Johns Hopkins and eCysticFibrosis Review *Present*

DANIEL

A Case for Early Intervention in *Pseudomonas aeruginosa* Eradication

WEBCAST

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PETER J. MOGAYZEL, JR, MD, PHD
Professor of Pediatrics
Director, Cystic Fibrosis Center
Johns Hopkins University School of Medicine
Baltimore, Maryland

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WELCOME

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LEARNING OBJECTIVES

- Evaluate the pros and cons of early *P. aeruginosa* eradication.
- Summarize the current evidence basis and expert opinion informing eradication best practices.
- Discuss key data from significant eradication trials including ELITE, EPIC, and ALPINE.
- Integrate evidence-based strategies to assess and improve eradication in the early stages of *P. aeruginosa* infection.

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The following relationships have been reported for this activity: PLANNERS

Faculty	Relationship
Michael Boyle, MD, FCCP	**SCIENTIFIC ADVISORY BOARD:** Gilead Sciences, Inc., Novartis Pharmaceuticals, Savara Pharmaceuticals, Vertex Pharmaceuticals Incorporated **PRINCIPAL INVESTIGATOR:** Vertex Pharmaceuticals Incorporated

No other planners have indicated that they have any financial interest or relationships with a commercial entity.

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ACKNOWLEDGEMENTS

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EDUCATIONAL SUPPORT

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- This activity is supported by an educational grant from Gilead Sciences, Inc. to Johns Hopkins University School of Medicine.

- All activity content and materials have been developed solely by the Johns Hopkins activity directors, planning committee members and faculty presenters, and are free of influence from Gilead Sciences, Inc.

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MARGARET ROSENFELD, MD, MPH
Professor, Department of Pediatrics
Director, Research Scholars Program
Associate Director, Center for Clinical and Translational Research
Seattle Children's Hospital

OFF-LABEL DISCUSSION: tobramycin inhalation solution

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WHY ERADICATION – A CLINICAL PERSPECTIVE

LEARNING OBJECTIVES

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- Describe the importance of early detection of *P. aeruginosa* infection.
- Describe the rationale for eradication therapy for newly acquired *P. aeruginosa* infection.
- Describe the accuracy of oropharyngeal cultures compared to cultures obtained by bronchoscopy for identifying *P. aeruginosa* infection.

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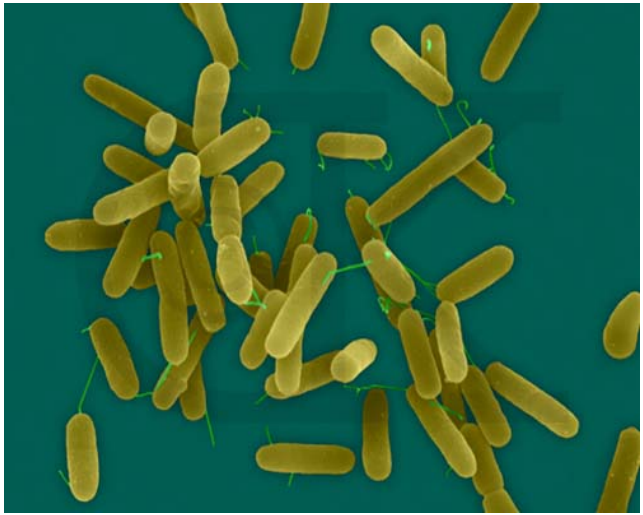
PSEUDOMONAS AERUGINOSA IN CF

- Sentinel pathogen in CF
- ~80% of U.S. adults with CF chronically infected
- Associated with:
  - More rapid lung function and CXR score decline
  - Poorer nutrition
  - More frequent hospitalizations
  - Poorer survival



INITIAL *PA* INFECTION

- Generally acquired from the environment (not patient to patient transmission)
  - Presumably enters lower airways by inhalation or from upper airway/sinus reservoir
- Typically non-mucoid
- Present at low density
- Highly antibiotic sensitive
- "Window of opportunity" to eradicate before development of chronic infection
- Current guidelines of care emphasize early detection and antibiotic treatment of initial/early *Pa*

INITIAL *PA* INFECTION: RISK FACTORS

- Risk of initial acquisition ~16% per year in infants and young children
- Few risk factors identified:
  - High risk CFTR mutations
  - Living in warmer, wetter climates

INITIAL *PA* INFECTION: CLINICAL OUTCOMES

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- Not associated with overt changes in clinical status
  - FEV_1
  - Height, weight
- Associated with greater likelihood of subsequent hospitalizations
- In pre-eradication era, *Pa* isolation prior to age 5 associated with poorer 8-year survival

Zemanick E, et al. Pediatr Pulmonol 2014; Emerson J, et al, Pediatri Pulmonol 2002.

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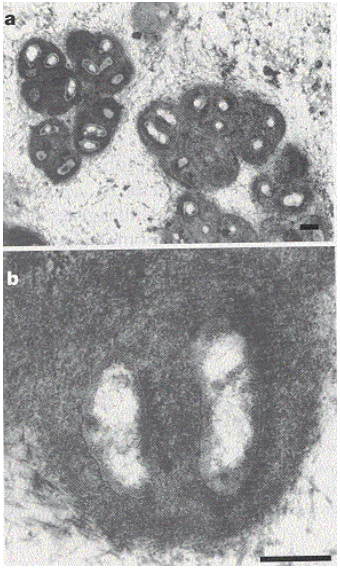
TRANSITION TO CHRONIC INFECTION

- Initial *Pa* infection generally progresses to chronic infection over a period of years
- Both host and pathogen characteristics promote chronic infection
- Host factors:
  - Dehydrated airway surface and abnormal mucociliary clearance
  - Impaired function of antimicrobial peptides
  - Neutrophilic inflammation damages airways

PA ADAPTATION TO THE CF LUNG

- *Pa* has multiple mechanisms to adapt to and chronically infect CF airway
  - Biofilm formation
    - Structured communities of bacteria encased in alginate matrix
  - Development of mucoid phenotype
  - Increased antibiotic resistance
- Chronic *Pa* infection is extremely difficult to eradicate



Singh PK et al. *Nature*, 2000; 407:659-818.

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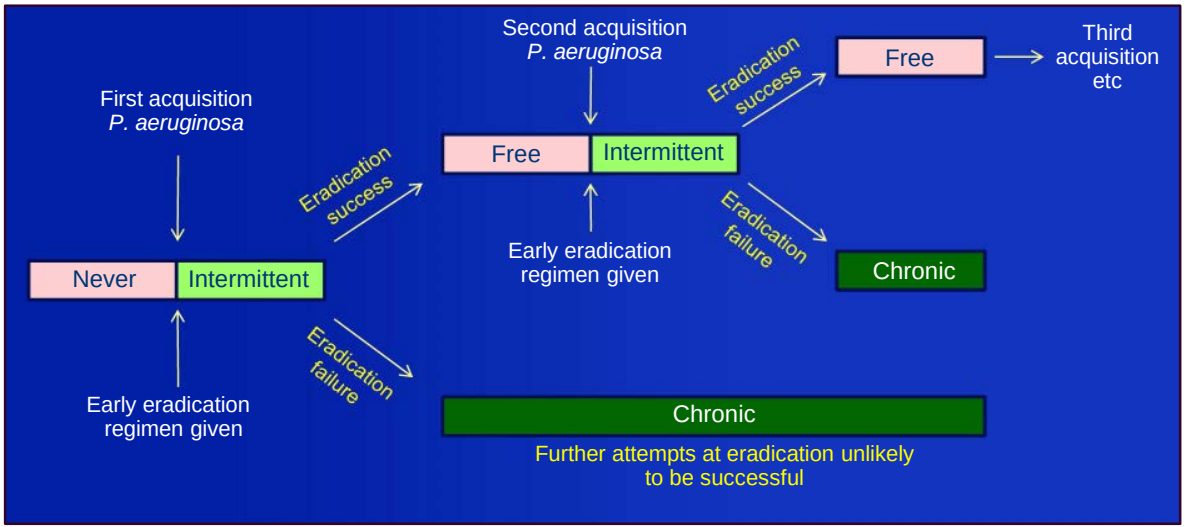
STAGES OF *PA* INFECTION



Lee TW. Chron Respir Dis. 2009;6:99-107.

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EARLY DETECTION OF *PA*

- Detection of early infection challenging as most at-risk patients do not expectorate sputum
- Debate continues regarding oropharyngeal (OP) swabs vs. BAL
  - Each has advantages and disadvantages
- In U.S., OP swabs usual source of micro specimens; recommended at least quarterly
- As oropharynx may serve as reservoir for lower airway infection, positive OP cx may be important in its own right – generally share genotype

DIAGNOSTIC ACCURACY OF OP CULTURES COMPARED TO BAL FOR *PA* DETECTION

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***Pa* Prevalence**	**8%**	**23%**
Sensitivity	44 (14, 79)	68 (43, 87)
Specificity	95 (90, 99)	94 (85, 98)
PPV	44 (14, 79)	76 (50, 93)
NPV	95 (90, 99)	91 (81, 97)

Rosenfeld M, et al, Pediatr Pulmonol 1999.

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ANTIBIOTIC TREATMENT OF EARLY *PA* INFECTION

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- Objective: to eradicate *Pa* while still antibiotic-susceptible and present at low density
- Originally proposed by Copenhagen CF Clinic in 1980s
- Now standard of care in most countries but no universal consensus on specific protocols

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EARLY ERADICATION THERAPY TRIALS

- Approaches have included inhaled, oral and IV antibiotics, alone or in combination
- In general have shown similar eradication rates
- Clinical efficacy more difficult to evaluate
- Difficult to compare study results due to differing eligibility criteria, endpoints, definitions of eradication success/failure

ERADICATION THERAPY GUIDELINES

- European Consensus Conference
  - 28 days of TIS when there is a positive culture is a recommended treatment strategy. However, … the optimal antibiotic regimen is unknown

    (Doring et al, *JCF* 2012:11;461-79.)
- Draft CFF Consensus Guidelines:
  - The CF Foundation strongly recommends inhaled antibiotic therapy for the treatment of initial or new growth of *P. aeruginosa* from an airway culture. Certainty of net benefit, high; Estimate of net benefit, substantial; Grade of recommendation, A. The favored antibiotic regimen is inhaled tobramycin (300 mg twice daily) for 28 days.

    (Mogayzel, et al, in press)

SUMMARY: WHERE WE ARE WITH *PA* ERADICATION

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- TSI most widely recommended treatment but optimal regimen not known
- Eradication success high but still ~20% failure rate
  - May need personalized approaches based on risk factor profile
- Despite eradication of *Pa*, we still see bronchiectasis, air trapping and abnormal lung function in young children
  - Inflammation?
  - Role of microbiome / other organisms?

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THE DECISION TO ERADICATE

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HARM TIDDENS, MD
PROFESSOR, PEDIATRICS PULMONOLOGY
ERASMUS MC-SOPHIA CHILDREN'S HOSPITAL
ROTTERDAM, NETHERLANDS

DONNA PEELER, RN, BSN
PEDIATRICS CLINICAL COORDINATOR, CYSTIC FIBROSIS CENTER
JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE
BALTIMORE, MARYLAND

Harm Tiddens, MD
FACULTY DISCLOSURE: Grant/Research Funding: Gilead Sciences, Inc., Chiesi Farmaceutici; HONORARIA: Gilead Sciences, Inc.

OFF-LABEL DISCUSSION: tobramycin inhalation solution, aztreonam inhalation solution, colistin, ciprofloxacin

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APPROACHES TO TREATING THIS PATIENT

LEARNING OBJECTIVES

- Describe effective approaches to eradication therapy for newly acquired *P. aeruginosa* infection.
- Describe advantages and disadvantages of various *P. aeruginosa* eradication strategies.
- Describe the importance of adherence and proper administration technique in the success of *P. aeruginosa* eradication therapy.

CONSIDERATIONS FOR SELECTING TREATMENT

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- Age of Daniel: 3 years
- Cooperative vs noncooperative (50%?)
- Socio economical
- *Pseudomonas aeruginosa (Pa)* history
- *Pa* phenotype (mucoid?)
- Evidence

Schelstraete, JCF 2013

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PA ERADICATION IN CHILDREN: CULTURE NEGATIVE RATES

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Reference Study	*Excl Pa Antibodies*	Drug	Dose	Mean Age (SD) *Years*	Patients *nr*	Children < 6 year *nr*	Pa after end of treatment *Weeks*	Rates Neg *Pa* %
Gibson, Ped Pulm, 2007	no	TSI	300 mg bid	2.4	8	100%	8	63
Ratjen, Thorax 2010 ELITE	yes	TSI 28 vs 58 days	300 mg bid	8.7 (7.2)	88	42%	4	~92
Ratjen, Thorax 2010 ELITE	yes	TSI 28 vs 58 days	300 mg bid	?	65	?	12	~86
Treggiari, Arch Pediatr Adolesc Med 2011 EPIC	no	TSI vs TSI + ciproflox acin	300 mg bid	5.5 (3.7)	152	60%	58	57

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Reference Study	*Excl Pa Antibodies*	Drug	Dose	Mean Age (SD) *Years*	Patients *nr*	Children < 6 year *nr*	Pa after end of treatment *Weeks*	Rates Neg *Pa* %
Taccetti, Thorax 2011	no	TSI +ciprofloxicin vs colistin + ciprofloxacin	300 mg bid $2x10^6$ U	~7,5	223	48%	24	66
Proesmans, JCF 2013	no	TSI vs colistin + ciprofloxacin	300 mg bid $2x10^6$ U	~9.8	58	?	12-20	44-65
Tiddens, JCF 2014 ALPINE	no	aztreonam	75 mg tid	6.3 (4.7)	105	47%	28	58
Tiddens, JCF 2014 ALPINE	yes	aztreonam	75 mg tid	?	49	?	12	86

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SERIAL PA CULTURE RESULTS BEFORE AND AFTER TIS OROPHANYNGEAL (OP) AND BRONCHOALVEOLAR LAVAGE (BAL)

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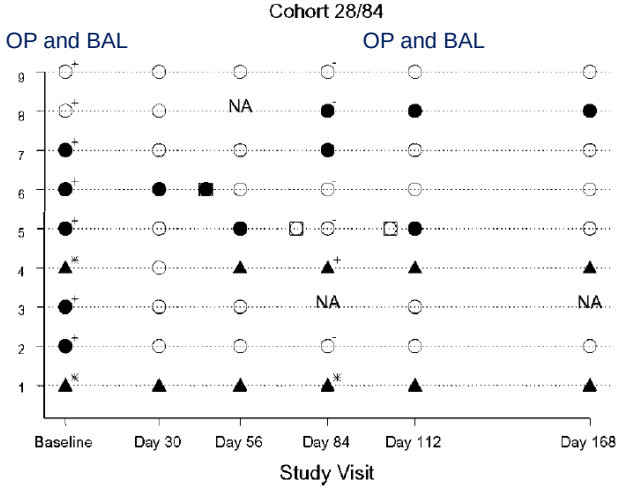

● = OP *Pa* +
▲= OP *Pa* + mucoid
■ = OP *Pa* + (acute visit)
+ = BAL *Pa*
*= BAL *Pa* mucoid
○ = OP *Pa* -
□ = OP *Pa* – (acute visit)
- = BAL Pa -

Gibson, Pediatric Pulmonology, 2007

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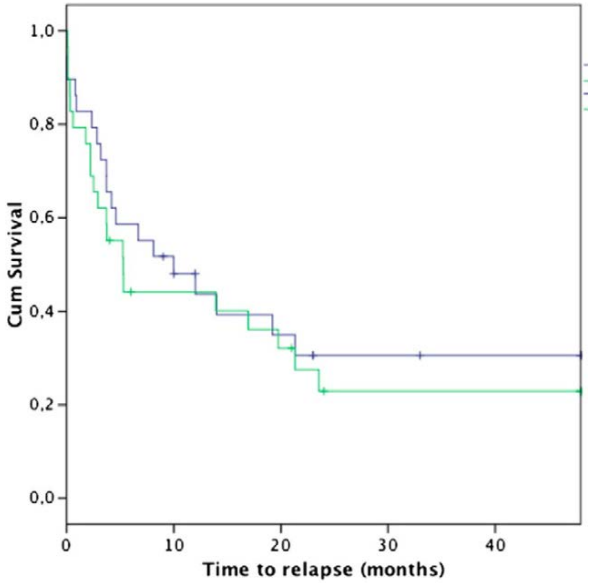
PA FREE SURVIVAL



- TSI (n=23)
- colistin + ciprofloxacin (n=26)
- Time from end of successful *Pa* eradication treatment

Proesmans, J Cyst Fibros, 2013

ALPINE: *PA* CULTURE RESULTS

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			Patients culture-negative for *P. aeruginosa*; n (%)			
		N	Week 4 (EOT)	Week 8	Week 16	Week 28
All patients completing 28-day treatment period		101	90 (89.1)	76 (75.2)	64 (63.4)	48 (47.5)
Subgroups						
Age	3 months to < 2 years	23	20 (87.0)	17 (73.9)	14 (60.9)	12 (52.2)
	2 to < 6 years	24	23 (95.8)	19 (79.2)	15 (62.5)	10 (41.7)
	6 to < 18 years	54	47 (87.0)	40 (74.1)	35 (64.8)	26 (48.1)
P. aeruginosa infection history	First	71	63 (88.7)	55 (77.5)	47 (66.2)	37 (52.1)
	Recurrent	30	27 (90.0)	21 (70.0)	17 (56.7)	11 (36.7)
P. aeruginosa culture at baseline[a]	Positive	42	36 (85.7)	23 (54.8)	18 (42.9)	11 (26.2)
	Negative	56	52 (92.9)	50 (89.3)	43 (76.8)	35 (62.5)
				p < 0.001	p = 0.005	p = 0.004
P. aeruginosa phenotype at baseline[b]	Mucoid	3	3 (100)	3 (100)	1 (33.3)	1 (33.3)
	Non-mucoid	39	33 (84.6)	20 (51.3)	17 (43.6)	10 (25.6)
Antibodies to *P. aeruginosa* at baseline[a,c]	Negative	62	57 (91.9)	49 (79.0)	42 (67.7)	35 (56.5)
	Borderline	19	17 (89.5)	13 (68.4)	11 (57.9)	6 (31.6)
	Positive	17	15 (88.2)	12 (70.6)	9 (52.9)	5 (29.4)

Tiddens et al., JCF, 2014

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DETERMINANTS FOR UNSUCCESSFUL ERADICATION *PA*

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- 'Known'
  - History of positive *P. aeruginosa*
  - Elevated *P. aeruginosa* antibodies at baseline
  - Positive culture at inclusion and at baseline
  - *P. aeruginosa* phenotype (mucoid vs non-mucoid)
- 'Unknown'
  - Young age?
  - Severe structural lung disease?
  - Distribution of lung disease (central vs small airways)?
  - Insufficient concentrations of inhaled antibiotics in diseased areas
  - Poor adherence to treatment
  - Poor inhalation competence?
  - Uncooperative character?
  - Poor socioeconomic conditions?

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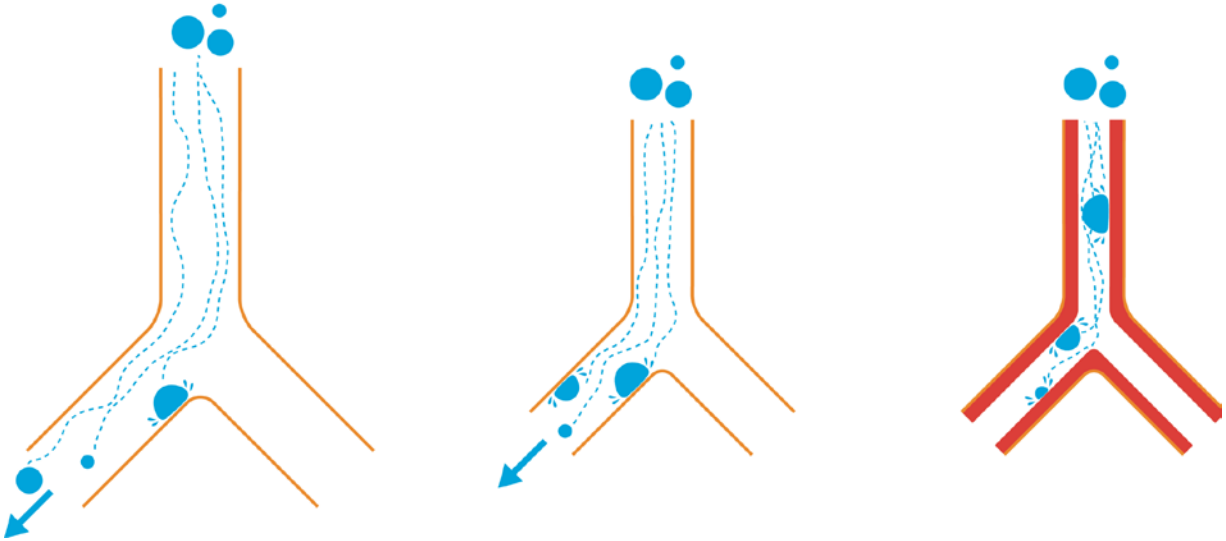
AGE AND CONCENTRATIONS OF INHALED ANTIBIOTICS IN AIRWAYS



Tiddens et al, Inhaled antibiotics: Dry or Wet, ERJ 2014 in press

SEVERITY OF STRUCTURAL LUNG DISEASE AND DISTRIBUTION OF INHALED ANTIBIOTICS

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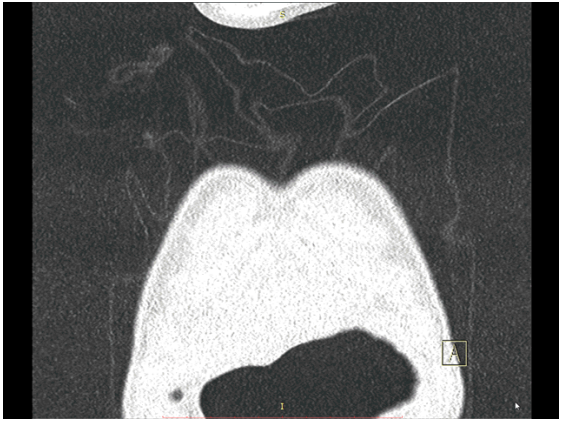
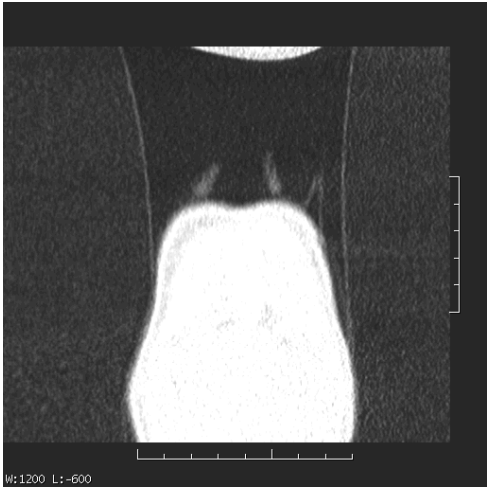


Age 2 years
P. aeruginosa negative



Age 2 years
P. aeruginosa positive

SEVERITY OF STRUCTURAL LUNG DISEASE: % OF DISEASED LUNG (NOT TRAPPED AIR)

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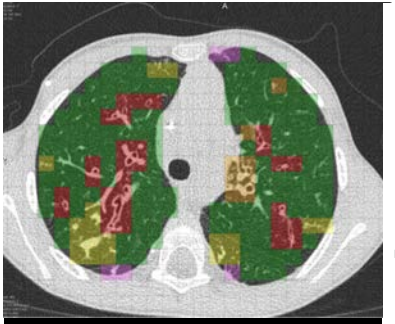
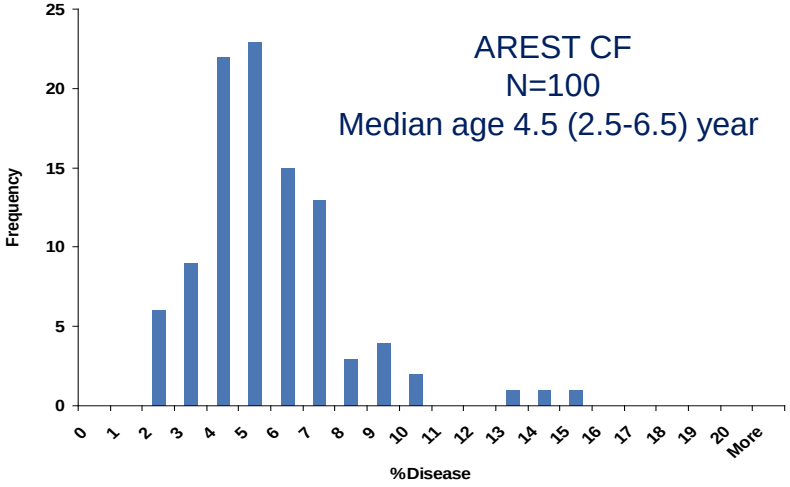


Legend: inspiratory

1. Bronchiectasis
2. Mucous plugging / consolidation
3 Bronchial wall thickening
4. Atelectasis
5. Normal lung



Kuo, Oudraad, Rosenow, Tiddens, Stick; manuscript in preparation

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SEVERITY OF STRUCTURAL LUNG DISEASE: TRAPPED AIR (= SMALL AIRWAYS INVOLVEMENT)

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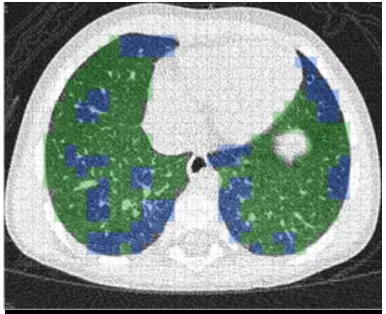
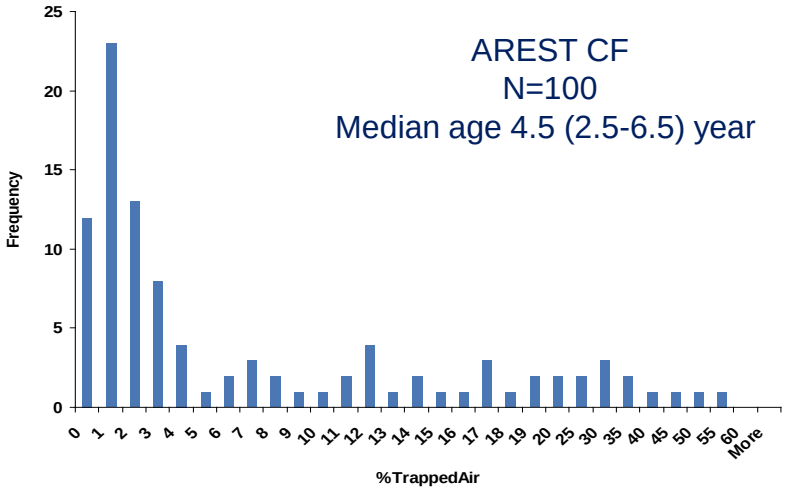


Legend: expiratory

1. Trapped air ≥ 50% of the cell

2. Trapped air < 50% of the cell



Kuo, Oudraad, Rosenow, Tiddens, Stick; Manuscript in preparation

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SEVERITY OF STRUCTURAL LUNG DISEASE AND DISTRIBUTION OF INHALED ANTIBIOTICS

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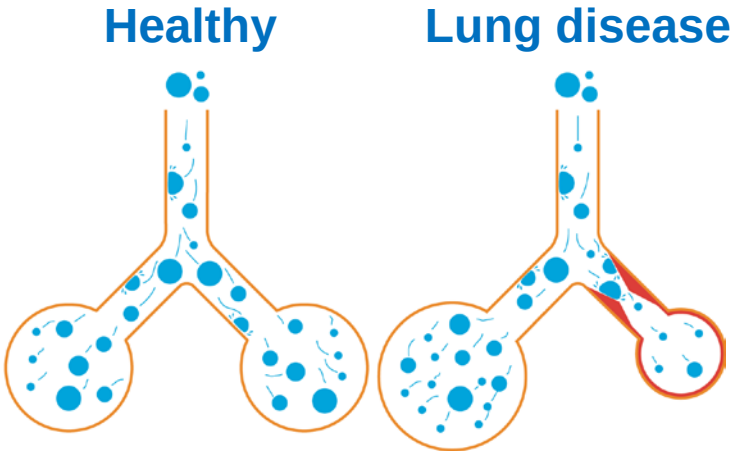

Tiddens et al, Inhaled antibiotics: Dry or Wet, ERJ 2014

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DISTRIBUTION OF LUNG DISEASE; DEPOSITION OF INHALED ANTIBIOTICS IN LARGE VS SMALL AIRWAYS

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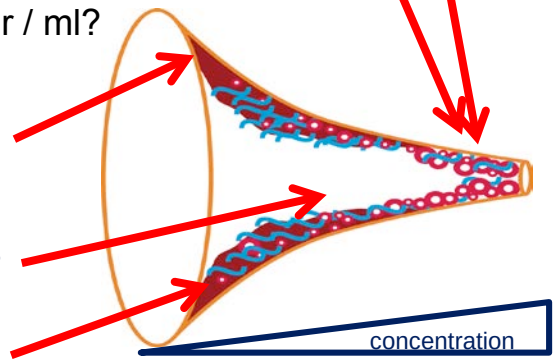
- Airway surface area 1 M2 -> 12 M2
- Epithelial lining fluid 7µm high
- Epithelial lining fluid 84 ml?
- 300 mgr TIS/ 27 mgr TIP => 300 µgr / ml?
- Adequate 125 µgr / ml

TIP 1979 ± 2770 µgr/ml
TIS 1074 ± 1182 µgr/ml



Concentrations small airways?

Questions Nebulized Antibiotics

Influence breathing pattern?

Influence particle size?

Influence structural lung changes?

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CONCENTRATIONS OF INHALED ANTIBIOTICS IN DISEASED AREAS

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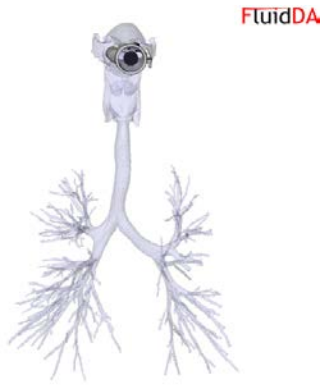
Hypothesis

- Concentrations of aztreonam depend on severity of CF lung disease
- Structural lung changes → local doses below MIC in small airways

Methods

- Computational fluid dynamics (CFD)
- Influence of tidal volume, particle size
- CF patients (5-17 yrs)
- 40 routine in and expiratory CTs
- CF-CT scores for disease severity
- Patient-specific 3D lung models
- Computation % total airway area with [aztreonam] < 10xMIC90 for *P. aeruginosa*



Bos, Submitted

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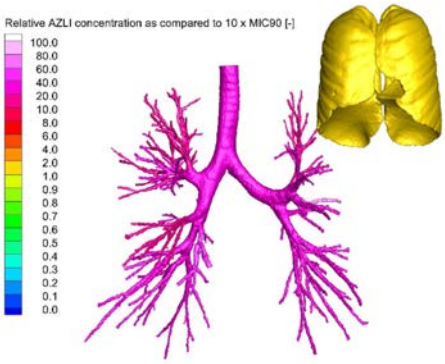
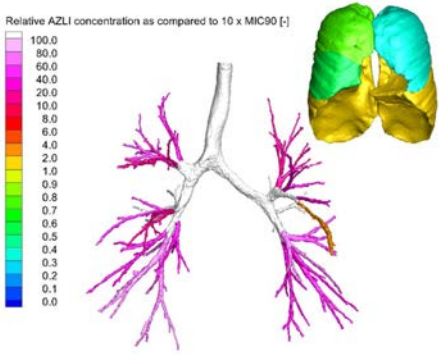
RESULTS

- Most lobes concentrations well above the 10xMIC90 threshold.
- Aztreonam concentration in lower lobes always > 10xMIC90
- Upper lobes more structural abnormalities and lower aztreonam concentrations than lower lobes
- Worst case scenario (large particles high TV) → up to 28% of lobes [aztreonam] < 10xMIC90.
- Aztreonam concentrations in lobes highly patient specific





SUMMARY

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- Success *Pa* infection eradication 44-92%
- Success rates lower when:
  - 2 or more positive *Pa* cultures before start therapy
  - Positive *Pa* antibodies
  - Mucoid phenotype *Pa*

- Other risks of failure
  - Poor adherence
  - Poor inhalation competence
  - Severe structural lung disease
  - Uncooperative child

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FAMILY COMMUNICATION

- Explain rationale for *P. aeruginosa* eradication protocol to patient and family.
- Explain medication side effects, order of medications and equipment cleaning and disinfection with patient and family.

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REINFECTION – HOW TO PROCEED

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CLAIRE WAINWRIGHT, MBBS, MRCP, FRACP, MD
RESPIRATORY SPECIALIST AND HEAD OF CYSTIC FIBROSIS SERVICES
ROYAL CHILDREN'S HOSPITAL
HERSTON, QUEENSLAND, AUSTRALIA

FACULTY DISCLOSURE: Grant/Research Funding: Novartis Pharmaceuticals, Vertex Pharmaceutics Incorporated
Advisory Board: Vertex Pharmaceuticals Incorporated
Honoraria: Vertex Pharmaceuticals Incorporated

OFF-LABEL DISCUSSION: tobramycin inhalation solution, aztreonam inhalation solution, colistin, ciprofloxacin

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WHAT TO DO WHEN REINFECTION OCCURS

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LEARNING OBJECTIVES

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- Identify risk factors for recurrent *P. aeruginosa* infection.
- Describe the approaches for treatment of recurrent *P. aeruginosa* infection.
- Describe methods used to define chronic *P. aeruginosa* infection.

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ACQUISITION AND ERADICATION OF *PA*

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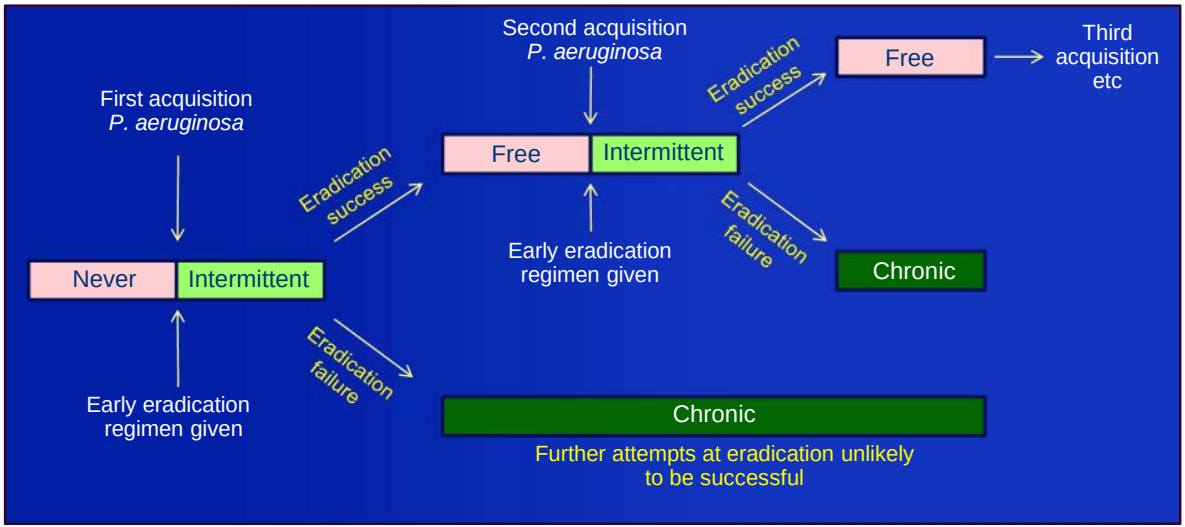

Lee TW. Chron Respir Dis. 2009;6:99-107.

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PREVALENCE OF REINFECTION WITH *PA*

- **Not many multisite longitudinal studies have followed children from birth.**
- **Prevalence of reinfection will depend on the time monitored and likely depends on:**
  - Treatment received for initial infection: timing/treatment given/adherence etc
  - Other treatments given: possibly staph prophylaxis?
  - Geographical site
  - Type of sample collected
  - Frequency of sampling
  - Definitions: eg, BAL does 100CFU/mL count?
  - Age

REINFECTION WITH *PA*: A COMPARISON HISTORICAL VS EPIC PROTOCOL DRIVEN TREATMENT

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- Historical data from epidemiological study of CF n=608
- EPIC trial n=304
- Mean age 5.5 years (range 0.1-13 years)
- Length of follow up approx 80 weeks (1.5 years)
- 35% children in EPIC study, and 54% in historical cohort had *Pa* recurrence

OP cultures only and no genotyping, frequency OP cultures inconsistent in historical group

Mayer-Hamblett et al. Pediatr Pulmonol 2013

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ACFBAL FOLLOWED 157 CHILDREN FROM CF DIAGNOSIS THROUGH NEWBORN SCREEN TO 5 YEARS

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- OP cultures in all, 1/2 had BAL, all BAL at 5 yrs
- Of 82/157 children who acquired *Pa* in first 5 years life - 36 (44%) reacquired *Pa*
- Average 2.8 years of observation post 1st acquisition

Wainwright et al. JAMA 2011

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SINGLE SITE STUDIES- OLDER COHORT

- Tacetti et al. *ERJ* 2005 – children and adults Florence – 24/47 **(51%)** patients reinfected over 7 years observation
- Munck et al. *Pediatr Pulmonol* 2001 – 19 children up to 14.5 years all reinfected **(100%)** over 3-25 months' observation
- Schelstraete et al. *J Cyst Fibros* 2010 – 41 children and adults with *Pa* given eradication, 7 failed and termed chronically infected, 18/34 **(53%)** with initial success reacquisition over median 50 months' observation

BEST ESTIMATE OF PREVALENCEOF RE-INFECTION WITH *PA* FOR YOUNG PRE-SCHOOL CHILDREN

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35% - 44% of children who receive initial prompt treatment over next 2-3 years

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IS IT RE-INFECTION OR TREATMENT FAILURE?

- Genotyping of samples
- Site of sample collection

SITE AND GENOTYPE

- Munck et al. *Pediatr Pulmonol* 2001- (sputum or catheter passed through nose to laryngeal aperture and aspirated) 14/19 acquired a new genotype
- Schelstraete et al. *J Cyst Fibros* 2010- (NPA, sputum) in 11 patients who became chronically infected 10 had identical *Pa* genotype, 7/14 who did NOT become chronically infected had identical genotypes

ACFBAL STUDY

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BAL GROUP

- 39/79 (49%) children cultured *Pa* in BAL
- 9/79 (11%) children in BAL group cultured *Pa* in OP culture ONLY
- 1 child with previous chronic *Pa* infection on BAL cultured Pa at age 5 and was counted as chronically infected

Wainwright et al, JAMA 2011

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ACFBAL STUDY

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Standard group (OP cultures not BAL until age 5 years)

- 43/76 (57%) in standard group had *Pa* cultured
- 2/43 (5%) had *Pa* cultured in BAL at age 5 having cleared infection previously on OP and might therefore have chronic infection

Wainwright et al, JAMA 2011

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IMPORTANCE OF SITE OF COLLECTION

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- Serial *Pa* BAL cultures 12/14 children had different genotypes
- Serial *Pa* OP cultures 3/11 children had different genotypes
- Genotype substitutions were more frequent among isolates from BAL than OP cultures

in both crude estimates (OR 16.0 [95% CI 2,118]; p = 0.007)

and when adjusted for time from diagnosing initial infection (OR 10.8 [95% CI 1,88]; p = 0.027)

T. Kidd et al. Submitted manuscript

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ACFBAL STUDY

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At age 5 years **NO** difference between standard-OP/BAL groups:

- Microbiology on BAL approx 12% *Pa* on BAL across both groups age 5 years
- Only 1 child with chronic *Pa* at 5 years in BAL group + 2 children in standard group who had cleared on OP but had same genotype on BAL age 5)
- On average all children had 3-4 OP cultures/year

Wainwright JAMA 2011

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- **Unclear** whether this is reinfection or failure to clear – no genotyping
- **Unclear** whether the infection is only in the upper airway or in the lower airway as well – he had OP cultures

Treatment, however, is likely to be successful for the lower airway, even if infection persists in the upper airway.

SO WHAT SHOULD WE DO?

Treat

Does it matter how we treat?

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PA ERADICATION THERAPY

Study	Design	Subjects n	Treatment	Results
Littlewood 1985	Cohort	7	colistin bd	↓ +ve cultures
Valerius 1991	RCT	26	colistin + ciprofloxacin 3/52	↓ chronic infection
Vasquez 1993	Cohort	16	ciproloxacin 2/52, colistin on going	↓ +ve cultures
Frederiksen 1997	Cohort	91	colistin + ciprofloxacin 3/52 vs 3 mths	↓ chronic infection, ↑ FEV1
Weisemann 1998	RCT DB PL	22	tobramycin 80mg 12 months	Faster time to negative culture
Munck 2001	Cohort	19	IV 18-21 days + colistin 2/12	100% clear reinfected by 3 years post
Ratjen 2001	Cohort	15	" "	93% clear 12 /12 60% clear 24/12
Griese 2001	Cohort	17	colistin + ciprofloxacin 3/52	88% clear 2 years

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PA ERADICATION THERAPY

Study	Design	Subjects n	Treatment	Results
Gibson 2003	RCT DB PL	21	Tobramycin 300mg 28 days	100% no Pa
Taccetti 2005	Cohort	47	colistin + ciprofloxacin 3/12	Free Pa median 18 mths
Gibson 2007	Cohort	31	tobramycin 28 vs 56 days	75-80% free up to 3/12 after
Ratjen 2010 ELITE	RCT	88	tobramycin 300mg 28 vs 56 days	93% cleared 1 mth. No difference 28/56
Hamblett 2009 Rosenfeld 2010 Treggiari 2011 EPIC	RCT	304	4 regimes cycled/culture tobramycin+ ciprofloxacin/placebo	No differences
Taccetti 2012	RCT	223	tobramycin+ciprofloxacin vs colistin +ciprofloxacin 28 days	No diffs 6 months 63-65% free
Tiddens 2014 ALPINE	Open label	105	aztreonam 75mg tds 28 days	75.2% free 4 weeks after

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PA ERADICATION

Optimal therapy still not known but successful eradication

- Reduces chronic infection *(Stuart et al. Paediatr Respir Rev 2010)*
- Health economic benefits *(Lillquist et al. J. Cyst Fibros 2011)*
- Minimal therapy should be one month inhaled tobramycin *(EPIC and ELITE)* or colistin + ciprofloxacin *(Tacetti 2012)*

SO EXACTLY WHAT DO WE NEED TO DO ONCE TREATMENT IS FINISHED?

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Check OP cultures once treatment completed.

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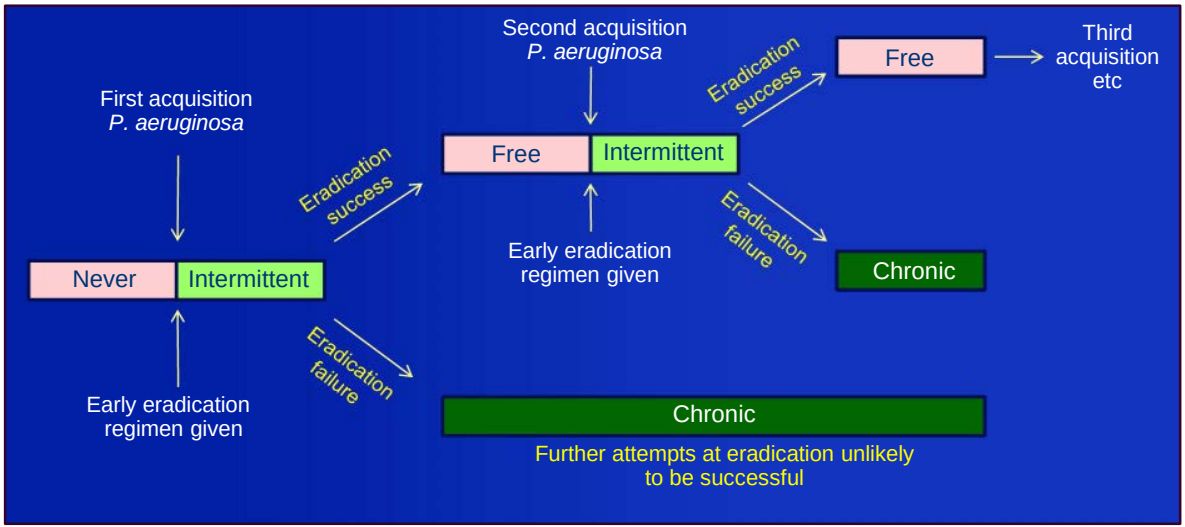

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SO EXACTLY WHAT DO WE NEED TO DO ONCE TREATMENT IS FINISHED?

If still *Pa* positive ?

Nearly evidence free zone

- Try a different treatment?
  - Switch therapies (e.g aztreonam and/or ciprofloxacin/colistin)
  - Hospitalize for IV antibiotics
- If OP cultures remain *Pa* positive, then may be chronically infected
  - Consider BAL to confirm chronic infection

SO EXACTLY WHAT DO WE NEED TO DO ONCE TREATMENT IS FINISHED?

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If *Pa* negative after treatment completion consider intermittent again

- Keep culturing (OP) and if becomes *Pa* positive start again with treatment

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SO EXACTLY WHAT DO WE NEED TO DO ONCE TREATMENT IS FINISHED?

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But if within 12 months you have had x 3 positive cultures? What do we do?

Again we are in an evidence free zone

- Change tack with treatment? Admit? Other eradication regimens?
- Consider BAL?

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ERADICATION CHALLENGES

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LEARNING OBJECTIVES

- Describe the value of treating *P. aeruginosa* infection in individuals who are asymptomatic.
- Describe differences in approach to *P. aeruginosa* eradication therapy in the US, Europe and Australia.
- Describe differences in *P. aeruginosa* eradication therapy in children and adults.

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KEY POINTS

- Should you treat aggressively when the patient is not sick?
- How to discuss with parents/patient
- Special cases: adults and other
- US vs Europe vs Australia

Q&A

OFF-LABEL DISCUSSION: tobramycin inhalation solution, aztreonam inhalation solution, colistin, ciprofloxacin

eCYSTICFIBROSISREVIEW.ORG

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A Case for Early Intervention in *Pseudomonas aeruginosa* Eradication

- Fifth volume launching in Fall 2014
- Monthly topic-focused literature reviews
- Case-based podcasts
- Designed for the whole Care Team
- Delivered via email

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THANK YOU

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WEBCAST

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