



# **HERPES ZOSTER IN HOSPITALIZED ADULTS:**

## **THE UCSF DERMATOLOGY CONSULT EXPERIENCE**

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# CONFLICTS OF INTEREST

- No conflicts of interest to disclose.



## OUR PATIENT

- 59yo F with history of AML s/p alloSCT
  - inactive chronic GVHD
  - recently off valacyclovir
- V1 zoster
- CNS dissemination
- Prolonged ICU stay



# OVERVIEW

Observations from UCSF and the literature:

- 1) Epidemiology
- 2) Isolation precautions
- 3) Diagnostic methods
- 4) Dissemination patterns
- 5) Treatment



# OVERVIEW

Observations from UCSF and the literature:

- 1) **Epidemiology**
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# HERPES ZOSTER – BURDEN OF DISEASE

- Since VZV vaccine introduced:
  - ↓ Varicella-related hospitalizations, expenditures
  - ↑ Zoster-related hospitalizations, expenditures
  - Annual hospital charges for HZ:  
\$1.2 billion in 1993 → \$1.9 billion in 2004
  - Adults > 60yo account for 75% of cost

*Patel MS et al. Infect Control Hosp Epidemiol. 2008 Dec;29(12):1157-63.*

- Immunocompromise and zoster incidence:
  - HIV → ~7x increase
  - Leukemia → 50 - 100x increase

*Friedman-Kien AE et al. J Am Acad Dermatol. 1986 Jun;14(6):1023-8.*

*Guess HA et al. Pediatrics. 1985 Oct;76(4):512-7.*



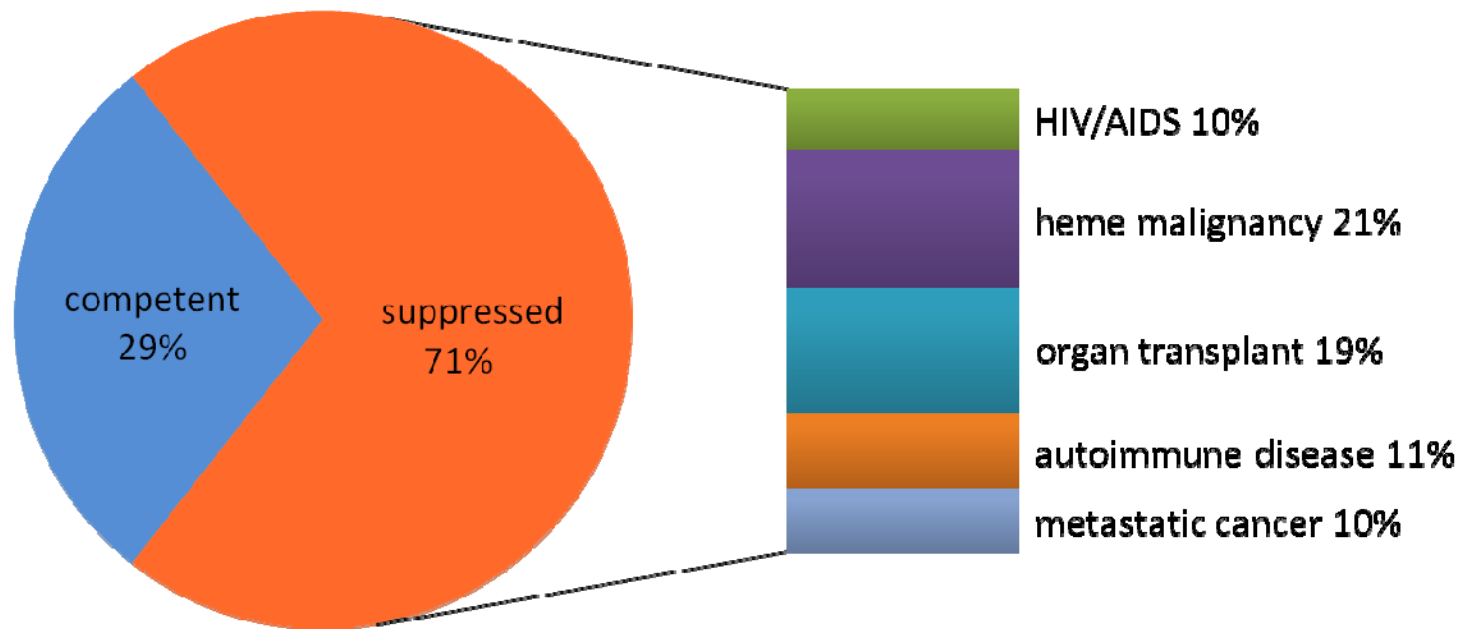
# UCSF STUDY POPULATION

- UCSF inpatient dermatology case log
  - Moffitt/Long Hospitals, adult patients
- 1733 dermatology consults, 12/2009 – 1/2014
- 52 clinical herpes zoster diagnoses
  - 26 female, 26 male
  - Ages 18 – 93, mean age 55.4 years



# RATES OF IMMUNOCOMPROMISE

- Our sample: 71% immunosuppressed



- Portuguese study: 11% immunosuppressed

*Mesquita M et al. Acta Med Port. 2013 Sep-Oct;26(5):531-6.*





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# CDC ISOLATION GUIDELINES FOR HZ

Immune status	Extent of disease	cover lesions	Isolation precautions		
			standard	contact	airborne
Competent	Localized	✓	✓		
	Disseminated		✓	✓	✓
Compromised	Localized		✓	✓	✓
	Disseminated		✓	✓	✓



# ZOSTER TRANSMISSION – NEW INSIGHTS

- VZV DNA has been found in:
  - **Vesicle fluid**
  - **Serum**
  - **Peripheral blood mononuclear cells**
  - **Saliva** (viral load correlates with acute pain)
- ...even in immunocompetent patients with localized zoster!

*Satyaprakash AK et al. J Infect Dis. 2009 Jul 1;200(1):26-32.*

*Mehta SK et al. J Infect Dis. 2008 Mar 1;197(5):654-7.*



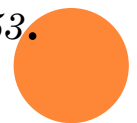
# ZOSTER TRANSMISSION – NEW INSIGHTS

- Similar rates of VZV transmission in children from primary varicella (15%) vs. zoster patients (9%).
- Transmission risk similar regardless of anatomic location of HZ!

*Viner K et al. J Infect Dis. 2012 May 1;205(9):1336-41*



- Case report: immunocompetent pt with localized zoster in care facility → varicella outbreak
  - Patient's lesions kept covered by gauze/clothing at all times
  - VZV found in environmental samples in patient's room

*Lopez AS et al. J Infect Dis. 2008 Mar 1;197(5):646-53.*



# ZOSTER TRANSMISSION – NEW INSIGHTS

- **Type of dressing does matter:**

Sample source	Gauze 	Hydrocolloid 
Dressing	22/23 VZV+	0/25 VZV+
Air	13/23 VZV+	0/24 VZV+

*Suzuki K et al. J Infect Dis. 2004 Mar 15;189(6):1009-12.*

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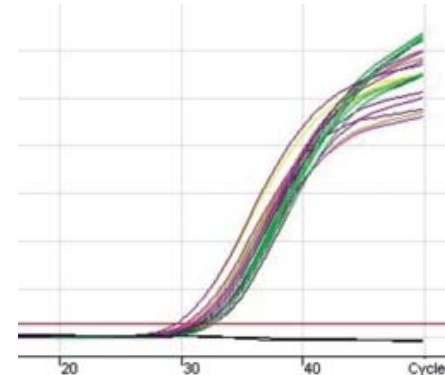
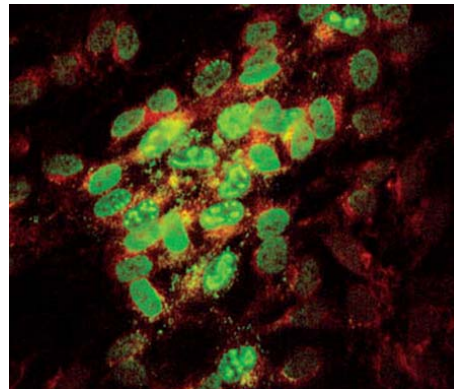
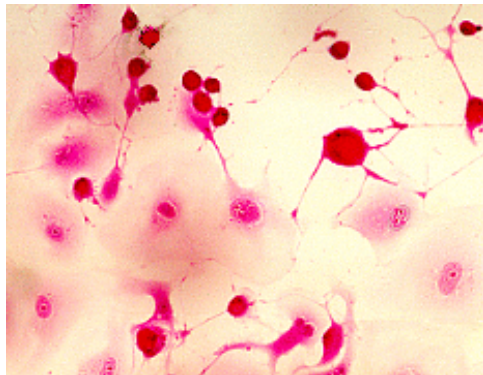
## UCSF: METHODS OF DIAGNOSIS

- Direct fluorescent antigen (DFA) checked in 46 (88%)
  - 75% positive, 15% negative, 9% insufficient sample
- Of the 6 who did not have DFA:
  - 2 had viropathic changes on skin biopsy
  - Both had positive VZV immunostain
- Remaining 4 patients diagnosed clinically



# LITERATURE: METHODS OF VZV DIAGNOSIS

	Sensitivity	Specificity	Turnaround
Culture	46.3%	100%	1 week+
DFA	87.8%	93.8%	24 hours
PCR	97.6 - 100%	90.6 - 100%	hours – days



*Wilson DA et al. J Clin Microbiol. 2012 Dec;50(12):4120-2.*





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# FORMS OF VZV REACTIVATION

- 1) **Localized** (classic) zoster
  - 1-2 dermatomes, unilateral
- 2) **Cutaneous dissemination**
  - >20 vesicles outside primary and adjacent dermatomes
- 3) Cutaneous zoster with **visceral dissemination** (lungs, CNS, liver, heart, GI)
- 4) Atypical **generalized cutaneous zoster** +/- visceral involvement
- 5) Visceral zoster **without skin lesions**

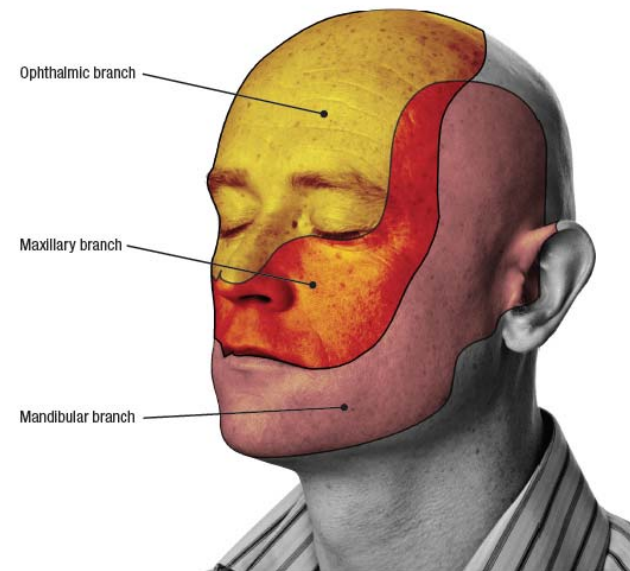
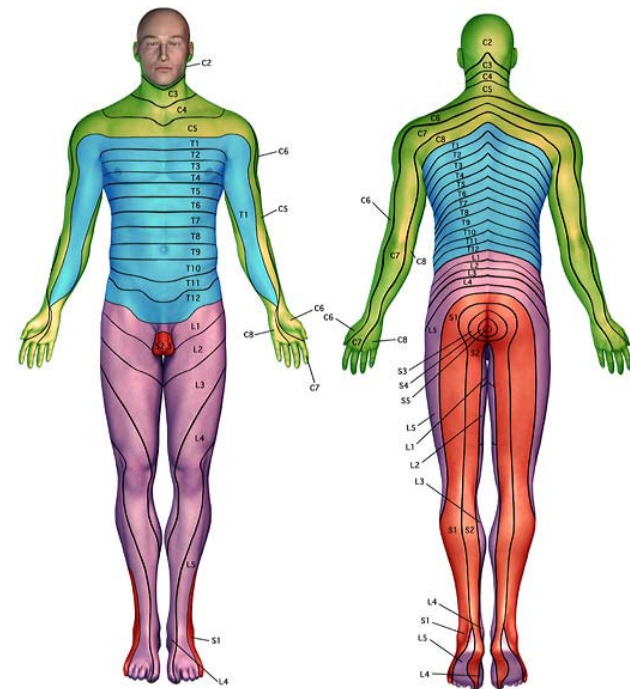


Figure 1. Distribution of the cranial nerve V: the ophthalmic nerve ( $V_1$ ), the maxillary nerve ( $V_2$ ), and the mandibular nerve ( $V_3$ ).

# UCSF: ZOSTER DISSEMINATION

- 23 (44%) disseminated zoster:
  - 19 (37%) cutaneous only
  - 8 (15%) CNS
    - 4 with CNS + cutaneous
  - 17 (74%) immunosuppressed
- No other visceral involvement



# LITERATURE: CNS ZOSTER

- Reported rates of CNS involvement in zoster: ~11%

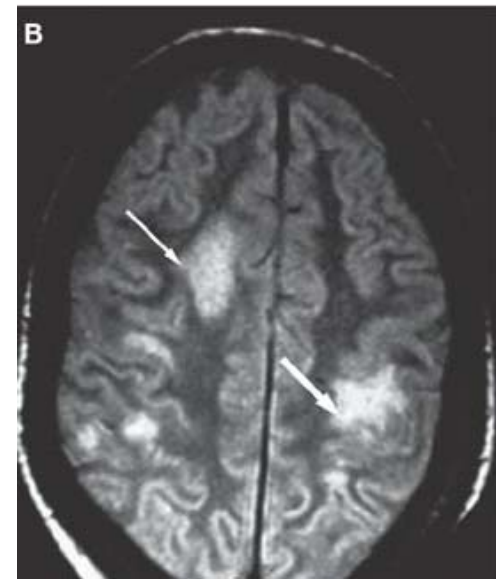
*Braun-Falco M et al. Int J Dermatol. 2009 Aug;48(8):834-9.*

- Syndromes of CNS zoster:

- Cranial nerve palsy
- Encephalitis
- Encephalopathy
- Aseptic meningitis
- Cerebrovascular disease

- Residual neuro deficits:

- 30% 1 month, 25% 3 months, 12% 6 months
- No correlation between CSF viral load and neuro sequelae at 3 months



*Persson A et al. J Clin Virol. 2009 Nov;46(3):249-53.*

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# UCSF: TREATMENT

# Pts (%)	Initial	Switched	Suppressive
Treatment			
Oral ACV/ VAL	20 (40%)	13 (25%)	5 (10%)
IV ACV/ GAN	31 (59%)	5 (10%)	-
None	1 (1%)	-	-



# CURRENT ZOSTER TREATMENT GUIDELINES

- Oral antiherpetic (acyclovir, famciclovir, valacyclovir)
  - start **within 72h** of symptom onset
- IV acyclovir for:
  - Visceral dissemination, retinitis
  - Severe immunocompromise
    - Within 4 months of alloSCT
    - HSCT patients with GVHD
    - Transplant patients on antirejection drugs
- Duration of treatment?
  - Lesions crusted → switch to PO
  - Total duration controversial
    - 7-10 days (immunocompetent)
    - Longer for visceral or immunocompromised

*Dworkin RH et al. Clin Infect Dis. 2007 Jan 1;44*



# TAKE HOME POINTS

- Increasing burden of HZ morbidity, especially in elderly and immunocompromised patients
- Contact plus airborne precautions if disseminated disease or immunocompromised patient
  - Extend to all hospitalized patients with HZ?
- DFA or PCR for diagnosis from vesicle
  - PCR for CSF
- Dissemination common in immunocompromised patients
  - Cutaneous dissemination may predict visceral disease
- Clearer guidelines needed for treatment of zoster patients with immunosuppression or dissemination





# THANK YOU...

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- Aaron Rowe, PhD
- UCSF Dermatology Residents, Faculty and Staff



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# WHO SHOULD GET ZOSTER VACCINE?



- Prevents HZ (51% decrease) and post herpetic neuralgia (66% decrease) in adults >60, also decreases severity/duration of HZ
- FDA approved for ages 50+, but CDC recommended for 60+
- 14x dose of virus compared to the VZV vaccine
- Not currently recommended in immunocompromised patients
- Preliminary data for inactivated vaccine suggests decreased severity of HZ
- Pre-vaccinate in anticipation of future immunosuppression?

*Oxman MN et al. N Engl J Med. 2005 Jun 2;352(22):2271-84.*

*Cohen JI. J Infect Dis. 2008 Mar 1;197 Suppl 2:S237-41.*

*Cheuk DK et al Cochrane Database Syst Rev. 2011 Mar 16;(3):CD006505.*



## LENGTH OF HOSPITALIZATION

- UCSF mean length of hospital stay:
  - 11.6 days in localized group
  - 15.3 days in disseminated/visceral group
  - Age does not correlate with LOS ( $r = 0.12$ )
- Italian study: mean hospital stay 8 days, increasing with age

*Gabutti G et al. Int J Environ Res Public Health. 2009 Sep;6(9):2344-53.*

- Portuguese study: Mean hospital stay 9.3 days, increasing with age.

*Mesquita M et al. Acta Med Port. 2013 Sep-Oct;26(5):531-6.*



# ISOLATION PRECAUTIONS

- Level of precautions in suspected HZ?
- Definitions:
  - **Standard**
  - **Contact:** standard + gloves and gown
  - **Droplet:** standard + contact + mask with eye shield
  - **Airborne:** standard + N-95 respirator mask + negative pressure room

