Ulster Med J 2014;**83(3):**135-139

Review

Perinatal Management of Major Congenital Heart Disease

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Accepted 27th January 2014

ABSTRACT

Congenital heart disease (CHD) is the most common form of congenital anomaly.

Prenatal diagnosis of CHD has been associated with decreased morbidity and mortality for some forms of major CHD. As most cases of major CHD are not identified prenatally, clinical examination of the newborn and pulse oximetry are also important means of identifying more cases.

Clinicians must suspect CHD as a diagnosis in a cyanosed or shocked neonate and be familiar with appropriate management, namely the commencement of prostaglandin if a duct dependent cardiac lesion is suspected.

Telemedicine can aid prompt diagnosis of CHD and therefore direct appropriate management.

INTRODUCTION

Congenital heart disease (CHD) is the most common form of congenital anomaly. If affects approximately 0.8% of all live births. Congenital malformations of the cardiovascular system accounted for 10.4% of infant mortality in Northern Ireland in 2010, excluding those infants with co-existent trisomy 13 or 18[1].

The correct management of neonates with suspected CHD is vital in improving the morbidity and mortality associated with these conditions. This may be facilitated by better prenatal diagnosis of CHD and the application of telemedicine in the form of transmitted echocardiography.

Major CHD is most often defined as a lesion that requires surgery or intervention catheter in the first year of life. Critical CHD may be defined as lesions that require surgery or catheter intervention in the first 28 days of life[2].

In the following paper we aim to summarise the role played by fetal echocardiography in the diagnosis of major CHD and also the identification and management of a neonate with major CHD. Both of these can be assisted by telemedicine.

PRENATAL DIAGNOSIS OF CONGENITAL HEART DISEASE

Prenatal diagnosis of CHD by fetal echocardiography is now a firmly established component of fetal medicine offered in many tertiary UK centres, including the Belfast Health and Social Care Trust. Image 1 shows an example of Hypoplastic Left Heart Syndrome (HLHS) identified on fetal echocardiography.

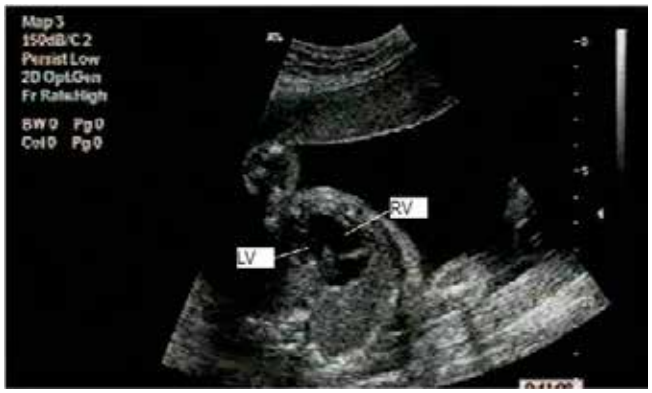

Image 1. Fetal Echocardiography of HLHS with a diminutive left ventricle (LV) and right ventricle (RV) seen.
Image provided by Dr AJ Sands

Prenatal diagnosis is increasingly playing an important role in paediatric cardiology. In the case of major or critical CHD it allows the opportunity to adequately counsel parents, to guide the timing and delivery of the baby in a suitable location and to plan perinatal management.

Approximately 90% of pregnancies affected by CHD occur in pregnancies where there are no known high risk features[3,4,5,6]. Therefore, initial antenatal diagnosis of CHD largely lies in the hands of those carrying out routine obstetric screening. Current national guidelines in the UK recommend that 4 chamber and outflow tract views are examined at the time of the fetal anomaly scan[6] as this allows for the possibility of >90% of major CHD to be detected[3,4].

When there is concern about the fetal heart on the obstetric anomaly scan or the pregnancy is deemed higher risk (refer to Table 1), referral is then made to a tertiary centre for fetal echocardiographic assessment.

Rates of prenatal detection of Congenital Heart Disease

Rates of prenatal detection of CHD vary considerably internationally and even nationally. In Northern Ireland between Sept 06 and Sept 07, 2.5 days of formal training on

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Table 1:

Pregnancies at high risk of fetal CHD that require referral for fetal echocardiography (excluding fetal indications)

Maternal Indications	Familial Indications
Maternal CHD	Paternal CHD
Maternal metabolic conditions, especially if poorly controlled in early gestation e.g. Diabetes Mellitus, Phenylketonuria.	Sibling with CHD or congenital heart block.
Maternal exposure to cardiac teratogens e.g Lithium, anticonvulsants, viral infections (rubella, cytomegalovirus, parvovirus, coxsackie) and toxoplasma	Chromosomal anomalies, gene disorders or syndromes with CHD in the family.
Maternal collagen disease with anti-Ro or anti-La	
Maternal use of Non-steroidal anti-inflammatory drugs after 25-30 wks	

Adapted from: Sharland G, Gnanapragasam J, Miller P, Narayanaswamy S. British Congenital Cardiac Association (BCCA) Fetal Cardiology Standards Working Group. Fetal Cardiology Standards. British Congenital Cardiac Association. March 2010. Revised March 2012.)[6]

fetal echocardiography was delivered to 90% of all obstetric radiographers in the province. The prenatal detection rate of major CHD rose significantly from 28% pre-training to 43% in the year of training[4] bringing Northern Ireland's rates close to the best previously quoted European rates of detection of 47%[7]. Diagnosis of four-chamber-view defects rose significantly from 38 to 54% and diagnosis of outflow-tract-view defects from 8 to 21%[4]. This study contributed to a change in regional guidelines, which now state that outflow tracts should also be routinely assessed during the anomaly scan.

Does prenatal diagnosis affect outcome?

The most important question is whether prenatal diagnosis of major CHD affects outcome of the infants. Some forms of CHD, namely those dependent on a patent ductus arteriosus, are associated with acute decompensation and risk of death often before a heart defect is suspected clinically. One would therefore expect that prenatal diagnosis of the defect and subsequent planning of the delivery with prompt postnatal management, would decrease the morbidity and mortality of the infant. This has however been hard to demonstrate. Prenatally diagnosed major CHD in some studies has been associated with a higher mortality. This is largely due to the fact that fetal echocardiography preferentially diagnoses the most severe/complex forms of CHD and there is also a higher frequency of associated extra cardiac abnormalities[3,4,8].

There have however been several studies since which have demonstrated that prenatal diagnosis of major CHD can improve outcome[9]. Research suggests that prenatal diagnosis of Transposition of the Great Arteries (TGA) and HLHS is associated with decreased perioperative morbidity and mortality[10, 11]. In coarctation of the aorta, collapse, pre-operative haemodynamic instability and death were more common in a postnatally diagnosed group[12].

POSTNATAL MANAGEMENT OF MAJOR CONGENITAL HEART DISEASE

Although the detection of major CHD in utero has improved substantially in recent years, many babies with CHD are undiagnosed at birth. This means that effective clinical examination of the newborn before hospital discharge and knowledge of the immediate management of a sick neonate with a duct dependent systemic or pulmonary circulation, is vital. Delayed or missed diagnosis of critical CHD accounted for 0.4-2.0 deaths per 10,000 livebirths in a UK series[13]. Perhaps the most important long term sequelae of delayed diagnosis in such patients who survive, is the risk of hypoxic/ischaemic brain injury. Periventricular leukomalacia has been reported on MRI imaging of the brain in up to 39% of neonates with critical CHD[13].

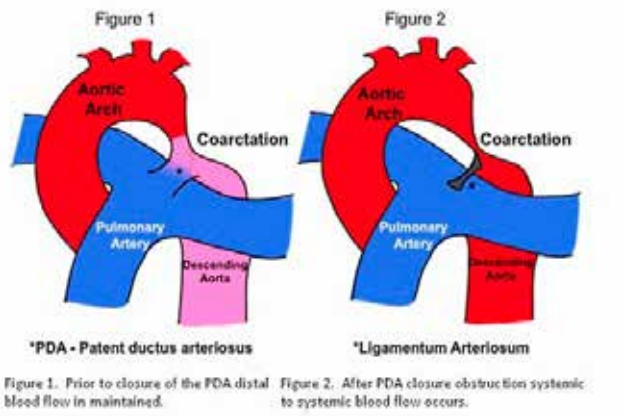

Fig 1. Duct Dependent Coarctation of the Aorta
Adapted from: http://www.uwhealth.org/american-family-childrens-hospital/pediatricpathways

Infants with a duct dependent systemic or pulmonary circulation and transposition of the great arteries are at risk of rapid demise and death in the first few days to weeks of life. Duct dependent systemic circulations often include the following conditions: HLHS; critical aortic stenosis; coarctation of the aorta; and interrupted aortic arch. Duct dependent pulmonary circulations may include the following conditions: pulmonary atresia; critical pulmonary stenosis; and tricuspid atresia. Circulatory collapse coincides with the closure of the ductus arteriosus and changes in the pulmonary vascular resistance. Figure 1 shows an example of critical

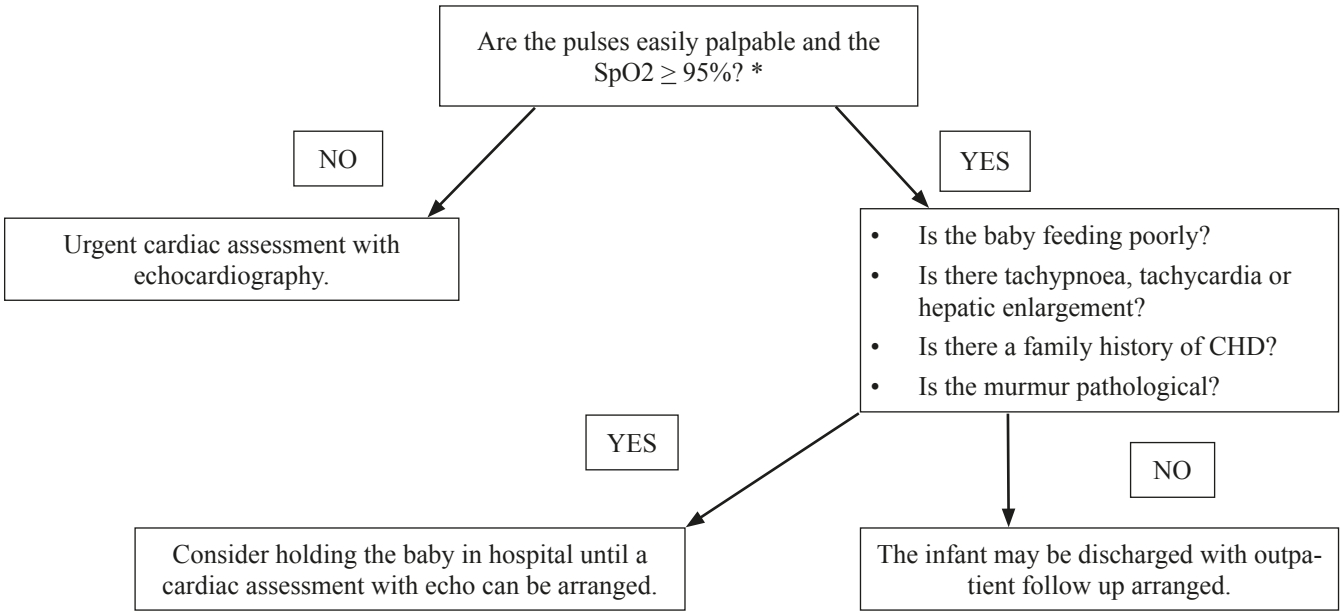

Fig 2. Assessment of a murmur heard on the newborn check pre-discharge.

*Confirming presence of femoral and brachial pulses should be mandatory before hospital discharge.

coarctation of the aorta where the systemic circulation is dependent upon a patent ductus arteriosus.

As these babies often look and examine well before these physiological changes occur, major CHD can go undetected at routine examination of the newborn. This is becoming even more problematic with a higher rate of early discharge of mother and baby after delivery.

Routine examination of the newborn

Routine examination of the newborn before discharge from hospital must incorporate the cardiovascular system. Signs such as cyanosis, heart murmurs and diminished peripheral pulses are sought and their discovery will prompt further expert cardiovascular assessment. As these signs are not always present before closure of the ductus and reduction of pulmonary vascular resistance, the clinical examination has low sensitivity. A study of 1590 babies with CHD in the UK showed that more than half were thought to have a normal cardiovascular system at their first routine examination and of these almost 40% presented with symptoms or died before their routine 6 week check[14]. Furthermore, the clinical examination is not specific. Cyanosis may be secondary to lung pathology and diminished pulses secondary to sepsis. However, discovery of these clinical signs will identify a sick newborn and further assessment and investigation must be undertaken with echocardiography often playing an important role in ruling out CHD as a cause. As heart murmurs have a prevalence of between 0.6-4.2% in all newborns, this decreases the specificity of the cardiovascular clinical examination of the newborn. The murmurs often represent physiological flow murmurs (e.g. mild turbulence in the branch pulmonary arteries), transient tricuspid regurgitation and small ventricular septal defects of no clinical significance. These babies may be wrongly suspected of having major congenital heart disease. Flow charts to help junior doctors and GPs decide when a neonatal murmur is significant may be useful as in figures 2 and 3.

Ongoing vigilance for CHD by the general practitioner and health care visitor is required, especially in cases of early discharge of the mother and baby.

Importantly, murmurs are often absent in major CHD and thus if any of the above features are present without a murmur, CHD must be ruled out.

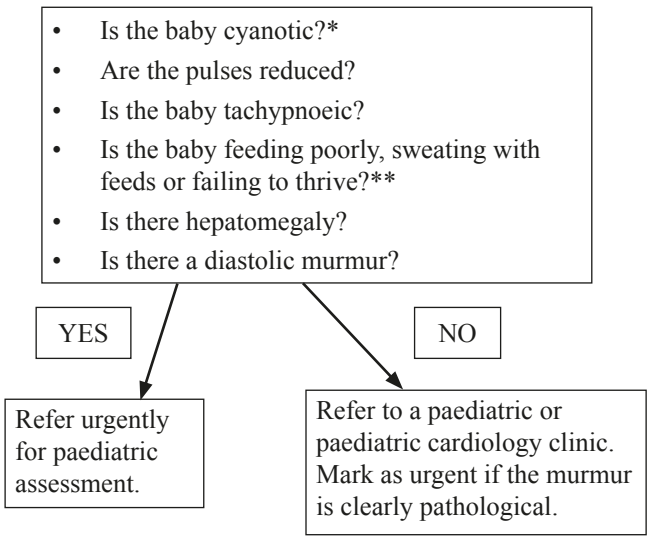

Fig 3. Assessment of a murmur heard on the 6 week baby check in primary care

*One must distinguish between peripheral and central cyanosis. SpO2 must be measured if there is any concern over cyanosis.

** Poor feeding may be the first sign of cardiac compromise

SpO2 screening with pulse oximetry

The addition of pulse oximetry screening to the newborn clinical examination has the potential to identify many more major congenital heart defects than clinical examination would alone. Post-ductal saturations (left hand or a foot) will be lower than pre-ductal (right hand) when there is mixing of pulmonary blood with arterial blood across the ductus arteriosus in duct dependent lesions. A positive result is post-ductal saturation of <95% or a 3% difference between pre and post-ductal saturations. A Swedish prospective study showed that introduction of pulse oximetry screening improved total detection rate of duct dependent circulation to 92%[15] and a case control study calculated that pulse oximetry had a sensitivity of 98.5% and a specificity of 96% for detecting these lesions[16].

Management of the collapsed neonate

As antenatal detection rates for major CHD remains around 50% at best and many cases are therefore unexpected, clinicians must have a high index of suspicion for CHD as a diagnosis in a cyanosed or shocked neonate presenting in the first hours or days of life. One must not forget that respiratory and metabolic conditions as well as sepsis can present very similarly and are more common than critical CHD. Nevertheless, if a duct dependent lesion is clinically suspected, commencement of prostaglandin infusion must not be delayed. Specialist paediatric cardiology advice must be sought as soon as possible. This will usually include echocardiographic assessment. In a remote hospital, a telemedicine facility would allow transfer of live echo images to a tertiary centre and avail of specialist opinion promptly. Of note, differentiating persistent pulmonary hypertension of the newborn (PPHN) from a duct dependent pulmonary circulation can be very difficult. Infants with PPHN may also show some improvement with the higher doses of prostaglandin. Use of echocardiography will often make a firm diagnosis, but usually the safest option is to commence prostaglandin in the interim.

Dose and rate of increase of prostaglandin may be administered as per the BNFC[17]. If a local protocol is available for both starting doses and rate of up-titration of prostaglandin, one must adhere to this.

The aim should be saturations between 75-85%, palpable femoral pulses and resolving acidosis. The dose may need to be doubled as frequently as every ten minutes if there is no improvement. However, at this point expert advice is required. When ductal patency has been established, attention must be paid to the balance between the pulmonary and systemic circulations. Pulmonary overcirculation will reduce systemic and myocardial circulation and so must be avoided. Measures to reduce pulmonary overflow include maintenance of systemic saturations between 75-85% and PaCO2 of 5-6 to avoid respiratory alkalosis, which may mean use of mechanical ventilation in order to achieve this[14]. Ventilation may also be required if the patient remains critically unwell (severe hypoxaemia, acidosis and/or cardio respiratory failure), suffers apnoea on administration of prostaglandin or on an elective basis when prostaglandin requirement reaches a pre-determined high level when apnoea becomes more common (e.g. >25nanograms/kg/min if PGE1 used)[18]. Apnoea is the most common side effect of prostaglandin, but other important side effects include hypotension, hypoglycaemia and fever.

If a baby is not responding to a prostaglandin infusion, there may be a variety of explanations[14,18]:

- Venous access may be inadequate.
- There may be inadequate flow across the duct and subsequently infusion rate may need to increase substantially (cardiology advice must first be sought).
- The patient may have been shocked and acidotic for a long period.
- The patient may have ventricular dysfunction secondary to an obstructed systemic lesion.
- The patient could have TGA with an intact atrial septum or obstructed total anomalous pulmonary venous connection. Specific catheter or surgical intervention may therefore be required urgently.

TELEMEDICINE

Telemedicine is a rapidly developing application of clinical medicine where medical information is transferred through modern telecommunications allowing for remote specialist consultation. Image 2 shows two doctors delivering a remote cardiac consultation via telemedicine. Images are received on the unit to the left of the picture and displayed on the television screen to allow viewing by those in the room. An audio unit seen on the table acts both as a microphone and a speaker to allow a conversation between both parties.

Telemedicine has proven to be very useful in paediatric cardiology. Transthoracic echocardiography is the gold standard for diagnosis of most CHD and thus transfer of echo images from district general hospitals to the specialist centre can aid prompt diagnosis. This is particularly important when dealing with duct dependent lesions in the newborn. In this situation, prompt diagnosis can improve outcome by rapid institution of the correct management and transfer to the appropriate centre. On the other hand, where cardiac disease is suspected but ruled out by expert viewing of echo images transmitted by telecommunication, transfer of the patient to the specialist centre can be avoided.

Accuracy of remote Echocardiograms

There have been many studies to determine the accuracy of remote diagnosis of congenital heart disease by telemedicine, which have largely shown very promising results. A review of the use of telemedicine for diagnosis of congenital heart disease in Northern Ireland over an 8 year period, confirmed that telemedicine diagnosis was accurate in 97% of cases[19].

Image 2. Telemedicine Suite in use, Royal Belfast Hospital for Sick Children.

Image provided by Dr AJ Sands

Telemedicine and prenatal diagnosis of Congenital Heart Disease

In addition to neonatal diagnosis of CHD and post-op follow up of surgical patients, tele-echocardiography can also be applied to prenatal diagnosis of CHD. A Northern Irish prospective study compared fetal echo performed by obstetric sonographers with live guidance and assessment by a fetal cardiologist via telemedicine, with fetal echo later performed by the specialist at the regional centre. This method was technically feasible, reliable and diagnostically accurate with diagnostic concordance in 97% of cases[20].

CONCLUSION

CHD is the most common congenital anomaly affecting approximately 0.8% of all live births.

Prenatal diagnosis of TGA, HLHS and coarctation of the aorta has been associated with decreased perioperative morbidity and mortality.

Clinical examination of the newborn will still miss many cases of major and critical CHD. The addition of pulse oximetry has the potential to detect of up to 92% of all cases of duct dependent circulations before hospital discharge.

Clinicians must have a high index of suspicion for CHD as a diagnosis in a cyanosed or shocked neonate presenting in the first hours or days of life. Prostaglandin infusion should be commenced promptly if a duct dependent circulation is likely.

Telemedicine has proven to be very useful in paediatric cardiology. Transfer of echo images from district general hospitals to the specialist centre can aid prompt diagnosis and therefore direct appropriate management.

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PUZZLING SYMPTOMS?

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	GAUCHER DISEASE	FABRY DISEASE	MPS I (mucopolysaccharidosis type I)	POMPE DISEASE (acid maltase deficiency)
Enzyme deficiency	β-glucocerebrosidase	α-galactosidase A	α-L iduronidase	Acid α-glucosidase
Substrate accumulation	Glucosylceramide – primarily in monocytes and macrophages	GL-3 - primarily in vascular endothelium	GAGs (heparan and dermatan sulphate) – primarily in connective and soft tissue, joints and cardiac cells	Glycogen – primarily in cardiac, skeletal and respiratory muscles
Spectrum of disease	Type I - Non-neuronopathic Types II & III - Neuronopathic	Both males and females affected, ranging from mild to classical phenotypes	Severe to attenuated (formally known as Hurler, Hurler-Scheie and Scheie)	Infantile to late onset
Incidence	1: 40,000–50,000 in general population[1] (1: 450 in Ashkenazi Jews[2])	1: 40,000 males[3] 1: 117,000 in general population[4]	1: 100,000[5]	1: 40,000 live births[6,7] (1: 14,000 in African Americans[8])
Inheritance	Autosomal recessive	X-linked	Autosomal recessive	Autosomal recessive
Key signs and symptoms	- Hepatosplenomegaly - Anaemia/ thrombocytopenia - Bone pain/crisis - Growth retardation - Avascular necrosis - Pathologic fractures - Osteopenia	- Cardiac dysfunction (esp. left ventricular hypertrophy) - Corneal/ lenticular opacities - Angiokeratomas - Renal dysfunction - Acroparesthesia/episodic pain crisis - Heat and cold intolerance - Cerebrovascular complications - Gastrointestinal manifestations	*Spectrum of clinical presentations from mild to severe* - Recurrent ear/nose infections - Corneal clouding - Enlarged liver and spleen - Obstructive airway disease - Valvular heart disease - Coarse facial features - Mental impairment in severe form - Musculoskeletal features - use pGALS to identify joint abnormalities and pattern of involvement; consider MPS I with toe walking / kyphoscoliosis / symmetrical joint contractures [in the absence of synovitis], especially upper limb [fingers / wrists / predominantly shoulder] involvement. Other features include hip dysplasia / trigger fingers / carpal tunnel syndrome	*Infants* - Cardiomegaly and/or cardiomyopathy - Profound, rapidly progressive muscle weakness - Respiratory insufficiency/frequent infections - Feeding difficulties/failure to thrive *Early childhood to late adulthood* - Progressive proximal muscle weakness - Respiratory failure/insufficiency - Gait abnormalities - Muscle pain
Diagnostic tests	Enzyme assay in leucocytes or cultured skin fibroblasts; bone marrow biopsy	Dried Blood Spot. Heterozygotes: DNA mutation or linkage analys	Lymphocytes assay Urinary GAGs	Dried Blood Spot with enzyme assay – or enzyme assay with blood leucocytes. Muscle biopsy and fibroblast skin biopsy
Lab assays	ACE, TRAP, CHITO, CCL-18/PARC	Plasma and urine GL-3	Urinary GAGs	Hex4, CRIM
	ACE: angiotensin-converting enzyme TRAP: tartrate resistant acid phosphatase CHITO: chitotriosidase CCL-18: CC-chemokine ligand 18 PARC: pulmonary activation-regulated chemokine	GL-3: globotriaosylceramide	GAGs: glycosaminoglycans pGALS: paediatric Gait, Arms, Legs and Spine	Hex: glucose tetrasaccharide CRIM: cross-reactive immunologic material

Lysosomal Storage Disorders Specialist Treatment Centres

If you would like further information please contact your local treatment centre:

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Department of Inherited Metabolic Disorders
University Hospital Birmingham (Adult)
Tel: 0121 627 1627 Ext 51592

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Addenbrookes Hospital (Adult)
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Lysosomal Storage Disease Unit
Great Ormond Street Hospital (Paediatrics)
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Charles Dent Metabolic Unit
The National Hospital for Neurology and Neurosurgery (Adult)
Tel: 0207 829 8778

Lysosomal Storage Disease Unit
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DUBLIN
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Children's University Hospital
Temple Street, Dublin 1
Tel: 01 878 4317

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Date of preparation: April 2014. Code: XLSD-UK-3/14-4936