Exposing NASH—a disease in stealth mode

Awareness of non-alcoholic steatohepatitis (NASH) and its symptoms is essential for early detection, and an informed public is also more likely to take action against NASH development.

A few weeks ago, at The International Liver Congress in Vienna, the results of a large population-based study in the UK, were presented. The data of the Avon Longitudinal Study of Parents and Children (ALSPAC) show that 20% of the 4,000 young adults (average age of 24 years) included in the study had distinct features of steatosis or non-alcoholic fatty liver disease (NAFLD). Among them, 2.4% also showed signs of liver fibrosis. With an estimated global prevalence of 20–30%, the rise of NAFLD in young people will undoubtedly pose a future challenge for healthcare systems worldwide. However, despite its widespread presence, NAFLD remains virtually unknown to the public. One reason may be that NAFLD is asymptomatic and is usually not diagnosed until it reaches a severe stage, often incidentally through routine blood analyses, abdominal imaging or surgery. Because of its silent nature, increasing awareness of NAFLD/NASH not only among the public but also among clinicians is of great importance.

NAFLD is characterized by ectopic accumulation of lipids within hepatocytes and is often associated with other features of metabolic syndrome such as obesity, insulin resistance and hyperlipidaemia. Although commonly considered a benign condition, NAFLD can progress to NASH, advanced liver fibrosis, cirrhosis and hepatocellular carcinoma. NAFLD is expected to become the primary reason for liver transplantation in the United States by 2020. The aetiology of steatosis is highly complex and depends on a combination of risk factors, including genetics, sex, age, ancestry, comorbidities

(for example, diabetes), environmental factors, lifestyle and diet. Free fatty acids, which are generated by excessive hepatic de novo lipogenesis from dietary carbohydrates or via adipose tissue lipolysis in obesity, are crucial in NASH pathogenesis, thus indicating that obesity and an unhealthy lifestyle are major contributors to the rise of the disease. With the ALSPAC study confirming that overweight and obese young adults are more susceptible to steatosis and liver fibrosis, and given that people with metabolic syndrome are likely to progress to advanced stages or NASH, the rising obesity pandemic among children and young adults is particularly worrying and indicates an urgent need for greater awareness of NASH among the public.

Last year, more than 150 experts issued a call for action against NASH and the current lack of general understanding of the disease. Their manifesto (<https://www.international-nash-day.com/about-international-nash-day/150-world-experts-manifesto/>) was published on the First International NASH Day, which took place on 12 June 2018. The second NASH day, on 12 June 2019, will involve a range of activities, including meetings with patients, conferences for clinicians and awareness campaigns in hospitals worldwide (<https://www.international-nash-day.com/>).

Awareness among the general public, clinicians and public health organizations, including the World Health Organization, is of pivotal importance to stop NASH in its initial phase when it is still reversible through lifestyle interventions, such as a healthful diet and regular exercise. Such

early intervention can be achieved only through patient education.

Simultaneously, investigating the mechanisms of NASH progression to develop new therapies will help people who cannot achieve disease regression. A particularly important question is why only a fraction of people with NAFLD develop liver fibrosis and NASH. Understanding this heterogeneity of progression is essential, because NAFLD will become an economic burden for healthcare systems. Knowing which patients do not need treatment because they are unlikely to develop NASH will aid in prioritizing treatments and managing resources.

Future therapeutic strategies and potential personalized approaches for patients with NASH can be achieved only through concerted efforts among hepatologists, diabetologists, endocrinologists and metabolism researchers to develop safe and efficient drugs. However, of note, disease regression is possible because of the remarkable regenerative capacity of the liver, especially in young adults and in patients with early stage disease. Ultimately, the personal commitments to a healthier lifestyle among the millions of people with NAFLD and NASH will also be essential. Consequently, community-driven initiatives, such as those organized during the International NASH Day, will be crucial in the battle against this silent liver disease. □

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