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Reply to Shoemark *et al.* and to Shapiro *et al.*

To the Editor:

We thank Shoemark and colleagues and Shapiro and colleagues for their thoughtful comments in response to our research letter (1). Shoemark and colleagues represent the European Respiratory Society in its positive position about the value of high-speed video microscopy (HVM) in primary ciliary dyskinesia (PCD), and Shapiro and colleagues represent the American Thoracic Society (ATS) in its negative stand with regard to its worth. How can one bridge this Atlantic Ocean difference in guidelines?

We believe that as with any conflict, the solution lies somewhere in the middle and largely depends on individual perspectives. Furthermore, even with guidelines, physicians should use their common sense and clinical judgment and make their decisions individually on a case-by-case basis (2).

Although the reason for the referral of our case was to determine whether the patient had PCD, the question that arose given the results of the HVM was, would there be any value in pursuing further tests in the evaluation, and would further testing, such as genetic and transmission electron microscopy (TEM) evaluations, make a clinical difference and change the management strategy or clinical decisions? We believe that given the HVM results, the decision to not pursue this further was the correct one. First, both genetic microscopy and TEM are susceptible to a high rate of false-negative results. Second, an abnormal TEM would not assist us, as our patient has chronic rhinosinusitis, in which case secondary TEM abnormalities would be highly likely. And lastly, the few pathogenic genes that were suggested as candidates for normal HVM findings (by Shapiro and colleagues) have either a severe or complete lack of cilia (e.g., CCNO and MCIDAS) or have an altered (albeit subtly) ciliary beat pattern (e.g., HYDIN, CCDC164, DNAH9, and GAS8) (3–9). With normal HVM performed in expert hands, these genetic mutations would have been very unlikely.

Despite the fact that both the ATS and European Respiratory Society guidelines advocate a combination of tests for PCD diagnosis rather than a single test, the ATS contradicts itself in its algorithm when it suggests that there is no need to pursue more testing when a single test (nasal nitric oxide) is abnormal for clinical diagnostic purposes in a patient with a compatible clinical presentation (*see* the ATS guidelines in Figure 1). The ATS explicitly states that further pursuit of more tests in these cases is justified only "for prognostic purposes, for further understanding of the disease, and to suggest potential future therapeutic considerations" (10).

As we noted in our research letter, had we followed the ATS guideline and stopped the evaluation after obtaining an abnormal nasal nitric oxide result, we would have incorrectly diagnosed PCD in our patient.

We stand behind our support for performing HVM in the diagnosis of suspected PCD. The evidence for the use of HVM is not limited to anecdotal reports but rather is derived from several studies that demonstrated its value in PCD (11). We understand that HVM has not been in common use in the United States in the past, and we acknowledge the limitations of the test and lack of standardization. However, we believe that rejecting it as a whole is unjustified. Our center has available devices, available

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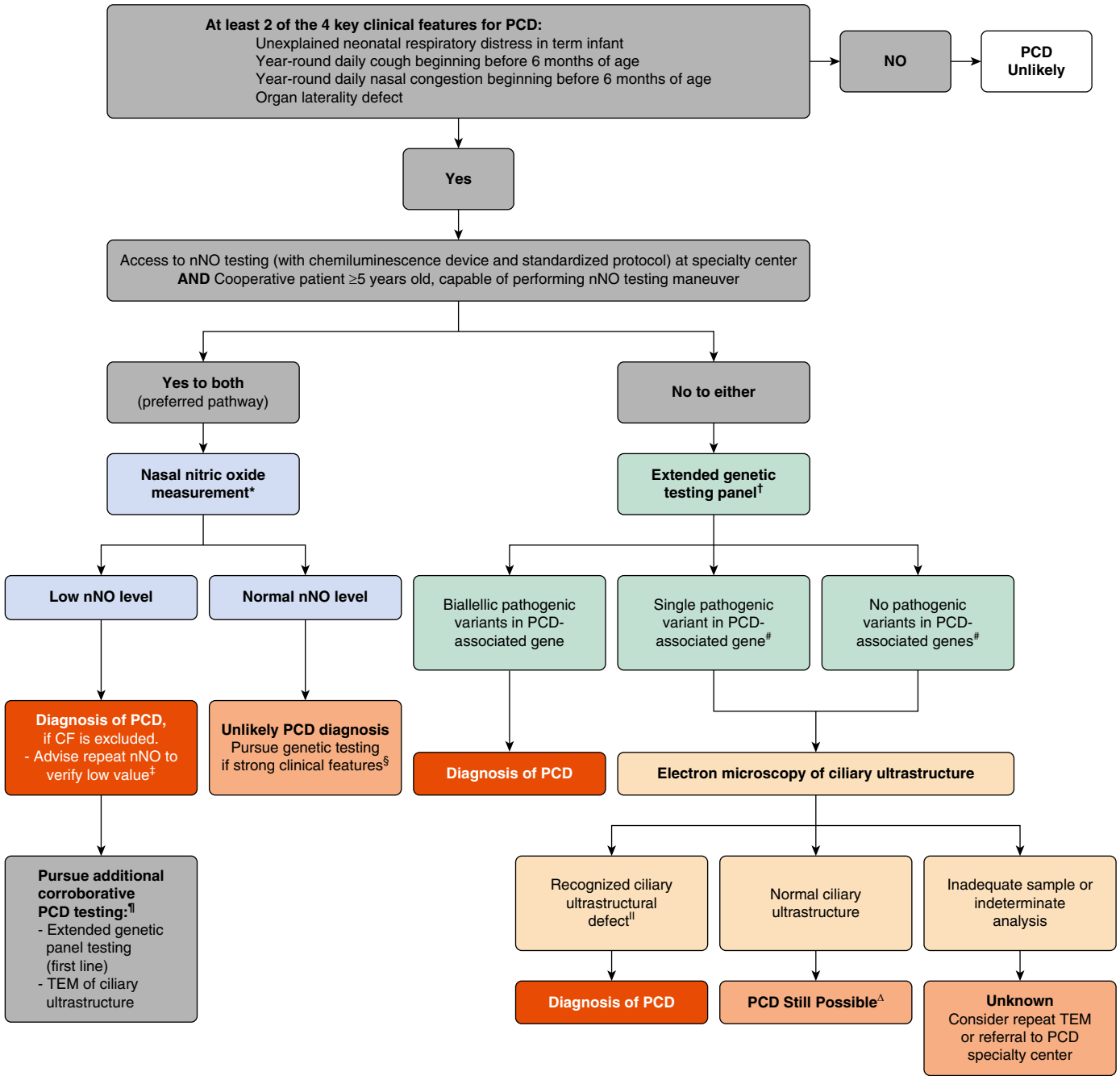

Figure 1. Suggested diagnostic algorithm for evaluating patients with suspected primary ciliary dyskinesia. ¶Additional corroborative testing may provide information on clinical prognosis, further understanding of the disease, and suggest potential future therapeutic considerations. Reprinted from Reference 10. For a complete list of footnote symbols, *see* Figure 1 in Reference 10. CF = cystic fibrosis; nNO = nasal nitric oxide; PCD = primary ciliary dyskinesia; TEM = transmission electron microscopy.

expertise, and available experience to carry out this test, which greatly supports our clinical practice.

Our friends and mentors Drs. Andy Bush and Clair Hogg best described our position long ago: "It is simply not good enough to dismiss videomicroscopy as 'difficult and limited in availability'; if it is the best test, it should be made available. No-one would advocate abandoning the sweat test because unskilled use leads to false positives and negatives, nor should functional ciliary studies be displaced because they are not easy and the equipment is sophisticated" (12). ■

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