MEDICAL NUTRITION THERAPY FOR HUMAN GASTROINTESTINAL DISORDERS AND APPLICATION TO CAPTIVE NON-HUMAN PRIMATES

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Abstract
Abnormal gastrointestinal function is considered to be a common problem among captive non-human primates. Certain nutrients and diet patterns are implicated in abnormal gastrointestinal function and disease. The human nutrition field uses medical nutrition therapies to prevent and/or manage a variety of gastrointestinal disorders. Some of these may be appropriate for application to non-human primates. Current evidence-based nutrition interventions for gastrointestinal disorders in humans are reviewed, and application to captive non-human primates discussed.

Introduction
Abnormal gastrointestinal (GI) function, ranging from chronic loose stool to diagnosed diseases, is considered a common problem among captive non-human primates. Chronic diarrhea is one of the issues most often reported in literature for many species of apes and monkeys, usually due to an infectious agent, but sometimes of no identifiable etiology (Lewis and Colgin, 2005; Munson and Montali, 1990; Rubio and Hubbard, 2002). For example, diarrhea was found to be the primary diagnosis for 32.5% of the clinical caseload at the Oregon National Primate Research Center (Wilk et al., 2008). Colitis is also a frequent post-mortem finding in animals with non-infectious diarrhea (Lowenstine and Rideout, 2004).

Diet and nutrition are fundamental to gastrointestinal health and function. Plant fiber, for example, positively impacts satiety, fecal consistency and overall GI health in primates (Cummings, 1978; Morin et al 1978; NRC, 2003). Dietary modifications may benefit primates when inappropriate diets are suspected as causal factors in GI abnormalities, although improvements are sometimes inconsistent (Janssen, 1994; Plowman, 2013). In humans, various medical nutrition therapies are used to prevent and manage GI disorders (AND, 2014; Dore et al., 2008; Eiden, 2003; Nahikian-Nelms et al., 2011; Stephen and Gyr, 2004). Some of these therapies may be appropriate or translatable to captive non-human primates with similar GI symptoms or conditions.

Medical Nutrition Therapy (MNT) for Human Gastrointestinal Disorders
Irritable Bowel Syndrome (IBS)
IBS is a chronic functional disorder of the gastrointestinal tract that commonly presents as cramping, abdominal pain, bloating, gas, diarrhea and constipation (Nahikian-Nelms et al., 2011). The most current nutrition therapy for IBS includes individualization along with:

- Low-FODMAP diet (fermentable oligo-,di-, and monosaccharides and polyols) (Ong et al., 2010; Heizer et al., 2009; Shepherd et al., 2008)
- Fiber intake based on tolerance and IBS type (AND, 2014)
- Elimination diet to identify food triggers
- Vitamin/mineral supplementation for suspected deficiencies

- Consideration of pre- and probiotics (Clark et al., 2012)
- Consideration of peppermint oil (Ford et al., 2008)

Inflammatory Bowel Disease (IBD)

IBD, which includes Crohn's Disease and Ulcerative Colitis (UC), involves chronic inflammation (often including ulcerations) in all or part of the intestinal tract, and presents with symptoms such as severe diarrhea, pain, fatigue, and weight loss (Eiden, 2003; Graham and Kandil, 2002). Nutrition therapy differs based on whether the disease is active or in remission.

<u>During active flare-up/exacerbation:</u>

- Bowel rest if needed; supportive nutrition (e.g. enteral or parenteral feeding) may be appropriate
- Progress to low-fat, low-fiber, high-protein, high-calorie, small, frequent meals with return to normal diet as tolerated
- Vitamin/mineral supplementation as needed to correct deficiencies or malabsorption

<u>During remission:</u>

- No particular diet is known to maintain IBD in remission; a normal "diet as tolerated" remains recommended (maintenance diet should strive to meet nutrient needs and support maintenance of a healthy weight) (Eiden, 2003)
- Avoid foods high in oxalate with Crohn's disease (AND, 2014)
- Consider supplementation with n-3 fatty acids and glutamine (Eiden, 2003)
- Consider use of pre- and probiotics (Gassull, 2005; Guarner, 2005)

Celiac Disease (Gluten allergy)/Gluten Intolerance

The only effective therapy for true gluten allergy is a strict gluten-free diet (Fasano and Catassi, 2001). For those suspecting or diagnosed with the less well-defined gluten intolerance, avoidance or minimization of gluten in the diet may provide relief, however, more recent research suggests this population may actually be intolerant to certain FODMAPs, as in IBS (Biesiekierski et al., 2013). Wheat contains both the protein gluten and the carbohydrate fructan, and the latter may be responsible for the symptoms attributed to gluten.

Diverticular Disease

Diverticular disease is characterized by the formation of tiny pockets, called diverticula, in the lining of the large intestine (colon), and includes diverticulosis, diverticular bleeding, and diverticulitis (Nahikian-Nelms et al., 2011). Nutrition therapy differs for diverticulosis and active diverticulitis.

<u>Diverticulosis:</u>

- High-fiber diet (≥16-17 g/1000 kcals/d) (gradual increase to ensure tolerance) (Makola, 2007)
- Avoidance of nuts, seeds, and hulls no longer considered necessary (Strate et al., 2008)
- Consider probiotics (Douglas, 2008)
- Adequate fluid intake in conjunction with high-fiber diet

Diverticulitis:

- Bowel rest (NPO) until bleeding and diarrhea resolve
- Begin oral intake with clear liquids, and slowly advance to low-fiber diet until inflammation and bleeding have fully resolved; then gradually return to high-fiber diet
- Consider probiotics

Gastroesophageal Reflux Disease (GERD) and Peptic Ulcer Disease (PUD)

GERD is a chronic disease in which stomach acid (or occasionally stomach contents) flows back into the esophagus, thereby irritating the lining of the esophagus and causing symptoms such as reflux or heartburn, and over time can cause damage to the esophagus. PUD involves an imbalance in digestive fluids in the stomach and small intestine that result in painful ulcers or sores in the lining of the stomach or duodenum (Shapiro et al., 2007). While the cause of both conditions can vary, dietary factors are often implicated, and the recommended nutritional therapy is similar for both (Dore et al., 2007; Shapiro et al., 2007):

- Avoid foods that can increase gastric acid secretion or damage the gastric mucosa (black and red pepper, coffee, tea, alcohol)
- Smaller, more-frequent meal pattern
- Eliminate/minimize foods that reduce lower esophageal sphincter pressure (chocolate, mint, high-fat foods)
- Lose weight if overweight
- Avoid eating 2-3 hours before bedtime
- Sit upright after meals

Constipation

Constipation is defined as infrequent and/or difficult bowel movements. While normal bowel movement frequency and consistency varies from person to person, a period of more than 3 days between bowel movements is considered abnormal, as is straining during a bowel movement or passing a hard bowel movement more than 25% of the time (Ternant et al., 2007). Nutrition therapy for constipation aims to improve the frequency of bowel movements and prevent straining during a bowel movement, using the following strategies:

- High-fiber diet (gradual increase to ≥25-38 g/d or 14 g/1000 kcals/d) (Ternant et al., 2007)
    - Insoluble fibers (found in whole grains and vegetables) appear to have the greatest effect on resolving constipation, but there is no definitive evidence of ideal fiber type(s); individuals are recommended to try different fiber formulations to find which work best for them (AND, 2014)
- Adequate fluid intake (≥64 oz/day)
- Regular physical activity
- Consider use of bulk-forming agents such as psyllium or methylcellulose (AND, 2014)
- Consider pre- and probiotic-containing foods as part of daily diet (AND, 2014)

Diarrhea

Diarrhea is characterized by loose and watery bowel movements, and can range in severity from acute and benign to chronic or indicative of serious disease, depending on the cause. Treatment

of the underlying cause is the most important aspect of diarrhea therapy. Nutrition therapy for diarrhea should aim to achieve the following:

- Restore normal fluid, electrolyte, and acid-base balance first (Guerrant et al., 2001)
- Reduce gastrointestinal motility
  - Avoid foods/beverages high in simple carbohydrates and sugar alcohols (AND, 2014)
  - Avoid high-fiber and gas-producing foods (AND, 2014)
- Improve stool consistency
  - Consider adding sources of pectin such as banana flakes to foods (Duro and Duggan, 2007)
  - Consider trial of coconut flakes or oil (Graedon and Graedon, 1999)
- Repopulate gastrointestinal tract with healthy microflora
  - Probiotic/prebiotic supplementation may assist with treatment and recovery but current research does not substantiate dosage recommendations (Canani et al., 2007; Douglas and Sanders, 2008)
- Stimulate the GI tract with slow introduction of solid food without worsening of symptoms
  - Low-fiber, low-fat, lactose-free foods recommended initially (Duro and Duggan, 2007; Steffen and Gyr, 2004)

Considerations in Application to Non-Human Primates

The aforementioned medical nutrition therapies (MNTs) have fair to strong evidence basis for use in humans (AND, 2014). Given the physiological similarities between many species of non-human primates (NHPs) and humans, and the similar nature of GI disorders observed in both, it may be appropriate to apply these therapies to NHPs in some instances. Before application, however, it is necessary to consider several factors. Each species' feeding ecology and digestive physiology should always be considered. Humans are omnivorous with a relatively simple GI tract, therefore certain nutritional therapies may not be appropriate for NHP species with different digestive strategies, such as foregut-fermenting colobines or hindgut-fermenting howlers (Bauchop and Martucci, 1968; Milton and McBee, 1983; Stevens and Hume, 1995). These highly folivorous primates need to maintain higher levels of plant fiber while minimizing readily fermentable carbohydrates for normal microbial fermentation and GI function (Edwards and Ullrey, 1999). The consequences of inappropriate diets for these species are reported in literature (Bauchop and Martucci, 1968; Janssen, 1994).

Another consideration is the common use of nutritionally-complete feeds in the diets of many captive NHPs. These items may contain ingredients commonly nontolerated by humans with certain GI disorders (e.g. wheat, soy, fructose, fibers), so it is possible these same ingredients may not be tolerated by individual NHPs with similar GI issues. If these fortified diet items are removed as part of therapy, the diet will need to be reassessed to ensure nutritional adequacy. Replacing nutritionally-complete feeds is a challenge in NHPs because there are fewer food groups/substitutions considered appropriate for NHPs from which to choose to meet nutrient needs compared to humans, and natural items (e.g. browse) often are not sufficiently available to supply key nutrients like protein and fiber.

Food preferences of individual animals also may complicate application of nutritional therapies. Animals with limited preferences may not accept replacement diet items or other modifications (e.g. will not consume more high-fiber leafy vegetables). Such animals may also resist novel ingredients like resistant starch and probiotics either mixed into diet items or as stand-alone supplements.

Yet another challenge is the potential difficulty monitoring and evaluating a therapy for efficacy in captive NHPs. This includes an inability to monitor an individual's response if maintained in a group setting (e.g. identifying one animal's stool from that of others), and the presence of confounding factors like stress, infection, and medications that may disguise or counteract any benefit the therapy is providing.

Some non-human primates are also prone to certain GI-related behaviors not seen in humans, for which human MNT may or may not be relevant. One common example is the regurgitation/reingestion behavior most commonly reported in captive gorillas and other apes. This behavior is observed only in captivity, and has been attributed mostly to stress and boredom, but also to certain diet items (Akers and Schildkraut, 1985; Baker and Easley, 1996). Recent research, however, suggests this behavior could also be related to GERD, but may not be recognized as such due to the difficulty diagnosing GERD in NHPs (Glover et al., 2008).

Finally, in deciding whether to apply human MNT for GI disorders or symptoms in NHPs, non-nutrition-related causes for symptoms should be considered. Behavioral dynamics and stress can have significant effects on stool quality and other GI symptoms, as has been documented in NHPs living in group situations (Wilk et al., 2008). Infection should be ruled out as a treatable source of GI dysfunction and dysbiosis. Recently, there is also a growing recognition of the role of obesity in gastrointestinal health and function, warranting consideration of an animal's weight or body condition status as a factor in any GI symptoms or disorders (Clemente et al., 2012; Moayyedi, 2008). These factors are important to recognize because the GI symptoms and conditions described above can occur in the context of an appropriate diet. Assessment of the complete clinical, nutritional, and behavioral situation is needed to properly apply human MNT to non-human primates.

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