E03/S(HSS)/d

2013/14 NHS STANDARD CONTRACT
SPECIALIST LIVER DISEASE SERVICE (CHILDREN)

PARTICULARS, SCHEDULE 2 – THE SERVICES, A – SERVICE SPECIFICATION

Service Specification No.	E03/S(HSS)/d
Service	Specialist liver disease service (Children)
Commissioner Lead	
Provider Lead	
Period	12 months
Date of Review	

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1. Population Needs

1.1 National/local context and evidence base

This service covers a large number of different conditions each with a separate evidence base that cannot readily be summarised here. Expert consensus, as evidenced by Royal College of Paediatrics and Child Health (RCPCH) approval, is that all of these conditions need to be managed in a specialist centre.

2. Scope

2.1 Aims and objectives of service

The aim of the service is to provide family-centred specialist care for children and families with all forms of medical and surgical liver disease, including metabolic liver disease, acute liver failure and pre-and post liver transplant management. The age range of new referrals varies from newborn babies to 16 year olds. Follow up care is provided until discharge, transition to adult specialist care (mainly between 16 – 18 years) or transition to end of life services. The majority of newly referred patients are infants or young children with neo-natal or childhood liver disease. The main diagnostic and monitoring methods include blood and urine analysis (e.g. serum biochemistry, haematology, microbiology and metabolic investigations), histological investigations (e.g. liver biopsy, skin biopsy, muscle biopsy), upper gastro intestinal endoscopy and endoscopic retrograde cholangiopancreatogram (ERCP), surgical diagnostics (e.g. operative cholangiogram) and radiological investigations (e.g. abdominal ultra sound scan, computed tomography (CT) / magnetic resonance imaging (MRI) scan and diagnostic interventional radiology procedures such as transjugular liver biopsy and hepatic angiography)

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Treatments offered include medical, surgical and/or interventional radiological management of liver disease, nutritional, psychological and physiotherapy support for the child and family, educational support and counselling about liver disease and preparation for liver transplantation. Treatment is delivered in an inpatient (ward or day unit based on paediatric intensive care unit (PICU) if required) and outpatient setting, with carefully monitored shared care arrangements in place with referring clinicians. The aim of the service is to assess, diagnose, manage and follow up paediatric patients with all forms of medical and surgical liver diseases set out in section 2.2 below, and promote their optimal future and quality of life as adults.

2.2 Service description/care pathway

The service is commissioned to provide:

- assessment, diagnosis and management of children with all forms of liver disease;
- provision of hepatobiliary surgery for patients with biliary atresia and choledochal cysts (<6 months of age only);
- provision of emergency, elective and planned care;
- a close working relationship with designated paediatric liver transplantation services;
- a close working relationship with local children's services to ensure as much care as possible is delivered closer to home.
- provision of a 24-hour national advisory service for patients/carers and healthcare professionals of all levels;
- provision of a dedicated adolescent transfer service to adult hepatology care

Care pathway:

- diagnosis tests;
- liver conditions and disorders;
    - acute liver failure, or;
    - chronic liver failure (parenchymal, biliary and vascular disorders)
- transplant – please see paediatric transplant service specification.

1.Highly specialised diagnostic test

Diagnosis may require the following surgical procedures:

- operative cholangiogram in suspected neonatal cholestasis for biliary atresia;
- muscle and skin biopsy in children with suspected metabolic/mitochondrial disorders;
- lip biopsy in neonates with suspected haemochromatosis.

High risk liver biopsies:

- biopsies requiring interventional radiology and surgical back up (e.g. in the presence of coagulopathy (PT.3 seconds prolonged, thrombocytopaenia<70x109 /1);
- post transplant or biliary surgery;

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- cystic disease
- obesity;
- anatomical abnormalities

2.Liver conditions and disorders

Acute liver failure and acute on chronic liver failure**:**

- acute liver failure of all known and unknown aetiologies;
- neonatal haemochromatosis;
- autoimmune hepatitis;
- Budd-Chiari syndrome;
- Veno-occlusive disease;
- Tyrosinaemia;
- mitochondrial electron chain;
- all children with acute decompensation of chronic liver disease.

Outcome:

- recovery (and discharge);
- chronic liver disease (and continued management);
- referral for transplant.

Chronic liver disease of childhood - involves a destruction of the liver parenchyma leading to fibrosis and cirrhosis:

- children with clinical and/or biochemical evidence of cryptogenic chronic liver disease or when local facilities do not allow rapid diagnosis of treatable conditions like autoimmune hepatitis or Wilson's disease (at least within two weeks from presentation);
- children with problematic complications of chronic liver disease such as cholangitis, intractable ascites, failure to thrive, malnutrition, pruritus, encephalopathy and recurrent gastrointestinal bleeding;
- children with recognised causes of chronic liver disease who do not respond satisfactorily to treatment (e.g. autoimmune hepatitis, Wilson's disease);
- children with chronic hepatitis B or C to be considered for anti-viral treatment;
- children with unexplained abnormality of liver function tests to be referred; immediately in the presence of coagulopathy not responding to vitamin K
- after no more than three months observation in the presence of normal synthetic function,
- children with unexplained hepatomegaly;
- children with chronic liver disease for consideration of liver transplantation (e.g. biliary atresia after Kasai porto-enterostomy).

Metabolic and genetic conditions requiring consideration for liver transplantation:

- primary oxaluria;
- fibropolycystic disease;
- methylmalonic acidaemia;
- primary immunodeficiencies

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Parenchymal disorders

In infancy:

Neonatal Hepatitis Syndrome (giant cell hepatitis) is an inflammatory condition of the neonatal liver:

- jaundiced infants who present with alcholic stools, hypoglycaemia, ascites (in utero or after birth) or severe failure to thrive and those with coagulopathy not corrected by intravenous vitamin K;
- neonatal hepatitis of unknown cause, which has not resolved completely with normal transaminases by four months of age.

In older children conditions:

- Alpha one antitrypsin deficiency
- Autoimmune liver disease
- Wilson Disease
- Non-alcoholic steatohepatitis (NASH)
- Hepatic storage disorders
- Liver tumours like Hepatoblastoma and Hepatocellular carcinoma and other rare tumours or secondaries to liver
- Single gene liver based metabolic disorders that could require liver or liver cell transplantation
- Chronic viral hepatitis B and C for treatment
- Drug induced hepatitis
- Unexplained hepato or hepatosplenomegaly
- Liver tests abnormalities in haematological conditions like sickle cell disease, liver complications of haematological malignancies
- Bacterial, parasitic and fungal infections of liver

Biliary disorders

- **Biliary atresia** - bile duct between liver and small intestine is blocked of absent. All suspected cases.
- **Choledochal cysts** - congenital cystic dilation of the bile ducts. Diagnosed antenatally or within six months of life, as they may represent cystic biliary dilatation with features of chronic liver disease (e.g. ascites, portal hypertension) or evidence of intrahepatic involvement.
- **Bile duct problems** - i.e. stones in the common bile duct, cyst of biliary system. All primary and secondary liver tumours (benign/malignant).
- **Cystic fibrosis related liver disease**
- **Inspissated bile syndrome**
- **Liver graft vs host disease**
- **Central (segments I, IV, V, VIII)** Multifocal where an extended partial
- hepatectomy may be required, which may require evaluation for total hepatectomy and transplantation (typically rare tumours such as liver/bile duct rhabdomyosarcoma.

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Vascular disorders

- **Vascular tumour with complications** (cardiac, mechanical)
- **Undiagnosed liver masses**
- **Portal hypertension:**
    - variceal bleeding (unless specialist paediatric therapeutic endoscopy is available);
    - children requiring consideration for shunt surgery or transplantation;
    - children requiring consideration for prophylactic treatment (e.g. air travel, living in);
    - children with ectopic variceal bleeding (e.g. gastric varices);
    - variceal bleeding associated with Budd-Chiari syndrome.
- **Congenital vascular anomalies** (e.g. congenital porto-caval shunts):
    - all cases will need specialist investigation (i.e. angiography) to determine relevant vascular anatomy;
    - a proportion will require specialist surgical reconstruction.

Care pathway

A sequential flow diagram of the integrated service user pathway(s) showing access, exit/ transfer points, potential routes and relationships with other health and/or social care providers is set out below.

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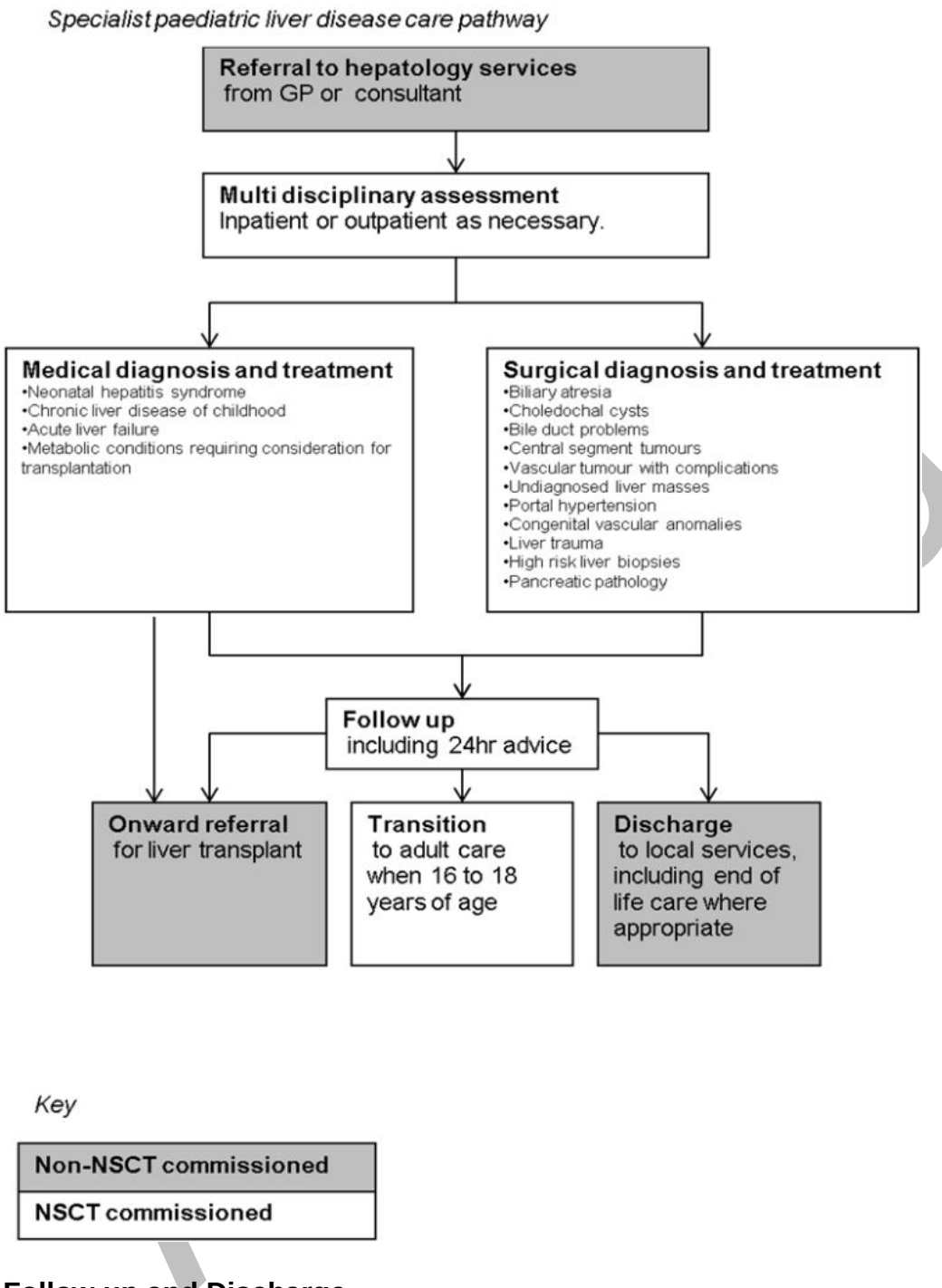

Follow up and Discharge

There are two elements described in the care-pathway for this service:

Follow up

- Discharge following admission for assessment and management:
    - discharge home;
    - transfer to referral/other unit.

Discharge from the service

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- Discharge from follow up:
    - no further follow up needed;
    - transition to adult liver services.

The three paediatric liver services work closely together and with adult services to develop and implement a national adolescent transition strategy to facilitate smooth transition for young people to adult liver services. Some elements of this service have already been implemented.

Days/hours of operation

The service is open at all times.

2.3 Population covered

NHS England commissions the service for the population of England. Commissioning on behalf of other devolved administrations is reviewed annually, and a current list is available from NHS England commissioners or via the website.

At the moment, NHS England contract includes provision for the service to treat eligible overseas patients under S2 [Under European Union (EU) regulations, patients can be referred for state funded treatment to another European Economic Area (EEA) member state or Switzerland, under the form S2 (for EU member states) or the form E112 (for Iceland, Norway, Liechtenstein and Switzerland)] referral arrangements. Providers are reimbursed for appropriately referred and recorded activity as part of NHS England contract.

Trusts performing procedures on EU-based patients outside of S2 arrangements will need to continue to make the financial arrangements directly with the governments involved, separately from their contract with NHS England.

With regard to S2, the mechanism for recovery of costs has been via the Department for Work and Pensions Overseas Healthcare Team. They are responsible for agreeing reconciliation and recovery of costs with European administrations. These arrangements were implemented in October 2009, though a similar process existed previously. The financial flows are therefore back into the treasury rather than back to trusts.

2.4 Any acceptance and exclusion criteria

The conditions included as set out in the ‘Referral List for Supra-regional Paediatric Liver Services’ approved by the Royal College of Paediatrics and Child Health (RCPCH) on 11 July 2002.

Referral criteria, sources and routes

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Patients are referred from general practitioners, hospital consultant paediatricians or paediatric gastroenterologists for medical or surgical assessment and management of liver diseases. Once referred the patient will be assessed by a multi-disciplinary team (MDT) as described in the service standards.

Referring for assessment of:

- Alagille's syndrome
- Alpha-1-antitrypsin deficiency
- Auto-immune liver disease, hepatitis B/C,
- Biliary atresia
- Budd-Chiari syndrome
- Drug-induced liver disease, hereditary fibrocystic disorders
- Haemochromatosis
- Hypopituitarism
- Lipid storage disorders
- Non alcoholic steato-hepatitis
- Parenteral nutrition associated liver disease
- Progressive familial intrahepatic cholestasis syndromes
- Sclerosing cholangitis, cystic fibrosis
- Tyrosinaemia type 1
- Wilson's disease

- *Chronic pancreatitis and pancreatic trauma to exclude*

Exclusion criteria

There are no exclusions from this service.

Non-NHS England commissioning - paediatric hepatology and paediatric liver transplantation:

- all paediatric liver and liver transplant care is supra-regionally directed as part of a clinical network;
- by its nature most care will be performed in NHS England commissioned highly specialised paediatric liver units;
- work in primary and secondary care will be performed in accordance with the clinical network principles of best possible care, equity of access and as close to home as possible;
- all chronic liver diseases should be managed by highly specialised NHS England commissioned services. Patients whose condition is benign and self-limiting may be managed entirely in primary or secondary care services, but require consultant input from a highly specialised paediatric hepatology NHS England commissioned unit in some form.

The following paediatric hepatology services and tasks can be commissioned outside the highly specialised paediatric hepatology NHS England commissioned units:

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In primary care, including by General Practitioners:

- Neonatal cholestasis/hepatitis - basic investigations to determine presence of conjugated hyperbilirubinaemia (appendix 1);
- Jaundice, hepatomegaly, abnormal liver function test (LFT) - direct referral to NHS England commissioned paediatric liver units or to secondary care for first line investigations – See B2 and appendix 3 beneath;
- providing prescriptions - including all basic routine medications and immunosuppression from 3 months after transplantation;
- routine vaccinations - and additional vaccinations on request;
- blood tests and taking part in share care programme;
- supervision of administration of medications at home - in situations of refractory non-adherence.

In secondary and tertiary care - General paediatric and paediatric gastroenterology units:

- first- line investigation of neonatal cholestasis/hepatitis - initial investigations to determine nature and risk of conjugated hyperbilirubinaemia - (appendix 2). With consultation with NHS England commissioned paediatric liver units in each case.
- first line investigation of abnormal liver function tests (LFT) - (appendix 3). - but should not delay referral to NHS England commissioned paediatric liver units;
- admission or supervision of home administration of parenteral drugs or parenteral nutrition;
- protocol first line management of complications of chronic liver disease and liver transplantation - (appendix 4) - with supervision by and transfer to NHS England commissioned paediatric liver units as indicated;
- providing defined preliminary components of protocol management of conditions such as treatment of chronic viral hepatitis;
- general out-patient review in collaboration with NHS England commissioned paediatric liver units;
- organising on-site outreach clinics - with a consultant Paediatric Hepatologist from a NHS England commissioned paediatric liver unit attending;
- providing outreach site for video clinics;
- blood tests and taking part in share care programmes.

Appendices:

1. Initial investigations to determine presence of conjugated hyperbilirubinaemia in primary care;
2. Initial investigations to determine nature and risk of conjugated hyperbilirubinaemia;
3. First line investigation of abnormal liver function tests;
4. First line management of complications of chronic liver disease and liver transplantation.

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2.5 Interdependencies with other services

Three units, King's College Hospital NHS Foundation Trust, Birmingham Children's Hospital NHS Foundation Trust and Leeds Teaching Hospitals NHS Trust all provide specialised paediatric liver services in the UK. Patients can be referred between the centres for reasons of family convenience and access to super-specialised services. Referrals will usually be received from general practitioners and local or regional general paediatricians or paediatric gastroenterologists. Where appropriate, patients will be discharged back to local care or follow up under shared care agreements. Integrated working relationships exist with on site paediatric liver transplant services and adult liver services for transition of care.

Issues of common interest are discussed among the paediatric staff at the Liver Steering Group of the British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN).

All units have a close but informal relationship with the Children's Liver Disease Foundation, the national charity that seeks to represent the perspective of children and families with liver diseases.

Relevant networks and screening programmes - Each of the three centres constitutes a hub for collaboration in medical and surgical management of complex liver disease, forming clinical networks, with joint clinics and shared protocols.

There are no relevant national screening programmes.

3. Applicable Service Standards

3.1 Applicable national standards e.g. NICE, Royal College

All service providers and provision areas must meet standard NHS governance requirements. Audit requirements are set out in the service standards.

4. Key Service Outcomes

No single outcome measure is possible because of the great variety of conditions included in the designation

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5. Location of Provider Premises

The service is delivered at the designated centres listed below.

Designated provider
King's College Hospital NHS Foundation Trust Denmark Hill, London. SE5 9RS
Birmingham Children's Hospital NHS Foundation Trust Steelhouse Lane, Birmingham, B4 6NH
Leeds Teaching Hospitals NHS Trust St James's University Hospital, Beckett St, Leeds, LS9 7TF

Appendix 1

Initial investigations to determine presence of conjugated hyperbilirubinaemia in cases of suspicion

- Inspect stool and compare with Children's Liver Disease Foundation (CLDF) stool colour chart;
- prescribe vitamin K 1mg/day;
- measure split (total and conjugated) serum bilirubin rapidly;
- refer to NHS England commissioned paediatric liver unit – *Note – stool colour interpretation is subjective resulting in frequent error and delay in referral.*

Appendix 2

Initial investigations to determine nature and risk of neonatal conjugated hyperbilirubinaemia

- defined as a conjugated fraction >30umol/l or >15% of total serum bilirubin;
- persisting >2 weeks after birth in term infants;
- persisting 3 weeks after birth in pre-term infants.

1. ensure given vitamin K parenterally at least once and regularly by mouth thereafter;
2. ensure not hypoglycaemic with BM stix before feeds for at least 24 hours – give IV dextrose to ensure blood glucose ≥4.0 mmol/l;
3. see and record colour of urine and stool personally;
4. take history and perform examination;
5. stop galactose in diet if any reason to suspect galactosaemia
    - Full Blood Count (FBC), retics, film, INR;
    - Renal, lipid, bone, and liver profiles, split bilirubin, creatine kinase;
    - α-1-antitrypsin phenotype (parents if transfused);
    - group and save;
    - random cortisol;
    - TORCHES Screen;

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- liver ultrasound.

6. Contact NHS England commissioned highly specialised paediatric liver units for consultant opinion. Do not wait for results to make contact;
7. preliminary investigations – blood and urine cultures, Cortisol – morning, T4, TSH, Toxoplasma, CMV, Rubella, Herpes, Adenovirus, EBV, Syphilis serology, Galactose-1-phosphate uridyl transferase, IRT, CF alleles according to practicability, Plasma amino acids, Urinary organic acids, liver ultrasound – other tests from KCH protocol may be suggested;
8. Liaise with NHS England liver centre to arrange transfer for investigation according to urgency depending on above information.

Appendix 3

First line investigation of abnormal liver function tests (LFT)

1. Investigations in liver disease with acute onset

- defined as sudden onset of jaundice with evidence of liver aetiology or incidental discovery of raised transaminases;
- age of onset >3 months;
- treat as neonatal jaundice before three months.

1. ensure given vitamin K parenterally at least once and regularly by mouth thereafter;
2. ensure not hypoglycaemic with BM stix before feeds for at least 24 hours – give IV dextrose to ensure blood glucose >4.0 mmol/l;
3. ask and record colour of urine and stool;
4. take history and perform examination especially for features of chronicity of liver disease;
5. bloods – HAV IgM, FBC, INR, DIC screen, renal, bone liver profiles, total and conjugated bilirubin levels, HBV Sag;
6. if INR>2 and vitamin K unresponsive treat as liver failure. Contact NHS England commissioned highly specialised paediatric liver units for consultant opinion. Do not wait for results to contact;
7. preliminary investigations – blood and urine cultures, urine drug screen, plasma paracetomol level if any indication, hepatitis C antibody, alpha-fetoprotein, liver ultrasound – other tests from paediatric liver units protocol may be suggested;
8. liaise with NHS England highly specialised paediatric liver unit to arrange transfer for investigation according to urgency depending on above information.

2. Initial investigations in likely chronic liver disease

- defined as evidence of liver dysfunction including incidental discovery of raised transaminases;
- clinical evidence of chronicity e.g. hepatosplenomegaly;
    - history of >6m duration.

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1. take history and perform examination especially for features of chronicity of liver disease.
2. ensure given vitamin K regularly. Oral administration is adequate unless coagulopathy or malabsorption is present:
    - FBC, retics, film INR;
    - Group and Save;
    - Renal, lipid, bone, and liver profiles, split bilirubin, creatine kinase;
    - Urine C&S. blood culture;
    - Hepatitis B and C status, Hepatitis A IgM if acute;
    - HIV status;
    - α-1-antitrypsin phenotype (parents if transfused);
    - Liver ultrasound;
    - Fatty liver disease in obese patients represents a particular low risk situation once Wilson Disease is excluded. After discussion with a NHS England Liver Unit selected patients can undergo copper and caeruloplasmin tests, penicillamine challenge, and eye review and remain under local supervision while dietary and exercise interventions are tried for 6 months following which review and investigation at a NHS England commissioned highly specialised paediatric liver unit is indicated;
3. Contact NHS England commissioned highly specialised paediatric liver units for consultant opinion. Do not wait for results to make contact;
4. Preliminary investigations –Immunoglobulins, C3, C4, auto-antibodies, pANCA, copper, zinc, caerulopasmin, hepatitis C antibody, alpha-fetoprotein, sweat test, cardiac assessment, liver ultrasound – other tests from KCH protocol may be suggested;
5. Liaise with NHS England commissioned highly specialised paediatric liver unit to arrange transfer for investigation according to urgency depending on above information.

Appendix 4.

First line management of complications of chronic liver disease and liver transplantation

1. Febrile illness that may be ascending cholangitis in patients who have had a Kasai operation

Defined as any septic episode of unknown cause, especially, but not only with evidence of worsening liver dysfunction e.g. jaundice:

- admit for antibiotic treatment;
- take history and perform examination;
- bloods – FBC, INR, renal, bone liver profiles, total and conjugated bilirubin levels, blood and urine cultures, throat swabs and viral serology if indicated;
- contact NHS England commissioned highly specialised paediatric liver units for consultant opinion. Do not wait for results to make contact;

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- first line antibiotics according to current network protocol;
- liaise with NHS England highly specialised unit to arrange transfer for investigation according to urgency depending on above information;
- if fever persists after 72 hours transfer to NHS England highly specialised unit is indicated. Patients showing rapid response may complete treatment in the secondary/gastro centre.

2. Investigations and treatment in portal hypertension with GI bleeding

Haematemesis/melaena leading to emergency local admission:

- achieve adequate intravenous access;
- BP/pulse/peripheral to core temp difference (if > 2 degrees = shock). Resuscitate and transfuse. Use APLS protocol. Do not over-transfuse as this may precipitate a further bleed;
- assess conscious level for encephalopathy;
- ensure given vitamin K daily IV;
- stop oral intake
- bloods – FBC, INR, renal, bone liver profiles, total and conjugated bilirubin levels, cross match 2-4 units of packed cells according to size of bleed and patient;
- start Octreotide 25 mcg/hr in 0.9% sodium chloride. Increase to 50 mcg/hr if no response. Prescribe to be given as 500mcg in 40ml of 0.9% sodium chloride and run at 2ml/hr;
- contact NHS England commissioned highly specialised paediatric liver units or consultant opinion. Do not wait for results to make contact;
- maintain oxygenation with facial oxygen;
- strict monitoring of urinary output and fluid balance. Catheterise if necessary. Check urinary electrolytes, urea, creatinine and osmolarity;
- start as 1st line antibiotics according to current network protocol;
- prophlylactic ranitidine plus oral antacid to prevent gastric/duodenal ulceration;
- liaise with SpR at NHS England commissioned highly specialised paediatric liver unit to arrange transfer.

3. Completion of therapeutic pathways.

Examples of patients completing treatments as close to home as possible when safe include:

- completion of antibiotics or antivirals after surgical interventions, liver
- transplantation or treatment of liver abcesses;
- nutritional rehabilitation after transplantation or continuation of established nutritional care before transplantation;
- steroid therapy after transplantation or in auto-immune liver disease;
- chelation therapy.

4. Febrile illness after liver transplantation

Defined as any septic episode of unknown cause:

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- admit for antibiotic treatment;
- resuscitation as necessary – APLS protocol;
- take history and perform examination;
- bloods – FBC, INR, renal, bone liver profiles, total and conjugated bilirubin levels, blood and urine cultures, immunosuppressive trough levels, EBV PCR, CMV PCR, throat swabs and viral serology if indicated;
- Contact NHS England commissioned highly specialised paediatric liver units for consultant opinion. Do not wait for all results to make contact;
- first line antibiotics according to current network protocol;
- Liaise with NHS England commissioned highly specialised paediatric liver unit to arrange transfer for admission.

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