Diseases of the Liver and Biliary System in Children

EDITED BY

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FOREWORD BY

DAME SHEILA SHERLOCK

SECOND EDITION
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Although the Ancient Egyptians believed that the liver had mystic powers of healing and Hippocrates gave a full description of hepatic encephalopathy, modern hepatology has only taken off in the last 50 years. Accelerated progress has followed discovery of the hepatitis viruses, now a virtual alphabet from A to E and beyond. Hepatobiliary imaging and endoscopy have added to the progress. Developments have depended not only on specialist hepatologists but on developments in other related disciplines of medicine, particularly virology, immunology, biochemistry and now, molecular medicine. A huge literature is available describing liver disease in adults but paediatrics has lagged behind.

This book covers all the essentials of paediatric hepatology and is therefore particularly timely. The material covered is wide, from such aspects as the psychology of parents of children on transplant waiting lists to the genetic disturbances of bilirubin and bile salt transport in the neonate. The chapter authors have been well chosen. They are international authorities, active both clinically and in research. They write lucidly from personal experience.

Many helpful algorithms and tables are included. The references at the end of each chapter have been carefully selected and are up-to-date. The book concludes with an Atlas of 75 carefully annotated plates. This is virtually a book in itself and covers all paediatric liver diseases. Candidates for higher paediatric examinations will find it particularly useful.

This book should be available in every paediatric department. It should be at hand at all times to offer practical advice on any childhood liver disease. General paediatricians will certainly benefit. It would be a suitable gift to reward a trainee.

This book fills a real gap in our knowledge of liver disease. It will be a well-deserved success.

Professor Dame Sheila Sherlock
Paediatric hepatology has come of age. The discipline is recognized as an essential component of paediatric gastroenterology, meriting its own curriculum and training programmes in Europe and the USA.

Paediatric liver disease is an important cause of morbidity and mortality in both the developed and the developing world. Significant advances, particularly in molecular genetics and the lessons learnt from functional genomics have increased our understanding of the aetiology and pathogenesis of paediatric liver disease, leading to the development of exciting new therapies. The natural history and outcome for many children with liver disease has improved substantially with the combination of modern management and liver transplantation. As survival following liver transplantation is almost assured, the search begins for alternative treatment, such as hepatocyte transplantation and gene therapy.

The investigation and management of significant paediatric liver disease rightly remains within the remit of specialist or transplant units, but the recognition of the incidence of liver disease, the implications of new therapies, and the necessity for multidisciplinary working is as important for general paediatricians as for paediatric gastroenterologists, surgeons and hepatologists.

The second edition of this book summarizes the recent advances of the last five years, and provides a practical approach to the diagnosis and management of paediatric liver diseases, highlighting the importance of multidisciplinary teamworking. New chapters describe the recent phenomenon of fatty liver disease and liver disease in the developing world. It should interest the non-specialist paediatrician and paediatric trainee as well as providing guidance to nurses and allied health professionals.

DEIRDRE A. KELLY
The investigation of paediatric liver disease requires many skills and a multidisciplinary approach. It would not have been possible to write this book without the skill and expertise of many of my colleagues in the Liver Unit and Birmingham Children’s Hospital.

I am delighted that I was able to call on so many distinguished contributors worldwide to share their own areas of expertise and learning.

I am indebted to many colleagues for help in providing clinical slides and material, particularly, Dr Helen Alton and Dr Rachel Brown.

Finally, I am grateful to Jennifer Shervington for all her help in editing and co-ordinating this book.

Dedications

First Edition
To my sons, Eoin and Lochlinn Parker
and
My husband, Ian Byatt

Second Edition
To the memory of my parents Frank and Kathy Kelly who started me on my medical career
Chapter 1: Supporting the Child and Family

GILL BROOK, JO HUNT, ANNE JOHNSON AND JULIE REED

Living with liver disease

‘In an age and culture in which good health is taken for granted, parents expect their children to be well and survive them. Diseases that threaten children’s autonomy and compromise their life expectancy, challenge our emotions and coping resources to the limit. Childhood disease can turn the world upside down’ (Eiser 1993a).

Most liver disease is life limiting. Medical therapy may control symptoms and long-term complications and thus optimize quality of life. However, for many children with liver disease there is no absolute cure and ongoing monitoring with regular hospital visits, for blood tests or admission, is required. Thus, from the time of diagnosis both child and family have to adapt to a life that is different from their expectations in order that the ‘upside down’ world becomes the norm for them. The child (infant–adolescent) with a chronic illness is automatically different to children of a similar age, while parents have an additional workload in caring for their child. ‘Normalizing’ processes within this context should be encouraged, using the knowledge, skills and active support of the different health professionals within the multidisciplinary team (Krulik 1980; Knafl & Deatrick 1986).

The child (depending on age) and family pass through numerous processes. First, both parents and child need to come to terms with the shock of the diagnosis as well as, for the parents, the grief of losing their child’s good health. Parents have to take in much information relating to diagnosis and prognosis as well as learning new skills in caring for their child. Ideally information should be shared with the parents and child at their pace, and in the context of their family and social setting.

Parents may find it difficult to accept the unpredictability of their child’s disease and the effect on immediate life plans. If the child’s condition deteriorates, with reduction in physical mobility, increasing symptoms, such as ascites and malnutrition, the intensity of the care required increases exponentially. As a result, the extra time and attention given to the child with liver disease may impact adversely on siblings and other members of the family (Eiser 1993b).

As the child’s disease progresses, the parent has to be careful to detect subtle changes in their child’s condition in order to seek appropriate help. As liver disease is relatively uncommon in the child population, many parents, children and young people become ‘experts’ in disease management and often know more about specific aspects of their disease than their local healthcare team. This may be an added concern to the family, and it is vital that efficient communication systems are established with local services. Ideally, the child and family should experience a ‘seamless web’ of care, treatment and support centred on the needs of the child, their siblings and their carers (Department of Health 2000). Multidisciplinary working is an essential feature of this ‘seamless’ care (Heywood 2002).

The role of the multidisciplinary team

In order to meet the physical and psychological needs of children and young people with liver disease and to maximize their quality of life, the skills of many appropriately trained health professionals are essential. At the specialist unit, this team includes the medical staff and ward-based nursing team and the following personnel:
Roles within the multidisciplinary team

Many of the roles within the team are self-explanatory, but the following personnel have particular skills and importance.

**Social worker**

To many families, the social worker is associated with child protection issues and not with their participation in the psychosocial aspects of care. Many social workers have a practical role by facilitating parents’ support groups and by liaising with community social workers and support organizations. They will also have the detailed knowledge to help the family gain maximum financial support from any benefits provided by central and local government.

**Play specialist and teacher**

The play specialist and hospital-based schoolteacher have a crucial role in the psychosocial support of the child (Webster 2000). They provide the ‘normal’ aspects of a child’s life, that of play and education. Using specialist skills, in conjunction with those of the clinical nurse specialist or liaison nurse, they can help children and young people understand how the body works, the nature of their liver disease, and how they may be treated. The play specialist is essential in preparing children for invasive procedures ranging from venesection to transplantation.

**Liaison nurse and nurse specialist**

Liaison nurses are usually the ‘key workers’ for a group of children and their families. Their critical activities within the team include:

- Provision of information. Children, young people, and their parents and other key family members should be provided with information about liver function, signs and symptoms of the child’s liver disease, the process of diagnosis, disease outcome, and management. The liaison nurse has a central role in the process of assisting children, young people and their parents in making informed decisions about treatment in partnership with the schoolteacher and/or play specialist.

The use of written information about specific liver diseases, liver transplantation and other treatments, procedures and medicines is helpful. The development of generic information leaflets (for instance those developed by the Children’s Liver Disease Foundation in partnership with Paediatric Liver centres in the UK) has proved beneficial to parents and families, as information is consistent.

- Coordination of discharge planning. The liaison nurse,
the social worker, the ward-based team and the family need to plan a safe and effective discharge from hospital. This includes teaching parents and children self-medication and other new skills (their age and ability taken into account) to ensure that they are able to give care safely at home; and liaising with local community teams to ensure resources, information and communication processes are established prior to discharge. It is essential that parents understand the arrangements for care and support at home as well as ongoing management between local and specialist centres. ‘Patient/parent-held records’ are helpful in achieving effective and open communication between all parties. If children have particularly complex care needs a case conference between all relevant professionals may be required.

- Continuing care. The liaison nurse or nurse specialist is often the best contact to ensure continuous communication between the family, the specialist centre and local shared-care team regarding any changes in treatment. The liaison nurse or nurse specialist should be easily contactable (by e-mail, telephone or pager) to provide further support and information for the child, family, or other healthcare professionals. It is vital that the child’s local health team are aware of the extent of the child and family’s knowledge in order to care for them appropriately.

In Birmingham, a nurse-led telephone consultation service has been developed (Gordon et al. 2002) in order to provide information and advice to patients, their families and medical teams. Advice is provided the same day on the following topics: immunosuppression monitoring (38%); information about outpatient appointments and admission dates and processes (16%); medication changes (15%); vaccination requirements (7%); and other issues relating to ongoing treatment (24%).

- Transition to adult care. The liaison nurse has a key part to play in the preparation and transfer of the young person to adult care. Establishing close links and working in partnership with the adult liver services in the early stages of transition helps facilitate a smooth and seamless transfer (see later).

**Shared-care protocols for patient management**

The development of shared-care protocols with the local centre makes a significant difference to the care that a child receives. These protocols should outline the management of the liver disease, identifying actions to be taken by the local shared-care team in specific problem situations and providing clear guidelines for referral. These protocols should include:

- overview of the liver disease and treatment
- potential complications and the medical and nursing management required
- medication regime and side-effects of relevant drugs, particularly unlicensed drugs
- contact information.

Copies of the protocol, discharge letter and subsequent correspondence could be given to the parents or young person which can be kept in the ‘parent/patient-held record’.

**Consent to treatment**

It is the right of all children and young people to be informed and have their views taken into account in all matters that affect them as stated in the United Nations Convention on the Rights of the Child of 1989. However, involving children and young people in decision making in relation to their care and treatment requires skill and sensitivity. Gillick (1986) established that children under the age of 16 could give consent (that is they are competent to do so) provided that they have ‘sufficient understanding and intelligence to understand fully what is proposed’. This is known as being ‘Gillick competent’. Although it may be difficult to define when a child or young person is competent, this can be overcome by establishing a clear process of information sharing and opportunity of shared decision making, involving all members of the multidisciplinary team with the child and their parents (Brook 2000). In Birmingham, we have developed a framework to empower children and young people, *with their parents*, to make choices in their care and treatment (Brook 2000).

The objectives of the framework are, for the team:

- to gain information of the child’s knowledge, understanding and experience of illness and health care in the context of the child’s life.

For the children and young people:

- to provide them with an opportunity to increase their knowledge and understanding of their disease and treatments and to express their feelings, fears and expectations
- to help them develop confidence in participating in decisions by providing opportunities for them to make choices in their care and treatment.

For the parents:

- to help them to gain knowledge and understanding of their child’s disease and treatment in order to make informed decisions *with* their child and as individuals
- to enable parents to impart information to their child and siblings
- to facilitate sharing information between the child and parent in order to help them make decisions together.

The complex issue of defining competence to consent at a practical level is at the centre of this work and is based on children and young people moving from ‘novice to expert’ (Benner 1984; Rushforth 1999) in their ability to make choices in their care and treatment provided they
have the opportunity to do so (Alderson 1991; Alderson 1993; Alderson & Montgomery 1996). This depends on their age and cognitive ability, their cultural and family background, their experience of living with liver disease and their wish to participate (Alderson 1991; Alderson 1992; Alderson 1993; Alderson & Montgomery 1996; Alderson 2000). Although children should be encouraged to participate, they should not be burdened with decisions that are too difficult for them to make (Alderson 1991; Alderson 1993).

Informed co-operation is vital to the outcome of many treatments, particularly transplantation, as long-term survival is dependent on compliance (Cameron 1996; Fielding & Duff 1999).

Many parents wish to protect their child from difficult information and it is important to help them understand that information provided with sensitivity by skilled personnel in an age-appropriate manner is preferable to an unexpected unpleasant experience in which the child has no control (Alderson 1991; Alderson 1993). Many parents require support in this process and should be given strategies to prepare themselves for difficult and emotional questions from their child and sibling(s).

In emergency situations, such as transplantation for fulminant liver failure, parents and children need sufficient information to make an informed decision. Time should limit only the quantity of information, not the quality. If the child is too ill to participate in the decision, parents need to be prepared for the child’s anger and grief during their recovery phase. Psychosocial support and information on the necessity of treatment will then be provided retrospectively to the child.

The process of information sharing

Information sharing between the child, family and healthcare team starts at the point of referral, preferably prior to the initial visit, perhaps by an introductory letter from the liaison nurse. In Birmingham, we attach a short questionnaire with a letter of explanation and activity sheets in order to find out about the child’s wishes and the extent of their understanding about their body and their disease. Plans are then made to meet the needs of the child and family, for example the play specialist may meet them to help with blood tests.

The process is continued during the hospital admission with the liaison nurse acting as the key contact for information and communication so that the child’s treatment can be planned accordingly. Information can be provided in a variety of ways using computer teaching sessions or games, innovative books and toys. In addition, the play specialist and nursing team encourage the child/young person to develop an information sheet — ‘Things you need to know about me . . .’. This enables the child to reveal their personal interests, wishes and fears, particularly if they are undergoing invasive procedures or being prepared for transplantation.

In order to make an informed decision, the information provided should include:
• the problem to be treated
• why the treatment is offered
• what the treatment involves
• alternative treatment(s)
• the risks and benefits.

It is crucial to check the child’s understanding by enabling the child to feed back to their parents the information they have received, or to write or draw the information they have remembered in a scrapbook.

This multidisciplinary approach relies on effective team working and a shared belief in the importance of allowing children and young people to develop their confidence and competence to make relevant decisions in relation to their health. The emphasis is on working with the parents and children together, helping them to share in decision-making whenever possible, thus parents gain confidence in their child’s ability to manage their own care, which is necessary preparation for adolescence and adult life.

Psychological support

The psychologist will be involved in providing psychological support to the child and family, neuropsychological assessment and evaluating psychosocial outcome.

Developmental, intellectual and neuropsychological assessment

Developmental assessment involves the administration of standardized tests (e.g. Bayley Scales of Infant Development, Griffiths Mental Development Scales) to babies and preschool aged children in order to measure their developmental ability. Intellectual assessment involves the administration of norm-referenced tests (e.g. Wechsler Preschool and Primary Scale of Intelligence-Revised, Wechsler Intelligence Scale for Children III) to preschool and school-aged children in order to measure their general intellectual ability. A neuropsychological assessment involves the administration of standardized tests of intellectual ability, learning, memory and attention and the interpretation of these measures in the light of known brain functioning.

Neuropsychological impairment can arise as a direct result of liver disease, e.g. cirrhosis, Wilson’s disease, or as a consequence of treatment, e.g. drug side-effects, transplantation. Assessment of a child’s intellectual or neuropsychological functioning may be clinically indicated where there are concerns about low attainment relative to intellectual potential, specific learning difficulties, problems with memory, attention and concentration.
Results of assessments may have important implications for a child’s education, psychological and psychosocial adjustment and professional–patient communication. Neuropsychological assessment may also be carried out as one component of a research protocol to investigate disease progression, effects of drug treatments or outcome after liver transplantation.

Research on disease progression suggests that prior to overt signs of encephalopathy, children with chronic liver disease may have specific neuropsychological impairment (visual–spatial skills and attention/concentration), with intact verbal and memory skills. These impairments have been shown in adult patients with nonalcoholic cirrhosis (Tarter et al. 1984) and it is likely that these changes would be at least as significant in the child population. In addition, some liver diseases, such as Wilson’s disease, are associated with decrement in visual–spatial and visual scanning tasks prior to neurological impairment (Tarter et al. 1987).

Studies investigating outcome following liver transplantation have been hampered by small heterogeneous samples; difficulties making comparisons between psychometric tests measuring developmental ability and those measuring intellectual functioning; lack of baseline data prior to the onset of end-stage liver disease; absence of comparison groups and a lack of research into specific components of neuropsychological functioning. Nevertheless, these studies suggest that post-transplant intellectual functioning is likely to be at least in the low average range (Stewart et al. 1989; Beath et al. 1993). Children who are under 12 months at the onset of their liver disease may have global intellectual deficits at post-transplant assessment (Stewart et al. 1994) with poor growth being an important mediating factor. If transplantation takes place before 12 months then this leads to improved growth and nutrition and reduces the possibility of developmental delay, with recovery to pretransplant intellectual level, or better, at 2 years post transplant (Van Mourik et al. 2000). Results of a recent longitudinal study suggest that there may be a dip in assessment scores following transplantation, with recovery to pretransplant intellectual level, or better, at 2 years post transplant (Van Mourik et al. 2000). This result requires further investigation but may have important implications for a child’s return to education. In older children, clinical observations and reports from patients suggest that liver transplantation may adversely affect memory, learning processes, attention span and vigilance.

In addition, cyclosporin A (until recently the most widely used immunosuppressant drug) is known to have neurological effects (Rubin & Kang 1987) and may affect neuropsychological functioning (Stewart et al. 1994), which has implications for the long-term educational prospects of survivors.

Treatment adherence

Children with liver disease pre or post transplant need to adhere to drug regimes with negative side-effects, dietary restrictions or repeated invasive procedures. Adherence difficulties are among the most frustrating and perplexing problems for the multidisciplinary team, especially before and after transplantation. Adherence to a specific treatment is affected by a number of interrelated variables including child’s developmental status, disease knowledge, health beliefs, and family support. Interventions to increase medical adherence need to address the immediate positive consequences of nonadherence vs. the delayed benefits of adherence (Schweitzer & Hobbs 1995). Treatment adherence can be particularly problematic during adolescence when patient concerns about not wanting to be ‘different’ are likely to be at their peak. During the teenage years parent support continues to be important, but peer support may have greater influence on a teenager’s adherence. Involving healthy peers or slightly older patients as mentors (e.g. Shroff Pendley et al. 2002) is a new and potentially promising area of research in treatment adherence.

Research focusing on children with liver disease is scant, but empirical work with other populations has demonstrated the efficacy of educational programmes (e.g. Beck et al. 1980), behavioural interventions utilizing stimulus control and positive reinforcement (e.g. Lowe & Lutzker 1979), and family support packages (e.g. Satin et al. 1989). While research has focused on quantitative investigations of adherence problems, there have been fewer investigations using qualitative techniques and/or identifying factors associated with good adherence. Treatment adherence is a complex issue and further research is needed to determine which intervention (or combination of interventions) is most suitable for an individual patient and their family (La Greca & Schuman 1995; Bryon 1998).

Altered physical appearance

Most children with liver disease are likely to experience abnormal changes in their appearance at some stage during their treatment. These changes may be due to disease processes, e.g. jaundice, or as a consequence of medical or surgical treatment, e.g. cushingoid features, scarring. Treatment adherence may be compromised by a patient’s wish to avoid the negative side-effects on physical appearance.

There are a number of reasons why it is important to consider the psychological effects of growing up with a distinctive appearance. First, children and adolescents describe themselves and their peers according to their physical appearance, and children as young as 3 years old are able to discriminate between attractive and unattrac-
Liver transplantation presents the child and family with ongoing medical and psychological challenges. As transplant survival rates have risen, transplant teams have become increasingly aware of the need to implement practices that enhance the child’s and their family’s quality of life throughout the transplant process (Burroughs & Rolles 1990).

As a consequence, psychologists and other members of the psychosocial team have become involved in pretransplant evaluation of children and their families, and support through the transplant process. Psychological intervention can help ameliorate both the child’s and parents’ distress, reduce the need for drugs, increase adherence to medical regimes, decrease hospital stay, and facilitate adjustment to daily life (Gold et al. 1986; Zitelli et al. 1986; Windsororva et al. 1991; Littlefield et al. 1996). Issues covered by the pretransplant assessment include the child’s cognitive and developmental functioning, coping styles and mental health of the child and family, family functioning, assessment of adherence, and in the case of live-related donation, evaluation of the donor.

**Cognitive and emotional development**

Research has shown that children’s experience of and recovery from medical intervention significantly improves when given age-appropriate information about the procedures (Lewandowski 1984). Consequently, transplant teams need to take into account both a child’s cognitive and emotional development when making decisions about how much, and in what way children should be informed about the disease, transplantation procedure and medical regimen. In addition, in specific cases it can be useful to assess the cognitive functioning of the parents, to determine whether they will require additional support in being able to comprehend and recall details of the child’s medical regimen. Hospital play specialists are trained to educate children about their transplant, guided by an understanding of their cognitive and developmental functioning, through innovative play activities and educational toys and books.

Assessment can also reveal anxieties about medical procedures which impact on the transplant process, for example, needle phobia. Psychological techniques have been developed to help children cope with specific medical procedures, including psycho education, play therapy, distraction, relaxation, behavioural therapy and cognitive behavioural therapy (Davis et al. 1988; Kendall 1992; Ollendick et al. 1994; Silverman & Kurtines 1996).

**Coping styles**

Assessment of family functioning and coping styles is integral to developing a transplant treatment plan, in order to minimize the impact of stressors on the family through the child’s illness and treatment. Common stressors impacting on the transplant process identified by Uzark (1992) include waiting and competition for a suitable organ (25% of patients die waiting for a donor (Paradis et al. 1988)), uncertainties of rejection, uncertainty of child’s future health and well-being, changes in role within the family, for example, siblings having to become more independent, social isolation, and financial burdens. Clinical experience suggests that families of children who require a second transplant find the process particularly stressful and further research is required to understand the issues that face this patient group.

**Mental health**

In the weeks after transplantation children can experience changes of mood, including mild depression and anxiety, which in most cases reaches a peak about a month after the operation (Mowat 1987; Zitelli et al. 1988). These...
changes in mood are often related to death anxiety, guilt due to perceived and real burdens on the family, survival guilt when other transplant patients have died, changes in family dynamics and body image concerns (Gardner et al. 1977). In addition, Walker et al. (1999) suggested that for some children the duration and severity of their emotional distress meets the diagnostic criteria for Post-traumatic Stress Disorder (PTSD), wherein the acute life-threat involved in the liver transplantation contributed to the development of PTSD. Consequently, it is important to monitor the child’s mental state from pretransplant to post transplant, enabling early psychological intervention if these symptoms reach clinically diagnostic levels.

**Family functioning**

Although not necessarily pathological, changes in the family system are inevitable when a child has a chronic illness such as liver disease and the family are subject to the transplant process, for example, parental role change, increase in care-giving burden, and separation from siblings through hospital stays (Zitelli et al. 1988; Uzark & Crowley 1989). Following transplantation, parents report a departure from practices of infantilization, inconsistent discipline, family social isolation, and resentment of the child by the siblings (Goodheart & Lansing 1996). However, conversely, the parents may become overprotective due to the awareness of the possibility of infection or rejection (Sexson & Rubenhow 1992). The child experiences increasing independence post transplantation, and is expected to engage in activities that have been neglected previously (i.e. school participation) which can induce anxiety and behavioural problems. There are also issues due to difficulties in adjusting to a change in the level of dependence of the child on their parents and their increasing autonomy from the family unit. Therefore, families often require ongoing psychosocial intervention to facilitate the adaptation to the different stages of the transplantation process.

**Evaluation of the live-related donor**

When a family decides to consider live-related surgery, the potential donor must undergo extensive assessment. This process may add to the stress of the parents with a child who is seriously ill. Boone et al. (1992) found that common concerns included: possible organ failure, increased risk of two family members undergoing surgery, increased financial burdens, feelings of guilt from nondonating parents and concern for other children.

The decision should be interdisciplinary, involving hepatologists, psychologists, social workers, and liaison nurses, to ensure that the donor is making a rational and voluntary decision, based on a good understanding of all the relevant information. The team needs to be aware of the contraindications of living organ donation, for example, pre-existing psychiatric disorders, inadequate parental coping behaviour and disturbed patterns in family functioning (Ozawa et al. 1992).

It is important that assessment of a live-related donor programme includes evaluation with particular reference to the quality of life of the family members (i.e. adult donor, partner of donor, siblings of recipient and recipient).

**Conclusion**

There is an emerging evidence base to show that psychological input has a positive impact on health outcomes for this group of patients (Roberts 1995).

**Nutritional support**

The need for dietetic support for a child with acute, chronic or metabolic liver disease will depend on the severity of the disease and symptoms (Fig. 1.1). Nutritional problems are multifactorial in origin, and their treatments diverse (Table 1.1; Chapter 14). Inability to provide satisfactory nourishment is distressing for both the families.

---

**Table 1.1 Causes of malnutrition in liver disease**

| Inadequate intake | • Anorexia, nausea and vomiting  
|                   | • Early satiety due to organomegaly and ascites  
|                   | • Recurrent infections and hospitalization  
|                   | • Unpalatability of prescribed feeds and diet  
|                   | • Behavioural feeding difficulties  
|                   | • Taste changes caused by medications and biochemical disturbances  
| Impaired digestion and absorption of nutrients | • Reduced bile flow causing fat and fat soluble vitamin malabsorption, and essential fatty acid deficiency  
|                                                      | • Enteropathy due to portal hypertension  
|                                                      | • Disease-related pancreatic insufficiency  
| Increased nutritional requirements | • Hypermetabolism due to infection or trauma  
|                                                      | • Insufficient protein synthesis and/or accelerated breakdown  
|                                                      | • Malabsorption  

Chapter 1: Supporting the Child and Family
and the child, and requires much support from the dietitian and the team.

**Chronic liver disease**

All infants with liver disease should have regular growth monitoring. Anthropometric measurements such as height, weight, mid-arm circumference (MAC) and triceps skin-folds (TSF) are useful tools in assessing nutritional status (Protheroe 1998), although weight may be affected by ascites and organomegaly, but because of their rapid growth infants are particularly at risk. All children with chronic liver disease are at risk of malnutrition and the dietitian should be in regular contact with the families and health professionals caring for the child, so that growth failure is identified early.

The aim of nutritional support is to provide adequate calories to prevent or treat malnutrition (Chapter 14). The dietitian has a key role in designing and prescribing nutritional support.

Infants require adequate calories in their milk feeds to grow, but may be unable to consume adequate volumes of feed or be fluid restricted because of ascites. It is best to concentrate formula milks to provide a more nutrient dense feed (Table 1.2). This should be done under supervision to ensure that excessive amounts of protein and electrolytes are not consumed. Concentrating milk formulas maintains the optimal protein:energy ratio for growth and provides additional vitamins and minerals. If the infant is not cholestatic, a high-energy infant formula, e.g. Infatrini (Nutricia) or SMAHigh Energy (SMA Nutrition) may be successful. Alternatively, extra carbohydrate in the form of glucose polymer, e.g. Maxijul powder (Scientific Hospital Supplies (S.H.S.)) or fat emulsions, e.g.
Calogen (Long Chain Triglyceride (LCT)) or Liquigen (Medium Chain Triglyceride (MCT) (S.H.S.)) can be added.

Children with end-stage liver disease may develop portal hypertension and ascites and require salt and water restriction (Table 1.3). In some circumstances a modular feed, designed to meet the specific needs of that individual child may be required (Table 1.4a,b). Cholestatic infants require specific feeds (see later).

For most infants, solids should be introduced between 4 and 6 months of age with no dietary restrictions. If additional calories are required, powdered foods can be mixed with infant formula, and/or energy supplements, e.g. M.C.T. Duocal (S.H.S.) or glucose polymer, can be combined with any solids to increase calorie density. For some babies this intervention can increase energy intake significantly (Tables 1.2 and 1.5).

Older children will benefit from paediatric or adult nutritional supplements, and advice on increasing energy and nutrient density of foods (Table 1.5).

### Cholestatic liver disease

There are many causes of cholestatic liver disease, which can be divided into two groups: those presenting in infancy, and those presenting in the older child (see also Chapters 4, 8 and 14).

#### In infancy

- Neonatal infection/hepatitis
- extrahepatic biliary atresia
- intrahepatic biliary hypoplasia (PFIC, Alagilles)
- total parenteral nutrition (TPN)-induced liver disease.

These babies usually have increased energy and nutrient requirements, up to twice the estimated average requirement (EAR), as a result of malabsorption, higher energy expenditure and infection (Chapter 4).

Most infants with cholestatic liver disease will require feed modification. If bile flow is limited from the liver into the gut, fat emulsification and digestion are reduced. This causes malabsorption of fat, fat-soluble vitamins, essential fatty acids and some minerals, leading to steatorrhoea, growth failure, and rickets.

Cholestatic babies often consume huge volumes (200–300 ml/kg) of standard infant formula or breast milk, because of malabsorption of LCT in dietary fat, which require bile for digestion and absorption. As fat is the major energy source at this age, the infants are not satisfied by their milk and consume large volumes to compensate. To promote growth it is essential to improve fat absorption, by manipulating dietary fat and substituting LCT with MCT. MCT does not require emulsification with bile and is absorbed directly into the portal vein.

Recommended practice is to change a cholestatic baby’s feed to one containing a proportion (50–75%) of fat as MCT, e.g. Pregestimil (Mead Johnson), Peptijunior (Cow and Gate), Caprilon (S.H.S.) or Generaid Plus (S.H.S.) (Table 1.3). MCT is well tolerated, but in large quantities can cause abdominal pain, with or without diarrhoea, and at high levels can cause vomiting (Table 1.6).

MCT does not contain essential fatty acids (EFAs) although the amount of EFAs required by cholestatic infants is unclear. Deficiencies may occur in children receiving supplements, but these are difficult to identify, as laboratory testing is difficult. The infant formulas prescribed should meet the ESPGHAN (European Society

### Table 1.2 Example of how to concentrate infant formula: Pregestimil (nutrient density /100 ml)

<table>
<thead>
<tr>
<th>Concentration (g/100 ml)</th>
<th>Nos of scoops in 180 ml (6 floz)</th>
<th>Energy, kCal (kJ)</th>
<th>Protein, g</th>
<th>CHO, g</th>
<th>Fat (g) 55% MCT</th>
<th>mmol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13.5%</td>
<td>6</td>
<td>68 (283)</td>
<td>1.9</td>
<td>6.9</td>
<td>3.8</td>
<td>1.4</td>
</tr>
<tr>
<td>16%</td>
<td>7</td>
<td>81 (335)</td>
<td>2.25</td>
<td>8.2</td>
<td>4.5</td>
<td>1.7</td>
</tr>
<tr>
<td>18%</td>
<td>8</td>
<td>91 (377)</td>
<td>2.5</td>
<td>9.2</td>
<td>5</td>
<td>1.9</td>
</tr>
<tr>
<td>20%</td>
<td>9</td>
<td>101 (419)</td>
<td>2.8</td>
<td>10.2</td>
<td>5.6</td>
<td>2.1</td>
</tr>
</tbody>
</table>

### Table 1.3 Treatment of disease-related symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Possible dietetic treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascites</td>
<td>• Sodium restriction&lt;br&gt;• Fluid restriction</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>• Protein restriction &lt; 1 g/kg (Gerber &amp; Schomerus 2000)&lt;br&gt;• Use branched chain amino acids (Teran 1999; Chin et al. 1992)</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
<td>• Continuous feeds, increased calorie density (Maintain glucose &gt;4 mmol/l)</td>
</tr>
<tr>
<td>Malabsorption/ feed intolerance</td>
<td>• Continuous enteral feeds&lt;br&gt;• Manipulation of feed composition&lt;br&gt;• Parenteral nutrition</td>
</tr>
</tbody>
</table>

Calogen (Long Chain Triglyceride (LCT)) or Liquigen (Medium Chain Triglyceride (MCT) (S.H.S.)) can be added.
Table 1.4a  Modular feed ingredients

<table>
<thead>
<tr>
<th>Nutritional component</th>
<th>Product</th>
<th>Comments</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>Maxipro</td>
<td>Whole protein</td>
<td>S.H.S.</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>Maxijul Powder</td>
<td>Glucose polymer</td>
<td>S.H.S.</td>
</tr>
<tr>
<td></td>
<td>Polycal Powder</td>
<td>Glucose polymer</td>
<td>Nutricia</td>
</tr>
<tr>
<td>Fat emulsions</td>
<td>Calogen</td>
<td>Long chain fat</td>
<td>S.H.S.</td>
</tr>
<tr>
<td></td>
<td>Liquigen</td>
<td>Medium chain fat</td>
<td>S.H.S.</td>
</tr>
<tr>
<td>Vitamins and minerals</td>
<td>Paediatric Seravit</td>
<td>(contains carbohydrate)</td>
<td>S.H.S.</td>
</tr>
<tr>
<td>Electrolytes</td>
<td>Sodium chloride</td>
<td>e.g. 1 mmol/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Potassium chloride</td>
<td>e.g. 1 mmol/ml</td>
<td></td>
</tr>
</tbody>
</table>

S.H.S., Scientific Hospital Supplies.

Table 1.4b  Example of an 800-ml modular feed for a 20-kg, 7-year-old child

<table>
<thead>
<tr>
<th>Product</th>
<th>Quantity</th>
<th>Energy, kCal/kJ</th>
<th>Protein, g</th>
<th>CHO, g</th>
<th>Fat, g</th>
<th>Na, mmol</th>
<th>K, mmol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maxipro</td>
<td>72 g</td>
<td>288 (1215)</td>
<td>54</td>
<td>5.4</td>
<td>5.4</td>
<td>6.3</td>
<td>11</td>
</tr>
<tr>
<td>Maxijul</td>
<td>184 g</td>
<td>700 (2925)</td>
<td>–</td>
<td>175</td>
<td>–</td>
<td>1.6</td>
<td>0.2</td>
</tr>
<tr>
<td>Paediatric Seravit</td>
<td>22 g</td>
<td>66 (276)</td>
<td>–</td>
<td>16.5</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Calogen</td>
<td>60 ml</td>
<td>270 (1130)</td>
<td>–</td>
<td>–</td>
<td>30</td>
<td>0.25</td>
<td>0.3</td>
</tr>
<tr>
<td>Liquigen</td>
<td>60 ml</td>
<td>270 (1130)</td>
<td>–</td>
<td>–</td>
<td>30</td>
<td>0.7</td>
<td>0.4</td>
</tr>
<tr>
<td>Sodium chloride (1 mmol/ml)</td>
<td>10 ml</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>10</td>
<td>–</td>
</tr>
<tr>
<td>Potassium chloride (1 mmol/ml)</td>
<td>22 ml</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>22</td>
</tr>
<tr>
<td>Per 100 ml</td>
<td>199</td>
<td>6.75</td>
<td>24.6</td>
<td>8.2</td>
<td>2.4</td>
<td>4.25</td>
<td></td>
</tr>
<tr>
<td>Per kg</td>
<td>80</td>
<td>2.7</td>
<td>9.85</td>
<td>3.3</td>
<td>0.94</td>
<td>1.7</td>
<td></td>
</tr>
</tbody>
</table>

Table 1.5  Suggestions on ways to add extra calories to food for infants and older children

- Use breast milk/formula to make powdered baby foods
- Mix baby rice and breast milk/formula with pureed fruit, vegetables, or commercial baby foods
- Add a cheese-based sauce to potato or vegetables
- Add cream to soups, sauces, puddings
- Use full-fat products, e.g. yoghurts, milk, puddings
- Add margarine/butter/grated cheese to potato, sweet potato, vegetables, spaghetti, baked beans, omelettes
- Fry/roast foods where possible, e.g. sausages, bacon, fish fingers, potatoes
- Add lentils, beans, etc. to soups and casseroles
- Use sugar on hot drinks, cereals and puddings
- Encourage sugary snacks, e.g. cakes, biscuits, sweets

Table 1.6  Treatment of feeding problems

<table>
<thead>
<tr>
<th>Problem</th>
<th>Possible cause</th>
<th>Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea</td>
<td>• MCT intolerance</td>
<td>• Change feed</td>
</tr>
<tr>
<td></td>
<td>• Medications</td>
<td>• Review timing/type of medication</td>
</tr>
<tr>
<td></td>
<td>• Enteropathy/</td>
<td>• ?P.N.</td>
</tr>
<tr>
<td></td>
<td>malabsorption</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>• Organomegaly</td>
<td>• Try continuous feeds</td>
</tr>
<tr>
<td></td>
<td>• Medication</td>
<td>• Review medication</td>
</tr>
<tr>
<td></td>
<td>• Reflux</td>
<td>• Start feed thickener?</td>
</tr>
<tr>
<td>Feed refusal</td>
<td>• Taste of milk</td>
<td>• Change milk</td>
</tr>
<tr>
<td></td>
<td>• Disease state</td>
<td>• Tube feed</td>
</tr>
</tbody>
</table>

P.N., parenteral nutrition.

for Paediatric Gastroenterology, Hepatology and Nutrition) guidelines for EFA (based on levels in breast milk), which recommend that 1–2% energy should come from linoleic acid (\(\omega-6\)), with the linoleic acid : \(\alpha\)-linolenic acid (\(\omega-3\)) being between 5 and 15 : 1. Walnut oil can be used as a natural source of EFAs, prescribing 0.5 ml/100 kcal to meet the recommended upper level.

Cholestatic breast-fed babies will demand frequent feeds, which is exhausting for the mother. Mothers are encouraged to continue breast feeding where possible, but the introduction of an MCT-containing formula, as a top up or supplementary feed, will reduce demand on the mother.
MCT-containing formula should continue until the infant’s bilirubin level is within normal range, or the child has been transplanted. Due to the strong flavour of these milks, the infant may reject them once solids are introduced. If growth is still failing, despite resolution of cholestasis, the introduction of a high-energy infant formula, e.g. Infatrini (Nutricia) or SMA High Energy (SMA), can be very successful in maintaining growth.

Older children (>2 years of age)

There are no specialized MCT-containing feeds available for this group of patients. Any paediatric energy supplements, e.g. Paediasure (1 kcal/ml, Abbott) or Fortini (1.5 kcal/ml, Nutricia), or adult supplements, e.g. Ensure Plus (1.5 kcal/ml, Abbott), can be used. Advice on fortifying foods with extra fat, carbohydrate and energy supplements (Table 1.5) can have a huge impact on energy intake. Following ‘healthy eating’ guidelines should be discouraged.

Nasogastric tube feeding

Supplementary nasogastric tube feeding should be considered at an early stage for any infant or child who is failing to thrive. Benefits are usually recognized and welcomed by all involved once commenced. These include:
- reduction in pressure on parents and child
- reduction in force feeding
- improved growth
- happier mealtimes.

Acceptance of tube feeding is enhanced by preparation, explanation and support by the multidisciplinary team before and after it has been instigated. Parents and child (depending on age) should be taught to pass the tube and become familiar with the mechanics of the pump, particularly if enteral feeding is nocturnal. They should be conversant with the mode of feeding (bolus, nocturnal or continuous). Parents should be expert in feed preparation and hygiene.

As up to 50–100% of energy requirements may be provided by tube feeding, this may impact on the oral feeding regime. However where possible the regime should suit family life, i.e. overnight feeding with or without bolus feeds during the day while maintaining oral feeding to stimulate speech and swallowing. Often continuous overnight feeding is better tolerated than bolus feeding for patients with organomegaly.

The use of gastrostomies in children with portal hypertension is controversial because of portal gastropathy and varices, but use of a soft nasogastric tube is safe.

Common problems

Intensive nutritional support in the ill infant or child may be problematic. A number of common problems are outlined in Table 1.6.

Parents of infants/children with liver disease feel immense pressure about feeding their child. They are aware of the importance of good nutrition and growth on prognosis and liver transplantation. They should not be burdened by unrealistic expectations, but should be reassured that the need for extra support and supplementary artificial feeding is often inevitable, particularly in end-stage disease.

Many children experience difficulty feeding. This may be behavioural, usually as a result of long-term hospitalization, tube feeding when young, delayed weaning or chronic illness, and will require different strategies (Table 1.7). Mealtimes can become a battle ground with both the child and carers using food as emotional manipulation. Often the carer will feel guilty because the child has been ill for so long and that tackling feeding issues is cruel. Resolution of these feeding difficulties will need long-term input from speech therapists, clinical psychologists, dieticians, health visitors, paediatric community nurses, and specialist liaison nurses. Reassurance and practical support are invaluable.

Acute liver disease

Dietary treatment will depend on symptoms at presentation, and speed of onset of disease. Initial assessment includes weight and height (length), and anthropometrical measurements such as MAC and TSF. If onset is rapid, the child is likely to be relatively well nourished at presenta-

---

**Table 1.7 Strategies for dealing with behavioural feeding difficulties**

- Never force/bribe/threaten a child to eat
- Try not to show anxiety or annoyance at mealtimes
- Reward good behaviour at mealtimes with attention and positive feedback, e.g. smiling, talking to them, and ignore bad behaviour, i.e. leaving the table before they should, throwing meals on the floor, etc.
- Encourage family mealtimes, sat at a table for social interaction
- Set a realistic time limit for the length of a meal, e.g. 30 min
- Encourage a regular meal pattern, which can include nutritious snacks
- Offer small portions and offer more when completed
- Discourage filling up on drinks between meals
- Allow infants to play with food and make a mess; this is part of normal development
Continuation of nutritional support post transplant is vital as it is important to maintain an adequate calorie intake (Chapter 20). The diet should normalize unless there are complications such as chronic rejection. Many children will require tube feeding for some time because of previous behavioural feeding problems (Kelly 1997).

**Liver transplantation**

Children awaiting liver transplantation may need more intensive nutritional support, requiring extra nutritional supplements, enteral tube feeding, or in some circumstances parenteral feeding (Chapters 4 and 20, Fig. 1.1; Table 1.8). Modular enteral feeds may be helpful as this provides the only method of achieving optimal nutritional input, e.g. when electrolytes or protein need to be modified or omitted, or if fluid is restricted (Table 1.4a,b). Modular feeds must be prescribed and supervised by an experienced dietitian. Dietary and fluid restrictions should be kept to a minimum. Removing favourite foods from the diet may limit energy intake and is difficult for the child to accept, while prolonged dietary constraints can lead to nutritional deficiencies. Oral nutritional intake should be encouraged in order to maintain feeding skills, even if amounts are of little nutritional benefit.

Parenteral nutrition

TPN is associated with inducing liver disease and the central venous catheters required are a potential source of infection, but may be necessary in children with liver disease if enteral nutrition has failed or there are complications such as feed intolerance or bleeding varices (Chapter 14).

**Conclusion**

Intensive nutritional support may make a big difference to the quality of life of many children. Skilled intervention by the multidisciplinary team is vital. Useful contact numbers and addresses for infant feed manufacturers are included (Table 1.9).

**Adolescence and transition to adult life**

Defining adolescence

Adolescence is best defined as the process of maturity in biological, psychological and social terms (Viner & Keane 1998). Adolescence starts around 10 years and may

### Table 1.8 Feed composition commonly used in the treatment of cholestatic children (per 100 ml)

<table>
<thead>
<tr>
<th>Feed</th>
<th>Manufacturer</th>
<th>Energy, kCal (kJ)</th>
<th>Protein, g</th>
<th>Fat, g (% MCT)</th>
<th>Na, mmol</th>
<th>EFAso6 : o3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregestimil (13.5%)</td>
<td>MJ</td>
<td>68 (283)</td>
<td>1.9</td>
<td>3.8 (55%)</td>
<td>1.4</td>
<td>Yes</td>
</tr>
<tr>
<td>Peptijunior (12.8%)</td>
<td>C+G</td>
<td>66 (280)</td>
<td>1.8</td>
<td>3.6 (50%)</td>
<td>0.9</td>
<td>Yes</td>
</tr>
<tr>
<td>Caprilon (12.7%)</td>
<td>S.H.S.</td>
<td>66 (280)</td>
<td>1.5</td>
<td>3.6 (75%)</td>
<td>0.8</td>
<td>Yes</td>
</tr>
<tr>
<td>Generaid Plus (17–34%)</td>
<td>S.H.S.</td>
<td>75–150 (315–630)</td>
<td>1.9–3.7 (35%)</td>
<td>0.5–1.0</td>
<td>Yes</td>
<td>56 : 1</td>
</tr>
<tr>
<td>MCT Pepdite (15%)</td>
<td>S.H.S.</td>
<td>68 (283)</td>
<td>2</td>
<td>2.7 (75%)</td>
<td>1.5</td>
<td>Yes</td>
</tr>
<tr>
<td>MCT Pepdite 1+ (20%)</td>
<td>S.H.S.</td>
<td>91 (380)</td>
<td>2.8</td>
<td>3.6 (75%)</td>
<td>1.8</td>
<td>Yes</td>
</tr>
<tr>
<td>Modular Feed</td>
<td>See individual products</td>
<td>70–200 (290–840)</td>
<td>Flexible</td>
<td>Flexible 50–65%</td>
<td>0–1.5 mmol/kg</td>
<td>No</td>
</tr>
</tbody>
</table>
extend to 20 years (Viner & Keane 1998). Using such a wide age range definition highlights the importance of the diversity in individual development, especially in the adolescent phase of life; we may be dealing with a mature 10-year-old and a less mature 20-year-old (Kuy Kendall 1989; Needham 2000).

Adolescence is a transitional stage in which the young person begins to move towards independence, from parents, and towards an increased reliance on peer group acceptance. Adolescents have to learn to accept their developing sexuality and to make choices relating to education, employment and a long-term career. These moves towards adulthood are challenging enough, but to a young person with chronic ill health they can be fraught with difficulties (Schidlow & Fiel 1990). It may be more difficult for them to develop their own autonomy due to the dependence on their parents. Acceptance by peers may be more difficult due to social isolation, missing school or college due to ill health and frequent hospital visits. Also young people with liver disease may look ‘different’ due to drug treatment (e.g. steroids) or the signs and symptoms of liver disease. Puberty may be delayed and growth stunted. The unpredictability of liver disease and treatment may make it difficult for young people and their families to plan realistically for the future.

Adolescents are a socially distinct group, not needing the protection and security accorded to children but not yet ready for full independence (Conway 1998). These young people and their parents require the support and guidance of the multidisciplinary team working within the specialist liver centre to help them move into the adult world towards independence. The traditional paediatric model of care focusing on the parent may avoid the important issues of sexual and reproductive health care, substance abuse, risk behaviours, career counselling, and independent living (Blum et al. 1993). The planning and development of adolescent-friendly services including the transition process must include the views of the young people themselves (Viner & Keane 1998). This group of patients require special provision for:

- their overall health care
- the psychosocial aspects of illness
- education and vocational training
- transition to adult care
- health promotion.

### Moving towards independence

The multidisciplinary team should positively promote and affirm the ‘moving on’ process in a supportive manner. This may require them to address their own feelings of ‘letting go’ the young people whom they have known for many years.

A good way to start is with self-medication (Tomlin 2001). Young people should be helped to take responsibility for medication from an early age as possible. This will include educating children about the reasons for medication as well as the potential side-effects. This information should be in written or another format appropriate to the child’s ability to understand. Parents will require encouragement to enable their child to take on this responsibility.

Young people need to take charge of their disease and be informed about effective ways of dealing with medical situations, such as recognizing deterioration in their health and making the appropriate responses. This should include how to seek help from health professionals initially in the paediatric/adolescent service and then in the adult service. Adolescents should also be encouraged to use patient-held records in which they record important medical events (Kurtz & Hopkins 1996).
Important information for adolescents and young adults with liver disease

Adolescents will need advice and guidance on:
- use of alcohol
- body piercing
- dental care
- sunbathing
- sexual health and contraception
- pregnancy
- healthy diet
- promotion of exercise.

This information will form part of the general education issues that should be addressed in the preparation for transition to the adult service.

‘Transition’ to adult services

Definition of transition:

Transition is ‘the purposeful planned movement of adolescents and young adults with chronic physical and medical conditions from child-centred to adult-orientated healthcare systems’ (Blum et al. 1993).

The optimal goal of transition is ‘to provide healthcare that is uninterrupted, coordinated, developmentally appropriate, psychosocially sound, and comprehensive’ (Blum et al. 1993).

Transition is an active process and not a single event. Planning for transition must begin early and be regularly reviewed. It must be age and developmentally appropriate.

There appears to be very little ‘hard’ evidence on the most effective model for a transition service. Blum et al. (1993) identify four key elements on which a potentially successful service should be based. These are:
- Professional and environmental support.
- Developing and maturing through adolescence into adulthood requires a service that supports all aspects of growth and development at this time.
- Decision making and consent.
- Young people must be given the opportunity to develop their autonomy and to make choices about their treatment and care with their parents in the early stages of their disease in order to gain confidence and competence in decision making. The parent, once confident in their child’s ability, will find it easier to let go.
- Family support.

Adolescents require parent support and encouragement to become independent while parents may need the help of health professionals to negotiate boundaries. Each individual transition plan should assist families to adapt their support in order to enable the young person to become more independent.
- Professional sensitivity to the psychosocial issues of the disease.

There is an increasing need for health professionals in the adult services to become skilled in the knowledge and management of paediatric health conditions as more children survive into early adulthood and beyond.

Young people should not be transferred to adult services until they have the skills to function in the adult service (Conway 1998). The following points highlight some of the important issues to take into account for transition and transfer of adolescence to adult healthcare services (Viner & Keane 1998; Kurtz & Hopkins 1996):
- Policy on transition should be established. The establishment of a well-planned and resourced transition programme reflects the strength of belief that chronic disease need not be a handicap (Sawyer 1998).
- The timing of transition must depend on the developmental readiness and health status of the adolescent. It is helpful to set a mutually agreed target transfer age for both staff and the young person in preparation for transition to adult care. Early discussion of transfer is essential (around 11 years of age may be an appropriate time, but this will depend on the age at onset of liver disease).
- The process of transfer should be coordinated. About a year prior to the agreed transfer date, it is recommended that the young person is provided with information on the adult service. There should be at least one visit to the adult clinic with parents and a trusted paediatric carer or paediatric team. A combined adult–paediatric clinic is very helpful as an introduction for the young person to the adult healthcare team, but this must not replace the coordinated transition process (Court 1993). Evaluation of transition and transfer should be made involving the users of the service (Lightfoot & Sloper 2002).
- It is helpful to identify a specific person within both the paediatric and adult teams to take responsibility for transition arrangements, usually the clinical nurse specialist or liaison nurse.
- The referring clinicians should provide a combined detailed report on the young person’s disease, treatment and holistic management and support, giving a copy to the adolescent and their parents.
- Transition plans must include communication with the local healthcare team.

Transition to adult care should be an integrated, smooth, coordinated process. It requires planning, adequate funding, a multidisciplinary patient-centred approach, and willingness by both adult and paediatric healthcare teams to learn and work together to achieve the best quality of life for the young people in their care.

References

Alderson, P. (1992) In the genes or in the stars? Children’s competence to consent. Journal of Medical Ethics 18, 199–204.


Gillilick vs. West Norfolk and Wisbech Health Authority (1986) AC 112;1985), 3 All ER 402;(1985), 5 WLR 830;(1986), 1 FLR 224.


Section 1: Supporting the Family


Chapter 2: Useful Investigations in the Assessment of Liver Disease

DEIRDRE A. KELLY

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The investigation of the liver relies on a multidisciplinary approach involving clinical chemistry, haematology, radiology, histopathology and microbiology. It is essential to understand the many functions of the liver and to recognize the effects of hepatic dysfunction on other body systems (Table 2.1).

Biochemical liver function tests

Baseline investigations

Biochemical liver function tests (Table 2.2) reflect the severity of hepatic dysfunction but rarely provide diagnostic information on individual diseases. Conjugated bilirubin is nearly always elevated in liver disease and is a particularly important investigation in the differential diagnosis of neonatal jaundice (Chapter 4). The presence of bilirubin is always abnormal if detected in a fresh urine specimen.

Aminotransferases are intracellular enzymes, which are mostly present in liver, heart and skeletal muscle. Increases in aspartate aminotransferase (AST) and alanine aminotransferase (ALT) indicate hepatic necrosis irrespective of aetiology (Table 2.2). ALT is more liver specific than AST but has a longer plasma half-life. A rise in AST is an early indication of liver damage and is a useful marker of rejection post-liver transplant (Chapter 20). These enzymes may be normal in compensated cirrhosis.

Alkaline phosphatase is found in liver, kidney, bone, placenta and intestine. In paediatric liver disease, increases in this enzyme indicate biliary epithelial damage, malignant infiltration, cirrhosis, rejection or osteopenia secondary to vitamin D deficiency. Gamma-glutamyl transpeptidase (GGT) is present in biliary epithelia and hepatocytes. The reference range is age related, with higher levels in neonates. It is elevated in many forms of liver damage, but may be normal in certain forms of intrahepatic cholestasis (e.g. familial intrahepatic cholestasis 1 and 2, Chapter 4).

The most useful tests of liver ‘function’ are plasma albumin concentration and coagulation time. Low serum albumin indicates chronicity of liver disease, while abnormal coagulation indicates significant hepatic dysfunction, either acute or chronic. Fasting hypoglycaemia in the absence of other causes (e.g. hypopituitarism or hyperinsulinism) indicates poor hepatic function and is a guide to prognosis in acute liver failure. If these baseline investigations suggest hepatic dysfunction, then more specific investigations for metabolic disease are appropriate to consider (Kelly & Green 1991; Kelly & Hull 1991; McKiernan 2001) (Table 2.3).

Second-line investigations (Table 2.3)

Hepatic dysfunction may be secondary to sepsis, particularly urinary sepsis, inborn errors of metabolism or endocrine disorders. It is usual to exclude sepsis by performing bacterial culture of the urine, and/or blood cultures if appropriate, and to exclude known causes of viral hepatitis.

If the infant is unwell, or has evidence of acute liver failure, then galactosaemia and tyrosinaemia should be excluded (Chapter 5).

In neonates, hypopituitarism may be difficult to exclude as thyroid function tests may be equivocal or in the low normal range. It is useful to perform a 09.00h
### Table 2.1 Functions of the liver

<table>
<thead>
<tr>
<th>Function</th>
<th>Effect of dysfunction</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metabolism/storage</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbohydrate/glycogen</td>
<td>Loss of glucose homeostasis</td>
<td>Hypoglycaemia on fasting/stress</td>
</tr>
<tr>
<td>Lipid</td>
<td>Lipid accumulation in hepatocytes</td>
<td>High/low cholesterol</td>
</tr>
<tr>
<td></td>
<td>↓Oxidation of fatty acids</td>
<td>↑Lactate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑Ratio FFA:BOH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑Acyl carnitine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Organic aciduria</td>
</tr>
<tr>
<td>Protein</td>
<td>↑Catabolism</td>
<td>Low BCAA, urea</td>
</tr>
<tr>
<td>Synthesis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin</td>
<td>Loss of muscle mass</td>
<td>Low albumin</td>
</tr>
<tr>
<td>Factors II, VII, IX, X</td>
<td>Coagulopathy</td>
<td>Protein energy malnutrition</td>
</tr>
<tr>
<td>Degradation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drugs</td>
<td>Prolonged drug effect, e.g. sedation</td>
<td>Clinical</td>
</tr>
<tr>
<td>Oestrogens</td>
<td>Telangiectasia</td>
<td>Clinical</td>
</tr>
<tr>
<td></td>
<td>Gynaecomastia</td>
<td></td>
</tr>
<tr>
<td>Toxic products</td>
<td>Encephalopathy</td>
<td>Abnormal EEG/clinical signs</td>
</tr>
<tr>
<td>Bile synthesis and excretion</td>
<td>Cholestasis</td>
<td>↑Conjugated bilirubin</td>
</tr>
<tr>
<td></td>
<td>Fat malabsorption</td>
<td>↑GGT</td>
</tr>
<tr>
<td></td>
<td>Fat-soluble vitamin deficiency</td>
<td>↑ALP</td>
</tr>
<tr>
<td></td>
<td>Pruritus</td>
<td>Cholesterol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Malnutrition</td>
</tr>
</tbody>
</table>

ALP, Alkaline phosphatase; BOH, beta-hydroxybutyrate; BCAA, branched chain amino acids; EEG, electroencephalogram; FFA, free fatty acids; GGT, gamma-glutamyl transpeptidase; Met, methionine; Phe, phenylalanine; PT, prothrombin time; PTT, partial thromboplastin time; Tyr, tyrosine.

### Table 2.2 Liver function tests

<table>
<thead>
<tr>
<th>Reference range of test</th>
<th>Abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated bilirubin &lt; 20 mmol/l</td>
<td>Elevated: hepatocyte dysfunction or biliary obstruction</td>
</tr>
<tr>
<td>Aminotransferases</td>
<td></td>
</tr>
<tr>
<td>Aspartate (AST) &lt; 50 U/l</td>
<td>Elevated: hepatocyte inflammation/damage</td>
</tr>
<tr>
<td>Alanine (ALT) &lt; 40 U/l</td>
<td></td>
</tr>
<tr>
<td>Alkaline phosphatase (ALP) &lt; 600 U/l (age dependent)</td>
<td>Elevated: biliary inflammation/obstruction</td>
</tr>
<tr>
<td>Gamma-glutamyltransferase (GGT) &lt; 30 U/l (age dependent)</td>
<td></td>
</tr>
<tr>
<td>Albumin 35–50 g/l</td>
<td>Reduced: chronic liver disease</td>
</tr>
<tr>
<td>Prothrombin time (PT) 12–15 s</td>
<td>Prolonged:</td>
</tr>
<tr>
<td>Partial thromboplastin time (PTT) 33–37 s</td>
<td>(i) Vitamin K deficiency</td>
</tr>
<tr>
<td></td>
<td>(ii) Reduced hepatic synthesis</td>
</tr>
<tr>
<td>Ammonia &lt; 50 μmol/l</td>
<td>Elevated: abnormal protein catabolism/urea cycle defect/other inherited metabolic disease</td>
</tr>
<tr>
<td>Glucose &gt; 4 mmol/l</td>
<td>Reduced in: acute or chronic liver failure/metabolic disease/hypopituitarism</td>
</tr>
</tbody>
</table>
cortisol level at the same time as measuring free thyroxine and thyroid stimulating hormone (TSH) (Spray et al. 2000).

α₁-Antitrypsin deficiency is the commonest inherited metabolic liver disease and should always be excluded at any age. As α₁-antitrypsin is an acute-phase protein, it is necessary to measure both concentration and phenotype in order to differentiate between homozygotes, heterozygotes and an acute-phase response. Although cystic fibrosis is a rare cause of liver disease in the neonatal period, it should be considered in the differential diagnosis of neonatal liver disease, and excluded by performing an immunoreactive trypsin test, a sweat test and mutation analysis if either are positive (Chapter 11).

Wilson’s disease rarely presents before the age of 3 years, but may mimic any form of liver disease and should always be excluded in older children (Chapter 13). An autoimmune screen and immunoglobulin levels should detect 75% of children with autoimmune hepatitis (Chapter 8).

The development of new technology, such as fast atom bombardment mass spectrometry and tandem mass spectrometry, has permitted the identification of specific metabolites in the urine and blood in a number of rare diseases, e.g. primary bile salt deficiencies (Chapter 4). Other specific tests include measurement of carnitine and acyl carnitine in fatty acid oxidation disorders (Chapter 5). These investigations are essential steps in the differential diagnosis of unresolved neonatal hepatitis.

Serum cholesterol is usually elevated in children with severe cholestasis, for example in Alagille’s syndrome or biliary atresia, and provides supporting evidence of these diagnoses. In contrast, low or normal cholesterol is characteristic of bile acid transport disorders, or of terminal liver disease (Chapters 4 and 20).

Plasma ammonia and amino acids (particularly phenylalanine, tyrosine and methionine) may be raised in either acute or chronic liver failure and are non-specific indications of hepatic dysfunction. An elevated plasma or urine tyrosine may indicate tyrosinaemia type I, which should be confirmed by measurement of urinary succinylacetone. Definitive diagnosis requires assay of fumarylacetase in skin fibroblasts or mutation analysis (Chapter 5). Primitive hepatic cells synthesize α-fetoprotein. The levels are highest in the newborn (>1000 mg/l) and fall in the first few months of life. It may be a useful screening test in the diagnosis of tyrosinaemia type I and hepatoblastoma, or for detection of hepatocellular carcinoma in chronic carriers of hepatitis B and C.

Radiology

Several radiological techniques provide valuable information in the investigation and diagnosis of paediatric liver disease, while the rapid development of interven-