Standardised Operating Procedure

Genetic Testing

chILDRANZ 2020

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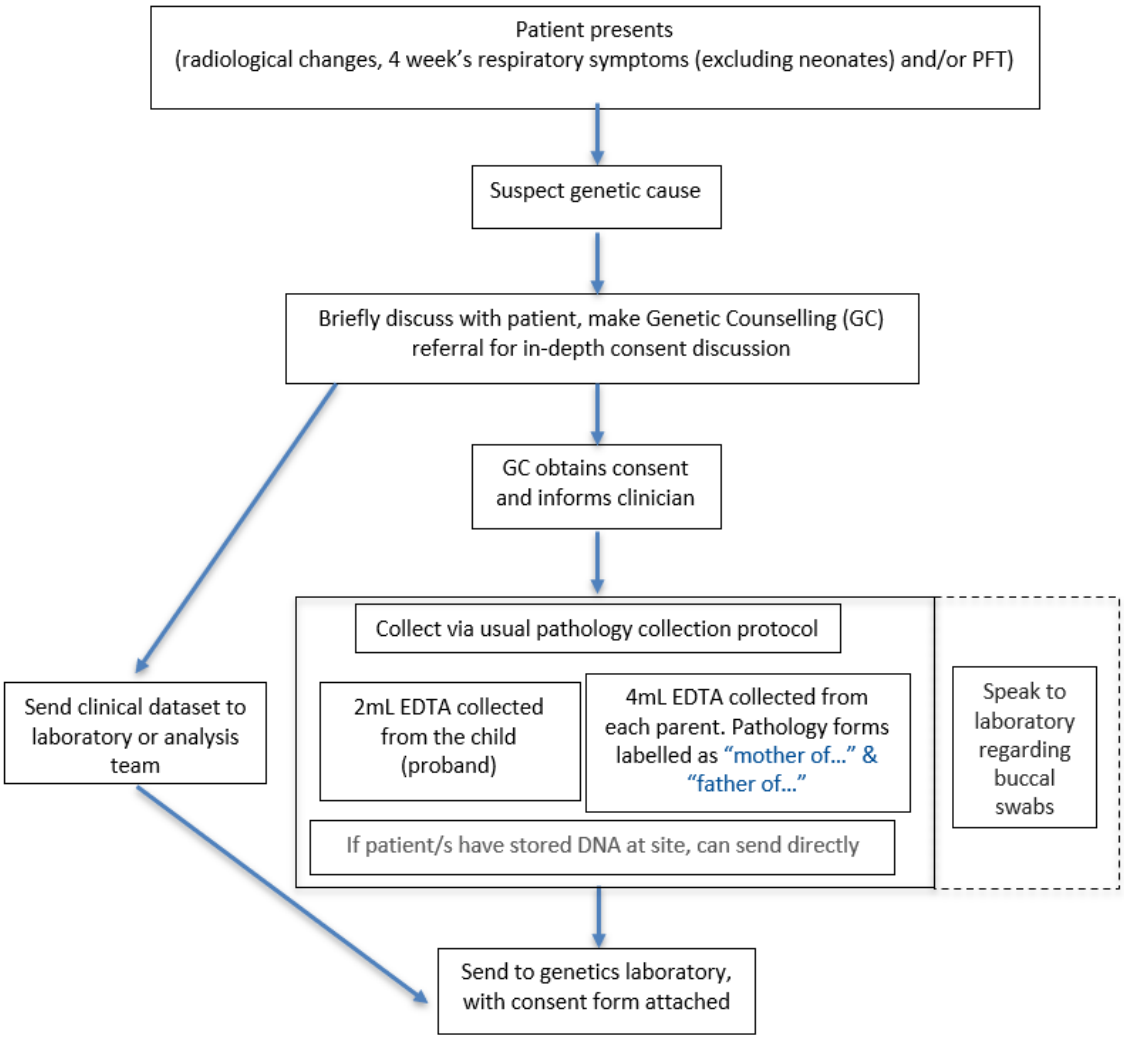
Best Practice Checklist

Genetic Testing for Interstitial (diffuse parenchymal) Lung Diseases in Children (chILD) Protocols

Inherited interstitial lung diseases (ILD) are rare diseases with varying phenotypes. Lung involvement may also occur in other inherited disorders such as immunological and rheumatological diseases. Here we outline a guide to the selection of genetic tests to confirm this suspicion.

Indications: Neonate, infant, toddler, child or adolescent with radiological evidence for interstitial or diffuse lung disease (please refer to Radiology SOP). In neonates, respiratory symptoms may occur soon after birth. Consider inherited ILD in children presenting with greater than 4 weeks' respiratory symptoms and/or abnormal pulmonary function tests with evidence of restrictive ventilatory defect.

Exclusion of infection, cardiac, metabolic or other causes of diffuse lung disease, age 10 days or older. If there is a positive family history inherited diseases are more likely.



Consent for Genetic Testing: Prior to testing, informed consent for genetic testing must be obtained from the patient, or their parent or guardian if the patient is under 16 or unable to consent. This ensures that information regarding the possible outcomes and implications of testing is provided. Genetic/Genomic testing is complex and it is important families understand the benefits and potential risks of testing – including the chance of incidental findings, insurance implications, possible identification of unexpected relationships (non-paternity/maternity, consanguinity), emotional impact of the result, data sharing and impact of results on other family members.

Type of test	Description	Indication	Turnaround Time	Analogy of a bookshelf to aid patient understanding
Chromosomal Microarray	Checks chromosomes to see if bits are missing or repeated	Baseline genetic test should be ordered before other genetic testing (or concurrently)	~2-4 weeks	Checks shelves in the library to see that correct number of books are there
Single Gene Test	Tests for one gene	Useful when clinician is certain of genetic cause	Variable	Takes a book off the shelf, and reads that one book to look for spelling mistakes
Surfactant Panel	Looks at numerous genes based on clinical phenotype (e.g.: surfactant)	Useful for minimising chances of incidental findings or if there is a very specific phenotype	~6 weeks	Takes numerous books off the shelf, reads all those books for spelling changes
Whole Exome Sequencing (WES)	Sequences all coding regions of genes (exons)	Analysis usually focuses on genes associated with clinical phenotype (e.g.: Surfactant genes) If needed, can broaden analysis to look at all genes, as more data is available	~4-6 Months*	Takes all books off the shelf, reads all important words in books looking for spelling mistakes
Whole Genome Sequencing (WGS)	Sequences all regions of genes (exons and introns)		~4-6 Months*	
Singleton v Trio	Genetic test on patient (singleton) or patient and both parents (trio).	Useful if segregation analysis is needed, best to order at the same time	As WES / WGS	Analogy for trio – taking child's books off shelf and reading through these, then if a spelling mistake is found also reading parents' books as a comparison to check spelling

Genetic Analysis: To aid the analysis it is essential to send accurate detailed clinical information to the analysis team and provide updates with any new phenotypic information. Identified variants will be discussed with the referring respiratory team.

Report: Anticipate 3-6 months until return of results, *which can be expedited if urgent or critically unwell. The Genetic Counsellor should be involved/present when genetic results are given to the family.

Other tests that should be performed: If a lung biopsy is going to be performed please collect a skin sample (please refer to Biopsy SOP) for potential functional analysis. Functional studies may help in assigning the causation of identified variants.

Acknowledgement:

European Management Platform for Childhood Interstitial Lung Diseases

Australian Genomics Health Alliance Acute Care Flagship

Further Support:

Please contact your local genetics health professional/s for further advice pertaining to your site.