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Air Swallowing and Breathing Exercises Reduce the Severity of Acute Gastroesophageal Reflux Symptoms and Give a Clue into the Role of Oxygen in Digestion: A Case Report with Extended Discussion

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Abstract

A case is reported where a patient, after using a tooth whitening gel containing the active ingredient hydrogen peroxide over 2 days, found that the expected onset of postprandial gastroesophageal reflux symptoms (RS) did not occur. Hydrogen peroxide can also be formed when oxygen in air dissolves in water contained in the gut lumen and so the role of oxygen, rather than potentially toxic hydrogen peroxide, was investigated as a treatment for RS. Air swallowing can provide oxygen to the gut lumen, and breathing exercises can supply oxygen from the blood to the gut epithelium. Air swallowing and breathing exercises (ASBE) were performed as required over 34 days, and it was found that a single ASBE session (3-8 ASBE over 30 seconds) brought temporary relief from RS over 1-2 hours. Up to 3 sessions of ASBE were required and resolved RS over 74% of days, reducing the need to take antacid tablets. To understand the impact oxygen could have on RS, the oxidation potential for oxygen, calculated as mmol electrons/100 ml (2-3 breaths) of swallowed air, was calculated and compared to the reported values for the antioxidant content of various foods. It was found that 100 ml of swallowed air has the potential to oxidize 1 serving of coffee, red wine, or orange juice, known refluxogenic or trigger foods that can cause RS. Based on the finding that ASBE can reduce RS and a brief review of the role oxygen plays in digestion, a hypothetical oxygen model for digestive reflux was proposed. For the model, the reflux of digesting food to the more oxygenated esophageal regions is triggered by refluxogenic foods high in antioxidants that react with oxygen in the lumen to create an inadequate supply necessary for aerobic digestion, resulting in gastroesophageal reflux. As the ASBE did not resolve all RS, with ≈26% remaining unresolved, the oxygen supply was considered only a part of the complex digestive reflux mechanism.

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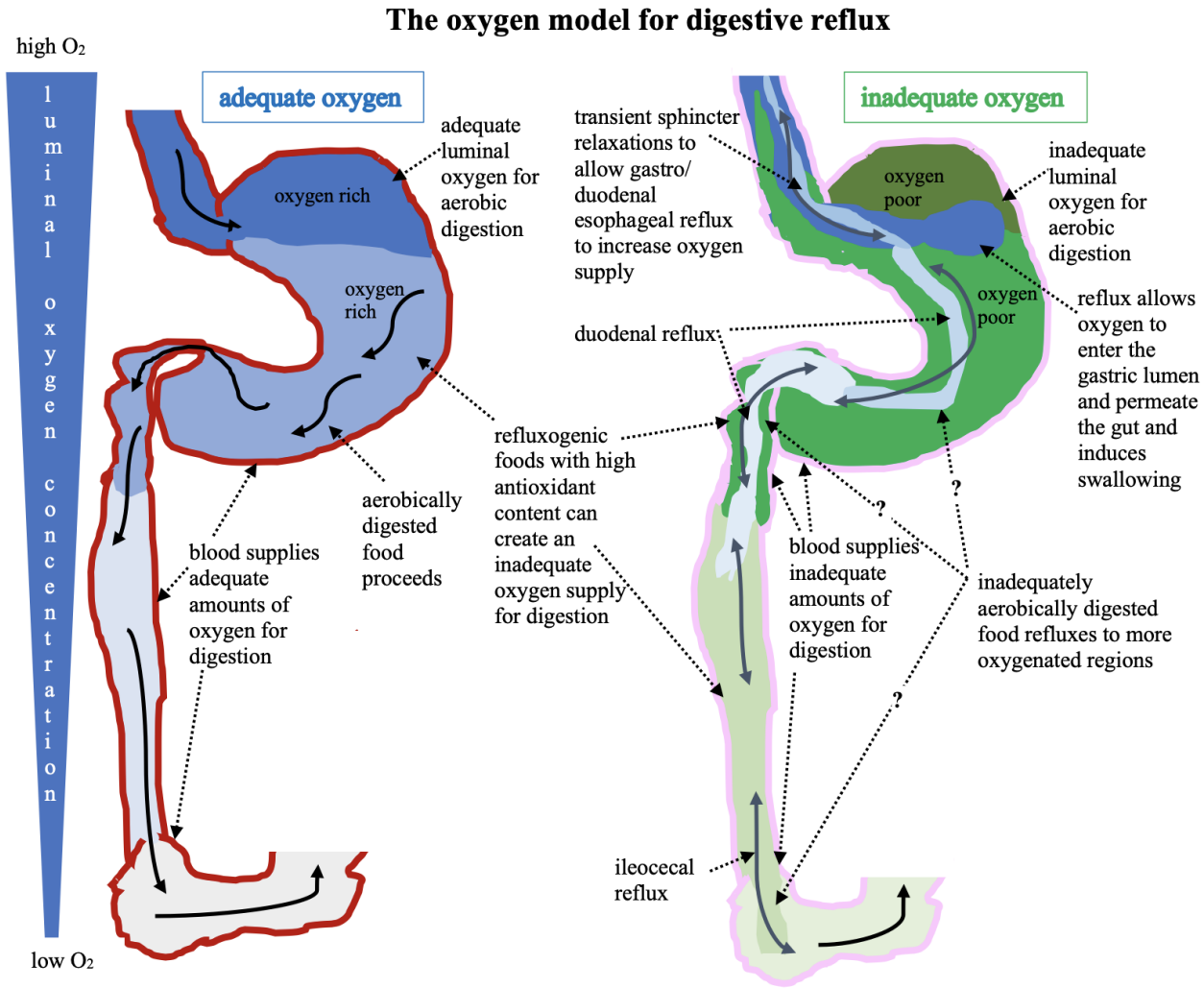
Abbreviations: air swallowing breathing exercises (ASBE), chronic obstructive pulmonary disease (COPD), ferric reducing ability of plasma (FRAP), gastroesophageal reflux disease (GERD), hypoxia inducible factor (HIF), irritable bowel disease (IBD), obstructive sleep apnea (OSA), positive airway pressure (PAP), reflux symptoms (RS), reflux symptom score (RSS), reactive oxygen species (ROS), transient lower oesophageal sphincter relaxations (TLESR).

Graphical Abstract



The hypothesised oxygen model for digestive reflux. Reflux of digesting food to the more oxygenated oesophageal regions is triggered by refluxogenic foods like coffee and orange juice which are high in antioxidants that react with oxygen in the lumen, to create an inadequate supply necessary for aerobic digestion, resulting in gastroesophageal reflux.
Several air swallowing and deep breathing events over 30 seconds, when reflux symptoms occur, increases oxygen supply and the probability that food can be aerobically digested as required, potentially reducing the number of reflux events and reflux symptoms, but excessive air swallowing can cause indigestion, bloating and burping

1. Introduction

A patient, after using a tooth whitening gel containing the active ingredient hydrogen peroxide over 2 days, reported that the expected onset of postprandial gastroesophageal reflux symptoms (RS) did not occur. This observation, together with the knowledge that oxygen from air can dissolve in water contained in the gut to form hydrogen peroxide, initiated the investigation into the potential benefits of air swallowing and breathing exercises (ASBE). Oxygen supply is likely the most central part of food digestion, and it is not surprising that, to digest an average meal, to produce molecules suitable for absorption, and to maintain a healthy microbiome, a significant amount of oxygen, including oxygen in the lumen, is required. A half equation for oxygen and the formation of hydrogen peroxide on dissolving in water allows a calculation of the maximum number of electrons able to be accepted during oxidation when 100 ml of air is swallowed. These values can be compared to reported values for the redox-active antioxidant in food [1]. A brief review of the literature for air and oxygen's association with gastroesophageal reflux disease (GERD) and other regions of the digestive system gives a clue to its central role. A hypothetical model is proposed suggesting that a diet consisting of foods requiring significant amounts of oxygen for digestion can create a lack of oxygen in regions of the gut, initiating reflux of digesting food to regions of higher oxygen content to increase oxygen supply and prevent cellular hypoxia or anoxia.

2. Case Report

A case is presented of a 65-year-old male with over a ten year history of postprandial RS that usually occur most nights, an hour or more after a meal, often becoming troublesome when lying down to sleep. No other diseases were reported or prescription medications currently used. After using a tooth whitening gel containing hydrogen peroxide (7.5%) in retainers covering the teeth for 60 minutes over 2 days, the expected onset of RS did not occur. Reflux symptoms were reported to be a feeling or awareness that stomach contents could reflux into the throat and were typically managed by using antacid tablets containing 300mg of calcium carbonate, taken before sleep. Consumption of refluxogenic foods like coffee and alcohol, eating 1-2 hours before sleep and large evening meals were minimised but not avoided altogether.

Awareness that hydrogen peroxide contained oxygen compounds that could also be obtained from ASBE and may be beneficial for digestion, ASBE was typically undertaken 1-2 hours after a meal when RS occurred. Symptoms would be scored nightly over 50 days as follows: no symptoms 0, mild 1, moderate 2, and severe symptoms 3. More complex RS scoring methods have been developed but may not necessarily be more accurate [2].

An ASBE involved breathing air to fill the mouth and deliberately swallowing the air and included several deep breaths over ≈30 seconds. Up to 3-8 ASBE were done at any one time, forming an ASBE session, performed when RS occurred. The first ASBE session often only brought temporary relief and had to be repeated, with up to 3 ASBE sessions required over 1-4 hours. Any discomfort resulting from ASBE or for whatever reason, the process could be discontinued, and antacid tablets could also be used if required to manage RS. The patient reported no significant side effects from ASBE but noted occasional burping and occasional mild transient indigestion immediately after ASBE of short duration.

3. Results

Air swallowing and breathing exercises

Over the 50 days, 10/50 days had no RS, and for 6/50 days, antacids were used in preference to ASBE due to going to sleep soon after a meal without time available to do the 3 ASBE sessions usually required (Supplementary material).

For 34 days, up to 3 ASBE sessions were undertaken to manage RS with up to 6 RS scores recorded (Fig 1A).

- The first ASBE session occurred ≈1-2 hours after the meal when RS emerged, bringing temporary relief to RS for 28/34 days, reducing the severity of RS for 4/34 days (7, 21, 27, 28), with RS unchanged for 2/34 days (22, 30) (Fig. 1B).
- About 1-2 hours after the first ASBE session, RS for 4/34 days (24, 32, 33, 34) had fully resolved, but RS for 30/34 days had re-emerged, requiring a second ASBE session (Fig. 1C).
- The second ASBE session brought temporary relief to RS for 25/30 days, reducing the severity of RS for 4/30 days (7, 20, 26, 27), with RS unchanged for 1/30 days (11) (Fig. 1C).
- About 1-2 hours after the second ASBE session, RS for 10/30 days (6, 12, 14, 15, 16, 18, 19, 25, 29, 30) had fully resolved (in addition to days 24, 32, 33, 34 after the first ASBE), but RS for 20/30 days had re-emerged, requiring a third ASBE session (Fig. 1D).
- The third ASBE session fully resolved RS for 11/20 days (1, 2, 3, 4, 8, 9, 10, 17, 20, 21, 23), but RS persisted for 9/20 days (5, 7, 11, 13, 22, 26, 27, 28, 31), with 7 days requiring the use of antacids and 2 days (5, 7) not requiring antacid use (Fig. 1D).
- In summary, the 3 ASBE sessions fully resolved RS for 25/34 ≈ 74% of days, and RS for 27/34 ≈ 79% of days did not require the use of antacids.

It is uncertain how much the RS scores would have reduced naturally over time, independently of ASBE sessions, potentially inflating the benefit of ASBE; however, ASBE had reduced the use of antacids to manage RS.

Relief from ASBE could take 10 minutes to occur after the session, while antacid tablets worked more rapidly, indicating redox reactions have a slower rate than acid neutralization. It was claimed that RS that developed approximately 30 minutes after drinking coffee in the mornings could be reduced by 2-3 ASBE sessions of 20-30 seconds, but RS score values were not recorded. The patient also found ASBE sessions worthwhile and would continue as a treatment option for RS after the 50 days, as the need for antacids had been reduced. There was no trend observed showing the severity or frequency of RS had reduced over the 50 days (34 days ASBE) from the ASBE. It is not known if air swallowing, breathing exercises alone, or both together provide the best option for RS reduction and resolution.

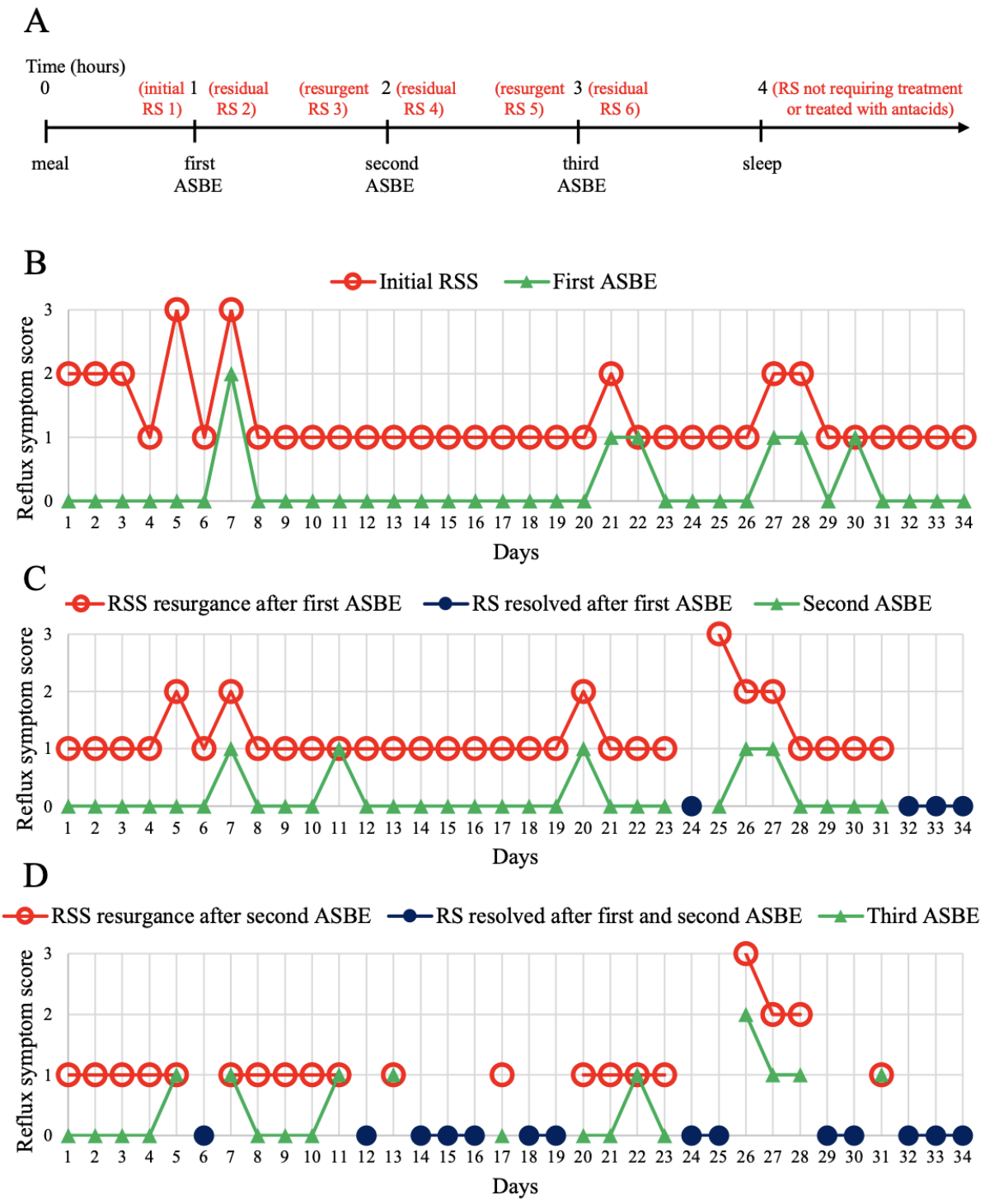


Figure 1. Changes in the RS score over 34 days from ASBE sessions: (A) typical timeline between meals with an initial RS score recorded before the 3 ASBE sessions followed by an additional 5 further RS scores, totalling up to 6 RS scores /evening meal (RS 1 -RS 6) before sleep, (B) the first ASBE session brought temporary relief to 28/34 days with RS persisting for 6/34 days (7,11,20,26,27), (C) over the following ≈ 1-2 hours, RS resolved for 4/34 days (24,32,33,34) but returned for 30/34 days requiring a second ASBE session, bringing temporary relief to RS for 25/30 days with RS persisting for 5/30 days (7,11,20,26,27), (D) again over a further ≈ 1-2 hours, RS returned for 20/34 days requiring a third ASBE session, fully resolving RS for 11/20 days with RS persisting for 9/20 days (5,7,11,13,22,26,27,28,31), overall ASBE sessions resolved 25/34 ≈ 74% of RS events over ≈ 1-4 hours with 9/34 remaining unresolved.

4. Discussion

To understand the finding that ASBE can reduce RS, a discussion with background information regarding the role of hydrogen peroxide, oxygen reactivity and supply, antioxidants in food, and a brief literature review of the role of oxygen in the gut was undertaken, resulting in a hypothetical oxygen model for reflux.

4.1. Hydrogen peroxide in humans and its formation by oxygen in water

Hydrogen peroxide could be considered a toxic substance with no beneficial role; however, it is produced by every cell in the body and is important physiologically, but when produced in excess, may cause disease [3]. For example, excessive production of hydrogen peroxide has been found to reduce lower esophageal sphincter tone in human esophagitis [4]. Although hydrogen peroxide can form when oxygen dissolves in water, at high concentrations it can be toxic. This was found when a solution of hydrogen peroxide (3%), when unintendedly ingested over several weeks as part of a dental mouthwash, caused chemical gastritis and colitis that completely resolved on cessation [5]. Hydrogen peroxide is contained in human breast milk ($H_2O_2 \approx 10^{-5}$ mol/L) and was found to promote gastric motility with an antimicrobial role in murine studies, and it may enhance gastric emptying in neonates [6]. The antimicrobial properties of hydrogen peroxide ($H_2O_2 \approx$ 0.1-0.03mol/L) were also shown by the eradication of *Helicobacter pylori* in vivo and in vitro from animal models [7].

The molecular oxygen present in air has a hypothetical redox half equation showing oxygen can react as an oxidizing reagent:

$$O_2 + 4e^- \rightarrow 2O^{2-} \qquad (1)$$

is soluble in water:

$$O_{2(g)} \leftrightharpoons O_{2(aq)} \qquad (2)$$

and can generate hydrogen peroxide, which can also react as an oxidizing agent:

$$O_2 + 2H^+ + 2e^- \rightarrow H_2O_2 \qquad (3)$$

$$H_2O_2 + 2H^+ + 2e^- \rightarrow 2H_2O \qquad (4)$$

$$O_2 + 4H^+ + 4e^- \rightarrow 2H_2O \qquad (5)$$

With oxygen able to accept a maximum of 4 electrons per mole as part of the oxidation process[8], many other reactive oxygen species (ROS), in addition to hydrogen peroxide, can be formed, including highly reactive oxygen free radicals that can remove a hydrogen atom from unsaturated fatty acids [9][10]. The thermodynamics and kinetics of redox reactions involving oxygen and the digestion of food can be pH dependent, as shown by eqs. (3-5), and catalysed by metals (Fenton reaction) [8][9][10][11][12].

4.2. The oxidizing potential of oxygen in 100ml swallowed air in mmol electrons

For 100 ml of swallowed air contained in the stomach, assuming 21% of the volume was oxygen or 21ml, with 78% nitrogen and 1% other gases, including water vapor, then the moles of swallowed oxygen can be calculated at standard temperatures and pressures from the ideal gas equation:

$$P\,V = n\,R\,T \qquad (6)$$

For oxygen, assuming a pressure (P) of 1 atmosphere or 101,325 pascals, a volume (V) of 21 ml of oxygen/100 ml of air (giving V = $21/10^6$ m^3), a gas constant (R) of 8.314, and a temperature of 25°C or 273.15 + 25 = 298.15K, then:

$$n = PV/RT = 101325 \times (21/10^6)/8.314 \times 298.15 = 8.58 \times 10^{-4} \text{ mol of oxygen} \qquad (7)$$

or the number of moles of oxygen (O_2) ≈ 0.86 mmol/100 ml of swallowed air.

From eq. (1), with a maximum of 4e/mole of oxygen that can be accepted, then from eq. (7):

$$0.858 \times 4 = 3.43 \text{ mmol electrons/100 ml of air} \qquad (8)$$

is the maximum number of electrons that can be accepted by 21 ml of oxygen (100 ml of air) from antioxidants or electron-rich food substances as part of the oxidation process.

4.3. The oxidizing potential of oxygen in 100ml of drinking water in mmol electrons

The concentration of pure oxygen that can dissolve in water is, on average, O_2 ≈ 1.22 mmol/L (pH ≈ 1-14, low ionic strength solutions) at 25°C and 1 atmosphere (atm), with solubility increasing with pressure but decreasing with increasing electrolyte concentration and temperature [13][14]. Air, with 21% oxygen, has a partial pressure P ≈ 0.21 atm, resulting in a concentration of O_2 ≈ 0.21x1.22 ≈ 0.256 mmol/L in water (≈ 0.0256 mmol/100 ml of water) at 25°C;[14].

From eqs. (3-5), with up to 4e/mole of oxygen available:

$$0.0256x4 \approx 0.10 \text{ mmol electrons/100 ml of water (dissolved oxygen)} \qquad (9)$$

is the maximum number of electrons that can be accepted by oxygen from air dissolved in 100 ml of water.

Swallowed air has a concentration of O_2 ≈ 0.86 mmol/100 ml of air compared to O_2 ≈ 0.0256 mmol/100 ml dissolved in water. As such, air contains ≈34 times more oxygen than oxygen (from air) dissolved in water at the same volume and temperature. Oxygen dissolved in water may be more reactive towards the contents of food than oxygen at the lumen/aqueous interface, but the depleted oxygen from water by reaction with food would allow more oxygen from air to dissolve in accordance with the equilibrium eq. (2).

4.4. Systemic oxygen supply to the human body

During the inhalation of air, with a 21% oxygen content, oxygen in the alveoli is exchanged for the waste product carbon dioxide from cellular energy production and exhaled as 16% oxygen and 5% carbon dioxide [15]. An adult at rest exchanges ≈500ml of air per breath (tidal volume) with 12 breaths a minute, resulting in ≈6 litres/minute of air ventilation [15]. With moderate exercise, the breathing rate can increase to 20 breaths/minute, with ≈2 litres/breath

resulting in ≈40 litres/minute of ventilation [15]. As such, from the values above, the amount of pure oxygen per minute, when breathing at rest, can be calculated as O_2 ≈ (0.21-0.16) x 6 ≈ 0.3 litres/minute or O_2 ≈ 300ml/minute, and with moderate exercise, O_2 ≈ (0.21-0.16) x 40 ≈ 2 litres/minute. In awake healthy subjects at rest, oxygen consumption has been reported to be O_2 ≈ 250ml of pure oxygen/min [16]. As 100ml of swallowed air contains 21ml of oxygen, then 21/250 or ≈8% of the body's systemic oxygen consumption/minute can be made available within the gastric lumen, indicating that multiple air swallowings can provide a significant increase in gastric oxygen availability for aerobic digestion when at rest.

4.5. Air Swallowing, Breathing, Luminal Oxidation of Lipids, and the Microbiome

Air swallowing naturally occurs on swallowing and when food is consumed. The swallowing of a 10ml liquid bolus is usually accompanied by 8-32ml of air, which can result in belching, but patients with excessive belching did not have more frequent gaseous gastroesophageal reflux [17]. Swallowed air has a higher partial pressure of oxygen in the stomach than in the blood, allowing oxygen to be directly absorbed by diffusion [18].

A meta-analysis of 7 studies on the effects of breathing exercises on patients with GERD found reduced symptoms, improved quality of life, and a decrease in acid suppression use, possibly due to strengthening the anti-reflux barrier function [19]. Diaphragmatic breathing exercises have been shown to reduce the symptoms of GERD and reduce acid exposure, attributed to respiratory physiotherapy; however, the proof of the mechanism of action was reported to be lacking [20][21]

In murine models, it was found that bacteria in the lumen consumed more oxygen than bacteria adherent to the mucosa throughout the length of the gut [22]. Oxygen was not only consumed by bacteria but was also involved in direct chemical oxidation processes of dietary lipids, and this may be one of the processes responsible for oxygen consumption [22]. It was also found that oxygen levels were highest in the duodenum, with oxygen levels in the lumen higher than the intravascular levels, followed by the stomach, with lower oxygen levels but with similar luminal and intravascular oxygen levels [22]. The existence of oxygen, other than in the stomach, was found by using a swallowed electronic capsule capable of sensing different gases, finding oxygen in the jejunum, ilium, and, with a high-fibre diet, the colon, with excess hydrogen mitigated by oxidation [23].

It has been reported that 5% of the total blood volume is present in the gut during fasting, increasing to 30% following the ingestion of a meal, creating daily fluctuations [24][25][26]. The oxygen gradients for the small intestinal epithelial cells, villus, and lumen are all at physiologically low O_2 levels (2-4%) and are depicted as tissue in constant low-grade inflammation [24][25][26]. Hypoxia and hyperoxia can alter the microbiome content of the gut; however, ASBE did not show a trend towards increasing or decreasing RS over the 50 days (34 days with ASBE), suggesting that any alteration of the microbiome did not greatly influence RS for this case report [26].

In summary, oxidative processes using oxygen in the lumen for digestion have been found to occur throughout the digestive regions of the gut, indicating an oxygen demand, but it is uncertain how much of this is supplied by air swallowing or systemically from the circulating haemoglobin in the blood. Dietary lipids can be considered potential trigger

foods, and if luminal oxygen is directly involved in their oxidation, they may have an important role in reducing RS, provided enough can be supplied from either swallowing or the blood supply.

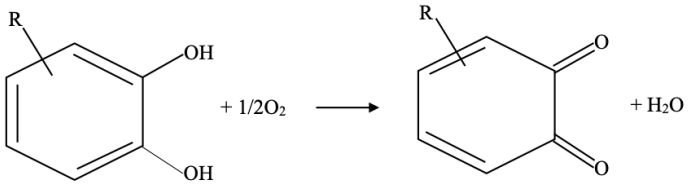
4.6. Antioxidants, foods, and their electron content

Foods, when consumed for digestion, can undergo oxidation or reduction (redox reactions) to involve the addition of oxygen, electron/hydrogen atom exchange, or free radical reactions as part of the digestive process [1][27]. The redox activity of 1113 food samples has been ranked according to their antioxidant contents as mmol electrons/100g or mmol/serving size with the aim of assessing the health benefits of antioxidants [1]. This was achieved by using the FRAP (ferric reducing ability of plasma) test to measure the relative oxidizing ability of foods towards 2,4,6-tripyridyl-*s*-triazine (TPTZ) as TPTZ-Fe(III)Cl_3, which, on mixing with food samples, accepts electrons to form a deep blue TPTZ-Fe(II)Cl_2 [1]. Foods that have relatively high antioxidant capacity per serving include coffee (2.96 mmol/serve), chocolate (2.52 mmol/serve), red wine (2.2 mmol/serve), pineapple juice (1.86 mmol/serve), oranges (1.26 mmol/serve), and iced tea (0.88 mmol/serve), often considered trigger foods for RS with high refluxogenic scores [1][28]. Foods with the lowest antioxidant activity include fats and oils (0.187-0.531 mmol/serve), meat products (0.052-0.509 mmol/serve) and substitutes, poultry products (0.072-0.388 mmol/serve), fish and seafood (0.025-0.141 mmol/serve), with the lowest values for eggs and egg dishes (0.009-0.047 mmol/serving) [1]. Fats and oils, despite the electrons available from the alkenes in polyunsaturated fats, were found to have low antioxidant activity, possibly due to any number of variables including slow reaction rate with the TPTZ-Fe^{3+} (a 4-minute incubation time was used), solubility, pH, ionic strength (electron conduction), and temperature [1].

Ideally, it is best to measure both the pro-oxidant and antioxidant properties of food, as no single test would reflect the many possible redox reactions for in vivo digestion [27]. If both pro-oxidant and antioxidant properties were measured using the FRAP and 3 additional testing methods, coffee and orange juice were found to have very high antioxidant potential, with sausage and white chocolate having both high antioxidant and high pro-oxidant properties at the same time [27].

Based on the calculated value in mmol electrons/100 ml of swallowed air, oxygen has the capacity to oxidize one serving of coffee, red wine, or orange juice, but not the highest scoring foods like one serve of blackberries (5.746 mmol/serving), walnuts (3.721 mmol/serving), strawberries (3.584 mmol/serving), or artichokes (3.559 mmol/serving), based on the FRAP analysis [1].

The polyphenols in red wine, which contain multiple aromatic hydroxy groups, have been reported to totally inhibit dietary lipid peroxidation when saliva is present in the acidic environment of the stomach [29]. Foods containing polyphenols can react directly with oxygen in the air, turning food brown, as shown from a slice of apple [30]. Polyphenols are likely to react directly with oxygen in the lumen, depleting the supply, and in this example, removing hydrogen from the polyphenol to form water, with the oxidation process not necessarily adding more oxygen atoms on forming the oxidised product:



(10)

4.7. Oxygen's Association with Reflux and the Digestion Process

Numerous studies give background information and provide a clue to a possible relationship between systemic or luminal oxygen supply, RS, and GERD in Table 1, and oxygen's role in other gut regions, Table 2, with some comments provided.

Table 1. Oxygen, reflux and the digestion process.

Research finding	Ref.
Chronic obstructive pulmonary disease (COPD) associated with abnormally high prevalence of oesophageal acid reflux where oxygen desaturation can coincide with periods of acid reflux in some patients.	[31]
Marked improvement in RS for patients with obstructive sleep apnea (OSA) treated with continuous positive air pressure (PAP) and nasal PAP suggested as a new treatment for nocturnal reflux disease.	[32][33]
The effect of PAP on productive cough was found to be mainly mediated through decreased in GERD.	[34]
Acute oxygen desaturation associated with pulmonary aspiration in patients with GERD and laryngopharyngeal reflux.	[35]
Gastric mucosal oxygen delivery and red blood cell flux decreased by 50% during hypothermic cardiopulmonary bypass despite constant systemic oxygen delivery. Comment: although the mechanisms were not discussed for the sedated patients, this result may indicate luminal oxygen has a role in increasing gastric mucosal oxygen levels in awake subjects.	[36]
Chewing gum is associated with an increase in air swallowing and a reduction in RS.	[37][38]
Consumption of carbonated beverages is associated with laryngopharyngeal reflux and GERD. Comment: the mechanism was not discussed but could involve the displacement of oxygen from the lumen by carbon dioxide, changing anerobic digestion conditions.	[39]
Magnetic resonance imaging of oxygen saturated water, claimed to increase health and athlete performance, found molecular oxygen remained present in the stomach or duodenum for ≈45 minutes. Comment: the use of the oxygen saturated water to relieve acute reflux symptoms was not reported.	[40]
Upper airway obstruction in newborn lambs had no significant effect over 3 hours but after 6 hours, mildly increased the number of gastroesophageal reflux events. Comment: hypoxia is likely to create reflux events.	[41]
Hypoxia of the esophageal mucosa related to ischemic heart disease leads to a decrease in both esophageal tissue resistance and lower sphincter dysfunction, leading factors in the development of GERD.	[42]
Air swallowing could promote belching but did not facilitate acid gastroesophageal reflux in both healthy and GERD patients. Comment: air swallowing may reduce the acidity of reflux.	[43][44]
Frequent belching was common in patients with functional dyspepsia who were found to swallow more air than controls (up to 80% incidence) resulting in an increased incidence of non-acid gaseous gastroesophageal reflux, with no signs of pathological acid reflux. Comment: gaseous reflux is likely to involve gas exchange with air in the oesophagus prior to returning to the stomach.	[45]
The gas component of the stomach remains relatively constant at ≈98-109±63 ml over 1 hour while digesting 500 ml of soup, even at low liquid volumes of 294±74 ml. Comment: retention of luminal gas during gastric digestion suggests an important role.	[46]
Oxygen demand is associated with high energy processes, like the transport functions of intestinal epithelial for electrolytes including Nå/K^+-ATPase with activity either increased or decreased during periods of hypoxia. Hypoxia has been found to reduce acid secretion and gastric emptying in murine models. Comment: how oxygen demand influences H^+/K^+-ATPase activity, an important component of GERD, requires further investigation.	[47][48][49]

Table 2. Both systemic and luminal oxygen with redox, irritable bowel disease (IBD), hypoxia inducible factor (HIF), oxygen in the gut and the microbiome but an association with bile and coloileal reflux was not found.

Research finding	Ref.
The metabolism of food, as it passes through the gut, involves specific regional redox potentials (Eh) and pH values with the oral cavity Eh≈800-1000 mV with pH≈7-8, the most oxidizing part of the gastric system due to the large amount of oxygen, followed by the stomach with a Eh≈400-500 mV, pH≈1-5, both forming the more aerobic regions of the digestive system, followed by the ileum Eh≈0-(-200) mV, pH≈7-8 and colon Eh≈-200-(-300) mV with pH≈5-6 with both forming the more anaerobic and reducing regions with low oxygen levels. Comment: redox potentials indicate the location of the oxidizing and reducing environments of the gut, presumably with different microbiome content, with reaction thermodynamics and kinetics likely pH dependent.	[50]
Biopsy specimens classified 20 aerobic and 12 anaerobic bacteria in the gastric mucosa, with the fundus redox potential ≈400-500 mV and the colon ≈-200-(-300) mV, with the redox balance influenced by the bacteria present and therefore antibiotics, both implicated in the development of diseases. Comment: the oxidizing environment of the stomach does not contain exclusively aerobic bacteria.	[51]
Cellular reductive stress, the counterpart of oxidative stress, is associated with a shift in the redox balance to a more reducing state, leading to inflammatory conditions, distorted transport, failed oxidation, and metabolic syndrome.	[52]
Colonic fermentation of indigestible carbohydrates in 9 patients with symptomatic GERD increased transient lower oesophageal sphincter relaxations (TLESRs), the number of acid reflux episodes, and GERD symptoms. Comment: Relaxation of the pyloric and/or ileocecal sphincters and an association with luminal oxygen supply was not investigated.	[53]
The role of oxygen in inflammatory bowel disease (IBD) may result from diminished tissue oxygen levels (anoxia) initiating hypoxia-inducible factor (HIF) pathways caused by a loss in intestinal epithelial barrier function, allowing luminal contents access to underlying cells.	[54]
Conditions that increase the epithelial oxygen content for intact epithelia, which may include the presence of dietary fibre, can create an imbalance in the anaerobic/aerobic bacteria ratio, resulting in dysbiosis in the colon.	[55]
Regurgitation of duodenal bile contents into the stomach and esophagus, known as bile reflux, can present as bile acids in the esophagus and is associated with GERD and hypopharyngeal cancer.	[56]
Coloileal reflux, classified as mild, moderate, or severe, has been reported at a 46.5% frequency from the analysis of 715 barium enemas, with the causes and consequences not widely investigated.	[57][58]
Oxygen pressure in the lumen of the small intestine was found to be <10mm Hg and in the lumen of the sigmoid colon <3-11 mm Hg, with the role of the epithelial-lumen interface together with the luminal oxygen concentration in intestinal diseases, not currently known.	[59]

4.8. The oxygen model for digestive reflux

This case report has found ASBE can reduce RS in one individual, but despite this limitation, ASBE must increase the oxygen concentration in the gastric lumen and other intestinal regions, increasing the probability of successful aerobic digestion of food. Increasing oxygen supply increases the probability for the oxidation of refluxogenic foods, changing their composition and therefore potentially reducing their influence on producing RS.

A hypothetical model is proposed suggesting that if the oxygen supply necessary for aerobic digestion is unavailable, the food/liquid contents can reflux from the stomach or duodenum towards more oxygenated regions of the oesophagus, preventing cellular hypoxia/anoxia (graphical abstract). Reflux between regions with different Eh and pH may also be beneficial, suggesting a possible bidirectional component for optimal human digestion. Reflux can also occur between the colon and the small intestine, although not refluxing into the oesophagus. Due to the possibility of multiple reflux processes, the model was termed the digestive reflux model, rather than the gastroesophageal reflux model.

Tables 1 and 2 provide supporting evidence and a clue into the role oxygen plays in both bringing relief and initiating digestive RS, in particular.

- ASBE in the current case report reduced RS and the need to use antacid treatments,

- breathing exercises were found to reduce the symptoms of GERD and reduce acid suppression medication[19][20][21],
- PAP (increased luminal oxygen) suggested as a new treatment for GERD[33],
- a remarkably high prevalence of oxygen desaturation associated with gastroesophageal reflux in patients with RS[60],
- acute oxygen desaturation (hypoxia) associated with pulmonary aspiration in patients with GERD and laryngopharyngeal reflux, suggesting reduced oxygen supply could initiate reflux [35].
- colonic fermentation of fibre can increase transient lower sphincter relaxations (TLESR) and GERD symptoms, and ingestion of fibre has been associated with increased oxygen concentration in the bowel, indicating TLESR (also associated with many other foods) may be initiated to increase luminal oxygen supply throughout the gut, but evidence is lacking [23][53][59][61].

Why the systemic blood supply cannot deliver sufficient oxygen for digestion may be due to many possible processes including a reduced respiratory drive as associated with obesity hypoventilation syndrome [62]. A unifying oxygen-related model for reflux would support the suggestion that GERD, functional dyspepsia, and irritable bowel syndrome could be overlapping disorders [63].

5. Conclusion

The process of ASBE was found to resolve or reduce most postprandial RS, although multiple ASBE sessions are required over several hours, reducing the need to use antacid treatments. A 100ml of oxygen from air swallowing was shown to have the capacity to oxidise several refluxogenic foods, changing their composition and therefore potentially reducing their influence on producing RS. A brief literature review gave a clue into the central role oxygen, both systemic and luminal, plays in the digestion process. A hypothetical model was proposed that suggests if there is insufficient systemic or luminal oxygen in regions available to carry out the necessary redox reactions, regions of the gut may initiate reflux of digesting food to regions of higher luminal oxygen concentration. Future research could consider what the role oxygen may have in digestive reflux diseases.

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