ELSEVIER
Journal of Cystic Fibrosis 1 (2002) 3–4
Journal of Cystic Fibrosis
www.elsevier.com/locate/jcf

Editorial

CF or not CF? That is the question

At many CF conferences there are case presentations, discussion groups, or even whole sessions devoted to the difficulties of categorising patients with some atypical (and usually relatively mild) features of cystic fibrosis who do not meet standard diagnostic criteria. They usually have at least one CFTR mutation. What diagnosis shall we give? Sometimes, the patient or family want a CF diagnosis to be made, sometimes not. Why do we have so much difficulty giving a firm, clear answer to the question?

For the great majority of patients, the old 'gold standard' sweat test criteria serve us well. The problem is that the sweat test often fails us just when we need it most. The group of atypical patients includes some who have genuinely borderline results, and repeating the sweat test several times confuses the clinician, when some results may be just above or below our cut-off level for normality. We than tend to select the results which best fit our clinical impression and ignore the others.

Twenty years ago, before the CFTR gene was discovered, we delayed making a diagnosis in these patients in the expectation that when the gene was found all would become clear. On the contrary, it has made things more difficult. With over 1000 mutations described, some of which are apparently innocuous, the mere identification of a mutation, or even two, does not of itself make the diagnosis of cystic fibrosis (although in the case of asymptomatic infants detected by neonatal screening, finding two 'severe' mutations allows the prediction that clinical features of CF will sooner or later emerge, probably sooner). However, the question remains whether a given young adult with mild clinical features, an equivocal sweat test and a single 'severe' mutation (such as F508del), either alone or in combination with a 'mild' mutation (such as R117H, in its 7T or 9T version), or with 5T variant, should be diagnosed as having CF. The decision remains a clinical one.

Several factors make us reluctant to use the CF diagnostic label too freely. The general public (in populations of European descent) are now much more aware of CF than they used to be. They have heard about the chronic lung disease, transplants, and anticipated breakthroughs in treatment. They know that it is a genetic problem, but often have a poor understanding of genetic principles. But they know that CF is a severe, life-shortening disease, to be feared.

Giving a CF diagnosis to this partly educated public implies a burdensome program of daily treatment and a prognosis, which may not be appropriate for the atypical patient with mild disease. It also produces a disturbance in the dynamics of the extended family (and careful counselling of close and more distant relatives may be requested, and required in any case). Furthermore, there are issues of employment, insurance, fertility and personal relationships to be addressed.

The accessibility of information about CF via the Internet has resulted in patients or families often learning correct and incorrect facts about the disease, and its management, sooner than their medical advisers have anticipated. They may suspect that the doctors are not giving them a true picture.

This is not an argument for withholding or delaying the diagnosis of CF, but rather one for widening our diagnostic options and vocabulary by calling those individuals with mild, atypical disease (and probably a much better than average prognosis) something other than 'classical' CF. The patient, the family, the health care professionals, employees and insurance companies need to recognise that the condition affecting these people does not have the same implications for health, treatment, employment and life expectancy as the stereotype of CF, which they may have seen on their computer terminal, medical textbook or television screens.

It was with these considerations in mind that a joint WHO/ICFMA/ECFS/ECFTN workshop looked at the current classification in the International Classification of Diseases 10th edition (ICD10) and found it wanting. A new, broader and more flexible classification was proposed, which it is hoped will find its way into the next edition (ICD11).

In addition, as we expand our knowledge of conditions which are clearly not CF, but in which CFTR muta-

PII: S1569-1993(01)00008-X

tions are common and probably have at least a contribution, the workshop proposed that these diseases (such as CBAVD and some cases of recurrent pancreatitis) should be classified along with CF in the same section of ICD 11, if at least one mutation has been identified. Further, for the first time it provides a code for neonatal hypertrypsinogenaemia where there has not been other evidence of CF, allowing those babies to be recorded and perhaps reviewed. The problem of whether, or how, to inform the parents of CF carriers that they have been detected by the screening test, remains: and it was not part of the workshop's brief to resolve this dilemma, only to provide an appropriate diagnostic code to be used or not, according to local policy.

The Working Group recommendations are reprinted on pages 5 to 8 by kind permission of the World Health Organisation.

J.A. Dodge
Center for Human Genetics, University of Leuven, B-3000, Leuven, Belgium
Els Dequeker
Department of Child Health, University of Wales Swansea, Singleton Hospital, Swansea SA2 8QA, UK