

to pinpoint and alleged culprit hepatotoxin in Herbalife products may be very challenging.

Despite aforementioned barriers, several cases of hepatotoxicity from herbal products distributing under the name of Herbalife have been published in peer-reviewed, high-impact journals, mainly from three case series from Switzerland (10 cases), Israel (14 cases) and Spain (20 cases).^{3–5} In our opinion, all of these series have adequately reported clinical information and have utilised generally-accepted causality assessment for herbal hepatotoxicity. Causality relatedness was 'probable' in most cases, although 'certain' (with positive rechallenge test) cases were also reported (two from Switzerland, three from Israel and one from Spain).^{3–5} Furthermore, three cases due to possible adulteration with bacteria have also been credibly reported.⁶

We do agree that some limitations exist among these reports, such as variety of the Herbalife product ingested, non-Herbalife product co-ingestion, inadequate ingredient analysis and possibility for other causes of liver disease, but these limitations do not preclude our drawing attention to these reports. These issues have been raised by Herbalife representatives as well.^{7–12}

We have searched the literatures regarding Herbalife hepatotoxicity and analysed available data carefully without bias, although some references that are letters to Editor from the manufacturer have not been cited in our review due to publishing space limitation.

In summary, we have a reason to believe that some ingredients in one of the various Herbalife products can be associated with liver injury, unless high-quality data regarding the safety of Herbalife product, other than post-marketing reports, emerges. Although the incidence is presumably very low, the possibility for Herbalife product-induced hepatotoxicity is important for practicing physicians to recognise, and it deserved to be reported in our review. Lastly, our conclusions are along the same lines as other authorities of drug-induced liver injury.^{13–16}

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Letter: an allergic phenotype in patients with eosinophilic oesophagitis and asthma

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SIRS, We read with great interest the study by Harer *et al.*¹ aiming to better define an allergic phenotype in adult patients with asthma and eosinophilic oesophagitis (EoE). Three issues arise.

First, the status of the oesophagus in the non-EoE group is not defined. EoE can be subclinical prior to presentation with dysphagia or food bolus obstruction.² Furthermore, the influence of gastro-oesophageal reflux

disease that can be associated with both asthma and eosinophilic infiltration in the oesophagus was not addressed.

Secondly, the definition of food allergy applied refers only to 'Type 1'³ IgE-mediated immediate hypersensitivity conditions (e.g. angioedema/anaphylaxis). Although this type of food allergy can occur in EoE patients, it is considered a separate condition, but this distinction is not made. Food challenge was documented too infrequently to be useful. The definition of food allergy in EoE patients and the need for reliable investigations is of current debate⁴ especially as, for example, 64% of adult EoE patients demonstrated histological improvement following the use of a six-food elimination diet, although only 13% had positive skin prick tests. Hence, either skin prick testing has limited utility or EoE may represent a disease with a range of immunological mechanisms including 'atopic' as well as delayed 'cell-mediated' immunity.

Thirdly, food allergy as documented was the strongest predictor of EoE, yet it was omitted from the multivariate analysis. The reason for this was not addressed.

While the development of a scoring scale/screening tool is to be applauded, its construction from an incom-

plete data set excluding food allergy based on limited investigations, and a potentially flawed definition of food allergy, is premature, given the evolving understanding of this condition. A prospective data set, with uniform investigation and a standardised definition of food allergy, is hence suggested.

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Letter: an allergic phenotype in patients with eosinophilic oesophagitis and asthma – authors' reply

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SIRS, We are most appreciative of the interest in our study from Philpott *et al.*, and the important issues they raised concerning our paper.^{1, 2} As regards their first point, this is important as we know from population studies undergoing endoscopy screening that subclinical cases of eosinophilic oesophagitis clearly exist. On the other hand, the prevalence is likely low, found to occur in 0.4% of Swedish patients undergoing endoscopy for abdominal pain.³ Although we suspect the prevalence of asymptomatic eosinophilic oesophagitis would be higher in the asthma population, we would hope it was low enough to not confound our results.

Their point about the influence of gastro-oesophageal reflux disease is also well made, and is a potential confounder. On the other hand, those factors identified on multivariate and split analysis, such as peripheral eosinophilia, lack of steroid inhaler use and presence of intrinsic asthma are not associated with gastro-oesophageal reflux.

As regards their next point, we agree with the mechanism by which symptomatic food allergy associated with an IgE response is not the likely mechanism of eosinophilic oesophagitis. On the other hand, eosinophilic oesophagitis is strongly associated with other manifestations of allergy including IgE-mediated allergic diseases such as food allergy and asthma and therefore we feel the association is valid. We also agree that IgE-mediated food allergy may be one of the strongest indicators of the presence of eosinophilic oesophagitis in asthma patients. In our prospective study, we will feel more secure evaluating this factor when we can be more rigid as regards its definition in patients.

Finally, there is no question that a prospective analysis will help us further validate the use of this scoring system. On the other hand, we attempted to do this in