



Indications in Hepatology and Liver Diseases

The various indications in hepatology represent a growing problem for the international health care systems and, first of all, for the patients. Therefore hepatology is an interesting market for the medical equipment manufacturers.

Alcoholism and resulting alcoholic liver disease is the an important factor in some Asian countries as well as in most industry countries but here the fastest growing segment in hepatology is NASH (nonalcoholic steatohepatitis). NASH is the most severe form of NAFLD, the major cause of cryptogenic liver cirrhosis. Nearly 10% of the US Americans (25 Million) are afflicted with liver-related diseases each year.

Chronic liver diseases are the biggest problem. An estimated 30% of the world's total population (2 billion) has been infected with hepatitis B virus and more than 350 million people (perhaps 400) are inflicted by chronic HBV. About 170 million persons have hepatitis C.

Chronic liver diseases from viral hepatitis might lead for one fifth of the patients to a liver cirrhosis which might end in the need of a liver transplantation (LTx). Again 20% of the cirrhotic patients are at risk to develop hepatocellular carcinoma (HCC), calling for liver resection.

A much smaller number of liver patients, about 12,000 per year, get fulminant hepatic failure or acute liver diseases.

www.liver-products.com

With the website www.liver-products.com the sananet GmbH, a German based consulting agency for the health care market, wants to give an insight into the hepatology market for manufacturers of liver diagnostic devices and liver therapy equipment. Below you will find some more details on the various indications in liver diseases.

www.liver-products.com is made for professionals in the hepatology market, be it as a doctor interested in the liver or a marketing manager of a medical company who wants to launch a new liver product.

Index

Indications in Hepatology and Liver Diseases.....	1
Index.....	2
Chronic Liver Diseases	3
Viral Hepatitis - HBV and HCV.....	3
HIV-Co-Infection	3
Hepatocellular Carcinoma - HCC.....	3
Liver Disease caused by Alcohol	3
Drug induced Liver Failure.....	3
Non-Alcoholic Steatohepatitis (NASH).....	4
Wilson Disease.....	4
Hemochromatosis.....	4
Primary Biliary Cirrhosis	4
Acute Liver Failure or Fulminant Hepatic Failure.....	5
Infectious Acute Liver Failure.....	5
Other Acute	5
Paediatric Liver Diseases.....	6
HAV (Hepatitis A) in Children.....	6
HBV (Hepatitis B) in Children.....	6
Mucoviscidosis / Cystic Fibrosis	6
Biliary Atresia	6
Further Information.....	7
ANNEX - List of Indications in Hepatology	8

Chronic Liver Diseases

More than 26,000 people die each year from chronic liver disease and cirrhosis in the USA. Above 350,000 are hospitalized with a diagnosis of cirrhosis. In hepatology the chronic liver diseases are the biggest burden for the worldwide health care systems.

Viral Hepatitis - HBV and HCV

HBV is 50 to 100 times more infectious than HIV. In Asian in a lot of countries, between 5% and 20% of the population are HBV carriers. More than 35,000 people contract hepatitis C virus each year in the US. Here it is more frequent than hepatitis B. Nearly 4 million Americans have antibodies against HCV indicating prior exposure or infection and about 1 million people against HBV.

Most people who become chronically infected by hepatitis B virus never know it. Dangerous is that two third of HBV cases have no or unrecognized symptoms. More than 500 million people worldwide are inflicted by either Hepatitis B Virus or by Hepatitis C. 20% of those patients with chronic viral hepatitis might develop liver cirrhosis which might end in the need of a liver transplantation (LTx).

HIV-Co-Infection

10% of the HIV-infected population worldwide, more than 40 million people, is co-infected with HBV. In Southeast Asia this might be 20% against 5% in Western Europe and North America. Dramatic effects on the development of cirrhosis might develop, if HIV is combined with a co-infection of HBV or HCV.

Hepatocellular Carcinoma - HCC

One of the most common tumours worldwide is hepatocellular carcinoma (HCC), the primary malignancy of the liver. HCC typically is secondary to either a viral hepatitis infection or cirrhosis caused by alcoholism in the Western World. At risk of hepatocellular carcinoma (HCC) are about one fifth of the chronic hepatitis patients. More than 1 Million new cases of HCC occur each year worldwide. The death rate is 100%. without medical treatment. The standard therapy of liver cancer is liver resection, but it can only be used for 5-15% of the patients. Non-surgical liver therapies like chemotherapy and ablation offer 5-year-survival rates of 30-40%. Therefore an estimated 550,000 people each year die of hepatocellular carcinoma.

Only 10 - 20% of hepatocellular carcinomas can be removed completely using surgery outside the western world. If the cancer cannot be completely removed, the disease is usually deadly within 3 to 6 months. This is partially due to late presentation with large tumours, but also the lack of medical expertise and facilities. 60% of liver cancer in Asian Americans is caused by chronic hepatitis B virus infection. In Eastern Asia (China, Hong Kong, Japan, Korea) alone each year 360,000 patients are dying, which makes HCC one of the top three causes of death by cancer in most of Asia.

Liver Disease caused by Alcohol

Between 10 and 25 per cent of alcoholics develop cirrhosis. Alcoholic liver disease can take a similar path as viral hepatitis. More than 2 million Americans suffer from alcoholic liver disease. 22000 patients die every year in the UK from alcohol related liver disease. Deaths from liver cirrhosis are rising here faster than anywhere else in Europe.

Drug induced Liver Failure

Today's birth control pills contain much less oestrogen than before. Before 300 - 3000 cases of chronic liver damage in otherwise healthy women occurred each year in Germany.

Non-Alcoholic Steatohepatitis (NASH)

NASH is a liver disease associated with Obesity and Type 2 Diabetes Mellitus. It is the fastest growing segment in hepatology. The reason for NASH is inflammation and damage to the liver cells, caused by fat in the liver. Untreated this can lead to cirrhosis.

NASH affects an estimated 2% to 5% of all US Americans.

Wilson Disease

Wilson's disease is an autosomal recessive disorder, with a male preponderance. Copper is accumulated in tissues, which manifests itself with liver disease and neurological symptoms. In the US 1 per 30,000 people suffer from Wilson disease.

Hemochromatosis

Hemochromatosis is characterized by improper dietary iron metabolism and a hereditary disease. Organ damage can be the result of iron accumulation in the tissue, manifesting as liver failure and diabetes mellitus respectively. In the US 0,3% to 0,5%, above 1 million are affected. In Great Britain the number is estimated to be roughly one in every 300-400 people. For Caucasians the rate in is estimated to be up to 5%.

Primary Biliary Cirrhosis

Primary biliary cirrhosis, an autoimmune disease affecting the liver by slow progressive destruction of the small bile ducts within the liver, can lead to scarring, fibrosis, cirrhosis, and ultimately liver failure. When these bile ducts are damaged bile builds up in the liver (cholestasis) and over time damages the liver tissue.

In 1996 there were 9,232 cases of primary biliary cirrhosis in the USA, the sex ratio being 9 to 1, women to men

Acute Liver Failure or Fulminant Hepatic Failure

Acute liver failure (ALF) used for both fulminant hepatic failure (FHF) and subfulminant hepatic failure. Relatively rare - only about 2000 cases annually occurring in the US - it is a potentially fatal disease, especially if complicated by hepatic encephalopathy and impaired protein synthesis.

Infectious Acute Liver Failure

More than 350 million people worldwide are inflicted by hepatitis B Virus. In many countries viral hepatitis is a common cause for FHF, especially hepatitis A and hepatitis B. In hepatitis C it is quite uncommon. Survival rates in HAV patients with FHF are about 50-60%, much more favourable than the outcome for patients with other hepatitis. These patients account for 10-20% of the liver transplants in children in some countries despite the relatively mild infection that is observed in many children infected with HAV. In the developing world, acute HBV infection dominates as a cause of FHF.

Sepsis can be another cause for an infectious acute liver failure.

Other Acute

Other causes for acute liver failure include:

- Acute Fatty Liver (as a result of pregnancy, tetracyclines, alcohol or Reye syndrome)
- Ischemic Liver Failure after surgical procedures and occlusion of hepatic artery.
- Multi Organ/Liver Failure after heart surgery
- The HELLP (hemolysis, elevated liver enzymes and low platelets) syndrome occurs in 0.1-0.6% of pregnancies and usually is associated with preeclampsia.
- Wilson's Disease (hereditary copper accumulation) may infrequently present with acute liver failure. Without OLT, this is almost uniformly fatal.
- Cryptogenic Acute Liver Failure (for nearly 15% of patients in the US, the cause of the acute liver failure remains indeterminate)

Paediatric Liver Diseases

In the US, there are about 15,000 children hospitalized each year due to liver disease. Reasons might be hepatitis infection or genetic defects like cystic fibrosis or biliary atresia.

HAV (Hepatitis A) in Children

Fulminant hepatic failure (FHF) in children can be caused by hepatitis A virus (HAV). It leads to a substantial proportion (10-20%) of the pediatric liver transplants in some countries, despite the relatively mild infection that is observed in many children infected with HAV.

HBV (Hepatitis B) in Children

A chronic infection and the development of a chronic liver disease is a major risk of a HBV infection during childhood. Of the children aged 1-5 years, infected with HBV, 30-60% will become chronically infected. Of older children and adults infected with HBV this is "only" 10%. Most people from Asia, the Pacific Rim, and Africa become infected with HBV during childhood. HBV is a high risk for newborn and children, especially in Asia, where 90% of newborn at birth with hepatitis B virus will become chronically infected and might therefore develop a chronic liver disease.

Mucoviscidosis / Cystic Fibrosis

Cystic fibrosis (CF) or mucoviscidosis is one of the most common and serious of all genetic (inherited) diseases which affects the liver of children. Without treatment, CF results in death for 95% of children before age 5. Advanced methods of diagnosis and treatment have greatly increased the survival rate. The recessive cystic fibrosis gene is carried by approximately 5% of population and about 1 in 500 parents are at risk for having children with cystic fibrosis. Mucoviscidosis affects the digestive tract and the lungs and is characterized by the production of abnormal secretions leading to mucous build-up, which can impair the pancreas and, secondarily, the intestine.

Biliary Atresia

One in every 15,000 live births is affected by biliary Atresia. Bile becomes trapped in the liver due to the congenital absence or closure of the ducts that drain bile. This is causing jaundice and (eventually) cirrhosis in children.

Untreated this is fatal and no curative therapy for biliary atresia exists. Kasai portoenterostomy, a surgical treatment, restores bile flow and clears jaundice, and if successful, achieves a 10-year survival rate. Yet even with early surgery liver transplantation plays an important role in the long-term treatment of biliary atresia. 60- 80% of children with biliary atresia require liver transplantation due to developing end-stage biliary cirrhosis.

Pediatric liver transplantation has evolved into a highly successful therapy and now offers significant hope for all children born with biliary atresia.

Further Information

If you are interested in further information on the hepatology market or you would like to give input to our website www.liver-products.com please contact:

sananet GmbH
Tilo Stolzke
Breite Strasse 6-8
23552 Lübeck
Germany

or call **Tilo Stolzke** at **+49 451 400 83 01** directly.

ANNEX - List of Indications in Hepatology

Chronic Liver Diseases

- infectious liver disease (HBV, HCV, HDV)
- toxic-chronic (alcoholic)
- NASH
- co-infection (HBV+HIV)
- toxic-chronic (drug induced)
- autoimmune (PBC, chronic-active autoimmune hepatitis)
- metabolic (hemochromatosis, Wilson's disease)
- biliary (cholestasis; SecondaryBiliaryCirrhosis)
- vascular (heart failure)
- other chronic (participation of liver in Crohn's, ulcerative colitis, Tuberculosis etc.)
- kryptogenic symptoms (suspected fibrosis / cirrhosis)

Acute Liver Failure or Fulminant Hepatic Failure

- infectious - viral (A, B, C, D, E), sepsis
- toxic-acute (paracetamol, alcohol, mushroom poisoning and other)
- other acute - acute fatty liver (pregnancy, tetracyclines, alcohol, Reye syndrome)
- other acute - multi organ (liver) failure after heart surgery
- ischemic (surgical procedures, occlusion of hepatic artery)
- vascular (heart failure; Budd Chiari syndrome)
- cryptogenic
- toxic-acute (intoxication with strongly albumin bound substances)
- Adult-onset Still disease
- Fructose intolerance
- Galactosemia
- HELLP syndrome of pregnancy
- Hemorrhagic viruses (Ebola virus, Lassa virus, Marburg virus)
- Idiopathic drug reaction (hypersensitivity)
- Neonatal iron storage disease
- Paramyxovirus
- Tyrosinemia

Paediatric Liver Diseases

- paediatric (mucoviscidosis, cystic fibrosis)
- paediatric (primary billiary artresia)