Pneumatosis cystoides intestinalis in Iran

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SUMMARY Nineteen cases of pneumatosis cystoides intestinalis all affecting adults and all involving the small intestine have been collected in two centres of Iran (Shiraz and Tehran) over a 20 year period, the pathological findings being divided into three groups: pure submucosal, combined submucosal and subserosal, and pure subserosal cysts. Experimental PCI was produced in cadavers using high pressure oxygen insufflation of the lungs, thus lending support to the theory that it has a mechanical origin. Other theories of aetiology include tumour, nutritional deficiencies, gas-forming organisms, alveolar rupture, and acid-base disturbance. In most of the cases presented high intraluminal pressure produced by obstruction appeared to force intraluminal gas through a breach in the mucosa into either the lymphatics or perivascular tissue to produce PCI. It is concluded that the aetiology in the vast majority of adult cases is mechanical in nature and that bacteria seem to play very little part, unlike their role in the PCI of infants.

Pneumatosis cystoides intestinalis (PCI) is a condition in which air is found, characteristically, in encysted form in any part of the gastrointestinal tract. However, although it is a rare disease, a steady stream of reports on it have been appearing in the literature since Du Vernoi (1783) first noticed the condition and Bang (1876) who reportedly gave a complete description of the first case observed in human necropsy. The extensive review by MacKenzie (1951), Koss in 1952, Romeo (1967), and the more recent review by Ecker *et al.* (1971) and the experience of the Mayo Clinic, reported by Shallal *et al.* (1974), give an idea of the accumulated world experience of this condition. As far as the aetiology of this 'disease' is concerned the reader should refer to the works of Finney (1908), Eveleth and Biester (1938), Koss (1952), Keyting *et al.* (1961), Doub and Shea (1960), Kenney (1963) and, in more recent years, to Stone *et al.* (1970) and Yale *et al.* (1974). The distribution of this disease appears to be world-wide and favours no particular geographical area, although, to our knowledge, no studies have appeared in the world literature with particular reference to this point. As far as the site of the cysts are concerned, no part of the gastrointestinal tract appears to be immune from gas cyst formation and cysts from the oesophagus (Vanasin *et al.*, 1971) to the rectum (Babb and Sox, 1970) have been reported. At one time, PCI of the left colon was thought to be rare; however, in recent

literature there have been more reports of colonic PCI (Smith *et al.*, 1958; Doub and Shea, 1960; Kristensen, 1974), which may point to a significant move in the pathophysiological behaviour of the disease. The age of the patient appears to be relevant, in that the PCI of the infant age group is significantly different, both in aetiology and prognosis, from that seen in adults (Stone *et al.*, 1970). This paper presents 19 cases of proven PCI from Iran collected from 1958-77 and describes experiments on cadavers which provide evidence confirming the mechanical theory as one of the aetiological factors of PCI.

Methods

SUBJECTS

Nineteen documented cases of PCI have been collected from 1958-77. These were collected as follows: the files of the two main Pahlavi University Hospitals, Shiraz, were searched between the years 1958-70 and documented cases of PCI were extracted; between 1970-72 all cases seen by F.N. or others in Pahlavi University Hospitals were added to the retrospective study, and between 1972-77, when one of the authors (F.N.) was transferred to Reza Pahlavi Medical Centre, Tehran, additional cases which were seen there were added. Each of these 19 cases was selected carefully on the basis of either definite pathological proof or observation at operation with photographic records. Other cases were rejected on the basis of incomplete evidence. Only

one case was included purely on radiological grounds and that was because both the clinical course and radiological appearances were so typical that it was felt justifiable to include it. Thirteen of the remaining 18 showed pathological proof either at necropsy (four) or surgical section (nine). The remaining five cases were direct observations at laparotomy with photographic proof (Table 1).

AGE AND SEX INCIDENCE

All 19 cases were adults with a peak age incidence in the fourth decade. There were only three females, giving a male/female ratio of approx 5:1; we were unable to find any PCI in the paediatric age group (Fig. 1).

PATHOLOGY

Group A: Submucosal pneumatosis

There were three patients in this group. The air

Fig. 1 Age and sex incidence of all the PCI cases collected between 1958-77.

cysts in this group were confined to the submucosa alone and in none of these cases could we find any evidence of chronic lung disease, peptic ulceration, or

Table 1 Relevant particulars of all cases of PCI collected between 1958-77

Unit no.	Age (yr), sex	Method of diagnosis		Location of gas		Type of ulcer seen	Other diagnosis	Outcome
		Op. obs. and hist.	Op. obs. only	Sub- mucosal	Sub- serosal			
A.B. S.132030	40 ♂	+	—	+	—	—	Carc. of bladder and peritonitis	Died
S.K. S.134487	55 ♂	+	—	+	—	—	Typhoid Ulcer perf.	Died
K.S. S.152553	50 ♂	+	—	+	—	—	Bowel gangrene	Died
S.N. A.3-72	65 ♂	+	—	—	+	—	GU	Died
A.A. S.78882	35 ♂	+	—	—	+	—	DU	Well
G.B. S.11449	48 ♂	+	—	—	+	—	DU	Well
R.J. N.119560	50 ♂	+	—	—	+	—	DU	Died (Lung abscess)
A.A. S.145969	46 ♂	+	—	—	+	—	DU	Died (Uraemia)
M.Z. N.86118	52 ♂	—	+	—	+	—	GU	Well
J.B. S.152039	38 ♂	—	+	—	+	—	DU	Well
R.M. C.M.H.	25 ♂	+	—	—	+	—	DU	Well
F.G. P.A.481-61	35 ♀	+	—	—	+	—	DU	Well
E.K. N.31267	60 ♀	+	—	—	—	+	DU	Well
F.M. N.36729	35 ♂	+	—	—	—	+	DU	Well
K.P. S.196776	55 ♂	+	—	—	—	+	DU	Died (Massive UGI bleeding)
G.E. S.227016	62 ♂	—	—†	—	—	+	DU	Well
H.R. R.P.05-96-78	54 ♂	—	+	—	+	—	DU	Well
S.M. R.P.06-27-57	60 ♀	—	+	—	+	—	—	Well
G.Z. R.P.01-23-86	40 ♂	—	+	—	—	—	DU	Well

Op. obs.: operative observation. PS: pyloric stenosis.

*Post-mortem. †x-ray diagnosis.

obvious obstructive disease. However, in all cases the terminal event included severe peritonitis with some form of terminal enterocolitis. In this group evidence points mainly to a bacterial aetiology somewhat similar to the PCI seen in infancy (Stone *et al.*, 1970).

Group B: Combined submucosal and subserosal pneumatosis

There were four cases in this group, three were confirmed pathologically, all having been found and resected at operation. The fourth case was included because of radiological proof of extensive PCI associated with evidence of both subserosal and submucosal involvement. In this group there were three males to one female, but all had duodenal ulcers with pyloric stenosis of varying degrees.

Group C: Subserosal pneumatosis

This group represents the majority of the cases of PCI that were seen and 12 cases are documented. All except two were male, nine had duodenal ulcer with varying degrees of pyloric stenosis, while two had gastric ulcers with other complications. Three of this group have proven chronic lung disease with emphysema and one had doubtful chronic lung disease noted only clinically.

MORTALITY

If we take groups B and C together, out of 16 cases four died (mortality 25%), but none of the deaths was directly related to PCI. Total mortality for all groups was approximately 37%.

EXPERIMENTAL PCI

Two cadavers, where death had occurred less than half-an-hour previously, were chosen and examined to rule out any chest injuries or conditions giving rise to lung injuries or pneumothorax before death. There was also no evidence of significant rigor mortis and the bodies had not been subjected to refrigeration. An anaesthetist (A.O.) passed an endotracheal tube on each and the cuff was blown to prevent leaks. O₂ was introduced under pressure for a variable number of minutes (about five minutes). Necropsies carried out immediately afterwards revealed rupture of alveoli with air tracking to the hilum of the lung and extensive mediastinal emphysema. From here, air was seen along the oesophagus, over the surface of the stomach, the duodenum, traversing the ligament of Treitz to the base of the mesentery, and from there involving both the small and large bowel throughout their length. The air appeared to follow the vessels of the mesentery and tended to accumu-

Fig. 2 Experimental PCI showing transverse colon with mesentery. Air bubbles can be seen tracking along the vessels to the surface of the colon.

late in cystic bullae subserosally, in a way very similar to extensive PCI. A photograph of this observation is shown (Fig. 2) illustrating the bubbles of air tracking along the vessels of mesentery of colon, reaching the subserosa of the transverse colon. Air was also felt submucosally, but these bubbles were difficult to demonstrate photographically. These experiments convinced us of the mechanism referred to by Doub and Shea that air under pressure can track from the lung *via* the mediastinum to the surface of the stomach, to the base of mesentery, and, once there, by following the vessels, it can reach virtually anywhere along the gastrointestinal tract and give rise to both submucosal and subserosal PCI. It also illustrates how, once air has found its way under the subserosal plane from a breach in the mucosa, it follows the vessels of the mesentery tracking distally or proximally to anywhere in the gastrointestinal tract. This may be the explanation for the often-noted observation of the cysts being found some distance from the site of obstruction or the breach in the mucosa. This, we believe, is the first time this mechanism has been shown in the human cadaver, previous experiments having been carried out on animals.

Discussion

Various hypotheses have been advanced to explain adult PCI, and in Table 2 a list of theories proposed by various authors is given.

Finney in 1908 suggested a gas-forming tumour as the main cause, but, so far, no histological or pathological proof of such tumour has been submitted. In 1938 Eveleth and Biester proposed a nutritional deficiency theory based on their observations in hogs fed on polished rice. This theory is somewhat similar to that postulated by Coello-Ramírez *et al.* (1970) that a temporary disaccharidase deficiency prevents digestion of carbohydrates and increases bacterial fermentation in the gut, producing large volumes of gas leading to distention, ischaemia, and subsequently submucosal dissection of gas. In 1952 Koss, in his extensive review of PCI, mentioned and supported the two theories that in some, gas-producing organisms are the main cause and in others a mechanical factor.

In 1960, Doub and Shea, and in 1961, Keyting *et al.* provided some experimental and statistical evidence that, in some patients suffering from obstructive lung disease, the air originates from the lung. Here they postulated alveolar rupture giving rise to pneumo-mediastinum and tracking of air from there to the gastrointestinal tract.

Trauma has been proposed as an aetiological factor and a recent report (Shuck *et al.*, 1974) has appeared in the literature.

Table 2 Theories of aetiology for adult PCI

Tumour	Finney (1908)
Nutritional deficiency	Eveleth and Biester (1938)
Gas-forming organisms	Koss (1952)
Mechanical	Koss (1952)
Alveolar rupture	Doub and Shea (1960); Keyting <i>et al.</i> (1961)
Acid-base disturbance	Kenney (1963)

In 1963 Kenney proposed that these patients have acid-base disturbances with difficulty in excretion of CO₂ and that the PCI may represent an attempt by the body to get rid of excess CO₂. Gas analysis of the contents of these cysts has shown variable contents of hydrogen, 10%-50%; oxygen, 7%-20%, and CO₂, 1%-15%, but relatively constant amounts of N₂, approximately 70%-75% (Stiennon, 1951; Mujahed and Evans, 1958; Hughes *et al.*, 1966). Recent reports of the disappearance of cysts in the distal colon with pure oxygen therapy (Forgacs *et al.*, 1973; Down and Castleden, 1975) and the gas diffusion theory of constant replenishment of the gas contents of these cysts, may be bringing us close to a unified theory of aetiology, mooted by various authors in recent papers who suggest that the spaces are created by mechanical means but that the gas in them is replenished by gas diffusion from the bowel (Wyatt, 1972). The fact that PCI has been found recently as a complication of jejunoileal bypass (Sicard *et al.*, 1976) may be yet another step towards finding a unified aetiology.

It appears that there are certain conditions—unknown or ill-proven as yet—which replenish the gas in the cysts or prevent its absorption. Our experiments show one route by which these cysts may initially be formed and possibly the air in them replenished for at least the initial period and, as these are people with chronic obstructive lung disease, the acid-base theory may continue the replenishment. However, this is not the full answer and it does not explain the majority of cases which are related to obstructive gastrointestinal disease. PCI is not a ‘disease’ by itself, and therefore cannot have a single aetiology. It is a ‘secondary manifestation of the reaction of the body to a variety of conditions’. It can be likened to pyrexia. We would be foolish if we attempted to seek a single aetiology for pyrexia. However, with our seven-year experience of this condition, one of the authors (F.N.) is convinced that the initial mechanism for the production of these cysts is, in the vast majority of cases, mechanical in nature. Most of these fall into the category of breach in the mucosa of the gastrointestinal tract with an accompanying obstruction. It can be seen in our cases that the majority had a gastric or a duodenal ulcer with an obstruction (mainly of the gastric outlet). The force of this type of obstruction and the air pressures produced must by

no means be underestimated, for we have seen some radiographic plates (Fig. 3) and witnessed clinically some distended abdomens which testify to very high pressures. The plate shown is a straight upright film of the abdomen of one of these patients with pneumoperitoneum forcing the liver downwards and to the midline; the distension of the stomach can easily be seen. We are convinced that in all cases the pressures in these circumstances are sufficient to force air through the breach in the mucosa submucosally, to reach the subserosal space and from there to travel anywhere along the small or large intestine. In the remaining cases the initial cause is as described by Doub and Shea (1960) and confirmed by our experiments; probably the maintenance of these cysts is either through repeated alveolar rupture or acid-base disturbance. We have not seen a case complying with this latter theory but it has been well established by reports in the literature. On one or two occasions we have had the opportunity to observe the repeated recurrence of pneumoperitoneum and signs of PCI confirmed at operation and the disappearance of

Fig. 3 Straight erect radiograph of the abdomen taken at admission of one of the cases showing massive pneumoperitoneum pushing the liver downwards and demonstrating gross gastric dilatation.

PCI and all symptoms once treatment was directed to the cause of obstruction and ulcer. This emphasises the fact that this condition is a secondary manifestation and treatment should be directed to the cause rather than to removal of the bowel involved with PCI.

Finally, we must mention the bacterial theory (Yale *et al.*, 1974) and the more recent reports of experiments performed (Yale, 1975) that support this theory. As mentioned earlier in this article, there is no doubt that bacteria are the main cause of PCI in infants and also in some adults, with devastatingly high mortality. In three of our cases (group A) this condition was found as a terminal event at necropsy. However, in our experience in the majority of our cases if the PCI was bacterial in origin then it would also have similar symptoms and similar course and mortality as that seen in infants, which it does not. There is no doubt that this variety of PCI is a benign phenomenon and if bacteria have been found in these cysts then we believe they are secondary in nature and do not contribute significantly to the cause of this phenomenon.

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References

- Babb, R. R., and Sox, H. C. (1970). Pneumatosis cystoides intestinalis diagnosed by rectal biopsy. *American Journal of Gastroenterology*, **54**, 609-612.
- Bang, B. L. F. (1876). Luftholdige kyster i væggen af ileum og i nydannet bindevæv påsammes serosa. Cysts in the walls of ileum and in neoplasm of connective and serous tissues. (Swedish.) *Nordiskt Medicinskt Arkiv*, **8**, 1-15.
- Coello-Ramírez, P., Gutierrez-Topete, G., and Lifshitz, F. (1970). Pneumatosis intestinalis. *American Journal of Diseases of Childhood*, **120**, 3-9.
- Doub, H. P., and Shea, J. J. (1960). Pneumatosis cystoides intestinalis. *Journal of American Medical Association*, **172**, 1238-1242.
- Down, R. H. L., and Castleden, W. M. (1975). Oxygen therapy for pneumatosis coli. *British Medical Journal*, **1**, 493-494.
- Du Vernoi, J. G. (1783). Anatomische Beobachtungen der unter der äussern und innern Haut der Gedärme eingeschlossenen Luft. *Physikalische und medicinische Abhandlungen der Kayserlichen Akademie der Wissenschaften in Petersburg*, **2**, 182-188.
- Ecker, J. A., Williams, R. G., and Clay, K. L. (1971). Pneumatosis cystoides intestinalis—bullous emphysema of the intestine. *American Journal of Gastroenterology*, **56**, 125-137.
- Eveleth, D. F., and Biester, H. E. (1938). Further studies on intestinal emphysema of swine. *American Journal of Hygiene*, **27**, 364-369.
- Finney, J. M. T. (1908). Gas cysts of the intestine. *Journal of*

- American Medical Association*, **51**, 1291-1298.
- Forgacs, P., Wright, P. H., and Wyatt, A. P. (1973). Treatment of intestinal gas cysts by oxygen breathing. *Lancet*, **1**, 579-582.
- Hughes, D. T., Gordon, K. C. D., Swann, J. C., and Bolt, G. L. (1966). Pneumatosis cystoides intestinalis. *Gut*, **7**, 553-557.
- Kenney, J. G. (1963). Pneumatosis intestinalis. *Clinical Radiology*, **14**, 70-76.
- Keyting, W. S., McCarver, R. R., Kovarik, J. L., and Daywitt, A. L. (1961). Pneumatosis intestinalis—a new concept. *Radiology*, **76**, 733-741.
- Koss, L. G. (1952). Abdominal gas cysts (Pneumatosis cystoides intestinorum hominis). *Archives of Pathology*, **53**, 523-549.
- Kristensen, J. K. (1974). Pneumatosis cystoides intestinalis. *Acta Chirurgica Scandinavica*, **140**, 501-504.
- MacKenzie, E. P. (1951). Pneumatosis intestinalis. Review of the literature with report of 13 cases. *Pediatrics*, **7**, 537-547.
- Mujahed, Z., and Evans, J. A. (1958). Gas cysts of the intestine (pneumatosis intestinalis). *Surgery, Gynecology and Obstetrics*, **107**, 151-160.
- Romeo, J. A. (1967). A review of pneumatosis cystoides intestinalis. *American Journal of Gastroenterology*, **47**, 142-147.
- Shallal, J. A., Vanheerden, J. A., Bartholomew, L. G., and Cain, J. C. (1974). Pneumatosis cystoides intestinalis. *Mayo Clinic Proceedings*, **49**, 180-184.
- Shuck, J. M., Malan, L. J., and Hammar, M. D. (1974). Pneumatosis cystoides intestinalis due to blunt abdominal trauma. *Journal of Trauma*, **14**, 435-440.
- Sicard, G. A., Vaughan, R., and Wise, L. (1976). Pneumatosis cystoides intestinalis: an unusual complication of jejunoileal bypass. *Surgery*, **79**, 480-484.
- Smith, W. G., Anderson, M. J., Jr, and Pemberton, H. W. (1958). Pneumatosis cystoides intestinalis involving left portion of colon. Report of 4 cases diagnosed at sigmoidoscopy. *Gastroenterology*, **35**, 528-533.
- Stiennon, O. A. (1951). Pneumatosis intestinalis in the newborn. *American Journal of Diseases of Childhood*, **81**, 651-663.
- Stone, H. H., Webb, H. W., and Kovalchik, M. T., III (1970). Pneumatosis intestinalis of infancy. *Surgery, Gynecology and Obstetrics*, **130**, 806-812.
- Vanasin, B., Wright, J. R., and Schuster, M. M. (1971). Pneumatosis cystoides esophagi. *Journal of American Medical Association*, **217**, 76-77.
- Wyatt, A. P. (1972). Pneumatosis cystoides intestinalis. *Proceedings of the Royal Society of Medicine*, **65**, 780-782.
- Yale, C. E., Balish, E., and Wu, J. P. (1974). The bacterial etiology of pneumatosis cystoides intestinalis. *Archives of Surgery*, **109**, 89-94.
- Yale, C. E. (1975). Etiology of pneumatosis cystoides intestinalis. *Surgical Clinics of North America*, **55**, 1297-1302.