

St Georges Paediatric Investigation Tool

Investigation Pathway for Primary Lymphoedema in Childhood

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This Investigation tool has been devised for the assessment of any child presenting with primary lymphoedema. There are numerous subtypes of primary lymphoedema and it is vital that children are thoroughly assessed to ensure that possible associated health problems are detected and treated accordingly.

Ideally, all children should be referred to a specialist unit: Derby Hospital or St George's Hospital where they can be assessed in a multidisciplinary clinic by a lymphoedema physician (Dr Keeley, Prof Mortimer or Dr Gordon) and a geneticist (Prof Mansour, Dr Suri). If this is not possible then all children must be assessed by a lymphoedema therapist and a physician (e.g. paediatrician or geneticist).

History

Full medical history needs to be taken, including a family history.

- Age of onset of lymphoedema.
- Distribution (ie legs, genitalia, arms etc). Are there any systemic lymphatic problems? (i.e. intestinal lymphangiectasia, pulmonary lymphangiectasia, pericardial effusions, chylothoraces, chylous ascites, chylous reflux)
- Progression of swelling?
- exacerbating and relieving factors?
- pain associated with swelling?

Associated features:

- vascular malformations / birthmarks / overgrowth of a limb
- structural abnormalities including cleft palate/structural heart disease/extra eyelashes
- steatorrhoea/chronic diarrhoea
- warts/cellulitis/recurrent infections/shortness of breath (chest infections)
- venous disease
- hydrocele in males

Pregnancy history:

- Antenatal: nuchal/neck thickness (was it normal or raised?)
- Non-immue hydrops fetalis/ pleural effusions (hydrothoraces) / pedal oedema

Family history

- 3 generation family history of swelling (including pregnancy losses), inherited health problems e.g. congenital heart disease, distichiasis, varicose veins.

Drug history and allergies

Past Medical History

- Overseas travel to area at risk of Filariasis
- Deafness
- Haematological disorders (eg myelodysplasia, leukaemia)
- Immune deficiency
- Learning difficulties

Examination

General Examination of the child

- Does child look dysmorphic?
- Height
- Head circumference (small, large, normal?)
- Yellow nails
- Cleft palate
- Ptosis
- Distichiasis
- Birthmarks
- Neck webbing
- Wide spaced nipples
- Heart murmur
- Pleural effusion
- ascites
- Hydrocele / genital lymphoedema

Examination of affected site (s):

- Distribution of the lymphoedema
- skin changes (eg epidermal naevi, other skin abnormalities)
- venous disease
- birthmarks (eg “port wine stains”)
- limb length discrepancy
- temperature discrepancy

Note presence of skin pathology e.g. eczema/psoriasis etc

Warts/molluscum

Investigations

Exclude other causes of oedema (select relevant investigations):

- Pelvic USS
- D-dimer
- LFT: low albumin
- Urinalysis
- Echo/BNP level

To further investigate the lymphoedema:

- Lymphoscintigraphy (usually if child aged 8 years or older)
- Consider venous duplex scan
- MRI if a lymphatic malformation or overgrowth is suspected

Specific genetic testing:

Array CGH (detailed chromosome analysis) if child looks dysmorphic or has learning difficulties.

Congenital lower limb lymphoedema:

- *VEGFR3* for suspected Milroy disease
- *KIF11* if microcephaly present
- Turner syndrome if female
- Noonan panel if dysmorphic

Congenital generalised lymphoedema (i.e. hydrops fetalis/chylous effusions/ascites/intestinal lymphangiectasia/pericardial effusions / widespread lymphoedema):

- consider *CCBE1* / *FAT4* / *PIEZO1* / Noonan gene panel.

Childhood onset of bilateral lower limb lymphoedema (after the age of 1 year):

- *FOXC2* (especially if distichiasis present)
- *GATA2* (especially if genital involvement, low monocyte count)
- *GJC2* (especially if hands are swollen too)
- Noonan panel (if dysmorphic and other associated features)
- Full blood count → refer to Haematology if any concerns.

Multisegmental lymphoedema with evidence of overgrowth:

- Consider taking a skin biopsy for *PIK3CA* gene testing.

Isolated genital lymphoedema:

- Consider Noonan syndrome (gene panel test).
- Consider anogenital granulomatosis: take skin biopsies of scrotum and/or penis looking for granulomas within the dermis.
- Refer to gastroenterology for consideration of endoscopy and biopsy looking for Crohn's disease.

If anything suggestive of intestinal lymphangiectasia (diarrhoea within an hour of ingestion of fatty foods / bloating):

- FBC/Albumin/ alpha1 antitrypsin
- Faecal alpha1 antitrypsin and calprotectin etc
- Needs referral to expert dietician to discuss MCT (medium chain triglyceride) diet.