

A17/S(HSS)/a

**2013/14 NHS STANDARD CONTRACT  
FOR CONGENITAL HYPERINSULINISM SERVICE (CHILDREN)**

**PARTICULARS, SCHEDULE 2- THE SERVICES, A- SERVICE SPECIFICATIONS**

<b>Service Specification No.</b>	A17/S(HSS)/a
<b>Service</b>	Congenital hyperinsulinism service (Children)
<b>Commissioner Lead</b>	
<b>Provider Lead</b>	
<b>Period</b>	12 months
<b>Date of Review</b>	

**1. Population Needs**

**1.1 National/local context and evidence base**

Congenital hyperinsulinism (CHI) is a complex condition requiring specialised care through a multidisciplinary team led by an expert paediatric endocrinology service. The management of CHI, particularly medically unresponsive diffuse CHI is challenging. Rapid  $K_{ATP}$  gene mutation analysis has been significantly beneficial to the diagnostic work up and clinical management of children with CHI

However, much remains unknown about the disease condition, particularly the natural history and the clinical relevance of gene mutation analysis to the clinical outcomes of patients..

It is estimated that the population incidence of CHI is 1 in 40,000 to 1 in 50,000, with the incidence rising to 1 in 2,500 in consanguineous populations. The true incidence of  $K_{ATP}$  mutations has not been fully investigated. In one large cohort of patients with CHI, the incidence of  $K_{ATP}$  mutations was 15%.. In another cohort, the incidence of  $K_{ATP}$  mutations was higher at around 40%.. A number of different genetic mutations have been identified in association with hyperinsulinism (HI), but the precise mechanisms have not been elucidated for many of the new mutations (3 & 6). Current research is underway to understand the genetic principles of CHI, not only to provide an efficient diagnosis and streamline treatment outcomes but also to improve our understanding of beta cell physiology. Further research is underway to investigate the cellular mechanisms underlying excess insulin secretion in children with CHI.

Treatment of CHI has been evolving over the past few years and there are a number of peer reviewed publications which support the evidence base for managing CHI

patients in centres of excellence (6, 8 & 9). Although medical treatment options are limited by the number of drugs available for this condition, genetic diagnosis, particularly those helping to identify focal CHI has been a significant improvement.

Likewise, the availability of positron emission tomography (PET)-computerised tomography(CT) scanning has been a significant advance in localising focal CHI in the preoperative period (7). It is important that clinical outcomes of children with CHI are analysed in the context of these new investigations (4) available to specialised centres.

## **2. Scope**

### **2.1 Aims and objectives of service**

#### **Aims**

The overall aim of the service is to provide the highest quality of care to children with CHI.

Specifically the CHI service aims to provide:

- high quality holistic care delivered through a multidisciplinary team (MDT)including: paediatric endocrinology, dietetics, speech and language therapy, clinical psychology, radiology, histology, intensive care and surgery
- specialised in-patient care to children, including critical care facilities
- diagnostic facilities to define the condition in order to specify appropriate treatment options
- to perform appropriate investigations to proceed to surgical treatment options if clinically indicated
- high quality pancreatic surgery and post operative management
- long term monitoring of the glycaemic status of children with CHI
- advice, education and support to local care providers on CHI and the management of CHI patients registered with one of the nationally designated providers
- to engage parents and families in the long term care of children with CHI
- continuous monitoring of risk and governance to ensure that clinical treatment is safe and effective
- clinical and service audits to ensure highest standards of safety, care and clinical effectiveness.

#### **General overview:**

Hypoglycaemia due to CHI is a relatively rare but potentially serious condition occurring soon after birth. The estimated incidence of CHI is 1:40,000 to 1:50,000, although it is likely that the incidence is higher, if less severe cases of CHI are also included. Current estimates based on activity within the nationally designated

centres suggest the incidence of CHI, within the scope of the nationally designated service, to be 1:30,000.

Hypoglycaemia in newborn babies is relatively common, but is often due to feeding problems, which are transient and easily reversed. In contrast, hypoglycaemia due to CHI is persistent. The resulting hypoglycaemia leads to hypoglycaemic brain injury which subsequently results in mental retardation, epilepsy and cerebral palsy.

In most other conditions with hypoglycaemia, compensatory ketogenesis offers the brain an alternative metabolite to function adequately. However, in HI, ketogenesis is suppressed. Therefore, children with CHI not only have low glucose but also lack the alternative metabolite ketone; the combined loss of brain metabolites may lead to abnormal brain development, affecting in particular, the occipital visual cortex. A number of observational studies have reported on the presence of neurodevelopmental abnormalities in children with CHI, suggesting that hypoglycaemia in the context of HI is likely to have long term sequelae, unless treated promptly.

Histologically there are two major subgroups of CHI, namely diffuse and focal. In diffuse disease there is an abnormality throughout the pancreas with all the beta-cells making too much insulin. However in focal disease the abnormality is confined to single region of the pancreas with the rest of the pancreas being normal in endocrine and exocrine function. The surgical treatment of the two groups is radically different. The diffuse form requires a near total pancreatectomy whereas the focal form requires a limited pancreatic resection. Children with the focal form can be “cured” after the limited resection.

Treatment of hypoglycaemia in children with CHI requires a multi-disciplinary team approach with paediatric endocrinology, dietetics, speech and language therapy, clinical psychology, radiology, histology, intensive care and surgery among others. The child may need to be stabilised initially on a critical care unit, while central venous access is secured. Frequent monitoring of blood glucose needs to be undertaken with alteration made to intravenous glucose as necessary. Treatment with anti-hypoglycaemic agents needs to be monitored for efficacy and side effects. Feeding difficulties are common in children with CHI with early establishment of feeding introduced with support from dietetics and speech and language therapy. If satisfactory glycaemic control is not achieved with maximal medical therapy, pancreatic surgery has to be considered.

The nationally designated providers must have appropriate access to investigations required including rapid CHI mutation analysis and specialised radiology investigations such as 18-fluorodopa PET-CT scanning. The provision of 18-fluorodopa PET-CT scanning must be accompanied by robust and transparent clinical and corporate governance arrangements and the prices must be approved by NHS England. It is the providers' responsibility to ensure that the price paid for 18-fluorodopa and PET-CT scanning represent best value for the NHS.

The nationally designated CHI service is commissioned on behalf of the NHS in

England and Scotland. Eligible residents of European Union member states are included under reciprocal arrangements.

Residents of Wales, Northern Ireland and the Channel Islands are excluded from this agreement as NHSE has no authority to commission services on behalf of these administrations.

## Objectives

- to provide an exemplary and comprehensive service for all eligible referred patients with CHI
- expert diagnosis of CHI utilising the most up-to-date validated diagnostic tools and knowledge
- expert management of patients with confirmed CHI through the use of the most up-to-date clinical protocols for prescribing and symptom management
- to provide access to 18-fluorodopa PET-CT scanning services in a select group of patients, with the ability to diagnose focal CHI early and offer surgical treatment with the prospect of a cure
- clinically appropriate consideration and provision of surgery within the CHI patient pathway
- effective monitoring of patients to ensure optimal functioning for the patient with regards to their CHI
- to operate a rolling programme of clinical audit to test current practice and inform the evolution of care in CHI
- to provide care with a patient and family centred focus to maximise the patient experience of care within the nationally designated providers
- to be seen as the leading clinical services and a source of expert advice for the diagnosis and management of CHI within the NHS
- to support local healthcare providers to manage patients with CHI whenever it is clinically appropriate and safe to do so
- provide high quality information for patients, families and carers in appropriate and accessible formats and mediums
- to develop the experience, knowledge and skills of the MDT to ensure high quality sustainable provision.

## 2.2 Service description/care pathway

The service aims to deliver high quality clinical care to patients with CHI. These patients are usually diagnosed in the newborn period with persistent hypoglycaemia. However occasionally infants and older children can also present with CHI. Once the diagnosis is made the baby/child is referred to one of the nationally designated providers. Referrals are responded to within 24 hours and if immediate transfer cannot be arranged then the provider will support the referring unit to provide appropriate care for the patient. The nationally designated provider may also require the referring hospital to carry out investigations to confirm the diagnosis of CHI.

The national providers use a core MDT including (at least):

- consultant paediatric endocrinologist
- clinical fellows
- clinical nurse specialist and other nurses
- psychologist
- pharmacist
- dietician.

In addition to this the service calls on the work of:

- radiology
- nuclear medicine
- paediatric anaesthesia
- pancreatic surgeons
- paediatric histopathology
- biochemistry
- speech and language therapy
- play specialists.

The service will liaise and work with a surgical team to manage those children whose condition and response to medical management indicates that surgery is a viable option.

Individuals work together with the same aims and clinical understanding of the condition and its management to create a multidisciplinary team approach.

Inpatients are reviewed every day on a ward round supported by a consultant paediatric endocrinologist with input from the core MDT as clinically required. Care plans are clearly documented in the notes. Relevant investigations will be carried out including genetic tests. Any referred patients that are waiting for admission are discussed and the plan to admit them as soon as possible is reviewed with any actions required updated.

It is recognised that rapid KATP mutation analysis is useful in the management of children with CHI early in the course of the illness. The presence of a paternal heterozygous mutation in *ABCC8* or *KCNJ11* or no identified mutations is a cue to undertake 18-fluorodopa PET-CT scanning to diagnose focal lesions, which would be amenable to focal lesionectomy. The following are the criteria for patient selection for PET-CT scanning:

- paternal heterozygous mutations in *ABCC8* or *KCNJ11*
- de novo heterozygous mutations in *ABCC8* or *KCNJ11*
- absence of gene mutations in *ABCC8*, *KCNJ11*, *GLUD1*, *GCK* or *HNF4A* with the child remaining on medical treatment for CHI and Diazoxide dose at least 5 mg/kg/day
- patients fulfilling above criteria and ratified by a MDT process
- exceptional circumstances ratified by a multidisciplinary team process.

If and when a patient requires surgery (pancreatectomy) the patient is then discussed with the surgical team and a date arranged for surgery.

There is a weekly MDT led by the senior consultant paediatric endocrinologist to discuss the needs of each inpatient (and other patients as required) in detail and review other non-medical aspects of their care.

The providers will hold other meetings regularly through the month to address clinical, service delivery and governance issues.

There are clinical protocols for the management of CHI patients.

Audit is an integral part of improving the delivery of care and an on-going audit programme provides the evidence to improve and enhance the delivery of the clinical care provided.

Throughout the care of the patient, the parents and/or carers of the patient must be supported by the team and provided with information on the condition, its treatment and the service.

This must include engaging and supporting patient groups when it is appropriate to do so.

### **Risk management**

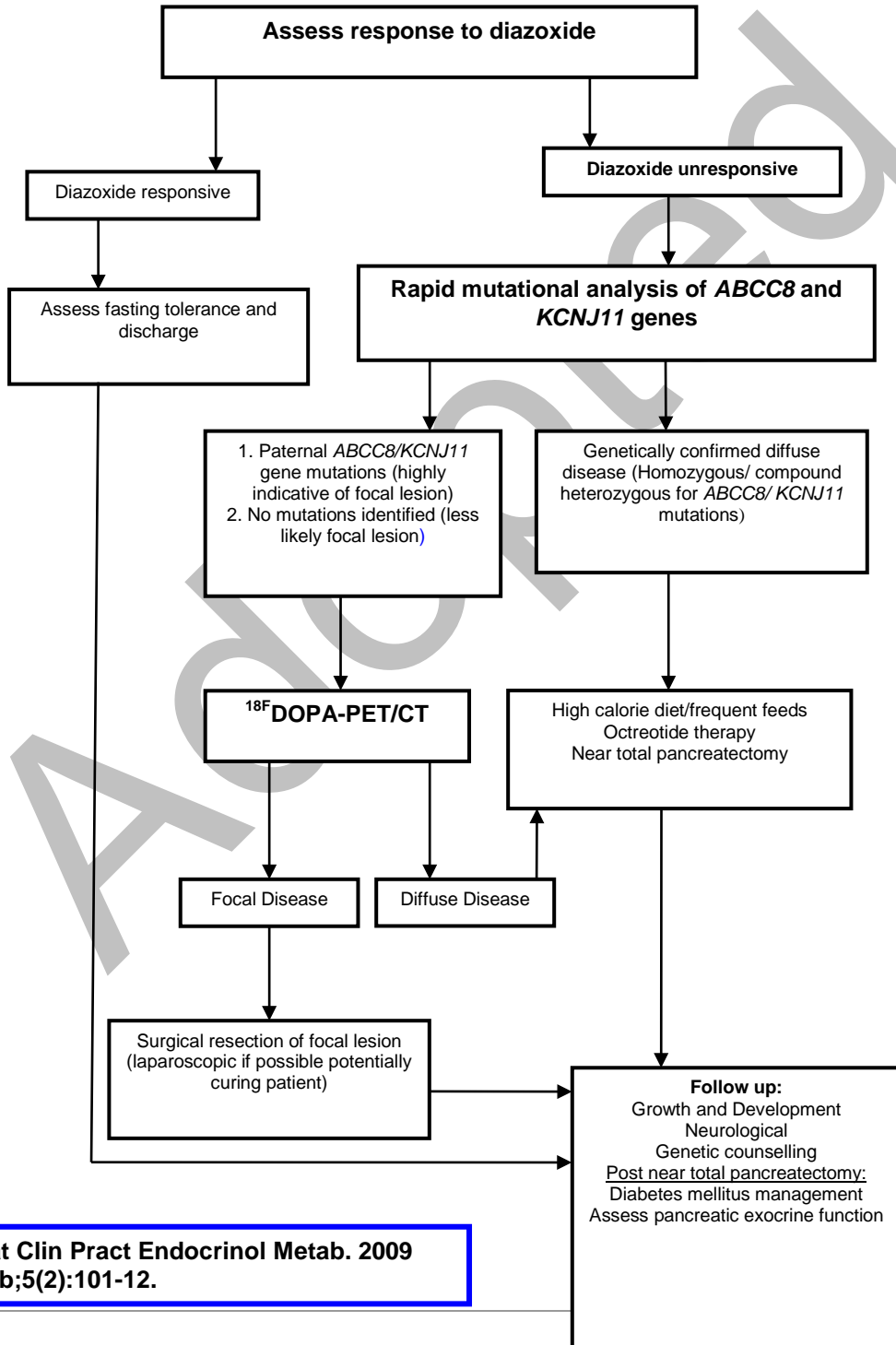
Care delivered by the CHI service providers must be of a nature and quality to meet the care standards, specification and agreement for the service. It is the trust's responsibility to notify the commissioner on an exceptional basis should there be any breaches of the care standards. Where there are breaches any consequences will be deemed as being the trust's responsibility.

Patients must be managed in line with the specification and care standards. Any deviation from these which has not been approved by NHSE is at the trust's risk both clinically and financially. It is the trust's responsibility to inform the commissioners of any such non-approved deviations on an exceptional basis.

Where a patient's presentation challenges the assumptions that underpin the specification, service standards and contractual arrangements it is the trust's responsibility to inform the commissioners on an exceptional basis, prior to any treatment (except for emergency treatment) so that the implications of the patient's requirements can be considered. This does not affect situations where the individual funding application process applies.

## Service model and care pathways

### Management of Congenital hyperinsulinism



Nat Clin Pract Endocrinol Metab. 2009  
Feb;5(2):101-12.

## **Days/hours of operation**

24 hours a day, 365 days a year

## **Discharge criteria & planning including any transition arrangements**

Criteria for discharge from inpatient care:

- satisfactory glycaemic stability achieved with or without medication
- no adverse neurodevelopmental outcomes anticipated
- no further investigation required
- clinically appropriate arrangements for local care and CHI service follow-up have been discussed and agreed by all relevant parties
- parents/carers have demonstrated competence in any care they will be required to provide in relation to CHI
- parents/carers understand and have the necessary information to contact their nationally designated CHI provider.

All discharge planning will be managed through the MDT with local health and social care providers being fully informed of the patient's condition and any responsibilities they will have to assume. This will be formalised in written communication to the patient's GP and all other relevant parties.

All patients who develop diabetes post pancreatectomy will be transferred to local diabetes services.

Transition to adult services will depend on local arrangements but adult care is currently beyond the scope of NHS England commissioned CHI service.

## **2.3 Population covered**

This service covers patients registered with an English GP, resident in Scotland, resident in the European Union and eligible for treatment in the NHS under reciprocal arrangements.

Patients from Wales and Northern Ireland are not part of this commissioned service and the trust must have separate arrangements in place.

## **2.4 Any acceptance and exclusion criteria**

Referrals are accepted from any qualified doctor where the patient has confirmed or suspected CHI. The receiving clinician at one of the providers may request the referrer to carry out further investigations to aid the proper diagnosis of the patient's condition.



Referrals will be accepted by the nationally designated providers via the on-call senior physician for the CHI service.

### **Exclusion criteria**

Confirmed alternative diagnosis to CHI

### **Response time & detail and prioritisation**

Initial telephone contacts from referrers are dealt with immediately by the senior CHI physician on duty. The referral may be accepted over the phone immediately and/or the CHI service provider may request the referrer to carry out further investigations. Advice on optimal management will be given and on-going support will be provided until the patient is transferred.

Transfer of patients to a nationally designated CHI service will be prioritised according to the needs of individual patients but in all cases where a transfer to the CHI service has been agreed that transfer will take place as soon as is practicable.

If necessary the nationally designated CHI providers will communicate with each other to coordinate appropriate care for patients at times when capacity at one or both the providers is under pressure.

## **2.5 Interdependencies with other services**

### **Whole system relationships and interdependencies**

Internally the CHI team will link into multiple clinical and administrative teams as a result of the composition of the broad MDT.

External to this the nationally designated CHI providers are the leaders in the NHS for patient care in this area. They provide a direct source of advice and support when other clinicians refer patients into the nationally designated providers. This support will continue until the patient is transferred into the nationally designated provider or it becomes apparent that the child does not have CHI.

The nationally designated providers also provide education within the NHS to raise and maintain awareness of CHI and its management.

The national providers will form a relationship with local health and social care providers to help optimise any care for CHI provided locally for the patient. This may include liaison with consultants, GPs, community nurses or social workers etc.

### **Relevant networks and screening programmes**

Not applicable at present

### 3. Applicable Service Standards

#### 3.1 Applicable national standards e.g. Institute for Health and Care Excellence (NICE), Royal College

The nationally designated CHI providers must be fully integrated into their trust's corporate and clinical governance arrangements.

The commissioners and service will conduct a formal joint service review at least every six months

See also NHS England Service Standards for CHI

### 4. Key Service Outcomes

#### Outcomes:

- to provide cure for those diagnosed with focal CHI after investigations and surgery
- to optimize neurodevelopment of patients with CHI through careful clinical management and support.

The providers will provide agreed performance monitoring data on a monthly basis. Where any elements of this deviate from the agreed plan, the service will provide a brief explanation accompanying the submission of the report. The commissioner may wish to follow this up and request further information to inform any necessary actions that will be agreed between the service and commissioners in the context of the terms and conditions of the agreement.

### 5. Location of Provider Premises

Great Ormond Street Hospital for Children NHS Foundation Trust

Royal Manchester Children's Hospital under sub-contract arrangements with Central Manchester University Hospitals NHS Foundation Trust

Alder Hey Children's NHS Foundation Trust