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Perspectives on Anemia and Iron Deficiency from the Cystic Fibrosis Care Community

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Anemia and the related problem of iron deficiency are prevalent in people with cystic fibrosis (PwCF) and are associated with worse lung function in adults (1, 2) but curiously not in children (2, 3). Because authors have heterogeneously defined anemia and iron deficiency in CF and humoral inflammatory mediators (i.e., interleukin-6 and hepcidin-25) affect biomarkers of iron homeostasis during CF pulmonary exacerbation (PEx) (4), discourse on these topics has lacked precision and consensus. Although some evidence suggests that oral iron supplementation does not trigger PEx or alter the lung microbiome in PwCF (5), the adverse potential for this treatment to enhance growth of airway pathogens concerns some providers. Uncertainties pertaining to anemia and iron deficiency in CF are surprisingly fundamental and include gaps in knowledge about which tests clinicians use to define these states, whether clinicians who care for adults or children foster similar or disparate opinions about these conditions, whether and to what extent clinicians believe these problems are common, and whether clinicians manage these problems.

Recognizing that no authors had queried CF clinicians about anemia and iron deficiency, we distributed a survey to 325 directors of CF Foundation-accredited centers and programs and to subscribers of the Leadership and Learning and Nutrition listservs hosted by Dartmouth College on behalf of the CF Foundation. We asked each respondent to answer questions with respect to his or her primary scope of practice as a clinician who treated children or adults with CF. We compared differences in the proportions of two groups with respect to a

categorical variable using proportion tests. We performed calculations using STATA MP 15.1 (STATACorp, College Station, TX). A p-value <0.05 was statistically significant.

Ninety-one clinicians completed the survey, 48 of whom (53%) identified as pediatric clinicians and 43 of whom (47%) identified as adult clinicians. Two-thirds of respondents (n = 63) had 15 years of experience treating PwCF. Most respondents (81%) worked at academic institutions that followed between 50 and 300 PwCF. Figure 1 shows the proportions of respondents from a given discipline.

Approximately two-thirds of pediatric clinicians who answered a question about prevalence of anemia in their practice (n = 31) believed that 10% or less of children with CF are anemic. Of the 43 adult clinicians who answered the same question, 30 (70%) believed that at least 11% of adults with CF are anemic. Most (80%) of the 30 adult clinicians who believed that at least 11% of PwCF in their practice are anemic also indicated that at least 11% of those individuals are iron deficient. More pediatric than adult clinicians felt that iron deficiency affects <5% of patients (40% vs. 5%, p = 0.0001). No pediatric clinicians felt that >30% of their patients are iron deficient, but 16% of adult clinicians held this belief (p = 0.004).

We asked clinicians to identify attributes of PwCF who are anemic. Fifty-four clinicians (26 pediatric, 28 adult) selected at least one of nine attributes presented to them in the survey in random order. Low BMI was the most common attribute of anemic PwCF identified by 19 (73%) pediatric and 24 (86%) adult clinicians. Frequent hospitalizations tied with worse lung function for second most common attribute of anemic PwCF among pediatric clinicians (n = 17, 65%) and was the second most common attribute among adult clinicians (n = 21, 75%). Forty-six clinicians thought that anemia causes symptoms in PwCF. Most of them (n = 44, 96%) felt that fatigue was the most prevalent symptom.

Eighty-six (44 pediatric, 42 adult) of the 91 clinicians who completed the survey said that they diagnosed iron deficiency in PwCF. Serum ferritin (Fer) was used most often for this purpose by 38 (86%) out of 44 pediatric and 36 (86%) out of 42 adult clinicians. Twenty-three pediatric (52%) and 31 adult (74%) clinicians used serum iron (p = 0.04 for comparison), and 9 pediatric (20%) and 20 adult (48%) clinicians used transferrin saturation (TSAT) (p = 0.008 for comparison). The median number of tests used by pediatric and adult clinicians, respectively, to diagnose iron deficiency were 3.5 (IQR: 1.5) and 4 (IQR: 2).

Seventy-four respondents said that they had treated anemia in PwCF. Of this total, 71 (96%) had used an oral iron supplement, 26 (35%) had used intravenous iron, 22 (30%) had referred a patient for bronchial artery embolization due to hemoptysis, and 16 (22%) had transfused a patient with packed red blood cells. We asked clinicians whether they had any concerns about treating anemia in PwCF with supplemental iron. Eighty-five clinicians answered this question. Forty of them (47%) had no concerns, 32 of them (38%) had one or more concerns, and 13 of them (16%) did not know or had no opinion. The concern most frequently cited by 22 of the 32 clinicians (69%) with one or more concerns was the possibility that supplemental iron could enhance the growth of lung bacteria.

We sought input from CF clinicians about research priorities. Fifty-nine clinicians (29 adult, 30 pediatric) answered the question, “Should research be conducted to identify strategies to minimize blood loss due to repeated phlebotomy in CF patients?” Adult clinicians were more likely than pediatric clinicians were to affirm that this research should be conducted (66% vs. 23%, $p = 0.001$). Of the 40 adult and 45 pediatric clinicians who identified at least one putative cause of anemia in PwCF, a higher proportion of adult ($n = 22$, 55%) than pediatric ($n = 11$, 24%) clinicians implicated phlebotomy. Eighty-four clinicians (92%) responded to the question, “Should research should be done to identify strategies to diagnose and/or treat anemia in CF patients?” Most respondents answered “Yes” ($n = 67$, 80%).

Our survey of primarily academic, early- to mid-career clinicians who treat either adults or children with CF suggests that their scope of practice strongly influences their opinions about anemia and iron deficiency. Raising awareness of these differences is an important prerequisite to the development of diagnostic and therapeutic strategies for anemia and iron deficiency that maximally benefit PwCF.

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Pediatric Clinicians (n = 48)

■ Pulmonologist
■ Dietitian
■ Associate Provider
■ Gastroenterologist
■ Other

Adult Clinicians (n = 43)

■ Pulmonologist
■ Dietitian
■ Associate Provider
■ Other

Figure 1.
Disciplines of pediatric and adult CF clinicians who completed the Diagnosis and Treatment of Anemia in CF (DATA-CF) survey