INTRODUCTION

It is estimated that by the year 2050, 23% of the United States population will be over 65-years of age (1). As the elderly population increases, 75% of healthcare expenditures will be focused on this group by the year 2030 (2). For this reason, it is important as gastroenterologists to not only understand the various biliary diseases in the elderly but also to have the knowledge for the variety of clinical presentations that may inflict this older adult population.

Physicians must also be attentive to the need to prevent complications, especially during diagnostic and therapeutic procedures as well as when prescribing medications. The value of interventions should be determined by their effect on the patient’s independence and quality of life, and the endpoint is often improvement rather than cure (3). Thus, chronological age alone cannot justifiably be used to preclude a curative approach, especially in biliary disease (4).

BILIARY TRACT MORPHOLOGY AND PHYSIOLOGY IN AGING

There are several physiologic and anatomic changes to the biliary tract that occur with aging (5). The speculated changes (Table 1) include increased lithogenecity of bile, deconjugation of bile pigments, increased bactobilia, and altered gallbladder motility (6). The decreased responsiveness to cholecystokinin and increased pancreatic polypeptide could depress gallbladder motility, but conflicting clinical data exists regarding this (6,7). Many suggest that these changes in the physiology of the biliary tract are responsible for the increased incidence of gallstone disease in the elderly (6).

The principal anatomic change is the increasing size of the common bile duct. In patients over 75-years of age in one study, the upper normal size of the CBD was up to 10mm with the gallbladder in situ and up to 14mm post-cholecystectomy (8). Overall, the number of descriptive studies that specifically look for the effects of aging on the biliary tract is small.

CHOLELITHIASIS

The prevalence of cholelithiasis increases with advancing age (9). The overall frequency of gallstone disease in the elderly has been estimated to be between 14% and 27% based on large population studies (6,10–13). Older adult patients have more complications as a result of cholelithiasis, specifically acute cholecystitis,
cholangitis, gallbladder perforation, gangrene, emphysematous cholecystitis, gallstone ileus, gastric outlet obstruction (Bouveret’s syndrome), gallstone pancreatitis, and choledocholithiasis (6,14–17). Because there is a significant increase in peri-operative risk of injury and death in these situations, much consideration should be placed on balancing the probability of benefit versus an undesired outcome from various therapeutic interventions. As a result, less invasive (and many times less effective) modes of therapy are contemplated and more likely to be attempted. This scenario may lead to a delay in gallstone removal that may result in net increases in major complications and emergency intervention (4,18,19). Clinicians should have a heightened awareness of atypical biliary symptoms in the older adult to avoid a delay in treatment, a scenario not dissimilar to acute appendicitis. An altered mental status may be the only manifestation of hepatobiliary disease (20). Surgery generally remains the most effective means of curative treatment of gallbladder stones. Laparoscopic cholecystectomy remains the standard therapy regardless of age (5). This accounts for the most common indication for abdominal surgery (21). Although data for laparoscopic cholecystectomy show a decisive advantage over open cholecystectomy, the results are not as favorable when compared with younger patients (5). Laparoscopic cholecystectomy in older adults is known to be associated with a higher conversion rate to open cholecystectomy in 7% to 32% compared with <5% in younger patients (21–23). This conversion rate is a manifestation of the increasing incidence of complicated gallstone disease in this age group. Of course, biliary endoscopic sphincterotomy remains an option in patients who are deemed to have high operative risk. However, it should not be considered the first line of therapy but evaluated as a therapeutic option on a case-by-case basis. Gallstone disease in the older adult population is a recurrent condition with worsening complications at repeated presentations, and it would seem that non-operative management may be associated with higher morbidity and mortality as shown by a study by Arthur, et al (24). In addition, dissolution therapy once reserved for the rarest of individuals who have prohibitive cardiac risk, small cholesterol stones, and functioning gallbladders has lost its popularity (25).

CHOLEDOCHOLITHIASIS

Choledocholithiasis is the most common cause of biliary obstruction (26). The reported incidence of common bile duct (CBD) stones in patients having cholecystostomy ranges from 20% to 54%. In a study of 330 patients over the age of 65 who underwent ERCP, mainly for the evaluation of jaundice, 30% were shown to have choledocholithiasis (27). In contrast, common duct stones are found far less frequently in younger patients (4).

The natural history of choledocholithiasis is difficult to determine (28). Common bile duct stones can present with biliary colic, acute cholangitis, acute pancreatitis, and even hepatic abscesses caused by the obstruction of bile duct or Ampulla of Vater, while approximately 10% are asymptomatic (28, 29). The symptoms of these entities can be subtle or even nonexistent (14). When obstruction of the bile duct occurs, the rise in biliary pressure results in the translocation of bacteria from the bile duct to the bloodstream. Patients presenting with CBD stones may have biochemical abnormalities most often demonstrating cholestasis (28).

The clinical approach to suspected choledocholithiasis is continuously evolving. With the use of less invasive imaging strategies, including CT, MRCP and EUS, performing ERCP can be restricted to those patients confirmed to have choledocholithiasis where the expected intent is therapeutic intervention and removal of stones (6). A recent National Institutes of Health (NIH) consensus statement found that ERCP,

### Table 1.

Age-Related Changes in Biliary Tract Physiology and Anatomy

- Increased lithogenecity of bile
- Deconjugation of bile pigments
- Decline of bile salt synthesis
- Increased bactobilia
- Altered (reduced) gallbladder motility
- Increased plasma levels of cholecystokinin
- Decreased responsiveness to cholecystokinin
- Increased prevalence of gallstones
- Pigment stones more common
- Increased common bile duct diameter
  (Pre/Post-cholecystectomy)
MRCP, and EUS were comparable in their sensitivities, specificities and accuracy rates for detection of choledocholithiasis (30).

Traditional methods of common bile duct stone extraction have included surgical removal and either dissolution or extraction of retained stones through a surgically introduced T-tube (31,32). Nevertheless, ERCP is indisputably associated with more rapid convalescence than surgery, results in fewer hospital days, and a less frequent need for a post-procedure intensive care unit stay. ERCP is comparable to surgery in younger patients, and safer than surgery in the very ill or elderly (33). Endoscopic sphincterotomy with stone extraction is the optimal treatment for a patient of any age with choledocholithiasis, with a success rate of 98%. (28,33–40). Biliary stents are an effective way of establishing free flow of bile, and can be used as a temporary measure in patients with common duct stones in whom sphincterotomy may be high-risk because of conditions such as bleeding diathesis and/or other significant co-morbidities present at that time. One advantage of biliary plastic stent placement over other endoscopic therapeutic modalities (i.e. sphincterotomy and stone extraction) is that stenting usually provides for a shorter procedure time. Therefore, this usually allows for less exposure to sedation and less risk for development of cardio-pulmonary complications. On the other hand, this approach often results in the need of a second procedure in the future for sphincterotomy and definitive stone extraction.

Complications occurring after endoscopic sphincterotomy and stone extraction are divided into early (within three months after the procedure) or later (more than three months after the procedure). Among the late complications are recurrent bile-duct stones, which occur in 4% to 24% of patients despite increasing experience and success with the procedure. Known risk factors for recurrent CBD stones are CBD dilatation (CBD diameter >13 mm), previous biliary surgery, and CBD angulation (CBD angle >145°). The prevalence of peri-ampullary diverticula increases with age, and is reported to be over 30% in patients above age 70 undergoing ERCP in some series. Peri-ampullary diverticula are also known to be a risk factor for recurrent CBD stones (37,38,41–49). With this, symptomatic recurrence of CBD stones was found to be significantly more common in older adult patients than in young patients (41).

**ACUTE CALCULOUS CHOLECYSTITIS**

Acute calculous cholecystitis may present atypically, especially in the older adult population. Hafif, et al reported that among 131 patients above 70-years of age with acute calculous cholecystitis, right upper quadrant pain was absent in 27%, and fever was absent in 45% (51). When this cannot be achieved in a particular patient, an innovative alternative option is temporary placement of a percutaneous cholecystostomy tube followed by an eventual laparoscopic cholecystectomy (52–54). In conjunction with intravenous antibiotics, this approach allows for clinical improvement in patients and decreases the subsequent chance for conversion to an open cholecystectomy (5). Laparoscopic cholecystectomy, performed two weeks following percutaneous cholecystostomy has been shown to have a conversion rate to open cholecystectomy of only 3% (55). Beyond this strategy of cholecystostomy followed by cholecystectomy, the role of nonoperative management is nearly nonexistent (5).

**ACUTE ACALCULOUS CHOLECYSTITIS**

Acute acalculous cholecystitis, or necrotizing cholecystitis, is an acute inflammation of the gallbladder in the absence of stones, and accounts for 5% to 10% of cholecystectomies performed in the United States. About 80% of patients are male, typically elderly, and critically ill. Risk factors for this disease entity include atherosclerosis, prolonged fasting, immobility, recent surgery, and hemodynamic instability (56). Therefore, in an immobile, fasting patient with hemodynamic instability, splanchnic vasoconstriction can result and the gallbladder can suffer both chemical and ischemic injury secondary to bile stagnation and decreased blood flow, respectively (56–58). The definitive treatment of acute acalculous cholecystitis is urgent cholecystectomy or cholecystostomy in patients unable to tolerate surgery. A technique using ERCP with selective cystic ductal cannulation by guidewire with nasobiliary catheter drainage has also been described and shown to be successful (59).

**CANCER OF THE BILIARY TRACT**

Cancers of the biliary tract tend to be more common in older age groups. The most common cause of jaundice in
the elderly is a malignant lesion that grows to obstruct the biliary system. The standard of care for management of biliary tract neoplasms has undergone significant changes over the past several decades, with careful attempts to preserve the patient’s quality of life. This has led to an explosion of minimally invasive procedures that can be performed endoscopically. These procedures can be employed as initial steps prior to surgery or as a mainstay of palliative therapy for patients who are deemed inoperable or have multiple and/or severe co-morbidities (14).

More sensitive techniques to determine tumor staging such as EUS and positron emission tomography (PET) scanning have provided more accurate information with which to plan management. Even though minimally invasive techniques are available to diagnose and treat biliary neoplasms, it is important to remember that surgery may be a viable option as age is no longer a contraindication for complicated surgeries such as pancreaticoduodenectomy (4,60,61). Patients with biliary neoplasms are best served by a multidisciplinary group that can work in a coordinated fashion with the geriatric specialist (14). It is crucial to have clear communication with the patient’s family and educate them concerning the nature of the disease, as well as all risks, benefits and alternatives of various invasive versus non-invasive treatment modalities. It is also important to take into account the patient’s wishes with respect to quality of life issues, while laying out all treatment options once a diagnosis has been made.

Cholangiocarcinoma

Overall, cholangiocarcinoma (CCA) is a rare neoplasm, but it remains the second most common primary hepatobiliary malignancy (62). Over the past three decades, the incidence of CCA has increased (63,64). During the 1970s, the average age at diagnosis of CCA was the sixth decade of life. In the late 1980s and during the 1990s, however, the age of diagnosis of CCA shifted toward the seventh decade of life. This age change of the affected individuals may reflect aging of the adult population with subsequent development of CCA (65).

Elderly individuals in Southeast and Eastern Asia have the highest incidence of CCA, as infestations of liver flukes are associated with intra-hepatic stones and the development of this malignancy. As such, patients from Asia can harbor flukes and may manifest with CCA after being in the United States for many years (66).

Diseases such as sclerosing cholangitis, biliary atresia, Caroli’s disease, and choledochal cysts are also associated with higher incidences of CCA. Choledochal cysts although often detected with symptom onset in the elderly, usually develop in early adulthood and often go undiagnosed until the patient presents with abdominal pain, elevated liver associated enzymes, with pancreatitis and/or cholangitis. According to its location in the biliary tree, CCA is classified into extrahepatic and intrahepatic types. The extrahepatic type accounts for approximately two thirds of all CCA and is further divided into [1] hilar or Klatskin, [2] middle, and [3] distal tumors. Intrahepatic CCA is classified into 4 growth types: [1] mass forming, [2] periductal infiltrating, [3] mass forming plus periductal infiltrating, and [4] intraductal (67). Whether CCA is intrahepatic or extrahepatic, the usual microscopic appearance is that of adenocarcinoma. Other histological variants include papillary adenocarcinoma, signet-ring carcinoma, squamous cell or mucoepidermoid carcinoma, and a lymphoepithelioma-like form (65). Sarcomatoid transformation has been observed in up to 4.5% of CCA cases (68).

The classic presentation of CCA includes jaundice, right upper quadrant pain, pruritus, and weight loss (66). The presentation of CCA is primarily governed by its anatomic location. Hilar and distal extrahepatic bile duct cancers present with symptoms of biliary obstruction, cholangitis, and right upper quadrant pain (62). Intrahepatic cholangiocarcinomas present as mass lesions and obstructive lesions are rare. Anorexia, fever and night sweats may also occur in addition to right upper quadrant pain (62,65). A dilated gallbladder (Courvosier’s sign) or an incidental abdominal mass (in asymptomatic patients) may be felt on physical examination (65, 66). Laboratory values usually show a pattern of obstructive cholestasis with increased alkaline phosphatase and bilirubin. The serum marker CA 19-9 may be increased.

Elderly patients who have a low CEA level, demonstrate an intraductal papillary growth pattern, curative hepatectomy and those who undergo post-operative chemotherapy tend to have the most favorable survival, although these trials have not focused on the elderly population per se (69). Data does suggest
that elderly patients with bile duct tumors should not be denied surgical evaluation based solely on age (4).

Since the natural history of CCA is short and most patients present with advanced disease, they are often candidates mostly for palliative therapy (62). Additionally, because CCA usually affects the elderly, a percentage of surgical candidates have comorbidities that preclude an operation for tumor resection. Palliative therapies aim at improving or resolving obstructive jaundice and subsequently ameliorating patient symptoms. It is important to note that relief of obstructive jaundice in patients with CCA improves symptoms and quality of life but not survival (65).

Surgical biliary bypass is associated with a high perioperative morbidity and mortality. Endoscopic palliative therapies of obstructive jaundice include biliary stenting, photodynamic therapy (PDT), and intraluminal brachytherapy (65). The endoscopically placed biliary endoprosthesis is widely accepted as a palliative treatment for malignant biliary obstruction (70–72). Metal stents remain patent longer than plastic stents and should be considered in patients with an anticipated survival of least three-to-six months, as these stents have been shown to be cost-effective in patients who survive greater than three months (65,73,74).

Gallbladder carcinoma
Carcinoma of the gallbladder accounts for approximately two-thirds of all cancers of the extrahepatic biliary tract, and tend to occur in older patients. Approximately 90% of these have histology consistent with adenocarcinoma, including papillary, intestinal type, mucinous, clear cell, and signet ring variants. Gallbladder adenocarcinoma has been found to correlate with the presence of gallstones, which can be present in 50% to 88% of patients (75). It is believed that the majority of patients with carcinoma of the gallbladder have gallstones although the converse is not true. Other risk factors for the development of gallbladder carcinoma are female gender, polypoid lesions of the gallbladder greater than 1cm, and a history of smoking (76–78). With the increasing use of ultrasound in modern practice, more and more polypoid lesions of the gallbladder are being detected. Although most gallbladder polyps are benign, some early carcinomas of the gallbladder do share the same appearance as benign polyps (78).

In the absence of jaundice as a part of the presentation, the diagnosis of carcinoma of the gallbladder is typically made at the time of cholecystectomy for what was thought preoperatively to be acute or chronic cholecystitis (4). Data demonstrates that approximately 10% of patients older than 60-years of age who presented with symptoms and physical signs consistent with acute cholecystitis had a neoplastic process involving their gallbladder. Indeed, many gallbladder carcinomas are found incidentally intra-operatively during routine cholecystectomy. Imaging studies, including CT scanning, ultrasound, nuclear scanning, and arteriography have all been used for the diagnosis of gallbladder carcinoma (79). Nonetheless, despite a detection rate of advanced gallbladder cancer in the range of 80% to 90%, only 20% to 30% of early lesions are diagnosed before operation even in the best of hands (80).

Clearly, the most important element in making a correct diagnosis is a high index of suspicion. Gallbladder polyps greater than 1cm are recommended for surgical removal in view of the higher chance of malignancy (78). For gallbladder carcinoma, surgical treatment provides the opportunity for long-term survival only when complete resection is performed (81). When the likelihood of gallbladder carcinoma is considered high, open, rather than laparoscopic cholecystectomy should be performed (79). Complete resection of the gallbladder cancer with enough margin and lymph node dissection should be performed, even for T1 tumors (82).

In the treatment of unrecognized carcinoma of the gallbladder, a radical second operation is recommended in aged patients for more than T2 tumors or when residual cancer is suspected in the cystic duct. Even in elderly patients, complete resection is an essential treatment for carcinoma of the gallbladder. However, it is important to remember that advanced carcinoma of the gallbladder results in a poor outcome even if resection is possible (83–85). More aggressive surgery including extended hepatectomy, pancreaticoduodenectomy, or both, is indicated for patients with advanced disease although these operations carry a higher risk of morbidity and mortality for advanced gallbladder malignancy (86–88).

(continued on page 22)
Rarely seen histologic types of gallbladder carcinoma include squamous cell, adenosquamous, undifferentiated carcinoma, carcinosarcoma, and small cell carcinoma (89). The median age at diagnosis is approximately 70-years of age (4). Melanoma has also been described in the gallbladder. Malignant melanoma is the most common tumor to metastasize to the gallbladder, accounting for 60% of all metastatic lesions. The mortality of melanoma metastatic to the GI tract is dismal, with a median survival of six-to-10 months after detection (90). Carcinoid tumors and lymphoma have also been reported in the gallbladder (89,91).

**OTHER DISEASES OF THE BILIARY TRACT**

**Benign Strictures**

There are many causes of benign biliary strictures. The most common are iatrogenic causes, particularly following cholecystectomy. Other causes relevant to the elderly population are traumatic, parasitic, inflammatory, and idiopathic including: gallstone perforation, blunt abdominal trauma, 
*Clonorchis sinensis*, 
*Ascaris lumbricoides*, papillary stenosis, ischemia, and post-radiotherapy (92). Even a low-grade biliary obstruction secondary to a benign stricture (i.e., as seen in chronic pancreatitis) carries a risk of stone formation and ascending cholangitis and it is important to identify and treat these patients accordingly. In general, differentiating between benign and malignant strictures, especially in the elderly, is of utmost importance and often can be particularly difficult. With the advent of intraductal cholangioscopy, it has become easier to identify intraductal lesions for better differentiation between benign and malignant strictures. Clinical findings may range from a subclinical derangement of liver function tests to the full picture of hepatic obstruction with jaundice, biliuria, and pruritus. If an elderly patient does require urgent relief of obstruction, ERCP should be performed. ERCP can serve a diagnostic and therapeutic purpose when brushings/biopsies are taken, and the obstruction is relieved after balloon dilation and placement of a plastic stent. Patients can be given the option of repeated endoscopic insertion of plastic stents. However, as the risk of recurrent cholangitis still remains, many patients do require surgical biliary bypass for definitive treatment of their stricture.

**Hemobilia**

Hemobilia occurs when there is a fistula between a vessel of the splanchnic circulation and the intrahepatic or extrahepatic biliary system (93). The age distribution of patients with hemobilia tends to peak in the sixth decade of life (94). With the increasing use of percutaneous liver and biliary procedures, especially in older adults, there has been an increase in the incidence of iatrogenic hemobilia such that this has become the most commonly reported cause (93). The incidence of hemobilia following percutaneous transhepatic cholangiography (PTC) is up to 4% (95). Stenting of biliary strictures is associated with an incidence of hemobilia in up to 10% of procedures (96–98). Other causes of hemobilia include blunt trauma, cholecystitis, vascular malformations, and tumors.

Quinke described a triad of signs and symptoms associated with the presentation of hemobilia (99). The symptoms include upper abdominal pain, upper gastrointestinal hemorrhage, and jaundice. All three may be present in up to 22% of patients, but this percentage may be lower in an older adult patient. The hemorrhage may be of rapid onset following liver trauma, or may be delayed by weeks. One has to be cautious in terms of relying on these symptoms in the elderly, as they may present atypically. Thus, a high level of suspicion must exist. For patients with upper gastrointestinal bleeding where hemobilia is suspected, esophagogastroduodenoscopy (EGD) is the first investigation of choice (93). Angiography is now recognized as the definitive investigation, and can be expected to detect a vascular abnormality in over 90% of cases of significant hemobilia (100). Angiography is a relatively safe procedure in an elderly patient who does not have chronic kidney disease or dye allergy. Many patients though, can be managed adequately on the basis of endoscopic findings (93). Cholangiography is useful if there is already percutaneous access or if ERCP is performed (101,102). Cholangiography with intervention is useful if biliary decompression and restoration of bile flow past clots is necessary. The management of hemobilia is directed at stopping bleeding and relieving biliary obstruction if present. Transarterial embolization (TAE) is now the first line of intervention to stop bleeding, as the success rate can be as high as 100%. With advancing technology and the advent of new diagnostic and therapeutic techniques, the mortality associated with hemobilia is low (93).
Biliary Papillomatosis

Biliary papillomatosis is a rare disorder. It is characterized by the occurrence of multiple papillary adenomata in the biliary tract with significant risk of malignant transformation (103). The natural history and pathogenesis of this disease is still unknown (103,104). Lam, et al described the mean age of presentation of biliary papillomatosis 72-years of age. Most patients present with recurrent cholangitis or jaundice, and malignant transformation can occur in up to 42% of patients. Various biliary conditions, including recurrent pyogenic cholangitis, have been associated with biliary papillomatosis. It has been postulated that long-term stimulation of the bile duct by stone, infection, or pancreatic juice and subsequent reactive biliary hyperplasia may contribute to the pathogenesis (105–107). A preoperative diagnosis of biliary papillomatosis could easily be missed at the first instance even if patients present typically with biliary obstruction and undergo appropriate investigations (108–110).

Typically during ERCP, a dilated papillary orifice with excessive mucin discharge could be observed. Multiple filling defects in the lumen of the biliary system and supple stenoses can also be seen. Histologic examination specimens taken after sphincterotomy have shown the typical lesions of papillomatosis in certain patient series (108). Radical surgery is recommended in patients who can withstand it because of the considerable risk of malignant transformation and the diffuse pattern of disease, and to date this is the only treatment to achieve long-term survival. If the patient is unfit or unwilling to undergo major surgery, local ablative procedures, palliative stenting, or drainage can be considered (104).

CONCLUSION

Biliary diseases in the elderly are becoming an increasingly important aspect of gastroenterology. Technological advances in imaging and therapeutics will allow more aggressive clinical care plans in patients who as recent as five years ago would have been deemed suitable only for palliation. It is estimated that by the year 2050, 23% of the United States population will be over 65-years of age (1). As this elderly population increases, 75% of healthcare expenditures will be focused on the elderly by the year 2030 (2). As biliary disorders represent some of the most common and feared conditions that affect the elderly, we believe that knowledge and awareness of the various presentations, approach, and management of these disorders in the elderly is of vital importance as well as mandatory for the practicing gastroenterologist today.

References

22. Bingener J, Richards ML, Schwesinger WH, Strodel WE, Sirinek KR. Laparoscopic cholecystectomy for elderly patients: gold stan-
Biliary Diseases in the Elderly

GERIATRIC GASTROENTEROLOGY, SERIES #19

47. Sugiyama M, Atomi Y. Risk factors predictive of late complications after endoscopic sphincterotomy for bile duct stones: long-term (more than 10 years) follow-up study [see comment]. J Gastroenterol, 2002;37(11):2763-2767.

(continued on page 26)
Biliary Diseases in the Elderly

GERIATRIC GASTROENTEROLOGY, SERIES #19

(continued from page 24)


