Update on Infection Prevention and Control in Cystic Fibrosis

The 9th Annual Fleming Infection Prevention and Infectious Diseases Symposium

Lisa Saiman, MD MPH
Department of Pediatrics
LS5@columbia.edu
Received honorariums for serving on Scientific Advisory Boards: Novartis, Gilead, AB Comm, Inc., Savara, Teva

Contract with Gilead
Learning Objectives

• Learn the current epidemiology of CF pathogens
• Consider routes of transmission of various CF pathogens
• Learn best practices to minimize the risks of acquisition and transmission of CF pathogens
Cystic Fibrosis Genetics

- Most common lethal genetic disease among Caucasians
- Autosomal recessive
- Mutation in cystic fibrosis transmembrane conductance regulator (CFTR) gene
- cAMP regulated chloride channel located in apical membrane of glandular epithelium
- Located long arm of chromosome #7
  - F508del most common mutation
  - 1700 identified mutations
Cystic Fibrosis Epidemiology

- 70,000 worldwide
- 30,000 affected individuals in the U.S.
- 1 in 3,200 live births among Caucasians
- 1 in 9,200 Hispanic
- 1 in 15,000 African Americans
- 1 in 25 carrier rate (unaffected)
- 1,000 new cases per year
  - Newborn screening (NBS) in all states
  - >60% of patients detected by NBS.
  - 8% new diagnoses adults >18 years of age
Median Survival over time in U.S.
Respiratory disease main cause of morbidity and mortality

Median Predicted Survival Age, 1986–2013
In 5-Year Increments

U.S. CF Registry
Half of patients with CF in U.S. are adults

Number of Children and Adults with CF, 1986-2012

- Children Under 18 Years
- Adults 18 Years and Older

U.S. CF Registry
Age-Specific Prevalence of Respiratory Infections in CF Patients

Source: Cystic Fibrosis Foundation Patient Registry, Annual Data Report
Changing Prevalence of CF Pathogens

Respiratory Organisms Prevalence, 1988-2012

- S. aureus
- P. aeruginosa
- MRSA
- H. influenzae
- S. maltophilia
- B. cepacia complex

US CF Foundation Patient Registry, 2012
P. aeruginosa: 2006-2012

Incidence

Prevalence

Salsgiver E et al. CHEST 2015.
MRSA, 2006-2012

Incidence

Prevalence
Explaining Epidemiologic Changes?

- Improving lung function decreasing risk of infection
- Successful early eradication strategies for *P. aeruginosa*\(^1\)
- Increase in community acquisition of MRSA\(^2\)
- More rigorous infection prevention and control practices at CF centers\(^3,4\)

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Discussion

- Changes to the CFFPR population during the study period
  - Increased number of patients identified by newborn screening
Major Routes of Transmission of CF Pathogens

Indirect Contact Transmission

- Occurs when infectious agents are transferred through contaminated intermediate object or person

- **Examples**: Transfer of infectious agents via contaminated hands, contaminated respiratory therapy equipment, common items: eating utensils, drinking glass, toys, etc.

Droplet Transmission

- Respiratory droplets carrying infectious agents travel from respiratory tract of infectious individual to susceptible mucosal surfaces of another person, generally over short distances (3-6 feet)

- Droplets generated by coughing, sneezing OR procedures, e.g., pulmonary function tests or chest physiotherapy

Airborne Transmission

- Dissemination of droplet nuclei of respiratory size containing infectious agents

- May remain suspended in air for prolonged periods of time and dispersed over long distances by air currents

- Inhaled by susceptible individuals without face-to-face contact with infectious individual

Strain variation of *P. aeruginosa* in ability to remain suspended in air.

Clifton IJ. JCF 2010; 9:64
Evolving View of Droplet Transmission

• Data from:
  • Epidemiologic studies of outbreaks
  • Experimental studies
  • Aerosol dynamics

• Infectious droplets can remain suspended in the air 45 min. - 2 hrs.

• Experimental data from smallpox and SARS ≥ 6 ft.

• Experimental data in CF ~ 6 feet.

CDC. Isolation Guidelines 2007; Festini F. Am J Infect Control 2010; 38: 244;
Transmission of CF Pathogens and Associated Morbidity and Mortality
Pseudomonas aeruginosa
Liverpool Strain and Increased Risk of Mortality/ Transplant

Aaron S, et al. JAMA 2011

HR 3.26 (95% CI 1.41, 7.53, P=0.01)

Strain A
Liverpool
n=67

Strain B
N=32

Unique Strains
n=218
Transmission of Multi-resistant *P. aeruginosa* (MRPA), Houston

- **2006**: average MRPA in U.S. 16% vs. 30.1% in Houston
- **2004-2009 PA strains**: 32 of 71 (45%) patients had strains with >95% similarity, aka Houston-1
- **12** more hospital-days year before Houston-1 acquisition
- **Improved** IP&C practices in clinic and hospital reduced acquisition

<table>
<thead>
<tr>
<th>Logistic regression for variables associated with Houston-1 strain</th>
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<tbody>
<tr>
<td><strong>Strata</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Days from clinic visit</td>
</tr>
<tr>
<td>&lt; 60</td>
</tr>
<tr>
<td>61-120</td>
</tr>
<tr>
<td>&gt;120</td>
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<tr>
<td>Days from hospitalization</td>
</tr>
<tr>
<td>&lt; 90</td>
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<tr>
<td>91-180</td>
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<tr>
<td>181-365</td>
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<td>4.02*</td>
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Burkholderia dolosa
Distribution of *Burkholderia* spp., U.S.

- *B. cenocepacia* and *B. multivorans* most common 1997-2007
- *B. multivorans* now more frequent than *B. cenocepacia*

LiPuma JJ Clin Microbiol Rev 2010
**B. dolosa: Morbidity and Mortality**

- Case-control study
  - 31 *B. dolosa*
  - 24 *B. multivorans*
  - 58 age-, sex-matched controls
- Increased decline lung function
- Increased 18-month mortality
  - 13% *B. dolosa*
  - 7% *B. multivorans*
  - 3% controls

MRSA

- Mean 5.3 years follow-up
  - 1,732 persistently (+)ve
  - 13,922 never MRSA
- 8-21 year olds
  - (+)ve MRSA FEV\(_1\) 71.0%
  - Never MRSA FEV\(_1\) 79.6%

Impact of MRSA on Survival (N = 19,833)

Ad HR 1.27 (95% CI, 1.11, 1.45)

**Pseudomonas, Burkholderia, and MRSA: Adversely impact recovery of FEV₁ in Exacerbations**

NTM Epidemiology
CFF Patient Registry

Figure 87: Mycobacterial Species Isolated*

- Tuberculosis
- Abscessus/Cheloneae
- Avium Complex
- Fortuitum
- Gordoneae
- Kansasi
Epidemiology of NTM in CF

- Described since 1970’s
- Variable prevalence 2-28%

<table>
<thead>
<tr>
<th>Country</th>
<th>Patients</th>
<th>Species (%)</th>
</tr>
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<tbody>
<tr>
<td>US</td>
<td>986</td>
<td>MAC (72%)&lt;br&gt;\textit{M. abscessus} (16%)</td>
</tr>
<tr>
<td>France</td>
<td>385</td>
<td>\textit{M. abscessus} (39%)&lt;br&gt;MAC (21%)&lt;br&gt;\textit{M. gordonae} (18%)</td>
</tr>
<tr>
<td>Israel</td>
<td>186</td>
<td>\textit{M. Simiae} (41%)&lt;br&gt;\textit{M. Abscessus} (31%)&lt;br&gt;MAC (14%)</td>
</tr>
</tbody>
</table>

M. abscessus subspecies massiliense

- **Index case**: CF adult with multi-drug resistant *M. abscessus ssp. massiliense* for 7 years
  - Transfer to clinic: AFB 4+ smear (+)ve

- **Transmission**: 4 additional CF adults (+)ve next 8 months
  - 4/5 overlapping CF clinic days
  - 3/5 died

M. abscessus ssp. massiliense

- Whole genome sequencing
  NTM isolates, 2007-2011)
- 31 patients (+) M. abscessus
  - 13 subsp. abscessus (6-patient cluster)
  - 15 subsp. massiliense (2 clusters of 9 and 2 patients)
- 9 patient massiliense cluster
  - More hospital exposure (10.8 vs. 1.2 d, p= 0.01)
  - CF inpatient ward (5.7 vs. 1.5 d, p=0.01)
  - CF clinic (3.9 vs. 2.3 d, p=0.02)
  - Hospitalized same time as infected patient (4.2 vs. 0.6 d, p=.005)

Role of Healthcare Environment

• *P. aeruginosa* in room air samples
  – obtained when waking up or after physiotherapy
  – 12/22 (55%) infected patients
  – 6/12 (50%) genetically identical to sputum strains

• Liverpool Epidemic Strain
  – 5/8 (63%) air samples in CF clinic hallway

• Non-epidemic *P. aeruginosa*
  – 3/15 (20%) PFT machine surface

• *Pseudomonas* and *S. aureus*
  • 13.6% of sites in CF clinics contaminated
  • hands (7%), exam room air (8%), environmental surfaces (1%)
  • No differences in adults vs. children; routine vs. sick visit

Zuckerman H et al. J Cystic Fibrosis 2009; 8:186
Hands of People with CF, USA

- 74 patients' hands cultured prior to performing alcohol hand hygiene at start of clinic visit
  - Hand hygiene reduced hand contamination
  - But...patients’ hands contaminated at visit end

KEY RECOMMENDATIONS
RECOMMENDATION KEY MESSAGES

- Whenever feasible, provided *choices* for implementation strategies in healthcare settings.
- Emphasized treating all people with CF the same... *regardless of respiratory tract cultures*. Assume all people with CF could have transmissible pathogens in respiratory tract secretions.
- No longer recommending different care practices for those infected with *Burkholderia cepacia complex*
- Recommendations for non-healthcare settings and for healthcare professionals with CF intended to *provide education to help make informed choices*.
Use Principles of Adult Education

• **Increase Knowledge of all providers**
  - Perceive relevance of information to their personal situation
  - Flexible
  - Encourage networking, critical analysis, self-reflection on practice, opportunities for open questioning
  - Increase awareness of guidelines
  - **Repeated exposures to information**
  - Educational materials that include “WHY”

• **Increase Skills**
  - Observations
  - Return demonstrations

• **Acknowledge Impact of Attitudes**
  - Reflect individual beliefs, professional and personal life experiences
  - Must believe practice change directly benefits themselves or patients

Matlow AG. AJIC 2012; 40: 260 [environmental service workers]; Ferguson PE. BMT 2010;45:656 [pt./families]; (Miroballi Y, Pediatric Pulm 2012;47:144 [CF patients and families].
Partner with Local IP&C Teams

• **Both teams** are data analysis/data driven

• **Expertise of IP&C Teams**
  • Implementation, prioritization and staging of recommendations, if appropriate
  • Identifying appropriate stakeholders, including C suite
  • Monitoring adherence to practices and providing feedback
  • Apply experience with improving hand hygiene, respiratory hygiene, environmental cleaning, transmission precautions, and collaborations with microbiology lab

• Audits of hand hygiene and cleaning practices

• Use existing tools for monitoring cleaning effectiveness
  • [www.cdc.gov/HAI/toolkits/Evaluating-Environmental-Cleaning.html](http://www.cdc.gov/HAI/toolkits/Evaluating-Environmental-Cleaning.html)

Hand Hygiene (HH)

• Improve HH among Healthcare Providers:
  – Prior to patient contact or after contact with body fluids or inanimate objects, e.g., equipment
  – Make improvement institutional priority
  – Make supplies readily accessible

• Improve HH among people with CF and families

CDC HH Guidelines 2002; WHO HH Guidelines 2003;
Use of Gowns, Gloves, Masks

• Gowns and gloves
  • **Staff** wear when caring for all people with CF in hospital and ambulatory care areas
  – **Patients and families** do **not** wear gowns and gloves

• Masks
  – **All people with CF** wear surgical masks (if tolerated)
  – **Staff only** wear surgical masks if suspected pathogen spread by droplets, e.g., influenza or pertussis
  – **Staff only** wear N95 masks if suspected airborne pathogen, e.g., TB or measles

• 6 foot rule

Implementing Contact Precautions

- Pediatric CF center, USA (n=180)
- Measure pathogen revalence before and after all staff wore gowns and gloves for all CF patients
- Change in *P. aeruginosa* prevalence
  - 30% → 21% (p<0.001)
- Change in MRSA prevalence
  - 10.8% → 8.7% (p=0.008)

Savant AP et al. BMJ Qual Saf 2014;Suppl 1:i73-80
Transmission Precautions for Non-tuberculous Mycobacteria

*Insufficient evidence* to place people with CF who are infected with NTM on Airborne Precautions, i.e., negative pressure room.

Scheduling CF Clinics

*Insufficient evidence* to routinely scheduling CF clinics based on specific pathogens isolated from respiratory tract cultures.
4 Options for Performing PFTs

1. In exam room at beginning of clinic visit
2. In a negative pressure room (Airborne Infection Isolation Room = AIIR)
3. In PFT lab with either portable or integrated high-efficiency particulate [HEPA] filters
4. In PFT lab without HEPA filtration, allowing 30 minutes to elapse before next person with CF enters PFT lab.

Psychosocial Impact IP&C Guidelines

• Centers should anticipate specific concerns regarding psychosocial impact of implementing IP&C recommendations

• Identify strategies to minimize negative impact

Bowmer G et al. J Cystic Fibrosis 2017;16(1):146-50
CF Foundation- and CF Center-sponsored Indoor Events

• Only one person with CF attend CFF- or CF Center-sponsored indoor events (e.g., CF Education Days) unless they live in the same household.

• Develop and utilize alternative CF education programs, (e.g., videotapes, video-conferencing, CD-ROM web-based learning, Apps)
**Cross-infection Policy**

Guidance for people with cystic fibrosis at events and meetings

- **UK CF Trust** “…it is our policy for only one person with CF to be present...at an indoor event organised by Trust staff or its volunteer branches, groups, and committees…

- **CF Canada** “For indoor events, a provision has made for organizers to invite one person with CF to attend.”

*CHEST JOURNAL*

- Sponsored Pro-Con debate on this recommendation
BALANCING INFECTION PREVENTION AND CONTROL WITH QUALITY OF LIFE
Updated Executive Summary

Summary and Conclusions

• The epidemiology of CF pathogens is changing; most notably the incidence and prevalence of *P. aeruginosa* are decreasing with the incidence and prevalence of MRSA are increasing.

• Infection prevention and control may be reducing acquisition of some CF pathogens.

• New knowledge mandated new guidance for IP&C practices for CF.

• To be effective at preventing transmission of CF pathogens, IP&C has to be understood and practiced by everyone.

• Research directions suggested by recommendations with *insufficient evidence*.
Questions, Comments, Thoughts, Concerns???