GASTROINTESTINAL ASSESSMENT AND MANAGEMENT PROCEDURES FOR EXERCISE-ASSOCIATED GASTROINTESTINAL SYMPTOMS

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INTRODUCTION

Incidence of exercise-associated gastrointestinal symptoms (Ex-GIS) are a common occurrence in many athlete populations. Ex-GIS are reported ≤10% in strength and power sports, team sports, and shorter duration (<2h) endurance exercise; whilst ultra-endurance sports consistently reports Ex-GIS incidence of ≥60%[1]. The type of Ex-GIS experienced can range from upper (i.e., regurgitation, urge to regurgitate, gastric bloating, belching, upper abdominal pain, and gastric acidosis), lower (i.e., flatulence, lower abdominal bloating and pain, urge to defecate, defecation with or without abnormalities (e.g., diarrhoea and/or faecal blood loss)), and other related symptoms (i.e., nausea, and acute transient abdominal pain) [2]. While the severity of Ex-GIS can vary from minor gut discomfort to severe symptoms that negatively impact on exercise performance through reducing workload and/or cessation of exercise[1]. The underlying pathophysiology of Ex-GIS has been thoroughly reviewed by Costa et al.[1,3], and appear to be explained by exercise-induced gastrointestinal syndrome (EIGS), with the two primary causal models: the circulatory-gastrointestinal and the neuroendocrine-gastrointestinal pathways (Figure 1). Clinical implications have been reported with respect to EIGS (e.g., acute reversible colitis)[4,5], including potential for fatality (e.g., septic shock) associated with systemic endotoxemia and responsive cytokinemia of the circulatory-gastrointestinal pathway[6-8]. More recently, concerns have been raised regarding the role of the neuroendocrine-gastrointestinal pathway of EIGS in promoting gastroparesis with or without paralytic ileus during exercise, which appears to be a potent factor of acute onset Ex-GIS[9,10]. For example, substantial anecdotal evidence from ultra-endurance athletes suggest rapid onset of Ex-GIS ~4 h into exercise stress (i.e., running and/or cycling), with accumulating laboratory research showing compromised gastrointestinal function (e.g., motility, digestion and/or absorption) and attempting to feed on a compromised gastrointestinal tract, are the main culprits in Ex-GIS[9-15]. Conversely, substantial injury and/or dysfunction to the intestinal epithelial with accompanying systemic endotoxemia and cytokinemia appears to not necessarily translate into Ex-GIS incidence and severity of clinical or performance significance[10,11,16,17].

It is now well established that in order to perturb gastrointestinal integrity and function, invoke a systemic inflammatory response to lumen originated bacterial

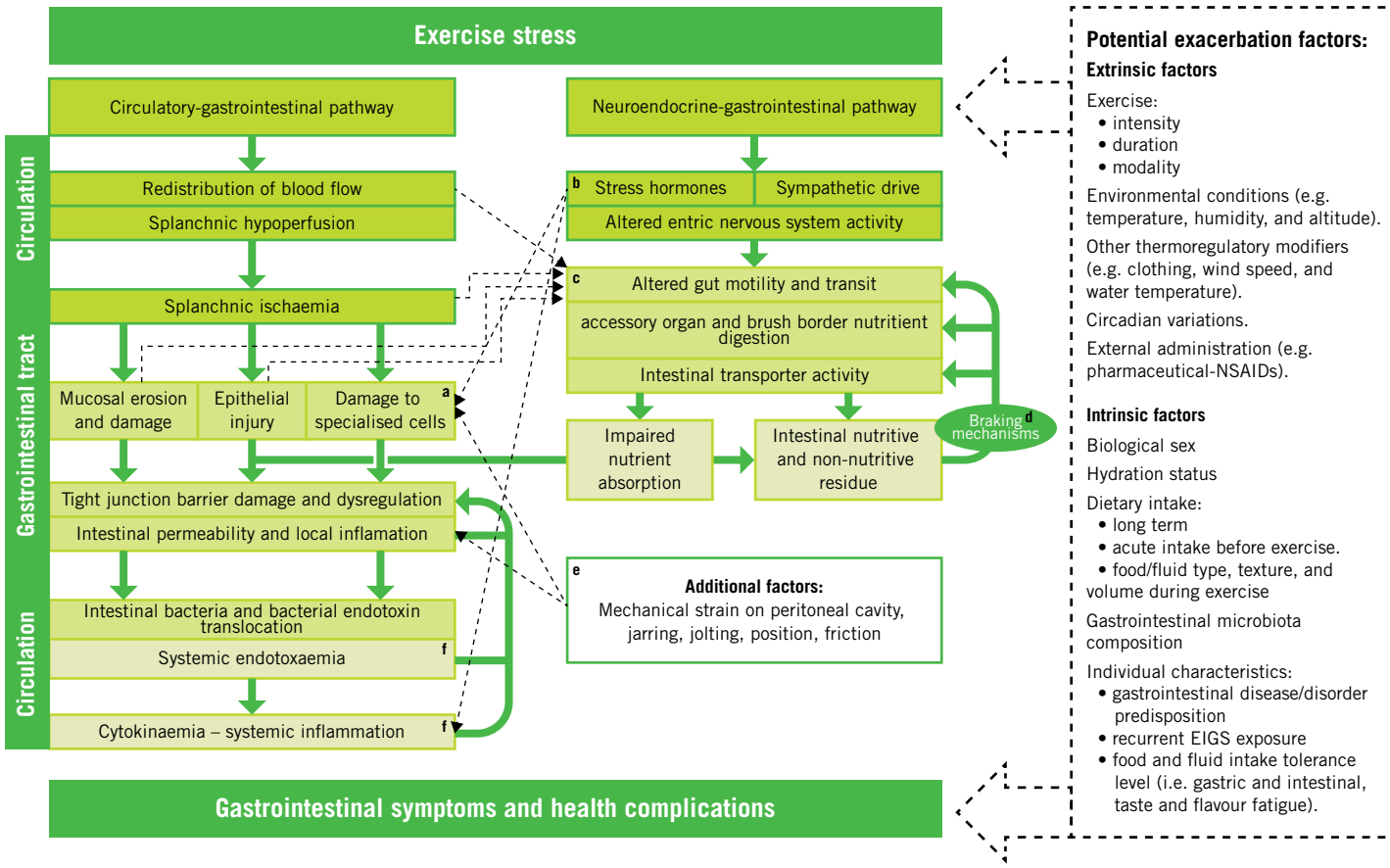


Figure 1: Schematic description of 'exercise-induced gastrointestinal syndrome' (EIGS) including the 'circulatory-gastrointestinal' and 'neuroendocrine-gastrointestinal' pathways, potential mechanical instigators, extrinsic and intrinsic exacerbation factors. Adapted with permission from "Systematic Review: Exercise-Induced Gastrointestinal Syndrome-Implications for Health and Disease," by Costa et al, 2017, Alimentary Pharmacology and Therapeutics, 46, pp. 246–265.

[a] Specialized antimicrobial protein-secreting (i.e., Paneth cells) and mucus-producing (goblet cells) cells, aid in preventing intestinal-originating pathogenic microorganisms gaining entry into systemic circulation. [b] Splanchnic hypoperfusion and subsequent intestinal ischemia and injury (including mucosal erosion) results from stress induced direct (e.g., enteric nervous system, and/or enteroendocrine cell) or indirect (e.g. braking mechanisms) alterations to gastrointestinal motility. [c] Increase in neuroendocrine activation and suppressed submucosal and myenteric plexus result in epithelial cell loss and subsequent perturbed tight junctions[18]. [d] Gastrointestinal brake mechanisms: Nutritive and nonnutritive residue along the small intestine, and inclusive of terminal ileum, results in neural and enteroendocrine negative feedback to gastric activity[13,19-22]. [e] Aggressive acute or low grade prolonged mechanical strain is proposed to contribute towards disturbances to epithelial integrity (i.e., epithelial cell injury and tight-junction dysregulation) and subsequent 'knock-on' effects into gastrointestinal functional responses[23]. [f] Bacteria and bacterial endotoxin microorganism molecular patterns (MAMPs) and stress induced danger associated molecular patters (DAMPs) are proposed to contribute towards the magnitude of systemic immune responses (e.g., systemic inflammatory profile)[24].

endotoxin translocation, and generate severe Ex-GIS of clinical significance (i.e., values consistent with gastrointestinal inflammatory or functional diseases/disorders) or limiting performance, a minimum threshold of exercise stress is warranted. This has previously been confirmed as ≥2 h at 60% $VO2_{max}$ in ≥35.0°C ambient temperature or ≥3 h at 60% $VO2_{max}$ in temperate conditions in laboratory-controlled studies[2,9-17], and ultra-endurance competition in field studies[25-28]. Exercise stress below this threshold appears inadequate in presenting clinical or performance implications in a variety of athlete populations (i.e., team, strength and power, endurance, and ultra-endurance sports)[1,3]. Alongside exercise intensity, duration and ambient conditions, there are several other extrinsic (i.e., modality, altitude, thermoregulatory modifiers, circadian variation, and pharmaceutical administration (e.g., NSAIDs)) and intrinsic (i.e., biological sex, hydration status, dietary intake, feeding tolerance, predisposition, and gut microbiota composition) factors that determine the incidence, type, and severity of Ex-GIS as a result of EIGS' dynamic and interrelated pathways (Figure 1). In addition, various assessment and analysis techniques have been explored for their validity and reliability in determining the magnitude of exercise-associated perturbations to gastrointestinal integrity, function, and systemic responses linked to the primary causal pathways and secondary outcomes of EIGS. Potential assessment and analysis methods that may be adapted to an athlete's individualised gastrointestinal assessment are depicted in Figure 2.

It is now clearly reported in the scientific literature that Ex-GIS is multi-factorial in

nature[1,3,29]. Therefore, it seems logical that prevention and management strategies are best approached through individual assessment, identification, and intervention implementation. To date, there have been a substantial number of studies investigating prevention and management for EIGS and associated Ex-GIS. These include, but not limited to gut training[11], cooling and heat acclimation strategies[30-32], hydration status[9], carbohydrate feeding[33], low fermentable oligo- di- mono- saccharide and polyols (FODMAP)[15], a variety of carbohydrate formulations (i.e., multi-transportable sucrose-glucose-fructose mixtures, carbohydrate density, modified starch, carbohydrate-protein co-ingestion, carbohydrate texture (e.g., solid vs. semi-solid vs. liquid), glucose polymers, etc.)[33-40], and acute or prolonged nutritional supplementation (i.e., probiotic, amino acids (e.g., glutamine, arginine, citrulline, glycine, and tyrosine), bovine colostrum, anti-oxidants, curcumin, nitrate, etc.)[3]. Research outcomes have shown a wide magnitude of positive, neutral, and negative outcomes with these diverse strategies; and are likely associated with, but not limited to, differences in exercise stress models, experimental design and confounder control, sample collection and analysis, and populations. From a translational and professional practice perspective, within such research, a large individual variation is observed and reported that suggests blanket prevention and management strategies may not work for all athletes suffering from Ex-GIS as a result of EIGS.

Considering the dynamic multifaceted and multilayers of EIGS (e.g., circulatory-gastrointestinal pathway, neuroendocrine-gastrointestinal pathway, mechanical instigators, extrinsic and intrinsic exacerbation factors), establishing the causal and exacerbation factor(s) for a particular Ex-GIS is difficult without an individual tailored exercise gastrointestinal assessment. In this article we present and discuss a suggested approach to the assessment and management of EIGS and Ex-GIS, and provide some reference examples.

EIGS and Ex-GIS assessment and management procedures

EIGS and Ex-GIS assessment and management procedures are depicted in Figure 3 and consist of 4 distinct phases:

Phase 1: Clinical assessment of the athlete gathering specific details about their Ex-GIS. This should include athlete characteristics, the symptom description (e.g., type, severity, timing of onset), and situation that prompted the Ex-GIS (e.g., modality, environmental conditions, pre- and during- exercise feeding and drinking habits, etc.) (Case Example).

Phase 2: Gastrointestinal assessment during exercise (GastroAxEx), in which an

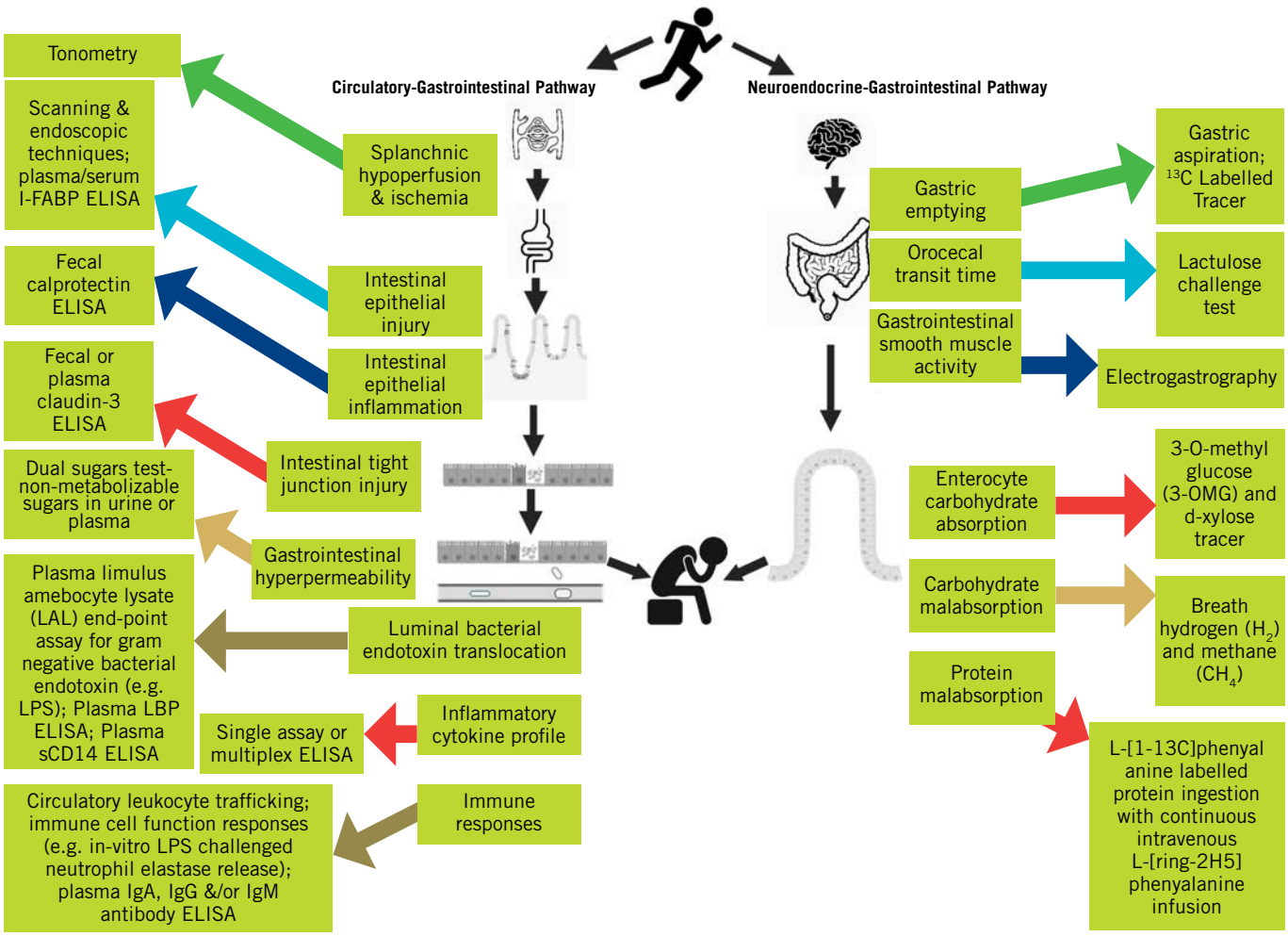


Figure 2: Schematic illustration of the available assessment and analysis technique to determine the magnitude of exercise-associated perturbations to gastrointestinal integrity, function, and systemic responses.

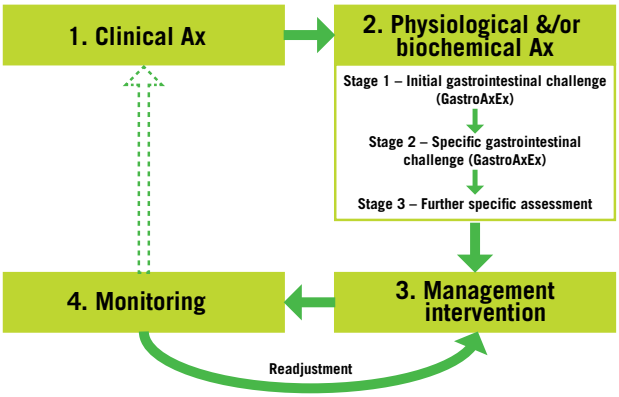
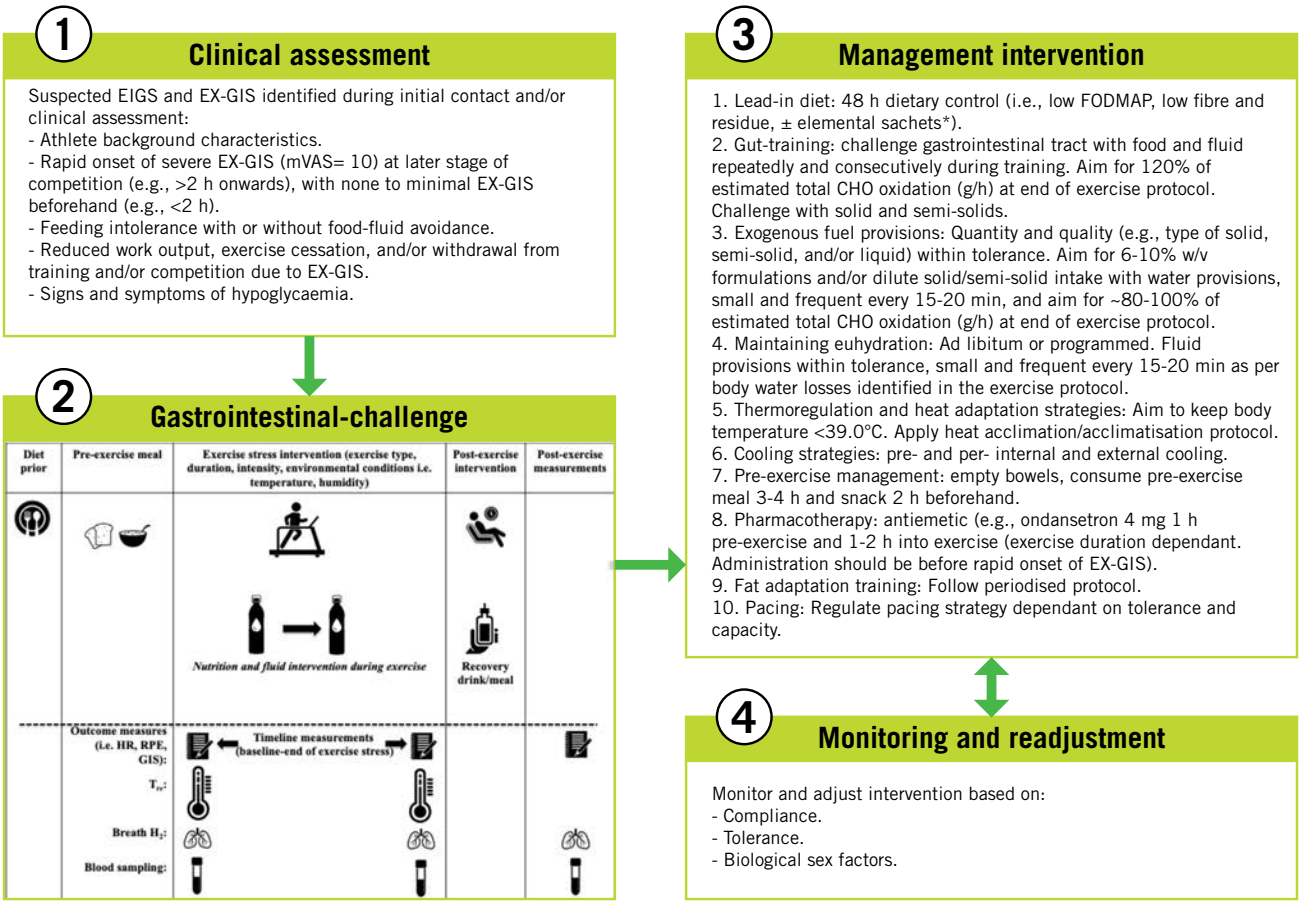


Figure 3: Four-phase EIGS and Ex-GIS assessment and management procedures. Elemental sachets: carbohydrate (CHO)= 60 g, protein (Pro)= 20 g, Energy= 325 kcal, Fat= 0 g, Fibre <1 g, FODMAP: <1 g. Ax=assessment, GastroAxEx=gastrointestinal assessment during exercise, GIS=gastrointestinal symptoms, HR=heart rate, RPE=rating of perceived exertion, TCR=thermal comfort rating, T_{re}=rectal temperature. Intervention based on original research providing evidence of positive outcomes, and avoiding those showing evidence of neutral to negative outcomes, on markers of EIGS (e.g., functional, integrity, and systemic markers) and Ex-GIS[1,3].



Case example

Biological Sex	*Age (y)*	*Anthropometry*	*Modality & training volume (h/week)*	*Dietary Practice*	*Presenting Ex-GIS*:*
Male	*31 y*	*Ht: 191 cm* *NBM: 75.1 kg* *BFM: 14.6 %*	*Amateur endurance and ultra-endurance trail runner.* *8 h*	*Vegan*	*3-5 h into racing experiences extremely severe stomach pain, this escalates to nausea and projectile vomiting. Over next 6 h period projectile vomiting 3-4 times. Unable to tolerate feeding and drinking at this time.*

Case Example Part 1: BFM: Body fat mass, Ex-GIS: exercise-associated gastrointestinal symptoms, Ht=height, NBM=nude body mass.

* Extreme Ex-GIS as determined by the modified visual analogue scale (mVAS)[2].

Case example for Stage 1 and 2

Exercise stress model		During exercise nutrition	
Mode	Running	Feeding During	20 g/h CHO for first 2h Sports confectionery, glucose tablets, and confectionery,
Start time of exercise	0900 h		
Duration (min)	180		
Intensity (km/h)	11.0-11.5		
T_{amb} (°C)	30	Water (ml/h)	174
RH (%)	29	(CHO % w/v)	11
RPE	13 (13-14)	(body water losses; L)	3.0
TC	10 (9-11)		
HR (bpm)	150 (138-162)		
T_{re} (°C)	37.6 (36.3-38.9)		
Physiological parameters		**Immune parameters**	
Plasma osmolality (mOsmol/kg)		Leukocytes ($x10^9$)	
Pre-ex	301	Pre-ex	4.6
Post-ex	304	Post-ex	9.5
		1 h post-ex	12.0
TBW (L (%))			
Pre-ex	46.9 (62)	Neutrophils ($x10^9$)	
		Pre-ex	2.6
ECW (L/%)		Post-ex	6.1
Pre-ex	19.2 (25)	1h post-ex	8.7
BML (%)	4.0	Lymphocytes ($x10^9$)	
		Pre-ex	1.6
BGL (mmol/L)		Post-ex	3.0
Pre-ex	5.5	1 h post-ex	2.7
Post -ex	6.4		
		Monocytes ($x10^9$)	
Oxidation rates		Pre-ex	0.3
Steady State		Post-ex	0.4
CHO (g/min)	1.6	1 h post-ex	0.6
Fat (g/min)	0.9		
		Neutrophil: lymphocyte ratio	
Oxidation rates		Pre-ex	1.6
Final measurement		Post-ex	2.0
CHO (g/min)	1.4	1 h post-ex	3.2
Fat (g/min)	0.9		
EIGS parameters		**Inflammatory cytokine parameters**	
Cortisol (nMol/L)			
Pre-ex	424	IL-β (pg/ml)	
Post-ex	1176	Pre-ex	0.8
		Post-ex	0.4
I-FABP (pg/ml)			
Pre-ex	1581	TNF-a (pg/ml)	
Post-ex	884	Pre-ex	15.7
		Post-ex	21.2
Claudin (ng/ml)			
Pre-ex	21.2		
Post-ex	16.3	IL-6 (pg/ml)	
		Pre-ex	33.5
sCD14 (ug/ml)		Post-ex	39.3
Pre-ex	2.5		
Post-ex	2.6	IL-8 (pg/ml)	
		Pre-ex	13.1
LBP (ug/ml)		Post-ex	19.8
Pre-ex	12.0		
Post-ex	12.6	IL-10 (pg/ml)	
		Pre-ex	22.0
OCTT (min)	90#	Post-ex	112.7
Gut Discomfort	13 (0-6)*	IL-ra (pg/ml)	
Total GIS	21 (0-14)*	Pre-ex	52.0
Upper GIS	0 (0)*	Post-ex	77.0
Lower GIS	13 (0-6)*		
Nausea	6 (0-6)*	SIR-P	133

Case example for Stage 1 and 2: BGL=blood glucose level, BML=body mass loss, CHO=carbohydrate, ECW=extracellular water, ex=exercise, HR=heart rate, OCTT=orocecal transit time, T_{amb}=ambient temperature, RH=relative humidity, RPE=rating of perceived exertion, TC=thermal comfort rating, T_{re}=rectal temperature, w/v=water volume equivalent, TBW=total body water, SIR-P=systemic inflammatory cytokine profile.

OCTT methodology[10], * modified visual analogue scale (mVAS)[2].

individual tailored laboratory-controlled simulation is designed and conducted. The design of the athlete specific GastroAxEx needs to take into consideration the modality, exercise intensity and duration, environmental temperature, routine race/event nutrition preparation (i.e., 24-48 h prior to event), and during race/event nutrition. In addition, the magnitude of exercise stress needs to be in accordance with previous published research reporting exercise-associated gastrointestinal disturbance of relative performance and clinical significance[9-11,15-17,30,33]. Appropriate gastrointestinal and physiological assessment markers need to be justified for determination based on individual clinical assessment from Phase 1.

Within Phase 2, there are three stages of real-time clinical, physiological and/or biochemical assessment.

• *Stage 1:* Initial GastroAxEx that includes the exercise stress with or without heat stress, simulation and gastrointestinal challenge of race nutrition, breath sampling to determine malabsorption of nutrients common in sports nutrition formulation and race nutrition, GIS and feeding tolerance assessment tool applied (i.e., pre-, during-, and post-exercise) in real-time, and also standard physiological and thermoregulatory strain markers measured (i.e., pre-, during-, and post-exercise) in real time.

• *Stage 2:* Includes further specialised assessment if deemed necessary that may include, but not limited to orocecal transit time (OCTT), specific food (i.e., volume, nutrient density, type, and/or texture) challenge, blood markers for detecting gastrointestinal epithelial perturbations such as plasma I-FABP, systemic endotoxin and/or inflammatory cytokine profiles, and/or immune responses.

• Stage 3: Involves more advanced or specific assessment, such as further specific food challenge(s), food allergens, food chemicals, luminal and/or systemic bacterial composition and/or short chain fatty acid concentrations, gastrointestinal microorganism infection (e.g., parasite or fungal determination) testing carried out by the relevant qualified medical or health professionals.

Phase 3: Intervention phase, which is based on the outcomes of the GastroAxEx from Phase 2, and should consist of specified aims, such as, but not limited to: 1) reduce pre-

Case example

Observations from GastroAxEx and proposed EIGS and Ex-GIS causal and exacerbation factors	*Therapeutic intervention and progress outcomes*
• *3 h into exercise: severe nausea (mVAS= 6); mild dizziness (mVAS= 2).* • *75 min post-ex: severe nausea (mVAS= 8) and severe urge to regurgitate (mVAS= 8).* • *Substantial post-exercise hypohydration (BML 4.0%) despite ad libitum fluid intake and carbohydrate provisions.* • *Peak T_{re} 39.3°C.* • *Low during ex CHO feeding (20 g/h for first 2 h).* • *Substantial post-ex cortisol response (+177%).* • *Slow OCTT response (90 min).* ***Neuroendocrine-gastrointestinal pathway predominance.***	*Strategies targeted at:* • *Reduce total gastric load leading into event.* • *Enter race with sufficient carbohydrate stores.* • *Increase carbohydrate provisions during exercise.* • *Better match fluid needs.* • *Implement thermoregulation strategies.* • *Pharmacotherapy strategy.* ***Action plan :*** ***Implemented intervention strategies****- 1, 2, 3, 4, 5, 6, 7 and 8 (Figure 3, Phase 3).* ***Additional comments:*** *Moderate-high carbohydrate lead-in diet.* *Outcome(s):* • *Due to injury and coronavirus pandemic not fully implemented and not tested in running competitions. However, completed multi-day endurance runs/hikes/mountain biking using intervention.* • *Become more consistent with during nutrition feeding (i.e., consuming carbohydrate early into sessions and more frequently in long training sessions), in which athlete reports improved gut comfort, and subsequent reduced Ex-GIS during prolonged endurance exercise.*

Case example 2: Assessment outcomes and informed management intervention. BML=body mass loss, CHO=carbohydrate, ex=exercise, mVAS=modified visual analogue scale, OCTT=orocecal transit time, T_{re}=rectal temperature.

exercise food and fluid gastrointestinal load and/or burden; 2) maintain gastrointestinal patency during exercise stress; and 3) ameliorate physiological strain to exercise stress (e.g., thermal strain and euhydration maintenance). All intervention procedures (Figure 2) are proposed to be practised in training and/or less important events, prior to using in targeted events. Based on the current understanding of effective, and not so effective, prevention and management strategies for EIGS and Ex-GIS, intervention may include the following: 48-h dietary control (i.e., low fermentable oligo-di-mono-saccharide and polyols (FODMAP), fibre and residue intake) +/- elemental sachets[15], gut-training[11,13], exogenous fuel provision within tolerance[11,13], hydration provision within tolerance[9], thermoregulation targeted and heat acclimation/acclimatisation strategies[41], pre- and/or per- internal and/or external cooling strategies[3], pre-exercise dietary management[15], pharmacotherapy application (i.e., ondansetron with medical collaboration and prescription, and NSAID avoidance)[42,43], fat adapt training and pacing strategies[44], and also taking into account the biological sex of the athlete[45].

Phase 4: Monitoring and readjustment of intervention, which includes checking the athlete is healthy leading into intervention, has followed the dietary intervention, menstrual status in female athletes[45], gut-training compliance, tolerance to food and fluid intake during exercise, tolerance and compliance with the thermal strain targeted strategy. In addition, measuring and recording Ex-GIS, physiological variables, and environmental conditions in training/racing where possible, checking other possible triggers (e.g., nutritional supplementation and anti-inflammatory medication). Further gastrointestinal assessment at rest and during exercise may be warranted if Ex-GIS persist (i.e., medical procedures for gastrointestinal disease/disorder diagnosis, gut microbiota composition, luminal pathogenic assessment (e.g., fungal, bacterial, parasitic, and/or allergen), specific food allergen or intolerance)[1,46,47].

What each phase of EIGS and Ex-GIS assessment and management procedure tells you?

In this article we present and discuss a suggested approach to the assessment and management of EIGS and Ex-GIS using a four-phase approach: 1) clinically assess athletes for EIGS and Ex-GIS using retrospective exploration; 2) to provide a GastroAxEx using valid and reliable gastrointestinal assessment tools; 3) implement an individualised EIGS and EX-GIS prevention and management therapeutic intervention informed by the GastroAxEx; and 4) assess outcomes of the therapeutic intervention in training and competition, and adjust accordingly. Using the case example given, the four-phase approach shows that a tailored GastroAxEx based on background characteristics and clinical assessment provided sufficient data to inform individualised therapeutic intervention, and subsequently reduced Ex-GIS in proceeding endurance and ultra-endurance activities. With repeated application of GastroAxEx in the clinical setting, from a translational research and practical perspective, it is now becoming apparent that no substantial disturbance is observed in the circulatory-gastrointestinal pathway of EIGS in the majority of cases, including gastrointestinal integrity and systemic endotoxin and immune markers. Conversely, disturbance

to the neuroendocrine-gastrointestinal pathway of EIGS (e.g., pronounced cortisol response and reduced OCTT) are common observations in athletes that undergo GastroAxEx and show severe Ex-GIS. These observations suggest gastrointestinal functional issues instigated by EIGS are likely culprits of Ex-GIS in the majority of athletes, and that targeting interventions to improve these debilitating gastrointestinal functional issues are likely to reduce the incidence and severity of Ex-GIS. Whilst prevention and management strategies targeting the circulatory-gastrointestinal pathway specifically (e.g., maintaining the integrity of the intestinal epithelium) are unlikely to resolve the Ex-GIS.

Each of the four-phases in supporting athletes presenting with Ex-GIS play a fundamental role in the prevention and management of EIGS and subsequent Ex-GIS. Phase 1 highlights the importance of a comprehensive clinical assessment of athletes presenting with EIGS and Ex-GIS in sports dietetic and/or sports medicine practice. Not all athletes present with the same Ex-GIS and/or experience Ex-GIS in the same exercise conditions (i.e., exercise stress, environmental conditions, and/or course topography), suggesting a dynamic and interactive relationship between primary causal mechanisms and exacerbation factors (i.e., extrinsic and intrinsic) with onset of Ex-GIS. For example, some athletes are prone to experience Ex-GIS in the heat, whereas others experience Ex-GIS in temperate ambient conditions. The onset of Ex-GIS in some athletes occur spontaneously and periodically along an endurance event, while in other athletes it occurs later into the event (>3 h) with rapid onset. In the latter case, it is common for athletes to report an inability to tolerate any food or fluid intake, and in some cases resulting in food and fluid avoidance for the remainder of the event/competition until completion or withdrawal. This scenario is supported by the scientific literature in which endurance and ultra-endurance athletes often report rapid and aggressive onset of Ex-GIS and inability to tolerate feeding when exercise duration is ≥3 h [29,48,49]. It is therefore important for practitioners to complete a clinical assessment in athletes presenting with EIGS, thoroughly looking at the exercise stress scenario, food and fluid intake around exercise, and background characteristics of each individual athlete. This information will be required to program the laboratory controlled GastroAxEx to best match the scenario resulting in Ex-GIS.

Phase 2 involves a laboratory controlled GastroAxEx, and it is essential that the assessment is individualised, since both laboratory and field research has demonstrated large individual variation in gastrointestinal integrity, function, and systemic markers that may impact on the incidence, type, and severity of Ex-GIS[6,7,9-13,15-17,30,33,46,50,51]. When designing and conducting the GastroAxEx, it is important to mimic the real-life scenario as close as possible that lead up to EIGS and Ex-GIS (i.e., replicate exercise stress, athletes should follow their typical lead-in race/event diet, pre-exercise meal and during exercise nutrition). This will then help identify the main causal and exacerbation factors of EIGS, and subsequent Ex-GIS, which will inform the individualised therapeutic intervention for the prevention and management of EIGS and Ex-GIS. For example, some athletes experience significant Ex-GIS and impaired gastrointestinal function during nocturnal compared to diurnal exercise, while other athletes are not affected[10]. In addition, there is large individual variability in tolerance to feeding nutrition during running[11,13], which therefore requires an individualised gut training approach in order to challenge individual tolerance levels. Such outcomes highlight the large individual variation in factors causing Ex-GIS in athletes and clearly show that the *'one size fits all'* approach is not appropriate. Therefore, practitioners should be cautioned against promotion of any one single prevention and/or management strategy claimed or marketed to prevent or attenuate markers of EIGS pathway perturbations and/or Ex-GIS. Such proposed singular strategies are notorious in the nutrition supplementation space targeting gut health in athletes (e.g., probiotic, amino acids (e.g., glutamine, arginine, citrulline, glyceine, and tyrosine), bovine colostrum, anti-oxidants, curcumin, nitrate, etc..), but do not have any effective role to play in EIGS and Ex-GIS therapeutic intervention due to the lack of research evidence efficacy, limited magnitude effect (i.e., positive effects of no clinical or performance significance or consequence), and substantial methodological limitation within research undertaken[1,3].

Phase 3 involves an individualised therapeutic intervention targeting

> ***The 'one size fits all' approach is not appropriate in Ex-GIS prevention strategies.***

EIGS. Considering the multifaceted and multilayers of EIGS and Ex-GIS, the therapeutic intervention needs to be targeted and individualised once the causal factor(s) for the GIS type(s) have been identified. For example, applying cooling strategies to an athlete presenting with EIGS who has shown no thermoregulatory strain during exercise appears irrelevant and potentially will be ineffective in managing their EIGS and Ex-GIS. Whereas, applying cooling strategies in athletes demonstrating poor thermoregulatory capacity (e.g., core body temperature reaching ≥39.0°C during exercise in temperate ambient conditions) would appear to be a targeted approach. Another example would be the administration of antiemetic pharmaceutical prescription for an athlete not presenting nausea, but presenting FODMAP intolerance, would potentially be ineffective, and therefore an inappropriate implementation strategy.

Nevertheless, considering the majority of athletes seeking professional support show neuroendocrine-gastrointestinal pathway associated EIGS and Ex-GIS from GastroAxEx outcomes (e.g., rapid onset Ex-GIS, delayed orocecal transit, carbohydrate malabsorption, and feeding intolerance during exercise), it seems logical to focus management attention to these causal factors. Whereas, targeting EIGS and Ex-GIS prevention and management strategies focused on the circulatory-gastrointestinal pathway (e.g., strategies promoting maintenance of splanchnic and villi microvascular perfusion, prevention of epithelial cell and tight-junction injury and dysfunction, and attenuation of luminal bacterial endotoxin translocation and associated inflammatory responses) would not be relevant and likely ineffective. Common therapeutic strategies currently used by athletes that have shown gastrointestinal functional improvements in laboratory research include short term (e.g., 24-28 h) low FODMAP, and reduced fibre and residue intake. These dietary strategies aim to reduce gastrointestinal load and reduce the risk of malabsorbed nutrients reaching the ileum potentially supressing gastrointestinal motility (i.e., reduction or cessation of gastric emptying and duodenal-jejunum motility) through braking mechanisms (e.g., ileal brake and gut hormones) potentially exacerbating Ex-GIS during exercise[11,13,15,19-22]. Other common

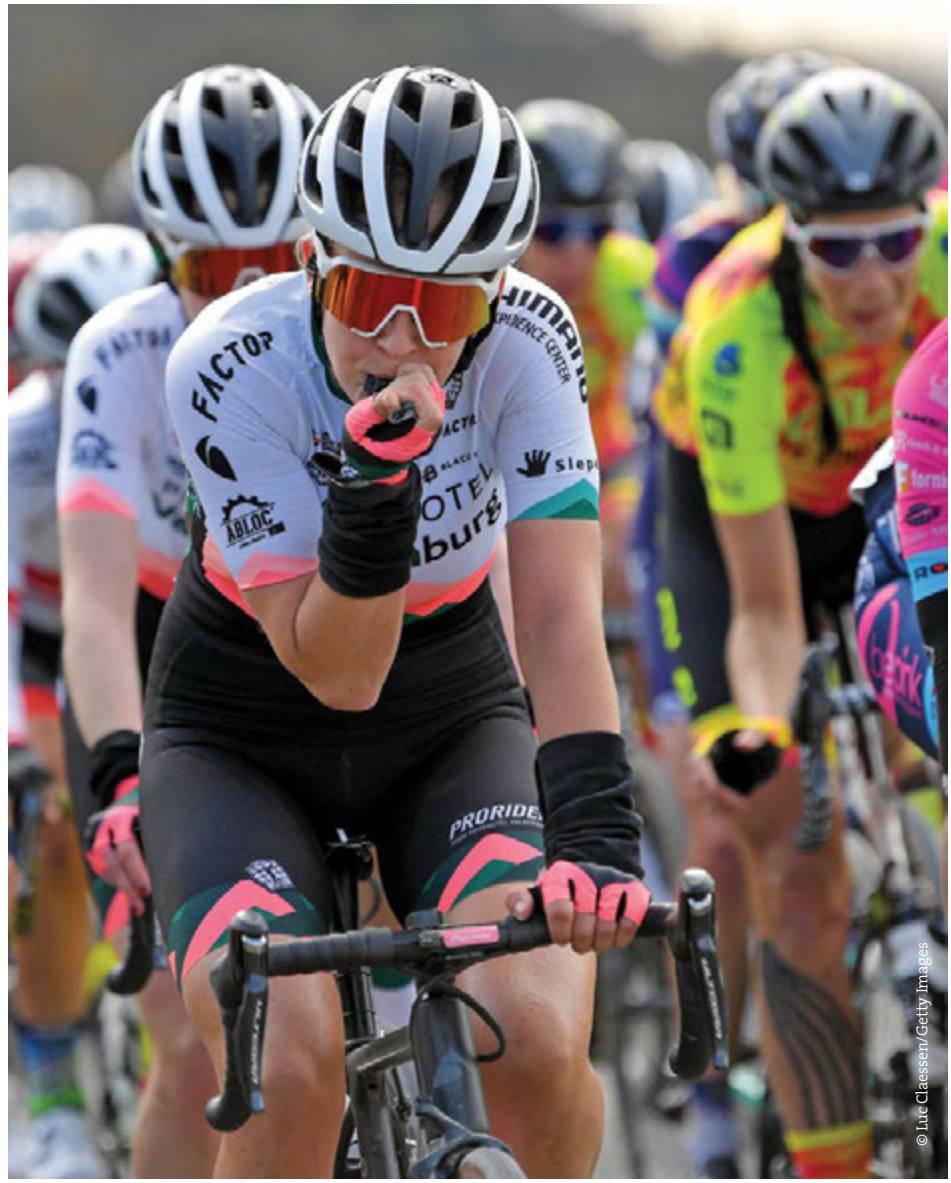


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Image: A quick bite during Women's Elite a 136km race from Siena to Siena – Piazza del Campo. March, 2021 (illustration).

themes of the therapeutic management plan amongst athletes is gut-training, as previously described by Costa et al., (i.e., repetitive gut-challenge)[11]. Gut-training has previously been shown to improve EIGS (neuroendocrine-gastrointestinal pathway), and subsequently reduce Ex-GIS, which translated into improved exercise performance (i.e., 1 h distance test)[11,13]. Small and frequent intake of a carbohydrate solution is recommended based on this method of carbohydrate ingestion and delivery being shown to maintain a consistent intragastric pressure resulting in an enhanced gastric emptying rate and improved stomach comfort[52,53]. Athletes identified as having significant body water losses (i.e., dehydration) during exercise despite water provisions aimed at maintaining euhydration (i.e., body water losses through sweating > water provisions and bioavailability), are advised to undertake fluid tolerance training, with repeated exposure to ingesting fluid shown to significantly improve gastrointestinal comfort, possibly due to increased gastric tolerance[54]. Pharmacotherapy intervention such as oral use of the antiemetic drug ondansetron may be appropriate for athletes who present with significant nausea, as it has been used successfully for alleviating this symptom in some competitive situations and is commonly found at endurance races for treating nausea and vomiting[55]. It is clear that there is not a '*one size fits all*' approach

to the therapeutic intervention for the prevention and management of EIGS and Ex-GIS, and that intervention is dependent on the causal and exacerbation factor(s) of EIGS that are identified through using appropriate (i.e., validated and reliability checked) assessment techniques (Figure 2).

Phase 4 consists of monitoring the athlete and adjusting the intervention based on their progress and feedback. It is important to recognise beforehand that the therapeutic intervention will likely need refinement and adjustment, based on each individual's response and subject to the specific event/competition targeted (i.e., distance, topography, environmental conditions, etc.). Monitoring the athlete is a significant aspect of phase 4 and plays a big part in whether the intervention will be successful or not in the long term. Without monitoring the athletes, it would be unknown the degree of intervention compliance, and subsequently the positive, negative, or neutral outcomes. This highlights the importance of two-way communication between the practitioner and athlete. It is apparent that Ex-GIS can only be reduced and managed by the athlete investing in following the therapeutic intervention recommendations, providing feedback to the practitioner on compliance and tolerance, and the practitioner adjusting therapeutic intervention based on this feedback and additional GastroAxEx as required and justified.

Future research and practice directions for managing EIGS and Ex-GIS

Areas of exercise gastroenterology research and practice that require further exploration and likely to have translational relevance and effect professional practice include:

- Gut training: Future studies should determine the impact of gut training protocols at points of exercise-induced gastroparesis and paralytic ileus (e.g., training at night with food (solid)).
- Dietary modifications: Long-term (e.g., ≥ 1 week) and acute (e.g. ~24 h) dietary intake, and food and fluid intake during exercise, may influence the incidence and severity of EIGS and Ex-GIS. Therefore, further exploration into singular and combined dietary and during exercise nutrition is warranted (e.g., determining the impact of different types and total intake of FODMAPs, fibre, and residue intake).
- Anti-emetic medications: Ondansetron is often provided at endurance races to alleviate nausea and vomiting, with anecdotal evidence and field research providing some strong justification for its administration. However to date there is a lack of laboratory-controlled randomised trial data supporting its use as an anti-emetic during exercise.
- Modification to the gut microbiota: The composition of resident bacteria (e.g., the α-diversity, and relative abundance of SCFA producing commensal and/or pathogenic-based bacteria) may influence the incidence and severity of EIGS and Ex-GIS. Despite the current research popularity of determining a role of the gut microbiota in athlete gut health and performance (i.e., both physical and mental) and predominantly focused on exploratory and descriptive taxonomical research outcome; a substantial amount of rigorously controlled dietary and/or nutritional supplementation research is needed to clearly articulate the role of gut microbiota compositional changes in the prevention and management of EIGS and Ex-GIS.
- External and internal pre and per cooling: This is a new area of exercise gastroenterology research exploration, with a scarcity of research available. Based on these limited, but promising outcomes, future studies should determine the impact of utilising both internal and external pre and per cooling strategies together on the prevention and management of EIGS and Ex-GIS.

SUMMARY AND CONCLUSIONS

Based on the clinical report of an athlete who is affected with EIGS and Ex-GIS, the signs and symptoms of training or competition, this information can be used to develop an individualised GastroAxEx aimed at identifying causal pathway(s) and exacerbation factor(s) of EIGS and subsequent Ex-GIS. Interpretation of outcome data from the GastroAxEx can inform the development and application of an individualised and targeted therapeutic intervention for the prevention and management of EIGS and Ex-GIS, with necessary intervention adjustments made in accordance with athlete's response of intervention (compliance and tolerance). Such translational research practice can result in decreased Ex-GIS incidence and severity during training and competition, and substantially result in improved work output, reduced exercise cessation and/or withdrawal.

References
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