CHAPTER II
Physicians examined the colon long before roentgen discovery. Ordinary physical examination which included palpation per abdomen yielded some results. Simple air insufflation of the large bowel aided both palpation and percussion thus enabling the clinician to determine the position of colon in reference to an abdominal tumour (Ziemssen, Runeberg).

Soon after the roentgen discovery, came the idea of artificially introducing a relative difference in density between the intestinal tube and the tissue surrounding it, thereby enhancing its roentgenologic contrast.

In 1896 Bacher in Germany and Cannon in America were successful in demonstrating roentgenographically various portions of gastro-intestinal tract with the salts of heavy metal. Cannon used capsules filled with bismuth sub-nitrate and showed the phenomena of deglutition exhibited by goose. Bacher produced roentgenograms of stomach and that of isolated loops of large intestines, after filling them with lead acetate as well as air. Even at that early date, he used both extremes of contrast scales to visualise the lumen of alimentary canal. This idea of double contrast
examination which came to early workers was naturally
due to common pre-roentgen use of air in insufflating
the colon.

Rumpel was apparently the first to use a suspension
of a metallic contrast substance to visualise a portion
of the alimentary tract of man. He used suspension of
bismuth subnitrate and showed a dilated oesophagus.

Earlier observers as Cannon, Raux, Balthazard and
Williams were concerned largely with the oesophagus and
stomach roentgenography, although Williams suggested
the use of gas for outlining the sigmoid and descending
portion of colon as early as 1901.

Hildebrand and Rumpel actually visualised the
colon of human being in vivo. They administered large
quantities of bismuth orally for several days, gave
opium to quieten the intestines, thus facilitating the
formation of opaque faecal masses and took roentgenograms
just after insufflating it with air.

Laurell produced useful roentgenograms of caecum
and proximal ascending colon using similar method.

It is evident thus that the combined method
actually had been used before the single contrast method
was established. In the same publication Hildebrand
claimed to have visualised human colon by injecting a
suspension of bismuth salt through rectum.
In 1909, Groedeal was responsible for developing radio-opaque bismuth clysm which was subsequently used by Rieder and Schule in their studies of colon.

Haenisch (1911) reported the superiority of the contrast enema over contrast meal for all purposes except for the study of motor function of colon. His observations were very well received and gave impetus to more intensive application of roentgen rays for the study of colon.

Pfahler in 1907 and Cole and Einhon in 1911 used only gas as contrast medium and were the first to submit their experience in roentgenography of colon pathology. However, they did not think that gases would ever replace metallic salts as contrast substances, but they felt that the gases may be used when for some reason or the other the use of opaque salt was inadvisable or contra-indicated. The chiefly recommended gases were air and carbon dioxide.

Krauss believed oxygen to be superior to other gases because he said it was easier to administer, afforded better contrast and was more comfortable to the patient.

Burkhardt applied the method of Krauss and demonstrated abnormal narrowing and widening of colon as well as the presence of foreign bodies and polypoid tumour.
The other group of workers as Ropke (1912) and Schitten Helm (1924) used air insufflation for demonstrating the lower border of liver, spleen, gall bladder and other extra colonic tumours. Rosenfeld and Meyer-Betz used air similarly. Philips demonstrated roentgenographically a large hypernephroma with the aid of air insufflation.

Schwarz, in his monograph on the clinical roentgenologic diagnosis of the colon, briefly considered the topic of colonic insufflation and dismissed the procedure as possessing little practical diagnostic value.

Since Haenisch's first publication in 1911, the opaque enema was the method of choice for the colon examination up to 1923. The sulphate of barium was first recommended by Krauss in 1910 and was found to be highly satisfactory. This gradually replaced the bismuth salts which occasionally were found to contain harmful toxic soluble substances. Barium sulphate could be obtained in pure form and was less costly. Thus it became standard opaque medium for the alimentary tract roentgenography.

Case in 1911 pointed out the advantages of stereo-roentgenography of colon filled with opaque material for more definite demonstration of certain significant roentgenologic abnormalities.
The studies of mucosal relief were initiated by Cole in 1915, and subsequently followed by Forssell, Bery, Knothe and Chaoul. Their observations essentially rested on the study of internal relief patterns of the colonic mucosa after the opaque enema had been evacuated.

In 1923, and again in 1925 A.W. Fischer of Germany described in detail his method for accomplishing the double contrast examination of colon. He did experiments with the surgically resected portions of the colon, and found that by using a suspension of barium sulphate, hydrated aluminium silicate and water, he could obtain excellent double contrast roentgenograms provided only a small amount of suspension was used and specimen vigorously shaken. This coated the walls of colon thoroughly after which he inflated it with air.

Fischer then applied this method on the patients. Depending upon each individual case he introduced air without permitting any evacuation of barium or at times allowed partial or complete evacuation followed immediately by insufflation under roentgenoscopic control.

The main advantages claimed by Fischer in his classic publication were the ability of air to penetrate stenosing lesion better than the heavy barium suspension; the ability of the examiner to see through overlapping loops of colon, plus the fact that the intra-luminal
polypoid tumours could be visualised which might get completely obscured by a solid column of barium. Thus Fischer laid the ground work for the method of double contrast examination of colon and claimed that his technique was superior to single opaque contrast method.

In 1928 while on a medical study trip in Europe, B.R. Kirklin who was then Head of the Section of Roentgenology of Mayo Clinic, Rochester, met Fischer and was greatly impressed with the potentialities of his technique. On returning home Kirklin relayed his impressions of the Fischer's method to one of his associates, Harry W. Weber.

After two years of constant efforts, Weber in 1930 modified and improved the double contrast examination of colon. He could produce diagnostic roentgenograms consistently with the help of double contrast technique. Besides Weber, Gershon-Cohen and Shay also started studying this technique. In 1930, Gershon-Cohen published a preliminary report on the diagnosis of early ileocaecal tuberculosis by double contrast enema. He stressed the usefulness of this method and showed additional findings over Stierlin's description in 1911.

Again in 1931 while enumerating the advantages of double contrast examination, Gershon-Cohen showed that the early neoplastic growths could be detected long
before they produce filling defects on single contrast; and provided a second check over the findings.

Weber (1930) used two ounces of castor oil in the evening before the examination for cleaning the colon followed by a soapy enema next morning. He also suggested the use of tincture belladona in three divided doses, two on the previous evening and one in the morning for patients feeling undue difficulty in retaining the enema.

Frick, Bluhbaum and Kalkbrenner (1928) used a colloidal solution of thorium de oxide which had the property of flocculating on the intestinal mucosa.

Raymond Sarasin in 1937 described the technique of colon examination in great detail which he divided into following three stages. This, subsequently, became standard procedure of examination:

Stage I - Filling, with opaque clysma.
Stage II - Evacuation of all excess.
Stage III - Air insufflation.

In 1939 J.C. Root injected air by two-bottle method. He flowed water from one bottle to other, displacing the measured quantity of air in colon. It also provided a constant flow of air. The clysma he used contained barium and water mixture with acacia as suspending medium.

Gershon-Cohen and Shay (1941) brought out a report on advantages of double contrast examination. They
pointed out that there was about 10% failure in establishing a diagnosis by simple barium enema, but many of such lesions could be shown by double contrast method. Out of 500 cases they found 7 lesions which could not be seen except only after air insufflation. They also successfully demonstrated the loops of bowel proximal to obstructive growths where barium could not pass. With double contrast examination the percentage of non-visualised pathology in the rectum also decreased. Smedal (1946) experienced that double contrast examination was not a simple procedure and its interpretation was not easy. In order to get a small amount of barium in right half of colon, the left side was over-filled rendering the air contrast roentgenograms valueless. He was of the opinion that simple enema must precede in all cases. Stevenson and Wilson (1952) also felt similarly and pointed out that it was not diagnostic in certain inflammatory diseases, and the lesions of right side of colon or terminal ileum. The air insufflation erases the mucosal details and also distended the segment so involved in mild inflammatory process. Reviewing again in 1954, they felt the importance of double contrast, but suggested that for utmost accuracy both examinations were necessary and should be carried out as two separate procedures with separate preparations. There should be at least a time interval of one day.
Martin L. Tracey (1946) and Bell et al (1948) stressed that a detailed colon examination was indicated when there was:

(a) A recent change in bowel habit
(b) An unexplained rectal bleeding
(c) A progressive anaemia without visible bleeding
(d) Indigestion or discomfort indicating interference with the passage of material through the bowel.

To overcome the difficulty of visualising rectum and pelvic colon, G.H. Fletcher in 1948 described a method, where he filled the urinary bladder by 200 to 400 cc. of saline water. This displaced the colon from the pelvis and presented a single loop for examination.

Till then the main obstacle in producing good double contrast roentgenograms was the presence of excess amount of barium suspension in colon. Moreton et al started working on those lines. In 1949 they performed the examination with limited suspension by stopping the opaque column when it reached a point just beyond the splenic flexure. He then rotated the patient to right causing the barium to gravitate as far as the hepatic flexure. Following evacuation he insufflated colon with air and exposed roentgen films. A routine use of double contrast was also stressed.

Same year Moreton, Stevenson and Yates tried to analyse the causes of fictitious polyps encountered in
double contrast studies. Those were usually due to various faecal particles, oil globules as indigested castor oil or mineral oil, non water soluble grease introduced by proctoscope or enema tips and air bubbles coated with barium.

C.A. Stevenson (1950) observed that a rapid introduction of air in the colon tends to lessen the fictitious polyp formation as against the slow administration of air.

A proper bowel wash and use of soap lubrication on enema tip instead of grease lessened the chances of such difficulty (Yates et al 1950).

For achieving similar advantages as barium-air contrast examination, Ladoux-Bebard and Garcia-Calderon proposed the use of a semi-transparent medium. According to them this study must be supplemented by a second enema of fully opaque barium as the previous one gave very poor fluoroscopic images. The medium used was expensive.

The idea of using higher kilovoltage came subsequently. In 1936 Riglerand Eriksen used over-exposed films for the demonstration of polypoid growth of stomach. Independently, few months later, Gianturco began to study the possibility of the over-exposed films by high kilovoltage technique for the examination of colon.
He showed that the barium mixture which was fully opaque to fluoroscopy could be rendered more and more transparent by increasing the kilovoltage in radiography. He published his first report in 1950 where he used a suspension of one part of barium in four parts of water and took roentgenograms at 100 K.V. or later at 120 K.V. With those factors he could see the second loop of the colon through superimposed other loop thus increasing the value of such a procedure. Gianturco objected the use of dilute suspensions as advised by Potter because of quick settling of barium in it and poor fluoroscopic image.

The routine use of high kilovoltage technique was again emphasised by F.K. Wietersen (1957) and S.J. Figiel et al (1958).

In 1957 G. Levene and S.A. Kaufman emphasised the use of compressed carbon dioxide instead of air in double contrast examination. While describing the advantages, they showed that carbon dioxide was 150 times more rapidly absorbed from the bowel and so was not attended by any discomfort as generally experienced with air. They also brought out that it was safer to use carbon dioxide as there was less danger of gas embolism. The gases other than air could not gain popularity because of the difficulty in insufflating the colon in dark room where fluoroscopy was being conducted.
The methods described so far were performed conventionally in three stages. R.D. Moreton, E.M. Cooper and E.F. Foegelle (1951) used a simple one stage procedure. They used a Y shaped adapter through which they injected suspension and air. After running the opaque enema up to splenic flexure they injected air by Weber's insufflator at a steady rate through the other limb of 'Y' adapter. By manipulating the position of the patient under fluoroscopy, keeping the barium column dependent, they visualised the whole of large bowel. The excess of barium if present could be drained through that adapter. They also used higher K.V. and lower M.A.S. values. After examining 2000 colons they brought out various advantages which included shortened time required for the examination and no reinsertion of catheter for air insufflation was required.

Templeton and Addington in 1951 combined the single and double contrast studies by developing an apparatus having a three-way valve which facilitated the filling of colon, then evacuating it partially and introducing air. They accomplished the evacuation by attaching the outflow channel to a source of negative pressure worked by water siphon. The chief drawbacks of this apparatus was its cost, repeated plugging of the drainage tube and problem of contamination.
The one-stage method was later used by many. Francis Polgar wrote about his contrast enema in lateral recumbency and aimed gas filling of the colon.

J.B. Douglas (1953) used similar one stage procedure as described by Moreton et al and found it very useful in some hospitalised patients.

J.C. Root and C.M. Greenwald (1954) also advocated a one-stage method using a Y tube connection. They reported two cases which revealed polypoid lesions, hidden on conventional examination.

In 1954 H.C. Crozier described a hand operated barium pump assembly.

A.M. Fraser (1955) described his variable contrast technique as a supplement to single contrast examination. He pushed water or dilute barium suspension after a normal opaque enema reached the splenic flexure. This he achieved by using two enema cans containing each type of suspension connected through Y tube.

L.B. Lusted and E.R. Miller (1955) described a pneumocolon bottle (BAIRBOT) by which they could perform examination in one stage. With the help of that they could regulate the filling of colon by opaque suspension or air.

Solve Welin while delivering Mackenzie Davidson Memorial Lecture in 1958 and again in 1962 described in detail his method of examination which was named as Malmo
modification. His procedure worked for regulated evacuation of the contrast medium from the colon and to avoid any unnecessary waiting time, thus completed the whole examination in less than 20 to 25 minutes.

He performed the examination in two steps. After cleaning the bowel, the patient was subjected to the first contrast enema with thick suspension of specific gravity of 6.5. This was not allowed to go beyond the splenic flexure. The patient evacuated this enema in toilet after necessary roentgenograms were made.

A second enema was given this time only up to middle of sigmoid colon after which air was injected and the patient manipulated for equal distribution of air and barium over entire intestinal wall. The excess of contrast medium was then drained off by ordinary enema pipe. He used clysodrast along with the barium suspension which contained tannic acid and performed over 9000 examinations with the above technique. He was convinced of the superiority of double contrast.

B.D. Braun (1959) followed a similar method and said that second enema of contrast medium provided a confirmation of a negative shadow, or any other pathology recognised at the first examination. During the second examination the bowel was better cleaned.

Nathan and Newman (1959) produced double contrast
roentgenograms without any fluoroscopic examination. He instilled a measured quantity of air approximately equal to the volume of barium suspension used.

Lately H.L. Steinbach et al (1962) used a disposable plastic bag for clearing as well as for barium enema. Though it was a little expensive but prevented cross contamination.

Pochaczevsky and Sherman in 1963 also used a disposable barium enema kit with prepacked barium sulphate. Before examination, the barium had to be mixed with added water but there was difficulty in proper mixing of the barium water suspension.

R.E. Miller (1964) suggested barium enema examination with large bore tubing of a diameter 3/8 inch. He drained the suspension by lowering the enema can below the level of the table top.

Steinbach, Burheume and Andren used similar method.

R.B. Pridie in 1965 following the same idea described a method for performing a double contrast examination in one stage and emphasised its routine use in a busy department, because the method was simple and needed less time than conventional methods.

A proper preparation of colon had been emphasised by many workers and was essential, specially for double contrast examination.
Yates, Moreton and Cooper (1950) analysed and found that where only a laxative was used without any bowel wash, 41 per cent had retained faecal matter. Further 51 per cent of double contrast studies had to be repeated for those patients who were allowed to eat supper and so they advised no supper on the previous day.

Though the ideal preparation of bowel has been the aim, it has not been achieved. S. Welin said that 'any attempt to get the intestines really cleaned was like crying for the moon'.

Swenson and Wigh (1948) believed that purgation was not really indicated and that morning cleansing enema was enough. Contrary to that Christie, Coe et al (1950) would purge their patients even at the risk of bleeding.

Hodges (1953) considered cleansing enemas useless as ordinarily carried out and prepared his cases with laxatives.

Besides castor oil which was used by earlier workers, various other cathartics had been tried for preparing the colon. These newer evacuants were found to be no way superior to castor oil.

Yates et al (1950) made a comparative study of three laxatives and found castor oil, phenolphthalin and compound licorice powder effective in that order. A similar study by C.A. Stevenson (1952) found that castor
oil cleaned the colon best as compared to phenolphthalein and compound licorice.

Kohler and Tahti stated that the results with castor oil and preliminary water enema were unsatisfactory in nearly one third of patients examined.

Other cathartics used were dulcolax, roenten, X-prep, which claimed to clean the colon in 64 %, 73 % and 64 % respectively. Andren, Frieberg Welins reported success with clysodrast.

In the experience of H.L. Steinbach and H.J. Burheune (1962) dulcolax and other agents were inferior to castor oil. In the observation of J.L. Ritan (1962) Dulcolax and X-prep proved to be as adequate as castor oil and enema.

R.D. Sloan and J.K. Goodrich (1962) conducted a comparative evaluation of the following three colon preparation techniques:

1. Castor oil and tap water enema
2. Castor oil and fleet enema disposable unit
3. Phosphosoda and fleet enema.

They found no significant difference but the colon prepared with castor oil and water enema appeared to be more adequately cleaned.

Moreton (1963) used one ounce of castor oil as advised by many previous workers (Welin 1930). He
believed that by giving 2 ounces one may produce confusing oil droplet shadows. Jones, Kaplan, Windholz (1951) did not encounter this difficulty and so advised to use 2 ounces of castor oil.

Hodge (1953) recommended two ounces as one would be certain that patient had ingested at least one ounce. Robinson in 1957 used castor oil in some quantity.

Govdin, Brailsford and Mucklow used hydrogen peroxide added in cleansing enema for cleaning the bowel.

G.N. Chucker and W.M.P. Gilmer (1958) brought out a detailed scheme to be followed for preparation prior to barium enema examination.

The universally accepted barium sulphate as a standard opaque medium was insoluble in water. A suspension in plain water though used by many workers was found to be unsatisfactory as it settled down rapidly due to immediate clumping of particles (Marks, 1951). Cochrane Shanks suggested a suspension containing barium sulphate 25 % W/W in water.

The characteristics of ideal suspension was brought out by Paul C. Hodges (1953). According to him the homogenised suspension should hold the bulk of barium in suspension for long periods and yet should get deposited on the colonic mucosa in a thin film. This should persist for some time even after evacuation.
Earlier the stable suspension was obtained by adding substances like kaolin starch, agar, gelatine or natural gums. Of these gum acacia was commonly employed.

Moreton and Yates (1950) made a comparative study of barium sulphate preparations, one with plain water and other containing suspending medium and found that the latter preparation was more suitable. The suspension showed better adherence to mucosa. He produced microphotographs showing uniform distribution of barium particles in suspensions with these media.

Poppel and Bercow (1944) found that mixture of 75 Gm. of barium sulphate, 5 Gm. of gum acacia and 2 quartz of water satisfied them fully while others advised its use in strength of 2 per cent.

Carboxy methyl cellulose sodium salt (C.M.C.), a synthetic gum, was shown to have many advantages. It was developed in Germany in 1918 and became commercially available in U.S.A. in 1945. It is a white odourless, tasteless, non-toxic powder which when dissolved in water gives a fibre free solution. This material is very hygroscopic and absorbs 18% of its weight of water in 48 hours. The C.M.C. is prepared by treating alkali cellulose with sodium chloroacetate. It is found to be extremely effective in holding barium sulphate in suspension. Initially the use of this suspending medium was advocated by Marks (1951) and then by Hodges.
(1953), Kirsh, Spellberg (1953), Zalac (1954) and others. They used in concentration of 2 to 2.5 per cent. Later it was shown by I.E. Kirsh (1956) and Beraubam (1964) that 1 per cent of this medium was quite enough to keep the suspension stable.

G.B. Brown (1963) brought out that rate of settling in aqueous suspension was in accordance with Stoke's law which deals with the motion of dispersed particles. The phenomenon depended on the size of the barium particles. Suspensions of micro sized particles were more stable as this decreased its fluidity.

C.A. Stevenson (1952) brought out that mixing of the suspension should be done at least for ten minutes, but preferably for twenty minutes.

Levene George in 1961 suggested the use of low temperature barium water suspension at 41° F. instead of using suspension at body temperature as advised by many (Cochrane Shanks). Several pints of cold fluid introduced in colon is uncomfortable to the patient as anus is sensitive up to pectinate line and may promote a peristaltic reflex of the gut.

In 1963 W.H. Shehadi advised the use of water soluble iodinated contrast media (as 40 % hypaque) specially in patients with known diverticulitis or with recent colon surgery where there is danger of impending
perforation or possibility of leakage or having complete obstruction. The drawback with this contrast medium is that one cannot do mucosal or double contrast studies.

R. Pyle and E. Samuel in 1960 and W.B. Seaman, Josephine Wells in 1965 reviewed the various complications met during colon study by barium enema and classified them. Though the various complications are rare but awareness and prompt recognition of these will minimise the associated mortality and morbidity.

The first probable death of a 11-year old child with Hirschsprung's disease by enema was described by Walker and Griffiths in 1893.

A. Jolleys (1952) met with similar accident. H.L. Steinback and coworkers in 1955 reported five more cases of fatality. They explained the death on the basis of water intoxication and suggested the use of isotonic saline solution for enema.

Perforation of colon during this procedure, specially during air insufflation, had been reported by many workers such as Kaulich (1930), Hummelman (1932), Kleinsasser and Warshow (1952), Issac (1952), Berk (1952) and H.F. Hamit (1955).

M.H. Nathan (1959) brought out that it required a pressure of more than 234 cm. of water to rupture the outer coat of normal colon and enema delivered from a
height of three feet was safe as the pressure so created was about 90 cm. of water.

The perforation is generally met with diseased colon and may produce retroperitoneal emphysema (Brown et al 1941, Spiro 1956, Lorine et al 1959, Buruton 1960 and others).

The case described by Shapiro and Refkin (1956) had emphysema extended up to mediastinum and neck.

Z. Lasser and Rigler found that perforation was relatively more frequent under three circumstances:
(1) When performed through colostomy stoma.
(2) When an inflatable balloon as Bradex rectal tube was used.
(3) When the examination followed shortly after endoscopy.

P. Lorinc and coworkers (1959) found its occurrence only twice in over 10,000 colon examinations.

Spector and Susman (1963) reported an unusual subserosal retroperitoneal perforation of sigmoid.

Massive fatal venous intravasation of barium suspension during enema examination had been reported by Isaacs et al (1950), Romen et al (1952) and Rosenberg et al.

Contaminated barium in peritoneal cavity would produce peritonitis, granulomas and dense adhesions.
Barium granuloma of rectum, a complication of enema examination, had been reported by many workers such as Beddoe et al (1954), Swartz (1955), Gorden et al (1957), S. Levene et al (1960) and McCurdy (1961).

Clinically this granuloma may simulate a carcinoma and at times difficult to distinguish (Carter 1963).

A very rare and unusual complication was recorded by Decarlo. While taking roentgenograms on a 65 days old premature infant, accidental dislodging of the clamp of enema tube produced filling of entire colon, small intestines and stomach causing vomiting of suspension and finally aspiration into the lungs.

I. Weissman (1962) reported enterogastric regurgitation in adults.

The other complications described may be due to toxic ingredients in the suspension as tannic acid.

In America J.B. Hamilton in 1946 after trying the methods used by G. Sackelts and Root (1939), advocated the use of tannic acid as an adjunct in the colon examination. According to Weber, tannic acid was being used as early as 1930 by some radiologists. This secured a better mucosal pattern on evacuation films because of the following properties:-

(a) Being sufficiently irritating, it stimulated the contraction of entire colon.
(b) The solution being astringent, inhibited the secretion of mucus.
(c) It had physical property of viscosity, thus causing suspension to adhere to bowel wall producing a uniform coating.

After the publications of Hamilton, its use became almost universal. In 1950 Christie, Coe, Hampton and Wyatt reported that they had carried out 4225 examinations using tannic acid and found that any lesion of size 1 cm. or more was seen. They concluded that its use had proved a valuable addition to the previous methods.

H. Weber was not so very optimistic and claimed that the addition of tannic acid to an opaque enema did not produce more satisfactory roentgenograms.

Toxicity of tannic acid, though known earlier, was not noticed until 1963 when McAlister and his coworkers reported death of 3 children from hepatic necrosis occurring few days after barium enema examination. Another report by Lucke, Hodge and Patt of similar fatalities came out the same year.

The hepatic toxicity of absorbed tannic acid was reported in 1942 by Wells, Humphrey Cole and Barnes, Rossiter in 1943.

In 1943 B. Handler produced hepatic necrosis in mice following subcutaneous injection of 1% tannic acid solution.
Its use was then prohibited by the Food and Drug Administration (F.D.A.) of U.S.A. from March, 1964. A similar caution was issued by the Ministry of Health to all radiologists in U.K.

Subsequent clinical and experimental study did not produce enough evidence to link tannic acid as the cause of death.

Staab and Vix were unable to demonstrate a significant rise of S.G.O.T. in 92 out of 94 patients subjected to barium enema examination containing 25% of tannic acid.

Marqulis and his associates demonstrated on animals (rats) that by giving 3 consecutive 1 minute retention enemas after every ½ hour interval, it did not produce any liver damage in concentration of 0.25 to 2%. However following a forced one hour retention enema liver damage was detected at 2.5% level.

Thomas (1963) estimated that over 600,000 enema examinations are being performed annually in United States alone, containing tannic acid in concentration between 0.5 - 3%.

A review of 60,000 examinations by Janower et al and 15000 by Kamp Harper was made in 1965. They did not find any case showing any untoward reactions.

Wyatt and coworkers in 1966 suggested the use of ammonium alum instead of tannic acid which produced comparable results.