Abnormal Gut Fermentation: The “Auto-Brewery” Syndrome

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Abstract/Résumé
The "auto-brewery" syndrome, caused by yeast or bacterial fermentation in the small intestine, is due to increased levels of blood ethanolic resulting from abnormal gut fermentation. This causes psychological, musculoskeletal, gastrointestinal and respiratory problems and is difficult to distinguish from other conditions, including food intolerance. Abnormal intestinal fermentation is associated with an alteration in gut permeability and a vitamin, zinc and magnesium deficiencies due to malabsorption. Diagnosis is based on an oral glucose challenge with positive results indicated when blood ethanolic concentration is greater than 22 μmol/L. Management of "auto-brewery" syndrome includes dietary restriction of fermentable simple sugars, refined carbohydrates, yeast products and mouldy foods. Antifungal drugs are recommended along with vitamin and mineral supplements. (J Can Diet Assoc 1997; 58:97-99)

Introduction
The following review developed as a result of a search for possible management strategies for several patients who attended the Allergy Nutrition Clinic, a component of the Allergy Nutrition Research Program at Vancouver Hospital and Health Sciences Centre, British Columbia. The patients were referred to the Allergy Nutrition Clinic with symptoms thought to be related to food intolerance. The symptoms did not fit the usual profile of food intolerance but were suggestive of an "auto-brewery" syndrome. This condition is described as abnormal gut fermentation (AGF) resulting from yeast or bacterial activity in the small intestine and causing increased levels of blood ethanolic (1). Although a clinical diagnosis of AGF was not confirmed in the patients attending the Allergy Nutrition Clinic, successful management outcomes supported what information there is currently available on AGF. The lack of research on AGF and the possibility that AGF may be more prevalent than previously thought, demonstrated a need for a review of the literature to encourage understanding of the etiology, diagnosis and management of AGF and to enhance recognition of this syndrome.

Symptoms
A wide range of symptoms accompany AGF and there is no single complaint which occurs exclusively in this condition. Increased fermentation and permeability of the gut may heighten an immune response causing the release of inflammatory mediators resulting in the polysymptomatic characteristics (3). The common symptoms are often multi-organ and tend to be indefinite, including fatigue, musculoskeletal aches and pains, abdominal discomfort, bloating, changed bowel habits and catarrhal discharge (1). Intense cravings for sugar are often reported (3). Table 1 identifies a list of symptoms associated with AGF.

The following case histories are representative of patients attending the Allergy Nutrition Clinic which led to this review focussing on AGF.

Case Histories: Client 1 was a two and a half year old boy, D.B. His mother described "bizarre behavior" after his son ate certain foods, especially candies and sweetened foods. He would start to giggle uncontrollably, stagger around "as if he were drunk" and finally wind down and fall asleep for about two hours.

Client 2 was a 35 year-old woman who had been very active in competitive long-distance running during her younger years. S.T. described herself as "a very hyper person" and needed extreme amounts of exercise (exceeding more than two hours per day) to "calm herself down". She had developed a pattern of eating large quantities of sweets and baked goods, and would eat a whole bowl of cookie dough before it was baked. She felt that these high sugar, simple carbohydrate foods made her feel "manic". She stated that "food does weird things to me" and that "this awful feeling" would not go away until she exercised (walking, running, bicycling) for at least two hours.

Client 3 described a multitude of symptoms, including bloating, abdominal pain, mental depression, hives, eczema and a chronic vaginal yeast infection. Thirty-two year old T.U. also complained of an over whelming craving for sugar with resulting mood swings when she ate excessive amounts of high sugar foods. Interestingly, both father and paternal grandfather, were alcoholics and had a similar history of abdominal discomfort.

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### TABLE 1

<table>
<thead>
<tr>
<th>Symptom Category</th>
<th>Common Symptoms Associated with Abnormal Gut Fermentation</th>
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<tbody>
<tr>
<td>Psychological</td>
<td>Decreased concentration, fatigue, difficulty in completing thoughts, lethargy, irritable bowel symptoms, vaginal itching</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Aches and pains, poor short-term memory, difficulty initiating physical activity, perineal/vulval itch</td>
</tr>
<tr>
<td>Gut</td>
<td>Abdominal discomfort, bloating, wind/gas, altered bowel habits, diarrhoea</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Nasal mucus discharge, recurrent sinusitis, catarhal discharge</td>
</tr>
<tr>
<td>General</td>
<td>Cravings for sugars and fermentable foods</td>
</tr>
</tbody>
</table>

1 compiled from Hunnisett 1990 (5); Eaton 1991 (1); Eaton 1992 (2); Eaton 1994 (4); Eaton 1995 (8).

2 In atopic and non-atopic patients

3 With or without association with asthma

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### Etiology and Pathology

**Gut Fermentation:** Normal gut fermentation occurs in the colon through bacterial action. This predominantly anaerobic process involves the extraction of glucose from soluble fibres and non-starch polysaccharides and is an integral part of digestion. By-products include short-chain fatty acids, ammonia, volatile gases and/or alcohols including butanols, methanols and propanols (4,5). In contrast, AGF takes place in the small intestine and produces ethanol (1,3). Yeast fermentation is suspected but bacterial metabolism may also be involved.

Alcoholic fermentation occurs in fungal species, such as Candida, that have metabolic pathways for converting pyruvic acid to ethanol. This process involves a decarboxylation of pyruvic acid to acetaldehyde under anaerobic conditions, followed by a reduction of the acetaldehyde to ethanol (Figure 1). Normally, the liver is able to detoxify the metabolites of yeast fermentation, but with AGF, sufficient ethanol accumulates in the blood to cause feelings of intoxication or the "auto-brewery" syndrome (6).

Gastrointestinal bacteria from the family Enterobacteriaceae can ferment glucose to ethanol and other alcohols. They are also capable of acidic fermentation producing a combination of acetic, lactic, succinic and formic acids. Some pathogenic bacteria, such as Clostridium spp. and Neisseria spp., can also produce ethanol (4). Overgrowth of aerobic and anaerobic bacteria within the lumen of the duodenum or jejunum may occur with intestinal stasis as in blind loop syndrome; it may occur with hypochlorhydria which increases the number of viable bacteria passing into the small intestine; and is seen in patients with common variable immunodeficiency (7,8).

**Gut Permeability:** Increased permeability of the small intestine to large undigested protein molecules was demonstrated in patients with AGF (9). Low blood levels of the B vitamins (specifically thiamine, riboflavin and pyridoxine), zinc and magnesium which accompany AGF may result from this altered gut permeability due to a possible competitive mechanism inhibiting absorption rather than a dietary deficiency (10).

Abnormalities in gut permeability were similar both in range and severity to food intolerance, perhaps explaining the clinical overlap between both entities (9). Compromised integrity of the small intestine has also been reported in long-distance runners (11) and chronic alcoholics (12).

### Diagnosis

Based on the theory that ethanol is produced in the gut from an oral glucose load then absorbed into the bloodstream, the Blood Ethanol Test (BET) or Oral Glucose Challenge (OGC) is a means to identify patients who ferment dietary carbohydrates to ethanol in the small intestine (3,5,6,9). The diagnostic protocol involves a 5g oral dose of glucose, following a three hour fast and a minimum 24 hour abstention from alcohol. Blood samples are taken two hours after the OGC to measure blood ethanol levels and compared to baseline ethanol levels in blood samples taken prior to the OGC. A positive test for AGF is indicated when concentrations of blood ethanol > 22 ummol/L. The validity of the BET has been confirmed in a number of other laboratories (9).

Increased levels of urinary β-alanine (BALA) has also been proposed as a marker for AGF (5). BALA is an isomer of the neutral amino acid, alanine, and is derived from the diet or produced during the metabolic degradation of cysteine and uracil. Although a major dietary source of BALA is the muscle protein of poultry, BALA can also result from enteral Escherichia coli activity through decarboxylation or transamination pathways so that increased production of BALA would be expected in AGF (5).
Other clinical or radiological examinations, including standard blood and urine analyses, have not been an adequate diagnostic tool for AGF (9). While breath hydrogen is related to bacterial fermentation, it has not yet been assayed in symptomatic subjects (8). Finally, no immunological basis to AGF has been identified to date (9).

Possible Source of the Problems:
"Auto-brewery" syndrome is not distinct from other diagnoses and may co-exist in patients who have a complex variety of symptoms involving psychological, musculoskeletal, gastrointestinal and respiratory problems (1). Historically, similar conditions have been labelled carbohydrate dyspepsia, intestinal carbohydrate dyspepsia, carbohydrate intolerance, carbohydrate indigestion and germ-carbohydrate fermentation, but were considered to be a psychological response rather than an organic syndrome (1). Candida infection, termed chronic candidiasis sensitivity syndrome (CCSS), was promoted as a causative factor of the multi-organ polysymptomatic complaints but inadequate research has been done to clarify the role of fungal involvement (1). Food intolerance and hyperventilation share some common symptoms with AGF but need to be identified separately (3).

Routine clinical examinations, standard laboratory tests and radiological examinations reveal little that is specific to AGF. Misdiagnosis is common and the epidemiology of AGF is unknown.

Management
The aim of treatment in AGF is the normalization of blood ethanol levels. Dietary restriction of fermentable simple sugars, refined carbohydrates, yeast products and mordant foods has been widely practised with varying degrees of clinical improvement (1,3) although no consensus on any ideal or precise dietary regimen has been achieved.

A concurrent course of antifungal drugs (e.g. Nystatin, Amphotericin) is recommended. In addition to a primary action inhibiting yeast fermentation, these drugs have been shown to stabilize cells in gut wall membranes which may reduce gut permeability, a condition associated with AGF (1). Management with antifungal drugs must be approached with caution because of the association of at least one preparation (ketoconazole) with irreversible liver damage (13).

Vitamin and mineral supplements may be necessary due to micronutrient malabsorption (10). Pancreatic enzymes have been used in past treatments of AGF, but the use of enzyme preparations should depend upon lab assessment of any enzyme deficiencies (1). Lactobacillus casei strain GG may also be of benefit in AGF by reversing intestinal permeability (14).

The bizarre behavior of Client 1 significantly lessened in frequency and intensity when processed sugars were removed from his diet. Initially Client 2 followed a reduced sugar (monosaccharides, disaccharides and "simple" starches) diet and found that her symptoms subsided. Unfortunately, she was overwhelmed with her craving for sweets and did not adhere to the recommended diet. Client 3 was advised to restrict fermentable sugars and starches. After following a strict diet for several months, she reported that her symptoms had improved and she was experiencing "less brain fog". However, "slipping off the diet" caused a return of her intense craving for sweets and associated abdominal and mental dysfunction.

Abnormal gut fermentation compared to food intolerance

Due to similar clinical presentations of AGF and food intolerance, a patient suspected of sugar, starch, yeast and/or cheese intolerance may actually be affected by AGF (11). However, AGF and food intolerance may co-exist in the same patient and are not mutually exclusive conditions. There may be a complex link between AGF and food intolerance, leading to a progression from one condition to the other. Sugar craving appears to be more in AGF than food intolerance which may be related to the fermentation products of sugar rather than sugar itself, comparable to the alcohol addiction in alcoholics (11). Differences between AGF and food intolerance are outlined in Table 2.

Conclusion
There is a scarcity of information on AGF with most references originating from a small group of researchers. This apparent lack of recognition of AGF may be due to the ill-defined symptom complex and clinical overlap with other conditions. More research is needed to answer further questions on etiology, definitive symptoms, diagnostic procedures and management. Documentation of cases would support efforts in this direction with comparison taken before and after treatment.

Examination of gut tissue through small bowel biopsy or microbiological studies might reveal possible AGF location and extent of fermentation activity. Finally, nutritional deficiencies associated with AGF need to be closely monitored to measure their impact on the satisfactory progression of management strategies.

References

TABLE 2

<table>
<thead>
<tr>
<th>Differences between abnormal gut fermentation and food intolerance'</th>
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<tbody>
<tr>
<td>Abnormal Gut Fermentation</td>
</tr>
<tr>
<td>may respond to allo-antigenic diet (no fermentable foods)</td>
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<tr>
<td>may respond to antifungal drugs</td>
</tr>
<tr>
<td>production of ethanol may respond to elimination and challenge diet</td>
</tr>
</tbody>
</table>

*compilied from Eaton 1994 (4); Eaton 1995 (8).*
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