Online supplement

A. Expected time course of selected chILDs

Currently there is limited knowledge on the long-term course of many chILDs and longitudinal multicentre studies with sufficient number of patients enrolled are needed. Here we summarise current ideas on the expected time course of selected chILD – see **eTable 1**.

eTable 1: Expected time course of selected chILDs

Disease	Manifestation and expected course of the disease	Recommended frequency of follow up
NEHI	• in infancy persistent tachypnoea, sometimes oxygen-dependency • regression of lung disease with age# o loss of oxygen dependence in the first 2-3 years or even more [1] o bronchial hyperreactivity / asthma possible in preschool and school age [2] o pulmonary exacerbations are also reported [3] • may be associated with TTF1 or other gene mutations; if TTF1 often very prolonged oxygen dependency	• in infants and toddlers every 3 months • in preschool age assess clinical signs of bronchial hyperreactivity (wheezing) and the occurrence of pulmonary exacerbations, perform spirometry with bronchodilation test • for symptomatic patients, continue follow-up every 3-6 months • in asymptomatic patients follow up may be less frequent but should be kept long-term • in adults – check up in case of breathing difficulties • Note that there are no data from adolescents
PIG	• RDS in full-term or slightly immature neonate, persistent pulmonary hypertension of the neonate • often associated with congenital heart disease • regression of lung disease, favourable course # [4,5] • administration of corticosteroids may accelerate regression [6] • may be associated with pulmonary growth disorders.	• in infants and toddlers every 3 months • until school age every 6 months, in asymptomatic ones it can be loosened but kept long-term • note that there are no data from adolescents and adults
EAA	• acute form with sudden onset of symptoms and	• depending on the severity of the pulmonary function

	which when early treated and the antigen is fully eliminated has a favourable prognosis • subacute and chronic form - gradual onset, often delayed diagnosis, risk of irreversible pulmonary involvement (progressive fibrosis, traction bronchiectasis) and side effects of treatment [7,8] • risk of exacerbations and relapses	deficit and the intensity of treatment every 3-6 months, regular monitoring of side effects of treatment is necessary • Thoracic HRCT in patients under treatment no more than 2 years before transition to adult care; in patients apparently in remission (i.e. off treatment) it may be considered to exclude asymptomatic progression. • due to the risk of late relapses, patients in remission should also be referred to adult care for
PIBO	• fixed bronchial obstruction, air-trapping, related to severe respiratory infection (often adenovirus) a few children may show partial reversibility after β2-agonists • oxygen dependence disappears with disease course (median 5 months after infection) • non-progressive / stationary course [9] • accentuation of dysanaptic lung growth [10,11] - disparity between alveolar growth (FVC) and bronchial growth (FEV1), decrease in FEV1 / FVC	• in infants and toddlers every 3 months • later every 6-12 months • refer to adult care, at high risk for COPD
JSSc	• pulmonary involvement in 30-70% of paediatric patients o chILD: alveolitis (GGO) and/or interstitial fibrosis o Pulmonary arterial hypertension - primary in vasculopathy or secondary in chILD • variable course according to disease activity and treatment effect, generally better prognosis than in adults [12]	• depending on the severity of the lung involvement and the intensity of treatment every 3-6 months, regular monitoring of side effects of treatment is necessary • follow up HRCT of the lung not more than 2 years before transition to adult care, in patients without respiratory symptoms and with a stable functional deficit not more than 5

	• monitoring - pulmonary function (FVC, FEV1, TLco) and HRCT [13]	years before transition • due to the risk of disease progression / late relapses, patients without respiratory symptoms should be referred to adult care †

data are available for children under older school age (approx. 12 years)

† similar approach to other rheumatic diseases (systemic connective tissue disease) with pulmonary involvement

NEHI - neuroendocrine cellular hyperplasia of infants; PIG - pulmonary interstitial glycogenosis; EAA - exogenous allergic alveolitis (hypersensitivity pneumonitis); PIBO - post-infectious bronchiolitis obliterans; JSSc - juvenile systemic scleroderma; GGO - ground glass opacity

B. Survey questionnaire

Country *

Centre *

Type of centre *

Outpatient only

Hospital based

University based

Other

Specialty of the responsible physician (head)

Pulmonologist

Pulmonologist - ILD specialist

Paediatric pulmonologist

Paediatric pulmonologist - ILD specialist

Other

Contact (e-mail of the person submitting the questionnaire – to clarify details, if needed. Not obligatory, but highly desirable)

GENERAL QUESTIONS

What is the general system of reimbursement of medical care in your country?

General health insurance (mandatory by law)

Individual health insurance

Government paid

Other

Is there any possibility for patients to buy specialized medications over the counter if not reimbursed through the system? Specify please:

Are the highly innovative and expensive new treatments (antifibrotics - nintedanib, pirfenidone, rituximab, belimumab….?) available in your country?

Yes, without limitations

Yes, limited to centres

Yes, but only limited- upon special request for individual reimbursement

No, in most cases not

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<u>For paediatric pulmonologists</u>

Is in your country Paediatric pulmonology (or equivalent paediatric respiratory specialty) formally established with training and certification?

Yes

No

Can you estimate how many patients with chILD are in your country? In total:

How many centres are specialised for the care of children with ILD in your country?

Please estimate the percentage of the children with ILD who are not registered in one of these expert centres?

% treated in centres with minor qualifications (and perhaps don't obtain optimal disease management)

% not diagnosed as chILD at all

How many patients with chILD do you register in your centre (even without official registry)?

What is the common time period of follow-up (months) for patients with chILD in your center (i.e. how often do you see the individual patients?)

Do you have a routine access to a pathologist specialised and skilled in chILD?

yes

no

Do you have a routine access to a radiologist skilled in chILD?

yes

no

Is in your country a routine formally defined co-operation between paediatric and adult pulmonologist ILD experts to guarantee smooth transition?

yes

no

Does your centre routinely co-operate with physicians caring for adult patients with ILD for transition?

yes

no

<u>FOR ADULT PULMONOLOGISTS</u>

Is in your country Adult pulmonology (or equivalent specialty) formally established with training and certification?

yes

no

Is the care for patients with ILD centralised?

yes

no

How many centres are specialised for the care of patients with ILD in your country?

Please estimate the percentage of the adults with ILD who are not registered in one of these expert centres?

% treated in centres with minor qualifications (and perhaps don't obtain optimal disease management)

% not diagnosed as ILD at all

How many patients with adult ILD do you have registered in your centre (whether or not there is an official registry)?

What is the common time period of follow-up (months) for patients with ILD in your centre? (i.e. how often do you see individual patients with adult ILD?)

Do you have a routine access to a pathologist specialised and skilled in ILD?

yes

no

Do you have a routine access to a radiologist skilled in ILD?

yes

no

Is in your country a routine formally defined co-operation between paediatric and adult pulmonologist ILD experts to guarantee smooth transition?

yes

no

Do you routinely co-operate with paediatric physicians caring for patients with chILD?

yes

no

<u>CENTRE SPECIFIC QUESTIONS</u>

Do you run or participate in a registry of adult ILDs? If yes, please specify.

Do you run or participate in a registry of children with chILD? If yes, please specify.

Do you have an established multidisciplinary team or board for ILDs?

Yes

No

If yes, who are the regular members (specialties)?

Do you routinely involve psychologist in your care for patients with serious chronic diseases?

yes

no

Do you routinely involve physioterapist in your care for patients with serious chronic respiratory diseases?

yes

no

TRANSITION SPECIFIC QUESTIONS

If you care for paediatric ILD, do you always know where to refer the chILD patient entering adulthood?

yes

no

What is the formal age (years) for transition from childhood to adulthood in your medical system?

Is the transition to adult care of individuals with chronic health problems reaching adulthood mandatory in your system?

yes

no

How long before the transition of the patients with chILD to adult care do you start planning?

Do you have any formal Standard Operational Procedure for transition of chILD patients in your centre?

yes

no

At transition time, is there a requirement for diagnostic re-evaluation?

yes

no

Do you have any standardised “Medical Summary/Transition report” that goes with the patient?

yes

no

Do you routinely organise pre-transition meeting?

No

Yes, parents/patient with peadiatric team only

Yes, parents/patients with adult team only

Yes, peadiatric team and adult team at the same time, withoutr parents/patient

Yes, all together at the same time

Does the adult team use any formal tools for Self-Care Assessment for the new patient?

yes

no

Is there any established system of long-term follow-up of patients with age specific chILD (eg. NEHI, PIG…) who reached remission?

yes

no

Please, optionally describe briefly your practice in transition

(free text window of about 250 characters)

Thank you very much for your help and co-operation.

C. Proforma transition report

Dear colleague:

Let me introduce my patient ***XXX***, born on ***XX***, who I have been treating up to now. I'd like to transfer him/her to your care as he/she has reached the age for transition. Below I summarize the most important medical details of his/her case:

The diagnosis of chILD was first suspected at the age of ***XX*** (calendar month/year) based on symptoms ***XXX***. Further investigation performed:

Lung function

Lab results

Imaging (X-ray, HRCT)

Bronchoscopy with BAL

Lung biopsy

Genetic testing

Please also note important medical history data: ***perinatal data, comorbidities, …***

The diagnosis was subsequently specified to ***XX*** (from the disease group ***XX***) in year ***XX***. The severity was ***X*** according to Fan.

He/She was treated as follows: ***pharmacological and nonpharmacological interventions*** (include also ***duration, effect on the disease and eventual side-effects***).

The course of the disease was then ***stable/improving/deteriorating (with acute exacerbations)***, which required specific treatment ***as follows***.

The patient's compliance was ***good/poor***, ***associated complications*** needed to be addressed with other specialists (***psychologist, dietitian, cardiologist, …***). The patient him/herself perceives following aspects of the disease as most important/problematic: ***XXX***.

In summary, currently the disease is ***well/poorly*** controlled. The latest examinations (lung function, imaging, bronchoscopy) show ***XXX***. I suggest following ***treatment*** and special attention to ***these aspects*** of the disease.

Thank you for accepting this patient.

Best regards ***XX***

D. Evaluation of pulmonary involvement

Longitudinal assessment of the evolution of lung disease is an important tool for management of the disease and may guide the transition process. It should be comprehensive and include various aspects that may not always be clearly correlated:

1. clinical symptoms,
2. lung function, including exercise tolerance,
3. structural lung involvement.

Although clinical signs (dyspnoea, cough, tachypnoea) are less sensitive indicators of pulmonary involvement, their impact on quality of life is crucial. They should be regularly evaluated during outpatient visits using e.g. Borg's dyspnoea scale and chILD specific quality of life score [14].

Pulmonary function tests (PFT) are currently the basic tools for monitoring children [15]; spirometry and transfer factor being the most commonly used. The role of PFT in chILD has been reviewed recently elsewhere [16] and important limitations have been identified (limited correlation between lung function parameters and subjective perception of the clinical status, limited data on its prognostic value, etc.). Use of appropriate reference values when interpreting PFT results is crucial. Currently, the GLI (Global Lung Initiative) standards, which are available for both spirometry [17] and

transfer factor testing [18] and span wide age range seem appropriate for long term follow up. We warn against switching between different reference values at the time of transition as it may distort the long-term trends in lung function.

Multidetector spiral computed tomography with thin sections reconstruction (HRCT), optimally using inspiratory and expiratory scans (possibly as spirometry guided CT) is currently the gold standard for evaluation of structural changes in chILD. This method has reasonable sensitivity for the early stages of the disease. Its main limitation is - especially in childhood - a significant radiation exposure. There is a consensus that HRCT should not be performed more frequently than once every 2 years, especially if the patient is stable. HRCT is also recommended to be performed prior to the referral to the care for adults as part of the outcome assessment. Its timing depends on the type of chILD, the severity of the lung disease, and disease activity in recent years (see **eTable 1**).

All these aspects evaluating the development of pulmonary involvement in patients with chILD should be summarized in the transition report in order to provide a comprehensive view of the course of the disease so far.

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