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Pepsin – The Aggressor

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Although pepsin as an entity was only discovered and named in 1836 (by Schwann) the etymology of the word is much earlier. Pepsis, peptos and peptein originate from 1694 and are derived from the Greek for digestion, with dyspepsia meaning 'bad digestion'. The word Peps-in thus means 'pertaining to digestion'. Therefore, although the enzyme was not discovered the vocabulary had developed to describe the digestion process and problems when they occurred.

Interestingly pepsin is a highly conserved molecule and is found in all mammalian species including horse, dog, pig and lower species such as fish. This highlights the importance of pepsin in digestion. The enzyme is the first stage in digestion of food in which proteins are broken into peptides to improve efficacy of digestion by downstream enzymes. The stomach mucosa is protected from auto-digestion by pepsin by an extensive mucus layer. As pepsin flows into the intestine it is of no consequence as the alkaline pH deactivates it and the tissues are columnar and protected by a mucus layer. In contrast if pepsin refluxes into the oesophagus and above it is damaging as there is no protective mucus layer and also the squamous tissue is more sensitive.

Evidence shows that compared to acid alone pepsin is damaging to the oesophagus [1-3] and laryngeal tissue [4, 5]. Even if damage is not accomplished pepsin is able to disrupt the defence mechanisms [6-8] thus making damage more likely in the event of further exposure.

As a marker of reflux pepsin has been detected in many and varied tissues beyond the upper oesophageal sphincter including middle ear [9], lung [10], trachea [11] and larynx [12]. Clinical measurement of pepsin is important as it can give an objective assessment of the presence of reflux in a patient and help to make a diagnosis.

A lateral flow *in vitro* diagnostic device to measure pepsin makes detection of pepsin rapid, sensitive (20 ng/ml) and semi-quantitative using two unique monoclonal antibodies to human pepsin. Evaluation of several different types of clinical samples including gastric juice, saliva/sputum and exhaled breathe condensate has been performed in hundreds of patients to date and only 30 µl of sample is needed.

In the event of a positive indication of reflux an appropriate treatment can then be initiated. However PPI therapy does not prevent reflux and only changes the pH [13, 14]. Indeed we have detected pepsin in clinical samples of patients on PPI. An

effective treatment option is available in the UK and Europe in the form of an alginate reflux suppressant^[15, 16]. Sucralfate may also be an alternative treatment while fundoplication is an appropriate option in young patients with severe reflux.

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