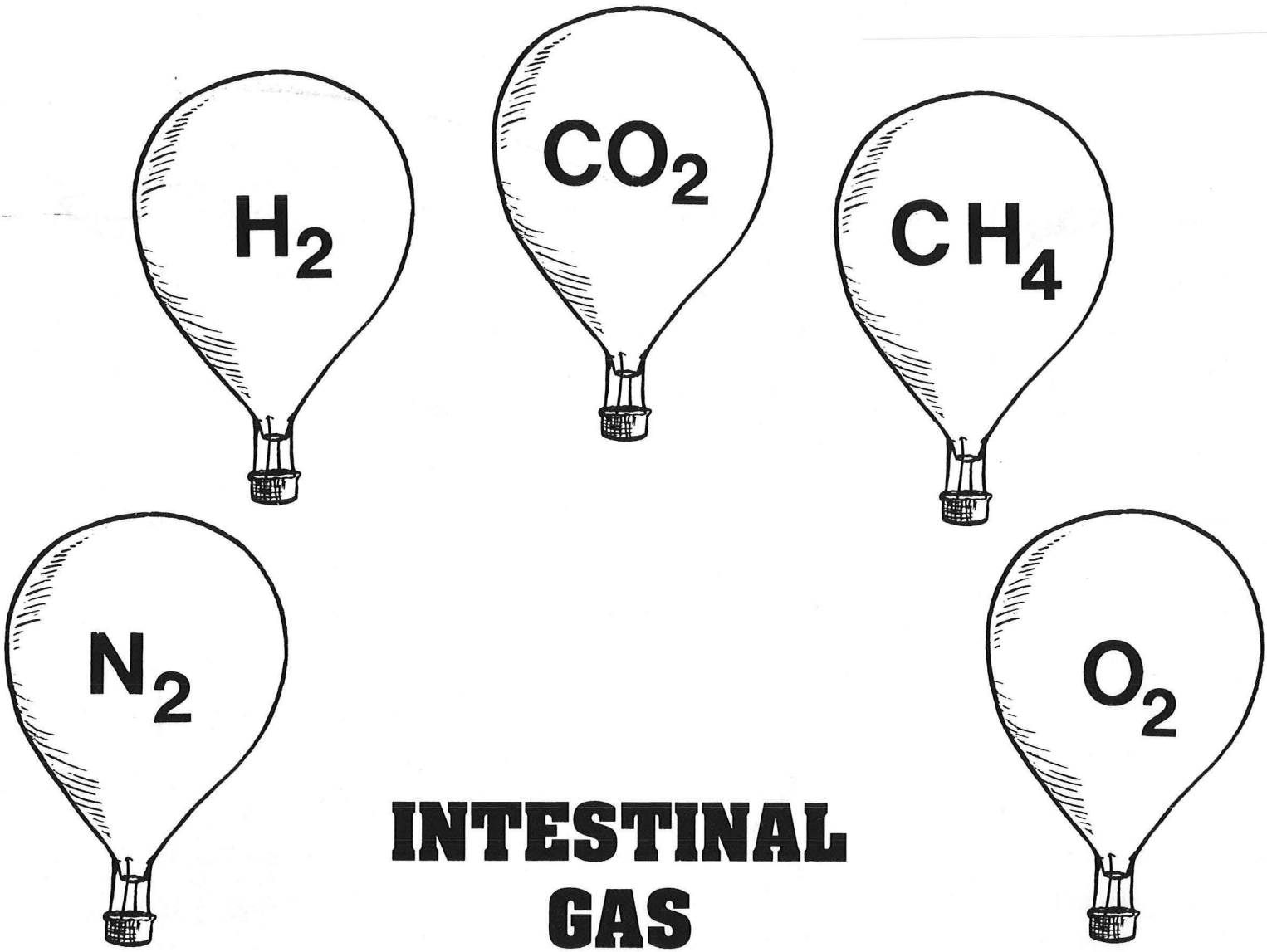


INTESTINAL GAS

MEDICAL GRAND ROUNDS

SOUTHWESTERN MEDICAL SCHOOL

Walter Peterson, M.D.

December 6, 1984

ACKNOWLEDGEMENTS

I wish to thank Kathy Weingarden and Pat Rollins for their diligent library research; Pat Ladd for her artistic prowess; the VA photography crew; Bobbie Bullard and Vickie Slagle for expert typing; and John Bond and Mike Levitt (University of Minnesota) for picking up the scent and providing modern-day insight into the field of flatology.

The subject of intestinal gas is one that attracts on a daily basis at least the momentary attention of virtually every human being. Such interest is not new:

"Passing gas is necessary to
well-being."

-Hippocrates-

"All Roman citizens shall be allowed
to pass gas when necessary."

-Claudius-

"The intestines are the home of
tempests: in them is formed gas,
as in the clouds; oxygen is found
in them, whilst the fat produces
hydrogen and carbon. The foods of
the animal kingdom give nitrogen;
an unknown process generates
sulphur and phosphorus, and hence
those emmissions of sulphuretted
hydrogen of which the effects are
known by every one, but of which
the author is never known."

-Brillat-Savarin-

Flatulence: rumbling, swelling, and
wandering pain coming suddenly, and
suddenly vanishing; a clear tumour
that yields to the touch, and that
sounds like a drum. Often belching
and farting are also signs, and ease
after breaking of wind doth follow.

-Fienus-

He took no more account of the wind
that passed from their mouth in words
than that they expelled from their
lower parts.

-Leonardo Da Vinci-

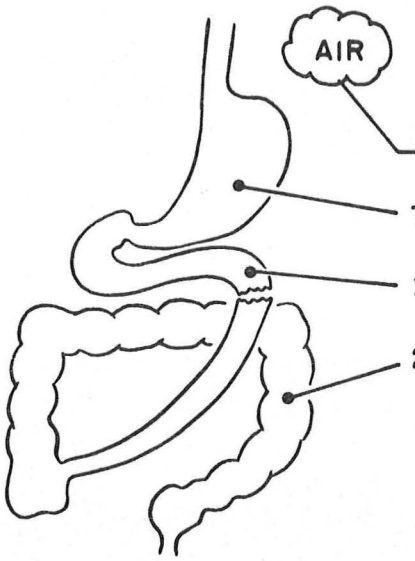
Such quotes would be no more than amusing if patients with "windy syndromes" did not appear in physicians' offices for relief. The degree of success customarily achieved in these encounters is nicely summarized by quotations from two well-known gastroenterologists:

> If the country's family physicians could vote on the most blatant failure of gastroenterologic research, as reflected in current clinical problems, it seems likely they would specify the inability to aid the patient with the complaint of intestinal gas.
>
> -Eddy D. Palmer, M.D.-

> Since interpreting symptoms in indigestion is difficult for most physicians, and the condition has heretofore been the province of mystics or basic physiologists, neither patient nor physician usually benefits from an encounter which has as its object the relief of gaseous symptoms.
>
> -Albert Mendeloff, M.D.-

This review will describe the constituents and mechanisms at work in "The Winds of War", with suggestions to achieve "Gone With The Wind".

COMPOSITION OF GAS IN AIR AND GASTROINTESTINAL TRACT



	N_2	O_2	CO_2	H_2	CH_4
AIR	79%	21%	Trace	—	—
	70 - 95%	< 20%	1 - 10%	—	—
	30 - 80%	2 - 10%	5 - 70%	—	—
	20 - 80%	1 - 2%	5 - 40%	< 1 - 30%	< 1 - 15%

Efforts to determine the constituents of intestinal gas may have begun as early as 1816. Magendie, examining the intestines of individuals recently decapitated *en guillotine*, found carbon dioxide, methane, and hydrogen present (1). Since hydrogen disappears during fasting, (see page 10), these hapless souls may at least have enjoyed a pre-decapitation meal. Further early efforts studying flatus (2), "stomach gas" (3), and small bowel gas after experimental obstruction (4), confirmed the presence of these gases and added nitrogen and oxygen. It is now clear that the normal composition of intestinal gas varies according to the individual studied, the location in the gastrointestinal tract, and whether the subject is fasting or fed (Figure 1).

Experiments using plethysmography or hypobaric pressure suggest that relatively little gas is present in the intestine at any given time (about 100 ml) (5,6). A more direct, and accurate, means of assessing the volume and composition of intestinal gas was reported by Levitt in 1971 (7). Infusing Argon at a rate of 45 ml/minute into the small intestine (Figure 2), washout curves for

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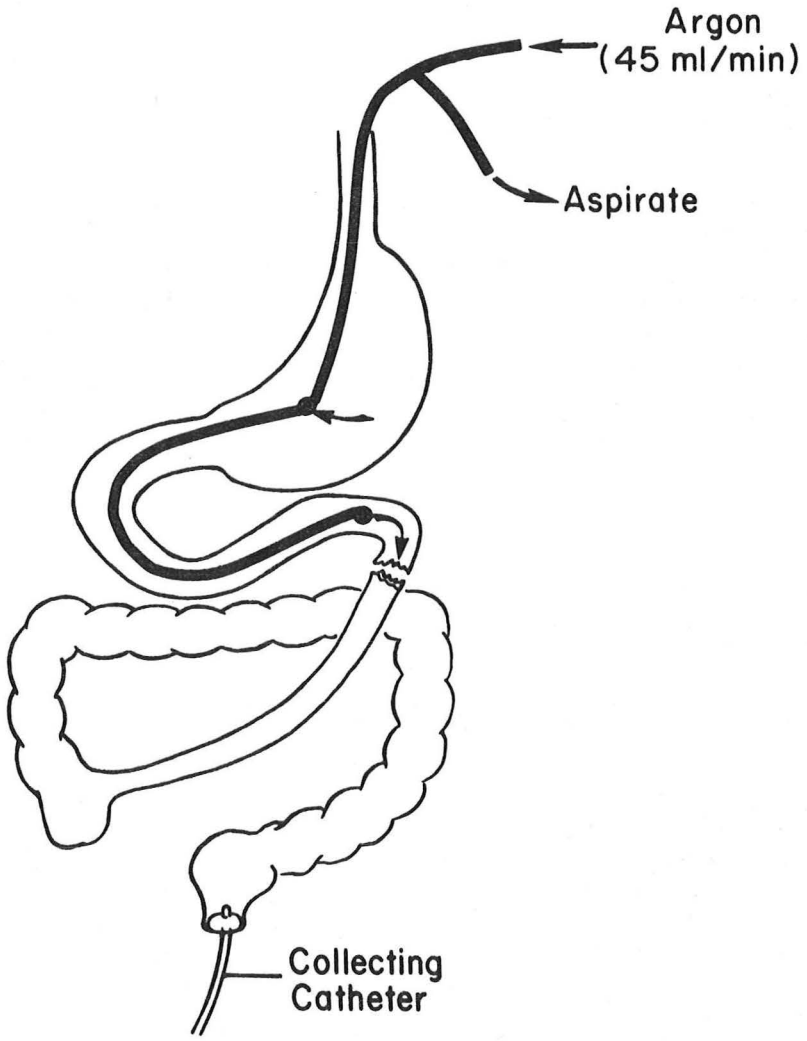
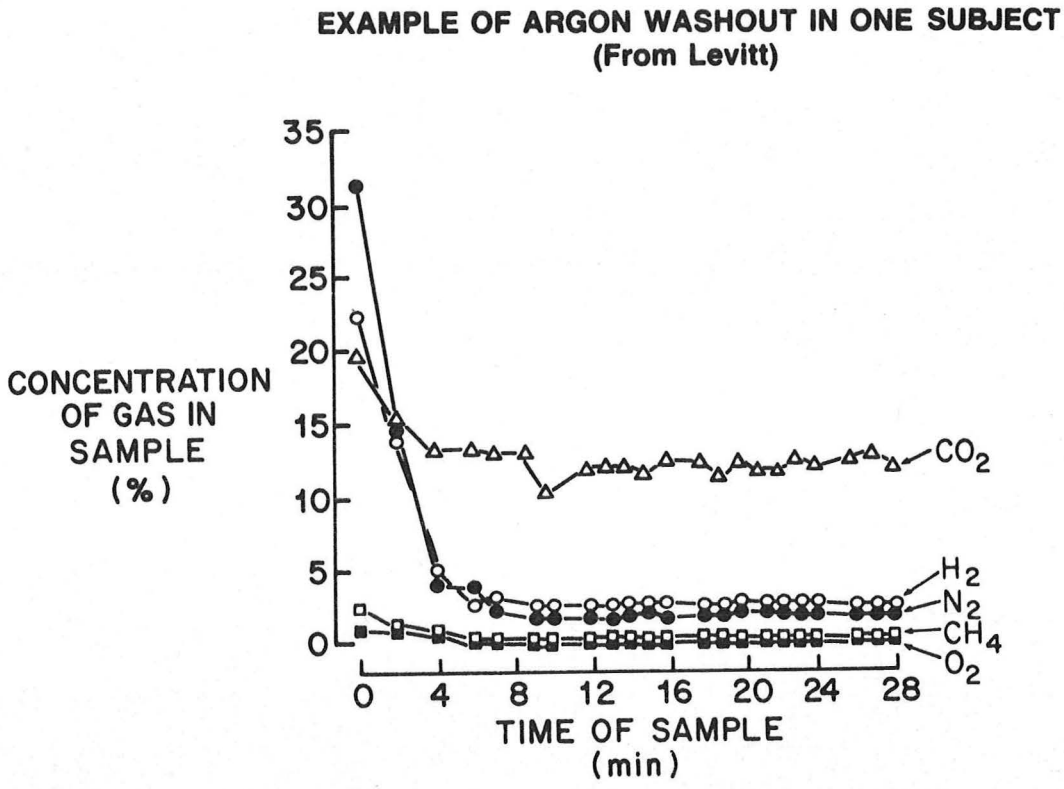
ARGON WASHOUT TECHNIQUE



gases present in the intestinal tract were generated. [Argon does not interfere with the analysis of the 5 major gaseous constituents of the intestine]. After correction for the amount of gas present in the steady state, volumes present at the start of the infusion can be calculated. An example of the washout in one subject is shown in Figure 3. Using the technique in 11 healthy subjects five to seven hours after breakfast, Levitt reported a mean ± SE intestinal volume of 90 ± 54 ml (range 30-200 ml) with concentrations of individual gases as shown in Table 1.

TABLE 1. Mean ± SE and range of concentrations of intestinal gases found in 11 healthy subjects. (From ref. 7)

Gas	Mean ± SE	Range
N_2	64 ± 21%	26-88%
O_2	0.7 ± 0.5%	0.1-1.8%
H_2	19.0 ± 16.0%	0.2-49%
CH_4	8.8 ± 9.0%	0-20% (7/11 had 0%)
CO_2	14.0 ± 7.0%	5.5-27%

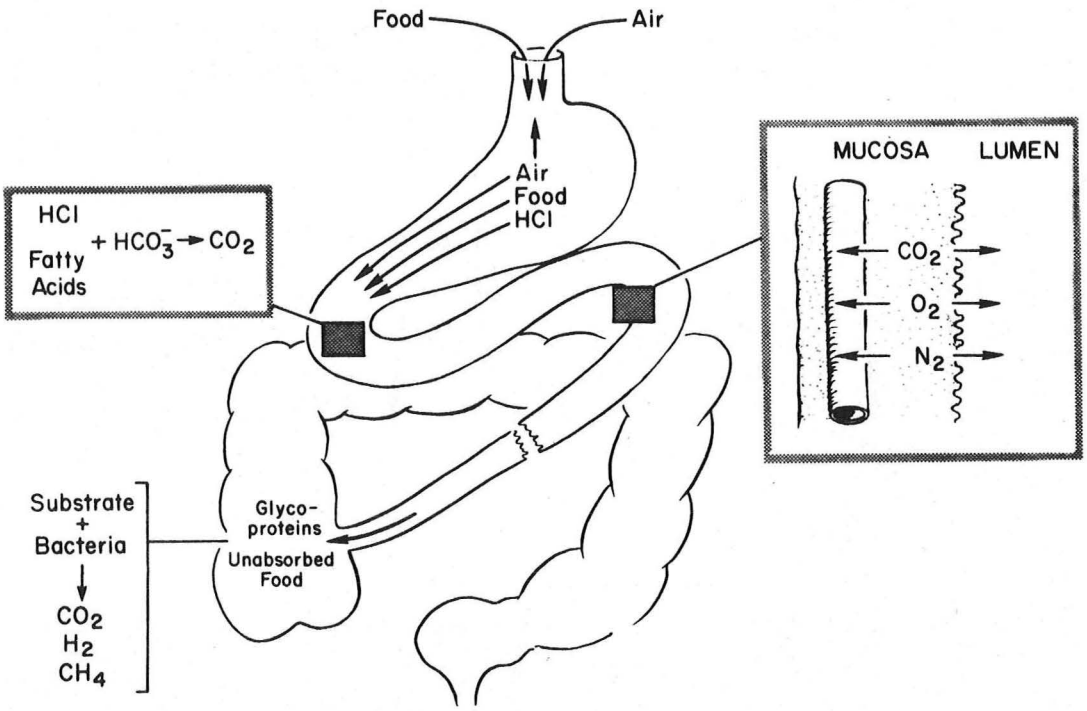


Several points can be made from these data: (1) Nitrogen, the largest component of air, is the predominant component of intestinal gas in most subjects; (2) oxygen exists in very low concentrations reflecting the anaerobic state of the intestine; (3) hydrogen, methane, and carbon dioxide - present only in negligible quantities in air - make up a substantial proportion of intestinal gas. This suggests they arise *in vivo*.

SOURCES OF INTESTINAL GAS

A summary of the potential sources for intestinal gas is displayed in Figure 4. Gases can enter the gastrointestinal tract either via swallowed air, diffusion from blood, or by *de novo* production.

SOURCES OF INTESTINAL GAS



SWALLOWED AIR

The only intestinal gases also present in air in important concentrations are nitrogen and oxygen, which may enter the stomach as constitutents of food. Such foods as meringues, souffles, light breads, ice creams, and carbonated beverages are obviously "airy" but other foods (such as an apple which is said to contain 20% air) have substantial amounts of air also. Each act of swallowing also brings with it small amounts of air. Finally some individuals bring in air as a nervous "tic". Such people do not swallow air as much as "suck it in" by developing more negative intraesophageal pressure in association with relaxation of the upper esophageal sphincter (8). This mechanism is employed by circus sword swallowers and those legendary beer drinkers who can literally pour large quantities of liquids down their gullet without "swallowing". Air in the stomach can be absorbed into the blood, emptied into the small bowel or brought back up via the esophagus.

DIFFUSION BETWEEN BLOOD AND GUT LUMEN

The net movement of gases depends on partial pressure gradients. Thus, in the stomach, oxygen (O_2) diffuses out of the lumen while carbon dioxide (CO_2) diffuses in. Since oxygen leaves at a greater rate than CO_2 enters, and since the lumen pressure is maintained at 760 mm of Hg, the partial pressure of nitrogen (N_2) rises. Nitrogen will then diffuse into the blood. Throughout the course of the intestine, gases diffuse back and forth depending upon the relative partial pressures.

DE NOVO PRODUCTION OF GASES

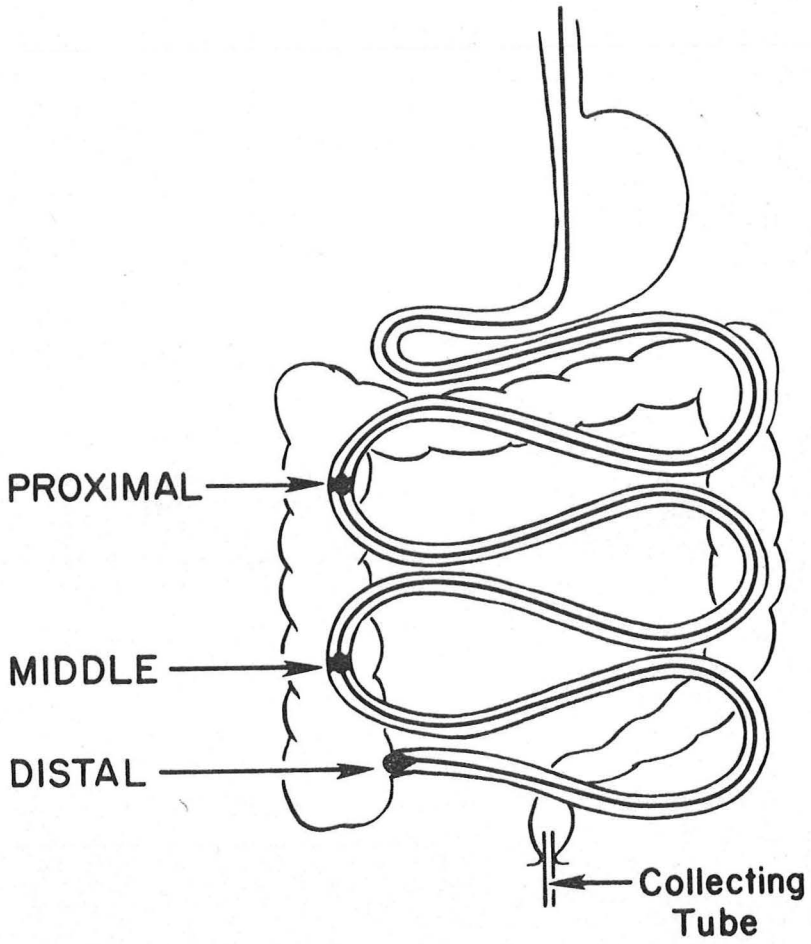
Three gases are produced in important concentration in the gut - CO_2, hydrogen (H_2), and methane (CH_4).

- Carbon Dioxide - CO_2 is generated by reaction of gastric HCl with either exogenous (9) or endogenous (10) sodium bicarbonate. Although solubility of CO_2 in water tends to limit its release into the gaseous phase (9), it is clear that substantial amounts can be produced. Fatty acids may also act as a source of duodenal CO_2 generation and the post prandial partial pressure of CO_2 can reach as high as 500 mm of Hg in the duodenum (10). Most of this CO_2 is absorbed as it moves down the gut.

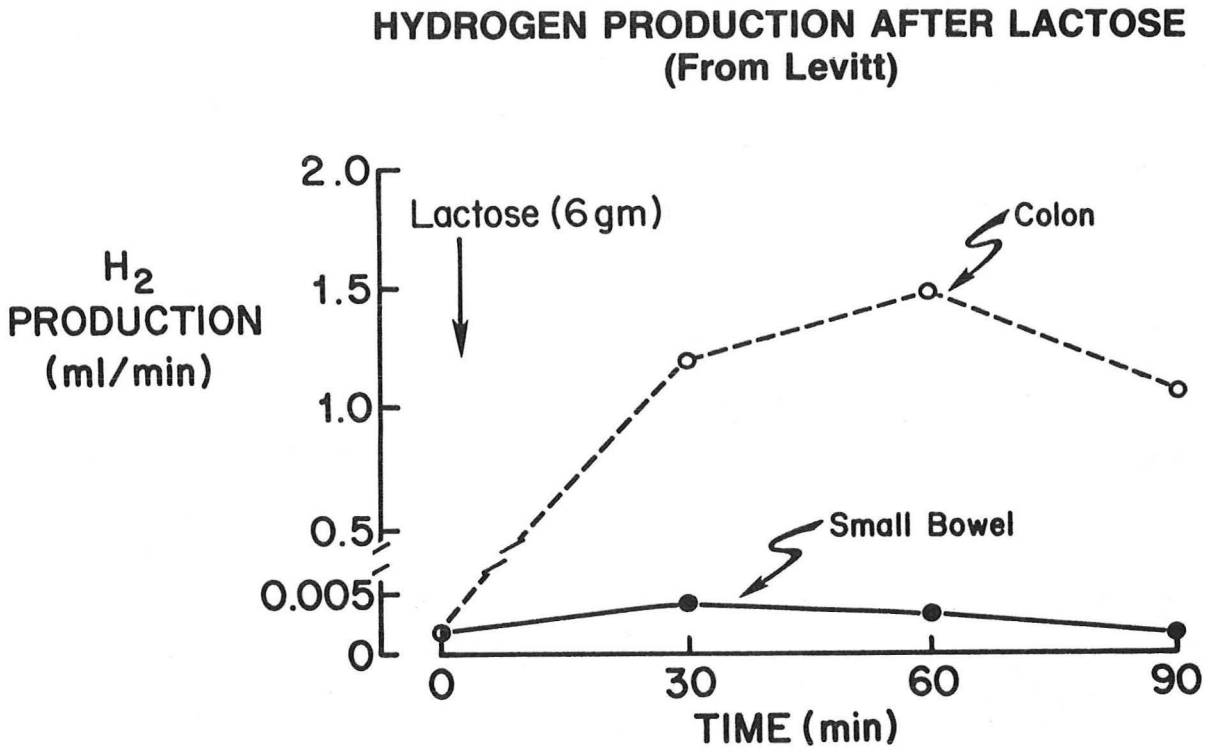
  Analysis of flatus (flatoanalysis) reveals the concentration of CO_2 to be too high to have come only from swallowed air or diffusion from blood. Rather, it is clear that certain foods are fermented to form CO_2. Steggerda studied five normal subjects fed a diet high (59%) in pork and beans ($\sim$ 225 gm/day) (11). Mean total gas expulsion during the post prandial period rose from 17 ml/hr during a basal diet to 170 ml/hr during the bean diet, with CO_2 output rising from 2 ml/hr to 87 ml/hr. Bond and co-workers have performed careful studies showing that colonic bacteria anaerobically metabolize malabsorbed carbohydrate (such as beans) to short chain fatty acids which then react with endogenous bicarbonate or are absorbed and metabolized to CO_2 (12,13).

- Hydrogen - When Steggerda did the bean study (11), it was also noted that hydrogen output rose from a baseline of 3 ml/hr to 26 ml/hr with pork and beans. Thus, as with CO_2, it appeared that hydrogen was also formed in the colon from bacterial conversion of malabsorbed carbohydrates. This was supported by work demonstrating that hydrogen was not produced in germ-free rats (14) or in newborn human infants (15). Sentinel work by Levitt (16), corroborated by Tadesse (17), further supports this concept. Levitt used a triple-lumen perfusion system (Figure 5), employing sulfur hexafluoride as a

INTESTINAL PERFUSION TECHNIQUE TO DETERMINE HYDROGEN PRODUCTION (From Levitt)



non-absorbable marker, to measure H_2 production in 10 normal subjects. As shown in Figure 6, fasting H_2 production is very low. In response to a lactose load (6 gm) substantial amounts of hydrogen were formed in the colon but

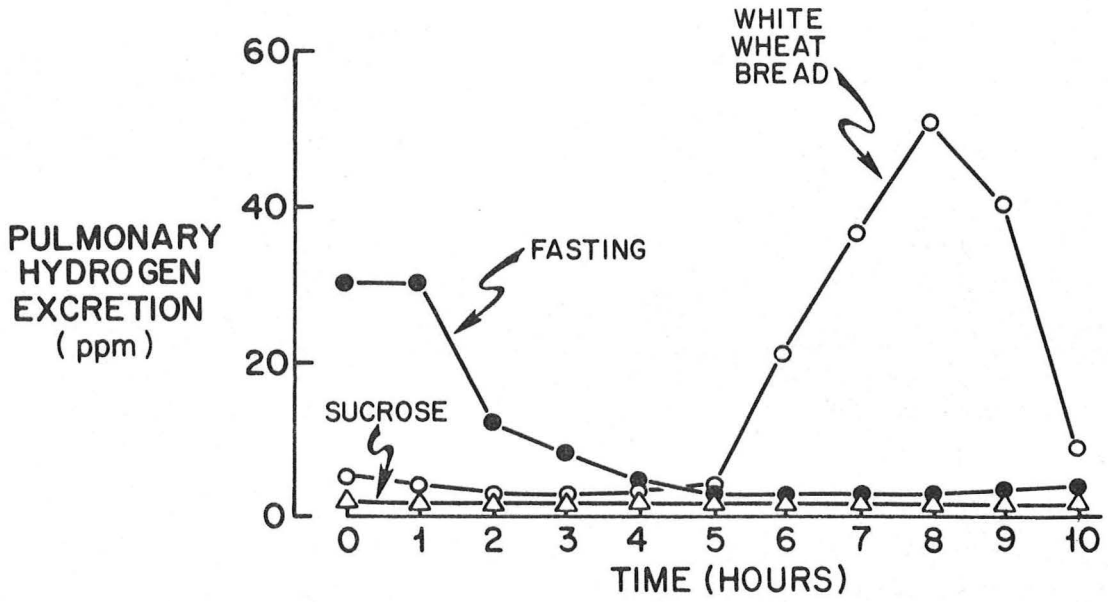


not in the small bowel, a finding consistent with the much higher bacteria counts in the colon. Similar findings were seen after a bean meal. In a second set of studies using the Argon washout technique (Figure 2), he noted a mean $\pm$ SE fasting volume of H_2 of 13 $\pm$ 9.8 ml in 10 normal subjects. After a standard breakfast, the production rate rose to 0.6 ml/min, within the range of results seen during the constant perfusion technique. Finally, he found a strong correlation between respiratory H_2 excretion and total H_2 production as measured either by the constant perfusion technique or Argon washout technique. Thus, breath H_2 was used for future studies investigating carbohydrate malabsorption.

It is well known that some individuals lack the enzyme (lactase) to digest lactose and thereby present substantial quantities of this disaccharide to the colon. Depending upon the amount malabsorbed and the efficiency of the bacteria present, some of the lactose will be metabolized ("salvaged") by colonic bacteria producing as byproducts CO_2 and H_2 (18). It is of interest that ingestion of lactose as yogurt results in less colonic gas production since some lactase is released from yogurt organisms (19).

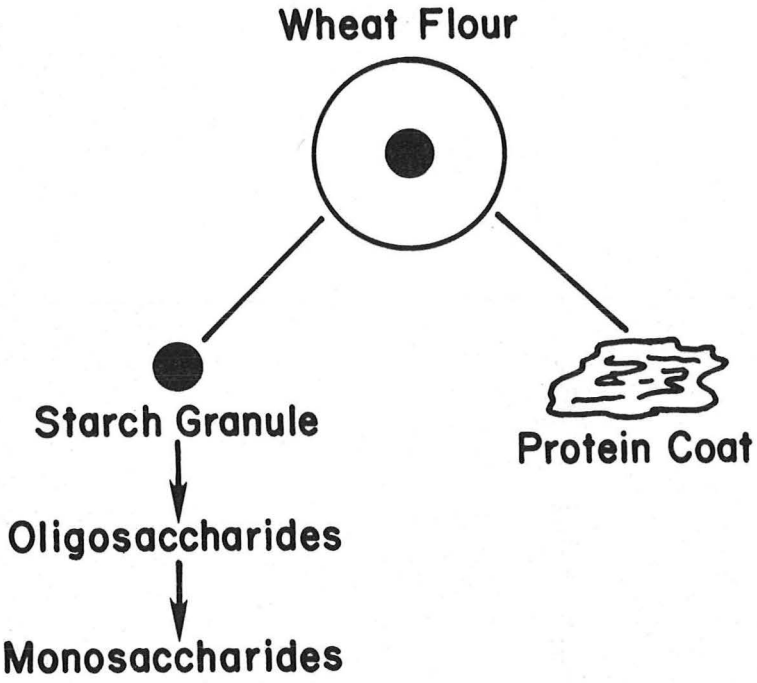
Less well-recognized is the fact that otherwise normal subjects also malabsorb carbohydrates - fructose (20), sorbitol (21), fruits (22) and starch products (23-26). For example, in one experiment (23), Anderson measured breath H_2 concentrations in normal, healthy volunteers fed 100 gm of sucrose or white wheat bread. While fasting levels and levels after sucrose were low (Figure 7), levels after wheat bread rose substantially. Ingestion of 100 gm of low gluten wheat bread did not result in elevated breath hydrogen levels. As

PULMONARY HYDROGEN EXCRETION IN FASTING STATE, AFTER SUCROSE MEAL, AND AFTER WHEAT BREAD
(From Anderson)



shown in Figure 8, wheat flour consists of a core starch granule surrounded by a protein coat (85% of which is gluten). If starch is presented to the small bowel extracted from its protein coat (low gluten bread), absorption is normal and hydrogen is not formed in the colon. Even if gluten is added back as a separate supplement to low gluten bread, absorption is still normal (23).

DIGESTION OF WHEAT FLOUR

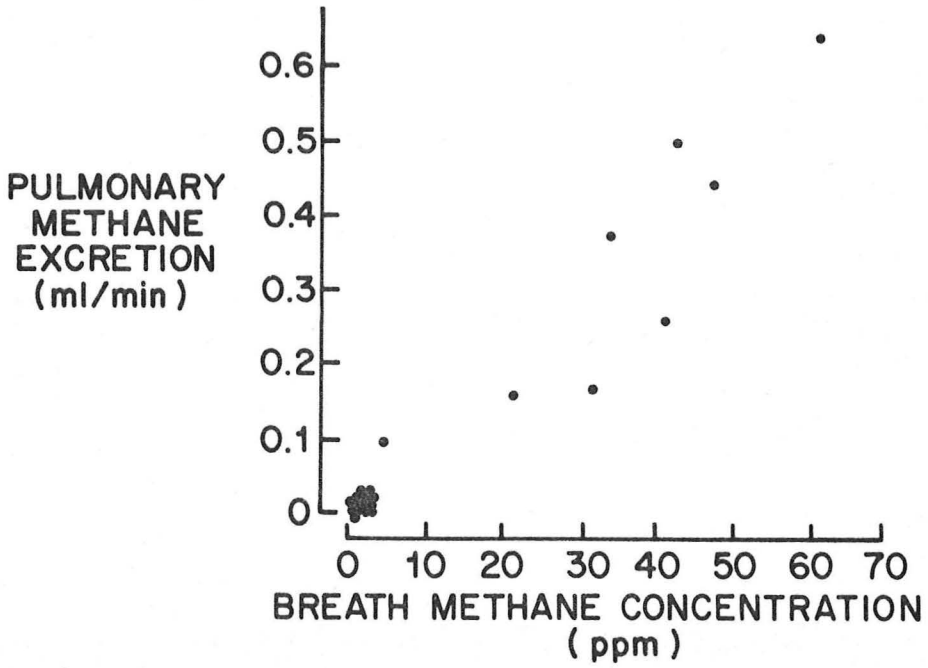


Thus, it appears that normal individuals are unable to degrade all the gluten away from starch granules, resulting in small but real malabsorption into the colon. Further work (24) demonstrated a similar phenomenon with oat flour, potatoes, and corn flour. Indeed, Stephens estimates that 2-20% of dietary starch escapes small bowel absorption (25). On the other hand, rice flour appears to be efficiently absorbed in the small intestine (23,24,27) and H_2 gas is not formed. Finally, although unprocessed bran and cellulose enter the colon virtually unchanged, gas does not form (28,29).

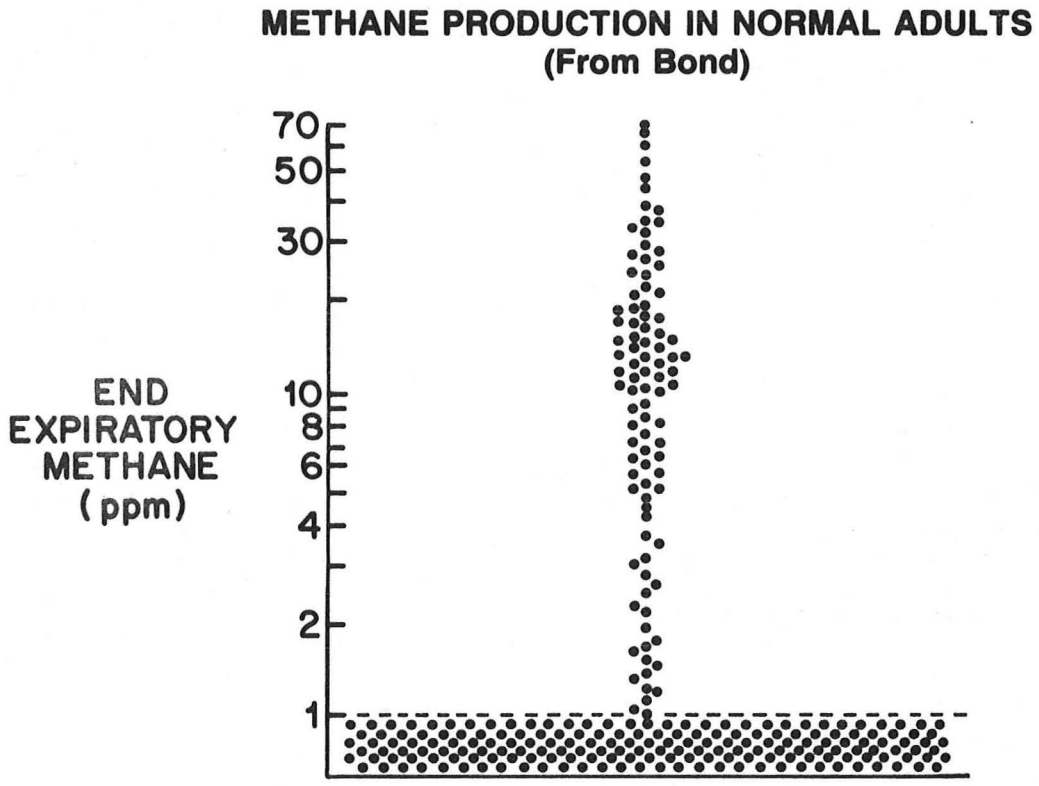
Two mechanisms are at work to limit the amount of H_2 which form from bacterial fermentation of unabsorbed carbohydrates. First, other bacteria present in stool can utilize H_2 up to 2 ml/hr/gm of feces (30). Second, as pH is lowered with fermentation, a feedback mechanism tends to inhibit further H_2 generation (26).

• Methane - Methane ("natural gas") production in animals is the result of metabolism of appropriate substrate by certain species of anaerobic bacteria (31,32). Such species have been isolated from human feces (33) so it is not surprising that methane can be found in human intestinal gas. Bond and coworkers have performed extensive studies in human subjects investigating methane production (34) using pulmonary methane excretion (35). After validating that breath methane concentration in ppm correlate well with actual methane excretion (Figure 9), they studied 280 adults. As shown in Figure 10,

CORRELATION BETWEEN PULMONARY METHANE EXCRETION AND BREATH CONCENTRATION (From Bond)

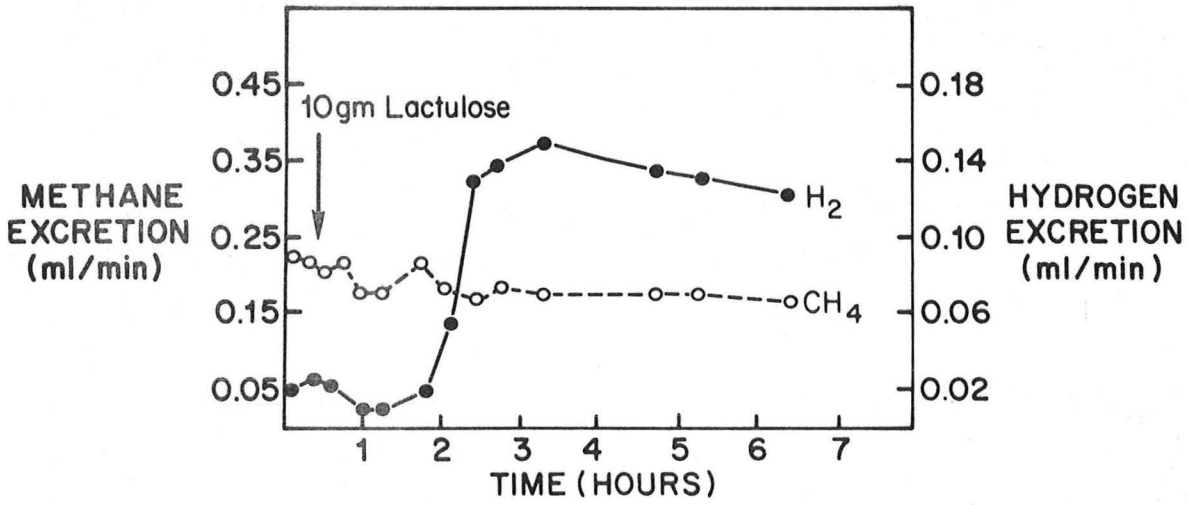


one-third produce methane in a breath concentration over 1 ppm. The champion methane producer in their studies generated between 4 and 5 liters per day. Putting this in perspective, cows can generate up to 250 L/day in their rumen, sheep 40 L, and goats 30 L (31). When one recognizes that bacterial fermentation of one day's manure from one cow could add 2000 L of methane (36), man's production pales by comparison. Although flatus in human methane producers can clearly be ignited to a blue, odorless flame, it is unlikely to be utilized as a major source of energy.

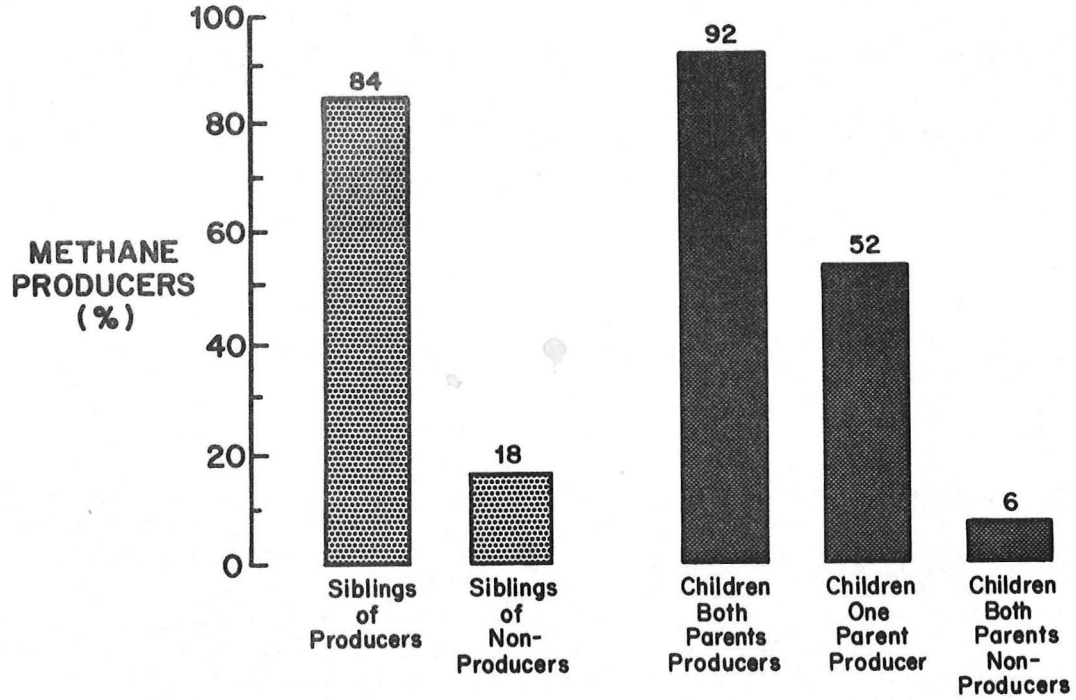


Further work from Bond's group showed that all human methane was produced in the colon, not the small bowel. Methane is not produced in germ-free rats or newborn infants (34). Further, as shown in Figure 11, methane production is not influenced by malabsorbed carbohydrate. In this case, lactulose, a non-absorbable disaccharide (galactose-fructose) was given to normal subjects. While breath hydrogen went up in expected fashion, levels of breath methane did not change. It appears then that some individuals possess a special bacterial flora in the colon capable of producing methane from some endogenous source. Recent work from Perman suggests that the substrate for methane production may be endogenous glycoproteins (37).

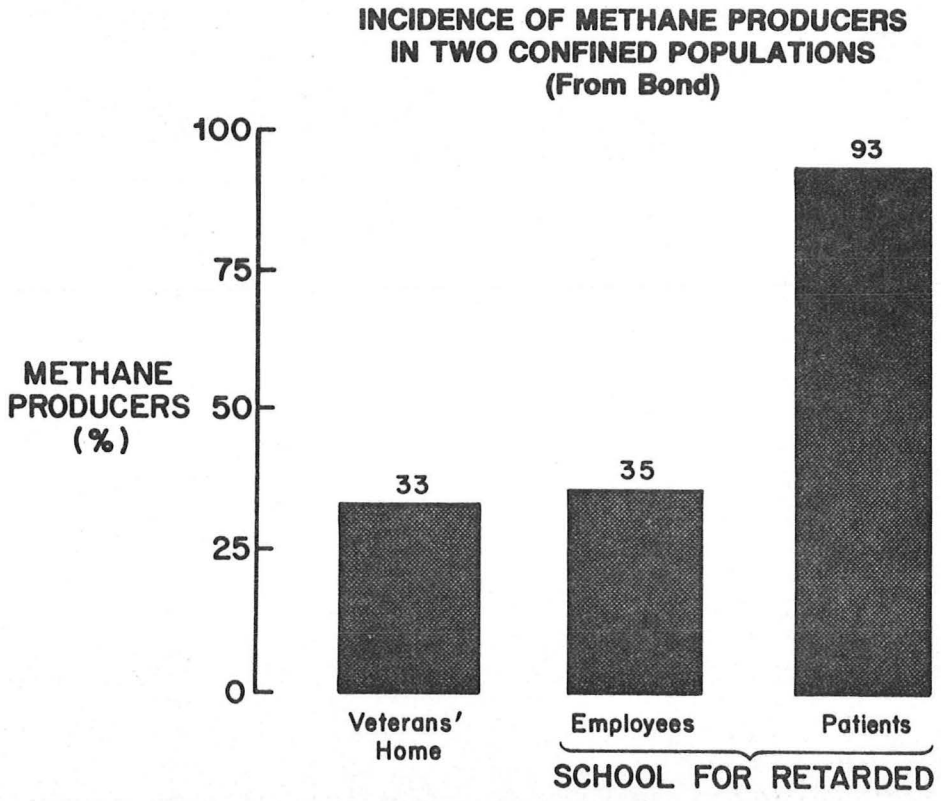
**EFFECT OF LACTULOSE (10 gm)
ON BREATH METHANE AND HYDROGEN
(From Bond)**



**INCIDENCE OF METHANE PRODUCERS IN FAMILIES
(From Bond)**



Development in some individuals of the bacterial flora necessary for methanogenesis may be familial (Figure 12). However, this is not solely a genetic phenomenon since over 90% of children in a school for the retarded were methane producers (Figure 13). Thus, close contact may be important although such contact evidently must occur at an early age since spouses have the same degree of concordance as the population at large and elderly members of a veterans domiciliary had no more than the expected incidence (Figure 13) (34).

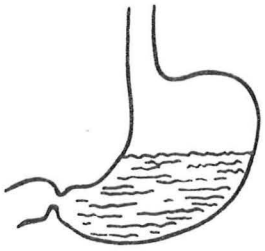


CLINICAL SITUATIONS ASSOCIATED WITH INTESTINAL GAS

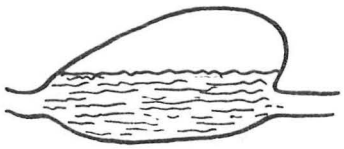
BELCHING

One way in which air can be removed from the stomach is by an active belch. When this occurs at random, there is a reduction in the size of the gastric air bubble. Patients with prior fundoplication may have difficulty belching as may individuals lying in the supine position (Figure 14). There are some individuals in whom belching is continuous and in whom the gastric air bubble does not change in size. Most such people are engaging in repetitive aerophagia in which air is "sucked in" to the esophagus (see page 7). The air is then immediately regurgitated, often without entering the stomach, a mechanism also employed for esophageal speech. Some air does reach the stomach and, in some individuals, may contribute to flatulence.

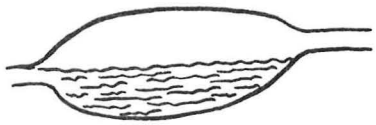
EFFECT OF POSITION ON STOMACH BUBBLE



UPRIGHT



SUPINE



PRONE

While some patients have organic problems for which they seek relief by belching, for most people it is simply a nervous "tic". Some such patients take this habit to the extreme of rumination (38). Treatment with drugs such as anticholinergics, antacids, enzymes therefore have no basis, and while some patients will respond to education (i.e., showing them what they are doing), others are more resistant.

EXPLOSIVE BELCHING

Cows suffer from a disease known as "foamy bloat", when ingestion of certain lush young grasses can result in such rapid production of gas that the rate of elimination cannot keep up. The animal's ruminant stomach distends to huge proportions which can cause respiratory embarrassment and death (39). Humans, even aerophagiacs with fundoplications, rarely develop such a problem since gas escapes downstream. However, there are situations where increased concentration of methane and/or hydrogen can create an explosive situation:

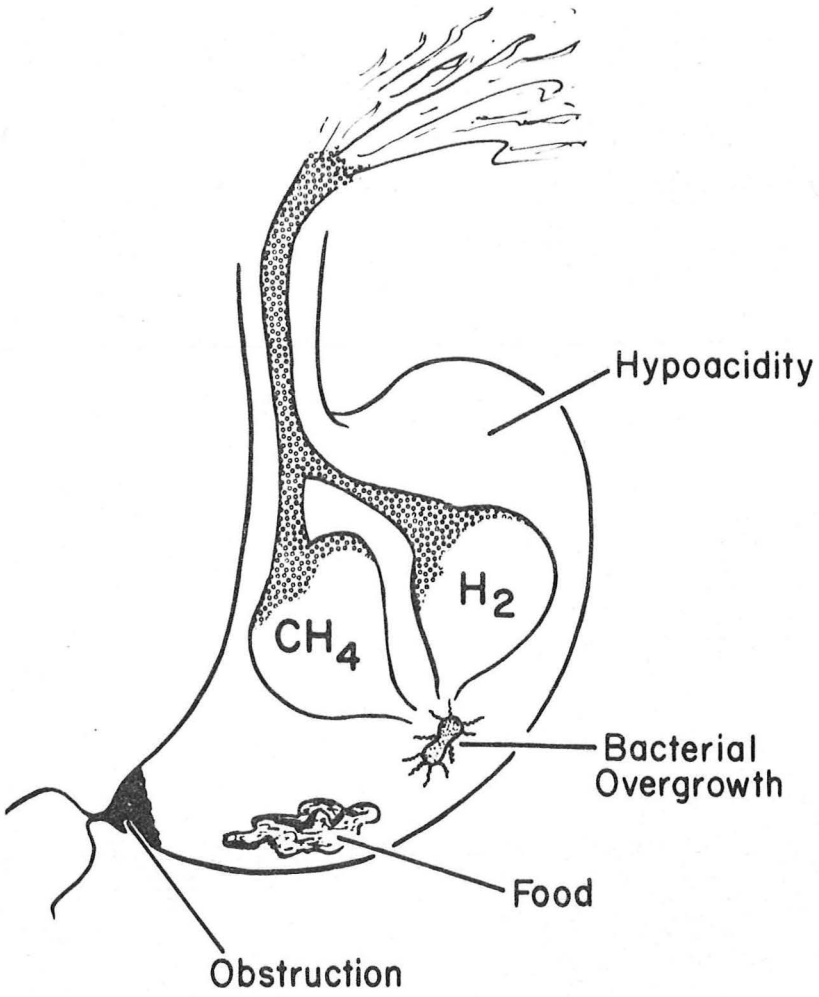
> The patient was a middle-aged man, rather thin and pale. He said that for a number of years he had suffered at times from pain in the region of the stomach after food. Recently vomiting had troubled him. This took place at irregular intervals, the amount being copious. On going into details he remembered bringing up material that he had eaten many hours before. The vomit was offensive as a rule. He also was prone to violent and foul-smelling eructations. But what really distressed him more than anything else was the following startling occurrence.
>
> One evening he had taken his wife to the cinema. There, in the darkness, feeling inclined to smoke, he had taken out a cigarette, and put it between his lips; he struck a match, bringing it up in his cupped fingers. Just at that moment a violent eructation occurred. To his alarm and astonishment, and of those seated near him, there was a flash and a sharp explosion; the cigarette was blown from his lips away across several rows of seats; his moustache was singed, and his lips and fingers burnt. In pain and confusion he had hurriedly to leave the cinema. The astonishment of the neighbours at this "fiery exhalation" can well be imagined.

This patient, reported by East in 1934 (40), had pyloric obstruction, as did the patient reported by Galley (41):

> The patient was playing bridge with friends when he was offered a light for his cigarette by his partner across the table. As he leant across the table he felt an undeniable necessity to belch. Unfortunately, he attempted to do this discreetly through his nose. He astonished the company by producing two fan-shaped flames from his nostrils. His partner, who accompanied him to the casualty department, described the incident as "just like a dragon, doctor."

Daniel described a patient who experienced explosive belching after a vagotomy and pyloroplasty (42) and Yu-li reported a patient with gastric cancer who ignited a belch (43). Dixon was moved to name this syndrome, which appears to require one or more of the conditions shown in Figure 15, as eluctation or belch flambe' (44).

EXPLOSIVE BELCHES IN HUMAN SUBJECTS



FLATULENT DYSPEPSIA

This condition, also termed burbulence,

> "How do I feel today? I feel as unfit as an unfiddle, and it is the result of a certain turbulence of the mind and a certain burbulence in the middle."
>
> -Ogden Nash-

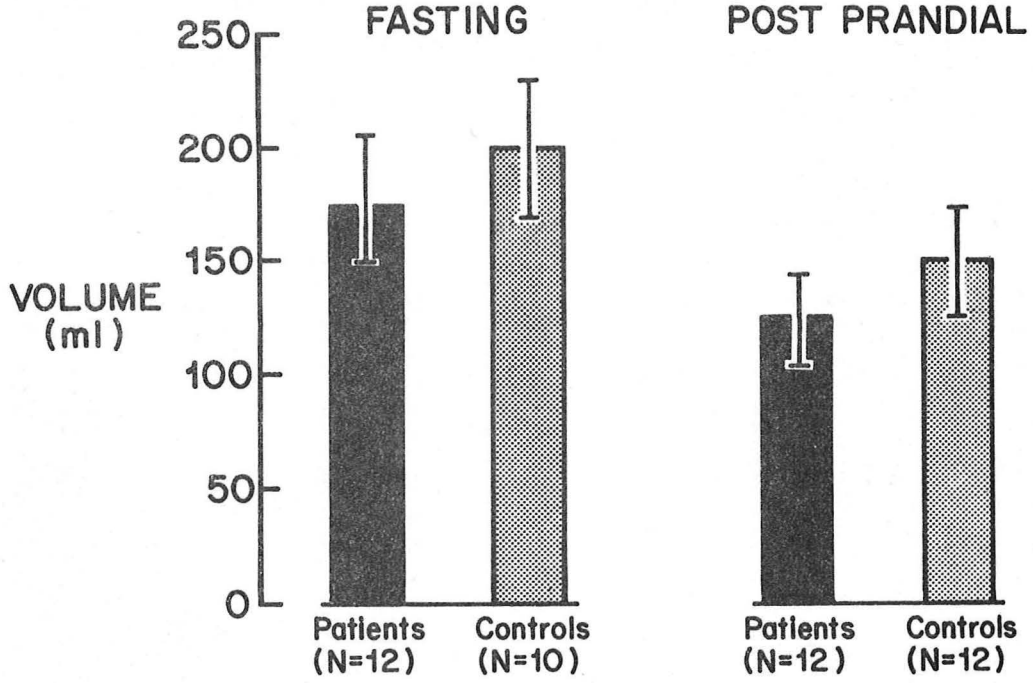
is a catch-all term for abdominal distress of unknown cause attributed by the patient to "gassiness". Robert Burton, 16th century author of Anatomy of Melancholy" wrote:

> The [symptoms] are these, beside fear and sorrow; "sharp belchings, fulsome crudities, heat in the bowels, wind and rumbling in the guts, vehement gripings, pain in the belly and stomach sometimes after meat that is hard of concoction, much watering of the stomach, and moist spittle, cold sweat; cold joints, indigestion, they cannot endure their own fulsome belchings, continual wind about their hypochondries, heat and griping in their bowels; midriff and bowels are pulled up; the veins about their eyes look red and swell from vapors and wind." [From their] crudities, windy vapors ascend up to the brain, which trouble the imagination and cause fear, sorrow, dullness, heaviness, many terrible conceits and chimeras.

In a nutshell, patients complain of excess gas, bloating, and abdominal pain. It is important to rule out organic causes for such symptoms which may thereby be specifically treatable. Features suggesting organicity include nocturnal discomfort, bleeding, weight loss, change in stool habits, older age, and recent onset. Remember that malabsorption of lactose, fructose, and sorbitol especially if taken in large quantities can produce symptoms in some individuals.

Danhoff evaluated patients with no organic cause for such symptoms (45). Using the "oxygen transit time", he suggested that some individuals had prolonged intestinal transit of gas which might predispose them to symptoms.

VOLUME OF INTESTINAL GAS IN PATIENTS WITH FLATULENT DYSPEPSIA AND CONTROLS



More recently, Levitt's group has assessed such patients using the Argon washout technique (46,47). Their results are summarized in Figure 16, where it can be seen there is no excess gas present in patients with flatulent dyspepsia, either in the fasting or the fed state. There was also no significant difference in the composition of intestinal gas. What was noted were differences in the intestinal transit times of gas and induction of symptoms with the Argon infusion (Table 2).

TABLE 2. Mean ± SE transit times, rate of gas passage, and induction of symptoms during Argon infusion (45 ml/min) in patients with flatulent dyspepsia and controls (From Lasser).

	Transit Time -Fasting-	Passage of Gas -Fed-	Induction of Symptoms	
Patients	28 ± 4 min* (N=17)	44 ± 6 ml/min (N=12)	72% (N=18)	
				(P < 0.05)
Control	22 ± 3 min (N=10)	28 ± 4 ml/min (N=12)	10% (N=10)	

* In 6 patients, the study was stopped because of pain. Their transit time was 40 ± 6 min (P <0.05).

It is of note that sham infusions of gas were also performed in each subject, none of whom developed symptoms. Thus, it appears that the symptoms of flatulent dyspepsis are related in some way to disordered intestinal motility and/or an abnormal pain response to "normal" gut distention.

- Treatment - As might be imagined, treatment for a syndrome with no good cause is difficult at best. Burton (see page 19) took a direct approach, recommending that one "attach a bellows to a clyster pipe, insert it in the fundament, and draw forth wind". Carminatives (from Latin Carminare - to card or comb out ... evil humors from the body) have been prescribed since the time of Hippocrates. Indeed, the Papyrus Ebers describes oil of wormwood (an oil used in pernod) used for "an obstruction of the abdomen" (48). Unfortunately, there are no data to support the use of these volatile oils (for example, oils of dill, peppermint, cinnamon, cloves, ginger, fennel, anise) for anything other than breath fresheners.

  Similarly, data to support the use of antacids, anticholinergics, simethicone alone (49) or simethicone with pancreatic enzymes (50) are less than persuasive. Nevertheless, Danhoff reports that simethicone does accelerate intestinal transit of gas (49). A recent double-blind, randomized, cross-over trial of metoclopramide suggests that 10 mg three times daily may relieve symptoms of flatulent dyspepsia better than placebo. (Table 3) 51).

TABLE 3. Results with metoclopramide or placebo in patients with post-cholecystectomy dyspepsia or ulcer-negative dyspepsia (From Johnson).

Syndrome	Metoclopramide Better	Placebo Better
Post-Cholecystectomy	6/8	1/8
Ulcer Negative Dyspepsia	17/29	6/29

FLATUS

Whether or not a patient's complaint of excess or foul-smelling flatus is real or perceived (52,53), the topic is one that has caught the fancy of at least several well-known authors.

> It is universally well-known, that in digesting our common Food, there is created or produced in the Bowels of human creatures, a great quantity of Wind..... Were it not for the odiously offensive Smell accompanying such escapes, polite People would probably be under no more Restraint in discharging such Wind in Company, than they are in spitting or in blowing their Noses.... A few stems of Asparagus eaten, shall give our Urine a disagreeable Odour; and a Pill of Turpentine no bigger than a Pea, shall bestow on it the pleasing Smell of Violets. And why should it be thought more impossible in Nature, to find Means of making a Perfume of our Wind than of our Water?
>
> -Benjamin Franklin-

> "Conversation as it was at the Social Fireside in the time the Tudors":
>
> > Yesternight took her Majestie, ye Queene, a fantasie such as she sometimes hath, and hadde to her closet certeain that do write playes, books & such like.... ...In ye heate of ye talke, it befel that one did breake wynde, yielding an exceeding mightie and distressful stinke, whereat all did laffe full sore, and then:
> > Ye Queene: Verily, in mine eight and sixty yeares have I not heard the fellow to this fartte.... Prithee, let ye author confess ye offspring. (Whereupon each member of the company denied authorship until, at last, Sir Walter Raleigh owned up.)
>
> -Mark Twain in "1601"-

Early studies have reported the "normal" flatovolume over 24 hours to be anywhere from about 20 ml/hr (11,54) to 40 ml/hr (55), with post prandial volumes ranging from 90 ml/hr on a regular diet to 140 ml/hr with a diet rich in brussel sprouts (56). The composition of flatus consists predominantly of CO_2, CH_4, H_2 and N_2, all of which are odorless gases. Hydrogen sulfide is present in concentrations of 0.0001-0.001%, which says volumes for the acuity of the human nose. Various skatoles, indoles, mercaptans, ammonia, and other volatile amines make up a very small, but potent percentage of flatus. Research into these areas has been sparse.

The origin of N_2 and some CO_2 in flatus is swallowed air and diffusion from blood to gut lumen. However, concentrations of CO_2 found in flatus suggest most is generated from bacterial fermentation by bacteria, as is H_2 and CH_4. Results of work by Steggerda (11) are shown in Figure 17 and Table 4.

EFFECT OF BEANS ON INTESTINAL GAS
(From Steggerta)

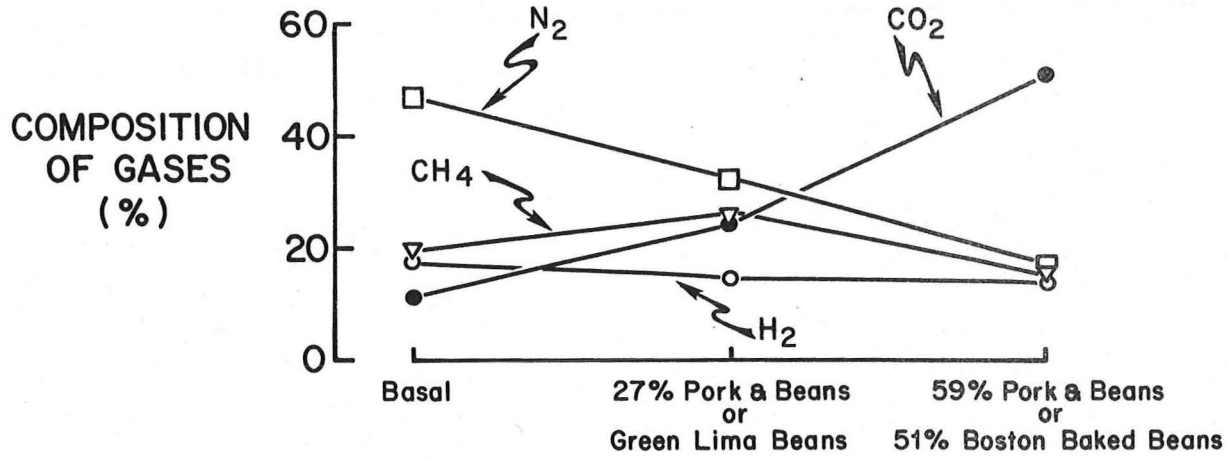


TABLE 4. Post-prandial volumes (ml/hr) of flatus produced by normal volunteers on three diets. (From Steggerda).

Diet	Total	N_2	CO_2	H_2	CH_4
Basal	17	8	2	3	4
27% Bean	67	21	17	10	17
59% Bean	170	30	87	26	27

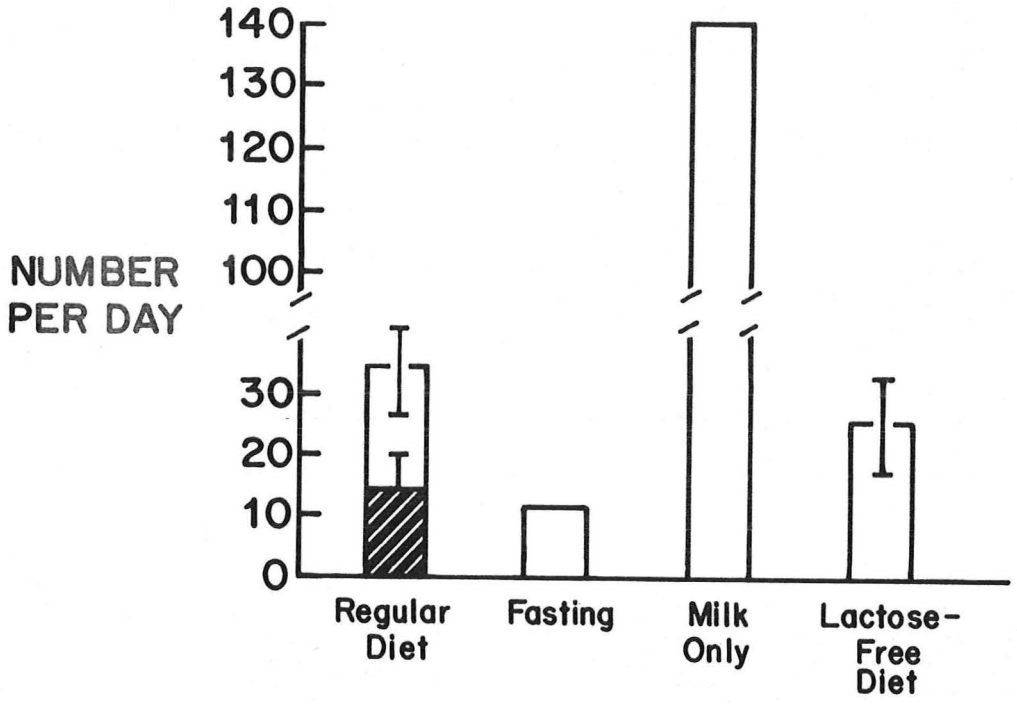
Although many other vegetables are "gas forming" (i.e., cauliflower, cabbage, broccoli, radishes, brussel sprouts, turnips), beans have assumed the favored role for experimentation. Whether *in vivo* or *in vitro*, beans result in the generation of CO_2 and H_2 (11,35,56-58), a phenomenon that does not improve by daily ingestion of beans over a month's period (59). Antibiotics have been shown either to prevent (58,60,61) or enhance (61) the effect of beans on gas production, depending upon the antibiotic used. Thus, beans clearly result in the generation of CO_2 and H_2 by colonic bacteria, much of which is consumed by other bacteria. As CO_2 and H_2 are produced, the partial pressure of N_2 decreases which leads to diffusion from blood. Thus, although the percentage of N_2 decreases, the volume increases (Figure 17, Table 4).

Beans contain two low molecular weight oligosaccharides - raffinose and stachyose. Raffinose (glucose-fructose-galactose) makes up about 0.5% of the bean *phaseolus vulgaris* while stachyose (glucose-fructose-galactose-galactose) makes up about 3.5% (62). These starches appear central to the flatulogenicity of beans (63-65), although some factor left in the bean residue after alcohol extraction of the oligosaccharides may also play a role (62). Stachyose and/or raffinose administered to humans (64), rats (14), or stool *in vitro* (60) leads to the formation of H_2 gas. Inasmuch as beans provide a substantial source of inexpensive nutrition, it makes sense that attempts are being made to render the bean less flatugenic.

Levitt has published the best case report of a patient (L.O. Sutalf) troubled with excess flatus (66). This young man passed a mean $\pm$ SE of 34 $\pm$ 7.3 expulsions per day (age matched control = 13.6 $\pm$ 5.6) (Figure 18) with a volume on his regular diet of 345 ml/hr (control $\sim$ 20 ml/hr). Treatment with simethicone, *Lactobacillus*, charcoal, neomycin, and anticholinergics had failed, prompting his referral to Dr. Levitt. Flatoanalysis disclosed the following concentrations of gas: N_2 17%, CO_2 44%, H_2 38%, O_2 1.3%, CH_4 0.003%. Since such values were inconsistent with air swallowing, Levitt tested this subject (who kept meticulous records) with various diets (Figures 18 and 19). Analysis of results shown in Figure 18 shows that the patient's flatopathy was clearly related to food, that a milk-only diet produced flatofrequency of near heroic proportions, and that marked improvement occurred with a lactose-free diet. The extent of the patient's lactose intolerance is demonstrated in Figure 19. On a regular test diet, he produced 4-hour volumes of almost 800 ml, far more than either normal controls or other lactose-intolerant controls. Removal of milk brought his flatovolume down to that of the lactose-intolerant controls but a 50 gm lactose load once again shows that this patient responds more dramatically than other lactose-intolerant subjects. Clearly his colonic bacteria are most efficient at metabolizing lactose.

However, even on a lactose-free diet (Figure 18), Mr. Sutalf still passed gas more often than normal controls. Although there is a report of charcoal reducing passages and breath hydrogen following a test meal (67), Mr. Sutalf had not responded to such therapy. He therefore kept careful flatugraphic records while systematically testing individual foods for their flatugenicity. Results of his work are shown in Table 5 (68).

FREQUENCY OF PASSAGES
(L.O. Sutalf)



VOLUME OF FLATUS
(L.O. Sutalf)

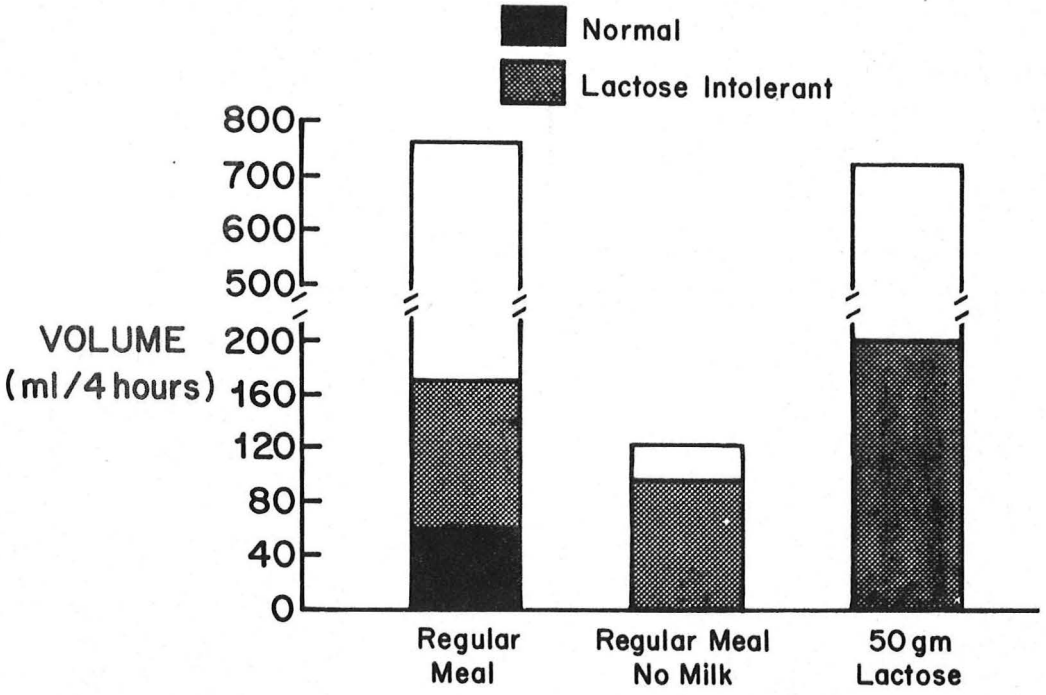
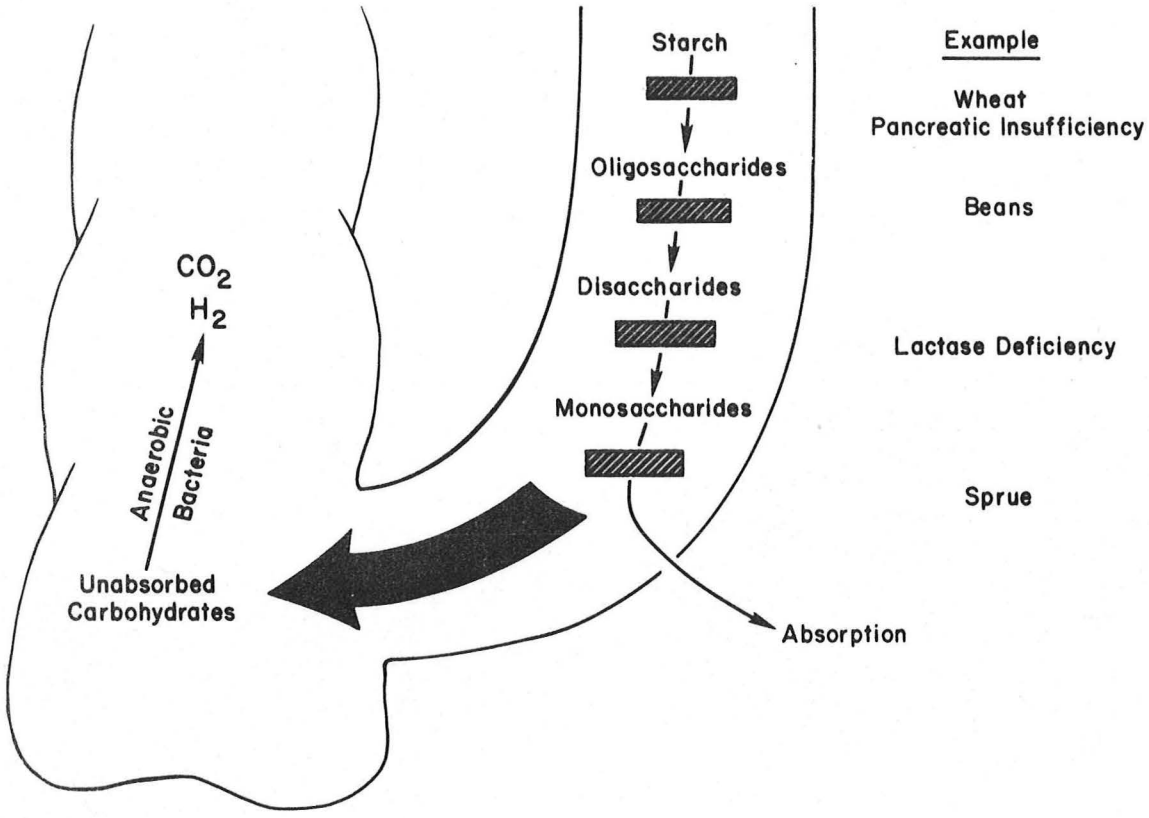


TABLE 5. Foods which are non-flatugenic (<19 passes/day), mildly flatugenic (20-40/day), and markedly flatugenic (>40/day). (From Sutalf)

Food	Non-Flatugenic	Mildly Flatugenic	Markedly Flatugenic
Animal Products	meat, fowl, fish	-	-
Vegetables	-	egg plant	brussel sprouts, onions, beans, celery, carrots
Fruits	cantaloupe, grapes, nuts, berries	citrus fruits, apples	raisins, bananas, apricots, prunes
Carbohydrates	rice, corn chips	potatoes, pastries, bread	pretzels, bagels, wheat germ
Other	eggs		milk

When Mr. Sutalf consumed a diet consisting only of non-flatugenic foods over a 3-week period, he noted a mean $\pm$ SE of only 16.8 $\pm$ 4.5 passages per day.

Thus, the cause of excess CO_2 and/or H_2 resulting in excess flatus can be summarized as shown in Figure 20. Unabsorbed carbohydrates which enter the colon are fermented by appropriate anaerobic bacteria to CO_2 and H_2. Treatment involves determining at what step in the absorptive pathway malabsorption occurs and adjusting the diet accordingly. Antibiotics are not indicated.



Not everyone is distressed at the thought of passing gas. Joseph Pujol, known as Le Petomane (69), evidently possessed the ability to "suck in" air *per rectum*. Once loaded, Le Petomane was able to discharge his ammunition in amazing ways, including the simulation of most every instrument in an orchestra. It is said his version of the Marseillaise never failed to rouse his audience to a standing ovation.

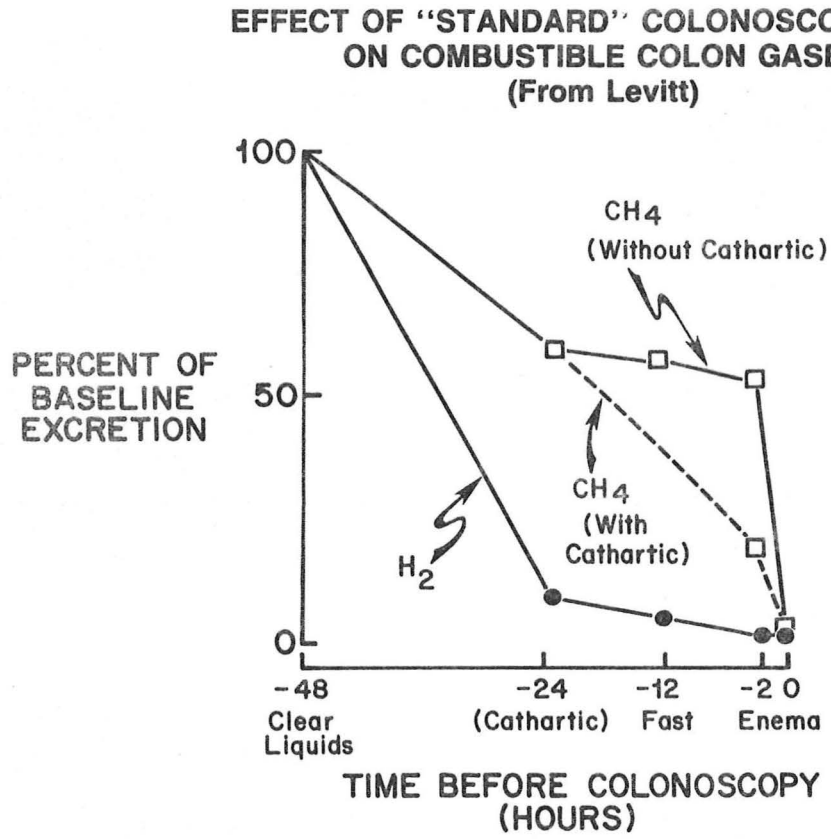
BOWEL EXPLOSIONS

Hydrogen and methane are explosive gases, with a combustible range of 4-75% for hydrogen and 5-15% for methane (70). Since these concentrations are often found in the colon, it is not surprising that numerous reports have been published of explosions occuring when electro-surgery was performed at proctosigmoidoscopy (70-78). The typical case report describes a loud retort with or without a blue flame (i.e., with or without methane) at the time of electrocoagulation. In each instant, pre-proctoscopy preparation consisted of only local enemas. In one instance (77), a breath sample taken shortly after the explosion disclosed a very high H_2 concentration. While most of these patients lived after urgent surgery to correct bowel rents, several authors proposed using CO_2 as an insufflation gas to dilute out the potentially explosive gases (70,75,79).

With the increasing use of colonoscopy, there was fear that not only would gases in the proximal colon be more explosive (inadequate cleansing enemas) but any explosion would produce more damage with the closed-end colonoscope (i.e., the explosive force could not be released as well as through the open-ended proctoscope). Several investigators, however, reported that as long as thorough cleansing regimens were instituted, the potential for explosion would not be present (80-82).

Ragins reported that 6/14 patients without any prep had H_2 or CH_4 or both in the explosive range, at the time of colonoscopy, but that thorough prep (clear liquids only for 24 hours prior to decrease hydrogen, castor oil or milk of magnesia the evening prior, and tap water enemas the day of the procedure to remove methane-producing bacteria) removed the potential for explosion in 52 patients (80). Bond measured breath H_2 and CH_4 in patients being prepared for colonoscopy with clear liquids, cathartics, a 12-hour fast, and pre-procedure enemas (81). A summary of their results is shown in Figure 21. The effect on H_2 of clear liquids and a 12-hour fast is marked whereas CH_4 is effected only minimally. If, however, oral cathartics are administered 24 hours prior and enemas 2 hours prior to the procedure, levels of both gases are negligible. In 60 patients prepared in this fashion, levels in the colon at the time of colonoscopy were $H_2 = 0.02 \pm 0.01\%$ and $CH_4 = 0.002 \pm 0.001\%$.

Such preps are time-consuming and tedious, not to say uncomfortable to patients. To obviate these problems, colonoscopists and surgeons began using oral lavage solutions to clean the colon just before a procedure. Since saline solutions may result in volume overload (83), non-absorbable solutions containing mannitol were employed. When Bigard (84) reported the first colonoscopic explosion (and death) following mannitol prep, interest in unabsorbed carbohydrates and carbohydrate alcohols as a source of explosive gases surfaced once again (85-92). Bond and Levitt showed that 200 mg of mannitol added to feces generated a five-fold increase in H_2 (89). La Brooy demonstrated that



administration of 100 gm of 10% mannitol one hour prior to colonoscopy resulted in H_2 concentrations in the explosive range in 6/10 patients while castor oil given the night prior produced such concentrations in 0/10 patients (90). Keighley studied 44 patients scheduled for operation for colon cancer (91) who received either no prep, oral mannitol alone, oral mannitol plus antibiotics, and total gut saline lavage. Results are shown in Table 6.

TABLE 6. Bacterial counts of E. coli and proportion with potentially explosive concentrations of colonic gas after four pre-op preps (From Keighley).

	E. coli Counts			Proportion With
Prep	$<10^6$	10^6-10^9	$>10^9$	Explosive Concentrations of Gas
No Prep (N=11)	0	10	1	4/11
Mannitol (N=11)	0	6	5	7/11*
Mannitol + Antibiotics (N=11)	10	1	0	0/11
Saline lavage (N=11)	6	3	2	1/11

*5/7 had counts $>10^9$

It is thus clear that mannitol lavage is an unacceptable way of preparing patients for colonoscopy or colon surgery. To obviate this problem, Davis and co-workers devised "Golytely" in which polyetnylene glycol (PEG) was substituted for mannitol (83). This solution, which produces no significant fluid shifts and is not metabolized to H_2, has become the standard prep today (93,94). Whether or not CO_2 should also be used as the insufflating gas remains controversial (91), although many colonoscopists feel that the "belt-and-suspenders" approach is preferable.

In summary, a clear liquid diet and a 12 hour fast will reduce the level of colonic hydrogen to below-explosive range. However, since methane levels are unaffected by food, thorough cleansing is needed to rid the colon of methanogenic bacteria. This is most conveniently accomplished by an oral lavage solution containing PEG but not mannitol.

FLOATING STOOLS

The clinical correlation of floating stools with steatorrhea has been believed to be related solely to the fat content of steatorrheic stools. However, 10-15% of normal subjects also pass stools which float. In an attempt to get to the bottom of this issue, Levitt and Duane studied normal subjects with (N=9) and without (N=24) floating stools and compared them to 7 patients with steatorrhea. Healthy "floaters" and patients with steatorrhea had stools with a specific gravity 0.9800 compared to healthy "sinkers" with a specific gravity of > 1.0400 (Figure 22). Of note, however, when the stools were degassed, the specific gravity of the healthy floaters and patients with steatorrhea rose to "sinking" levels. Thus, stools float because of their gas content, not their fat content. Breath and stool methane concentrations in the three groups are shown in Table 7.

SPECIFIC GRAVITY OF STOOLS BEFORE AND AFTER DEGASSING FROM HEALTHY SUBJECTS AND PATIENTS WITH STEATORRHEA

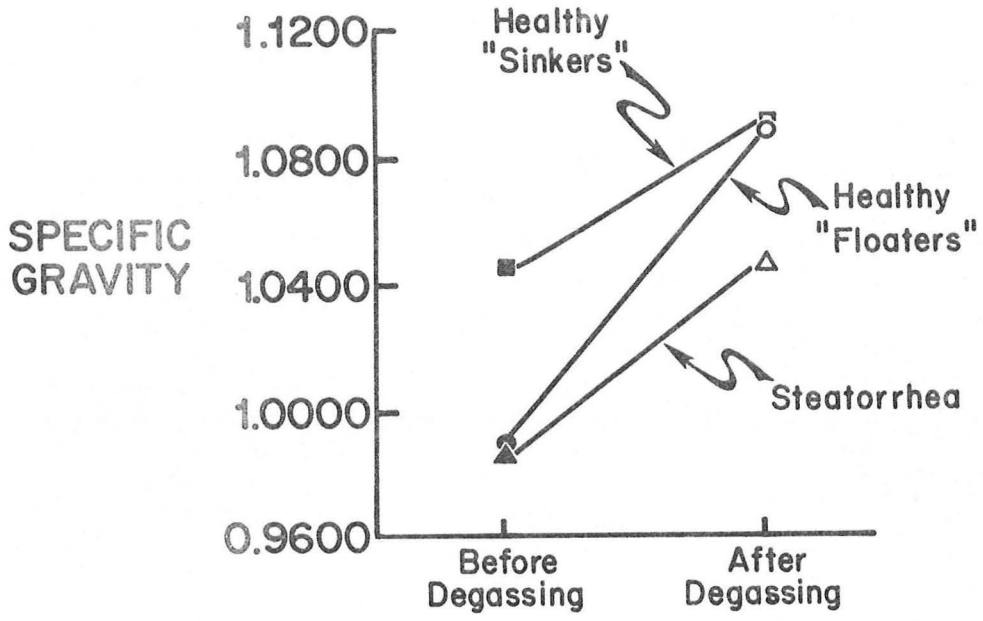


TABLE 7. Breath and stool methane in normal subjects and patients with steatorrhea. (From Levitt).

	Breath CH_4 (ppm)		Breath CH_4 > 7 ppm	Stool CH_4 (N=4)***
Normal Floaters	26.2 ± 4.6	(N=9)	8/9	64%,72% (N=2)
Normal Sinkers	1.82 ± 0.3**	(N=24)	2/24	<1%,<1% (N=2)
Steatorrhea*	-	(N=7)	1/7	-

* 17-38 gm/day stool fat
** Atmospheric
*** H_2 <2% in all 4

Thus, normal individuals whose stools float do so because of high levels of stool methane, while patients with steatorrhea must have high levels of H_2 and CO_2 as a result of malabsorption.

All of this moved Chatton (96) to verse in honor of Dr. Duane, whose own extraordinary methane production prompted the research:

Our thanks to frank Doctor Duane
Who takes the time to explain
Just how he had noted
That his stools often floated
Before they were flushed down the drain.

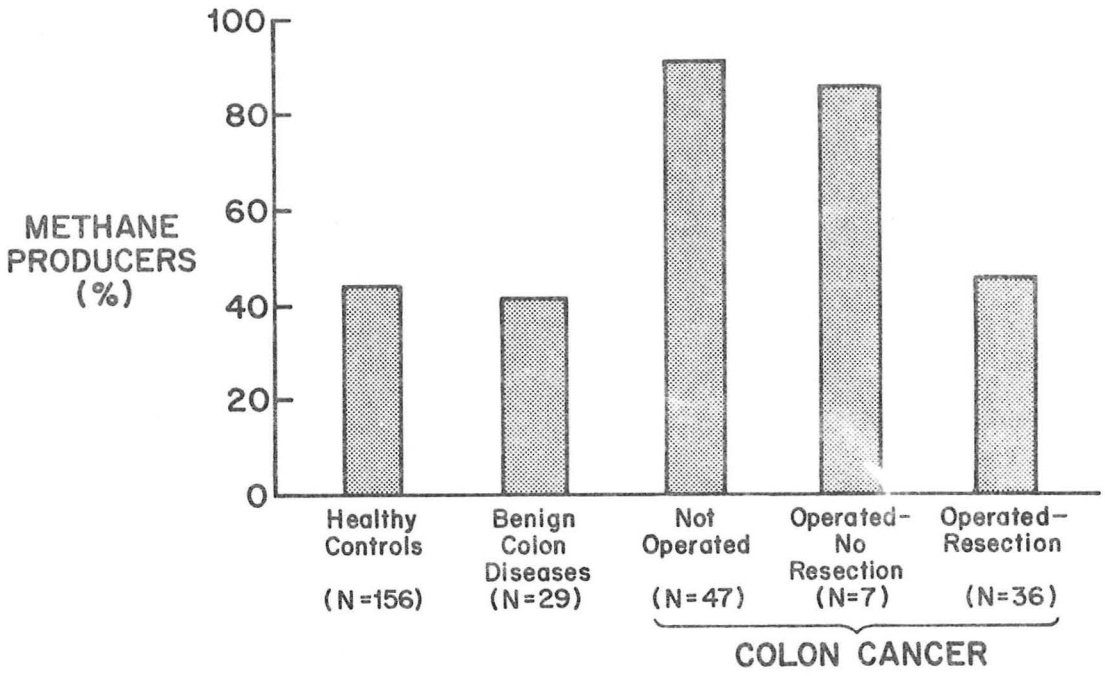
He must have thought first, "Mama mia!
Do I suffer from steatorrhea?
But it cannot be that -
There's no trace of fat."
Which led to another idea.

Well aware of the gas he unloosed
The doctor quite shrewdly deduced,
(Almost clairvoyant)
His feces were buoyant
Because of the methane produced.

METHANE AND COLON CANCER

Haines in 1977 reported that 80% of patients with untreated colon cancer excreted >1 ppm CH_4 in their breath compared to 40% of controls (97). Pique extended these observations to include patients with benign colon diseases and patients whose colon cancer was resected (98) (Figure 23). Inasmuch as surgical

INCIDENCE OF METHANE PRODUCERS IN CONTROLS AND PATIENTS WITH COLON CANCER
(From Pique)



resection brought the incidence of methane producers back to control levels, it appears that high methane levels in patients with colon cancer is effect rather than cause. Although Karlin's report was contradictory (99), his patients had had laxatives and enemas prior to breath analysis which might have affected results. Perman (100) offers several possible explanations for the possible relationship between methane and colon cancer:

- Tumors may secrete increased amounts of glycoproteins (a substrate for methanogenic bacteria) or mucoproteins with an increase in protein to carbohydrate ratio.

- Colonic organisms adhere to secretion and mucosa by a lectin-like mechanism. Tumor-induced changes in binding sites may enhance colonization with methanogenic organisms.

- Slow transit due to relative colonic obstruction may favor colonization of methane-producing bacteria.

- Patients with colon cancer have higher stool pH levels which may favor the development of methanogenic bacterial strains.

The clinical relevance of any relationship between methane and colon cancer, while intriguing, remains to be determined.

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