Eur Respir J 2005; 26: 561–562
DOI: 10.1183/09031936.05.00091405

EDITORIAL

Case detection of α_1-antitrypsin deficiency: does it help the patient or the doctor?

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Alpha$_1$-antitrypsin (α_1-AT) deficiency is a common genetic disorder, with homozygous genotype Z as the most relevant deficient type for clinicians. In some parts of Europe, this phenotype is as prevalent as cystic fibrosis and for both disorders there is presently no cure for the disease, which has implications for genetic testing in many countries. In 2003, the European Respiratory Society and American Thoracic Society published a joint statement of standards for diagnosis and management of individuals with α_1-AT deficiency [1]. Recently, a full chapter on genetic testing addressed the pros and cons of this issue.

In pulmonary practice, diagnostic testing of a single case with onset of symptoms related to chronic obstructive pulmonary disease (COPD) at early age is most frequently performed. Predispositional detection of the related family of the newly detected case is already more questionable and relates to the care that doctors can provide to cases detected by family screening. Case detection is somewhat different from screening, as screening activity is usually employed for subjects with no symptoms of disease. Public health authorities often only allow for (neonatal) screening if it is possible to establish the diagnosis in a cost-effective way and if efficacious therapy is available shortly after the diagnosis is made. Neonatal screening for phenylketonuria is a classic example of how screening results in effective treatment. Screening for breast carcinoma in females aged >40 yrs shows that other issues of screening for disease should also be taken into account [2].

Subjects with type ZZ α_1-AT deficiency are at risk of liver damage shortly after birth and after the 4th decade of life, and are at risk for emphysema after the 2nd decade of life. Although there is no cure for these two risks, both prevention of cigarette smoking and drinking alcohol will reduce morbidity later in life. These two interventions may justify the approach of case detection in a population at risk (including family screening), rather than neonatal screening of the general population.

De la Roza *et al*. [3] describe in this issue of the *European Respiratory Journal* the approach of testing for α_1-AT deficiency by initial detection of α_1-AT concentration and reserving further testing for PiZ and PiS genotypes to patients with α_1-AT levels <110 mg·dL^{-1} as the most cost-effective screening method for COPD patients. This approach reduced the cost per sample by ~30% (€13.43 *versus* €19.41 (US$16.35 *versus* US$23.64)) and the cost per PiZZ individual detected also by ~30% (€3,589 *versus* €5,189 (US$4,370 *versus* US$6,319)) compared with screening all samples for genotype without prior notice of plasma concentration.

With the recent introduction of intravenous α_1-AT augmentation treatment in Spain and other European countries, physicians are now able to offer management of newly detected ZZ cases shortly after diagnosis. I intend to mention management and not therapy, since the efficacy of this costly treatment remains to be proven in a placebo-controlled study. It is also one of the reasons why medical journals would like to know about the conflict of interest that authors might have concerning their scientific publications, as case detection is of direct interest to pharmaceutical companies that sell augmentation therapy.

The logistics of sampling by dried blood-spot sample, as described by De la Roza *et al*. [3], are remarkably simple. Several companies provide kits for this, accompanied by clear instructions for a doctor's nurse or assistant. All that is needed are drops of blood by finger prick from the patient to fill four circles of 1-cm diameter present on filter paper. When the blood has dried, the paper can be mailed in an envelope by regular mail to the detection lab; this is far more convenient to all involved than sending a tube of whole blood. Since the quality of the filter paper seems to be a critical step in collection of the sample, I wonder if the provider of this material is able to deliver such material for the following decades.

It would be of interest to know the impact of detection of genetic deficiency on newly diagnosed subjects. Does this contribute to a better chance of successful smoking cessation by the patient? Is lifelong weekly intravenous augmentation therapy more acceptable to the patient when the genotype is known rather than just a serum level? The current literature has no answer to these questions. The only neonatal screening study published did indeed address some related questions. Neonatal screening can have important psychological consequences both on the parents and the child. Experience in Sweden has shown that the mothers of α_1-AT-deficient children suffered increased anxiety compared with controls [4]. Insufficient counselling at the time of identification was reported by the majority of parents, which

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reinforces the importance of patient/parent education. However, there were some beneficial effects of screening. Half of the α_1-AT-deficient individuals thought that the knowledge of their high-risk condition had affected their lives, particularly their awareness of the dangers of smoking and environmental pollution. The majority, 88%, knew that they should avoid smoking to protect their lungs [5]. Indeed, the majority of those who were identified through screening and their parents would recommend screening for α_1-AT deficiency.

Despite clear recommendations from the World Health Organisation and American Thoracic Society/European Respiratory Society, many physicians, as well as patients with chronic obstructive pulmonary disease, remain completely unaware of the risk of rapid lung function decline by α_1-antitrypsin deficiency. With currently available improved strategies to help patients stop cigarette smoking as the most important intervention to stop the progression of lung disease, testing of patients with chronic obstructive pulmonary disease and their siblings is justifiable.

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