Leading article

Nutcracker, neurosis, or sampling bias?

Claims that motility disorders of the oesophagus are a common cause of pain are probably overstated. A recent review estimated that the oesophageal chest pain industry in the United States was worth more than 300 million dollars a year. Investigating atypical chest pain is not a common task for the British gastroenterologist but what of the future? Do Americans with atypical chest pain benefit from all the investigations lavished upon them? This important question could only be answered with certainty by a randomised controlled trial in which one group of patients with atypical chest pain underwent treatment with the benefit of oesophageal investigation and the other group was treated empirically. What is the evidence that abnormal oesophageal motility causes chest pain?

To be certain that oesophageal motility disorders cause chest pain, pain and abnormal contractions need to be closely linked. Pain occurring with disordered motility must be the same as the presenting pain and abnormalities must be genuine departures from the normal range and not just artefacts of the method used. Resolution of the abnormality should be associated with improvement in pain and vice versa. Psychiatric disorders must be recognised because they can affect the perception and reporting of pain. Finally, to ensure that the frequency of the abnormality is not overestimated the patient population must be representative, otherwise inferences will not hold true in the general population. Thus, establishing the relationship between contractile activity and pain is a formidable task, compounded by the complexities of monitoring and measuring motility, the uncertainty of psychological assessment, and capricious referral patterns.

The relationship between motility and chest pain can be examined in three ways. First, with routine oesophageal manometry, where pain during manometry is unusual so that abnormalities of motility without pain only provide supportive evidence of a diagnosis. Second, to improve the sensitivity of the investigation various pharmacological agents (usually cholinergics) are injected to provoke changes in motility and pain. The occurrence of both together is considered strong evidence for a diagnosis. Finally, in recent years ambulatory motility has been used to link motor events with episodes of pain. The rationale is the same as that for ambulatory electrocardiography and provides the best evidence for a causal link between abnormal motility and pain.

Several abnormalities of baseline oesophageal motility have been associated with pain. The commonest and most controversial is the ‘nutcracker’ oesophagus. This attractive term is used to define a group of patients who have exceptionally powerful oesophageal peristalsis (mean amplitude for 10 wet swallows in excess of 180 mmHg). In one series, 48% of abnormal tracings of patients with atypical chest pain showed a nutcracker oesophagus. These high pressures may represent artefact rather than pathology. Nervous patients are probably not excluded from studies as readily as nervous volunteers. It is likely, therefore, that patients, as a group, react more to intubation than volunteers and this adverse reaction might lead to spuriously high estimations of amplitude. Externally applied stress can increase the amplitude of peristalsis and there are two mechanisms by which this could occur. First, patients who are anxious or stressed may hyperventilate and hyperventilation is recommended to help them relax. In a controlled study short periods of hyperventilation increased the strength of oesophageal contractions by as much as 30%. In the second place, anxiety may alter the force with which subjects swallow, and swallowing forcefully can increase the power of peristalsis by up to 30%. There are other problems with these types of studies, most notably the control groups used. When assessing a diagnostic test it is important for the test to distinguish between patients with similar symptoms and not between those with symptoms and those without. In the case of oesophageal motility, disease or symptoms may lead to disordered motility. When oesophageal motility in patients with chest pain with and without coronary disease is compared the differences between the groups is usually less marked.

Provocation tests are often done as an extension to manometry. Cholinergic drugs enhance contractility of the oesophagus and, in some cases, pressures up to 400 mmHg may be recorded. Such very high pressure waves might be painful. Hence, the validity of the test depends on whether the pain is identical to that of which the patient complained. Furthermore, it is possible that these drugs affect afferent pain pathways or other organs and that the high amplitude contractions are an epiphenomenon.

The best method for connecting motility abnormalities and pain is the ambulatory study because prolonged studies are more likely to identify spontaneous episodes of pain. Abnormal oesophageal contractions immediately preceding or during an episode of pain constitute good evidence that the abnormality caused the symptoms. Unfortunately, patients are not good at using event markers reliably during such studies and it is difficult to correlate events accurately. To overcome the problem of storage capacity some solid state recording devices record oesophageal motility for only a few minutes either side of an event so that a great deal of baseline motility is not recorded and abnormalities not associated with pain can be missed. If the recording is very abnormal but pain is infrequent then pain could coincide with abnormality by chance.

Patient selection is the most significant methodological problem encountered in estimating the prevalence of chest pain related to oesophageal motor disorder. Information about the source of patients is rarely provided. The cardiologists working in this specialty have recognised the problems of sampling bias and the limited application of their findings to unselected populations. The crux of the problem is how patients are referred for further investigation. What are the factors that lead to patient presentation and referral? What affects the threshold for seeking advice? What factors determine whether a patient is sent for complicated cardiac blood flow measurements or for oesophageal manometry? There are general factors applicable to the entire population that influence presentation, referral, and investigation. In North America, for instance, patients have ready access to specialist physicians who are acting under two forces that might reduce the threshold for investigation: litigation and the prospect of remuneration. In Britain the general practitioner acts as an effective filter for the specialist.
Furthermore, British physicians, with limited resource, tend to be more selective in their decision to investigate patients. Hence, the provision and pattern of health care affects the threshold for investigation. Moreover, as the perceived and real wealth of a country improve, then expectations of good health and health provision increase, thus lowering the threshold for consultation and requests for further investigation.

There are also specific factors about the patient which determine the pattern of referral and investigation. There is a tendency to assume that the severity of symptoms is the overriding factor. While this may be true for some patients, there are probably other factors not related to the severity of the presenting symptoms which lead to complaint and referral. The first and most obvious is the degree to which the patient is concerned about the symptom. Inappropriate concern, or neurosis, can be innate or secondary to external factors, such as a recent cardiac death of a friend. The neurotic is much more likely to complain than the stoic person. Hence, it is no surprise that populations of patients with functional disorders have a higher rate of neurosis than control populations.21,22 Other psychological disorders may enhance perception and reporting of symptoms as well as increase concern about them.21,22 Furthermore, psychiatric and other physical symptoms can change the thresholds for seeking advice in a number of ways. First, although other symptoms may originate as the presenting complaint, they can be ignored or overlooked by the organically orientated doctor; second, they may enhance the apparent seriousness of the presenting complaint.

Faced with an apparently healthy patient, it is easy to focus on a specific symptom such as chest pain, while ignoring more nebulous possibilities whether or not these are psychological. The patient quickly gets the message and, to ensure continued attention, shifts the emphasis to the chest pain. Alternatively, patients readily realise what does not interest their doctors and automatically focus on what does. This happens in the irritable bowel syndrome and there is no reason to believe it cannot happen with atypical chest pain. Patients with irritable bowel syndrome frequently have non-colonic symptoms23; indeed nearly half the patients with the irritable bowel syndrome will rank a non-colonic symptom as the most troublesome one.23 Why do so many of these patients get referred for investigation of colonic symptoms when it is not those symptoms which bother them most?

Finally, while chest pain alone might not be enough to take the patient to the doctor, other symptoms, such as shortness of breath, palpitations, or dizzy spells in combination with chest pain, might affect the patient or primary physician’s threshold for seeking advice. Hyperventilation has been linked on many occasions with atypical chest pain,24,25 and it is possible that the symptoms of hyperventilation in combination with chest pain result in increased numbers of these patients presenting for advice. Hyperventilation is well known to mimick symptoms of organic cardiac disease, such as a rapid pulse,24,25 breathlessness, and dizziness.24 It is easy to imagine how chest pain with these symptoms is treated more seriously than chest pain without them.

Many patients with atypical chest pain, like those with the irritable bowel syndrome, never consult their doctor.26 Those who are referred for investigation might have a high frequency of disorders of the oesophagus and microcirculation of the heart. However, it seems increasingly likely that such disorders are uncommon in unselected populations and that the emphasis should be switched to why people present for investigation and why doctors decide to investigate further. We do not yet know what the true prevalence of oesophageal motor disorders is in patients with atypical chest pain, and until investigations in unselected populations are reported clinical gastroenterologists should not purchase manometry equipment for the investigation of chest pain.