Time to make the change from 'primary biliary cirrhosis' to 'primary biliary cholangitis'

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The prognosis of patients with primary biliary cirrhosis (PBC) has improved substantially since the disease was first described >150 years ago by Addison and Gull (1). Over the past three decades, the improvement in transplant-free survival has been mainly driven by the widespread use of ursodeoxycholic acid (UDCA) and the timely detection of disease (2). The moniker 'primary biliary cirrhosis' was adopted in 1950 (3). However, it has been subsequently acknowledged that the use of the term 'cirrhosis' is a misnomer in patients presenting with early stage disease and histological evidence of chronic nonsuppurative destructive cholangitis (4). In early reports, a significant proportion of PBC patients presented with jaundice and decompensated cirrhosis, and virtually all of these patients died from cirrhosis and liver failure within 10 years of their diagnosis (3,5). Now, <50% of patients are documented to develop cirrhosis and the median transplant-free survival of UDCA treated patients is >20 years (2).

Because many patients with PBC do not have and will never develop cirrhosis, this label has understandably upset many patients with PBC, who have now pushed for a change. During the European Association for the Study of Liver Monothematic Conference on Primary Biliary Cirrhosis in May 2014, representatives of patient advocacy groups initiated discussions with hepatologists to change the eponym 'primary biliary cirrhosis' to one that would more accurately reflect the features of the disease. From the patient perspective, the term 'cirrhosis' is misleading on several fronts, and may lead to stigmatization and confusion with alcohol-induced cirrhosis, as well as a lack of clarity concerning the stage of disease and the prognosis. This initiative for a name change was supported by patients around the globe, including members of the PBC Foundation (United Kingdom), the PBCers (United States) and the PBC Society (Canada).

Over the past year, patients and physicians have worked together to achieve a consensus regarding the name change. In a poll involving more than 50 hepatologists from around the world, 95% agreed that the name should be updated, and >80% believed that it would be best to maintain the acronym 'PBC'. Similarly, the vast majority of >1000 patients surveyed supported the name change. Several terms were considered to replace 'cirrhosis', including 'cholestasis' and 'cholangiopathy'. The final consensus was that 'primary biliary cholangitis' provided the most accurate description of the disease, echoing the histological description first coined by Rubin et al (4) in 1965.

Understandably, there is concern that the terms 'primary biliary cholangitis' and 'primary sclerosing cholangitis' (PSC) are now fairly similar, differing in acronym by only a single letter. This may lead to confusion and misinformation, given that patients with either disease may develop biochemical evidence of cholestasis and symptoms of fatigue, pruritus and jaundice. Despite some similarities in presentation, however, there are currently substantial differences in available treatments and prognosis. It is, therefore, imperative that the medical

community strives to minimize inaccuracies and misconceptions that may develop from this initiative.

While this change in terminology more accurately reflects the natural history of PBC in the current era, it also highlights the knowledge gaps in our understanding of PBC. In fact, some hepatologists have raised the concern that 'primary biliary cholangitis' is a non-specific moniker that underscores our lack of understanding of the etiology and pathogenesis of PBC. The risk factors that trigger different phenotypic manifestations of PBC and the response to UDCA therapy are largely unknown. Genome-wide association studies have demonstrated a strong association with human leukocyte antigen alleles and multiple single nucleotide polymorphisms associated with genes along the interleukin-12 axis (6,7). However, the role that specific risk alleles play in PBC has yet to be defined and no risk loci specific to PBC have been identified (7). Whereas several environmental factors have been linked with PBC, including xenobiotics and infectious agents such as proteobacteria and retroviruses, none have categorically been associated with the development of disease (2,7). Clearly, a better grasp of the disease process would lead to a more appropriate name for PBC.

Despite these concerns, it is timely that the Canadian Association for the Study of the Liver and the Canadian Liver Foundation formally recognize the change from 'primary biliary cirrhosis' to 'primary biliary cholangitis' in conjunction with the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. While this revised terminology is, in part, a reflection of our patients' need for more clarity in understanding PBC, we hope that it will also usher in a revolution in the research and management of primary biliary cholangitis.

REFERENCES

1. Addison T, Gull W. On a certain affection of the skin vitiligoidea – α -plana, β -tuberosa. *Gastroenterology* 1851;31:574-82.
2. Poupon R. Primary biliary cirrhosis: a 2010 update. *J Hepatol* 2010;52:745-8.
3. Ahrens EH Jr, Payne MA, Kunkel HG, Eisenmenger WJ, Blondheim SH. Primary biliary cirrhosis. *Medicine (Baltimore)* 1950;29:299-364.
4. Rubin E, Schaffner F, Popper H. Primary biliary cirrhosis. Chronic non-suppurative destructive cholangitis. *Am J Pathol* 1965;46:387-407.
5. Sherlock S. Primary biliary cirrhosis (chronic intrahepatic obstructive jaundice). *Gastroenterology* 1959;37:574-86.
6. Hirschfield GM, Siminovitch KA. Genetics in PBC: What do the "risk genes" teach us? *Clin Rev Allergy Immunol* 2015;48:176-81.
7. Hirschfield GM, Chapman R W, Karlsen TH, Lammert F, Lazaridis KN, Mason AL. The genetics of complex cholestatic disorders. *Gastroenterology* 2013;144:1357-74.

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