Introduction

Liver disease and cirrhosis remain common causes of morbidity and mortality worldwide [1–3]. The significant advances in our understanding and treatment of liver disease, including liver transplantation over the last 25 years, have resulted in hepatology increasingly becoming a separate specialty. Although in many countries hepatologists have received background training in gastroenterology and endoscopy, subspecialization often means that they are no longer practicing endoscopists.

On the other hand, there are healthcare systems where hepatologists come from an internal medicine background with no prior training in endoscopy. It is therefore important for the modern hepatologist to have a full appreciation and up to date knowledge of the potential of endoscopy in liver disease and to ensure that there is a close collaboration between hepatology and endoscopic departments. In parallel to this, endoscopy has undergone a period of rapid expansion with numerous novel and specialized endoscopic modalities that are of increasing value in the investigation and management of the patient with liver disease.

The role of endoscopy in liver disease is both diagnostic and interventional. Endoscopy is commonly offered to patients with relevant symptoms (unsuspected liver disease may be diagnosed in this manner) and has a role in the management of inpatients with pre-existing liver disease, mainly for variceal screening and therapy. Furthermore, such patients can be challenging to sedate and the complexity and number of endoscopies in liver disease continue to increase with rising numbers of end-stage liver disease patients, patients who are considered for liver transplantation, and in post-liver transplant patients.

It is therefore not surprising that advanced endoscopic modalities, such as endoscopic ultrasound (EUS), endoscopic retrograde cholangiopancreatography (ERCP), cholangioscopy (e.g., SpyGlass™), confocal endomicroscopy, and double balloon enteroscopy, have all become integral in the detailed investigation and treatment of liver-related gastrointestinal and biliary pathology (Figure 1.1).

It is now clear that the role of endoscopy in liver disease is well beyond that of just treating varices. As endoscopic technology advances, so do the indications and role of the endoscopist in the management of liver disease.
Endoscopy Room Setup

Optimum design and layout of the endoscopy room are important to ensure maximum functionality and safety while accommodating all the state of the art technology likely to be needed in the context of investigating complex patients with liver disease. The endoscopy room needs to be spacious with similar design principles to an operating theatre. Gas installations and pipes should descend from the ceiling and the endoscopy stack unit and monitors should be easy to move around and adjust according to the desired procedure, or mounted on pendants to maximize floor space.

A multifunctional endoscopy room able to accommodate different endoscopic procedures, such as esophagogastroduodenoscopy (EGD), enteroscopy, ERCP, and EUS, is advantageous. As such, the room design should be able to contain the following equipment:

1) An endoscopic stack system containing a light source and video processor unit that has advanced features (e.g., high definition (HD), alternate imaging modalities, image processing), HD capable monitor, and HD video and image capture device.
2) A physiological stats monitor to monitor vital signs such as blood pressure, heart rate, blood oxygenation levels, and electrocardiographic (ECG) readings.

3) An ultrasound (US) scanner/processor compatible with EUS endoscopes. Such a scanner usually includes modalities such as tissue harmonics, Doppler, color and power flow, contrast, and elastography.

4) A reporting system that allows for the speedy capture of images and the generation of reports connected to the central patient record system. This should be compatible with the hospital Picture Archiving and Communication System (PACS) for high resolution image transfer or videos.

5) A C-arm installation connected to a central PACS system for image archiving can be used in a well-equipped endoscopy room shielded for radiation. Alternatively, in many hospitals, ERCP or other interventional procedures requiring fluoroscopic guidance are carried out in the radiology department in order to benefit from regular updates of high quality radiology equipment and the presence of a radiographer.

6) Basic equipment required for patient treatment and safety, such as suction, water jet units, argon plasma coagulation (APC), electrosurgery, and emergency trolleys for acute cardiorespiratory arrest, as well as equipment for elective and emergency intubation and for delivery of general anesthesia.

7) Onsite pathology facilities (e.g., for real-time assessment of samples from EUS guided fine needle aspiration) may be found in many endoscopy units.

Endoscopic Stack

Modern endoscopic stacks have many common components – the light source to provide illumination and the video processor, which takes the endoscopic image from the charge coupled device (CCD) chip within the tip of the endoscope, processes the image and then displays it on the monitor in real time.

At present there are two methods employed for the transmission of light and display of the received image (Figure 1.2). One method is to transmit separate red (R), green (G), and blue (B) color spectrum wavelength components generated by RGB rotating filter lenses via an optical fiber bundle into the gastrointestinal tract. The reflected light intensity changes obtained from each RGB light are detected via a monochrome CCD where the video processor combines these with the appropriate R, G, or B color to generate a “white light” or color image, where each element of the CCD is one pixel of each frame of the video. The second option is to transmit white light, without alteration, and then detect the image using a color or RGB CCD, where multiple elements of the CCD are used to create one pixel in the video frame. A newer method, not widely used currently, that removes the need for the fiber transmission bundles, is the introduction of light emitting diodes (LEDs) built into the tip or bending section of the endoscope. The anatomy is imaged using a RGB CCD. Each transmission method has advantages and disadvantages, but in general visible resolution and detail definition of the image, due to advances in CCD manufacture and technology, have greatly improved irrespective of the technique used.

Furthermore, as camera chip or CCD technology has increased in resolution and decreased in size, manufacturers have been able to take advantage of improvements in display technology to visualize the gastrointestinal tract in high resolution, thus giving the endoscopist a new dimension in detecting pathology.
Image Enhancing Modalities

Manufacturers have introduced various image enhancement techniques (Figure 1.3) to aid in the detection and delineation of pathology for more accurate diagnosis and targeted treatment [4]. Examples of these include narrow band imaging (NBI; Olympus Corp., Tokyo, Japan), flexible spectral imaging color enhancement (FICE; Fujinon Corp., Saitama, Japan), and i-Scan (Pentax Corp., Tokyo, Japan). NBI operates on a different principle to the other systems, as it limits the transmitted light to specific narrow band wavelengths centered in the green (540 nm) and blue (415 nm) spectra. This allows for detailed mucosal and microvascular visualization, thus facilitating early detection of dysplastic changes. Alternatively, FICE and i-Scan use post-image capture processing techniques that work on the principle of splitting the images into “spectral” components. Specific spectral components are then combined, with the “white light” image, in a number of permutations, thus creating different settings that aim to enhance the original endoscopic image and delineate the gastrointestinal mucosa or vascular structures.

New Advances in Image Enhancement

An alternate image enhancement technique to NBI, i-Scan, and FICE has been introduced by Fujifilm with the release of the ELUXEO™ endoscopy system, consisting of a new video processor and light source. Within the light source, Fujifilm have replaced the standard xenon lamp and have instead incorporated four LEDs with wavelengths in the red, green, blue,
Figure 1.3 (a) Narrow band imaging (NBI) using a monochrome charge coupled device (CCD) camera (mainly used in UK and Japan). (b) Altered version of NBI for use with the color CCD camera (Europe and USA/rest of world). (c) Flexible spectral imaging color enhancement (FICE). B, blue; G, green; R, red; WL, white light.
and blue-violet spectra. They have replaced FICE with two dedicated image enhancement techniques: (i) blue light imaging (BLI); and (ii) linked color imaging (LCI). The incorporation of a dedicated blue-violet LED takes advantage of the short wavelength absorption of hemoglobin (410 nm), which can enhance the underlying superficial vascularity and mucosal patterns (Figure 1.4). LCI is an image processing technique that separates the four color channels to allow for the enhancement of the difference in the red color spectrum and improve the detection and delineation of mucosal inflammation (Figure 1.5).

Endoscopes
The quality of modern endoscopes has greatly improved; they are far more ergonomic in design and lighter, with superior picture resolution and definition. Endoscopes have also become slimmer and this has significantly impacted on patient safety and comfort. The incorporation of high resolution (up to 1 million pixels) and high definition (>1 million pixels) camera technologies into modern endoscopes and the introduction of new image enhancement techniques have significantly enhanced the endoscopist’s arsenal in the detection and treatment of gastrointestinal pathologies. With such advanced optics, fine mucosal details can be visualized which may reveal subtle pathology, such as angioectatic lesions, watermelon stomach, portal hypertensive gastropathy, enteropathy, and ectopic varices at a far earlier stage than with older generation endoscopes.

Modern endoscopes are far more advanced than previous generation ones, resulting in more space being available in the insertion tube, and therefore larger working channels can be included, allowing for more powerful air suction and insufflation, as well as water irrigation to clean the lenses. Powerful air insufflation can often flatten even large varices. This has to be taken into account when grading varices using a commonly used classification system by Westaby et al. [5], which depends on the percentage of circumference of the esophageal lumen occupied by a varix and whether the varix can be flattened by air insufflation.

In general, the types of upper gastrointestinal endoscopes used in the context of liver disease are the standard endoscopes that possess a working channel of 2.8 mm, the therapeutic endoscopes with a working channel of 3.2 or 3.6 mm (often used in the context of upper gastrointestinal bleeding), and more recently the high resolution ultrathin endoscopes (5.9 mm). The latter have become more popular in the last few years, not only in diagnostics, but also in the assessment of varices, particularly for patients who have been finding frequent surveillance endoscopies to monitor variceal progression stressful.

Such endoscopes can be used transnasally, which has been shown in some studies and select patient populations to be more comfortable than standard endoscopy [6]. Ultrathin endoscopes improve patient tolerance while maintaining an adequate or even near standard size working channel (2.4 mm) for endoscopic biopsies. Such endoscopes, however, are not suitable for endoscopic variceal banding (Figure 1.6).

Endoscopic Ultrasound
Side and front optical viewing endoscopes with appropriate technology have been used to perform EUS, and these are commonly used for diagnosis and therapy in the patient with liver disease. This technique can be of value in the diagnosis of varices, particular ectopic varices (Figure 1.7), in assessing eradication of varices, and in delivering EUS guided therapies, such as thrombin or cyanoacrylate injection for variceal obliteration [7]. EUS guided measurement of the hepatic venous pressure gradient (HVPG) is possible, as are biopsies of the hepatic parenchyma
Figure 1.4 (a) The function of the four light emitting diodes (LEDs) in relation to the depth of penetration of the light spectra from the new ELUXEO™ light source. (b) The difference in the transmitted spectra when in white light, blue light imaging (BLI) and linked color imaging (LCI) modes. (c) The short wavelength absorption characteristics of hemoglobin in comparison to the transmitted light spectra of BLI. (d, e) Images of a polyp captured using (d) white light, and (e) BLI. Source: Reproduced with permission of Aquilant/Fujifilm.
and masses in the left lobe of the liver. Both linear and radial echoendoscopes (Figure 1.8) should be available with appropriate clinical expertise in a center dealing with complex patients with liver disease. Additional modalities, such as tissue harmonics, Doppler color and power flow, contrast, and elastography (for assessing tissue stiffness), are also of value in the context of liver disease. The use of high frequency (12 or 15 MHz) ultrasound miniprobe through the working channel of a standard or double channel therapeutic endoscope can also be used for a quick assessment of variceal obliteration (Figure 1.9).

Endoscopic Retrograde Cholangiopancreatography
The latest ERCP scopes, together with the SpyGlass™ technology [8], have enabled direct visualization of the biliary tree and this has significantly improved our ability to diagnose malignant biliary disease. In 2007, the first generation SpyGlass™ Direct Visualization System (Boston Scientific Corp., Natick, MA, USA) was introduced (Figure 1.10). This relied on a small fiber-optic bundle with an external CCD, introduced into a dedicated catheter, to visualize the biliary tree. The SpyGlass™ DS system introduced in 2015 has evolved
to be a small digital endoscope, with improved optical resolution (approximately $\times 4$), a wider field of view (60%), and dedicated LED illumination.

Recently there have been safety concerns about the design of the ERCP endoscopes and their ability to be sterilized adequately as bacterial transmission of resistant bacteria from patient to patient has been reported [9–12]. As can be appreciated by the complex design of the tip of the ERCP endoscope (Figure 1.11), meticulous cleaning is required to ensure high level decontamination of such endoscopes. This has led to the revision of decontamination protocols [13] and calls for the revision of the design of the latest ERCP endoscopes [14].

**Figure 1.8** Endoscopic ultrasound (EUS) equipment with (a) a miniprobe 2.6 mm in diameter; (b) and (c) are 360° radial views, one with side viewing optics and the other with front viewing optics, respectively; and (d) the linear or fine needle aspiration EUS instrument.

**Figure 1.9** (a) Injection of thrombin for variceal obliteration using an endoscopic ultrasound miniprobe (grey arrow) and an injection needle (blue arrow). (b) Appearance of varices under a 12 MHz miniprobe (white arrow). (c) “Snow storm” appearance of an obliterated area of a varix (white arrow) following thrombin injection.
There has been an increase in the use of deep enteroscopy (both single and double balloon) in the management of patients with chronic liver disease [15]. These endoscopes are used for deep intubation and access to the common bile duct (double balloon assisted–ERCP) in the context of altered anatomy (e.g., Roux-en-Y in cases of hepaticojejunostomy) or for the investigation and treatment of small bowel pathology in the patient with liver disease (e.g., treatment of ectopic varices or biopsies of the small bowel in the post-liver transplant patient to exclude sinister pathology such as lymphoma). Such procedures require special expertise, are time consuming, and preferably should be performed under general anesthesia.

**Colonoscopy**

Colonoscopy in the patient with liver disease is not dissimilar to other patients. HD colonoscopes should be used to ensure diagnosis and therapy are optimized. Appropriate enhanced imaging modalities, such as NBI and FICE, are available although their value in the colon has been debated compared with that in the upper gastrointestinal tract.

High quality colonoscopy is particularly important in the workup of patients prior to liver transplantation to ensure that colon cancer is not missed. This is particularly important in the context of primary
sclerosing cholangitis. Colonoscopy may also be required in the evaluation of gastrointestinal bleeding and the treatment of colonic (mainly rectal) varices.

**Wireless Endoscopy**

Wireless capsule endoscopy is valuable in the assessment of esophageal varices in a selected group of patients with liver disease who for a number of reasons may not be keen to undertake routine endoscopic surveillance [16] and in patients with suspected small bowel sources of bleeding [17]. The basic schematic of the capsule and the procedure setup are detailed in Figure 1.12. They mainly consist of a power source (batteries), a CMOS (complementary metal oxide semiconductor) or CCD chip, lens and associated imaging board, illuminating LEDs, and a transmitter to wirelessly transmit or stream the video to an external recorder. Several companies now compete and produce high quality wireless systems with slightly different capsule characteristics (Figure 1.13).

**Accessories and Consumables**

A number of accessories are routinely used in the context of endoscopy in liver
disease. These include variceal band ligators, endoloops, injection needles for delivering sclerosants (rarely used nowadays), thrombin or cyanoacrylate (superglue), and fine needle devices for the deployment of coils. All these techniques have been shown to be relatively minimally invasive but effective in controlling variceal bleeding [18–20]. Other modalities include APC for the
delivery of coagulation for bleeding from gastric vascular ectasia, as well as recently introduced radiofrequency ablation (RFA) probes for the therapy of obstructing cholangiocarcinoma. It is now widely accepted that single use accessories and consumables should be used to ensure maximum infection control.

In conclusion, a well-designed and well-equipped endoscopy unit is important for the delivery of state of the art endoscopic therapy for patients with liver disease, whose diseases for the most part are high risk and of high complexity.

**Patient Safety and Training**

Patient safety is best achieved by high standards of equipment disinfection and maintenance, appropriate patient selection, and endoscopy of high risk patients in a safe environment (e.g., critical care unit) with adequate support from anesthesiologists and an appropriately trained team of endoscopists and nurses.

**Cleaning and Disinfection of Endoscopes**

Endoscopes need to go through a complex disinfection/sterilization procedure to eliminate the transmission of bacteria, viruses, parasites, fungi, and spores, as well as prions that can transmit spongiform encephalopathy. As such, strict operating protocols should be in place and followed in a very rigorous manner based on published guidelines and standards relating to disinfection/sterilization processes. This improves the safety and minimizes the risk of infection in patients undergoing endoscopy. Publications such as the *Guidelines and Tools for the Sterile Processing Team* [21] and sterile processing accreditation surveys [22] published by the Association of periOperative Registered Nurses’ (AORN) journal, and important communications and updates from regulatory bodies such as the Food and Drug Administration and Centers for Disease Control, raise awareness among healthcare professionals and ensure that a high level of safety is maintained [23,24].

Accreditation surveys performed by specialist agencies and professional organizations are peer reviewed and focus on safety and quality of patient care, thus encouraging the development and adherence to robust processes for endoscopy units in order to achieve accreditation.

In most endoscopy units, automated cleaning/washing machines are available for cleaning and reprocessing the endoscopes. Depending on the number of endoscopy rooms and the volume of endoscopic procedures per week, specific guidelines exist regarding the design of decontamination facilities to ensure effective risk control. The *Choice Framework for Local Policy and Procedures 01-06* by the UK Department of Health [25] details the best evidence based policies and gives comprehensive guidance on the management and decontamination of reusable medical devices.

It is particularly important to ensure that the workflow within the endoscopy unit is from dirty to clean. Such workflow avoids recontamination of reprocessed endoscopes from unprocessed, and thus contaminated, devices. An example of a high throughput reprocessing unit is illustrated in Figure 1.14.

Employment of appropriately trained staff accountable to a management structure is important to ensure adherence to decontamination protocols and best utilization of resources. The purchase of suitable automated endoscope reprocessors is important. Optimal reprocessing also depends on the local quality of water used, the decontamination agents used, and the endoscope manufacturer to ensure compatibility and minimization of the damaging effect of disinfection on endoscopes.
The previously used aldehyde based detergent (glutaraldehyde) should be avoided as this may result in fixing prions inside the endoscopes, thus increasing the risk of transmission of prions, leading to spongiform encephalopathy. In general, neutral pH or neutral enzymatic agents are recommended because of their effective decontamination while having the least damaging effect on endoscopes.

Rigorous and regular microbiological tests reflecting the best evidence based practice are necessary to ensure that the decontamination process remains of high standard. The decontamination room staff should constantly be in communication with the infection prevention and control teams, which typically include medical and nursing personnel and a microbiologist trained in infection control.

Transmission of hepatitis viruses is very rare if all standard operating procedures are followed. It is, however, particularly important in the context of liver disease to ensure that there are robust systems in place for tracking all endoscopes used through a unique endoscope identifier, as well as being able to trace the journey of a particular endoscope through its decontamination and clinical usage. Such information is critical in the unfortunate event of a safety breach, which may expose several patients to risks of infection, so as to be able to recall all patients who underwent procedures with inadequately sterilized endoscopes and provide prophylactic therapy as appropriate.

Specifically in the context of prion transmission, it is of paramount importance that early action be taken in the event that the guidelines have not been followed during a procedure with a high risk for transmission of variant Creutzfeldt–Jakob disease (vCJD), thus potentially contaminating the endoscope. Such endoscopes need to be quarantined immediately, as once they have been contaminated there is no safe method of disinfection. These endoscopes should be reserved exclusively for an individual patient at high risk of vCJD if future endoscopic procedures are required. Specific guidelines regarding prion transmission are in place through the British and American Societies of Gastroenterology. A summary of these guidelines is presented in Figure 1.15 [26,27].
Figure 1.15 Endoscopic procedures considered high risk for prion transmission in pink and low risk in green. APC, argon plasma coagulation; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; I, invasive; NI, non-invasive; TNE, transnasal endoscopy. Summarized from Transmissible Spongiform Encephalopathy Agents: Safe Working and the Prevention of Infection: Annex F: Endoscopy, 2015.
It is now recommended to routinely use single use endoscopic accessories, which minimize the risk of transmission of infection. Storage of disinfected endoscopes should be in designated clean and dry areas, preferably in dedicated storage cabinets with HEPA (high efficiency particulate air) filtered air, which allows the endoscopes to be stored and dry for 72 hours without the need for reprocessing. This is particularly useful in busy units with regular off hours endoscopy.

**Patients**

A detailed history of previous infection should be taken to ensure that high risk patients for viral hepatitis, as well as vCJD and other infectious diseases, are identified. In that respect, important information, such as travel to endemic areas for infections and previous blood transfusions or administration of blood products or surgery in the past, needs to be carefully recorded.

Patients with liver disease at risk of cardiopulmonary compromise should receive the endoscopy under anesthetic support. This is particularly important for patients with encephalopathy and those with alcohol withdrawal symptoms who are far more sensitive and run a high risk of permanent brain injury even after short periods of hypoxia following aspiration or cardiac arrest.

Endoscopy in patients at risk of multiorgan failure should be performed in a critical care environment. The decision and timing of endoscopy should always be balanced against the risks for the individual patient with liver disease. Optimization of the patient’s clinical condition by correction of coagulopathy, prophylactic antibiotics, and judicious use of blood transfusion is the cornerstone of safe endoscopy in such patients.

**Health Personnel and Training Issues**

Since each patient or health staff member is a potential source of infection, precautions are necessary from the personnel point of view to avoid being infected or to pass infection to patients. Personnel should be vaccinated in case of hepatitis A or B or other infection, such as typhoid, depending on the prevalence of such infections in their environment. Meticulous hand washing before and after treating each patient should be practiced. It is also desirable that operators wear protective gowns during endoscopic procedures, as well as gloves, designated shoes, and, whenever appropriate, masks and protective eyewear. Training and operating protocols should be available in each endoscopy room, reviewed at regular intervals, and evaluated to ensure that they are followed. Any incident should be immediately notified to the hospital safety team to ensure that the incident is investigated. Such incidents should be reviewed at regular endoscopy quality improvement meetings to ensure that policies and procedures can be modified to avoid similar incidents in the future.

All practitioners performing endoscopy in patients with liver disease should have adequate training to recognize and treat esophagogastric varices in the elective and acute setting. Familiarization with appropriate equipment and accessories on models and simulators in “hands-on” workshop sessions can greatly enhance training prior to participating in real life cases.

Medical teams should be particularly aware that the patient with liver disease is often likely to have hepatic decompensation in the context of significant bleeding or a complication. Therefore, further management is often required in a critical care environment. This is particularly important for the cirrhotic patient with bleeding varices who has become encephalopathic and runs the risk of aspiration. Appropriate training to recognize such patients for transfer to a critical care unit and assisted ventilation is important. Close collaboration between the endoscopist and hepatologist is necessary, so that the endoscopist is fully aware of
hepatic complication risks and, likewise, the hepatologist is fully aware of the latest endoscopic developments available that can be used to maximize the quality of care of the patient with liver disease.

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References


