DISCUSSION I

Question: **Professor Tytgat, you mentioned a study from the UK in which patients with gastric cancer had previously undergone endoscopy but in whom an early lesion was missed. Which study was this and where was it published?**
Professor Tytgat: The study was published in *Gut* in 1997.[1] The study looked at a large group of patients with gastric cancer. Approximately 70% of these patients had peptic symptoms prior to the diagnosis of early malignancy, and a substantial proportion of these had undergone endoscopy prior to detecting overt malignancy. Undoubtedly, at the time of endoscopy, the lesion must have been present. This is the very first paper to indicate that we probably miss a lot on endoscopy—at least that is the message that I took from the paper.

Question: **Why were the early malignancies missed? Could it be due to the fact that not enough biopsies were taken?**
Professor Tytgat: These early malignancies are tiny abnormalities, just tiny discolourations or elevations, and perhaps we should be looking for these instead, particularly in patients over the age of 45–50 years.

Question: **How long should a patient be off antisecretory or antiulcer medication before he/she can be considered to have a normal endoscopy?**
Professor Tytgat: I do not think that we know the answer to that one yet.
Professor Dent: In the case of gastro-oesophageal reflux disease (GORD), follow up studies suggest that it can take at least three months for the majority of patients to show endoscopic relapse, which I find a bit surprising. I am also not sure we really know the answer.
Professor Talley: The Rome Committee struggled with this issue in the absence of any good data.[2] In fact, this is an area for clinical research for anyone who might be interested in a new project. It was suggested that if you waited for a period of perhaps a month, and the patient was symptomatic, it was reasonable to endoscope. There was concern about endoscoping patients who were still receiving potent acid suppression and finding nothing, and then not really being sure whether a lesion had been missed.
Professor Tytgat: This time period also allows for *Helicobacter pylori* to recolonise in sufficient numbers and for gastritis levels to return to the original level but, as Professor Talley said, we require further studies.

Question: **In a new patient with uninvestigated dyspepsia, is there any correlation between the duration of symptoms and endoscopic findings?**
Professor Tytgat: Again, I am afraid that we do not know the answer.

Question: **Can you improve the clinical diagnosis of heartburn by asking the patient about the response to antacid consumption?**
Professor Dent: There have been analyses on the diagnostic value of the response of heartburn to antacids, and a Scandinavian study that evaluated a list of questions found that such a response was of substantial predictive value.[3] In the questionnaires that we have been developing, response to antacids has been included, as our analyses have also shown that it is helpful.[4] While it is most important to get the diagnosis of heartburn right, there are other key questions that add diagnostic value. We probably get a good yield from the evaluation of symptom patterns using only four diagnostic questions, so this is a very simple instrument, and yet it can improve the recognition of reflux symptoms very substantially.
Professor Tytgat: I do not think that you can use response to antacids as an indicator that GORD is present. I am becoming increasingly convinced that there are various sorts of "burning"—heartburn is different to epigastric burning and to non-reflux related gastric burning, which may also respond to antacids. So, unfortunately, you cannot use antacids to determine whether the burning sensation is due to GORD.

Question: **When should 24 hour oesophageal pH monitoring be used? Is it relevant at all, or should we abandon it?**
Professor Dent: No, we should not abandon it—everything has its place. It is true that 24 hour oesophageal pH monitoring is costly and invasive, and there is the problem of access to it for most patients. In the routine diagnosis of GORD, the pattern of symptoms is perfectly adequate and pH monitoring is both redundant and of undue expense. pH monitoring however is of use in the evaluation of the "problem" patient with atypical persistent symptoms. Thus pH monitoring belongs much further down the management tree.

Question: **Dr Agréus, did you control for non-steroidal anti-inflammatory drug use, aspirin use, and over the counter prescriptions in your long term follow up study?**[5]
Dr Agréus: The true answer is no. We did not control for such drug use because we already have data on drug consumption from the first and second surveys,[6] but not from the third survey.[5] From the first two surveys we knew that about 30% of individuals with functional gastrointestinal disorders took some kind of acid suppressing drug—antacids, H_2 receptor antagonists, and proton pump inhibitors—and we also knew that the symptom pattern did not change between the first and second survey. However, we do not know what happened in the third survey—proton pump inhibitor consumption could have increased about 10-fold during that time but, on the other hand, as we have seen today, these drugs reduce symptoms only in about 50% of individuals.

Question: **Is intestinal metaplasia a precancerous lesion, how do you manage it, how accurate is endoscopy at recognising it, and what is its clinical significance?**
Professor Tytgat: Only a fraction of patients with intestinal metaplasia are recognised endoscopically. I believe that it is a significant lesion if it is sufficiently advanced to raise the pH in the stomach, and usually its presence goes hand in hand with the risk of developing dysplasia. Throughout the gastrointestinal tract, the precursor lesion for adenocarcinoma is intestinal metaplasia—this is true in the oesophagus, in the stomach, and perhaps even in the colon. Therefore, intestinal metaplasia is a universal precancerous lesion in the gastrointestinal tract.

Question: **How many people develop malignant disease over a seven year follow up, and is this an important consideration in the population?**
Dr Agréus: We checked the data files for 1290 people from the endoscopy units in two hospitals and, after the survey in 1995, none was found to have malignant disease.[7] I think that about 8% of this population had undergone an upper endoscopy, and less than 3% showed a structural disease.

Question: **Dr Moayyedi, could you comment on the differences in prevalence, incidence, and cost of dyspepsia, by sex, ethnic group, and age in the Swedish studies?**
Dr Moayyedi: I do not have any information on the Swedish data. As far as the UK data are concerned, there was no difference in either the prevalence of dyspepsia or resource consumption due to sex. There was an increase in prevalence in populations with a lower socioeconomic status, and this was associated with an increase in cost. We could not really address ethnicity as only 2% of our sample were from ethnic minorities. We did not see any differences between this population and Caucasians, but we were not really getting a representative sample of ethnic groups. None of the data is published yet however.

Question: **Professor Dent, is endoscopy negative reflux really a disease? For example, we do not consider headache to be a disease. Therefore, do patients with heartburn, who have a small impairment in their quality of life, really have a disease?**
Professor Dent: Yes, I think that endoscopy negative reflux is a disease. When you look at the burden of symptoms in endoscopy negative patients enrolled into clinical trials, the intensity and severity of their heartburn are comparable with patients with reflux oesophagitis, and this is reflected in impaired quality of life for these patients. It is fair to say that it is unlikely that a patient without oesophagitis is at any significant risk of local

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complications in the oesophagus resulting from gastro-oesophageal reflux. As clinicians, we have to make a judgement about whether a patient's symptoms are severe enough to warrant intervention; if the symptoms are mild and intermittent, maybe all the patient needs is an explanation about what is causing the symptoms and to hear that there is no cause for concern.

Dr Agréus: I think that we also have to realise that in patients with any kind of reflux symptoms, between 5% and 10% will also have peptic ulcer disease at the same time.

Questioner: I certainly do not dispute that patients with symptomatic heartburn have an impaired quality of life and may require treatment, and that we need to take these symptoms seriously, but I am really not certain why we consider it to be a true disease. To me, a disease is something that defines some form of pathological entity, for which we have some objective measures; in the case of oesophagitis, this could be 24 hour pH monitoring. However, consider the following examples: a patient who has chronic pain that means he/she cannot work, or someone with backache but no abnormality on which to operate, or someone who suffers from tension headache and takes a lot of time of work—these people are not considered to have a disease, they are individuals with symptomatic problems who have a significantly impaired quality of life.

Professor Dent: This is to some extent a semantic argument. These patients do have objective indicators of disease. However, if you perform an oesophageal motility study on them you demonstrate that they have defective gastro-oesophageal competence, which can be cured by antireflux surgery. Furthermore, these patients respond very well to acid suppressive therapy. Using your definition, you might as well deny that asthma is a disease because it does not produce any lasting pathological evidence that you can see. Ultimately, what matters is how the patient feels and how much you can help them.

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