1 The rise of intravenous nutrition products among professional team sport athletes – reasons to be 2 concerned? 3 4 Nathan A. Lewis ^{1,2} 5 Andrew Hodgson³ 6 Tamim Khanbhai⁴ 7 8 Jen Sygo⁵ 9 Jordan Mazur⁶ Casey Smith⁷ 10 Paul Catterson⁸ 11 Charles R Pedlar^{1,9,10} (Corresponding Author; email: charles.pedlar@stmarys.ac.uk; phone: 12 13 +44772524373914 15 ¹Orreco, Business Innovation Unit, NUIG, Galway, Ireland 16 ²English Institute of Sport, Sports Training Village, University of Bath, UK ³Department of Haematology, Sligo University Hospital, Sligo, Ireland 17 ⁴Tottenham Hotspur FC, Enfield, London, UK 18 19 ⁵Toronto Raptors, OVO Athletic Training Center, Toronto, Ontario, Canada 20 ⁶San Francisco 49ers, Santa Clara, California, USA ⁷Dallas Mavericks, Dallas, Texas, USA 21 22 ⁸Newcastle United Football Club, Darsley Park, Benton, UK ⁹St Mary's University Twickenham, London, UK 23 24 ¹⁰Institute of Sport, Exercise and Health, University College London, London, UK 25 26 27 Orcid IDs: 28 C Pedlar: 0000-0002-3075-9101 29 N Lewis: 0000-0001-8896-344X

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1 Use of intravenous nutrition products in sport

2 The authors regularly interact with professional team sport players in European and American 3 leagues and their multidisciplinary support teams, and we are aware of players receiving regular 4 intravenous nutrition (IVN) products. Furthermore, this is often evident in blood biomarker 5 profiles where specific nutrients are beyond the upper-bound measurement limit of the clinical 6 laboratory. The precise prevalence of IVN use is not known, however, anecdotally some players 7 are receiving IVN as often as weekly as part of a pre- or post-game routine. So called 'drip bars' 8 and concierge IVN services are easily accessible, albeit seemingly devoid of appropriate 9 regulation (1). These offer a menu of IVNs containing nutrients such as B vitamins, amino acids, 10 glutathione, vitamin C and electrolytes, claiming to boost health and performance, restore 11 hydration, accelerate recovery and so on. Further, players might request parenteral 12 administration of nutrients such as iron and B12 from a team physician when not otherwise 13 indicated. Typically, sports physician-administered IVNs are reserved for clinical presentations 14 such as anaemia, significant deficiencies with accompanying symptoms, or in race medicine (e.g. severe dehydration/collapse caused by ultra-marathon running in the desert) (2). Whilst 15 16 these are distinctly different from the self-directed IVN use described above, there is cross-over 17 regarding the potential risks and benefits.

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19 Guidance for players and practitioners in the peer reviewed Sports Medicine/Sports Science 20 literature describing the evidence base and risks associated with IVNs is largely absent. IVNs 21 are not mentioned in recent nutrition consensus statements, and this is consistent with the 22 principle of reducing needle use in sport and a 'food first' approach taught in sports nutrition 23 courses around the world. A ban on needle use by athletes at the Olympic Games has been in 24 place for all recent Games except for appropriate medical use, and where a Therapeutic Use Exemption (TUE) is obtained. Similarly, the World Anti-Doping Agency (WADA) prohibit IV 25 26 infusions over 100mls (per 12 hours) unless a TUE is obtained; however, these controls are not 27 mirrored across all sports leagues.

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29 Is there any evidence of benefit to athletes beyond placebo?

30 IVN products are often used as a means of addressing tiredness, fatigue, or recovery, but the

31 evidence is sparce and not supportive. We are aware of just two studies assessing vitamin

1 injections in otherwise healthy participants; neither of which yielded an effect for the injection 2 group. Mya-Tu et al. observed no effect of 1mg of cyanocobalamin (synthetic B12) or placebo 3 injections (3/week) for 6 weeks in a double-blind manner, on various tests of physical 4 performance, or any difference versus the placebo (3). A cross-sectional study of elite Polish 5 track and field athletes reported 34% (n=82) received vitamin B12 injections across a 6-year 6 period (4). Whilst a beneficial effect of vitamin B12 was observed on red cell parameters, there 7 was no additional benefit when the athlete's vitamin B12 concentration was above 700 pg/mL. 8 Furthermore, where a vitamin B12 deficiency exists, one study found no additional benefit of an 9 injection over oral supplementation (5).

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11 **Risks**

12 It is well known that the gut-liver axis actively protects the human from infection, from the 13 acidity of bile to the intricate immune pathways in the epithelial mucosa, and the dynamic role of 14 the gut microbiota providing protection against toxicity (e.g. heavy metals) (6). Bypassing these 15 mechanisms appears foolhardy unless there is a significant clinical rationale, and no studies have 16 addressed the long-term impact. However, via biomarker profiling we have observed vitamin B6 17 and cobalamin (vitamin B12) often beyond the measurement range of the laboratory, in a sub-18 group of professional players. These observations may be the direct result of IV therapies, 19 although inadvertent intake via fortified foods may also be causative. Whilst the long-term 20 effects of high cobalamin are unknown, the long-term effects of vitamin B6 are classically 21 associated with peripheral neuropathy (7). Athletes regularly receiving parenteral iron risk liver 22 disease, and indeed high body stores (hepatic iron concentration) have been observed in road 23 cyclists (8).

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Given that the long-term effects of supratherapeutic doses of B vitamins and other nutrients are unknown in athletes, it does not appear to be worth the risk, especially given the lack of evidence-based benefits. There are also the direct risks related to venous access including infection and thromboembolic complications. More than this is the reputational risk to sport if it is normalised for athletes to regularly partake in self-directed IVN use with a worrying shift away from what 'works' (according to scientific standards), to that which is unproven.

1 Furthermore, some athletes risk an anti-doping violation by participating in self-directed IVN 2 use. 3 4 **Future directions** 5 A greater understanding of the prevalence of regular IVN use among athletes needs to be 6 established. Qualitative study may provide important information on the draw and motivating 7 factors for athletes to seek IVN, perhaps informing alternative strategies for education and 8 resources to meet nutritional and performance needs. In parallel, governing bodies and players 9 associations in the professional leagues need to provide guidance over the potential risks of IVN 10 use. The 'food first' and 'no needle' messages need to be amplified among all athletes and 11 multidisciplinary support teams to avoid what was previously a 'last resort' treatment becoming 12 normal without scientific evidence of benefit. 13 14 References 15 16 1. Shmerling RH. Drip bar: Should you get an IV on demand? In: Harvard Health 17 Blog2018. Givan GV, and Diehl JJ. Intravenous fluid use in athletes. Sports Health 4: 333-339, 18 2. 19 2012. 20 3. Tin May T, Ma Win M, Khin Sann A, and Mya-Tu M. The effect of vitamin B12 on 21 physical performance capacity. Br J Nutr 40: 269-273, 1978. 22 Krzywański J, Mikulski T, Pokrywka A, Młyńczak M, Krysztofiak H, Fraczek B, 4. 23 and Ziemba A. Vitamin B(12) Status and Optimal Range for Hemoglobin Formation in Elite 24 Athletes. Nutrients 12: 2020. 25 Wang H, Li L, Oin LL, Song Y, Vidal-Alaball J, and Liu TH. Oral vitamin B(12) 5. 26 versus intramuscular vitamin B(12) for vitamin B(12) deficiency. Cochrane Database Syst Rev 27 3: Cd004655, 2018. 28 Duan H, Yu L, Tian F, Zhai Q, Fan L, and Chen W. Gut microbiota: A target for 6. 29 heavy metal toxicity and a probiotic protective strategy. Sci Total Environ 742: 140429, 2020. 30 Hemminger A, and Wills BK. Vitamin B6 Toxicity. In: StatPearls. Treasure Island 7. (FL): StatPearls Publishing 31 32 Copyright © 2022. StatPearls Publishing LLC., 2022. Deugnier Y, Loréal O, Carré F, Duvallet A, Zoulim F, Vinel JP, Paris JC, Blaison D, 33 8. 34 Moirand R, Turlin B, Gandon Y, David V, Mégret A, and Guinot M. Increased body iron 35 stores in elite road cyclists. Med Sci Sports Exerc 34: 876-880, 2002