L’enfant avec mucoviscidose à l’âge adulte

From a respiratory and digestive disease of children to a multisystem diseases predominantly of adults

Cystic Fibrosis 3rd Edition 2007 M. Hodson, D Geddes, A Bush

SSP/SGP
Congrès annuel
Crans-Montana 17 juin 2010

Prof. JM Tschopp, Centre Valaisan de pneumologie, CHCVs
The child with CF as an adult

- Evolution of life expectancy
- CF = a spectrum of disease
- CF and lung transplantation
- CF a chronic disease. What did we learn from pediatricians?
- CF: ways for improvement
Not everything that counts can be counted, and not everything that can be counted counts
Cystic fibrosis (CF)

- The most common life-shortening inherited disease of Caucasian people (1/2000)
- Children disease: death from pneumonia and malnutrition
1940: antibiotics

1950: sweat test
postural drainage
meconium ileus equivalent
liver cirrhosis
comprehensive and preventive treatment programme

1960: National and International organisations
First clinic for adults
1970: pseudomonas infection
Nutrition: resistant acid pancreatic enzymes

1980: physiotherapy
Antibiotics (carbenicilline + aminoside)
Liver-lung-transplantation; heart-lung transplantation
More aggressive nutritional support
(fat-soluble vitamins, enteral feeding etc)

1989: gene identification
Survival of children with cystic fibrosis

**FIGURE 1**

*Tuchman LK Pediatrics 2010;125:566*
Survival of children with cystic fibrosis: median survival

Cystic Fibrosis Foundation
Vignette clinique : Jean-Charles 1961

- 1961: ileus méconial; test à la sueur +
- 1976: diabète insulinodépendant
- 1988: insuffisance respiratoire sévère (paO\textsubscript{2} 55 mmHg /7.3 kPa; paCO\textsubscript{2} 50 mmHg/6.7kPa) → concentrateur O\textsubscript{2} >22h/j puis ventilation non invasive à domicile
- 1989: visite à Londres: transplantation cœur-poumons ?
- 1990 janvier: liste de transplantation cœur-poumons
- 1994: transplantation bipulmonaire et greffe d’îlots de Langerhans: insuffisance pancréatique exo- et endocri ne
End-Stage Cystic Fibrosis*

Improved Diabetes Control 2 Years After Successful Isolated Pancreatic Cell and Double-Lung Transplantation

Jean-Marie Tschopp, MD, PhD, FCCP;
Martin H. Brutsche, MD; Jean-Georges Frey, MD;
Anastase Spiliopoulos, MD; Laurent Nicod, MD, PhD;
Thierry Rochat, MD, PhD; and Philippe Morel, MD, PhD

Table 1—Spirometry and Diabetic Parameters Before and 6 Months After Bilateral Sequential Single-Lung and Pancreatic Cell Transplantation

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Transplantation Time</th>
<th>Before</th>
<th>After, 2 mo</th>
<th>After, 24 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁, L/s*</td>
<td></td>
<td>0.4 (11%)</td>
<td>3.1 (92%)</td>
<td>3.0 (79%)</td>
</tr>
<tr>
<td>FVC, L*</td>
<td></td>
<td>1.0 (21%)</td>
<td>3.4 (75%)</td>
<td>3.5 (77%)</td>
</tr>
<tr>
<td>Venous glucose, mmol/L†</td>
<td></td>
<td>6.1±2.8 (2.3-12.1)</td>
<td>9.0±1.2 (4.2-10.9)</td>
<td>5.8±0.9 (3.8-8.5)</td>
</tr>
<tr>
<td>Daily insulin, IU/d†</td>
<td></td>
<td>102±13</td>
<td>60±2</td>
<td>66±2</td>
</tr>
<tr>
<td>Fasting C-peptide, mmol/L</td>
<td>≤0.04</td>
<td></td>
<td>1.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Hypoglycemic events/wk†</td>
<td>3</td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hyperglycemic events/wk†</td>
<td>3</td>
<td></td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

*For FEV₁ and FVC, values in parentheses represent percent of predicted values.
†Mean ± SD (range). Venous glucose levels measured three times daily over a period of 1 month.
‡Values represent mean number of symptomatic hypoglycemic events per week.
Jean-Charles 1961

- 1995: rejet A1
- 1998: infarctus diaphragmatique
- 2003: HT artérielle
- 2005: sinusite chronique à pseudomonas
- 2006: mariage
- 2008: oséoporose
- 2008: décès de sa mère; père malade
Jean-Charles 1961

- 1995: rejet A1
- infarctus diaphragmatique
- HT artérielle
- Ostéoporose avec hyperparathyroidisme
CF and lung transplantation: problems

- Pre-
- Per-
- Post-transplantation
Evolution clinique

« fenêtre de transplantation »

Longueur des listes d’attente

Courtesy of Prof T Rochat
Multivariate survival mode

- Improved survival: 5/514 listed patients
- Improved survival: 1/248 transplanted patient
- Revise Allocation score
- Prospective randomised controlled trial

_Lung transplantation and survival in children with cystic fibrosis_
_N Eng J Med 2007;357:2143_
Lung Transplantation in Cystic Fibrosis — Primum Non Nocere?

Julian Allen, M.D., and Gary Visner, D.O.
Lung Transplantation for Cystic Fibrosis

Frederick R. Adler¹, Paul Aurora²,³, David H. Barker⁴, Mark L. Barr⁵, Laura S. Blackwell⁴, Otto H. Bosma⁶, Samuel Brown⁷, D. R. Cox⁸, Judy L. Jensen⁷, Geoffrey Kurland⁹, George D. Nossent⁶, Alexandra L. Quittner⁴, Walter M. Robinson¹⁰, Sandy L. Romero⁴, Helen Spencer², Stuart C. Sweet¹¹, Wim van der Bij⁶, J. Vermeulen⁶, Erik A. M. Verschuuren⁶, Elianne J. L. E. Vrijlandt⁶, William Walsh⁷, Marlyn S. Woo¹², and Theodore G. Liou⁷

The Importance of Measuring Health-Related Quality of Life

Alexandra L. Quittner, David H. Barker, Laura S. Blackwell, Sandy L. Romero, and Marlyn S. Woo

Alternate Models of Selection for Lung Transplantation: What Distinguishes the British System?

Paul Aurora and Helen Spencer

Pediatric Lung Transplantation for Cystic Fibrosis: Overview and Historical Perspective

Stuart C. Sweet

DOI: 10.1513/pats.2009008-088TL
When to refer a patient with CF for lung transplantation?

Guidelines for Referral

- FEV$_1$ below 30% predicted or a rapid decline in FEV$_1$
- Exacerbation of pulmonary disease requiring ICU
- Increasing frequency of exacerbations requiring iv antibiotics
- Refractory and/or recurrent pneumothorax.
- Recurrent hemoptysis not controlled by embolization.

Guideline for Transplantation

- Oxygen-dependent respiratory failure.
- Hypercapnia.
- Pulmonary hypertension

Orens JB et al, JHLT 2006
Swiss Lung Transplant Registry
Demographics

- CF (31%)
  - n=78
- COPD (32%)
  - n=79; 23 α1AT
- IPF (19%)
  - n=47 IPF; 5 SAR, 4 HIS
- PHT (12%)
  - n=30; 8 TPH, 1 EIS
- LAM (3%)
  - n=4
- REDO (3%)
  - n=3

3 Heart-Lungs
2 Liver-Lungs
1 Kidney-Lungs

Courtesy of Prof T Rochat
n = 120 transplantations
n = 22 transplantations pour mucoviscidose
n = 12 vivants, dont 7 avec VEMS normal
survie de 1 à 16 ans (médiane 11,5 ans)
n = 10 dcd, dont 3 après re-transplantation

Courtesy of Prof T Rochat
Survival (%) vs. Years

- ALPHA-1 (N=1,356)
- COPD (N= 4,955)
- PPH (N= 737)
- CF (N = 1,923)
- IPF (N = 2,119)
- SARCOIDOSIS (N = 317)
Vignette clinique 2
Michel (28 ans)
- naissance: mucoviscidose
- VEMS: 60%
- 2002: assistant en pharmacie
- 2003: Bishorn (4150 m)
- Health promoting Hospital (OMS)
- 2004: Europe nord → sud
- 2005: chauffeur de bus
Composition de la Cour : Jean-Michel Zufferey, Président ; Jocelyne Zufferey, assesseur ouvrier ; Serge Métrailler, assesseur patronal ; greffier : Jean-Pascal Fournier
Enfant avec mucoviscidose à L’âge adulte = Partenaire actif et responsable
La mucoviscidose est une maladie génétique mortelle qui détruit les poumons. Cette maladie héréditaire est la plus fréquente. Elle touche un nouveau-né sur 1'800. Les personnes atteintes sont privées du fonctionnement adéquat de leurs poumons. Même si ces dernières années la recherche a progressé, cette maladie n’est pas guérie et tue toujours.

Ce voyage d’espoir à vélo à travers le continent américain a pour but de sensibiliser un large public et de récolter des fonds dans la lutte contre la mucoviscidose. Grâce à vos dons et à votre soutien, vous apportez un peu de réconfort aux malades et les aidez dans leur combat au quotidien. L’itinéraire, le projet complet et plus d’infos, visitez : www.muco-velo.ch

Voici le CCP où vous pouvez verser vos dons

Association Muco-Velo
Raid à vélo pour la mucoviscidose
1936 Verbier, CCP 17-771621-7

Merci pour votre générosité. Même un petit geste peut faire beaucoup
San Francisco: dyspnée +++; VEMS = 35%
→ Asthme bronchique difficile à contrôler
Mexique: retour en CH refusé
IgE spécifique pr Aspergillus fumigatus: 3000 kU/l
\paO_2 = 42 \text{ mm Hg}/ 5.5 \text{ kPa}; \ SaO_2 = 78% 
malgré ventilation mécanique (VNI) → trachéostomie)
Aspergillose invasive → détresse respiratoire → transplantation
CF: from Allergic bronchopulmonary aspergillosis (ABPA) to invasive aspergillosis

- Corticoresistant asthma $\rightarrow$ respiratory insufficiency $\rightarrow$ allergic disease to severe infectious disease
- $pO_2 = 42$ mm Hg/ 5.5 kPa
- $Sao_2 = 78\%$
Aspergillus Infections in CF Lung Recipients

31 CF recipients

Aspergillus pre-transplant
7/31 (22%)

Aspergillus post-transplant
15/31 (48%)

Invasive Aspergillus infection
4/15 (27%)

3 anastomosis infections

No infection
11/15 (73%)

1 bronchial infection

Nunley DR et al, Chest 1998
The child with CF as an adult

- Evolution of life expectancy
- CF a spectrum of disease
- CF and lung transplantation
- CF a chronic disease. What did we learn from pediatricians?
- CF: ways for improvement
Psychosocial aspects of Cystic fibrosis

- Pediatrician/Physician
- Geneticist
- Physiotherapist
- Gastroenterologist
- Immunologist
- Patient
- (Parents?)
- Microbiologist
- Pulmonologist
- Dietician
- Psychologist
- Social worker
- Nurse
- Hospital
This article is the second in our “Transition to Adult Care Series.” New articles in this series will appear in subsequent issues of Pediatrics.

**AUTHORS:** Lisa K. Tuchman, MD, MPH, Lisa A. Schwartz, PhD, Gregory S. Sawicki, MD, MPH, and Maria T. Britto, MD, MPH

Division of Adolescent and Young Adult Medicine, Center for Clinical and Community Research, Children’s National Medical Center, Washington, DC; Divisions of Oncology and Clinical Medicine.
Motivational Interviewing for Adherence Problems in Cystic Fibrosis

Alistair J.A. Duff¹ star and Gary J. Latchford¹,²

- Adherence in adult medicine: 50% (WHO 2003)
- Cognitive dissonance
<table>
<thead>
<tr>
<th>Element</th>
<th>Example techniques and skills</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Agree on an agenda for discussion</td>
<td>Draw up list of topics together Physician and patient both add possible topics</td>
</tr>
<tr>
<td>2. Develop rapport with patient</td>
<td>Communication skills: e.g., open questions, reflection statements, summary statements Stance: collaboration between patient and physician</td>
</tr>
<tr>
<td>3. Facilitate consideration of discrepancy in behavior</td>
<td>Communication skills: e.g., reflection statements Feedback of test results using elicit-provide-elicit technique Scaling questions Decision matrix</td>
</tr>
<tr>
<td>4. Successful management of resistance</td>
<td>Communication skills: e.g., empathic listening Avoidance of confrontation and simple advice giving</td>
</tr>
<tr>
<td>5. When patient is ready, successful planning of change</td>
<td>Increase confidence and self efficacy: e.g., affirming and morale boosting statements Behavioral strategies: problem solving, goal planning, etc.</td>
</tr>
<tr>
<td>6. Planning for the next appointment</td>
<td>Review intention of patient: If ready to change help plan If unsure explore further If unwilling respect decision but ask permission to discuss again another time</td>
</tr>
</tbody>
</table>
Identifying Barriers to Treatment Adherence and Related Attitudinal Patterns in Adolescents With Cystic Fibrosis

Eric J. Dziuban, MD, Lisa Saab-Abazeed, MD, Sarah R. Chaudhry, BS, Daniel S. Streetman, PharmD, and Samya Z. Nasr, MD
Poem: a life with cystic fibrosis
Jane, 19 years, 1982
The Cleveland treatment programme: a paradigm for modern CF care (p6)

- Patient and families = partners
- Intensive and comprehensive care
- National and international organisations
  Matthews LW et al J Pediatr 1964;65:558
- CF a paradigm for modern medicine
Hypertonic Saline Research

About Hypertonic Saline

Hypertonic Saline (HIS) is just a strong salt-water solution. The concentration used is typically about 7% salt - that is, about twice as salty as seawater — although sometimes weaker or stronger concentrations are used. Hypertonic saline can be turned into a mist by a simple device called a nebuliser. The mist can then be inhaled into the lungs.

How Does Hypertonic Saline Help in CF?

When Hypertonic Saline is inhaled into the lungs, the body tries to dilute the strong salt concentration. The cells lining the airways are triggered to release water. This restores the layer of moisture lining the airways, which helps the mucus to clear the same way it does in healthy lungs. You could think of it as the lungs “flushing out” the stagnant, infected mucus.

Studies done during the mid 1990s showed that inhaling nebulised Hypertonic Saline temporarily increases the speed at which mucus is cleared from the lungs. Subsequent short-term trials showed that inhaling nebulised Hypertonic Saline on a regular basis (usually twice per day) improves lung function in PWCF.

What was the recent trial about?

Although the short-term trials were favourable, it was not known whether Hypertonic Saline is safe and effective when used for long periods. The National Hypertonic Saline Trial tested 164 stable subjects with CF aged at least 6 years of age. These subjects were randomly allocated to inhale either 4mL of Hypertonic Saline (7% saline) or 4mL of placebo (a very weak salt solution — less than one third as salty as sea water). Both solutions contained an inert substance to disguise the taste, so subjects didn’t know which solution they were inhaling. The subjects inhaled their allocated solution twice daily for 48 weeks. They kept up all their other standard therapies, and received whatever additional treatment they normally would whenever they had a flare-up. Patients were checked regularly for signs of improvement, as well as for any possible adverse effects.

“The subjects who were inhaling Hypertonic Saline had far fewer flare-ups.”

What did the trial show?

The main outcome of the trial was lung function — a breathing test, which measures how well the lungs can shift air in and out. The subjects who were inhaling the Hypertonic Saline had a modest rise in their lung function at the first measurement point (that is, after 4 weeks). This improvement was maintained until at least the last measurement point (that is, 48 weeks).
Nadine 42 ans, Marie 35 ans

- Mucoviscidose naissance
- à 30 ans: VEMS = 55%
- Cure antibiotique 2x/an: pseudomonas sensibles
- Vit en couple
- traductrice

- Mucoviscidose naissance
- à 30 ans: VEMS = 35%, fume 30 cig./j
- Cure antibiotique ?x/an: pseudomonas sensibles
- Vie sentimentale ?
- Sans profession
Adult CF: sexual and reproductive life (1)

- Pregnancy: success rate 74%
- Pregnancy: spontaneous abortion 7%
- Pregnancy interruption: 13%
- Indication: FEV$_1$ > 50% (?)
- Genetic counselling

Teenager sexual life: information

Hubert D, Pneumologie 2nd edition, in Aubier

Sawyer J Adoles Health 1995;17:46
Adult CF: sexual and reproductive life (2)

- Men azoospermic
- Infertility: 98%
- Better information: 1/93 unaware of CF infertility

  Sawyer Thorax 2005:60:326

- Options: adoption? Donor?
- Oocytes in-vitro fertilisation? (MESA, TESA + ICSI):
  62% success rate
Jean 36 ans

- Naissance: mucoviscidose
- 14 ans: pseudomonas aeruginosa (cure antibiotique)
- 28 ans: mariage
- Tentative de fertilisation: échec; séminome
Jean 36 ans

- VEMS = 34%
- Capacité pulmonaire totale = 77%
- Gazométrie (500m):
  - $p_{aO2} = 47 \text{ mm Hg/6.2 kPa}$
  - $S_{aO2} = 80\%$
  - $p_{aCO2} = 42 \text{ mm Hg/5.6 kPa}$
  - $pH = 7.49$

Peut-il encore piloter?
Mme Clara non fumeuse 72 ans: « bronchite chronique »
The child with CF as an adult

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- CF: ways for improvement
Airway disease: CF

- Mucus
- Infection
- Inflammation
- Obstruction
- Destruction
Hypertonic saline improves the LCI in paediatric patients with CF with normal lung function

Reshma Amin, Padmaja Subbarao, Alisha Jabar, Susan Balkovec, Renee Jensen, Shawn Kerrigan, Per Gustafsson, Felix Ratjen

- Lung clearance index (LCI)
- RCT: n = 20 patients with CF
- New way for early intervention: Strategies?

Thorax 2010;65:379
Conclusion

- CF in adults = multisystemic disease
- CF = a paradigm for modern medicine: comprehensive and intensive care
- CF = the longest chronic disease at least in some patients
- CF still a challenge
Merci de votre attention