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Reply

Sir—I would not disagree with Dr Ogundipe's view that the way geriatric medicine is integrated into the medical student's curriculum is the key issue. However, we must recognise that ageism is institutionalised in this country, and hospitals and universities are not exempt from this form of discrimination. There remains a strong view that one way to ensure geriatric medicine continues to get a look-in is to maintain its presence as a distinct part of the curriculum.

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Metformin and vitamin B12 deficiency: the role of H2 receptor antagonists and proton pump inhibitors

SIR—Liu *et al.* highlighted an important point, which is well described with regard to metformin therapy [1]. Interestingly, they have categorically stated that: 'These two patients had B12 deficiency associated with metformin therapy'.

However, we feel that in both the patients described in their report, there are alternative causes for the deficiency of vitamin B12, which has not been discussed.

The first patient described was also on treatment for gastritis with *famotidine*, an H2 receptor antagonist (H2RA). The chronic use (>2 years) of H2RA or proton pump inhibitors (PPI) has been associated with B12 deficiency [2]. H2RAs decrease acid secretion by the gastric parietal cells and gastric acid and pepsin produced by these cells are required for the cleavage of vitamin B12 from dietary sources [2, 3], hence, the potential to cause B12 deficiency. Indeed, the uptake of food-bound B12 in patients on treatment with cimetidine has been demonstrated to be decreased, from a mean of 5.3% without the drug to 2.5% after it, a fall of 53%; $P < 0.0001$ [4]. This impairment of B12 absorption had raised the possibility more than two decades ago that long-term, full-dose therapy with cimetidine may produce B12 deficiency similar to that seen in other *hypochlorhydric states* [4].

In the second patient described, no comment has been made on other medications that the patient could have been taking. Nonetheless, this 'patient had taken *over the counter* metformin for 8 years, with diarrhoea for 2 years'. It is therefore, likely that the patient could also have been taking an H2RA/PPI *over the counter*, especially having suffered with gastrointestinal (GI) side effects for 2 years. Neither of the patients had been reassessed for B12 status after suspending metformin for a satisfactory period.

Intrinsic factor (IF), also produced by gastric parietal cells, is required for B12 absorption from the GI tract. As Liu *et al.* suggested [1], metformin treatment could have been one of the possibilities in the cases reported, as it can result in B12 deficiency mediated by depression of IF secretion.

GI symptoms can be a limiting factor in optimising metformin therapy [5], and the underlying cause remains unclear. Many a time, these patients are prescribed H2RAs/PPIs to help the GI side effects and gradually optimise the dose of metformin. H2RAs/PPIs may therefore impair the absorption of protein-bound dietary B12 and could contribute to the development of B12 deficiency with prolonged use. Patients taking these medications for extended periods of time should be monitored for B12 status. The role of H2RA/PPI affecting the absorption of B12, especially in diabetic patients on metformin therapy with GI side-effects is less commonly perceived in routine daily clinical practice and also needs to be appreciated and recognised even further (Figure 1).

Competing interests

GIV is a Specialist Registrar and JHBS is a Consultant Physician in Diabetes and Endocrinology and both the authors are involved with the management of elderly diabetic patients in routine daily clinical practice.

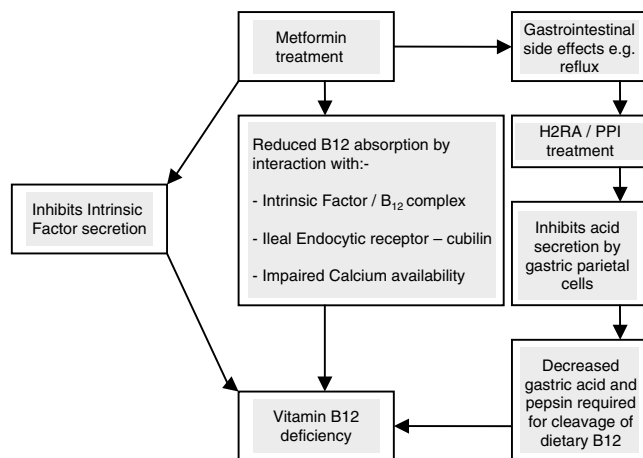


Figure 1. Role of metformin and H2RA/PPI in the evolution of B12 deficiency.

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Response to letter of Varughese and Scarpello

SIR—I am grateful for Varughese and Scarpello raising these important points regarding the contribution of pharmacological achlorhydria to the aetiology of B12 deficiency and their clear, expert explanation.

We fully accept that association does not mean causation, and the case report acknowledged that there are many causes of B12 deficiency in elderly diabetic people.

The main point is to alert geriatricians, who see these patients with falls, to this problem so that neuropathy is not attributed to diabetes but investigated further.

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Re: 'Falls definition validation'

SIR—As older people may be the only witnesses of their fall event self-report, remains a crucial source of information about falls. Dickens *et al.* [1] made a valid point, that for clinical use, a standardised full definition of a fall [2] may not be necessary for patients' understanding of 'what is a fall'. However, for effective meta-analyses of data from different researchers, it is vital. For example, Tai Chi hit the United Kingdom with gusto after the publication by Wolf showing that older people taking part in Tai Chi halved their risk of falls [3]. Yet, on closer analysis, Wolf was considering trips and falls and so despite seeming to be more effective than previously published fall-prevention exercise, it could not be usefully compared. Without standardisation of falls definitions, we will not be able to extract useful data for clinical guidelines on fall prevention interventions [4]. Self-report of falls is notoriously inaccurate, a recent trial looking at the use of diaries to record falls for 6 months followed by a retrospective self-report of falls [5], found that falls were generally under-reported on questioning compared to a falls diary. A significant difference in falls self-report was seen between those in the intervention and those in the control group, suggesting that self-report varies depending on access to care. The assumption that an injury will assist in the recall of fall was not confirmed in this study as the self-reporting of injuries was worse than the self-reporting of falls [5]. However, these were falls over the last 6 months, whether or not a fall had precipitated a visit to an Accident and Emergency Department. The use of different methods of self-report of falls must be tailored to the setting and the use of the data. While we agree with Dickens that simplicity is optimal in the clinical setting, the limitations of these approaches need to be recognised. For research purposes we urge readers to adopt high quality standardised definitions, such as those developed by the ProFaNE consensus statement of outcome definitions [6].

On behalf of ProFaNE (Prevention of Falls Network Europe) www.profane.eu.org.