PART 1
Diagnosis and pathophysiology
CHAPTER 1
Clinical clues to the diagnosis of cirrhosis

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Introduction

Cirrhosis is a diffuse process characterized by replacement of normal liver tissue by fibrosis and regenerative nodule formation [1]. The development of cirrhosis is usually an irreversible process. However, the reversal of fibrosis has been shown in certain conditions like hepatitis C, biliary obstruction, iron overload, and non-alcoholic steatohepatitis. Thus, cirrhosis is considered as a dynamic process involving pro- and anti-fibrogenic mechanisms, the former being more marked than the latter. The term cirrhosis is a histologic diagnosis and has its own unique constellation of clinical manifestations such that a clinical diagnosis of cirrhosis can be made with confidence most of the time.

The diagnosis of cirrhosis in clinical practice is based on risk factors, history and clinical findings, biochemical tests, imaging, endoscopic and histologic findings. The diagnosis of cirrhosis is not based on a single clinical parameter but a combination of above parameters and the identification and interpretation of these findings. This chapter focuses on the clinical clues that aid in the diagnosis of cirrhosis.

Clinical presentation

Cirrhosis occurs clinically as compensated cirrhosis or decompensated cirrhosis.

Compensated cirrhosis is usually diagnosed incidentally during a routine examination or biochemical test, during surgery for some other reason, or sometimes with nonspecific symptoms like fatigue, anorexia, dyspepsia, weight loss, or right upper abdominal discomfort. Up to 30–40% of patients with compensated cirrhosis remain without clinical signs [2]. These patients decompensate at the rate of 10% per year and have a 50% 10-year survival rate [3].

 Decompensated cirrhosis is cirrhosis complicated by one or more of the following: jaundice, ascites (with or without hepatorenal syndrome, hyponatremia, spontaneous bacterial peritonitis), hepatic encephalopathy, or variceal bleeding. The presence of these features of decompensation have a high specificity but low sensitivity for the diagnosis of cirrhosis. Decompensated cirrhosis has a 50% survival rate at 18 months [3]. These clinical manifestations are discussed subsequently.

Patient history

Abdominal distension (ascites)

Cirrhosis is the most common cause of ascites (85%) and ascites is the most common complication of cirrhosis. Up to 60% of patients with compensated cirrhosis develop ascites within 10 years [3]. Clinically, patients present with gradually progressive abdominal distension with or without pedal edema, history of weight gain, increase in waist size of clothing, sometimes with a decrease in urine output, or the development of abdominal hernias as a result of increased intra-abdominal pressure. The ascites in cirrhosis resulting from portal hypertension is usually responsive to diuretic therapy, hence such a history must be sought in any patient presenting with ascites. History of cardiac failure, renal disease, malignancy, and tuberculosis must be ruled out. A history of ascitic tap is a
strong clue to the presence of ascites, hence the nature of fluid tapped may add further valuable information to the diagnosis.

**Jaundice**
Jaundice as a clinical manifestation may be seen in cirrhosis depending on the degree of decompensation. Jaundice (icterus) is a clinical manifestation of hyperbilirubinemia and presents as yellow discoloration of the skin and mucous membranes. It is the most obvious sign of liver disease and is best seen in the conjunctivae. It is usually detectable when the serum level of bilirubin exceeds 2 mg/dL (34 mmol/L). Elevation of both unconjugated and conjugated bilirubin occurs in patients with hepatocellular disease resulting from impaired canaliculic excretion or biliary obstruction. Unconjugated hyperbilirubinemia in cirrhosis is caused by either associated hemolysis or decreased conjugating enzyme in the endoplasmic reticulum of hepatocytes, namely bilirubin uridine-diphosphoglucuronate glucuronosyltransferase (UGT) or associated Gilbert’s syndrome. Serum bilirubin levels are usually below 5 mg/dL; however, values above this may also be seen in certain patients who are in a decompensated state. A serum bilirubin level >5 mg/dL is one of the clinical defining criteria for acute on chronic liver failure [4]. The clinical significance of jaundice in cirrhosis lies in assessing the decompensated state of cirrhosis as jaundice is not specific to cirrhosis alone as it is seen in many other liver disorders and even in nonhepatic disorders.

**Upper gastrointestinal bleeding**
Gastroesophageal varices are present in approximately 50% of patients with cirrhosis. Up to 40% of patients with Child A cirrhosis have varices which increases to 85% in Child C cirrhosis [5]. Variceal bleeding occurs at a rate of 5–15% per year [6]. Variceal bleeding presenting as hematemesis with or without melena is one of the most common complications of cirrhosis with portal hypertension. The presentation is usually a painless, effortless bleed and may be precipitated by drugs like nonsteroidal anti-inflammatory drugs (NSAIDs). There may be associated melena which is passage of black tarry stools, which are offensive, semi-solid, and difficult to flush down the toilet. Patients may have postural hypotensive symptoms such as light-headedness and fainting episodes in cases of a significant bleed. Once a patient has a variceal bleed, the portal pressure (i.e., hepatic venous pressure gradient; HVPG) is usually >12 mmHg [7], because the development of varices occurs with HVPG >10 mmHg. However, variceal bleed alone is not a feature of cirrhosis; it may well be seen in noncirrhotic portal hypertensive conditions such as extrahepatic portal vein obstruction (EHPVO) or noncirrhotic portal fibrosis (NCPF).

**Hepatic encephalopathy**
Hepatic encephalopathy is a neuropsychiatric syndrome with multiple variable manifestations. It may be covert (which includes minimal hepatic encephalopathy; MHE) and stage I encephalopathy) or an overt (stage II–IV) encephalopathy. Patients with MHE may present only with cognitive dysfunction in cirrhosis. The prevalence of MHE is 30–84% [8] and that of overt hepatic encephalopathy is 30–50% in cirrhotic patients [9,10]. The presentation of hepatic encephalopathy has marked variability among patients. Drowsiness, disorientation with reference to time, place, or person, delirium, and confusion can occur. Disturbance in sleep develops early with hypersomnia and altered sleep rhythm. There is further development of apathy, somnolence, tremors, apathy, and slowness of response. As further worsening occurs, the patient may become aroused on noxious stimuli or may become deeply unresponsive and comatose. Seizures may occur, especially in deeper grades of encephalopathy. Personality disturbance is another mode of presentation in the form of irritability, euphoria, and features of social disinhibition. Patients often present with loss of bladder and bowel control. Intellectual deterioration, memory impairment, and cognitive dysfunction also frequently occur. Constructional apraxia, micrographia, slow slurred monotonous speech, dysphasia, and perseveration can all occur.

A clinician must always look for a history of precipitating factors for encephalopathy: gastrointestinal bleed, use of diuretics, infections, hyponatremia, surgery, constipation, renal failure, anemia, hypoglycemia, and, in the absence of any precipitating event, a thorough search should be made for the presence of spontaneous porto-systemic shunts [11]. Any patient with hepatic encephalopathy must have any neurologic cause like meningitis, stroke, intracranial bleed, chronic subdural hematoma (especially in alcoholics) ruled out. There are various criteria for staging of hepatic encephalopathy. One of the most commonly used is the West Haven criteria as shown in Table 1.1 [12].
**Etiologic history taking**

**Alcohol intake: how much is significant**

Fatty liver develops in up to 90% of patients who drink more alcohol than 60 g/day [13]. Fibrosis progression and development of cirrhosis may occur in up to 5–15% of patients despite abstinence. Continued alcohol use increases the risk of progression to cirrhosis in 30% of patients [14]. The risk of developing cirrhosis increases with the ingestion of >60–80 g/day of alcohol for 10 years or longer in men, and >20 g/day in women. Yet, even drinking at these levels, only 6–41% develop cirrhosis [15–17]. Hence, there are several other risk factors involved in the development of alcoholic liver disease: sex (female), drinking patterns (early age of drinking, daily heavy drinking, episodic binge drinking), obesity, dietary factors, non-sex-linked genetic factors, cigarette smoking, other chronic liver disorders (hepatitis B or C, hemochromatosis, nonalcoholic fatty liver disease; NAFLD).

In a population-based cohort study of almost 7000 subjects in two northern Italian communities, even among patients with very high daily alcohol intake (>120 g/day), only 13.5% developed alcoholic liver disease (ALD). Homemade brew has variable amounts of alcohol and associated trace metals which may cause the development of liver disease with fewer years of consumption.

The history of alcohol consumption should be obtained both from the patient and family members, enquiring about alcohol-associated illnesses like pancreatitis and peripheral neuropathy, driving under the influence of alcohol, and history of any withdrawal symptoms. The amount of alcohol for reference purposes is 30 mL whisky, 360 mL beer, 120 mL wine – all equivalent to 10–11 g alcohol, and each of them is considered as one unit. The CAGE questionnaire is frequently used to assess the degree of alcohol-related problems and alcohol dependence [18].

**History of other risk factors**

A history including blood transfusion, surgery, needle-stick injuries, sexual contact, tattooing, skin piercing, dialysis, sharing of razors or toothbrushes must be taken to assess the risk of exposure to hepatitis B and C viruses. Metabolic risk factors include diabetes mellitus, hypertension, obesity, and dyslipidemia which must be asked about in view of nonalcoholic steatohepatitis-related cirrhosis. A family history of chronic liver disease may be relevant in certain situations like Wilson’s disease, autoimmune disorders, and even hepatitis B and C-related cirrhosis. A history of abnormal involuntary movements like choreoathetosis should arouse the suspicion of Wilson’s disease. Autoimmune disorders like vitiligo, diabetes mellitus, thyroid disorder, pernicious anemia, and inflammatory bowel disease are associated with autoimmune hepatitis. A past history of biliary obstruction and biliary surgery could give a clue to the diagnosis of secondary biliary cirrhosis as pruritus and fatigue may be seen in primary biliary cirrhosis. A personal history of sexual dysfunction like loss of libido, loss of secondary sexual characteristics, breast enlargement

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**Table 1.1 West Haven criteria for staging of hepatic encephalopathy.**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Intellectual impairment</th>
<th>Neuromuscular impairment</th>
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<tbody>
<tr>
<td>Stage 0</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Minimal hepatic encephalopathy</td>
<td>Normal examination findings, subtle changes in work or driving</td>
<td>Normal</td>
</tr>
<tr>
<td>Stage 1</td>
<td>Personality changes, attention deficits, irritability, depressed state</td>
<td>Minor abnormalities of visual perception or on psychometric or number tests</td>
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<td>Stage 2</td>
<td>Changes in sleep–wake cycle, lethargy, mood and behavioural changes, cognitive dysfunction</td>
<td>Tremor and incoordination</td>
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<tr>
<td>Stage 3</td>
<td>Somnolence, confusion, disorientation, amnesia</td>
<td>Asterixis, ataxic gait, speech abnormalities (slow and slurred)</td>
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<tr>
<td>Stage 4</td>
<td>Stupor and coma</td>
<td>Muscular rigidity, nystagmus, clonus, Babinski’s sign, hyporeflexia</td>
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<tr>
<td></td>
<td></td>
<td>Oculocephalic reflex, unresponsive to noxious stimuli</td>
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in males and amenorrhea or infertility in females are clues to hypogonadism, often seen in cirrhosis. A history of smoking is also important as it has been shown to have a role in progression of chronic liver disease: hepatitis C and alcoholic cirrhosis [19].

**Examination**

**General examination**

A patient with cirrhosis appears malnourished, with shrunken eyes, temporal hollowing, parched lips, muddy complexion of the face, dried skin (xerosis), and hyperpigmentation, with features of various nutritional deficiencies. Patients have a hyperkinetic circulation. They may also have petechiae, purpura, or ecchymotic patches suggestive of underlying coagulopathy and thrombocytopenia. Fetor hepaticus is a sign of hepatocellular failure characterized by a sweetish, slightly faecal smell of the breath similar to freshly opened corpses of mice.

Pallor indicates anemia, which may be multifactorial in cirrhosis as a result of anemia of chronic disease, hypersplenism, acute or chronic blood loss, a nutritional cause, bone marrow suppression, or an autoimmune process. Scleral icterus is usually present in patients with decompensated cirrhosis. However, all patients who are decompensated do not have scleral icterus, especially those who present with upper gastrointestinal bleed or ascites. Patients with compensated cirrhosis are usually anicteric. Scratch marks may be present in cholestatic liver disorders. Xanthelasmas and pruritic scratch marks are a clue to biliary cirrhosis. Xanthelasma often develops as a painless, yellowish, soft plaque with well-defined borders, which may enlarge over the course of weeks. Clubbing is seen in patients with cirrhosis, especially in the setting of biliary cirrhosis, hepatopulmonary syndrome, or cystic fibrosis. Cyanosis may be seen in severe degrees of hepatopulmonary syndrome. Presence of a Kayser–Fleischer ring or sunflower cataract should arouse suspicion for underlying Wilson’s disease as the etiology.

**Nutritional status**

Malnutrition is a common complication of cirrhosis with a prevalence of 65–90% [20]. There is severe reduction of body fat and overall muscle mass [21]. These patients also have various micro and macronutrient deficiencies often manifesting clinically. Nutritional status should be assessed in all patients. Nutritional assessment by body mass index in cirrhotic patients with ascites is difficult as it overestimates the true body weight in these patients. Hence, in patients with ascites, weight correction should be carried out by reducing 14 kg in massive ascites, 6 kg in moderate ascites, and 2.2 kg in minimal ascites from the observed weight [22].

**Cutaneous clues**

**Spider angioma**

A spider angioma consists of a central arteriole with numerous small radiating vessels from it resembling a spider’s legs. These spider angiomas may range from a pinhead to 0.5 cm in diameter. They are mostly seen along the vascular territory of the superior vena cava, “V” of the neck, chest, face, arms, hands, and back. They are reckoned to be distributed in relation to a gradient of skin vascular reactivity and temperature [23]. These skin lesions blanch on pressure and if large enough can be seen or felt to be pulsating [24]. A study showed the prevalence of spider angiomas was 50% in patients with alcoholic cirrhosis compared with 27% in patients with nonalcoholic cirrhosis. Overall, up to 33% of patients with cirrhosis have spider angiomas [25].

The number and size of vascular spider angiomas have been found to correlate with the severity of liver dysfunction. They may disappear with improvement in liver function or may increase in number with progression of liver dysfunction. Sometimes they may bleed profusely. They are mostly seen in association with alcoholic cirrhosis. Patients with spider angiomas have a higher frequency of variceal bleeding (36%) than patients without spider angiomas (11%). Spider angioma profile also predicts the risk of variceal bleeding, which is greater when there are >20 spider angiomas (50%) or multiple atypically located spider angiomas (66%). Large spider angiomas (>15 mm) correlate with large varices and higher risk of bleeding [26]. Other causes of spider angiomas include viral hepatitis and under normal conditions in children and adults (including pregnancy). They are mainly caused by an increase in ratio of serum estradiol to free testosterone in male patients [27]. Young age, elevated plasma vascular endothelial growth factor, and basic fibroblast growth factor have been attributed as significant independent predictors of spider nevi in cirrhotic patients [28]. For cosmetic reasons, spider angiomas can be treated with laser therapy [29]. Differential diagnosis for vascular spider angiomas include cherry
hemangiomas, insect bites, Rendu–Odsler–Weber syndrome, angioma serpiginosum, ataxia telangiectasia, senile angioma, disseminated essential telangiectasia, and angiokeratomas.

Palmar erythema
Palmar erythema manifests as bright red discoloration of the palms, mostly on hypothenar, thenar eminences, and pulps of the fingers. Also known as liver palms, it is a less frequent finding than vascular spider angiomas. Of patients with cirrhosis, 23% manifest palmar erythema [30]. The soles of feet may also be affected. The mottling blanches on pressure. Other causes also include familial inheritance, thyrotoxicosis, pregnancy, rheumatoid arthritis, diabetes mellitus, gestational syphilis, human T-cell lymphotropic virus type 1 (HTLV-1) associated myelopathy, leukemia, chronic febrile illnesses, and drugs (amiodarone, gemfibrozil, cholestyramine, topiramate, and albuterol or salbutamol). Similar to vascular spider angiomas, the pathogenesis of liver palms lies in the hyperestrogenic state and regional differences in the peripheral circulation of patients with cirrhosis [31].

Dupuytren’s contracture
Dupuytren’s contracture is a flexion contracture of the ring and little fingers brought about by thickening of the palmar fascia of the hands. It is thought to be caused by fibroblastic proliferation and disorderly collagen deposition. Normally, the palmar fascia consists of type I collagen but in Dupuytren’s contracture this is replaced by type III collagen which is significantly thicker than type I. According to Wolfe et al. [32], Dupuytren’s contracture was present in 66% of male alcoholic patients with cirrhosis. In Nazari’s series a similar association was found in 55% of patients with alcoholic (Laënnec’s) cirrhosis [33].

The exact pathogenesis and causal association in cirrhosis is not clear. It is also seen in other conditions like diabetes mellitus, alcoholism, repeated trauma, and phenytoin therapy. Male gender, age more than 40 years, people of northern Europe and Scandinavian descent, and a positive family history are risk factors for Dupuytren’s contracture. The contractures are divided into three grades (based on the joint with the greatest degree of flexion contracture): grade I contractures of 5–30 degrees, grade II contractures of 30–60 degrees, and grade III contractures of 60–90+ degrees [34].

Leukonychia
Leukonychia means white nails (Terry nails) and was first described in 1954. Terry nails is a physical finding in which fingernails and/or toenails appear white with a characteristic ground glass appearance with a dark band (pink or brown) at the distal tip and the absence of a lunula. This is mainly caused by hypoalbuminemia, and can also be seen in those with chronic kidney disease, type 2 diabetes mellitus, congestive heart failure, or advanced age. The pathogenesis of these nail changes is unclear but is thought to be caused by a decrease in vascularity and an increase in connective tissue within the nail bed. Holzberg postulated that the vascular changes (dilated vasculature in the dermis of the distal band) were related to the premature aging of the nail bed, which resulted in the abnormal appearance of the nail [35–38].

Muehrcke’s nails
Muehrcke’s nails are paired horizontal white bands separated by normal color. The exact pathogenesis is not known but it is believed to be caused by hypoalbuminemia, hence may be seen in other conditions such as nephrotic syndrome.

Bier spots
Bier spots are small, irregularly shaped, hypopigmented patches on the arms and legs caused by venous stasis associated with functional damage to the small vessels of the skin. Bier spots disappear when pressure is applied. Raising the affected limb from a dependent position also causes Bier spots to disappear, which is not the case in true pigmentation disorders [39].

Paper-money skin
Paper-money skin (or “dollar-paper” markings) describes the condition in which the upper trunk is covered with many randomly scattered, needle-thin superficial capillaries. It often occurs in association with spider angiomas. The name comes from the resemblance to the finely chopped silk threads in American dollar bills. The condition is commonly seen in patients with alcoholic cirrhosis and may improve with hemodialysis [40].

Hypogonadism and gynecomastia
Diminished libido and potency, loss of secondary sexual hair, decreased frequency of shaving, gynecomastia, and testicular atrophy are the usual features of hypogonadism
in cirrhosis. Gynecomastia is the enlargement of the male breast, defined as glandular breast tissue that is >4 cm in diameter and is often tender [41]. It is mostly seen in those with alcoholic liver disease, although spironolactone use is also a common cause for this in cirrhotic patients. It is present in up to two-thirds of patients with cirrhosis. The prevalence of gynecomastia in cirrhotic patients in one study was reported to be 44% [42]. Female patients with cirrhosis may present with infertility or amenorrhea. In cirrhosis there is a decrease in the hepatic androgen receptors and an increase in the hepatic estrogen receptors, resulting in increased estrogen: androgen ratio [43]. Hypothalamic pituitary dysfunction is also one of the mechanisms for these features. The conjugation of steroid hormones occurs in the liver and any failure of hormonal metabolism may result in steroid hormonal imbalance. Testicular atrophy is ideally measured by orchidometer; however, in the absence of the same, small volume testes, with loss of testicular sensation, is also an adequate clue for atrophy.

Parotidomegaly
Parotidomegaly is usually seen in those with alcoholic cirrhosis. It is usually caused by glandular hypertrophy as a result of adipose infiltration or acinar hypertrophy. Some authors also suggest a role for glandular dysfunction [44]. In sialosis of alcoholic origin, 60% of patients with alcoholic cirrhosis present with parotidomegaly [45], the glandular enlargement being observed already in the pre-cirrhotic phase in 12% of cases [46,47].

Other manifestations
Muscle cramps occur frequently in those with cirrhosis and are characterized by severe pain, occurring in the calf muscles, mostly during sleep or at rest, lasting for few minutes and occurring several times a week [48]. They occur in more than 70% of patients after diagnosis of cirrhosis and are related to the duration of recognized cirrhosis and the degree of liver dysfunction. The mechanism proposed includes reduced effective plasma volume and correlates with the presence of ascites, low mean arterial pressure, and plasma renin activity [49]. Neurogenic, muscular origin, deficiency of calcium, magnesium, and zinc have also been proposed as mechanisms. Lid lag and lid retraction also occur more frequently in cirrhotic patients than healthy individuals with no evidence of any thyroid dysfunction. Other oral and cutaneous manifestations include onycholysis, gingivitis, and candidiasis.

Abdominal examination
Abdominal veins
Portal hypertension caused by cirrhosis may result in dilatation of periumbilical collateral veins. Blood from the portal venous system may be shunted through the periumbilical veins and ultimately to the anterior abdominal wall veins, manifesting as caput medusa. It involves a prominent vein, the thoracoepigastric vein, which interconnects the superficial epigastric vein with the lateral thoracic vein, which is a tributary of the axillary vein. It therefore connects the superior vena cava (axillary vein) with the inferior vena cava (superficial epigastric, which drains into the femoral vein). The dilated veins appear to radiate from the umbilicus and the flow of veins when examined is away from the umbilicus. The presence of visible veins alone does not indicate portal hypertension; the distension of these veins is more important. In cases of suspected Budd–Chiari syndrome (with inferior vena caval involvement), the infra-umbilical vein flow is directed upwards and there is opening up of back veins as well.

Cruveilhier–Baumgarten murmur
A venous hum is heard in the epigastric region on auscultation because of collateral connections between the portal system and the periumbilical veins in portal hypertension, seen rarely in cirrhotic patients. Congenital patency of the umbilical vein may also cause this venous hum. These patients are associated with an increase in spontaneous hepatic encephalopathy [50].

Examination of the liver
Liver examination should focus on the size, surface, margin, consistency, and presence of any bruit. The liver span is usually 10–12 cm in men and 8–11 cm in women. A reduced liver span is a clue to the diagnosis of liver cirrhosis. A shrunken liver is usually a feature of post-necrotic cirrhosis while an enlarged liver indicates an alcohol etiology, autoimmune liver disease, hemochromatosis, or Budd–Chiari syndrome. The cirrhotic liver usually has a firm consistency, irregular or nodular surface, and irregular margins. Presence of an arterial bruit may denote the development of hepatocellular carcinoma, although it may also be seen in alcoholic hepatitis or other vascular lesions of liver. A firm liver
has a sensitivity and specificity of 73% and 81%, respectively, for the diagnosis of cirrhosis [51]. The left lobe is often enlarged in cirrhosis and is a useful sign, with a sensitivity and specificity of 86% and 67% [52].

**Examination of the spleen**

Splenomegaly indicates portal hypertension and is a valuable sign in a suspected case of cirrhosis, especially if there are other features suggestive of cirrhosis; however, it may be enlarged in other conditions. The spleen is usually mild to moderately enlarged in cirrhosis. An unduly massive spleen should make the physician suspect coexisting portal or splenic vein thrombosis or noncirrhotic portal hypertension. Presence of splenomegaly has a very high specificity (90%) but low sensitivity (34%) [51].

There are three methods of percussion of the spleen: Nixon’s method, Castell’s method, and percussion of the Traube’s space. Percussion of Traube’s space has a sensitivity and specificity of 67% and 75%, respectively, for detecting splenomegaly [53]. Patients presenting with upper gastrointestinal bleed and splenomegaly usually indicates a diagnosis of portal hypertension and evidence of one of the features of cirrhosis may form a clue to cirrhosis. Splenomegaly is almost universal in NCPF and the average spleen is about 8 cm. In comparison to EHPVO, the spleen is usually >7 cm below costal margin in NCPF and <7 cm in EHPVO [54]. The splenomegaly in EHPVO is mild (5 cm) in 42% of patients, moderate (6–10 cm) in 40%, and massive in only 18% [55].

**Examination for ascites**

Jugular venous pressure can help in differentiating between cardiac ascites and hepatic ascites as it is commonly raised in cardiac but not in liver disease. Lack of rise in jugular venous pressure (negative hepatojugular reflux) can be a useful clue in cases of Budd–Chiari syndrome [56]. The hepatojugular reflex has a reported sensitivity of 24–72% and a specificity of 93–96% as a marker of right heart dysfunction [57]. The clinical finding of ascites by means of shifting dullness has a sensitivity of 83% and a specificity of 56% [58]. In cases where the shifting dullness is absent, the patient has a <10% chance of having ascites. The amount of ascites required for detection by various methods includes 30 mL for ultrasonography, 1500–2000 mL for shifting dullness. However, in the setting of a tense ascites, shifting dullness may not be apparent. A puddle sign detects up to 120 mL of free fluid [58]. Development of ascites also correlates with the degree of portal pressures such that with an HVPG of >8 mmHg, patients start developing ascites.

**Neurologic examination**

Asterixis, or flapping tremors, is the most characteristic neurologic abnormality detected on clinical examination in patients with overt hepatic encephalopathy. The patient’s arms are outstretched, with forearms fixed and hyperextension at the wrist joint. The physician observes a rapid flexion–extension movement at the metacarpophalangeal joint, and wrist joint. Sometimes, arms, neck, jaw, protruded tongue, retracted mouth, and tightly closed eyelids are involved and the gait is ataxic. Absent at rest, less marked on movement, and maximum on sustained posture, the tremor is usually bilateral. Alternatively, asterixis can be evaluated having the patient grip the evaluator’s fingers in steady fashion and is present if the patient’s grip tension oscillates. Asterixis can be graded: grade 0 (no flapping motions), grade I (rare flapping motions, 1–2 per 30 seconds), grade II (occasional, irregular flaps, 3–4 per 30 seconds), grade III (frequent flaps, 5–30 per 30 seconds), and grade IV (almost continuous flapping motions) [59]. It may be seen in certain other conditions such as cardiac failure, respiratory failure, and uremia. There is no ideal test for the diagnosis of MHE. However, the Working Party recommends that the diagnosis of MHE requires a normal mental status examination and impairment in the performance of at least two of the following tests: Number Connection Test, Part A (NCT-A), Number Connection Test, Part B (NCT-B), block design test (BDT), and digit symbol test (DST) [11]. There are various neuropsychologic, neuropsychiologic, and computerized tests that can be used for making the diagnosis of MHE.

The patient may have hypertonia in the initial stages and hypotonia as coma supervenes, exaggerated deep tendon reflexes or areflexia (in deep coma), flexor or extensor plantar response. In cases of hypertonia, ankle clonus must be checked. The gait is often ataxic. Patients with Wilson’s disease may have extrapyramidal features like chorea, athetosis, dystonia, rigidity, dysphonia, dysarthria, and dysphagia.

A recent study analyzed the diagnostic accuracy of overall clinical impression and combination indices and models for detection of cirrhosis. The sensitivity and specificity of the overall clinical impression for the diagnosis of cirrhosis are 54% and 89%, respectively [51].
Thus, cirrhosis can be diagnosed by a combination of history and clinical examination. This diagnosis has to be confirmed by imaging or endoscopy. Its presence indicates a close observation on follow-up for development of hepatocellular carcinoma.

References