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Congenital Short Bowel Syndrome

Short bowel syndrome is a clinical disorder characterized by diarrhea, malabsorption and needs of parenteral nutrition for life support. In newborns, short bowel syndrome is most commonly an acquired disorder after surgical bowel resection due to conditions such as necrotizing enterocolitis, gastroschisis, volvulus, extensive aganglionosis in Hirschsprung's disease, or intestinal atresia. Born with a short bowel known as congenital short bowel syndrome (CSBS) is a very rare condition in newborns associated with a high mortality rate and prognosis. According to autopsy reports, the length of the small intestine as measured from Treitz to ileocecal valve correlates with crown-to-heel length. The mean length of the small bowel in full term infants is approximately 240 cm and increases to 600 cm in adulthood. Short bowel syndrome manifests in newborns when the small bowel length is less than 75 cm. Newborns with CSBS can be as short as 20 cm in length, with a mean length of 50 cm. The pathogenesis of CSBS is poorly understood. CSBS occurs most often in association with malrotation (> 96%). The normal elongation, rotation and herniation of the small bowel is interrupted or delayed due to lack of space between the developing digestive tube and umbilical celom. Other believe is a defective neuroenteric development since intestinal dysmotility is an important component of the syndrome. Children born with CSBS have a loss of function nonsense mutation in the CLMP (Coxsackie- and adenovirus receptor-like membrane protein). CLMP encodes a tight-junction membrane protein of the bowel, located in chromosome 11, and expressed during embryonic development. Mutations in CLMP cause a recessive form of CSBS. In other patients a mutation in FLNA gene was found in chromosome X, which encodes for a cytoskeletal protein called filamin A that binds to actin. Other congenital anomalies associated with CSBS include pyloric stenosis, appendiceal agenesis, acheiria, dextrocardia, hemivertebrae and paten ductus arteriosus. Clinically, most babies with CSBS develop bilious vomiting, diarrhea, failure to thrive with signs/symptoms consistent with intestinal obstruction. Onset of intestinal volvulus associated with acute mesenteric ischemia is rare in these patients since a short bowel length precludes twisting. CSBS is diagnosed by barium-contrast studies and confirmed by exploratory laparotomy. Management of CSBS consist of parenteral nutrition with early introduction of enteral nutrition. In the event of failed adaptation and liver failure with reduced venous access from treatment, transplantation becomes the hope for these children. Survival beyond the first year with CSBS is 75% and improving. Most common cause of death is sepsis.

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Biliary Dyskinesia

Biliary Dyskinesia (BD) is characterized by an abnormal gallbladder contractility identified using cholecystokinin-stimulated hepatobiliary iminodiacetic acid (HIDA) nuclear scans. BD is a diagnosis of exclusion so other causes such as irritable bowel syndrome, dyspepsia, GE reflux disease needs to be rule out. The diagnosis is established when the gallbladder has an ejection fraction less than 35% and the child has typical symptoms of biliary colic without gallstones. Gallbladder dyskinesia is becoming the most common indication for gallbladder removal in adults and pediatric population. The most accepted pathogenesis of BD is uncoordinated contractions and relaxation of both the gallbladder and sphincter of Oddi. Subsequent distension of the gallbladder leads to inflammation, hypersensitivity and dysfunction. 75% of affected cases are females, most cases are white adolescents and almost 50% are obese. Major preoperative symptoms in children with BD include nonspecific vague chronic right upper quadrant/epigastric abdominal pain, nausea, postprandial pain, fatty food intolerance, vomiting, constipation and diarrhea in this order of frequency. Children with symptoms and BD undergo a series of preoperative studies without significant pathologic findings such as US, CT-Scan, MRI, UGIS and upper/lower GI endoscopy. Most of these cases are referred by pediatric gastroenterologist after trying several medical management options. Initially more than 80% claim pain improvement after cholecystectomy, but two years or more after surgery 30-40% continue with similar symptoms. The difference between short and long-term results may be due to true recurrence of symptoms or inaccurate reporting by parents who wants to please the surgeon. Two-third of gallbladders removed due to BD shows chronic cholecystitis. Patients with chronic inflammation are more likely to persist with symptoms at long-term follow-up. An ejection fraction below 15% is usually associated with a higher resolution of symptoms after cholecystectomy. BMI percent, pain during CCK administration during the HIDA scan and presence of chronic cholecystitis does not predict which patient will have short or long-term improvement in symptoms. Factors independently associated with short term pain improvement after cholecystectomy includes shorter duration of pain before surgery, history of vomiting preop, no history of fevers or obstructive sleep apnea. Factors independently associated with short-term complete symptoms, resolution includes history of epigastric pain and lower GI disease. Longer duration of symptoms predicts poor outcome after

cholecystectomy in BD. Symptoms of functional dyspepsia overlap with symptoms of BD in children. There is no well-defined nonsurgical management of BD. Some researchers advocate medical over surgical management of BD since BD is not a life-threatening condition, there are no serious complications, and some children continue to experience symptoms after cholecystectomy. With persistent abdominal pain after cholecystectomy there is a high index of suspicion for sphincter of Oddi dysfunction. Studies comparing cholecystectomy to nonsurgical medical management show same results in both groups.

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Pancreatic Cyst Fluid Analysis

The extensive use of ultrasound has uncovered symptomatically as well as asymptomatic pancreatic cysts. The majority of pancreatic cysts are found incidentally when abdominal imaging is performed for other indications. Pancreatic cysts can either be simple (retention) cysts, pseudocysts and cystic neoplasm. Cystic neoplasms are further subdivided into serous cystadenomas, mucinous cystic neoplasms, intraductal papillary mucinous neoplasms or papillary cystic neoplasms. The majority of pancreatic cystic lesions identified are mucinous cystic neoplasms. Since some of these pancreatic cysts can develop into malignancy, a diagnosis performing aspiration and analysis of the cyst fluid must be undertaken. Accurate diagnosis leads to effective and standard management. This can be achieved using either US- or CT-guided percutaneous aspiration or endoscopic ultrasound fine needle aspiration. The diagnostic accuracy after aspiration is very high (~ 95%). The fluid is analyzed for cytology, viscosity, extracellular mucin, tumor markers (CEA, CA 19-9, CA 15-3, CA 72-4, CA 125), enzymes (amylase/lipase) and DNA quality/content or mutational analysis. Mutational analysis can further characterize allelic imbalances, loss of heterozygosity (LOH) and K-ras mutation. Estimates of the cyst fluid volume can be approximated using the formula $4r^3$, where r is the radius of the cyst. Imaging is the less accurate in the diagnosis of pancreatic cystic lesions. Surgical resection is recommended if a cyst has both a solid component and dilated main pancreatic duct. Viscosity is lower in

pseudocysts (1.3) and serous cystadenomas (1.27), compared with mucinous cystadenoma (1.84) and mucinous cystadenocarcinomas (1.90). CEA levels are high in mucinous cystadenomas and very high in mucinous cystadenocarcinomas when compared with pseudocysts and serous cystadenomas. Elevated CEA and viscosity accurately predict mucinous cysts. The presence of extracellular mucin is predictive of a mucinous neoplasm. Cytological identification of extracellular mucin and CEA elevation are predictors of mucinous neoplasm and malignancy. Cytology detects mucin containing cells, malignant cells, glycogen-rich cuboidal cells, branching papillae and abundant enucleate squamous cells and debris. Cytology is diagnostic in less than 60% of pancreatic cysts. CA19-9 cyst fluid levels above 50,000 U/ml are found in mucinous cystadenoma and cystadenocarcinomas. Levels below 37 U/ml suggest serous cystadenomas or pseudocysts. CA 19-9 is suitable for detection of malignancy but is insensitive for premalignant lesions. CA 72-4 cyst fluid levels above 40 U/ml are significantly high in mucinous cystic tumors. CEA levels greater than 400 ng/ml are characteristic of mucinous tumors and cystadenocarcinoma, while CEA levels less than 4 ng/ml are associated with serous cystadenomas. Cyst fluid CEA is the most accurate test available for diagnosis of mucinous cystic lesions of the pancreas with a cut off value of 192 ng/ml for diagnosis. In some centers CEA is the only tumor marker routinely use for diagnostic work-up. Amylase/lipase high levels (above 250 U/L) are commonly seen in pseudocysts. Cyst fluid amylase is of limited utility in evaluation of pancreatic cysts. Low values are associated with a neoplastic tumor. DNA analysis has found that a K-ras mutation followed by allelic loss is most predictive of malignancy in a pancreatic cyst. In malignant cysts, elevated CEA is more predictive of histology than K-ras or LOH mutations. DNA mutational analysis should be used selectively rather than routinely. Costs are significant with DNA analysis. Confocal laser endomicroscopy (CLE) is a novel technology for real time in vivo microscopic imaging using a probe inserted through a 19-G needle. CLE findings of mucinous tumors include finger-like papillae with layers of a thick band-like epithelium. Serous cysts have a superficial network or fern-type pattern, while pseudocysts contain bright particles. Cytology, CEA levels and -K-ras mutation analyses are the most important in clinical practice. Is important differentiate between benign and malignant lesions to determine whether surgical resection or conservative management is required. (See attached Table).

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Table: Pancreatic Cyst Fluid Analysis

	Pseudocysts (inflammatory)	Serous Cystadenomas	Mucinous cystadenomas/Intraductal papillary mucinous cystic neoplasms	Solid pseudopapillary tumors
Appearance/Viscosity	Thin-brown fluid viscosity = 1.3	Thin-clear fluid Viscosity = 1.27	Thick-clear fluid Viscosity = 1.84 to 1.90	Bloody
Amylase/lipase	High levels amylase > 250 U/L	Low	variable	Low
Cytology	Inflammatory cells, debris	Glycogen rich cuboidal cells	Mucin-containing columnar cells, atypia	No typical findings; inflammatory cells and debris
Tumor Markers	CEA low; < 5 ng/ml CA 19-9 < 37 U/ml	CEA low CA 19-9 < 37 U/ml	CEA > 192 ng/ml (most accurate) CEA > 400 ng/ml for IPMC CA 19-9 > 50,000 U/ml CA 72-4 > 40 U/ml	CEA low
Mucins	No typical finding	No typical finding	Positive staining	No typical finding
DNA	K-ras mutation absent	K-ras mutation absent	K-ras mutation specific for mucinous cysts; allelic loss	K-ras mutation absent
Laser Endo-microscopy	Bright particles (inflammatory cells)	Superficial vascular network/fern pattern	Finger-like papillae/thick layer of band like epithelium	Not well defined

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