capacity 83% predicted. During the preceding
5 years, the patient had required 2–3 monthly
courses of intravenous anti-pseudomonal che-
motherapy administered at home by an indwelling
subcutaneous vascular access port. During a routine
clinic review, the patient mentioned that her
great-nephew had recently been diagnosed with
cystic fibrosis (mutations Q43X and D1152H).
Subsequent genetic testing of our patient revealed
her to be a compound heterozygote for two
recognized cystic fibrosis alleles: delta F508 and
D1152H.

Delta F508 is the most common mutation world-
wide and occurs in up to 80% of cystic fibrosis
patients in the UK. D1152H is far less common,
having first been identified in Ashkenazi Jews and
Northern Europeans, with most data on this muta-
tion arising from studies on infertile males.1 The
many different phenotypes observed in cystic
fibrosis are believed to relate to the effect of the
specific mutation on the production of the cystic
fibrosis transmembrane conductance regulator pro-
tein. Low values of the protein (class I mutations) are
associated with severe disease, and intermediate
values (class V) with mild disease.2–5 D1152H is a
class IV mutation, and is generally associated with
late presentation, mild pulmonary disease, pan-
creatic sufficiency, normal sweat chloride values and
advanced survival.4,5

It is not common for cystic fibrosis to be
diagnosed after adolescence, let alone beyond
60 years of age. Although the clinical implication
in our patient was limited, her family has received
appropriate genetic counselling. Moreover,
despite the absence of extra-pulmonary symptoms,
advanced age and other plausible causes of
bronchiectasis being present (previous ‘chest infec-
tions’, tuberculosis and allergic bronchopulmonary
aspergillosis), the diagnosis of cystic fibrosis was still
made in this particular patient.

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References
Fibrosis Gene in Patients with Congenital Absence of the Vas
2. McKone EF, Emerson SS, Edwards KL, Aitken ML. Effect of
genotype on phenotype and mortality in cystic fibrosis: a
3. Hubert D, Bienvenu T, Desmazes-Dufeu N, et al. Genotype-
phenotype relationships in a cohort. Eur Respir J 1996;
C, Aymard P. Mild course of cystic fibrosis in an adult with
mutation (D1152H) in a family with mild lung disease and
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Angioedema may not be a class
side-effect of the angiotensin-
converting-enzyme inhibitors

Sir,
Angioedema is a well-documented and poten-
tially life-threatening side-effect of treatment
with angiotensin-converting-enzyme (ACE) inhibi-
tors, occurring in 0.1–0.2% of patients treated with
these drugs.1 Given the growing number of patients
with hypertension or heart failure treated with these
drugs, and the long duration of treatment, the
frequency of this complication is probably set to
rise. Although most cases of angioedema occur
within the first week of treatment, recent reports
indicate that late-onset angioedema may be more
prevalent than initially thought. This side-effect of
ACE inhibitors is not an allergic reaction and can
occur after many years of uneventful drug use.2
Black patients appear to be at increased risk.

We report the case of a 57-year-old Caucasian
man, who was admitted to hospital because of
severe dyspnoea. Clinical examination revealed
intense swelling of the lips and the tongue that did
not allow intubation, and emergency tracheotomy
was performed to relieve airway obstruction. He had
been treated for hypertension with an ACE inhibitor
(ramipril 2.5 mg/day), with no side-effects over the
last three years. His blood pressure was not well-
controlled, however, and a family physician decided
to change from ramipril to another ACE inhibitor
(trandolapril 2.0 mg/day). Two days later, the patient
presented with symptoms of angioedema.

Angioedema is a swelling involving the deeper
layers of the skin or submucosal tissue, and usually
presents as episodic attacks of swelling of the face,
lips, tongue and airways, although it may also
involve visceral tissues. If angioedema occurs in the upper airways it can become life-threatening; in the gastrointestinal tract it can become very painful. Two patients with recurrent severe abdominal pain, nausea and vomiting underwent three unnecessary laparotomies before the correct diagnosis was made. Angioedema associated with ACE inhibitors appears to be linked to the decreased degradation of bradykinin, because ACE not only converts angiotensin I to angiotensin II, but also inactivates bradykinin. Angioedema due to C1-inhibitor deficiency and ACE-inhibitor-related angioedema are the two forms of angioedema that result from a bradykinin-mediated increase in vasopermeability. Plasma bradykinin increases during acute angioedema in patients with hereditary C1-inhibitor deficiency, but is normal or marginally increased during remission. In three patients with a history of angioedema related to the use of ACE inhibitors, bradykinin levels were high during ACE inhibitor treatment. In another patient, the increased levels of bradykinin during an acute attack were decreased by 93% after withdrawal of the ACE inhibitor. The appearance of angioedema with trandolapril in a patient previously uneventfully treated with ramipril shows that angioedema may not be a class side-effect of ACE inhibitors, and that safe treatment with an ACE inhibitor does not rule out the occurrence of angioedema with another drug of the same family. Patients should be advised to report mild and self-limited episodes, and physicians must stop the ACE inhibitor immediately. If the diagnosis is missed, recurrent and more severe episodes may occur, with potentially serious consequences.

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References
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