LETTERS TO THE EDITOR

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Transoesophageal echocardiography and lung cancer staging

Carole J M Connolly

Cardiac involvement by tumour is found in 25% of patients who die from lung cancer and, in the majority of these patients, the involvement is asymptomatic.1 With a significant proportion of patients subjected to lung cancer surgery dying from disease progression within 6 months of surgery, the British Thoracic Society guidelines on the selection of patients with lung cancer for surgery may help to reduce this number.1,2 These guidelines acknowledge the excellent staging potential of PET scanning but only mention echocardiography in the context of valvular or ischaemic heart disease. Echocardiography is an excellent modality for detecting cardiac malignancy.3 An increasing number of anaesthetists are joining the already large number of cardiologists able to perform transoesophageal echocardiography (TOE). We suggest that patients presenting for lung cancer surgery who have either ECG abnormalities or poorly differentiated paracardiac tumours should undergo TOE before thoracotomy. The TOE examination would add little to the total operative time but would add contemporary information to existing older information regarding disease stage. Moreover, there would be a small number of patients who would be spared thoracotomy.

A recent case in which left atrial extension of a lung cancer was demonstrated by intraoperative TOE but missed by preoperative PET scanning and the standard staging methods lends anecdotal weight to our argument. Not only did our patient suffer an unnecessary thoracotomy, but also left popliteal artery tumour embolism. This is not the first time a patient has had a thoracotomy abandoned because of tumour involvement of the left atrium revealed only by intraoperative TOE.4 In both cases TOE in the anaesthetic room would have prevented thoracotomy and, in our case, distant tumour embolisation may not have occurred.

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Self-management of asthma in general practice

We welcome the paper by Thoonen and colleagues on the management of asthma.1 We agree that general reference to the potential problems in this patient group might be appropriate and we will consider this in the next version of the guideline.

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References

Authors’ reply

We thank Dr Allen and colleagues for raising these issues. As they point out, the difficulties of diagnosis and treatment are mainly features of the co-morbidity which increases with age, not age itself, and we had not felt it desirable or possible to cover all the changes to routine practice which might be required because of the presence of other diseases. We cannot comment on the items of evidence included in their letter since references are not given, except to say that their points seem correct in principle but some of the evidence levels look unrealistic—for example, one of the flaws of the current grading system is that, however good the evidence on something like asthma mortality, it cannot be level 1 evidence since that is possible for randomised controlled trials only. Nonetheless, we agree that general reference to the potential problems in this patient group might be appropriate and we will consider this in the next iteration of the guideline.

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and 78% for the UC and SM groups, respectively, a difference reported to be statistically significant. As we do not expect that these specific outcomes were analysed on an intention to treat basis, non-random withdrawal might have biased the findings—for example, when most patients who withdrew from the SM group did so because they were not able to comply with the SM programme and their asthma was badly controlled, this would affect the outcomes, inflating the differences in favour of the SM group.

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Reference

Authors’ reply
In their letter van der Wouden and colleagues question the issue of selective withdrawal of subjects from the two study groups which may have had consequences for the validity of our conclusions. As a possible source of bias in calculating successfully treated weeks this may be an important issue which was not discussed in depth in our original paper.

To address this question we performed an additional analysis of the study records of all subjects excluded from the calculation of the successfully treated weeks. We divided all these subjects into two categories: (1) those excluded from the calculation because of side effects to inhaled steroids, poor asthma control, referral to a pulmonary physician, or non-compliance with the study protocol (categorised as “unable to comply”), and (2) subjects excluded because of a change of address or GP, pregnancy, or unknown reasons (categorised as “other reasons”).

The number of subjects in the “unable to comply” subgroup was four out of 15 in the self-management group (4% of all self-management subjects) and five out of eight in the usual care group (5% of all usual care subjects). The number of withdrawals for asthma related reasons (including poor asthma control) was therefore relatively small in both study groups and was, in fact, relatively higher in the usual care group. We therefore believe that the impact on the number of successfully treated weeks must have been limited and, if present at all, was in favour of the usual care group rather than the self-management group.

We conclude that, even if there were differences in the withdrawals between the two groups, this does not change our conclusion that self-management of asthma is at least equally as effective as the asthma treatment usually provided in Dutch primary care. This conclusion supports the view of van der Wouden and colleagues that self-management of asthma is a promising innovation in general practice.

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Reference

Atopic cough: little evidence to support a new clinical entity

A cough is by far the most common reason for a patient to seek medical advice. Most of these consultations are for acute cough caused by a myriad of respiratory viruses. In practice, we do not attempt to differentiate rhinovirus infection from adenovirus because no important consequence arises from this diagnostic precision. In chronic cough numerous studies have shown that the overwhelming majority of patients are suffering from one of three conditions: a form of asthma, gastro-oesophageal reflux, or rhinitis. The question is whether any further subdivision is justified or merely muddies the water.

In their recent paper published in Thorax Fujimura and colleagues, by investigating a diagnostic nosology of “atopic cough”, have succeeded in adding further unnecessary complexity to the area. There are many aspects of this paper which cannot be left unchallenged and we have outlined these below.

The evidence to support a new clinical entity of “atopic cough” is weakened by the extremely vague term “probable atopic cough”. This point is well illustrated in their table 2 which outlines a variety of diagnostic permutations possible after interpretation of symptoms and investigations. We suspect the authors have, in a significant number of these “probable” patients, merely described atopic individuals with cough predominant asthma. Certainly the demonstration of bronchial hyperreactivity (BHR) in 15 such patients (median PC20 2.5 mg/ml, range 1.25–5.0), many of whom had airway eosinophilia and all of whom appear atopic, is suggestive. Such diagnostic imprecision may yet have therapeutic consequences, but the authors do not provide sufficient information in the paper to conclude that these patients failed to respond to steroids, and have indicated that response to bronchodilators was tested in neither a randomised nor a controlled way.

The authors have relied heavily on the “absence of transformation to typical asthma” to differentiate atopic cough from asthmatic cough. Such a conclusion can hardly be supported by a telephone follow up which relies on patient recall and subjective assessment of symptoms. In some series up to one third of patients identified as having cough variant asthma may have had typical asthma symptoms, although in a year follow up of 63 patients with cough variant asthma typical wheeze occurred in only 6%. Thus, lack of progression to typical asthma is not described and cannot be used to support the proposition that atopic cough is unique.

The statement “the defining physiological feature is increased cough sensitivity without BHR” is not applicable to the non-asthmatic atopic cough described and cannot be used to support the proposition that atopic cough is unique.

We believe our clinical understanding of asthmatic cough is enhanced by the recognition that an individual patient may show different features of the disease process. The unnecessary subdivision into arbitrarily defined “diseases” such as atopic cough (or, indeed, eosinophilic bronchitis) is not helpful either diagnostically or therapeutically.
independent. or bronchial responsiveness are entirely
tations of eosinophilic airway inflammation,
medical science. It is very important to recog-
insistence runs counter to the progress of
all of these should be categorised as “asth-
ese chest specialists have used the same
Since we proposed atopic cough as an
productive cough are generally recognised:
mechanisms. We do not yet fully understand
why eosinophilic airway inflammation in-
represent eosinophilic bronchitis without asthma are as
areas A + B represent probable
cough, and areas A + C as cough variant asthma regard-
Figures 1 shows a consensus opinion of the
Worldwide problems regarding the diagno-
sis of cough variant asthma, atopic cough, and
eosinophilic bronchitis without asthma. Both are non-specific to the actual cough
mechanism. We continue to suggest that such
insistence runs counter to the progress of medical science. It is very important to recog-
prise of bronchodilator therapy in individual
patients in a randomised and placebo con-
rolled manner, the assessment we used is not
difficult. Although the placebo effect may lead to an incorrect diagnosis of cough variant
asthma, no effect is meaningful enough to exclude cough variant asthma or cough
predominant asthma.
One fundamental feature of cough variant
asthma is mildly increased bronchial responsive-
siveness unrelated to cough sensitivity. It is
well known that cough sensitivity is in-
creased in some patients with cough variant
asthma and asthma (asthmatic patients), as
pointed out by McGarvey and Morice. Our
opinion is that increased cough sensitivity is
a complication in asthmatic patients but it is
not a fundamental aspect of the asthmatic
airway. We label such patients as having “cough variant asthma” or “asthma compli-
cated with cough hypersensitivity”. In these
patients bronchodilator therapy is not suffi-
cient; histamine H1-antagonists are useful, as
shown by Shioya et al.7 Corticosteroids do, of
course, relieve the cough because they im-
prove both cough hypersensitivity and BHR
which are caused by eosinophilic airway
inflammation via possibly different mecha-
nisms.
The data presented in our paper showing that six of 20 patients with cough variant
asthma not taking long term inhaled cortico-
steroid therapy developed typical asthma are
consistent with previous reports. Although
Orejas et al14 reported that typical asthma
occurred in only 6% of 63 patients with cough
variant asthma during a 3 year follow up period, there exists an important problem in
the diagnostic criteria for cough variant
asthma. Orejas et al14 and many other investiga-
tors have diagnosed cough variant asthma based on BHR without assessing the efficacy of
bronchodilator therapy or measuring cough
sensitivity, resulting in the inclusion of non-asthmatic patients who, in fact, have
atopic cough.
McGarvey and Morice and other investiga-
tors feel that subdividing eosinophilic airway
airway inflammation disorder causes unwieldy complexity in the
diagnosis of chronic cough. We hold that
delineating the pathophysiology of specific subdivisions such as atopic cough and cough
variant asthma will allow more effective and
specific treatments to be used rather than
relying solely on inhaled corticosteroids
which are non-specific to the actual cough
mechanism. We continue to suggest that
atopic cough should be considered as an
entity separate from cough variant asthma
with a unique pathophysiology and its own
rate of asthma onset.

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Authors’ reply
Since we proposed atopic cough as an
atiological entity in 1992, a number of Japa-
nese chest specialists have used the same
arguments as McGarvey and Morice to criti-
cise the concept. They insist that, because
corticosteroids are effective in atopic cough
as well as in asthma and cough variant asthma,
all of these should be categorised as “asth-
matic”, and continue to suggest that such
insistence runs counter to the progress of medical science. It is very important to recog-
prise that there are different clinical manifes-
tations of eosinophilic airway inflammation,
and cough sensitivity and bronchomotor tone
or bronchial responsiveness are entirely
independent. Two mechanisms of non-
productive cough are generally recognised:
cough triggered by increased bronchomotor tone and cough based on increased cough
sensitivity. Both may result from eosinophilic
airway inflammation, although via different
mechanisms. We do not yet fully understand why
eosinophilic airway inflammation in-
creases cough sensitivity in atopic cough
while both asthma and cough variant asthma
exhibit mild bronchial hyperresponsiveness
(BHR) without increased cough sensitivity.
We believe that future studies will
unlock the mechanism, thereby contributing to
both our understanding of the pathophys-
iology of atopic cough and to better specific
treatment.
In our study patients with a definite
diagnosis of atopic cough did not go on to
develop typical asthma, indicating that atopic
cough is not a precursor to asthma. Only one
of 58 patients with a probable diagnosis of
atopic cough developed typical asthma 11.3
years after her first visit. Although the
patient’s bronchial responsiveness was in-
creased, her bronchomotor reversibility and
airway obstruction in peak expiratory
flow rate were within normal limits; broncho-
dilator treatment was not effective, leading
to a probable diagnosis of atopic cough.
Although some investigators believe that
BHR is the key criterion for a diagnosis of
cough variant asthma, this is incorrect. The
most important feature of cough variant
asthma is isolated chronic cough responsive
to bronchodilators. Furthermore, it has been
already shown that measurement of bronchial
responsiveness cannot predict the efficacy of
bronchodilators in the treatment of cough.

Figure 1 Recognition of cough variant
asthma, atopic cough, and eosinophilic
bronchitis without asthma based on bronchial
responsiveness and bronchodilator response
in chronic coughers with eosinophilic airway
inflammation.

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