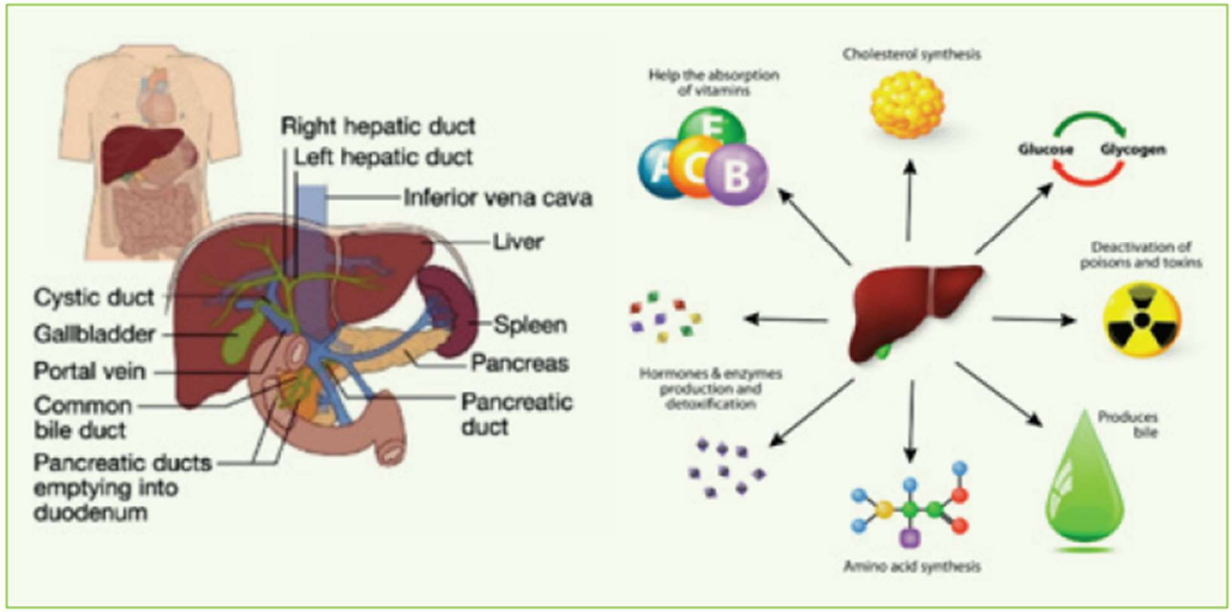
The Liver and its functions



The liver is dark reddish brown in colour and is divided into two main lobes (the larger right and the smaller left) which are further subdivided into approximately 100,000 small lobes, or lobules.

About 60% of the liver is made up of liver cells called hepatocytes which absorb nutrients and detoxify and remove harmful substances from the blood.

A hepatocyte has an average lifespan of 150 days. There are approximately 202,000 in every milligram of your liver tissue.

The liver receives its blood supply via the hepatic artery and portal vein.

Liver functions include:

- Processing digested food from the intestine;
- Controlling levels of fats, amino acids, and glucose in the blood;
- Combating infections;
- Clearing the blood of particles and infections, including bacteria;
- Neutralising and destroying all drugs and toxins;
- Manufacturing bile;
- Storing iron, vitamins, and other essential chemicals;
- Breaking down food and turning it into energy;
- Manufacturing, breaking down and regulating numerous hormones including sex hormones;
- Making enzymes and proteins which are responsible for most chemical reactions in the body, for example those involved in blood clotting and repair of damaged tissues.

Https://britishlivertrust.org.uk/

ABOUT CHILDHOOD LIVER DISEASE

There are many different childhood liver conditions and problems which are collectively referred to as childhood liver disease. In fact, there are over a hundred different childhood liver diseases, including:

Biliary Atresia, Alagille syndrome, Alpha-1-antitrypsin deficiency, Autoimmune disease, Choledochal cyst, Cystic fibrosis, Gilbert's syndrome, Hepatitis, NAFLD, Primary Sclerosing Cholangitis, Progressive familial intrahepatic cholestasis (PFIC), Wilson's disease and Acute liver failure.

1 baby is born in New Zealand every month with a serious liver disease.

KNOW THE EARLY WARNING SIGNS

Signs and symptoms can be subtle or non-specific and so it can take a while for parents and health care professionals in the community to recognize that a baby may have liver disease.

There are many different causes of liver disease in babies. Some of these are extremely rare while others, such as **Biliary Atresia**, are more common.

Each of the different causes of liver disease may have specific signs and symptoms related to that disease and it is not possible to mention all of them in one guide.

Key warning signs have been recognised as an early alert to signal that medical examination is warranted. Beware Yellow is a campaign to raise awareness of these signs.

Parents know their babies best. If you have any concerns about your baby's health, then you should contact your midwife or GP. Sometimes, a straightforward blood test, usually done as a heel prick is enough to tell doctors whether to worry about liver disease

Beware Yellow, promotes awareness of 3 Key signs for Parents and Medical professionals to be alert for in young babies.

1. JAUNDICE

Jaundice is a yellow colour to the eyes, skin and even the hair. It can range from subtle to obvious. Sometimes it can be difficult to see in babies' skin but is usually easier to see in the whites of the eyes.

Jaundice on the first day of the life is rare. Babies with jaundice on day one should be seen by a doctor.

Common causes include incompatibility between the blood of the baby and his or her mother, and infections. As babies are usually seen by a doctor prior to discharge from hospital, the jaundice is usually noticed.

However, for babies born at home or discharged early, it is important that mothers let their midwife or doctor know if their baby becomes jaundiced on this first day.

Jaundice in the first 2 weeks of life is often physiological jaundice. Sometimes the baby needs to undergo light therapy known as phototherapy. Usually, physiological jaundice is short-lived and has no long-term effects on a baby's health. Physiological jaundice is not due to liver disease.

Occasionally, jaundice will last longer than 2 weeks and this is commoner if babies who are breast fed. No-one really knows why breast-fed babies become jaundiced but, again, this is harmless and has no long-term effects. Breast-milk jaundice goes away once breast feeding is stopped. However, there is no need to stop breast feeding if the baby has been checked by a doctor and no serious cause of liver disease found.

Jaundice after the first 2 weeks of life should always be checked out. However, there is no need to wait 2 weeks if you are worried about your baby before this time, see your GP if your baby has any of the childhood liver disease symptoms listed.

Jaundice is due to high levels of a waste substance called bilirubin. There are 2 types of bilirubin: unconjugated and conjugated. A simple blood test will tell whether your baby has high levels of unconjugated or conjugated bilirubin. Unfortunately, the laboratory will often only look at the total bilirubin level which then does not help tell between the 2 types of bilirubin.

The test which does distinguish between them is a split bilirubin test. It is the conjugated bilirubin which is high

in liver disease and any baby with a high conjugated bilirubin level should be referred urgently to a paediatrician (a doctor specialising in child health).

Conjugated bilirubin levels are normal in babies with physiological or breast-milk jaundice and so it is easy to distinguish between which babies need referral to hospital and investigations for liver disease and which do not.

The Liver and its functions

2. PALE STOOLS (POO)

Normal baby stools (poo) range from yellow to green to brown. Any other colour is not normal. Baby poo is yellow, green, or brown because bile, the waste product of the liver, comes into the intestine and mixes with the digested milk.

In liver disease, the stool may be especially pale, for example white, cream or a very pale yellow. This happens for 2 reasons. Firstly, there may be a blockage meaning that bile cannot get out of the liver and so the poo resembles just digested milk – a creamy colour.

In addition, bile contains useful substances which help babies absorb the fats in their milk.

If there is not enough bile being made, the fats may not be absorbed well leading to too much fat in the poo. Fat in poo gives it a pale, loose, greasy look and it may smell worse than a normal baby poo.

Sometimes parents find it difficult to describe the colour of their baby's poo and of course, it can be different at each nappy change! Take a dirty nappy along with you when you see the midwife or doctor to show them. They will be able to tell whether there is enough colour in the poo or not.

3. DARK URINE

Usually, the urine of a new-born baby is colourless (like water). However, when a baby becomes jaundiced with a high level of conjugated bilirubin, the bilirubin can come out in the urine. The urine then looks yellow or brown.

This can easily be seen in the nappy. It is not normal for a baby's urine to be yellow or brown so, again, take your baby along to see your doctor and take a wet nappy along with you.

OTHER SYMPTOMS TO BE AWARE OF:

Itching

When babies are jaundiced, the bilirubin (yellow colour) in their skin makes them itch. This is commoner in older babies who have more advanced liver disease. However, in both ***Alagille syndrome & Progressive Familial Intrahepatic Cholestasis (PFIC),*** the itch may be especially severe and can occur very early in life. Sometimes these babies itch even when their skin is only mildly jaundiced or not jaundiced at all. Severe itching without much jaundice suggests testing for these two diseases.

Poor weight gain

Babies with liver disease often have difficulty putting on weight. This can occur for many reasons. In some liver diseases, especially Alagille syndrome, the baby may already be small at birth. In addition, babies with liver disease are often losing fat into their poo (as described above) and their metabolic rate is higher.

These two facts mean that they need more calories than other babies. So, you may notice that your baby is feeding well and yet not gaining enough weight. In addition to all of this, some babies with liver disease lose their appetite. This is commoner as they become older. If their liver and spleen become large, then their stomach may be a little compressed so that they feel full easily and take only a small volume of feed.

Also, children with liver disease may vomit more easily than other children. If you are worried about your baby's growth in any way then this is always a reason to consult with your GP, midwife, or Plunket nurse

Bleeding

The liver performs all sorts of important functions but one of these is making substances which help the blood clot. These substances need vitamin K to work properly. Vitamin K is absorbed from milk but there is less vitamin K in breast milk than cows' milk.

If your baby has bleeding, this can be a sign that they have a problem with their liver. It is unusual for babies to have bleeding so if you notice blood in the nappy or from the nose or mouth, you should consult a doctor urgently.

Equally, bruising in babies is also uncommon and should be taken seriously. It is because of this risk of bleeding that babies with liver disease usually receive vitamin K supplements.

TYPES OF CHILDHOOD LIVER DISEASE

Biliary Atresia (BA)

Biliary Atresia is the leading cause of childhood liver disease occurring in 1 in 8,000 live births, 1 in 5,000 in Māori and Pacific Island children (www.https://starship.org.nz/).

Biliary Atresia is a physical defect of the bile ducts developing abnormally in the womb and causes the bile ducts to become inflamed or obstructed in the new-born baby. Bile ducts on the inside and outside of the liver may be affected, leading to a blockage of bile flow from the liver. This in time, can lead to scarring or fibrosis of the liver. In the first weeks of life babies with Biliary Atresia may seem well, apart from being jaundiced (yellow hue of skin and of the whites of the eyes) and in some cases feeding more often.

Jaundice extending beyond the first 2 weeks after birth, or newly occurring jaundice, are red flags, and baby should have a 'split bilirubin test' asap. If Biliary Atresia is suspected from this blood test, specialist care will quickly follow, including investigative surgery (operative cholangiogram) to confirm the diagnosis and establish how many bile ducts are affected.

A "Kasai procedure", may be completed under the same general anaesthetic at the same time, to help bile drain from the liver into the gut.

Treatment for BA is surgical (Kasai portoenterostomy) which is most successful if performed early, preferably before 6 weeks of age. Approximately 60% of infants with BA will have a successful Kasai (bilirubin <25mmol/L by 6 months of age).

Infants with BA who have unsuccessful Kasai will require transplantation. Those with successful Kasai may still require transplantation due to portal hypertension, recurrent cholangitis, and complications of cirrhosis.

Alagille syndrome

Affecting I in 30,000 live births. Individuals with Alagille syndrome may have fewer bile ducts than normal, meaning bile can get trapped in the liver and cause damage, leading to jaundice (yellowing) of the skin and eyes.

Liver damage can cause issues such as malabsorption (not properly absorbing fats and nutrients) which can lead to slower growth and development, and sometimes, the formation of harmless lumps or fatty deposits underneath the skin.

Other parts of the body may also be affected e.g., sometimes the baby also has a heart murmur, and they may have a harmless extra membrane at the back of their eye and an unusual but harmless shape to the bones in their spine. None of these things can be seen from the outside and need special tests at the hospital to look for them. In addition, some children with Alagille syndrome may have a characteristic facial appearance.

Alpha-1-antitrypsin deficiency

Alpha-1-antitrypsin is a protein produced in the liver. It protects the body's tissues from damage caused by the release of enzymes from white blood cells during the immune response to infections. Individuals with alpha-1 antitrypsin deficiency, produce an abnormal form of this protein which becomes trapped in the liver rather than circulating in the blood. This can lead to damage to the lungs and the liver. Around ten percent of children who have alpha-1 antitrypsin deficiency have problems with their liver.

Autoimmune disease

There are two types of autoimmune liver disease: Autoimmune hepatitis (AIH) and AIH/sclerosing cholangitis overlap syndrome known as autoimmune sclerosing cholangitis (ASC). Each type has different types of autoantibody present:

Type 1: Anti-nuclear (ANA) and/or anti-smooth muscle (SMA) antibodies. Type 1 makes up two out of three of all cases of AIH and most ASC cases.

Type 2: Liver kidney microsomal (LKM) antibodies. Type 2 is less common, more likely to affect younger children and can present with acute liver failure. Type 2 is rare in ASC.

Choledochal cyst

A choledochal cyst is a swelling or dilatation of the bile ducts. There are various types, affecting the external common bile duct or hepatic ducts, or in some cases affects the internal, liver intrahepatic ducts. Most choledochal cysts are detected in childhood, following symptoms of Jaundice/abdominal pain, and confirmed by ultrasound scan.

The Liver and its functions

Cystic fibrosis
Children with cystic fibrosis may develop liver problems due to fibrosis of the liver. Small bile ducts and surrounding liver tissue can become damaged and scarred.

Gilbert's syndrome
Gilbert's syndrome is a common genetic condition (affects around 1% of the population), mild liver condition that causes jaundice (yellowing of the skin). It is not thought to cause liver damage.

Hepatitis
Hepatitis B and C can both damage the liver. Viral infection and the body's immune system response to this, can damage the liver cells.

Non-Alcoholic Fatty Liver Disease (NAFLD)
NAFLD has increased in both adults and children in recent years and is now one of the most common forms of chronic liver disease in children and adolescents.

Primary Sclerosing Cholangitis (PSC)
PSC is a rare, progressive liver disease in which bile ducts inside (intrahepatic) and outside (extrahepatic) the liver may narrow or become blocked due to inflammation and scarring.

Progressive familial intrahepatic cholestasis (PFIC)
PFIC is a complicated group of diseases. There are several types and all rare, PFIC type 1 can involve other parts of the body. Frequently these babies have diarrhoea which can become quite severe. Any baby with jaundice, diarrhoea and itching should be seen by a specialist paediatrician.

Wilson's disease
Wilson's disease is a rare, inherited condition in which the body cannot handle copper correctly, resulting in a toxic build-up of copper in the liver. It is estimated that Wilson's disease affects 1 in 30,000 of the population.

KASAI

The liver has ducts, so that the bile it produces can drain into the intestine and help with digestion of food. If these ducts are blocked, the Kasai procedure is a way to surgically bypass them and prevent liver damage. It is often the preferred initial treatment for Biliary Atresia.

During the Kasai Procedure surgeons first carefully remove the damaged ducts outside of the liver. They use a small segment of the patient's own intestine to replace the ducts at the spot where bile is expected to drain. This segment not only connects to the liver, but also connects to the rest of the intestine. The Y-shaped passageway formed by the Kasai operation allows bile to flow from the liver into the intestine.

Although the Kasai procedure is not a permanent cure for Biliary Atresia, in many cases it allows patients to grow and remain in good health for several years. This delays (or in about 25% of children, eliminates) the need for a liver transplant.

LIVER TRANSPLANT

A liver transplantation is an operation performed to replace a diseased liver with a healthy one from another person. An entire liver may be transplanted, or just a section. The liver may come from an organ donor, or from a family member who is willing to donate a part of his/her liver and is a suitable candidate to donate. The specialist medical team will advise when liver transplant is being considered as a treatment option for your child, explaining clinical details, the procedure and what to expect. A range of patient information has been developed to answer the questions of patient families facing this situation. IDFNZ has hundreds of paediatric liver transplant patients in our membership. Patient networking and sharing transplant stories is a valuable way of achieving first-hand information and supporting others.

Childhood Liver Disease - 'Need to Know' Facts

Jaundice is common in babies and usually harmless but a small number of jaundiced babies have serious liver disease

Jaundice on day 1 of life and after 2 weeks of age requires investigation

A simple blood test called split bilirubin can tell whether your baby needs further tests for liver disease

Baby poo is usually yellow, green or brown - pale poo which is white or cream needs investigation

Baby urine is usually colourless - if you can see urine in a baby's nappy because it is yellow or brown, then your baby needs investigations

Itching, poor weight gain and bleeding may also be signs of liver disease

Liver disease is rare in babies but early diagnosis is essential to prevent complications

Do not hesitate to consult your doctor if you are worried about yout baby's health