

fact that mean values for MCV remained the same for both the iron deficient subgroup and the iron replete subgroup. Also among subjects who had progressed to iron deficiency, the mean value for haemoglobin (Hb) was 132.7 g/L vs 139.2 g/L in the iron replete subgroup.<sup>1</sup> In a study where iron deficiency was defined as serum ferritin of  $\leq 30$   $\mu\text{g/L}$  in men and  $\leq 20$   $\mu\text{g/L}$  in females, or transferrin saturation as  $\geq 20\%$  or reticulocyte haemoglobin as  $\leq 28$  pg, there were 770 subjects with IDWA. Among them were 463 who had MCH amounting to  $\leq 28$  pg vs 209 with MCV of  $\leq 80$  fL.<sup>2</sup> Accordingly, given the fact that MCH of  $\geq 28$  pg is more prevalent than MCV of  $\leq 80$  fL in IDWA subjects, a MCH of  $< 28$  pg should be a *red flag* for IDWA, prompting further investigation along the lines proposed by Al-Naseem *et al.*<sup>3</sup>

The recognition of IDWA has implications for correction of incident iron deficiency and for identification of its underlying cause. Correction of incident iron deficiency (regardless of Hb level) is a matter of urgency in patients with congestive heart failure (CHF). In Wienbergen *et al.*, where iron deficiency was defined as serum ferritin  $< 100$   $\mu\text{g/L}$  or  $100$ – $299$   $\mu\text{g/L}$  in association with transferrin saturation  $< 20\%$ , predicted mortality in CHF subjects with IDWA was significantly greater ( $p=0.002$ ) than in CHF subjects without iron deficiency.<sup>4</sup> Furthermore, among CHF patients in whom iron deficiency has been defined according to the criteria cited by Al-Naseem *et al.*, treatment with intravenous iron improves symptoms, functional capacity and quality of life irrespective of presence or absence of anaemia.<sup>3,5</sup> The rationale for these outcomes might be the one that comes from animal studies.<sup>4–7</sup> In one study, IDWA was shown to be responsible for decreased left ventricular function and reduced mitochondrial complex 1 activity in mice.<sup>6</sup> In another murine experimental model, deficiency of transferrin in heart muscle was shown to lead to lethal cardiomyopathy.<sup>7</sup>

Also, of some importance is the identification of the underlying cause of IDWA. In the meta-analysis undertaken by Chan *et al.* (five studies), 13 gastrointestinal malignancies were identified in 3,329 participants. Prevalence of gastrointestinal malignancy in those with IDWA was predominantly in the age group of  $> 50$  years with little risk in younger age groups. Overall, the number needed to endoscope (to discover one case of malignancy) amounted to 263. When stratified according to age, number needed to endoscope amounted to 39 in those aged  $\geq 50$  years.<sup>8</sup> In a separate study (a retrospective analysis not included in the previous meta-analysis), among 287 CHF patients of mean age 70 years with IDWA, 30 were diagnosed with gastrointestinal malignancies.<sup>9</sup> In the latter study, anaemia was defined as Hb  $< 12$  g/dL in both men and women, and iron deficiency was defined according to the criteria cited by Al-Naseem *et al.*<sup>3</sup> In that study, serum ferritin  $< 30$   $\mu\text{g/L}$  had a specificity of 90% for generating a positive endoscopy result but this was at the cost of poor sensitivity (13%), in other words, at the cost of rejecting many potential candidates for endoscopy simply because they had higher serum ferritin values. Conversely, a serum ferritin cut-off level of  $< 100$   $\mu\text{g/L}$  had higher sensitivity (93%) in identifying potential candidates for endoscopy but at the cost of a higher ratio of 'numbers needed to endoscope' (ie lower specificity, amounting to 31%) for obtaining a positive endoscopy result.<sup>9</sup>

In conclusion, the emerging picture is that of a compelling urgency to identify IDWA in patients with CHF because of its adverse effects on prognosis, and because those adverse effects

can be mitigated by treatment. There is a compelling need to identify the underlying cause of IDWA in subjects aged  $\geq 50$  years but not such a compelling need in younger subjects. ■

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## COVID-19 multidisciplinary working group

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Editor – We write in support of the process outlined by Satta *et al.* in their recent commentary which explored the methods for creating an expert multidisciplinary team (MDT) to support decision making and governance around therapeutic options during the COVID-19 pandemic.<sup>1</sup>

Within our own organisation, a large district general hospital, we established a similar COVID-19 oversight group (COG) by mid-April 2020, drawing in multiple experts, like those reported by Satta *et al.* We developed the trust-wide guidelines for managing COVID-19 and maximised the delivery of clinical trials, overseeing study outcomes with early implementation of efficacious treatments through this group.

During the COVID-19 pandemic, up to 10 May 2021, our organisation recruited 5,431 participants into research studies of which 6% ( $n=333$ ) were recruited to interventional trials including RECOVERY ( $n=222$ ) and REMAP-CAP ( $n=15$ ).<sup>2,3</sup>

The COG was also able to review, through weekly virtual meetings, the outcomes from various research studies and interim position statements released from the department of health. Various novel therapeutic agents were implemented into updated guidelines

within 7 days of release of the interim position statements with effective transition into standard care within this time period.<sup>2–4</sup>

In order to evaluate the impact of the COG guidelines, we undertook a trust-wide audit of randomly selected COVID-19 patients admitted between 01 May 2020 and 30 Nov 2020. The majority of patients received appropriate therapeutic interventions during the audit time periods: dexamethasone (93%) and remdesivir (84%). Tocilizumab guidance was received in January 2021 and a further audit suggested that 86% of our patients received this treatment appropriately.

We agree with the authors and feel confident that the establishment of a local MDT has enabled our organisation to provide rapid access to therapeutic interventions in COVID-19 with high levels of concordance with local guidelines. Although NHS organisations have a wide degree of heterogeneity, we believe that the effective implementation of a local COVID-19 MDT group could have beneficial impact across the wider healthcare system. ■

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## Probiotics for atopic dermatitis

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Editor – We read with great attention the holistic and exhaustive review by Plant and Arden-Jones about atopic dermatitis.<sup>1</sup>

However, we think that the increasing use of probiotics in the prophylactic and curative management of this condition deserves more attention.

In fact, probiotics were increasingly used during the last 2 decades, notably in infants and children; and the cumulated evidence is now conclusive through several systematic reviews and meta-analyses.

Particularly, treatments with mixed-strain probiotics have greater prophylactic and curative effects to both lower the risk of atopic dermatitis and reduce symptoms in children.<sup>2</sup>

Interestingly, regarding the preventive effect of such probiotics, strong evidence-based proofs recently demonstrated that supplementation with probiotics in both the antenatal period (in pregnant mothers) and postnatal period (in breastfeeding mothers then in infants) was efficient to reduce the incidence of atopic dermatitis in infancy and childhood.<sup>3,4</sup>

The era of microbiome-targeting drugs is here, and probiotics ought to be considered as a powerful, adjunct, preventive and curative therapy; especially in the paediatric population. ■

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## Novel psychoactive substance

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Editor – We read with interest the article entitled 'Acute neurological consequences of novel psychoactive substance use: a retrospective review in a large UK hospital' by Tanti *et al*.<sup>1</sup> The team have effectively highlighted the high rates of psychiatric comorbidity, unemployment, homelessness and incarceration in this vulnerable group in society. However, the paper may have benefitted from involvement of a clinical or analytical toxicologist to prevent several inaccuracies. Lack of analytical confirmation in any patient is a major limitation; self-reporting of substances of abuse (especially novel psychoactive substances (NPS)) is known to be unreliable. It is misleading to state 'unfortunately, drug screens do not detect novel psychoactive substances' since, while basic point-of-care immunoassay-based tests will not detect