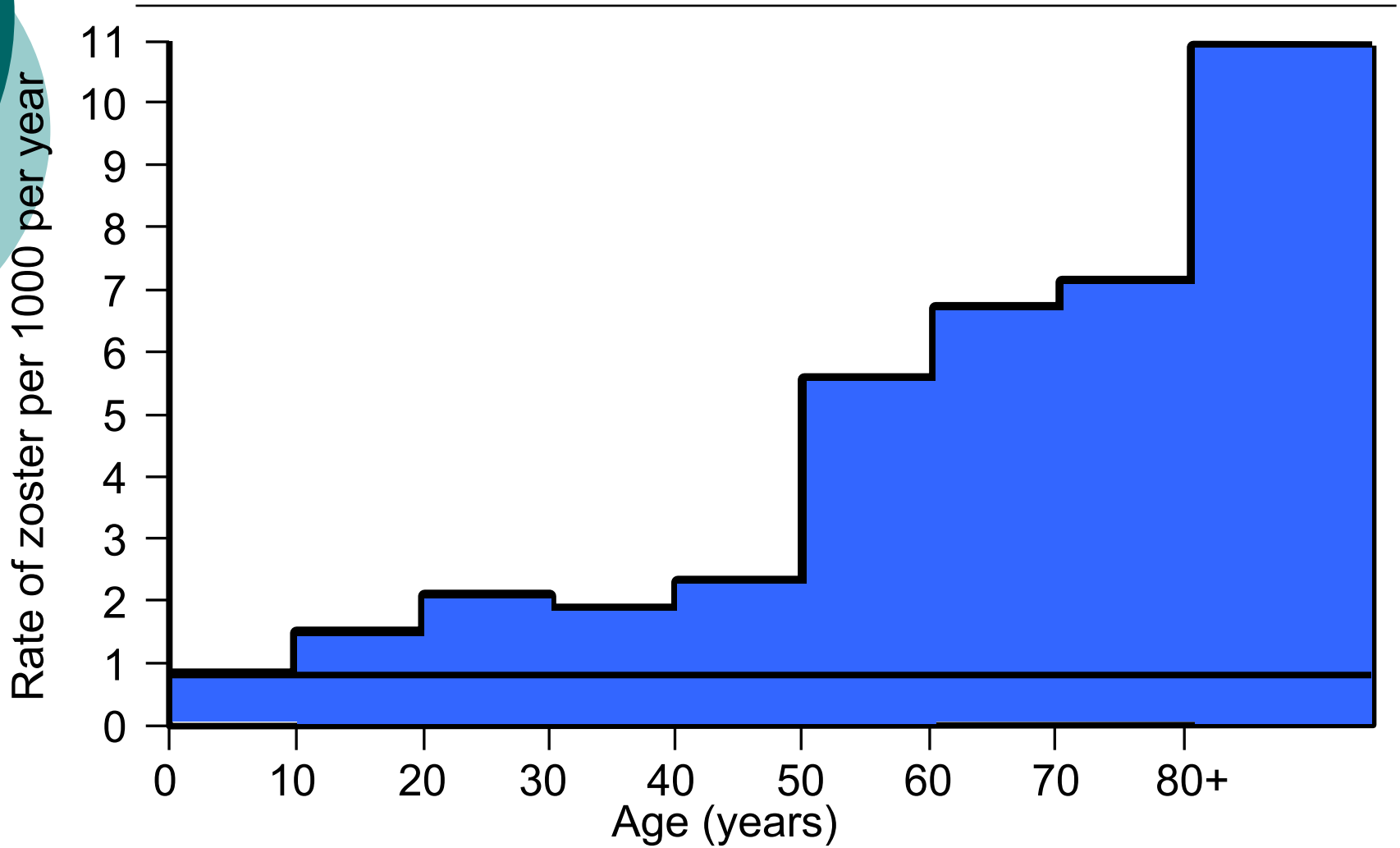
- Annual rate 3 to 4 per 1000 population per year (6 studies)
- ~1 million cases in the U.S. annually
- Rate appears to be increasing in recent decades
- Lifetime risk of developing zoster: about 30%
- Repeated episodes of zoster occur
  - Rate of repeats comparable to rates of first episode?

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:
(inconsistant, 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

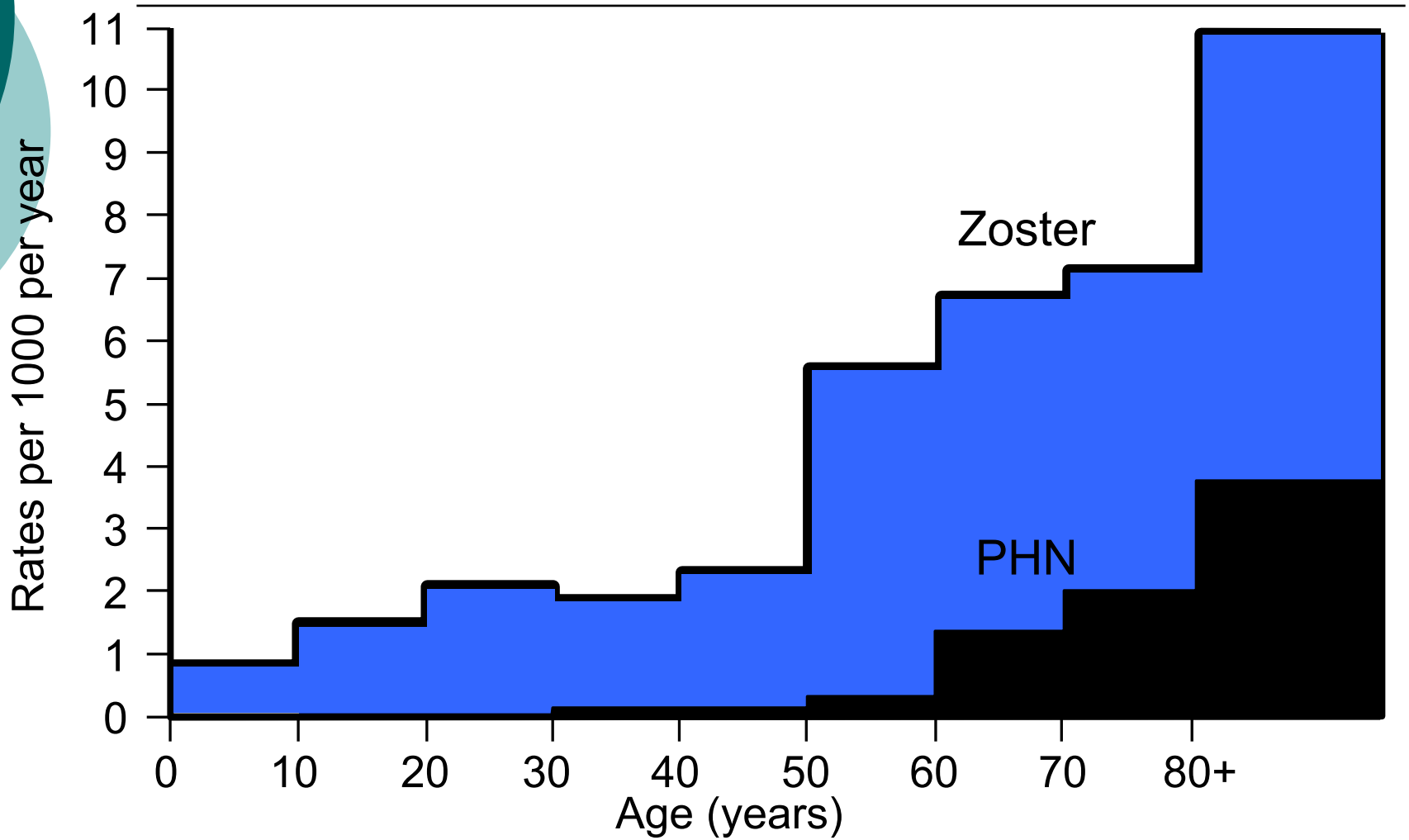
Risk factors for PHN:

- 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

Hope-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 ≥ 90 days)
- ~1/3 of zoster episodes involve ≥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 ≥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

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

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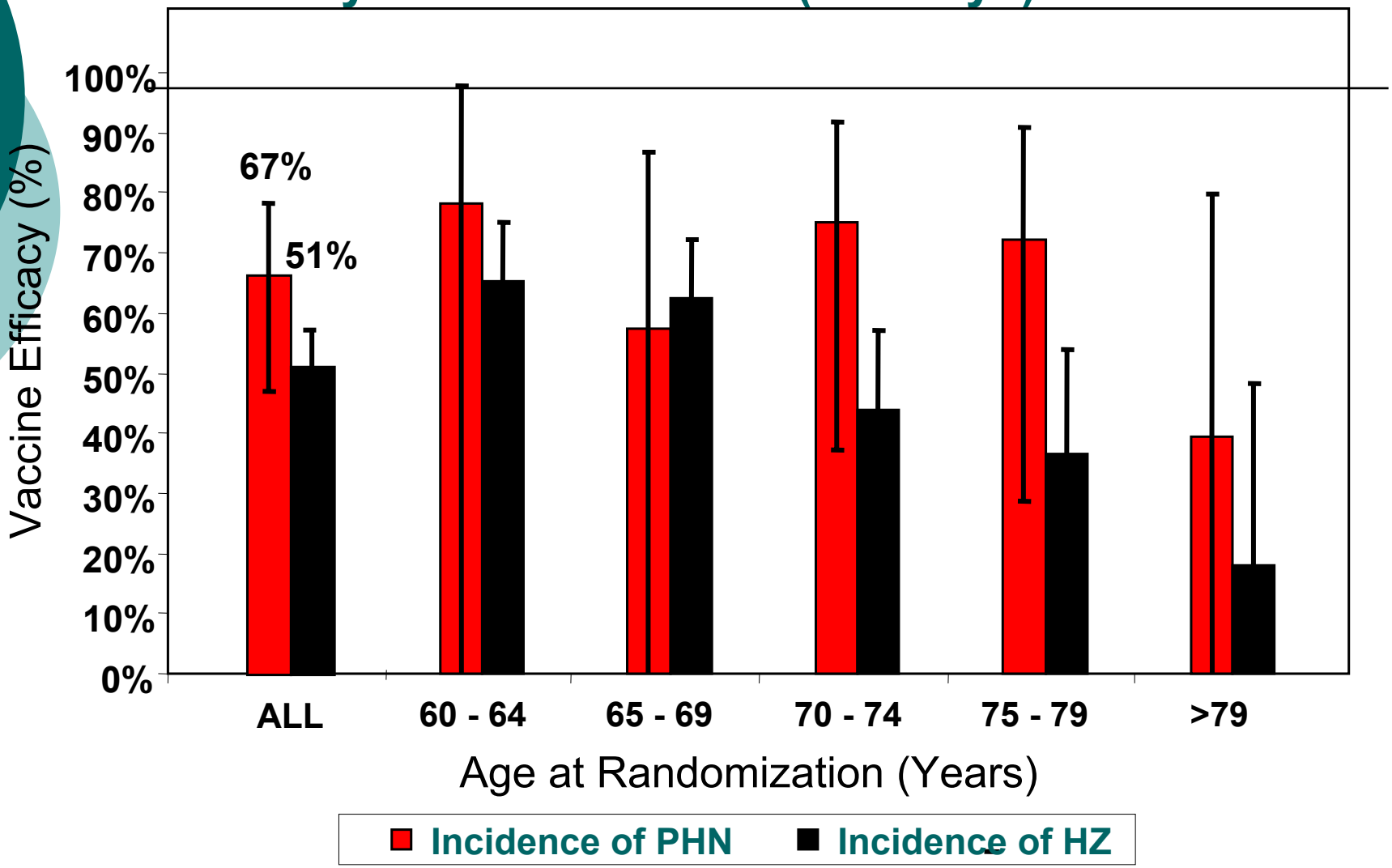
The Shingles Prevention Study: Results

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)

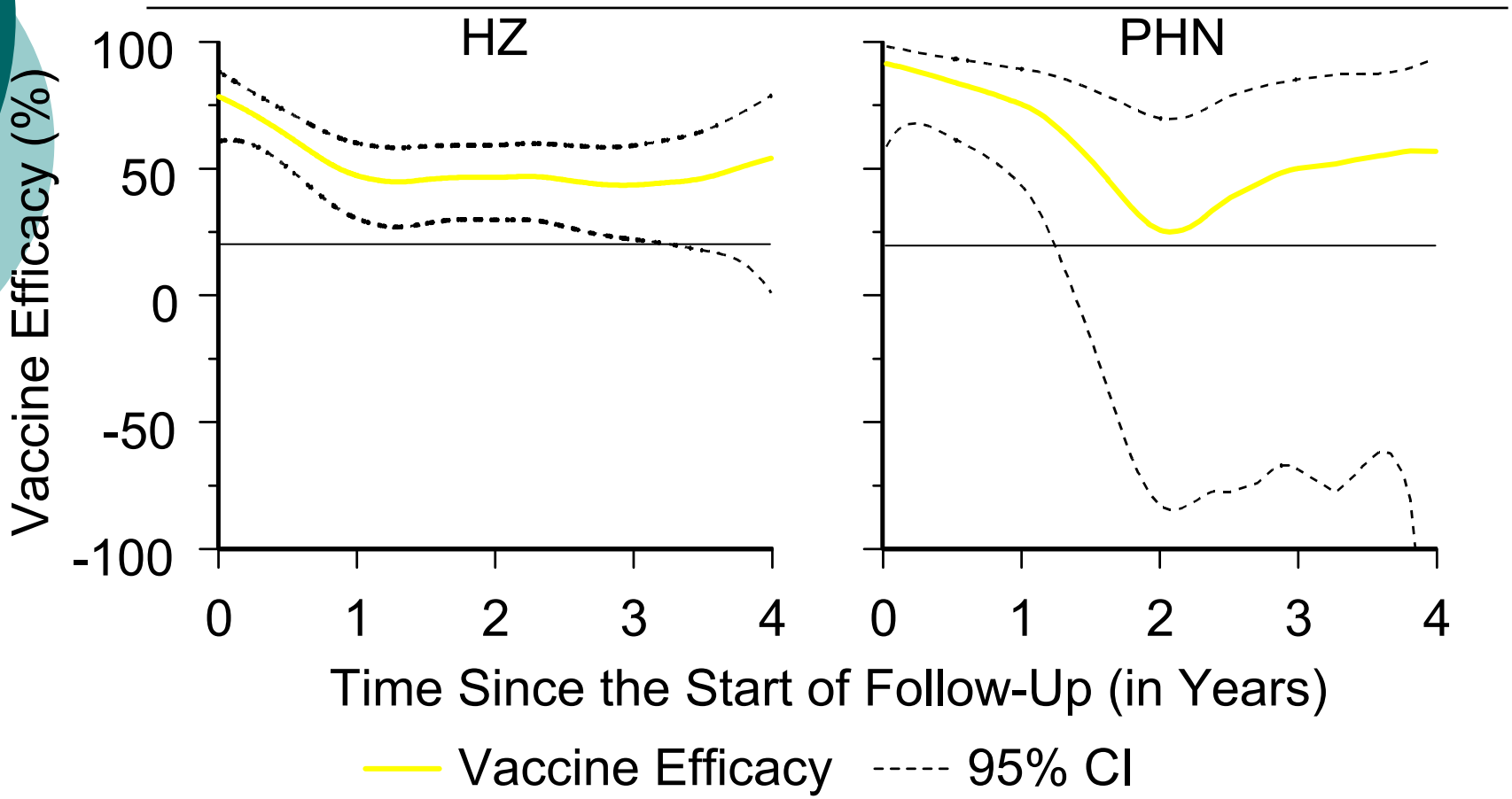
Shingles Prevention Study: Results
dverse Events

AAppears to be safe:

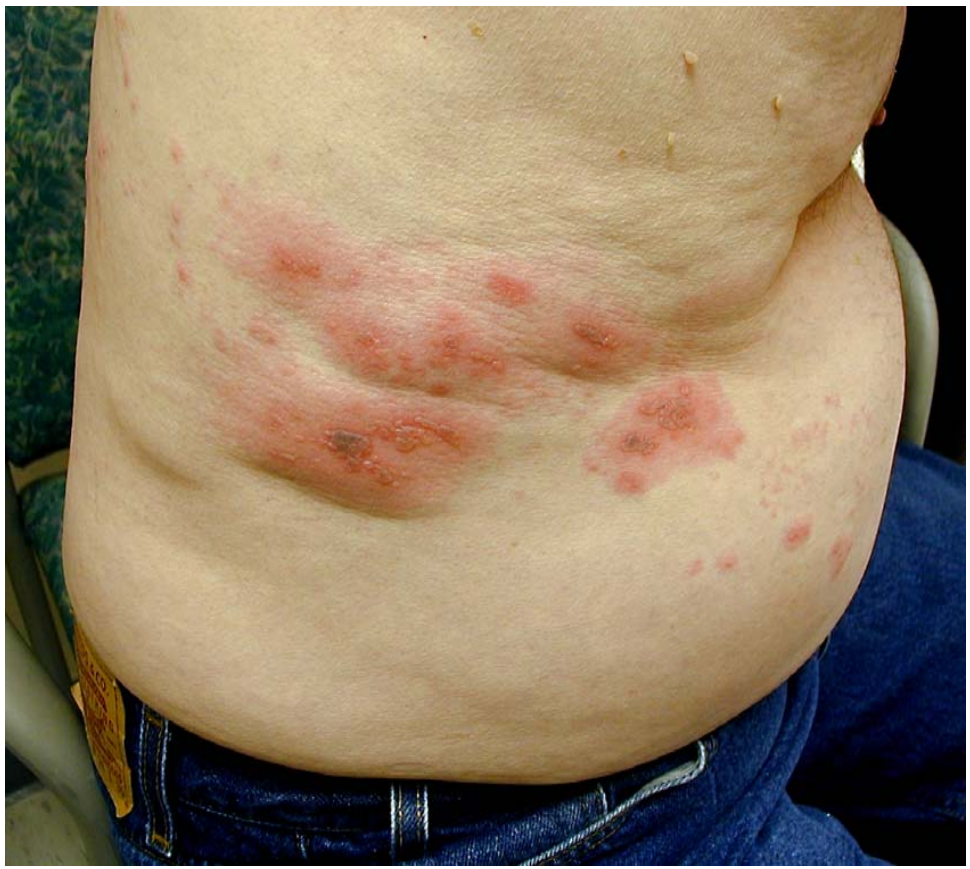
- No pattern suggesting a causal link to serious adverse events
- Vaccine rashes did not occur in the trial
- Excess of mild reactions in vaccines:

	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??