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ENTEROCLYSIS AND COMPUTED TOMOGRAPHIC ENTEROGRAPHY IN MEDICAL IMAGING

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ABSTRACT

Enteroclysis is an X-ray examination of the small intestine that looks at how a liquid called contrast material moves through the small intestine. This test is done in a hospital radiology department. The health care provider will insert a tube through nose or mouth into the stomach and into the beginning of the small bowel. Contrast material and air will flow through the tube and X-rays are taken. The X-ray images appear in real time on a monitor that is similar to a television screen. This means they are seen as the contrast is actually moving through the bowel. Sometimes a CT scan is also used. The goal of the study is to view all of the loops of small bowel. It is to be asked to change positions during the examination. The test usually lasts several hours, because it may take a while for the contrast to move through the whole small bowel. It is prescribed to drink clear liquids for at least 24 hours before the test. Laxatives may be prescribed to make sure the bowel is clear of any particles that might interfere with the study. It is suggested to stop taking medications, including narcotic pain relievers, on or before the day of the examination. It is recommended not to change or stop taking any medications without first talking to health care provider. If the patient is anxious about the procedure, it is suggested to be given a sedative before it starts. It is to be asked to remove all jewelry and to wear a hospital gown. It is best to leave jewelry and other valuables at home. It will be asked to remove any removable dental work, such as appliances, bridges or retainers. The placement of the tube may be uncomfortable. The contrast material may cause a feeling of abdominal disturbances. This test is performed to examine the small bowel. It is the most *complete way of telling if the small intestine is normal. There are no problems seen with the size or shape of the small intestine. Contrast travels through the bowel at a normal rate without any sign of blockage.*

Many problems of the small intestine can be found with enteroclysis. Some of these include: Inflammation of the small bowel (Crohn disease), Mal absorption, Narrowing or stricture of the intestine, Small bowel blockage, Tumors of the small intestine. The radiation exposure may be greater with this test than with other types of X-rays because of the length of time, but most experts feel that the risk is low compared to the benefits. Pregnant women and children are more sensitive to the risks of X-ray radiation. If there is a chance that if one is pregnant, it must be informed to health care provider. Rare complications include: Allergic reactions to medications prescribed for the examination (drug sensitivity), possible injury to bowel structures during the study, Barium may cause constipation. It must be informed to health care provider if the barium has not passed through the GIT system by 2 or 3 days after the test, or if feeling of constipation.

KEYWORDS: Contrast media, MRI, X-ray, GIT, Ultrasound, Barium meal, Thorotrast, Enteroclysis, CT enterography, Barolith.

INTRODUCTION

A **medical contrast medium** (or **contrast agent**) is a substance used to enhance the contrast of structures or fluids within the body in medical imaging. It is commonly used to enhance the visibility of blood vessels and the gastrointestinal tract. Several types of contrast media are in use in medical imaging and they can roughly be classified based on the imaging modalities where they are used. Although other types exist, most common contrast agents work based on X-ray attenuation and magnetic resonance signal enhancement.[1,2]

X-ray attenuation

Iodine and barium are the most common types of contrast medium for enhancing X-ray-based imaging methods. Various sorts of iodinated contrast media exist, with variations occurring between the osmolarity, viscosity and absolute iodine content of different media. Non-ionic dimers are favored for their low osmolarity and toxicity, but have a correspondingly higher price attached to their use.[3,4]

MR signal enhancing

Gadolinium is used in magnetic resonance imaging as a MRI contrast agent. In the 3^+ oxidation state the metal has 7 unpaired **f** electrons. $_{64}Gd^{157}$: $1s^2 2s^2 2p^6 3s^2 3p^6 3d^{10} 4s^2 4p^6 4d^{10} 5s^2 5p^6 \mathbf{4f^7} 5d^1 6s^2$. This causes water around the contrast agent to relax quickly, enhancing the quality of the MRI scan.[5,6]

Ultrasound scattering and frequency shift

Micro bubble contrast agents are used to aid the sonographic examination, specifically echocardiograms, for the detection of a cardiac shunt. These bubbles are composed of agitated saline solution, most of which are too large to pass through the lung capillaries. Therefore, the only ones that reach the left side of the heart pass through an abnormal connection between the two sides of the heart, a so-called right-to-left shunt. In addition, pharmaceutically prepared micro bubbles are composed of tiny amounts of nitrogen or per fluorocarbons strengthened and supported by a protein, lipid, or polymer shell. These are small enough to pass through the capillaries and are used to increase the contrast in the left ventricle, improving the visualization of its walls. The drop in density on the interface between the gas in the bubble and the surrounding liquid strongly scatters and reflects the ultrasound back to the probe. This process of backscattering gives the liquid with these bubbles a high signal, which can be seen in the resulting image.[7-9]

Figure-1: MRI Scan in enteroclysis

Adverse effects

While modern contrast media are generally safe to use, medical conditions can be caused by the administration of various contrast media. Reactions can range from minor to severe, sometimes resulting in death with death being about 0.9 per 100,000 cases. To better understand the reactions and to efficiently manage patients at risk, it is useful to classify them. Risk factors for developing severe reactions include strong allergies, bronchial asthma, cardiac disease and β-blocker use. While the previously suspected IL-2 medication is no risk for the acquisition of adverse events.[10,11]

A common misconception that even exists among healthcare professionals is that an allergy to contrast media is related to an allergy to seafood (shellfish) because both share iodine in their construction, implicating iodine as a source. Numerous studies have shown that although iodine is common in contrast media, iodine is not the cause of allergic reactions to contrast media and instead the more likely culprit are the inert ingredients and the patient's past history of having other strong allergic reactions. One important distinction is that allergic effects are by definition immunoglobulin E related histamine storms and studies have shown that contrast media cause no such reaction *in-vivo* thereby refuting the possibility that contrast media or the iodine in it is likely to be an allergen. Although it may seem contradictory, the few rare cases of contrast medium mediated IgE are exceedingly rare compared to all adverse reactions and when they happen, are often because the patient already has multiple risk factors that suggest the patient has other allergy related problems.[12] Historically, contrast media was sometimes highly dangerous but these dangers were not well-understood during the development of the early types of contrast media, such as Thorotrast.[13]

Upper Gastrointestinal Series also called Upper Gastrointestinal Studies or Barium X-rays of the upper gastrointestinal tract are medical radiography diagnostic tools used to examine the gastrointestinal tract for abnormalities. Barium sulphate mixed with water is ingested or instilled into the gastrointestinal tract and standard X-rays are made of the regions under examination. Because Barium is an X-ray contrast medium, it enhances the visibility of the relevant parts of the gastrointestinal tract by coating the inside wall of the tract and appearing white shadow/patch on X-ray film. This in combination with standard X-rays allows for the imaging of parts of the upper gastrointestinal tract such as the pharynx, larynx, oesophagus, stomach and small intestine such that the inside wall lining, size, shape, contour and patency are visible to the examiner. In combination with fluoroscopy it is also possible to visualize the functional movement of examined organs such as swallowing, peristaltic or sphincter closure. Depending on the organs to be examined, Barium X-rays can be classified into

Barium swallow, Barium meal or Barium follow through and Enteroclysis. To further enhance the quality of images, air or gas is sometimes introduced into the gastrointestinal tract in addition to Barium and this procedure is called double contrast imaging. In this case the gas is referred to as the negative contrast medium. Traditionally the images produced with Barium contrast are made with X-rays but Computer tomography is also used in combination with Barium contrast in which case the procedure is called CT enterography. Barium sulphate as a contrast medium was evolved from the prior use of bismuth preparation which was too toxic. The use of bismuth preparations had been described as early as 1898.[14]

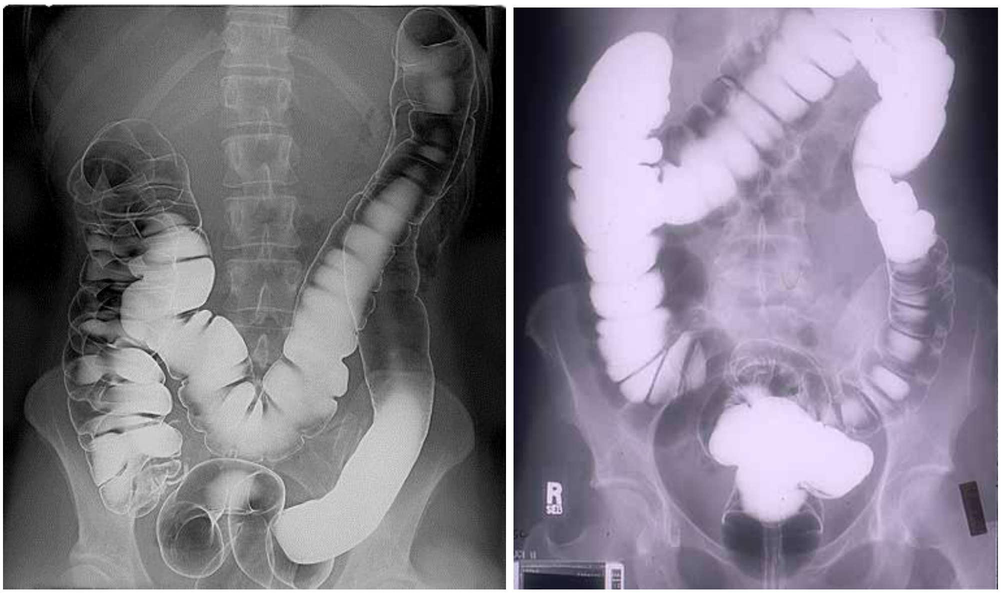

Figure-2: X-ray imaging of barium meal

Types: Various types of Barium X-ray examinations are used to examine different parts of the gastrointestinal tract. These include Barium swallow, Barium meal, Barium follow through and Barium enema. The Barium swallow, Barium meal and Barium follow through are together also called an Upper Gastrointestinal Series while the Barium enema is called a Lower Gastrointestinal Series. In Upper Gastrointestinal Series examinations, the Barium sulphate is mixed with water and swallowed orally, while in the Lower Gastrointestinal Series (Barium enema) the Barium contrast agent is administered as an enema through a small tube inserted into the rectum.[15]

(a) Barium swallow X-ray examinations are used to study the pharynx and oesophagus (b) Barium meal examinations are used to study the lower oesophagus, stomach and duodenum (c) Barium follow through examinations are used to study the small intestine (d) Enteroclysis also called small bowel enema is a Barium X-ray examination used to display individual loops of the small intestine by including the jejunum with a small tube and administering Barium sulphate followed by methylcellulose or air (e) Barium enema examinations are used to study the large intestine and rectum and are classified as Lower gastrointestinal series.[16]

Uses: Barium X-ray examinations are useful tools for the study of appearance and function of the parts of the gastrointestinal tract. They are used to diagnose and monitor Esophageal reflux, Dysphagia, Hiatus hernia, Strictures, Diverticula, Pyloric stenosis, Gastritis, Enteritis, Volvulus, Varices, Ulcers, Tumors and gastrointestinal dis-motility as well as to detect foreign bodies. Historically Barium X-ray examinations are the standard approach used to assess and diagnose diseases of the gut, but they are increasingly being replaced by more modern techniques such as computer tomography, magnetic resonance imaging, ultrasound imaging, endoscopy and capsule endoscopy. However, Barium contrast imaging remains a common diagnostic test, which has the advantage of lower costs and being more widely available as compared to newer techniques. Newer techniques are also not able to assess superficial mucosal lesions in as much detail as some Barium X-ray techniques such as enteroclysis.

Mechanism: Barium sulfate in suspension is frequently used clinically as a radio contrast agent for X-ray imaging and other diagnostic procedures. It is most often used in imaging of the GI tract during what is colloquially known as a "barium meal". It is administered orally, or by enema, as a suspension of fine particles in thick milk like solution (often with sweetening and flavoring agents added). Although barium is a heavy metal and its water-soluble compounds are often highly toxic, the low solubility of barium sulfate protects the patient from absorbing harmful amounts of the metal. Barium sulphate for diagnostic purpose must be free from chloride and it should pass the Cl^- limit test. Barium sulfate is also readily removed from the body, unlike Thorotrast, which it replaced. Thorotrast is a suspension containing particles of the radioactive compound thorium dioxide, ThO_2, which was used as a radio contrast agent in medical radiography in the 1930s and 1940s. Due to the relatively high atomic number 56 and atomic weight 137 ($_{56}Ba^{137}$: $1s^2 2s^2 2p^6 3s^2 3p^6 3d^{10} 4s^2 4p^6 4d^{10} 5s^2 5p^6 6s^2$) of barium (oxidation state 2^+), its compounds absorb X-rays more strongly than compounds derived from lighter nuclei. Barium sulphate is swallowed, which because it is a radio opaque substance does not allow the passage of X-rays. As a result areas coated by Barium sulphate will appear white on an X-ray film. The passage of Barium through the gastrointestinal tract is observed by a radiologist using a fluoroscope attached to a TV monitor. The radiologist takes a series of individual X-ray images at timed intervals depending on the areas to be studied. Sometimes medication which produces gas in the gastrointestinal tract is administered together with the Barium sulphate. This gas distends the gastrointestinal lumen, providing better imaging conditions and in this case the procedure is called double contrast imaging.[17]

Barium swallow examination

Little or no preparations are required for the study of the larynx, pharynx and esophagus when studied alone. A thick Barium mixture is swallowed in supine position and fluoroscopic images of the swallowing process are made. Then several swallows of a thin Barium mixture are taken and the passage is recorded by fluoroscopy and standard X-rays. The procedure is repeated several times with the examination table tilted at various angles. A total of 350-450ml of Barium is swallowed during the process.[18]

Figure-3: Enteroclysis by barium meal

Barium meal and Barium follow through examinations

For Barium meal or Barium follow through examinations a 6hour period of fasting is observed prior to the studies. Barium is administered orally, sometimes mixed with Gastrografin (diatrizoic acid) to reduce transit time in the bowel. Metoclopramide is sometimes also added to the mixture to enhance gastric emptying. X-ray images are then taken in a supine position at intervals of 20–30minutes. Real time fluoroscopy is used to assess bowel motility. The radiologist may press or palpate the abdomen during images to separate intestinal loops. The total time necessary for the test depends on the speed of bowel motility or transit time and may vary between one to three hours.[19]

Enteroclysis

For small bowel examinations, in addition to fasting for eight hours prior to examination, a laxative may also be necessary for bowel preparation and cleansing. Enteroclysis involves the continued infusion of 500-1000ml of thin Barium sulphate suspension into the intestine through a duodenal tube. Then methylcellulose is instilled through the tube. Barium and methylcellulose fill the intestinal loops which can be viewed continuously using fluoroscopy, or standard X-rays are taken at frequent intervals. The technique is a double contrast procedure which allows detailed imaging of the entire small intestine. However the procedure may take 6 hours or longer to complete and is quite uncomfortable to undergo.[20]

Result analysis: (a) Enteroclysis has shown to be very accurate in diagnosing small bowel diseases, with a sensitivity of 93.1% and specificity of 96.9%. It permits detection of lesion which may not be seen with other imaging techniques. There is no significant difference in terms of detection of clinically significant findings, sensitivity or specificity between Enteroclysis and Computer Tomographic Enterography. Enteroclysis compares favorably with wireless capsule endoscopy and double-balloon endoscopy in the diagnosis of mucosal abnormalities of the small bowel.[21]

(b) The interpretation of standard barium swallow examinations for assessing dysphagia is operator and interpreter dependent. It has poor sensitivity for subtle abnormalities but is more sensitive in detecting esophageal webs and rings than gastroscopy. The best initial evaluation of suspected oro-pharyngeal dysphagia is a barium study. Barium swallow studies remain the main investigation of dysphagia. Barium studies may detect pharyngeal tumors that are difficult to visualize endoscopically.[22]

(c) Barium follows through examinations are the most commonly used imaging technique in assessing patients with Crohn's disease, although Computer Tomography and Magnetic Resonance Imaging (MRI) are widely accepted as being superior. However, Barium examinations remain superior in the depiction of mucosal abnormalities. The features of Crohn`s disease are well described by Barium follow through examinations, appearing as a typical "cobblestone pattern", but no information is obtained regarding extra-luminal disease.

Radiographic imaging in Crohn’s disease provides clinicians with objective evaluations of small bowel regions that are not accessible to standard endoscopic techniques. Because of its length and complex loops, the small intestine is the most difficult part of the gastrointestinal tract to evaluate. Most endoscopic techniques are limited to the examination of proximal or distal segments, hence Barium follow through remains in most centres the test of choice for the investigation of abdominal pain, diarrhoea and in particular diseases manifesting mucosal abnormalities such as celiac and Crohn's disease.[23]

Figure-4: Barium sulphate suspension to be swallowed by patient

(d) Barium swallow studies are better than endoscopy at demonstrating the anatomic findings in gastro-esophageal reflux disease after anti-reflux surgery.[24]

(e) Barium fluoroscopic examinations have some advantages over computed tomography and magnetic resonance techniques, such as higher spatial resolution and the ability to examine bowel peristalsis and distension in real time.[25]

(f) Many infections and parasitic infestations produce patterns of the luminal surface, which are best seen on Barium examinations. Certain parasites are seen as filling defects outlined by Barium and Barium examinations play an important role in the diagnosis of intestinal infections and infestations as compared to other techniques. Barium studies show Tapeworms and Ascaris as thin, linear filling defects of the bowel. Because Ascaris have a developed alimentary tract, Barium may outline the parasites’ intestinal tracts on delayed images. In Strongyloidiasis Barium studies show intestinal wall edema, thickening of intestinal folds with flattening and atrophy of the overlying mucosa. Schistosomiasis caused by infection with Flatworms have an appearance resembling colitis ulcerosa, with inflammatory polyps, ulcers, fibrosis, wall thickening, loss of haustration and stenosis in Barium X-rays. Anisakiasis is demonstrated by Barium X-rays as bowel wall edema, thickening, ulceration, or stricture due to inflammation. Sometimes worms are seen as long, thread-like, linear filling defects up to 30cm long. In Typhlitis Barium studies show edema, ulceration and inflammation of bowel wall resulting in wall thickening. In Pseudo membranous colitis Barium studies show pan colitis with thumb printing and shaggy margins as well as plaque-like eccentric, nodular or polyploidy appearance.[26]

(g) Barium studies and computer tomography are the most common tools used to diagnose gastrointestinal Lymphoma. Barium chloride, along with other water-soluble barium salts, is highly toxic. Sodium sulfate and magnesium sulfate are potential antidotes because they form the insoluble solid barium sulfate $BaSO_4$, which is also less toxic, but less harmful because of its insolubility. Barium contrast is more sensitive in the demonstration of subtle mucosa and sub-mucosa abnormalities but computer tomography is the method of choice for determining the extent of disease and staging as well as related complications such as fistulation and perforation. Sub-mucosal nodules or masses form a bull's-eye or target appearance on barium studies.[27]

Figure-5: CT Enterography of GIT

Adverse effects: Radiographic examinations entail the exposure to radiation in form of X-rays. Although Barium ions are toxic, their use is generally regarded as safe because the small amounts of Barium ions available in solution and absorbed by the Gastrointestinal tract are deemed to be of no practical importance. However isolated cases of Barium encephalopathy have been described following absorption of Barium from the intestinal tract. Constipation and abdominal pain may occur after Barium meals.[28] The formation of Baroliths (barium clog), which may need to be removed surgically, is a complication of the use of Barium sulphate. Baroliths are rare complications of barium contrast roentgenography that occur almost exclusively in the colon. Baroliths are often asymptomatic, but may be associated with abdominal pain, appendicitis, bowel obstruction, or perforation. We present an unusual case of a barolith which developed within the lumen of the small bowel, and resulted in the detection of an otherwise occult carcinoid tumor of the ileum. Barium sulphate may cause serious peritoneal irritation. Leakage of Barium sulphate into the abdominal cavity may occur in people with duodenal ulcers or other perforations and may lead to peritonitis, adhesion, granulomas and is associated with a high mortality rate.[29] Leakage of Barium into the mediastinum or peritoneal cavity may lead to endotoxic shock which is often fatal. As a result, the use of Barium as a contrast agent is contraindicated when there is a suspicion or possibility of compromise of bowel wall integrity. Aspiration or inhalation of Barium sulphate into the lungs during oral application can lead to serious respiratory complications leading to fatal aspiration pneumonia or asphyxiation. Hypersensitivity and allergic reactions are rare but some additives contained in Barium preparations may induce immune reactions. Complete gastrointestinal obstruction is also a contraindication for Barium studies.[30]

CONCLUSION

Computed Tomographic (CT) Enterography is a non-invasive technique for diagnosis of small bowel disorders.

ADVANTAGES

- evaluates the entire thickness of the bowel wall
- offers information about the surrounding mesentery, the mesenteric vasculature and the perienteric fat
- useful in the assessment of the solid organs and provides global overview of the abdomen

Disadvantages

- exposure to ionizing radiation

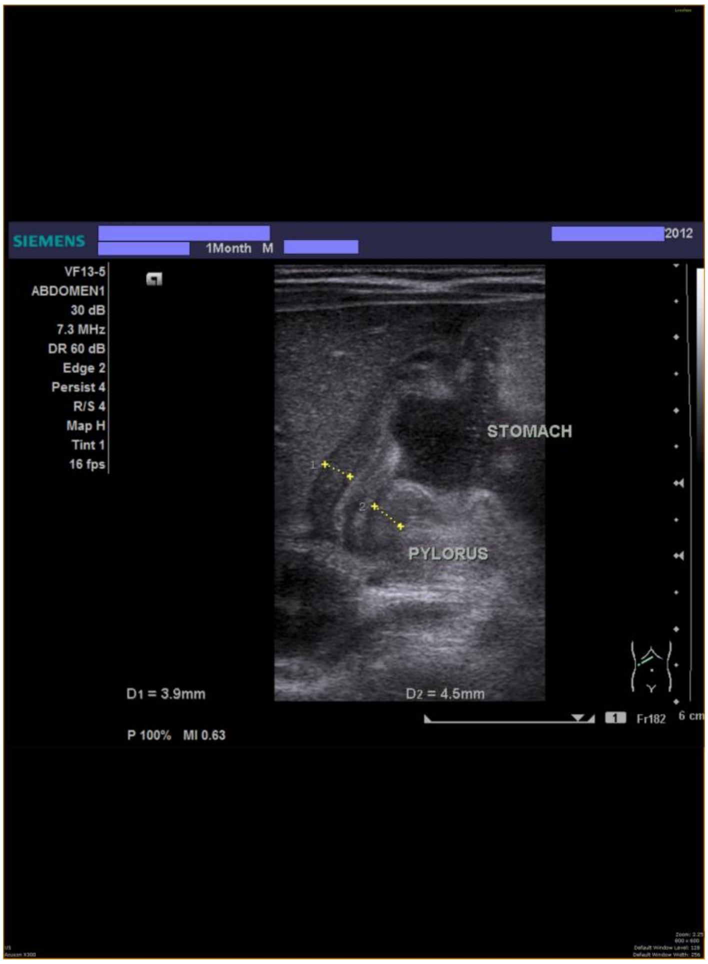

Figure-6: Computed Tomographic Enterography

Technique

Adequate luminal distension is necessary as collapsed bowel loops may mimic pathology. CT enterography utilizes two types of contrast:

- neutral oral contrast agents
  - these have attenuation similar to that of water e.g. water, PEG electrolyte solution, methyl cellulose
  - intravenous contrast is used with neutral agents
  - these agents allow better assessment of mucosal enhancement, mural thickness as well as mesenteric vasculature, this is important especially in the evaluation of Crohn's disease [2]

- **positive contrast agents**
  - such as a dilute (1%) barium solutions

- they are not routinely used in CT enterogrpahy
- pathologic mural enhancement and intestinal hemorrhage are obscured by positive contrast agents
- mainly used to detect lower grades of small bowel obstruction and internal fistula

Procedure

Actual procedure will vary depending on institutional protocol/guidelines but below is a typical description:

1. Abstain from all food and drink 4-6hours before the exam
2. Patients drink about 1.5-2L of oral contrast over 40-60minutes
3. Administration of intravenous contrast injection at a rate 4ml/sec
4. CT scanning is ideally performed on a multi-detector computed tomography (MDCT) scanner about 45-65seconds after contrast material injection in a single (venous) phase or dual (arterial & venous) phases for the evaluation of mesenteric vasculature or GI tract bleeding.
5. Data interpretation with the use of axial and coronal reformatted images for proper evaluation.

Findings

(a) Inflammatory bowel disease and its complications e.g. Crohn's disease or ulcerative colitis

(b) small bowel tumors, including benign tumors (e.g. hamartomatous or hyperplastic polyps) or malignant tumors (e.g. adenocarcinoma, carcinoid, lymphoma and gastrointestinal stromal tumors)

(c) mesenteric ischemia and gastrointestinal tract bleeding

(d) Coeliac disease

REFERENCES

1. Sen D.J., Prajapati M.K., Sheth A.H. and Patel V.V.; *Study of viscera by X-ray contrast media in diagnostic radiology*: International Journal of Drug Development and Research: 2(1): 171-181, 2010.
2. Patel J.B, Patel K.M., Shah D.H., Patel J.S., Garg C.S., Brahmbhatt K.J. and Sen D.J.; *Functional magnetic resonance imaging: a new diversion in medical diagnosis*: Research Journal of Pharmacy and Technology: 4(8): 1169-1178, 2011.
3. Thomson K. and Varma D.; *Safe use of radiographic contrast media*: Australian Prescriber: 33: 19-22, 2010.

4. Caro J.J., Evelinda T., Maurice M.G.; *The Risks of Death and of Severe Nonfatal Reactions with High- vs Low Osmolarity Contrast Media: A Meta-analysis*: American Journal of Roentgenology: 156(4): 825–832, 1991.
5. Böhm I., Heverhagen J.T., Klose K.J.; *Classification of acute and deleayed contrast media-induced reactions: proposal of a three-step system*: Contrast Media & Molecular Imaging: 7(6): 537-541, 2012.
6. Brockow K. *et al*.; *Management of hypersensitivity reactions to iodinated contrast media*: European Journal of Allergy & Clinical Immunology: 60(2): 150–158, 2005.
7. Boehm I.; *Contrast media and patients at risk: asthma*: Acta Radiologica: 50(3): 348, 2009.
8. Boehm I.; *Is interleukin-2 (still) a risk factor for adverse reactions in concert with radiographic contrast medium injection?*: Acta Radiol: 50(7): 752-753, 2009.
9. Coakley F. and David M.P.; *Iodine Allergy: An Oyster Without a Pearl?*: American Journal of Roentology: 169(4): 951–952, 1997.
10. Boehm I.; *Seafood Allergy and Radiocontrast Media: Are Physicians Propagating a Myth?*: The American Journal of Medicine: 121(8): e19, 2008.
11. Carr D.H. and Archi C.W.; *Contrast Media Reactions: experimental evidence against the allergy theory*: British Journal of Radiology: 57(678): 469–473, 1984.
12. Murphy K.P., McLaughlin P.D. O'Connor O.J. and Maher M.M.; *Imaging the small bowel*: Current opinion in gastroenterology: 30(2): 134–140, 2014.
13. Kuo P., Holloway R.H. and Nguyen N.Q.; *Current and future techniques in the evaluation of dysphagia*: Journal of gastroenterology and hepatology: 27(5): 873–881, 2012.
14. Levine M.S., Rubesin S.E., and Laufer I.; *Pattern approach for diseases of mesenteric small bowel on barium studies*: Radiology: 249(2): 445–460, 2008.
15. Maglinte D.D., Kohli M.D., Romano S. and Lappas J.C.; *Air (CO_2) double-contrast barium enteroclysis*: Radiology: 252(3): 633–641, 2009.
16. Grant P.D., Morgan D.E., Scholz F.J. and Canon C.L.; *Pharyngeal dysphagia: what the radiologist needs to know*: Current problems in diagnostic radiology: 38(1): 17–32, 2009.
17. Bhatt N.A. and Sen D.J.; *Pharmacopoeia reflects on permissible pharmaceutical impurities in parts per million limit*: Journal of Drug Discovery and Therapeutics: 3(28): 01-09, 2015.

18. Dambha F., Tanner J. and Carroll N.; *Diagnostic imaging in Crohn's disease: what is the new gold standard?*: Best practice & research. Clinical gastroenterology: 28(3): 421–436, 2014.
19. Deepak P., and Bruining D.H.; *Radiographical evaluation of ulcerative colitis*: Gastroenterology report: 2(3): 169–177, 2014.
20. Baker M.E., and Einstein D.M.; *Barium esophagram: does it have a role in gastroesophageal reflux disease?*: Gastroenterology clinics of North America: 43(1): 47–68, 2014.
21. Fidler J.L., Fletcher J.G., Bruining D.H., and Trenkner S.W.; (*Current status of CT, magnetic resonance, and barium in inflammatory bowel disease*: Seminars in roentgenology: 48(3): 234–244, 2013.
22. Sinha R., Rajesh A., Rawat S., and Rajiah P.R.; *Infections and infestations of the gastrointestinal tract. Part 1: bacterial, viral and fungal infections*: Clinical radiology: 67(5): 484–494, 2012.
23. Sinha R., Rajesh A., Rawat S., and Rajiah P.R.; *Infections and infestations of the gastrointestinal tract. Part 2: parasitic and other infections*: Clinical radiology: 67(5): 495–504, 2012.
24. JuEngin G., and Korman U.; *Gastrointestinal lymphoma: a spectrum of fluoroscopic and CT findings*: Diagnostic and interventional radiology: 17(3): 255–265, 2011.
25. Schott G.D.; *Some observations on the history of the use of barium salts in medicine*: Medical History: 18(1): 9–21, 2012.
26. Paulsen S.R., Huprich J.E. and Fletcher J.G. *et al*.; *CT enterography as a diagnostic tool in evaluating small bowel disorders: review of clinical experience with over 700 cases*: Radiographics: 26(3): 641-657, 2006.
27. Elsayes K.M., Al-Hawary M.M. and Jagdish J. *et al*.; *CT enterography: principles, trends, and interpretation of findings*: Radiographics.: 30(7): 1955-1970, 2010.
28. Maglinte D.D., Bender G.N. and Heitkamp D.E. *et al*. *Multidetector-row helical CT enteroclysis*. Radiol. Clin. North Am.: 41(2): 249-262, 2003.
29. Ilangovan R., Burling D., George A. *et al*.; *CT enterography: review of technique and practical tips*: Br. J. Radiol.: 85(1015): 876-886, 2012.
30. Raptopoulos V., Schwartz R.K., McNicholas M.M. *et al*.; *Multiplanar helical CT enterography in patients with Crohn's disease*: AJR Am J Roentgenol.: 169(6): 1545-1550, 1997.