

Adenovirus 14

A New Cause of Severe Community Acquired Pneumonia

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Case Presentation

- Identification: 18 year old previously healthy male
- Chief complaint: cough for 5 days
- Illness onset: Nausea, “dry heaves”, loose stools, non-productive cough
- Illness progression: Fever to 104° F begins 2 d prior to evaluation, confusion begins on day of evaluation

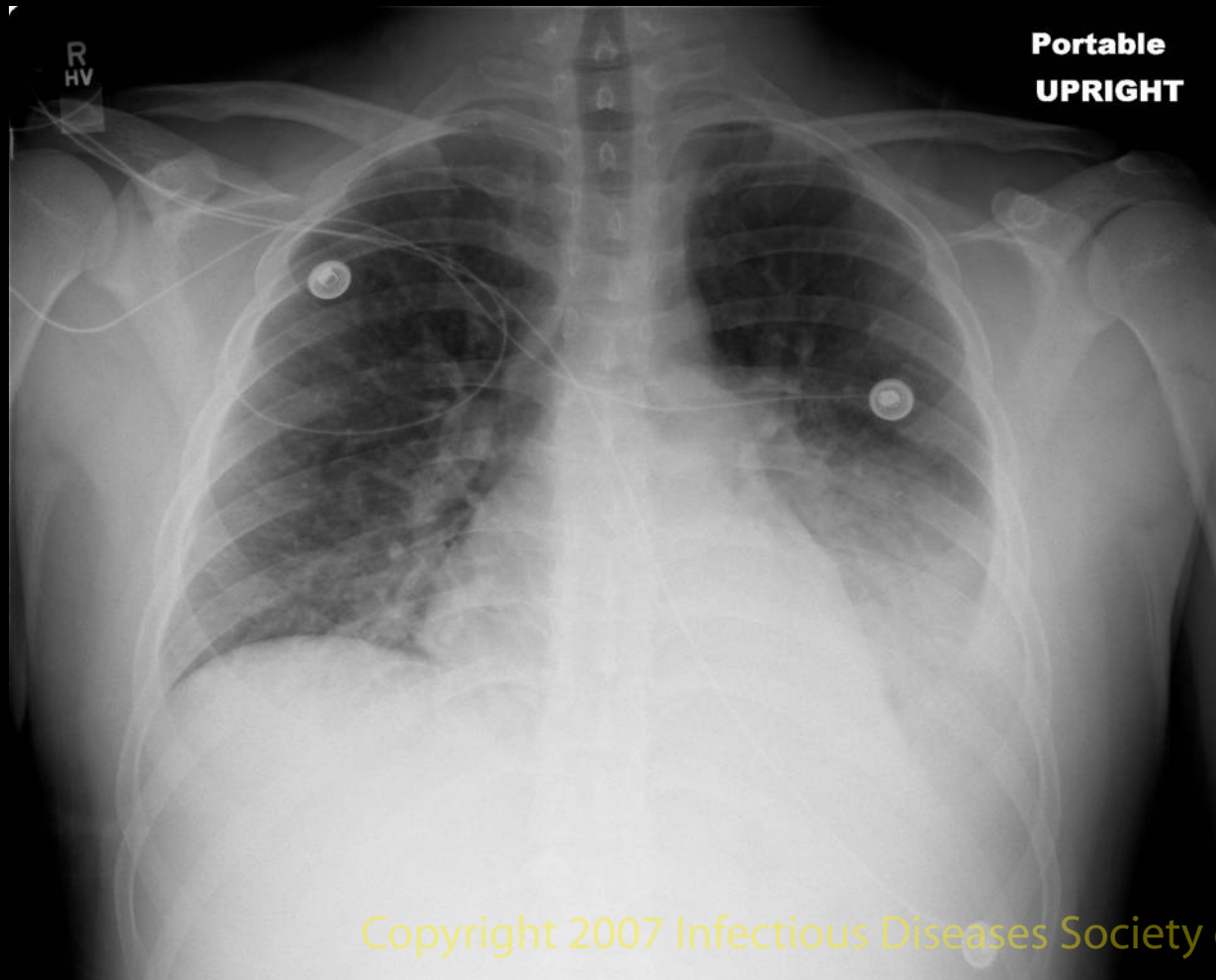
Past Medical History

- Previously well
- Severe “mono” 5 months earlier treated with steroids, famcyclovir and clindamycin
- No chronic medications
- No alcohol
- Occasional recreational smoking

Examination on admission

- Fever
- Oxygen saturation =79% on ambient air
- Decreased breath sounds at bases

Admission Radiograph



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Hospital Course

- Respiratory failure rapidly developed
 - Mechanical ventilation x 14 days
 - Prone, FiO₂=1.0
- Progressive hypotension
 - Fluid boluses, vasopressin
- Empiric ceftriaxone, azithromycin, moxifloxacin

Diagnostic Evaluation

- Blood and sputum bacterial cultures no growth
- *S.pneumoniae* and *Legionella* urine antigen tests negative
- Bronchoscopy
 - Mild airway erythema
 - PCR negative for *Legionella* and *Pneumocystis*
 - Respiratory viral panel negative for influenza A and B, and Respiratory Syncytial Virus
 - Adenovirus detected by culture and Polymerase Chain Reaction

Case Outcome

- Mechanical Ventilation x 14 days
- Discharged home on room air after 17 day hospitalization

Adenovirus Background

- Non-enveloped double stranded DNA virus
- 51 known serotypes
- Clinical Spectrum
 - Respiratory Tract- upper, lower
 - Conjunctivitis (usually types 8, 19, 37)
 - Gastroenteritis (usually types 40, 41)
 - Urinary Tract in normal and compromised hosts
- Year round, winter/spring predominance

Severe Adenovirus Disease

- Immunocompromised hosts and neonatal age group at risk of disseminated disease and death
- Cluster at chronic psychiatric facility 1995
 - Immunocompetent adults
 - 18 pneumonia, 6 ICU care(3 had serious underlying medical disease), 4 septic shock
 - Adenovirus 35
- No community-based outbreaks of severe disease previously reported

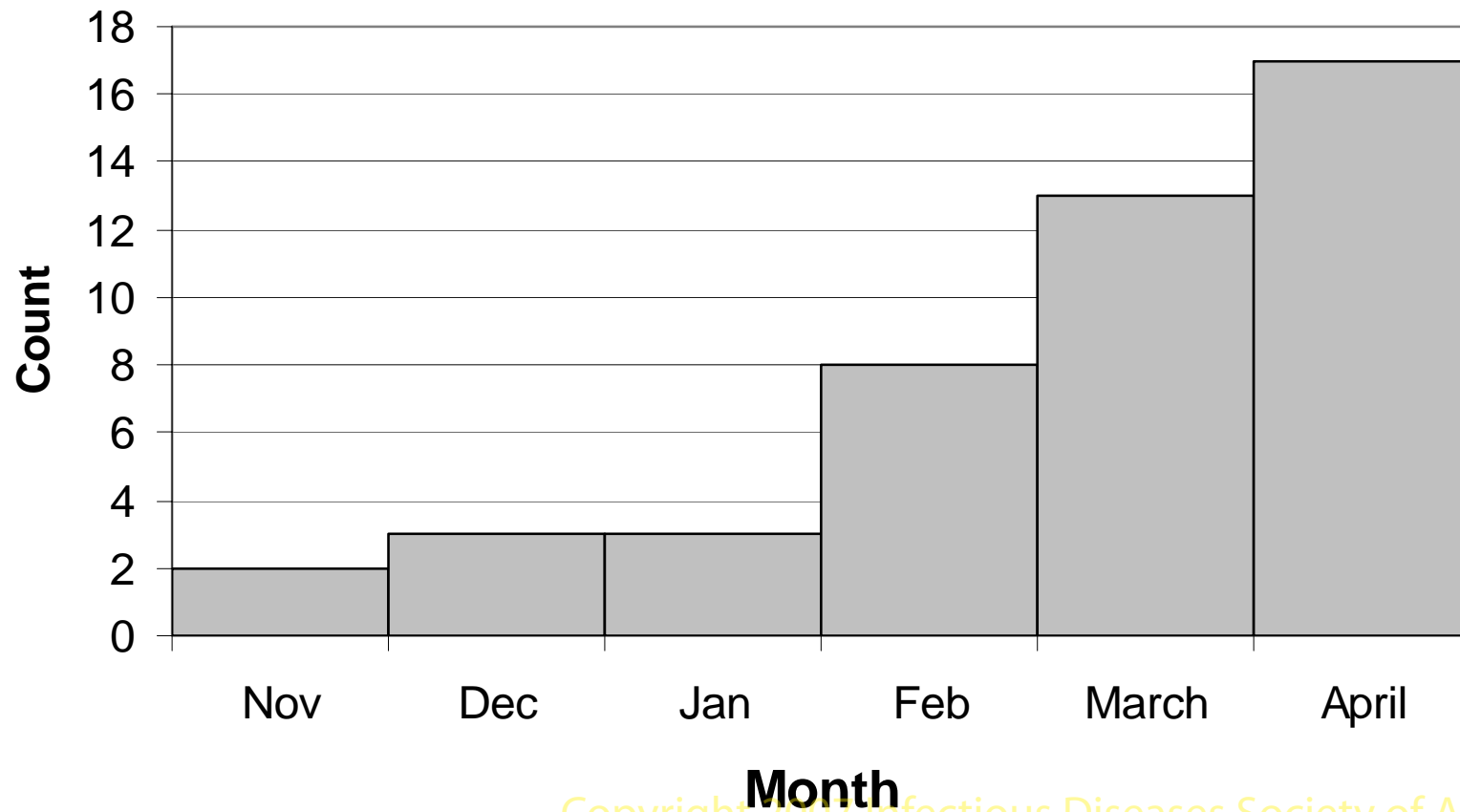
Identification of Cluster, April 2007

- 4 of 13 ICU patients at Portland, Ore hospital had adenovirus pneumonia as primary problem
- Posted to Emerging Infections Network
 - No responses
- Oregon Public Health informal survey of other hospitals suggested larger problem
- Systematic review of all adenovirus cases identified by Oregon labs from November 2006 through April 2007

Methods

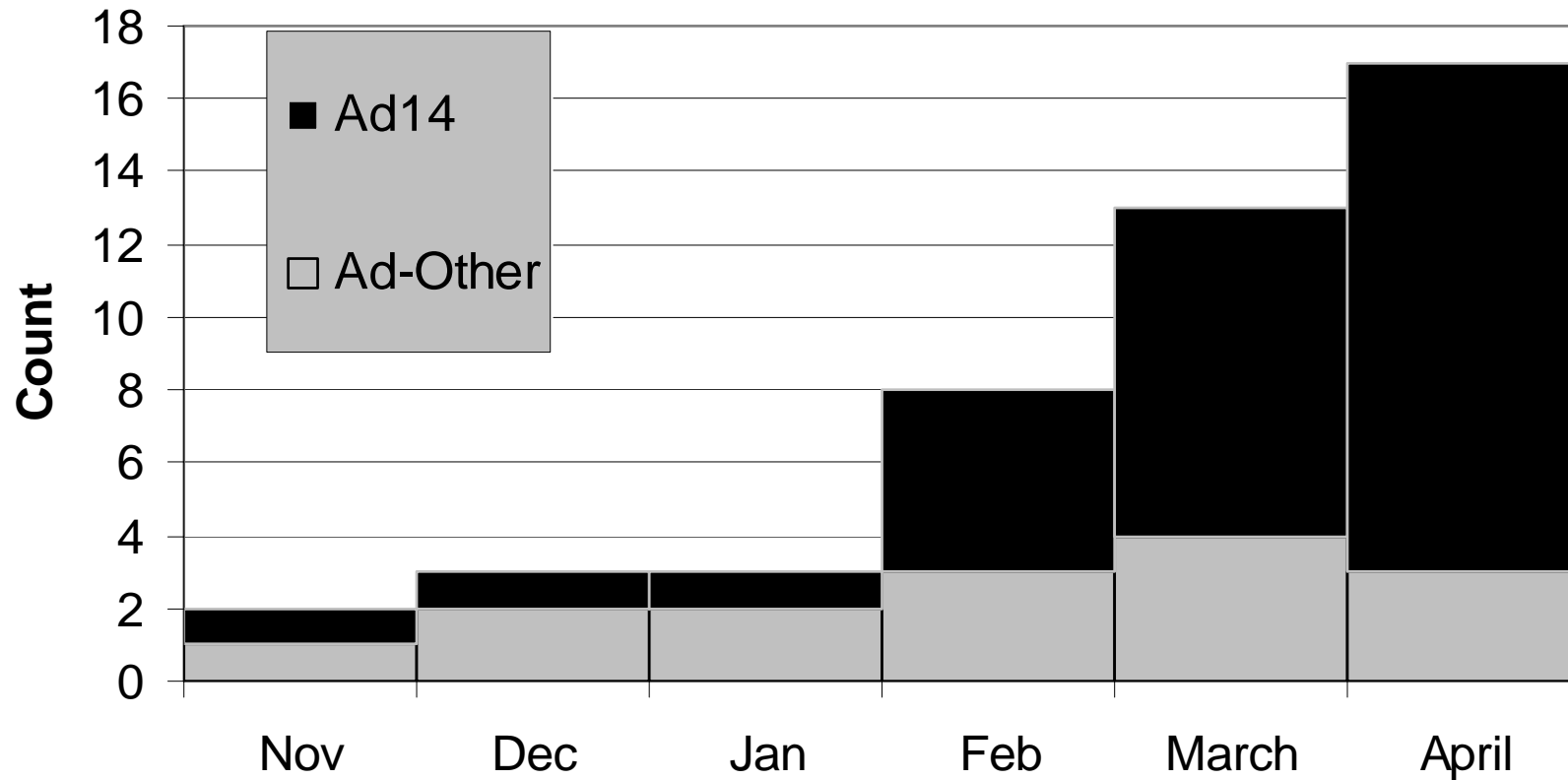
- Study period: Nov 1, 2006-April 30, 2007
- Case finding: Survey of all Oregon virology labs for adenovirus detection during study period
- Case definition: Clinical illness with positive adenovirus detection (culture or PCR) during study period
- Data collection: standardized abstraction tool used by MD; data entered into Access database
- Adenovirus typing by hexon gene sequencing validated realtime PCR assay
- Data analysis: SAS 9.1

Adenovirus, Oregon Active Surveillance 11/06 - 4/07



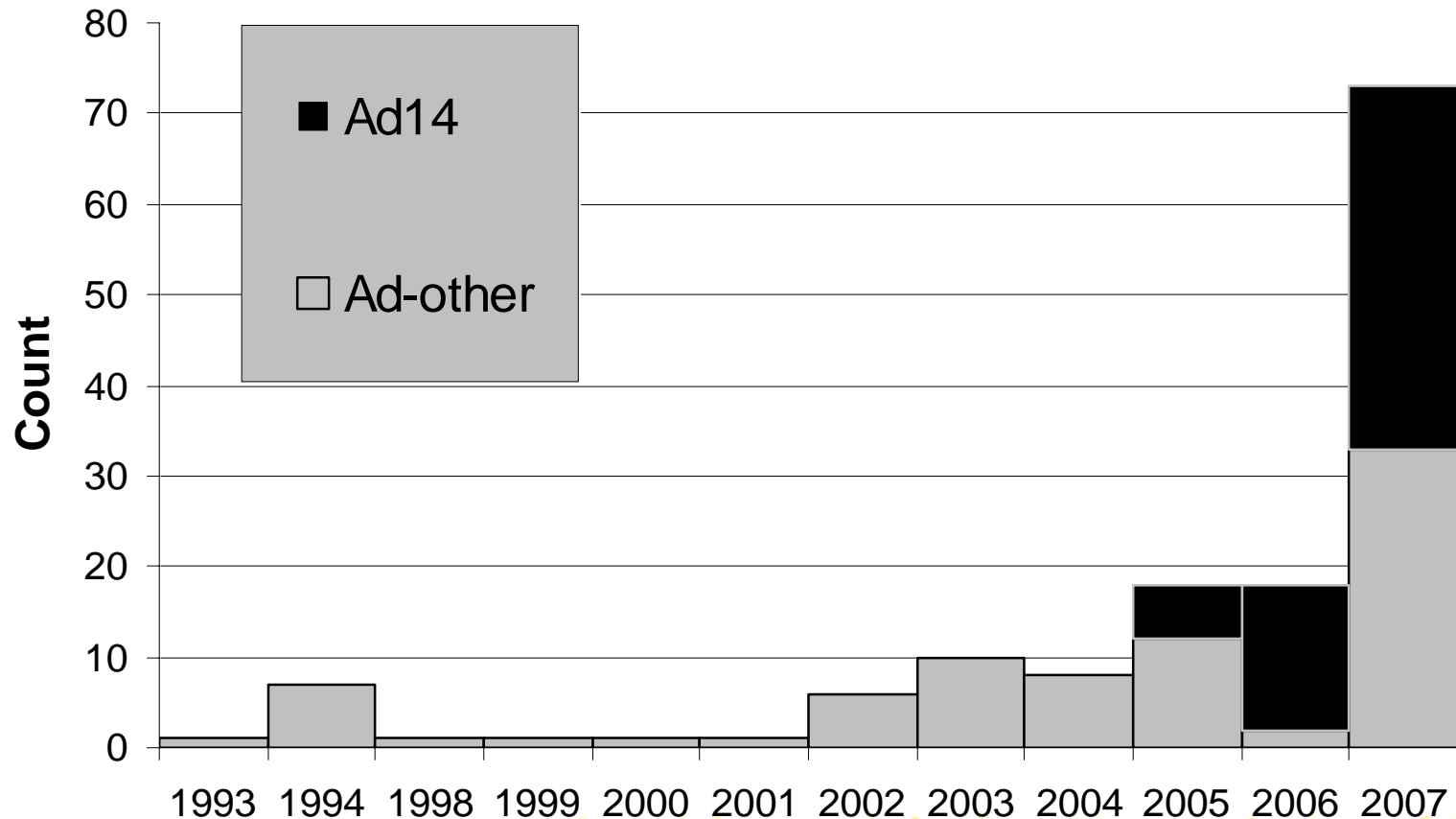
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Adenovirus 14, Oregon Active Surveillance 11/06 - 4/07



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Adenovirus14, Oregon State Public Health Lab 1993-2007

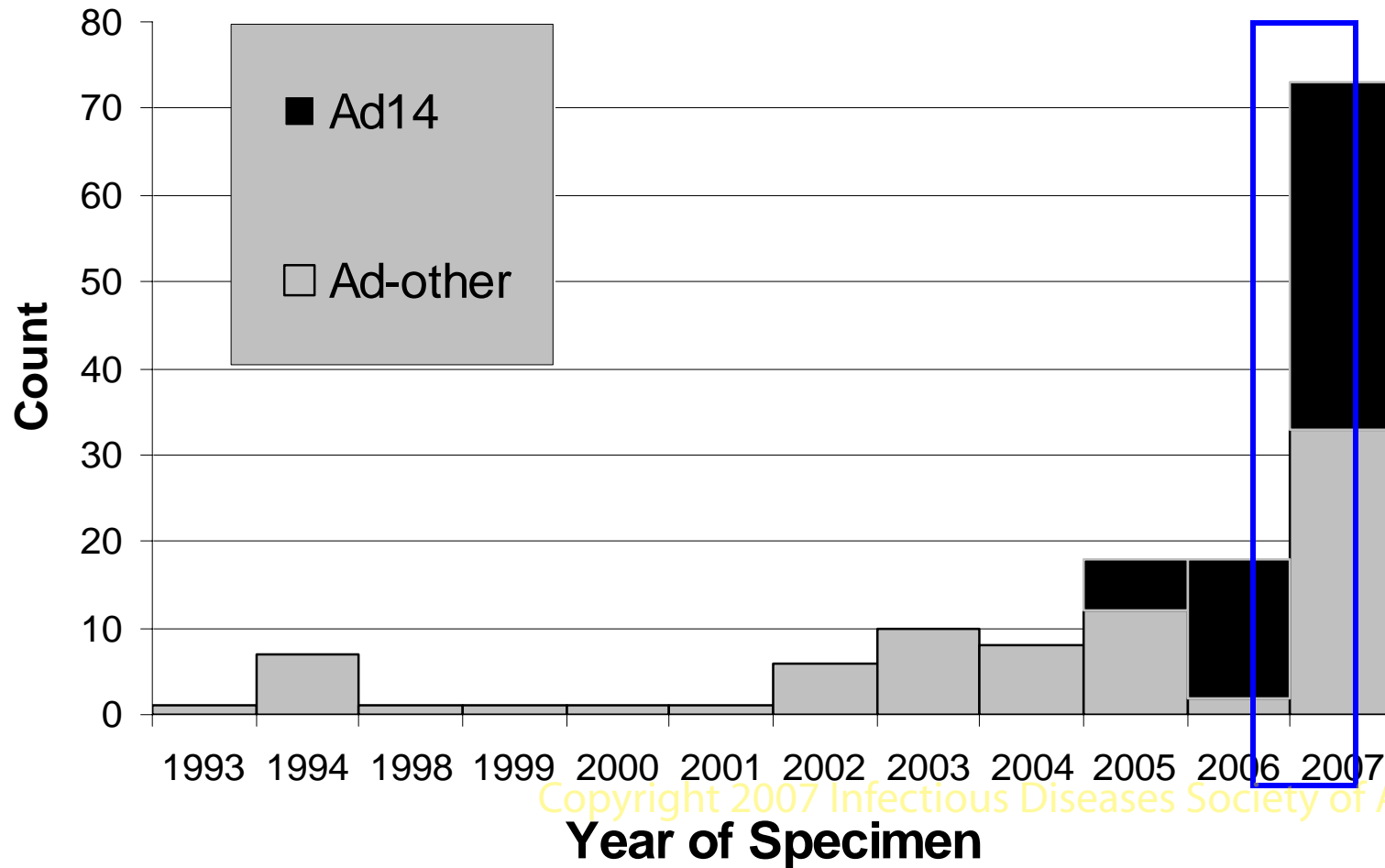


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Year of Specimen

Adenovirus14, Oregon State Public Health Lab 1993-2007

Study Period



Adenovirus in Oregon, Nov 06-Apr 07

	Ad14	Ad-other	Stats
Number	31	14	
Age median (range)	52.9 y (0-82 y)	1.1 y (0-33 y)	P<0.0001
Male #(%)	23 (74%)	11(79%)	NS
Hospitalized	22 (71%)	2 (14%)	OR 15.9
Smoker	14 (70%)	0 (0%)	

Adenovirus in Oregon, Nov 06-Apr 07

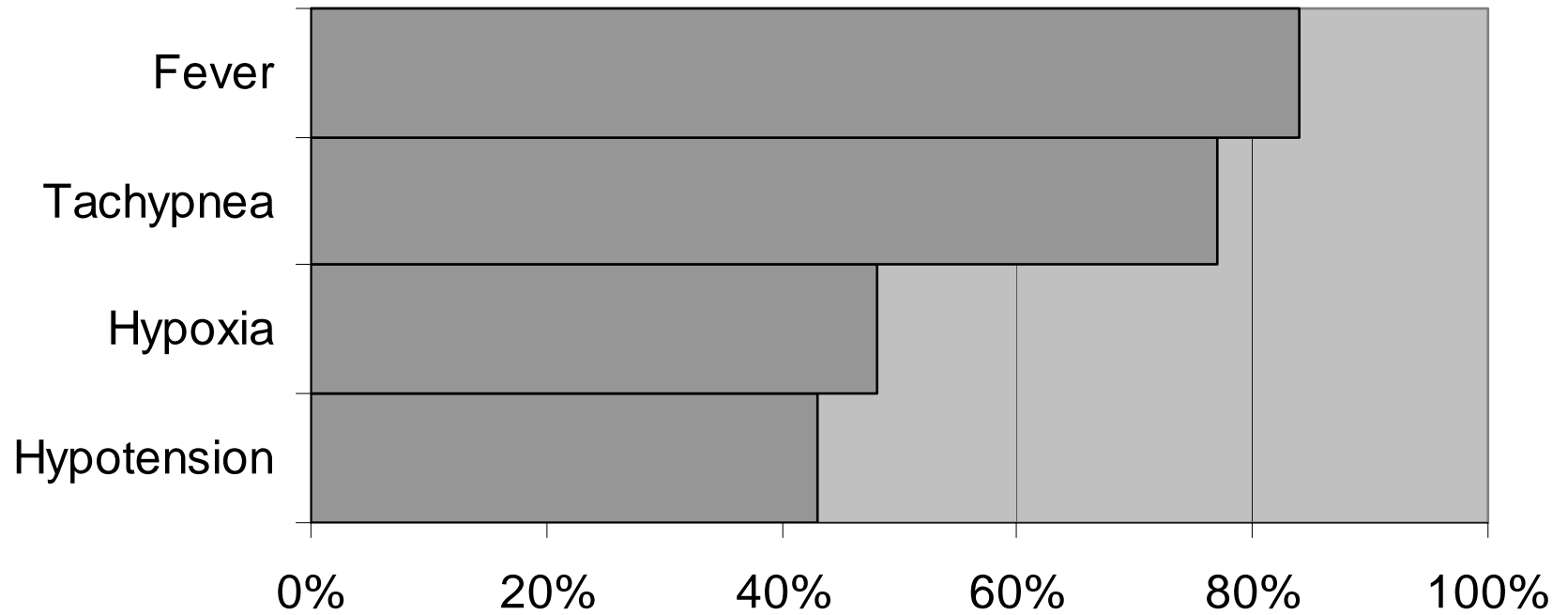
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Adenovirus 14, Underlying Illness

<u>Illness</u>	<u>Number (%)</u>
Hypertension	8 (27%)
Lung Disease	7 (23%)
Malignancy	6 (19%)
Steroid Use	5 (16%)
Diabetes Mellitus	4 (16%)

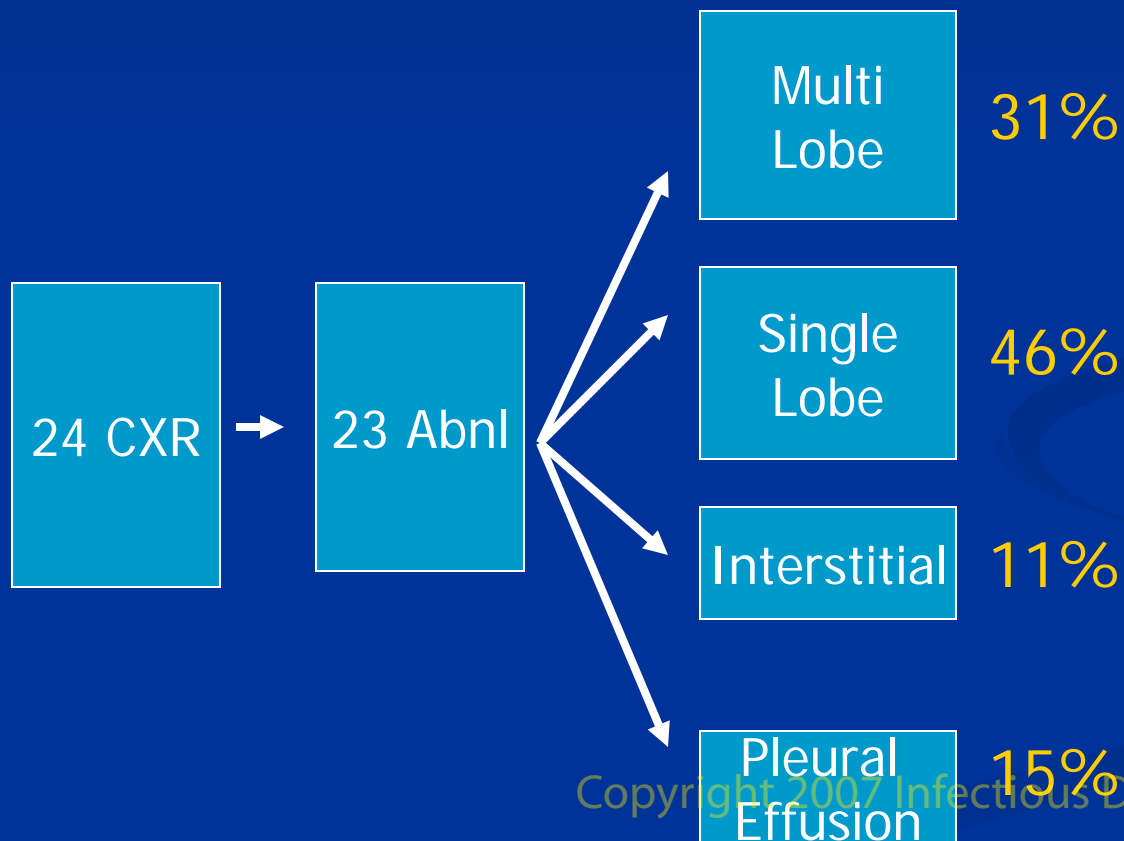
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Adenovirus 14 Clinical Features on Presentation

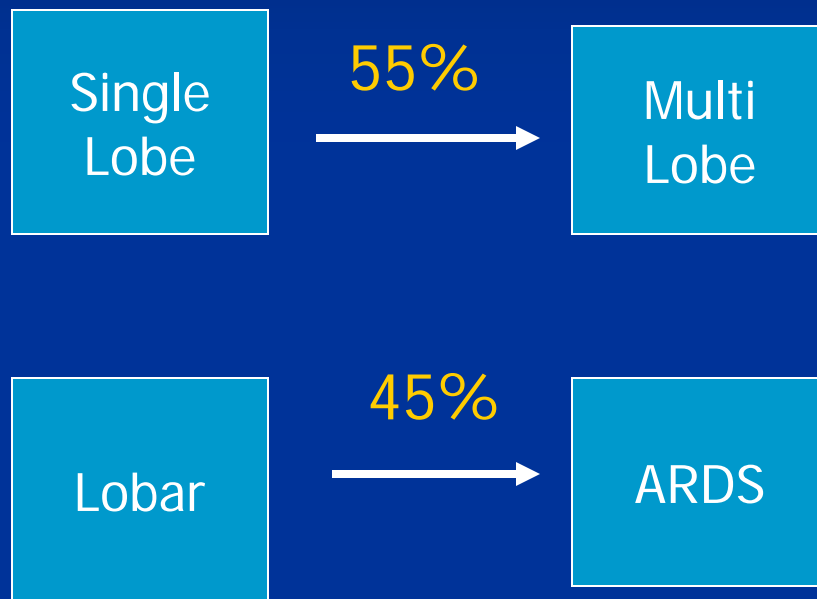


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Initial Radiographs



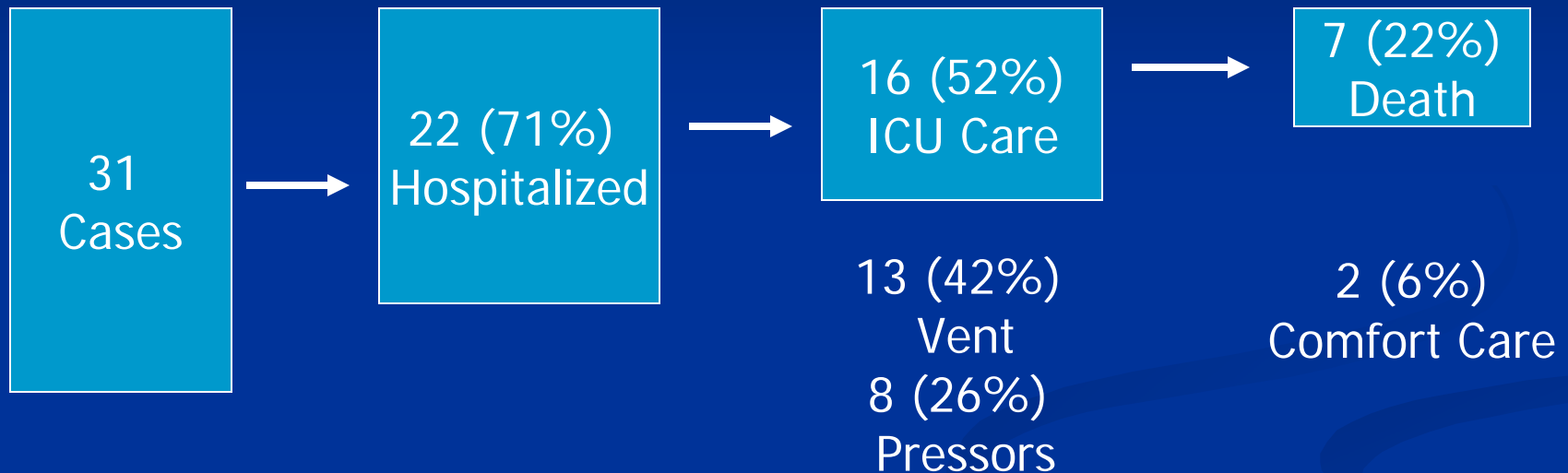
Radiograph Progression



Treatment

- Broad spectrum antibiotics used in all patients
- Cidofovir used in 6 patients
 - 2 deaths
 - 4 survivors
 - Dosing limited by nephrotoxicity

Adenovirus 14, Outcome



Hospital LOS
Median 7 days
Range 2-42

ICU LOS
Median 7 days
Range 2-19

Risk Factors for Death or ICU Care

<u>Univariate Analysis</u>	<u>OR</u>
Creatinine >1.2 mg/dl	12 (1.2-115)
Lymphocyte Count <100/ul	5.6 (1.1-22)
Other Pathogen	12 (1.2 -115)
<u>Multivariable Analysis</u>	
Creat >1.2, Lymph<100, Other pathogen	Similar OR, not significant

Infection Control

- Many patients placed in contact plus droplet isolation
- One possible case of healthcare worker illness linked to hospital exposure
 - CDC investigation of nosocomial transmission conducted, analysis pending

Limitations and future directions

- Limitations include:
 - Retrospective Study
 - Incomplete ascertainment
 - Testing bias
 - Prolonged adenovirus shedding
- Future Study
 - Transmission
 - Pathogenicity
 - Other populations

Adenovirus 14, conclusions

- Adenovirus type 14 emerged in 2005 in Oregon
- During the November – April study period
 - Most cases male
 - Typically 5th or greater decade of life
 - Current smokers
 - **n.b. females and infants were also affected**
- Outcomes
 - most hospitalized
 - > 20% died
 - Elevated creatinine, low lymphocyte count, and co-pathogens may predict severe outcome

Adenovirus 14 Recommendations

- Obtain viral culture in pneumonia patients who lack a specific etiology, especially those with severe disease
- If adenovirus 14 detected, anticipate stormy course
- Consult infectious disease regarding risk/benefit of specific therapy