Pediatric Gastrointestinal Endoscopy:

European Society of Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) and

European Society of Gastrointestinal Endoscopy (ESGE) Guidelines.

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Abstract

This Guideline refers to infants, children and adolescents aged 0-18 years. The areas covered include: indications for diagnostic and therapeutic esophagogastroduodenoscopy and ileo-colonoscopy; endoscopy for foreign body ingestion; corrosive ingestion and stricture/stenosis endoscopic management; upper and lower gastrointestinal bleeding; endoscopic retrograde cholangio-pancreatography and endoscopic ultrasonography. Percutaneous endoscopic gastrostomy and endoscopy specific to inflammatory bowel disease (IBD) has been dealt with in other Guidelines [1-3] and are therefore not mentioned in this Guideline. Training and ongoing skill maintenance are to be dealt with in an imminent sister publication to this.

Time definitions used:

Emergent/emergency: <2 hours.

Urgent/urgently: <12 hours or <24 hours and defined in text.

Early: <48 hours but may be at clinician's discretion.

Introduction

Gastrointestinal (GI) endoscopy in the pediatric population has evolved during the last thirty years with an increasing number of diagnostic and therapeutic applications. Technological improvements in endoscope design and endoscopic devices have contributed to the evolution of pediatric endoscopy.

Endoscopy in the pediatric population has generally, to date, been performed by both non-pediatric endoscopists and pediatric endoscopists.

The aim of this evidence-based and consensus-based Guideline, commissioned by the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) and the European Society of Gastrointestinal Endoscopy (ESGE) is to provide a comprehensive review of the clinical indications and timing of diagnostic and therapeutic endoscopy in pediatric patients. It is not meant to be a comprehensive overview of a patient's care and investigation/therapy for each area will, of course, involve the clinician's discretion in terms of the place of endoscopy in overall management, encompassing, as it must, complementary non-endoscopic approaches. The role of endoscopy in the overall management will depend on a number of factors including but not limited to the specific clinical features, the availability/appropriateness of non-endoscopic approaches, and the available skills of the endoscopist. This Guideline tries to address this issue of endoscopist skills, and certainly the upcoming ESPGHAN/ESGE Guideline on training in pediatric endoscopy will help in this respect. How, where and when endoscopy may be employed in pediatric management is particularly important in the areas of GI bleeding and ERCP/EUS.

This undertaking is the first joint endoscopy review between pediatric and adult endoscopy representative groups in Europe. Our aspiration is that the Guideline may lead to a degree of standardization in the utility and practice of endoscopic approaches for children, thereby contributing to excellence and appropriateness of care.

Percutaneous endoscopic gastrostomy and endoscopy specific to inflammatory bowel disease (IBD) have been dealt with in other Guidelines [2–4], and are therefore not mentioned in the pediatric GI endoscopy [1] Guideline. Training and ongoing skill maintenance will be addressed in an imminent sister publication.

Methods

ESPGHAN and ESGE agreed to develop a joint Guideline. Two guideline leaders (MTh for ESPGHAN and AT for ESGE) invited the listed authors to participate in the project. The key questions were prepared by the coordinating team (AT, MTh, MMT, RF, YV, JMD) and then approved by the other members. The coordinating team established task force subgroups, each with its own leader, and assigned the following key topics among these task forces: esophagogastroduodenoscopy (EGD) and ileo-colonoscopy (IC); foreign bodies (FB); corrosive ingestion; corrosive ingestion and esophageal strictures/stenoses; GI bleeding; endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasonography (EUS). Each task force performed a systematic literature search to prepare evidence-based and well-balanced statements on their assigned key questions. Searches were performed in PubMed and/or EMBASE and/or Cochrane (publication year from 2000 to May 2015 or before if strictly needed) including as a minimum the key words 'pediatric' and 'endoscopy'. All articles studying the application of diagnostic and therapeutic endoscopy in the pediatric age range were selected by title or abstract. The results of the relevant publications were summarized in literature tables and graded by the level of evidence and strength of recommendation according to the GRADE system (Grading of Recommendations Assessment, Development and Evaluation) [4,5]. Each task force proposed statements on their assigned key questions which were discussed and voted on during the plenary meeting held in February 2015 in Munich. In November 2015, a draft prepared by AT, CH and MTh was sent to all group members. After agreement from all the authors on a final version, the manuscript was reviewed by two members of the ESGE Governing Board, ESGE individual members and the ESPGHAN Council. The manuscript was then submitted to the *Journal of Pediatric Gastroenterology and Nutrition* for publication in full length, and to

Endoscopy for publication of an executive summary. Both the Guideline and Executive summary were issued in 2016/17 and will be considered for review and update in 2021/22 or sooner if new and relevant evidence becomes available. Any updates to the Guideline in the interim will be noted on the ESPGHAN and ESGE and websites: http://www.espghan.org/guidelines/; http://www.esge.com/esge-guidelines.html

ESOPHAGO-GASTRO-DUODENOSCOPY (EGD)

ESGE/ESPGHAN suggest diagnostic and therapeutic EGD for the indications listed in Tables 1 and 2, respectively.

(Weak recommendation, low quality of evidence)

ESGE/ESPGHAN do not suggest EGD in the case of uncomplicated gastroesophageal reflux, functional gastrointestinal disorders or for diagnosing perforation.

(Weak recommendation, low quality of evidence)

ESGE/ESPGHAN suggest routine tissue sampling even in the absence of visible endoscopic abnormalities in all children undergoing EGD.

(Weak recommendation, low quality of evidence)

ESGE/ESPGHAN suggest using ESPGHAN guidelines (eosinophilic esophagitis, eosinophilic esophagitis, Helicobacter pylori (H. pylori), celiac disease (CD), and [IBD])) for precise indications and preferred sites for biopsy during EGD in children suspected of a specific disease. (Table 3)

ESGE/ESPGHAN suggest performing EGD in children under general anesthesia (GA) or, only if GA is not available, deep sedation in a carefully monitored environment.

(Weak recommendation, low quality of evidence)

ESGE/ESPGHAN suggest performing EGD in a child-friendly setting with appropriate equipment and by an endoscopist trained in pediatric gastroenterology.

(Weak recommendation, low quality of evidence)

ESGE/ESPGHAN suggest that when adult endoscopists perform pediatric procedures, collaboration between adult gastroenterologists and pediatricians is always warranted.

(Weak recommendation, low quality of evidence)

ESGE/ESPGHAN suggest that the choice of the gastroscope type should depend on the child's weight and age (Table 4).

EGD is a useful diagnostic and therapeutic tool in children [6], from which information can be obtained from visualization and biopsy of the mucosal surfaces of the esophagus, stomach and duodenum. Although one third of children have a sore throat or hoarseness after EGD, EGD is generally considered to be safe for all ages [7]. In a pediatric cohort including 345 procedures (231 EGD alone, 26 colonoscopy alone, 44 combined EGD and colonoscopy) in 301 children with a median age of 7 years, 20 (5.8%) adverse events were reported (12 secondary bleeding following variceal banding/sclerotherapy, 2 colonoscopy-related perforations, 6 anesthesia-related) [8]. Fourteen events were procedure-related (12 secondary bleeding after banding or sclerotherapy, 2 bowel perforations during colonoscopy) and 6 were anesthesia/sedation related. None of the adverse events were fatal. However, it is important in order to minimize risk of complications, that EGD only should be performed for appropriate indications and by well-trained endoscopists [6]. A diagnostic EGD is indicated in the presence of symptoms listed in *Table 1* in order to confirm an underlying disease. A selection of therapeutic indications are also listed in *Table 2*. Non-

indications are uncomplicated gastroesophageal reflux and functional GI disorders. Contraindications include diagnosis of perforation *(Table 1)*.

Routine tissue sampling according to the indication, even in the absence of visible endoscopic abnormalities, is of major importance in all children undergoing EGD. Two studies in children assessed the value of routine esophageal, gastric and duodenal biopsies and new diagnoses based on biopsy samples alone were identified in 17% and 11% [9,10]. A study including 823 infants younger than 1 year of age, a group in which both symptoms and signs are notoriously difficult to interpret, the histological findings during EGD and/or colonoscopy were helpful in diagnosis in 63.8% of the cases [11]. One pediatric study showed that biopsies from the first and third part of the duodenum were important when assessing a patient for suspected celiac disease: biopsies from the duodenal bulb had an incremental diagnostic yield of 10.6% compared with biopsies only from the third part of the duodenum [12]. *Table 3* sets out the ideal location for biopsies to allow the greatest diagnostic yield with respect to suspected diagnosis [2,13-15]. In contrast to adults, in children EGD should be performed with GA or, if not available, under deep sedation with a specifically trained pediatrician in charge only of the sedation leaving the endoscopist to concentrate on the procedure alone. Propofol-based sedation is likely to be the safest and most convenient way of sedation however this remains the subject of debate [16]. Furthermore, endoscopy should be performed in a child-friendly setting. This is a very important point and pertains to not only the child but the family. The 'journey' that a child and their parents/carers take should involve wherever possible a pre-visit to the unit, a play specialist to allow an age-specific approach to prepare the child, a non-threatening environment with age-appropriate wall decorations and toys, an anesthetist with the requisite human skills to allay the fears of the child and their family and a recovery area that is child-specific with parents/carers invited to be present before their child fully wakes. A multidisciplinary team consisting of a pediatric anesthetist, pediatric gastroenterologist, endoscopic nurse and specialized pediatric nurses, should be available to take care of the specific needs of pediatric patients. In some hospitals, adult endoscopists are needed to perform advanced therapeutic procedures which are not routinely performed by a pediatric gastroenterologist and these are

dealt with further on in this Guideline, however the advanced training of pediatric endoscopists is occurring and it is envisaged that upper GI endo-therapeutic procedures in the near future in children will and should be performed routinely by such individuals, as already occurs in a small number of supra-regional centers at present. A retrospective study suggested that 'adult' endoscopists when supported by pediatricians are able to safely conduct EGD and IC in children but this Guideline Group suggest that this should not be the ideal arrangement and that pediatric endoscopists should manage the child and perform the procedure thereby providing a seamless service [17]. The choice of the equipment including the actual endoscope depends on a child's weight and age. *Table 4* details the different endoscope sizes as adapted from American Society for Gastrointestinal Endoscopy (ASGE) [18].

ILEO-COLONOSCOPY

ESGE/ESPGHAN suggest ileo-colonoscopy for the diagnostic and therapeutic indications listed in Table 5.

ESGE/ESPGHAN suggest against ileo-colonoscopy in the case of toxic megacolon, recent colonic perforation (<28 days), recent intestinal resection (< 7 days) or functional GI disorders.
(Weak recommendation, low quality of evidence)

ESGE/ESPGHAN suggest performing ile-ocolonoscopy in children under GA or, only if GA is not available, deep sedation in a carefully monitored environment.
(Weak recommendation, low quality of evidence)

ESGE/ESPGHAN suggest that ileo-colonoscopy should be performed in a child-friendly setting with appropriate equipment and by an endoscopist trained in pediatric gastroenterology.

ESGE/ESPGHAN suggest that when non-pediatric endoscopists perform pediatric procedures in older children, collaboration with a pediatrician is always warranted.

(Weak recommendation, low quality of evidence)

ESGE/ESPGHAN suggest that the choice of the colonoscope type should depend on child's weight and age (Table 4).

In children, IC is primarily indicated for suspected IBD, in cases of per-rectal bleeding and/or unexplained anemia [6] and for genetic polyposis syndromes including familial adenomatous polyposis (FAP) [19-21] (*Table 5)*. The recommendations concerning environment, endoscopists and type of endoscopes are similar to those formulated for EGD. There are no published data to support specific colonoscope choice in children but recommendations based on experience state that the lower weight limit for use of a standard adult colonoscope is around 10 kg *(Table 4).* The largest safety report was a 5-year retrospective database study of 7792 procedures with an overall complication rate of 1.1% of which approximately 50% were GI-related, most commonly bleeding, 30% were cardiopulmonary complications, and 10% were miscellaneous which included allergic drug rash reactions amongst others. Perforation was very uncommon (0.01%) [22] and as in adults, perforations in children are mostly due to advancement of the endoscope itself or are related to polypectomy, not to biopsy.

BOWEL PREPARATION FOR ILEO-COLONOSCOPY IN CHILDREN.

ESGE/ESPGHAN recommend low-volume preparation for bowel cleansing in children, using either polyethylene glycol (PEG) plus ascorbate or picosulphate magnesium citrate/Senokot.

(Strong recommendation, high quality of evidence)

ESGE/ESPGHAN recommend against the use of sodium phosphate for bowel cleansing.

(Strong recommendation, high quality of evidence)

Success and safety of IC relies very much on the quality of bowel preparation. In adults, ESGE Guidelines recommend a low-fiber diet on the day preceding ileo-colonoscopy and a split regimen of 4L PEG solution; alternatives include a split regimen of 2L PEG plus ascorbate or of sodium picosulphate plus magnesium citrate [23]. The ESGE advised against the use of oral sodium phosphate due to the risk of renal insufficiency. Furthermore, PEG is the only recommended regimen in patients with renal failure [23]. In children, a national working group performed a systematic review and a national-based survey of all endoscopy units performing IC in Israel [24]; six different protocols were compared but none of these showed significant advantages. Another publication concluded that the most used agents in children include PEG-3350 solutions, picolax, senna, bisacodyl, and magnesium salts [25]; their efficacy was found to be similar. Recently a randomized controlled trial (RCT) including 299 children evaluated four different regimens [26]: the three low-volume regimens were non-inferior in terms of bowel cleansing compared with the "high-volume" regimen (PEG at a dose of 100 ml/kg, maximum 4 L). Of note, low-volume regimens were better tolerated and were associated with a less frequent need for nasogastric tube placement compared with the high-volume regimen. The authors suggested that the most suitable low-volume preparation was sodium picosulphate plus magnesium citrate. Regimens using sodium picosulphate with magnesium citrate (sodium picosulfate 0.01 g, magnesium oxide 3.5g, citric acid 12.0g per sachet) are used as follows: two doses 5-10 hours apart (0.25 sachet/dose for <6 year, 0.5 sachet/dose for 6-12 years, 1 sachet/dose for >12 years) with liberal drinking of clear fluids such as cold tea/sport drinks and approximately 40 ml/kg after each dose.

ILEO-COLONOSCOPY IN CHILDREN: BIOPSY, CARBON DIOXIDE INSUFFLATION, ILEAL INTUBATION, POLYPECTOMY TECHNIQUE.

ESGE/ESPGHAN suggest routine biopsy even in the absence of visible endoscopic abnormalities in all children with suspected IBD undergoing ileo-colonoscopy.

ESGE/ESPGHAN suggest using ESPGHAN guidelines relating to ulcerative colitis and the revised Porto criteria for diagnosis of IBD for precise indications and preferred sites to biopsy.

ESGE/ESPGHAN did not find any evidence to recommend against or for the use of routine CO_2 insufflation during IC in children. Pain seems to be rare and mild after IC in children.

ESGE/ESPGHAN suggest that ileal intubation should be attempted in symptomatic children with abdominal pain, intestinal bleeding, diarrhea or with any suspicion of IBD.

ESGE/ESPGHAN suggest removal of very small polyps (<3 mm) by cold biopsy forceps and 3-8mm polyps by hot or cold snaring. Cold snaring is advisable in the right colon where the perforation risk is higher. For polyps >8 mm, hot snaring is suggested.

A study on 390 pediatric ileo-colonoscopies reported 84% agreement between endoscopists and pathologists, especially when an endoscopist reports normal-appearing colonic mucosa and if histology was considered the gold standard, endoscopy was found to have a 90% sensitivity and 78% specificity [27]. When children present with diarrhea, abdominal pain, weight loss or other symptoms where initial investigations are normal and in the absence of macroscopic lesions of the colon, biopsies should be taken

from different colonic segments in order to exclude conditions such as collagenous or microscopic colitis [28]. Collagenous colitis is rare in children. One very small study found that 5/26 children with chronic diarrhea and macroscopically normal colonic mucosa had histological abnormalities (3 lymphocytic colitis and 2 collagenous colitis) [29]. In suspected pediatric IBD, recent ESPGHAN Guidelines highlighted the importance of biopsies in all segments of the lower digestive tract in order to differentiate Crohn's disease from ulcerative colitis and to determine the extent of the inflammatory process [3,15]. At the initial diagnostic stage, the presence of a granuloma allows differentiation between Crohn's disease and ulcerative colitis and when combined with EGD can make this distinction in up to 15-20% of cases over and above that which is made by IC alone [30]. Granulomas are more frequently observed when the biopsies are performed at the edges of ulcerative lesions [31,32]. In severe acute colitis, a careful examination limited to the rectum and sigmoid may be performed initially because of the risk of perforation when the risk/benefit is managed by the possibility of performing a subsequent IC [3]. Other pathologies such as acute graft-versus-host disease (GVHD) can be safely investigated using endoscopy and in one retrospective study of 48 children a sensitivity of recto-sigmoid biopsies of 77% for GVHD diagnosis was reported [33]. Biopsies taken proximal to the recto-sigmoid only contributed to the GVHD diagnosis in 2/48 however. This compares to a study of adults with acute intestinal GVHD in the lower GI tract, of whom 20% had lesions only in the ileum [34]. To increase the sensitivity of endoscopic exploration for suspected intestinal GVHD, a lower GI endoscopy may be accompanied by an EGD.

Two meta-analyses studied the usefulness of CO_2 insufflation during colonoscopy in adults [35,36]. Both found that CO_2 insufflation significantly reduced pain during and after colonoscopy [35,36]. In a retrospective pediatric population, post-IC pain was reported using CO_2 only by 2/68 (3%) children [37]. A recent RCT [38] compared insufflation of CO_2 versus air during IC in children 7 to 18 years of age: CO_2 insufflation significantly decreases post-procedural discomfort. CO_2 has been used in large series of double balloon enteroscopy (DBE) in children as the rapidity of gas reabsorption is particularly useful during this procedure - no adverse events such as clinically significant rise in blood CO_2 were identified [39,40].

Caution should be taken in small children because the amount of insufflated CO_2 could induce adverse effects due to the smaller blood volume of young children.

A registry of newly diagnosed IBD cases in children in 44 centers in 18 countries reported a successful intubation of the ileum in 75% of 1995 colonoscopies [41]. In an adult study of 500 consecutive colonoscopies where the ileum intubation rate was 99%, time and probability of ileal intubation were significantly correlated to the quality of bowel cleansing and to the experience of the endoscopist [42]. In a pediatric cohort of 44 complete colonoscopies with an ileal intubation rate of 61%, ileal examination did not modify the patient-reported symptoms after endoscopy but this is essentially irrelevant as the diagnosis clearly needs to be established histologically in order to inform subsequent management [37]. The aim of 100% terminal ileum intubation is to be highlighted in children especially in the IBD situation [43].

Polyps

In a study including 11637 children, polypectomy was performed in 6.1% of procedures and this rose to 12% where lower intestinal bleeding was a symptom [44]. Performing a polypectomy, the endoscopist has 3 goals: to remove the lesion; to retrieve it for histological examination; and to avoid adverse events. The 3 main adverse events of polypectomy are bleeding, perforation and post-polypectomy syndrome, also known as trans-mural burn syndrome. The specific technique of polypectomy is generally chosen based on polyp localization, morphology and size. In an RCT adult study, the use of a cold snare vs cold forceps polypectomy to remove diminutive (≤ 5 mm) polyps was significantly correlated with a shorter procedure time and a more complete polyp eradication rate (93% versus 76%, respectively). [45] Cold snaring is a safe technique with no adverse events reported in large series in adults [46]. Hot biopsy forceps on the other hand induced a larger histological lesion compared to conventional snare procedure in a porcine model, especially when the snare diameter is large (5 mm versus 2.5 mm) [47] and necrosis depth is increased after hot forceps polypectomy with a more frequent inflammatory reaction under the submucosa due to the smaller area for electrical current diffusion vs polyp snares. Cytological artefacts are more

frequent in polyps removed by hot forceps technique compared to cold forceps [48]. For both of these reasons it is suggested that hot forceps polyp removal should be avoided in children.

FOREIGN BODY INGESTION

ESGE/ESPGHAN recommend an early referral to the emergency room and X-ray evaluation in all patients with suspected foreign body ingestion even if asymptomatic. Biplane radiographs should be obtained of the neck, chest, abdomen, and pelvis if indicated. Computed tomography (CT) scan can be considered for radiolucent foreign bodies (FB).
(Strong recommendation, moderate quality of evidence)

ESGE/ESPGHAN suggest early EGD if the foreign body is in the esophagus.

The approach to the endoscopic management of foreign bodies should take in to consideration the type (food, batteries, magnets, sharp, blunt, drug packets and size), the symptoms, the time since probable ingestion, the probable GI location, any suspected impaction etc. In the case of batteries symptoms are immaterial especially if the battery is impacted in the esophagus. Indeed any patient who is symptomatic with an ingestion of a sharp or a blunt FB should have endoscopic removal attempted. The standard approach to resuscitation of Airway, Breathing and Circulation (ABC) is pertinent in this clinical context. If drooling is present and the patient is not able to swallow their secretions, there is a risk of aspiration. In cases of proximal esophageal FB ingestion, it will be necessary to ensure airway protection and endoscopy for FB removal should be performed under GA [49].

FB ingestion leading to impaction and food bolus impaction are quite common and the majority occur in the younger child with a peak incidence between the ages of 6 months and 6 years [49].

Pre-endoscopic series have shown that 80% or more of FBs will pass without the need for any intervention. Mortality due to FB ingestion was not reported in a large pediatric series [50,51]. A case of death has been

reported in a 2-year old boy due to an aorto-esophageal conduit caused by an impacted sharp FB in the esophagus [52].The patient's age and size, the type and form of the ingested object, its location as well as the clinical symptoms and duration since ingestion will all contribute to the decision whether to intervene endoscopically and to the timing of any intervention.

Symptoms associated with FB ingestion varied among studies from vomiting, drooling, dysphagia, odynophagia, globus sensation and also included respiratory symptoms of coughing, stridor and choking. Some children are completely asymptomatic. In 9/12 studies [53] where coins were most the most frequent or only FB ingested, vomiting and drooling were the predominant symptoms. It should also be remembered that evaluation for peritonitis or small-bowel obstruction should occur in any case of FB ingestion and in such situations endoscopy should not delay surgical consultation but simultaneous endoscopy can complement the surgical approach [49,54,55].

For the purpose of initial diagnosis, radiographs can confirm the location, size, shape, and number of ingested FB and can help to exclude aspirated objects [49,56]. Radiographs identify most radio-opaque FBs but radiolucent FBs are common, limiting the reliability of radiographs in this initial evaluation [56]. Fish bones, wood, plastic and thin metal objects are some of the most common radiolucent objects [49,56]. Thin fragments of aluminum, such as pull-tabs or pop-tabs of beverages, present a relatively high radiolucency [57]. Biplane radiographs should be obtained of the neck, chest, abdomen, and pelvis if indicated. In addition to localization of radio-opaque objects, the presence of free mediastinal or peritoneal air should be assessed. A contrast examination should not be performed routinely in the patient with suspected proximal esophageal obstruction because of the risk of broncho-aspiration. Furthermore, opaque contrast agents, such as barium, coat the FB and esophageal mucosa, compromising subsequent endoscopy and Gastrografin® (amidotrizoeacid), a hypertonic non-opaque contrast agent, which can produce a severe chemical pneumonitis if aspirated, should not be used. There are no pediatric studies evaluating CT-scan in the diagnosis of FB ingestion in the digestive tract. A pediatric study [58] showed a 93% PPV and 100% NPV using spiral and cine CT-scan in the diagnosis of radiolucent FBs in the airways. CT scanning can be

considered in the diagnosis of radiolucent ingested FBs in selected cases considering also the risk of X-ray exposure in children.There is not enough evidence for use of metal detectors or ultrasonography in localizing ingested coins in children [59,60]. Magnetic resonance imaging is not helpful in detecting FBs [61].

BLUNT FOREIGN BODIES AND COINS

ESGE/ESPGHAN recommend removal of blunt FBs and coins or impacted food from the esophagus urgently (<24 hours), even in asymptomatic children. If the child is symptomatic an emergent (<2 hours) removal is indicated especially for button batteries.

ESGE/ESPGHAN suggest removal of blunt FBs from the stomach or duodenum if the child is symptomatic or if the object is wider than 2.5 cm in diameter or >6cm in length. Otherwise blunt FBs in the stomach can be followed and retrieved only if they produce symptoms or do not pass spontaneously after 4 weeks.

As noted above the timing of endoscopy depends on a number of factors including age, the patient's clinical status, the time of the patient's last oral intake, type of FB ingested, location within the GI tract and the time that has elapsed since ingestion. In addition, an assessment of the relative risk of aspiration, obstruction or perforation may determine the timing of any endoscopy [49]. Generally speaking, timing can be divided into emergent (less than 2 hours from presentation, regardless of nil by mouth status), urgent (less than 24 hours from time of ingestion) and elective (more than 24 hours from ingestion). Patients who are clinically stable without symptoms of proximal esophageal obstruction do not require emergent endoscopy because the ingested FB will usually pass spontaneously [49]. However, even in asymptomatic

children esophageal FBs and food that has impacted in the esophagus should be removed urgently (<24 hours from presentation) as any delay decreases the likelihood of successful removal and increases the risk of adverse events, including the risk of perforation. These data are based on adult studies as those in children are not available [49,62,63]. If the FB is located in the stomach and there is no risk of impaction distally (for example due to strictures) then most FBs will pass in 4 to 6 days. Therefore conservative outpatient management is appropriate for most asymptomatic gastric FBs. If a child with a FB ingestion is being followed on an out-patient basis he/she should continue a regular diet and the child and their parents should be instructed to observe the stools for evidence of having passed the object and they should be advised that small blunt objects (including coins) may take as long as 4 weeks to pass spontaneously. Coins are the most common ingested FB objects among children but radiologically can be mistaken for button-batteries (BB) and therefore a careful history is mandatory [64,65]. A child with witnessed or suspected ingestion of a coin or another blunt FB should undergo radiography as mentioned above. One should not mistake a coin for a BB therefore it is essential to closely examine the edges of the image of the coin on the Xray to exclude the double halo sign of a possible button battery.Lateral films also can be helpful to distinguish one from the other.

Localization of the ingested coin in the GI tract, age of the child and coin size all are factors that influence the likelihood of spontaneous passage. Depending on the localization in the child's esophagus spontaneous clearance occurs in about 30-60% of children and is more likely if the coin is stuck in the distal esophagus at the time of diagnosis [66,67].

Blunt FBs and coins stuck in the esophagus should be removed urgently (within 24 hours) to avoid significant esophageal injury or erosion into the mediastinum and as detailed below BBs require emergency (<2 hours) removal from the esophagus - this also applies to other FBs if the patient is symptomatic, unable to manage secretions or with respiratory or other concerning symptoms. A radiograph should be repeated immediately prior to GA in order to avoid an unnecessary procedure in case the FB has spontaneously

passed through the esophagus but this should not delay emergency endoscopy in the case of a disc/button battery [68].

Large or long objects which do not pass the pylorus and are trapped in the stomach should be removed electively or urgently in the case of a symptomatic child. There exists only expert opinion regarding the definition of "large" and "long" FBs. If the diameter of the FB is more than 2.5cm it is unlikely to pass the pylorus, especially in younger children. In one adult study [49], 80% of FBs longer than 6cm were unable to pass the pylorus in the 48 hours following presentation. Furthermore it is unlikely that FBs longer than 6cm in length will pass from the first to the second part of the duodenum and are equally unlikely to pass through the ileo-cecal valve if the duodenum is traversed [49,68]. After each extraction one should examine the mucosa to exclude significant injury.

SHARP POINTED OBJECTS

ESGE/ESPGHAN recommend emergent (<2 hours) removal of sharp-pointed objects located in the esophagus (all cases).

ESGE/ESPGHAN recommend emergent (<2 hours) removal of sharp-pointed objects in the stomach or proximal duodenum even in asymptomatic children.

There are many reports of ingested sharp objects in children [69-71].The frequency and type of ingested sharp objects are highly dependent on cultural and environmental factors. One can see more young children with fish bone ingestions in Asian and Mediterranean families, where fish is a main food and introduced early in life [72]. Symptoms of ingestions are quite common if the FB is lodged in the upper-mid esophagus (pain, dysphagia, odynophagia, drooling). However a significant percentage of patients remain asymptomatic for weeks and delayed intestinal perforation, extra-luminal migration, abscess, peritonitis, fistula formation [68,73-75], appendicitis, liver, bladder, heart, and lung penetration [76-78] and rupture of

the common carotid artery [79] have been described. The ileo-cecal region is the most common site for intestinal perforation but perforations have been reported in the esophagus, pylorus, at the junction between the first and second parts of the duodenum and in the colon [80]. Rates of complications are higher in patients who are symptomatic, have a delay in diagnosis beyond 48 hours [81] or have swallowed a radiolucent foreign body [82,83]. Toothpick and bone ingestions present a high risk of perforation [76,82] and are the most common FB that require surgical removal [82]. Patients suspected of having swallowed sharp-pointed objects must be evaluated to define the location of the object. Many sharp-pointed objects are not visible by radiographs, so endoscopy should still follow a radiologic examination with negative findings when a high index of suspicion is present. Sharp-pointed objects lodged in the esophagus are a medical emergency due to the potentially high risk of perforation and migration. Direct laryngoscopy is an option to remove objects lodged at or above the cricopharyngeus. Otherwise, flexible endoscopy may be performed if laryngoscopy is unsuccessful and for treatment of objects lodged below this area. Sharp-pointed objects in the stomach or proximal duodenum should also be removed emergently but if these pass through the duodenum then enteroscopy, if available, or surgery, in a symptomatic patient must be considered. If observation rather than removal is chosen in the asymptomatic patient, then monitoring in a hospital setting with daily abdominal X-ray may be considered. Patients should be instructed to immediately report abdominal pain, vomiting, persistent temperature elevations, hematemesis or melena [61,71]. The average transit time for a foreign object ingested by children has been reported as 3.6 days [70] and the mean time from ingestion of a sharp object to perforation has been reported as 10.4 days [84]. If the foreign body has not progressed on imaging in three days or the patient becomes symptomatic, surgical removal may be considered [70,84].

BATTERIES

ESGE/ESPGHAN recommend to emergently (<2 hours) remove BBs impacted in the esophagus.

ESGE/ESPGHAN suggest to remove BBs in the stomach emergently (<2 hours) if the child is symptomatic and/or has a known or suspected anatomical pathology in the GI tract (e.g. Meckel's diverticulum), and/or has simultaneously swallowed a magnet.

ESGE/ESPGHAN suggest that BBs larger than >20 mm present in the stomach should be checked by radiograph and removed if still in place after more than 48 hours.

ESGE/ESPGHAN recommend an urgent endoscopic removal (< 24 hours) for single cylindrical battery ingestion when impacted in the esophagus and as soon as possible elsewhere in the GI tract when the child is symptomatic (Strong recommendation, moderate quality of evidence)

ESGE/ ESPGHAN suggest that a single cylindrical battery in the stomach can be observed and the child monitored as an outpatient and followed by X-ray 7-14 days after ingestion if the battery is not passed in the stool.

BBs and Cylindrical Batteries

The US Poison Centers, from 1985-2009, reported an incidence of 6.3-15.1 cases of batteries ingested per million population [85,86].

An observed increase in poor outcome was attributed to the emergence of the larger, 20-mm diameter, lithium coin cells as an increasingly popular battery type. Thirteen deaths related to tissue damage in the esophagus or airway and 73 major outcomes (with debilitating and prolonged compromise of feeding

and/or breathing that required multiple surgical procedures, enteral tube feeding and/or tracheostomy) were described [85,86]. These devastating cases occurred predominantly in children who were younger than 4 years [85,86]. Almost all of these major outcomes involved esophageal BB injuries and therefore impaction at this site represents the highest risk for injury and this leads to our recommendation to emergently (<2 hours) remove BB impacted in the esophagus [87]. The removal of BBs in the stomach is controversial. The largest retrospective study of 8648 cases is reassuring with no reported significant gastric injuries from BB ingestion [85]. However there are case reports of severe gastric injury [88] and also fatalities reported from aorto-esophageal fistulae due to gastric BBs that had caused esophageal injury before reaching the stomach [89]. The recommendation with respect to removal of BBs from the stomach is based on expert opinion and in the knowledge that only two cases of BB-induced gastric lesions have been reported during the last 30 years. Consistent with other guidelines [49] BBs larger than 20mm in the stomach should be checked by radiography and removed if still in place after more than 48 hours. Less evidence exists regarding cylindrical battery ingestion and although these batteries do not typically discharge electrical current in the way that BBs do they nevertheless have the potential to leak caustic fluid if the outer casing is compromised. In the largest published series identified of 62 children with cylindrical battery ingestions, about 82% were unaffected and no patient had major complications or death. [90] Of particular interest to the practitioner caring for adolescents, a suicide attempt was the reason for ingestion in only 1.3% of the 2,382 total battery ingestions in this series, which is lower compared with other objects or poisons sought out for the same purposes [91]. For single cylindrical battery ingestions we suggest urgent endoscopic removal (<24 hours) when impacted in the esophagus but if located in the stomach the patient can be monitored as an outpatient and followed by X-ray if the battery is not observed to pass in the stool. Once these batteries pass the pylorus they almost universally pass the remainder of the GI tract without incident. For the adolescent with multiple gastric cylindrical batteries as the result of intentional ingestion one paper advocates endoscopic removal of the batteries at the time of presentation [92].

MAGNETS

ESGE/ESPGHAN recommend urgent (<24 hours) removal of all magnets within endoscopic reach. For those beyond endoscopic reach, close observation and surgical consultation for non-progression through the GI tract is advised.

Ingestion of a single magnet is typically innocuous and would be expected to behave much like another blunt FB. In contrast, multiple magnets or a magnet and another metallic FB can lead to bowel wall necrosis with fistula formation, perforation, obstruction, volvulus or peritonitis [93] by attracting themselves and trapping a portion of the bowel wall.

FOOD BOLUS IMPACTION

ESGE/ESPGHAN recommend removal of impacted food from the esophagus as an emergency 2 hours from the time of presentation (and ideally from the time of ingestion) in case of symptoms (drooling, neck pain). If the child is asymptomatic an urgent (< 24 hours) removal is indicated.
(Strong recommendation, moderate quality of evidence)

ESGE/ESPGHAN suggest investigation for underlying pathology of the esophagus in all cases of food impaction.
(Weak recommendation, low quality of evidence)

Food bolus impaction in the esophagus is the most common type of impaction in adults [94]. Data in children are rare but several studies show that underlying esophageal pathology, such as eosinophilic esophagitis, peptic or other strictures, achalasia and other motility disorders often are the cause of food bolus impaction [94-98]. Esophageal food bolus impaction in a symptomatic patient with drooling or neck pain is an indication for emergent endoscopic removal. If the child tolerates their secretions, endoscopic

removal may be postponed and an urgent (<24 hours) endoscopic removal may be considered, allowing an elective procedure and providing additional time for spontaneous clearance. The technique of removal can include piece-meal extraction, suction and/or gentle pushing of the bolus down into the stomach, though visualization of the distal esophagus is necessary to ensure that there is no stricture distal to the bolus. Use of glucagon to relax the lower esophageal sphincter to hasten spontaneous clearance has been studied with equivocal results and has not generally been recommended in this setting [99]. Recent data suggest that it may be particularly ineffective in cases with underlying eosinophilic esophagitis [68,99,100].

DRUG PACKETS

ESGE/ESPGHAN recommend against endoscopic removal of drug-containing packets.

(Strong recommendation, low quality of evidence)

In regions of high drug trafficking, so called "body packing" can also involve teenagers. Illegal drugs are packed into latex condoms, balloons or plastic and swallowed for transportation [101]. Leakage or rupture of these packets can be fatal, therefore endoscopic removal should not be attempted. Surgical removal is indicated when packets fail to progress or if signs of intestinal obstruction are present. If packet rupture is suspected, surgery and urgent medical consultations for drug toxicity are indicated.

EQUIPMENT FOR FOREIGN BODY REMOVAL

ESGE/ ESPGHAN suggest that flexible endoscopy is an effective and safe procedure for removing FB from the GI tract, with a high success rate using retrieval nets, polypectomy snares and rat-tooth forceps.

(Weak recommendation, very low quality of evidence)

Flexible Endoscopy

Most ingested FBs are best removed using flexible endoscopes and have a high success rate. Chaves et al performed a prospective mixed child and adult study showing that flexible endoscopy is an effective and safe procedure to remove FBs from the GI tract, with a high success rate using only polypectomy snares and rat-tooth forceps [102].

Rigid endoscopy

Some studies have shown that rigid esophagoscopy carries a higher complication rate than flexible endoscopy in performing esophageal FB extraction and its routine use is not recommended [103]. Rigid endoscopy can be considered only for proximally located blunt objects, since the rigid tube provides protection [103,104].

Magill Forceps

In a retrospective study, coins located in the proximal third of the esophagus where successfully removed using Magill forceps. Using direct laryngoscopy under anesthesia coins were visualized and grasped with Magill forceps. The coin was removed in 96% of 165 children with a proximal esophageal coin, 82% at the first attempt [105].

Retrieval Devices/Overtubes

Devices used for retrieving FBs include alligator and rat-tooth forceps, retrieval nets, polypectomy snares, tripod forceps and baskets. The availability of latex cone and overtubes to protect the cardia and esophagus when removing sharp foreign bodies is important for procedure safety. There are no studies performed in children on the use of different retrieval devices or overtubes.

Pharmacological agents

One RCT did not find an advantage in spontaneous passage of a coin from the esophagus to the stomach when using glucagon compared to placebo [106].

CORROSIVE INGESTION

ESGE/ESPGHAN suggest that every child that has ingested a corrosive substance should have a thorough follow-up, with endoscopy dictated by symptoms and dependent on the symptoms/signs, the timing should be within 24 hours.
(Strong Recommendation, high quality of evidence)

ESGE/ESPGHAN recommend that every child with a suspected caustic ingestion and symptoms/signs (e.g. any oral lesions, vomiting, drooling, dysphagia, hematemesis, dyspnea, abdominal pain etc) should have an EGD in order to identify all consequent digestive tract lesions.
(Strong recommendation, high quality of evidence)

ESGE/ESPGHAN suggest that in the case of suspected corrosive ingestion, EGD is withheld if the child is asymptomatic (no drooling of saliva/other symptoms and no mouth lesions) and that adequate follow-up is assured.
(Weak recommendation, moderate quality of evidence

Ingestion of corrosive substances can cause serious injuries to the digestive tract and occurs most commonly in children (about 80% of the cases) [107,108]. Corrosive ingestion is mostly accidental in children (but intentional ingestion has been described in teenagers [109,110]) and although reported at any age it is more frequent under 5 years with a maximum incidence at 2 years of age [107,109]. In the developed world with the advent of child-unfriendly packaging, corrosive ingestion has become quite rare

[111]. Household, industrial and farm products, especially if stored in non-original containers, represent the most frequently ingested caustic agents.

The ingested substance varies between rural and urban living areas and also with the level of economic development. In developing world countries the most frequent accidental poisoning are medications (48.3%), followed by corrosive acidic substances (23.1%), carbon monoxide intoxication (12.5%) and batteries [112,113]. A variety of substances have been reported that were ingested leading to caustic injuries ranging from alkaline bases with pH up to 12 (e.g. sodium hypochlorite and sodium hydroxide), to acidic substances with a pH as low as 2 (e.g. hydrochloridic acid and salicylic acid) and also bleaching substances where the pH is around 7 [114,115]. More recently so-called hair-relaxers and liquid tabs (pods) containing detergents are a new addition to the long list of ingested products but fortunately it seems that the upper digestive tract is not as severely damaged by these substances [116,117].

The extent of the esophageal damage is related to the nature and the concentration of the caustic substance, the duration of contact with the mucosa and quantity ingested [118]. Strong alkalis produce liquefaction necrosis with deep ulcerations and risk of esophageal stricture and/or perforation. Acids usually cause coagulative necrosis with limited tissue penetration and superficial scar formation [119]. Upon swallowing, acids cause severe oropharyngeal pain and therefore they are usually consumed in small volumes compared with alkaline substances [107], resulting in a lower incidence of stricture formation and/or esophageal perforation. Other substances that may result in stricture formation are bleaching agents, non-phosphoric detergents, ammonia and sodium bicarbonate.

Gastric lesions, with or without outlet obstruction syndrome, are almost always related to acidic ingestions, as alkalis are neutralized by gastric acid [120].

If not actually observed then corrosive ingestion may be inferred from oral burns, however their absence does not exclude ingestion and esopohageal/gastric damage [121] and the consequent need for EGD. Although there are some discrepancies between studies, it is known that up to 70% of corrosive ingestions may be asymptomatic at presentation [120,122,123]. It has been proposed that routine EGD is not

performed in asymptomatic patients in the absence of oral lesions [119,124-126]. Drooling saliva and oral lesions have been noted significantly more frequently in high-grade injury and symptoms such as pain, hyper-salivation, swallowing difficulties and bleeding are other suggestive symptoms of esophageal injury [113,121]. Some children may even develop dyspnea and other respiratory symptoms (cough) and in very severe cases hemodynamic instability and/or circulatory collapse, however none of these presenting symptoms is completely predictive of esophageal injury [114], although hematemesis or dyspnea as single symptoms have a very high positive predictive value for esophageal lesions after caustic ingestion [122,124,126]. Both in retrospective and prospective studies, the presence of three or more symptoms that occurred after caustic ingestion was positively associated with severe lesions seen at EGD [124,126]. Young children presenting with suggestive symptoms in the absence of an observed ingestion of corrosives require EGD to exclude esophageal lesions [120,122-124,127,128].

Esophageal lesions after corrosive ingestion are described according to the Zargar Classification [129]:

Grade **0**   Normal.

Grade **I**   Edema and hyperemia of mucosa.

Grade **IIa**   Friability, hemorrhage, erosion blisters, exudates or whitish membranes, superficial ulcers.

Grade **IIb**   Grade IIa plus deep discrete or circumferential ulceration.

Grade **IIIa**   Small scattered areas of necrosis, areas of brownish-black or grey discoloration.

Grade **IIIb**   Extensive necrosis.

Images of the lesions are important for an accurate follow-up.

Patients with low grade lesions at endoscopy (grade 0 to IIa) who have in addition a normal physical examination and who can eat and drink normally can be discharged [126,127] but if not then admission to a hospital environment for observation should occur.

ESGE/ESPGHAN recommend to have the same grade of suspicion for both acidic and alkali ingestion regarding potential mucosal injury. (Alkali ingestion, especially lye, is associated with more severe esophageal lesions and severe gastric lesions can occur in acidic ingestion.) Stricture development has been associated with both acidic and alkali ingestion.

ESGE/ESPGHAN recommend high doses of intravenous dexamethasone ((1g/1.73m2 per day) administration for a short period (3 days) in IIb esophagitis after corrosive ingestion as a method of preventing esophageal stricture development. There is no evidence of benefit from the use of corticosteroids in other grades of esophagitis (I, IIa, III)

Efforts should be undertaken to prevent vomiting after corrosive ingestion. Small amounts of water can be allowed if the child asks for it or even stimulated to rinse the mouth and esophagus. However, if the child has severe pain and if perforation is suspected, nothing should be given by mouth.

Experimental studies showed decreased incidence of grade III burns and stricture formation with early corticosteroid and antibiotic use compared with controls [119,130,131]. However, their efficacy and safety in children with esophageal burns is under discussion [132,133] because of many inconsistent variables including the type of corticosteroids used, the dosage and duration. A recent RCT has concluded that corticosteroids are beneficial for stricture prevention in grade IIb esophageal burns [131]. As yet unstudied is the possibility of the anti-fibrotic Mitomycin-C used topically to prevent post-ingestion fibrosis.

BENIGN ESOPHAGEAL STRICTURES

ESGE/ESPGHAN recommend esophageal dilation using balloon or bougies for benign esophageal strictures only when symptoms occur.

Esophageal strictures in children may have multiple etiologies including congenital or inflammatory disorders, caustic ingestion, eosinophilic esophagitis (EE) and gastroesophageal reflux disease (GERD) [134]. The relative proportions of etiologies vary between countries (e.g. higher proportion of caustic strictures in developing countries) [135,136].

EE will not be discussed as this topic is covered by another recent Guideline [14]. Safety and long term efficacy of esophageal dilation for benign esophageal strictures has been confirmed in children [137,138]. Data on the ideal timing of esophageal dilation are scarce. Two retrospective studies including 100 and 76 esophageal atresia (EA) patients compared routine esophageal dilation every three weeks starting three weeks post-surgery versus when symptoms developed. No difference in outcome and complications were found between the two groups after 2 and 3 years of follow-up but significantly fewer dilations were needed in the on-demand dilation group [139,140].

Through-the-scope balloons and wire-guided polyvinyl bougie dilators (Savary Gilliard) are most frequently used to dilate benign esophageal strictures in children and similar results are reported – a retrospective study [141] compared 125 balloon dilations vs 88 bougie dilations in children with benign esophageal strictures and reported 4 failures in the bougie group related to unsuccessful passage of the stricture.

Expert opinion suggests that both anesthesiology and surgical assistance should be available during esophageal dilation procedures in children - the latter in case of complications [141].

Balloon dilation.

Balloon dilation can be performed under direct endoscopic view or fluoroscopic view. The size of the balloon catheter can vary from 4-22 mm and the balloon inflation duration varies between studies from 20 to 120 seconds [142]. A study [137] on 77 children (median age 1.8 years) that underwent 260 balloon dilations of benign esophageal strictures under endoscopic view (mean 3.4 dilations/patient), reported 4 (1.5%) esophageal perforations, with one requiring surgery - the remaining patients were all asymptomatic

after a median follow-up of 6.6 years. Strictures shorter than 5cm in length appeared to have a significantly better outcome [143,144]. In a retrospective study of 34 patients with EA and symptomatic esophageal strictures, balloon dilation appeared to be more effective and less traumatic than bougienage [145].

Bougies

Bougie dilation is a safe and effective dilation technique for esophageal strictures. In a study of 107 children, dilation was performed at 2-3 week intervals using Savary-Gilliard bougies and was considered adequate if the esophageal lumen could be dilated to 15mm diameter (12mm in children <5 years of age) with complete relief of symptoms [146]. Subsequently, dilation was performed on an "as needed" basis dependent on symptoms. Dilation was successful in all but 3 cases. Dilation was also successful in patients with strictures 5cm or more in length and/or in patients with multiple corrosive strictures, although these required a higher number of sessions to achieve adequate dilation and also higher number of subsequent sessions for recurrence. Six esophageal perforations occurred during 648 dilation sessions (0.9%) with 1 requiring surgical repair.

Size, number and interval between dilations

There are no data on the "optimal" increase in size that should be aimed for at each dilation session. The 'rule of three' is often invoked: no more than 3 times the diameter of the stricture - so a 3mm stricture should not be dilated to more than 9 mm etc. Balloons are to be preferred over bougies if financially possible. There exists no consensus in regard to the interval between dilations and the frequency of this intervention is often individualized according to relief of dysphagia and the severity of the stricture observed during repeat endoscopy. Most studies used a minimal period of three weeks between dilation sessions [144,146,147] and for balloon dilation an average of three dilations appeared to be required [142].

ESGE/ESPGHAN suggest the following definition of a benign refractory or recurrent stricture in children: "An anatomic restriction because of cicatricial luminal compromise or fibrosis that results in dysphagia in the absence of endoscopic evidence of inflammation. This may occur as the result of either an inability to successfully remediate the anatomic problem to obtain age-appropriate feeding possibilities after a maximum of 5 dilation sessions (refractory) with maximal 4-week intervals, or as a result of an inability to maintain a satisfactory luminal diameter for 4 weeks once the age-appropriate feeding diameter has been achieved (recurrent)".

To define refractory and recurrent strictures in children, we adopted the definition used in adults based on Kochman's criteria [148]. In an online survey of the working group members, the number of sessions, intervals and target diameter were assessed. Seventeen of 18 members (94%) supported the definition stated above, with 39% and 61% of respondents mentioning a maximum of three and five sessions, respectively. Proposed intervals between sessions were: two or three weeks (39% of members each) or four weeks (22%). Refractory and recurrent stenosis is reported in about 30% of the cases [142].

ESGE/ESPGHAN suggest temporary stent placement or application of topical mitomycin C (MMC) following dilation for refractory esophageal stenosis in children. ESGE/ESPGHAN do not suggest the routine use of intra-lesional steroids for refractory esophageal stenosis in children.

There is no standard treatment for refractory stenosis.

Local application of mitomycin C (MMC) is a therapeutic option for the treatment of refractory esophageal strictures in children [149,150]. A systematic review identified eleven publications including 31 cases [151] of various etiologies. In one study, cotton pledgets soaked in a solution (0.1mg/ml) of MMC were applied endoscopically directly onto the mucosa post-dilation with a frequency of 1-12 times over 12 weeks. After a mean follow-up of 22 (6 to 60) months complete relief of symptoms was reported for 21/31 children

(67.7%), and 6/31 (19.4%) had a partial relief. In four children (12.9%) MMC application failed. No direct or indirect adverse effects were reported. Two double blind RCTs showed that MMC application significantly reduced the number of esophageal dilations sessions needed to alleviate dysphagia following EA and corrosive strictures [152,153].

MMC is a cytostatic agent, therefore dysplasia of healthy tissues after application should be considered as a theoretical risk. [151] This complication was not observed in a study performing esophageal biopsies during a 24 months mean follow-up [149]. Future studies with long-term follow up are required to evaluate the potential side effects [149,151].

With the advent of removable, fully covered, self-expandable metal stents (FCSEMS), the use of esophageal stents in children has expanded in particular for the treatment of refractory stenoses. In three studies that included a total of 25 children, complete clinical response following stent removal with no recurrence of dysphagia or need for subsequent dilations was reported in 50-85% of patients. [154] Most patients suffered from nausea or chest pain in the days following stent placement, in some cases leading to premature removal of the stent. Duration of stenting varied from 1 to 24 weeks. Stent migration was the most commonly cited complication and occurred in 0-29% of patients. In a recent retrospective study in children with perforations and refractory strictures after EA repair a total of 41 plastic and FCSEMS were placed in 24 patients, including 14 patients who had developed esophageal leaks. Success in the treatment of refractory strictures was limited due to a high stricture recurrence rate after stent removal (39% at 30 days and 26% at 90 days). Stent-related adverse events included migration (21% of plastic and 7% of FCSEMS), granulation tissue (37% of FCSEMS and none of plastic), and deep ulceration (22% of FCSEMS and none of plastic) [155].

A recent uncontrolled study in 10 children with intractable esophageal strictures due to caustic ingestion reported symptom resolution using stricture dilation preceded by intra-lesional triamcinolone injection

[156]. However, in a recent double-blind RCT in adults with benign anastomotic strictures, no benefit of intra-lesional triamcinolone could be demonstrated [157].

In patients operated for EA, ESGE/ESPGHAN suggest long-term endoscopic surveillance for Barrett's esophagus and cancer. Frequency would be dictated by the presence or not of dysplasia and should follow standard guidelines already published in the literature.

A systematic review and meta-analysis to define the prevalence of chronic long-term problems in 907 EA operated patients showed, compared with controls, a 40.3 relative risk for dysphagia during adolescence and adulthood due to altered peristalsis [158]. Gastroesophageal reflux is a known risk factor for subsequent development of esophageal intestinal metaplasia. The overall estimated prevalence of Barrett's esophagus was 6.4% in EA patients, which is 4 times and 26 times higher than its prevalence in adults and pediatric general population respectively. In a systematic review the prevalence of esophageal carcinoma was low (1.4%) and only squamous cell carcinoma was described. However, cases of adenocarcinoma in EA patients have been reported [159]. In view of the high incidence of Barrett's esophagus in EA patients at a young age [160], endoscopic surveillance is warranted in adolescence and adulthood [161]. The question of whether endoscopic surveillance should occur for metaplastic change following corrosive ingestion is not one that can be adequately answered with the present medical evidence.

UPPER AND LOWER GI BLEEDING.

ESGE/ESPGHAN suggest that, having employed all necessary medical interventions as standard, EGD be performed very early (<12 h) in acute upper GI bleeding (AUGIB) cases which require ongoing circulatory support or where a large hematemesis or melena occurs.

ESGE/ESPGHAN recommend that, having employed all necessary medical interventions as standard, EGD be performed very early (< 12 h) in AUGIB in cases with known esophageal varices. (Strong recommendation, moderate quality of evidence)

ESGE/ESPGHAN suggest that, having employed all necessary medical interventions as standard, EGD be performed within 24 hours in AUGIB cases which require transfusion due to hemoglobin drop below 8 g/dL, where an acute drop of 2 g/dL is identified, and in those who are stable but whose bleeding score is above a recognized threshold/validated score for probable endoscopic intervention requirement.

ESGE/ESPGHAN suggest that EGD be performed before hospital discharge in children with AUGIB and pre-existing liver disease or portal hypertension.

ESGE/ESPGHAN do not suggest routine use of wireless capsule endoscopy/enteroscopy in AUGIB in children.

ESGE/ESPGHAN suggest that urgent therapeutic ileo-colonoscopy is not usually necessary in lower GI bleeding unless severe enough to cause circulatory compromise but diagnostic IC is needed as soon as is practical and safe.

Adult studies are the primary guides for evaluation of pediatric practice, but are not entirely applicable to children. Distinction is drawn between the speed of intervention required for acute upper and lower GI bleeding in children. It is rare to require intervention for lower GI bleeding as the majority of massive hemorrhage (fresh red blood/melena) originates in the upper GI tract with the occasional exception of a Meckel's diverticulum or severe colitis.

Scoring systems of intervention in children are emerging but require prospective evaluation of predictive accuracy and reliability.

In adults with AUGIB validated scoring systems have been published [162-164] while, to date, only one such scoring system exists in pediatrics ('Sheffield Scoring System') which might predict the requirement or otherwise for endoscopic hemostatic therapy, is undergoing prospective multi-center validation at present [165]. This retrospective case-control study reliably predicted which children most likely require endoscopic intervention. Particular weighting was given on modelling to such factors as: transfusion requirement; signs of hypovolemia (raised HR> 20 bpm above age-appropriate median and prolonged CRT); large hematemesis; melena; and drop of Hb> 2 g/dl. The timing of such intervention is clearly dependent on the circulatory stability of the child. For uncontrolled bleeding requiring volume support immediate intervention is suggested. For children in whom the threshold score is reached but who are stable then endoscopic intervention within 12 hours is suggested. Finally, for children whose clinical bleeding risk score does not reach the intervention threshold and in whom AUGIB would appear to have ceased then elective or no endoscopy is suggested [165].

The matter is further complicated by the wide variability of the following important practical factors in the provision of such life-saving techniques for children: availability of appropriately trained pediatric therapeutic endoscopists; availability of units with adequate and appropriate equipment/skills within geographical proximity; and agreed guidelines/algorithms of care for this clinical emergency with, to date, no universal view of when and how to intervene endoscopically.

This is further compounded by an absence of knowledge of the size of the clinical problem in pediatrics. Many pediatric endoscopists would not encounter an acute upper GI bleeding case more than a handful of times each year. A case, then, may be made for centralisation of such units and skills, but the caveat to this is the need then for safe transport of a child who may be actively bleeding to such a center.

There seems to be little requirement for urgent or early use of the wireless capsule endoscope or enteroscopy in acute bleeding in children [40,166,167].

Endoscopy has been advocated for the management of AUGIB, but the optimal timing is still uncertain. Ideally, endoscopy should occur after the stabilisation of the patient and various studies have been conducted comparing various timing of endoscopy performed within 6, 12 and 24 hours of presentation [168]. Adult literature recommend that endoscopy in AUGIB should be performed within 24 h of presentation [169,170] or within 12 hours when bleeding continues at a rate considered potentially life-threatening [170-174]. A clinical benefit of endoscopy performed of presentation is reported in acute variceal bleeding in children [175]. In the pediatric population endoscopy in AUGIB is recommended within 24 hours [165,170,172].

Lower GI Bleeding

Most cases of acute colonic bleeding (or lower GI bleeding) in children presenting either as hematochezia (bright red blood, clots) or melena will stop spontaneously, thus not needing urgent evaluation [176], but IC following adequate bowel preparation need to be planned before discharge from the hospital. However, for children with severe hematochezia, defined as continued bleeding within the first 24 h of hospitalization with a drop in the hemoglobin of at least 2 g/dl and/or a transfusion requirement, urgent diagnosis and intervention are required to control bleeding [165,177]. When hematochezia is not severe, elective IC need to be scheduled.

ENDOSCOPIC HEMOSTASIS TECHNIQUE FOR GI BLEEDING IN CHILDREN

ESGE/ESPGHAN recommend hemostasis of esophageal variceal bleeding in children using band ligation, if feasible, or sclerotherapy as an alternative.

ESGE/ESPGHAN suggest that the treatment of peptic ulcers and Dieulafoy's lesion should not be carried out with epinephrine injection alone but in combination with thermal or mechanical techniques.

Minimal data exist comparing endoscopic equipment and techniques in children. Adult studies are the primary guides for evaluation of pediatric equipment. Working channel size is the major factor limiting the choice of accessories [18]. In children >10 kg, endoscopes for therapeutic endoscopy are generally identical to those used in adults (Table 4).

Standard pediatric gastroscopes have a 4.9-6.0 mm outer diameter and a 2.0 mm working channel. They will accommodate needles for injection therapy (4-6 mm length), bipolar and argon plasma coagulation probes but not heater or multipolar probes, or ligating or mechanical devices [178]. Removing the Teflon sheath from a hemostatic clip allows use with pediatric endoscopes. Patient electrodes and grounding pads are available in neonatal (< 3 kg) and pediatric (< 15 kg) sizes.

Non-variceal bleeding

Dieulafoy lesion

In a review of 24 pediatric cases, half were treated surgically, the others were managed endoscopically by injection therapy, band ligation and thermocoagulation [179]. Epinephrine combined with either mechanical treatment or heater probe is preferable to epinephrine alone for hemostasis [180]. One should consider tattooing the bleeding site to aid location in the event of re-bleeding [181].

Bleeding ulcer

A report describes the successful treatment of a newborn by heater probe thermocoagulation [182]. Argon plasma coagulation with a 1.5 mm or 2.3 mm probe was used in 12 children [183]. Generally, for older children standard adult GI practice should apply to AUGIB [184].

Variceal Bleeding

A randomized prospective study in 49 children showed that band ligation is safe and effective, superior to sclerotherapy in terms of variceal eradication and was associated with a lower re-bleeding rate [185]. Most

studies support band ligation but if that is impossible due to patient size then sclerotherapy can be used [185-187]. The use of band ligation sets for gastroscopes with a diameter of 8.5-9.2 mm is limited primarily by the narrowness of the pharynx, and not only by body weight. Recently band ligation sets are available for pediatric gastroscopes and although previously sclerotherapy was the method of choice for children weighing <8 kg [188] this may change soon. Evidence is limited concerning the management of gastric varices in children. In case reports, N-buthyl-2 cyanoacrylate 'glue' injection has been successful [186,189]. Small cohort studies in children using variceal banding as prophylaxis exist [190]. It has been found that variceal grading can be a subjective assessment. There is no evidence that PPI use post-banding is beneficial [191]. A retrospective review of the safety and efficacy of expanded polytetrafluoroethylene-covered transjugular portosystemic shunt in 12 children showed a satisfactory result and therefore this may be a useful alternative in acute or recurrent medically or endoscopically uncontrollable variceal bleeding [192].

ESGE/ESPGHAN suggest adopting general anesthesia in children undergoing endoscopy for GI bleeding. General anesthesia is recommended when there is variceal bleeding. Deep sedation may be used in less severe bleeding in older children.

ESGE/ESPGHAN suggest using video capsule endoscopy (VCE) in children when there is suspected small-intestinal bleeding and in addition balloon enteroscopy for therapeutic purposes.

The majority of studies are retrospective analyses focusing on the diagnostic yield and therapeutic success of endoscopy in children with GI bleeding. The type of sedation/anesthesia used when performing upper GI endoscopy in children for AUGIB is not always reported, but most of the procedures were performed under GA with endotracheal intubation, while conscious or deep sedation should *not* be preferred [193].

VCE in children finds a main indication in the study of obscure GI bleeding and suspected or known Crohn's disease. The youngest VCE patient investigated was 8 months [194]. If the capsule cannot be swallowed it is placed endoscopically using various devices [166]. In a meta-analysis including 723 VCE examinations in children, the diagnostic yield of VCE was 65.4% with retention rates comparable to those of adults [195]. Interventional studies on small bowel endoscopy mostly reported on double-balloon enterosocopy using an endoscope with either 9.4 mm or 8.3 mm diameter [39,40,196]. Angiodysplastic lesions, polyps, Meckel's diveritculi, chronic mucosal erosive/inflammatory diseases such as diaphragm disease and congenital lesions such as duplication cysts are all noted in the literature as causes of bleeding either acutely or in a more chronic fashion. Diagnostic approaches include VCE, double balloon enteroscopy, CT-scan, CT-angiogram, intra-vascular angiography and isotope labelled bleeding scans.

ENDOSCOPIC RETROGRADE CHOLANGIO-PANCREATOGRAPHY (ERCP).

ESGE/ESPGHAN suggest ERCP in pediatric patients (>1 year old) for therapeutic purposes following diagnostic information from non-invasive diagnostic modalities such as magnetic resonance cholangio-pancreatography (MRCP). Diagnostic ERCP can be considered in selected cases where advanced non-invasive imaging is inconclusive.

ESGE/ESPGHAN recommend that therapeutic ERCP in pediatric patients (>1 year old) is considered for diseases listed in Table 6 following diagnostic information from non-invasive modalities such as magnetic resonance cholangio-pancreatography (MRCP). Results and complication rates of ERCP in children are similar to those reported in adults.

Published series on pediatric ERCP are retrospective data collections. Indications for ERCP in children are more frequently related to congenital abnormalities or trauma than to malignancy, which is more frequent in adults [197]. The division between biliary and pancreatic indications is age-dependent: pancreatic and biliary indications prevail in children of 7-12 years and 13-17 years, respectively while they are similarly distributed in children younger than 6 years [198]. Indications for ERCP in pediatric patients are summarized in *Table 6*.

Currently, the majority of ERCPs in children are therapeutic as MRCP has mostly replaced diagnostic ERCP but this is not reflected in the literature. [199]. MRCP accurately depicts pancreatico-biliary anatomy and related diseases in children and secretin stimulation can enhance the visualization of non-dilated pancreatic ducts thereby improving diagnostic sensitivity [200]. Two large retrospective series in children with a mean age of 10 years [199,200] reported an 11-13% non-diagnostic rate of MRCP and in such cases diagnostic ERCP can be considered.

Technical success for diagnostic and therapeutic ERCP in children (>1 year old) is high, with adverse event rates similar to those in adults [201,202]. The success rate reported in pediatric ERCP case series is > 90%, with a complication rate of 2.3-9.7%, and no procedure-related mortality [197,198,201-213]. A retrospective case-controlled study [201] compared results of ERCP in children and adults performed at the same center. Pediatric and adult patients were matched according to indications, diagnostic findings and technical complexity. ERCP success rate was 97.5% in children vs 98% in the adult cohort and complications rates were similar (3.4% in adults vs 2.5% in pediatric patients). The risk of post-ERCP pancreatitis is increased in therapeutic vs diagnostic ERCP, in the case of pancreatic duct injection and in more (vs less) complex procedures in children [202,211,214].

Chronic pancreatitis (CP) is a frequent indication for therapeutic ERCP in children. ESGE recommend endotherapy as a first-line therapy for CP in children starting at 8 years in the same conditions as in adults [215]. Two recently published large series [216,217] confirmed good results of endoscopic treatment of CP in children with complete pain resolution in 63.6% of the cases and improvement in 21.6% [216], while

pancreatic duct stenting significantly decreased the number of pancreatitis after a mean follow-up of 4.5 year [217].

ESGE/ESPGHAN suggest that diagnostic ERCP in neonates and infants (≤ 1 year old) with cholestatic hepatobiliary disease is considered if non-invasive investigations are not conclusive in order to allow timely referral to surgery for suspected biliary atresia or to avoid unnecessary surgery if biliary atresia is excluded.

The first-line imaging modalities in neonatal cholestasis are abdominal ultrasound (triangular cord sign) and cholescintigraphy; ERCP and MRCP are not routinely recommended for the diagnosis of cholestatic jaundice in infants [218].

In the setting of neonatal anatomy, and in particular, the minute structures of biliary hypoplasia or atresia (BA), MRCP still appears to have unsatisfactory diagnostic accuracy (70% in a recent series on 190 infants) [219]. As the diagnosis of BA at MRCP is based on the absence of visualization of the extrahepatic bile ducts and a prospective evaluation [220] of normal infants by MRCP visualized extrahepatic bile ducts in 62.5% of the cases, the authors concluded that MRCP led to a high level of false positivity in the setting of neonatal cholestasis.

In this particular indication, retrospective series [221-227] report that ERCP has a greater than 85% success rate but also report a complication rate of up to 10%, although this included cases of increased pancreatic enzymes. All complications resolved by conservative treatment. Procedure-related mortality was not reported. Keil et al [221], in a series of 104 infants, reported 86% sensitivity and 94% specificity of ERCP for BA and 100% sensitivity and 90% specificity for choledochal cyst. According to published data [221,222,224-227] ERCP avoided unnecessary laparotomies in 18-42% of the infants. Liver biopsy is indicated as a complimentary investigation especially if ERCP is inconclusive [218].

ERCP currently offers superior diagnostic visualization of the biliary tree in infants and neonates [221]. However ERCP remains an invasive procedure, thus its indication in infants needs to be carefully evaluated

in a multidisciplinary setting, balancing risks and benefits.

ESGE/ESPGHAN recommend that ERCP in children is performed by an experienced endoscopist, in a high-volume tertiary care center and with pediatric involvement.

The annual number of pediatric ERCPs performed even in a referral endoscopy unit is usually low. The two largest published series [206,210] report 24 and 36 pediatric ERCPs/year; in neonates and infants this figure is lower with a minimum of 2.7 ERCP/year and a maximum of 20 [224]. Most pediatric endoscopy training programs offer limited exposure of their trainees to ERCP. Training in ERCP requires performance numbers that often exceed the number of patients an average pediatric gastroenterologist will encounter in their training. Pediatric gastroenterologists undoubtedly perform a lower volume of ERCP compared with adult-trained endoscopists at expert centers and it could be argued that initial numbers for competency should be the same [228,229]. North American Society for Pediatric Gastroenterology, Hepatology and Nutrition [230] suggests a minimum of 200 diagnostic and therapeutic ERCPs to achieve competence in pediatric patients, although this is a suggestion rather than based on evaluation of prospective competence. The combination of a pediatric gastroenterologist, who is knowledgeable about the pediatric GI disease, with an experienced ERCP endoscopist is perhaps an ideal alternative.

ESGE/ESPGHAN suggest GA for ERCP in children. Deep/conscious sedation can be considered for teenagers (age 12-17 years) although GA is the preferred choice.

Given the long duration and degree of difficulty of ERCP in small children and neonates, as well as the softness of their tracheal wall, it is recommended to perform ERCP in children under GA with endotracheal intubation. Some series report the use of conscious/deep sedation in 70% of cases but this should be

considered to be historical and age-dependent and should not be considered for children under 12 years of age [207,208,211].

Prophylaxis of post-ERCP pancreatitis with NSAID (diclofenac/indomethacin suppository) is recommended in children older than 14 years.

No RCTs on the prophylaxis of post-ERCP pancreatitis (PEP) in children have been published. In a series of 423 ERCPs, prophylactic pancreatic stenting was associated with higher rates of post-ERCP pancreatitis in high-risk patients and did not eliminate severe PEP [214]. Pharmacologic prophylaxis with diclofenac/indomethacin suppositories are recommended in adults [231] and may be used in children although evidence is lacking to date.

Protection of radiosensitive organs (thyroid gland, breasts, gonads and eyes) is recommended together with adjustment of collimation to the smaller size of children.

Children are more sensitive than adults to radiation exposure and the life-time risk of cancer induction is possibly 3-5 times higher. ESGE guidelines on radiation exposure [232] recommends to adjust collimation to the smaller size of the patient and to protect with radiation protection shields the most radiosensitive organs (thyroid gland, breasts, gonads, and eyes) and to keep these organs outwith the main X-ray beam.

ESGE/ESPGHAN recommend the pediatric 7.5 mm duodenoscope for children weighing <10 kg and that a therapeutic duodenoscope can be used in those weighing ≥10 kg.

ERCP in infants and neonates *(≤ 1 year old)* is feasible with a 7.5 mm pediatric duodenoscope. This endoscope has a 2 mm working channel limiting the array of devices that can be used, however double-

lumen sphincterotomes, extraction baskets, and retrieval balloons are commercially available. Previously specific pediatric ERCP scopes with a standard 3.2 mm working channel or a therapeutic 4.2 mm working channels were available but are no longer commercially available. Commercially available therapeutic duodenoscopes have an insertion tube diameter of 11.3-11.6 mm and a distal end of 13-13.5 mm. (*Table 4*)

ENDOSCOPIC ULTRASONOGRAPHY (EUS).

The endobronchial ultrasound (EBUS) can be adapted for EUS in children with a weight below 15 kg. A standard linear echoendoscope should only be employed in children under general anesthesia, considering the stiff and potentially traumatic distal part.

ESGE-ESPGHAN suggest the use of EUS in children only in tertiary referral centers with experience in therapeutic endoscopy. Strict collaboration between adult and pediatric gastroenterologists is required in the case of EUS with standard echoendoscopes.

Experience of EUS in pediatric patients is limited partly because commercially available echoendoscopes have a distal end diameter of 11-14 mm for radial probes and 14 mm for linear probes which cannot traverse from D1 to D2 small children. GA and careful insertion of the rigid tip of the linear echoendoscope is needed. The use of adult echoendoscopes was recently described [233] in children aged >3 years with weight ≥15 Kg. In smaller children the Endobronchial Ultrasound (EBUS) endoscope can be considered (*Table 4*).

Reported experiences with standard EUS scopes and mini-probes in children are limited to small series [233] [234-251], with only 2 papers including more than 50 cases [233,243]. Many papers are from adult endoscopy centers, which routinely perform EUS with standard echoendoscopes.

Mini-probes can be used with standard endoscopes in small children [234-240] and allow EUS in special anatomic situations such as stenoses through which standard EUS scopes may not feasibly be passed.

ESGE-ESPGHAN suggest the use of radial EUS with mini-probes to diagnose congenital esophageal strictures (tracheobronchial remnants vs fibromuscular stenosis subtypes).

Congenital esophageal stenosis (CES) is an esophageal malformation with a stenosis generally located in the middle or more often in the lower esophagus. Three CES subtypes have been described: fibromuscular, tracheal cartilaginous remnants and the membranous web. In about 10% CES is associated with esophageal atresia [247] and differentiation between the CES subtypes is possible by histopathology after surgical resection [234,235,239,240,247].

A systematic review [247] from 144 CES cases confirmed the importance of EUS as the main diagnostic tool to distinguish CES subtypes and modify patient management. In tracheal cartilaginous remnant CES, some authors suggest stenosis resection and anastomosis to avoid the risk of post-dilation esophageal perforation [235,247]. A recent series reported CES dilations effective in all the different CES subtypes in 96% of the cases and suggests that surgery is reserved for cases of endoscopic dilation failure [252].

ESGE/ESPGHAN suggest consideration of EUS for the diagnosis of pancreatico-biliary diseases in children where non-invasive imaging modalities (ultrasonography, MRCP) are inconclusive (Table 7).

ESGE/ESPGHAN suggest EUS-guided drainage of pancreatic pseudocysts in children should be performed in in large EUS centers with specific experience and expertise.

EUS and EUS-guided fine-needle aspiration (FNA) have been reported as feasible in small series of children for assessing pancreatico-biliary diseases [233,241-246] where non-invasive imaging modalities (e.g. MRCP) are inconclusive. Therapeutic EUS with the drainage of pancreatic pseudocysts can be

performed with the same technique as that described in adult patients although in large cysts EUS guidance may not be necessary [233,250,251].

Indications for EUS in children are summarized in *Table 7*.

ESGE and ESPGHAN guidelines represent a consensus of best practice based on the available evidence at the time of preparation. They may not apply in all situations and should be interpreted in the light of specific clinical situations and resource availability. Further controlled clinical studies may be needed to clarify aspects of these statements, and revision may be necessary as new data appear. Clinical considerations may justify a course of action at variance to these recommendations. ESGE and ESPGHAN guidelines are intended to be an educational device to provide information that may assist endoscopists in providing care to patients. They are not rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment.

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Table 1. Typical diagnostic and therapeutic indications, non-indications and contraindications for esophagogastroduodenoscopy (EGD) in pediatric patients.

Diagnostic indications	Therapeutic indications	Non-indications	Contraindications
Weight loss, failure to thrive	Percutaneous endoscopic gastrostomy (re)placement	Uncomplicated Gastroesophageal Reflux Disease (GERD)	To diagnose perforation
Unexplained anemia	Duodenal tube placement	Functional Gastrointestinal (GI) disorders	
Abdominal pain with suspicion of an organic disease	Foreign body removal		
Dysphagia or odynophagia	Food impaction		
Caustic ingestion	Hemostasis		
Recurrent vomiting with unknown cause	Percutaneous jejunostomy placement		
Hematemesis	Esophageal varices		
Hematochezia	Dilatation of esophageal or upper GI strictures		
Unexplained chronic diarrhea	Perforation closure if this occurs during an endoscopy itself		
Suspicion of graft versus host disease	Achalasia pneumodilation or occasionally botulinum injection		
GI allergy	PEGJ tube insertion		

	Cysto-gastrostomy for drainage of pancreatic pseudocyst (preferably with endoultrasound guidance)	
Chronic GERD to exclude other diseases or surveillance of Barrett's esophagus	Polypectomy, endomucosal resection	

Table 2. Diagnostic indications for EGD in pediatric patients. Symptoms/signs according to suspected disease.

Symptoms/Signs	Suspicion of:
Weight loss, failure to thrive, chronic diarrhea, malabsorption, anemia, abdominal pain with suspicion of an organic disease	Celiac disease, IBD, giardia, allergic enteritis/enteropathy, bleeding lesions, graft versus host disease, peptic ulcer disease.
Dysphagia, odynophagia, chest pain, feeding difficulty	Foreign-body ingestion, food impaction, post-caustic ingestion, eosinophilic esophagitis, achalasia, aberrant vasculature affecting the esophagus, congenital webs or other abnormaities such as Schatzki's ring, stricture post-surgical e.g. post-repair of tracheo-esophageal fistula
Hematemesis, hematochezia, melena	Polyps, angiodyspasia, arterio-venous malformations, peptic ulcer with or without H.pylori infection, less common conditions such as duplication cysts
Family history of polyposis syndromes	Polyps (diagnostic and surveillance)
Vomiting	Any obstructive or partially obstructive pathology involving the upper GI tract e.g. pyloric stricturing, duodenal webs and strictures, bezoars, superior mesenteric artery syndrome etc; allergic GI pathology; peptic ulceration; assessment of esophagitis associated with reflux.

Table 3. Indication and site of tissue sampling during upper and lower endoscopy in pediatric patients.

Indication	'Tissue samples: sites and numbers'
Eosinophilic esophagitis	At least 3 biopsy sites should be targetted with 1-2 biopsies from proximal, middle and distal esophagus, regardless of the endoscopic appearance of the esophagus
Helicobacter pylori infection	2 biopsies from both the antrum and the corpus (±fundus)
Celiac disease	At least 1 biopsy from the duodenal bulb and at least 4 biopsies from the second or third portion of the duodenum
IBD	Multiple biopsies (2 or more per section) from all sections of the visualized GI tract, even in the absence of macroscopic lesions

Table 4. Type/size of GI endoscope in pediatric patients according to body weight.

Weight or age	EGD	Colonoscopy	ERCP	EUS
< 10 kg or < 1 year	≤ 6 mm gastroscope preferred. Consider standard adult gastroscope if endotherapy required.	≤ 6 mm gastroscope, standard adult gastroscope or pediatric colonoscope (<5-8kg or <6 months then an upper GI endoscope can be used and the size of the scope would depend on the size of the child – neonatal colonoscopy is rare but may require a paediatric upper GI endoscope).	7.5 mm duodenoscope.	Miniprobe or 7.4 mm EBUS-scope.
≥ 10 kg or ≥ 1 year	Standard adult gastroscope. Therapeutic gastroscope if needed.	Pediatric or adult colonoscope.	Therapeutic duodenoscope. (4.2 mm operative channel)	Miniprobe or 7.4 mm EBUS-scope.
≥ 15 kg or ≥ 3 years	-	-	-	Adult radial / linear Echoendoscope

EGD, esogastroduodenoscopy;

ERCP, endoscopic retrograde cholangiopancreatography;

EUS, endoscopic ultrasonography;

EBUS: Endobronchial Ultrasound.

Table 5. Typical diagnostic and therapeutic indications, non-indications and contraindications for ileo-colonoscopy in pediatric patients.

Diagnostic indications	Therapeutic indications	Non-indications	Contraindications
Unexplained anemia	Polypectomy, endomucosal resection or extended submucosal dissection and removal of sessile polyps	Functional GI disorders Constipation with normal fecal calprotectin	Toxic megacolon
Unexplained chronic diarrhea	Dilatation of ileo-colonic or colonic stenosis		Recent colonic perforation
Peri-anal lesions (fistula, abscess)	Treatment of bleeding lesions		Recent intestinal resection (< 7days)
Rectal blood loss	Foreign body removal		
Unexplained failure to thrive	Reduction of sigmoidal volvulus		
Initial work up for IBD	Cecostomy or sigmoidostomy		
Suspicion of graft versus host disease			
Rejection or complications after intestinal transplantation			
Radiological suspicion of ileo-colonic stenosis/stricture			
Polyposis syndromes			

Table 6. Typical ERCP indications in pediatric patients.

Biliary		Pancreatic	
Diagnostic	**Therapeutic**	**Diagnostic**	**Therapeutic**
Cholestasis in neonates and infants	Common bile duct stones	Evaluation of anomalous pancreatico-biliary junction	Chronic pancreatitis
Choledochal cyst	Bile leak (post-surgical/ post-traumatic)		Recurrent acute pancreatitis
Primary sclerosing cholangitis (brush cytology)	Benign biliary strictures		Pancreas divisum
	Primary sclerosing cholangitis		Pancreatic duct leak (post-surgical/ post-traumatic)
	Malignant biliary strictures		Pancreatic pseudocyst
	Parasitosis (Ascariasis, Fasciola)		Injection of botulinum toxin for sphincter of Oddi dysfunction

Table 7. Typical EUS indications in pediatric patients.

Esophagus	Stomach	Duodenum	Pancreatico-biliary
Congenital esophageal stenosis	Gastric duplication	Duodenal duplication	Bile duct stone
Eosinophilic esophagitis	Gastric varices		Pancreatic pseudocyst (diagnosis and treatment)
Esophageal duplication			Pancreatic disease (± FNA)

FNA: Fine-needle aspiration.