מרכז שניידר לרפואת ילדים בישראל
مركز شنايدر لطب الأطفال في اسرائيل
Schneider Children's Medical Center of Israel

Induced sputum in infants aged ≤ 24 months- routine use in the CF and pulmonary clinic

Hannah Blau, MBBS

The Kathy and Lee Graub Cystic Fibrosis Center and Pulmonary Institute

SCHNEIDER CHILDREN'S MEDICAL CENTER OF ISRAEL

1. Identifying bacterial pathogens is a vital guide for treatment in chronic suppurative lung diseases in children

Infection & inflammation develop early, especially in CF

Chronic *P aeruginosa* infection worsens prognosis

- We need a tool that can be used at every clinic visit, to guide treatment
- BAL cannot do this!

2. Can results of sputum culture in infants support a likely diagnosis of CF?

BACKGROUND – PAST STUDIES

Induced Sputum in the Very Young*

A New Key to Infection and Inflammation

Huda Mussaffi, MD; Elizabeth M. Fireman, PhD; Meir Mei-Zahav, MD; Dario Prais, MD; and Hannah Blau, MBBS

CHEST 2008; 133:176-182

- **20 CF, 8 months to 8 yrs (median 3y); 8 with other lung disease**
- assessed feasibility and safety of IS with hypertonic saline
- compared pathogens cultured: IS Vs oropharyngeal cough swabs
- inflammatory markers: neutrophil %, IL-8, neutrophil elastase
- correlated with clinical state.

BACKGROUND – PAST STUDIES (cont)

Microbiology:

Mussaffi et al, CHEST 2008

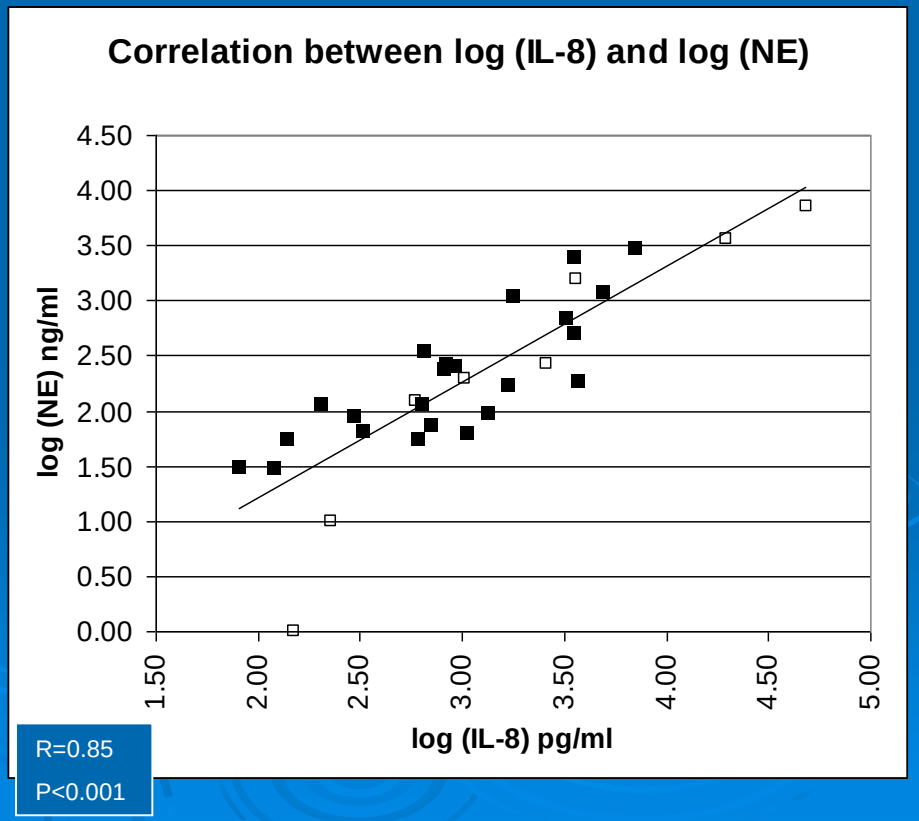
Bacteria	Paired specimens (n=29)	
	I.S	Cough swab
P. Aeruginosa	11	5
S. Aureus	2	1
No growth	13	21
Total pathogens	22	8

BACKGROUND – PAST STUDIES (cont)

Markers of inflammation: high in both CF & non CF chronic lung disease

Mussaffi et al, CHEST 2008

	CF	Non-CF
n	23	8
IL-8 pg/ml, Median (range)	834 (81-6920)	1809 (150-48550)
NE , ng/ml Median (range)	171 (30-3005)	229 (0-7030)
% neutrophils Median (range)	64.5 (4.5-87)	46 (0.5-94)



BACKGROUND – PAST STUDIES (cont)

Induced sputum compared to bronchoalveolar lavage in young, non-expectorating cystic fibrosis children ☆

Hannah Blau [a,b,*], Barry Linnane [c], Rosemary Carzino [d,e], Esta-Lee Tannenbaum [d], Billy Skoric [d]
Philip J. Robinson [d,e,f], Colin Robertson [d,e,f], Sarath C. Ranganathan [d,e,f]

Journal of Cystic Fibrosis 13 (2014) 106 – 110

- To assess sensitivity and specificity of induced sputum as compared to BAL the 'Gold Standard', for bacteriologic diagnosis in a group of young, non-expectorating patients with cystic fibrosis
- Compared to BAL as part of AREST CF and ACFBAL studies, at RCH, Melbourne

Microbiology findings of BAL and induced sputum specimens.

Patient no.	Age (y)	Between BAL & IS (d)	Patient group	Microbiology			
				BAL		IS	
				Microorganism	Antimicrobial susceptibility	Microorganism	Antimicrobial susceptibility
1	4.24	13	AREST	URTF +	n/a	URTF +++	n/a
2	4.19	12	AREST	*S. aureus* + mixed neg. bacilli +	*S. aureus*: pen-s, clindamycin-s, vanco-s, erythro-s, flucox-s, and teicoplanin-s	*S. aureus* +++	*S. aureus*: pen-r, clindamycin-s, vanco-s, erythro-s, flucox-s, and teicoplanin-s
3	4.04	5	AREST	No bacterial growth	n/a	*S. marcescens* + *H. parainf* ++ URTF	*S. marcescens*: ampicillin-r, cephalothin-r, cefotaxime-s, gentamicin-s, ceftazidime-s, augmentin-r, cotrimoxazole-s, cefpodoximer-I, tobra-s and cipro-s
4	4.98	6	ACFBAL	*P. aeruginosa* +++ *S. maltophilia* +++ *A. fumigatis* +	*P. aeruginosa*: genta-s, ceftaz-s, tobra-s, cipro-s, meropenem-s amik-s, piper-s, cefipime-s, norflox-s, tim-s, pip/tazobactam-s, and aztreonam-s *S. Maltophilia*: cotrimoxazole-s	*P. aeruginosa* + *S. maltophilia* +	*P. aeruginosa*: genta-s, ceftaz-s, tobra-s, cipro-s, meropenem-s amik-s, piper-s, cefipime-s, norflox-s, tim-s, pip/tazobactam-s, and aztreonam-s *S. Maltophilia*: cotrimoxazole-s
5	5.3	8	ACFBAL	URTF ++	n/a	URTF + *C. albicans* ++	n/a
6	5.08	5	ACFBAL	*S. aureus* +++ URTF ++	*S. aureus*: pen-r, clindamycin-s, vanco-s, erythro-s, flucox-s, and teicoplanin-s	*S. aureus* ++ URTF +++ *C. albicans* +	*S. aureus*: pen-r, clindamycin-s, vanco-s, erythro-s, flucox-s, and teicoplanin-s
7	5.19	9	ACFBAL	URTF +	n/a	URTF +++	n/a
8	7.44	1	Clinical	MRSA +++ *C. glabrata* +	*S. aureus*: pen-r, clindamycin-r, vanco-s, erythro-r, flucox-r, and teicoplanin-s	MRSA +++	*S. aureus*: pen-r, clindamycin-r, vanco-s, erythro-r, flucox-r, and teicoplanin-s
9	4.03	6	AREST	URTF +	n/a	URTF +++	n/a
10	3.02	4	AREST	*H. influenza* (not type b)	Ampicillin-r, augmentin-s, cefotaxime-s, and cotrimoxazole-r	URTF +++	n/a

Blau H et al. J Cyst Fibr 2014

We now asked: What are our clinic sputum culture results in ≤ 2 yr olds?

Retrospective analysis 2007-2015 of:

- Cultures for bacteria
- Comparing CF and non CF chronic lung disease
- 1st bacterial culture
  - could this be helpful in suggesting a specific 'CF profile'
- All cultures, over the 1st 2 years

Method of inducing sputum as per ECFS CTN standards of practice

- 2 hours fasting
- Inhalation of 2 puffs salbutamol 100mcg via vlaved spacer device
- Inhalation 5ml, 4.5% hypertonic saline, 10 min.
- Monitoring O_2 saturation, cough and wheeze.

- Oropharyngeal suction using a size 6 catheter following and together with chest physiotherapy
- Secretions collected in a sterile mucus extractor

Demographics

- Age at culture: (2-24) months
- 23 children with CF
- 124 children with non CF chronic suppurative lung disease

Cultures/ patient, bacterial diversity

	CF n=23	non CF n=124
Total cultures < 2y of age	207	348
Cultures/subject median (range)	7 (1-31)*	2 (1-18)*
Different bacteria/subject median (range)	3 (1-14)	2 (1-8)

*p<0.001

Bacteria in 1st culture:

	CF, n=23		Non CF*, n-124		p value
Enterobacter sp	5	21.7%	16	13.1%	0.33
K. pneumoniae	4	17.4%	12	9.7%	0.28
P. aeruginosa	3	13%	13	10.4%	0.72
Acinetobacter	2	8.6%	12	9.7%	1
Chryseobacterium indol.	2	8.6%	3	2.4%	0.17
E coli	2	8.6%	10	8%	1
H. Influenzae	2	8.6%	20	16%	0.53
Proteus mirabilis	2	8.6%			0.02
Serratia sp	1	4.3%			0.16
S. aureus			17	13.7%	0.08
Citrobacter			4	3.2%	1

*In non-CF only: 2 cases each of: *Pseudomonas sp, Proteus mirabilis, K. oxytoca, Haemophilus sp, H. parainfluenza, Corynebact striatum, Chryseobacterium sp;*
1 case each of *S. pneumonia, Sphingomonas paucimobili, Gram neg bacillus*

Sputum cultures, 0-24 months: CF, n=23; non-CF: n= 124

Bacteria*	CF n**	%	Non-CF n**	%	p value
Pseudomonas aeruginosa	17	70.8	32	25.6	<0.0001
Enterobacter sp	12	50	28	22.4	0.01
Klebsiella pneumoniae	9	37.5	31	24.8	0.21
Staphylococcus aureus	9	37.5	34	27.2	0.33
Escherichia coli	8	33.3	18	14.4	0.037
Hemophilus influenzae	8	33.3	34	27.2	0.623
Acinetobacter sp	6	25	13	10.4	0.086
Klebsiella oxytoca	6	25	7	5.6	0.007
Serratia sp	6	25	4	3.2	0.001
Chryseobacterium indol	4	16.7	6	4.8	0.064
Pseudomonas sp	4	16.7	6	4.8	0.064
Stenotrophomonas maltophilia	3	12.5	5	4.0	0.129

* ≥1 bacteria/patient; n** = number of patients with ≥1 infection with that bacteria

P. Aeruginosa in CF and non CF subjects aged<2y

P. aeruginosa positive	CF n=17	non CF n=32
Chronic *P. aeruginosa* (≥ 3 pos. cultures over >6mths)	1	4
Positive cultures/subject till 2y median (range)	1.5 (1-4)	1 (1-8)

Conclusions comparing CF and non CF patients:

- At 1st culture no bacteria was found more frequently in CF than non CF patients, including *P. aeruginosa*
- Over 2 years, the following were more frequently found in CF:

  P. aeruginosa, Enterobacter species,

  E. coli, K. oxytoca, Serratia
- CF patients had more sputum cultures than non CF patients

Conclusions (cont):

Induced sputum has an important role in our pulmonary clinic, in all non-expectorating subjects with productive coughs:

- in guiding antibiotic therapy
- frequently identify *P. aeruginosa* and enable aggressive therapy and eradication in most cases

Thanks to..

- Dr. Huda Mussaffi
- Dr. Meir Mei Zahav
- Dr. Dario Prais
- Dr. Guy Steuer
- Dr. Patrick Stafler
- Dr. Hagit Levine

- Nurses:
- Tammy Taizi
- Shlomit Katz

- Physiotherapist
- Hadas Mantin

The team at the Graub CF Center, Schneider Children's Med Cr.