New Frontiers in Inflammatory Bowel Disease Monitoring

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THE GLOBAL health burden of inflammatory bowel disease (IBD) is increasingly prevalent in today's world, partly due to unhealthy lifestyle choices and growing obesity rates. The remitting and relapsing nature of IBD means treatment is complicated and non-linear. Coupled with the complex interactions between genetic and lifestyle factors, a streamlined approach to treatment is yet to be defined. Nevertheless, there have been huge advancements in the field, with several key publications paving the way in IBD research. Experts at United European Gastroenterology (UEG) Week 2024 highlighted several of the latest key advancements, and hinted at what's to come for IBD management in the coming years.

MODERN INFLAMMATORY BOWEL DISEASE MONITORING

Robert Hirten, Icahn School of Medicine at Mount Sinai, New York, USA, began with a forward-thinking approach to IBD management. In a world driven by technology, non-invasive and wearable-based monitoring is an exciting new frontier in medicine.

The current state of disease monitoring in IBD has two key features. First, care is primarily received in clinical settings, with patients required to make frequent visits to their clinician and attend further appointments for blood tests, stool tests, endoscopies, and imaging. Second, current monitoring in IBD is cross-sectional. At an appointment, the clinician assesses the patient at a single point in time, despite IBD being a complex, chronic, and progressive disease. Thus, Hirten argued, the clinician is forced to build a complicated picture of the patient's health with only snippets of information from each visit. This leads to delays in receiving and interpreting results, and therefore delays in changes to therapy; a challenge given the dynamic remitting and relapsing nature of IBD.

Therefore, Hirten emphasised the need to work towards a dynamic, granular, and longitudinal assessment of IBD. This would include long-term, at-home monitoring of physiological signals, blood markers, activity levels, symptoms, the exposome, and the microbiome. Hirten acknowledged that this is not a novel concept, and has already been applied to other diseases, such as the use of wearable patches for at-home glucose monitoring in patients with diabetes. Currently, the landscape of health wearables is dominated by optical sensors, such as the Apple Watch (Apple, Cupertino, California, USA) or the Fitbit (Fitbit Inc, San Francisco, California, USA), and sweat sensors, a more recent innovation on the rise.

Hirten provided examples to validate his proposal that at-home monitoring with wearable devices is the way forward. By combining machine learning algorithms with heart rate variability data, measured using optical sensors, research has shown that a wearable device can differentiate between inflammatory and non-inflammatory states in patients with IBD.[1] This approach illustrates the feasibility of using wearables to identify, and potentially predict IBD flares, offering an appealing alternative to current monitoring methods that depend on invasive and inconvenient assessments.

> **A wearable device can differentiate between inflammatory and non-inflammatory states in patients with IBD**

On the other hand, sweat sensors detect changes in electrolytes, metabolites, small molecules, proteins, and vitamins using non-invasive sweat patches. In IBD, recent research has demonstrated that sweat sensors can detect elevated expression of calprotectin in patients with active IBD, compared to those in remission, highlighting a strategy for monitoring disease activity and guiding timely interventions in IBD.[2]

Overall, Hirten proposed a remote monitoring paradigm in which select individuals, such as those in remission or starting a new medication, are provided with a wearable device, and the data collected are analysed to assess the likelihood of a flare-up or remission. When a specific threshold, such as the risk of a flare, is reached, both the patient and clinician would be notified, ensuring timely intervention and personalised care.

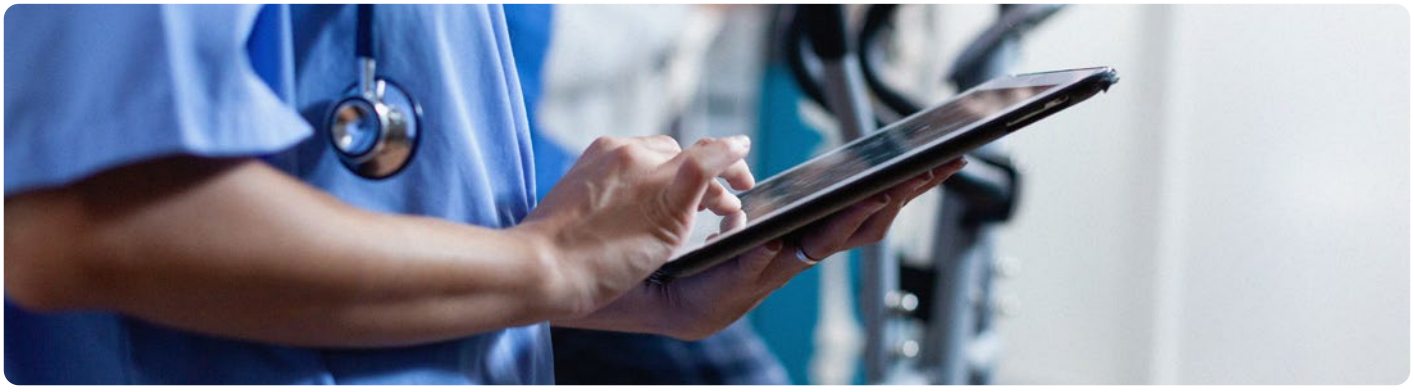
NEW DRUGS ON THE HORIZON

Sreedhar Subramanian, Cambridge University Hospital NHS Foundation Trust, UK, provided a comprehensive summary of new and upcoming developments in drug research for IBD.

Following a period of relative stagnation between 2017–2020, there has been a sudden explosion of new therapeutic agents for IBD, particularly for ulcerative colitis, with even more in the pipeline. Notable emerging therapies include new drugs based on existing mechanisms of action, innovative strategies like combination treatments and bi-specific antibodies, as well as entirely new approaches, including cell-based therapies and microbiota modulation.

One therapeutic with a novel mechanism of action involves antibodies that target tumour necrosis factor-like cytokine 1A (TL1A), a cytokine encoded by the *TNFSF15* gene, which is associated with disease susceptibility and progression. Research behind targeting TL1A has been building for almost two decades, with an emerging body of evidence implicating TL1A in the pathogenesis of IBD. Tulisokibart, a TL1A monoclonal antibody, has been shown to significantly increase the percentage of patients who achieve clinical remission.[3] Similarly, the anti-TL1A antibody PRA023 has demonstrated efficacy in Crohn's disease, where patients receiving PRA023 achieved significantly greater rates of endoscopic response and clinical remission.[4]

Another promising therapeutic strategy involves upregulating anti-inflammatory microRNAs (miRNAs). Interest in miRNAs has surged, especially following the recent awarding of the 2024 Nobel Prize in Physiology or Medicine to Victor Ambros and Gary Ruvkun for their discovery of miRNAs and their groundbreaking work on post-transcriptional gene regulation. Currently, the medical use of microRNAs is limited to diagnostic strategies, but emerging research is expanding the landscape of possibility for miRNA-based therapeutics, although none have yet been approved.



> A diet high in ultra-processed foods has been associated with an increased risk of Crohn's disease, but not ulcerative colitis

Hirten also touched on the recent excitement surrounding JAK inhibitors, and explained that there are more gut-selective JAK inhibitors on the horizon. However, he claimed that a "more interesting" therapeutic agent are TYK2 inhibitors. By selectively inhibiting TYK2 signalling pathways, they interfere with fewer molecular mechanisms, and therefore have a better safety profile.

Hirten concluded his talk with "a note of caution", warning that not all therapies will come to fruition, despite the excitement they may have surrounding them. The downfall of cobitolimod, a TL9 agonist, known for its notable Phase II success, but early termination during Phase III due to lack of efficacy,[5] highlights the need to be "cautiously optimistic about what the pipeline holds". Looking ahead, Hirten identified three key research priorities: discovering new therapeutic targets, deepening our understanding of the mechanisms behind both new and existing drugs, and better understanding individual differences in treatment responses. These steps will help clinicians to select the most effective, personalised strategy for each patient.

LIFESTYLE INTERVENTIONS

Iris Dotan, Rabin Medical Center, Petah Tikva, Israel, wrapped up the meeting with "the most important lecture of this entire session". Whilst showing appreciation for the previous talks, Dotan noted that not all patients will undergo continuous monitoring with wearables, or receive one of the many novel drugs in the pipeline, but all patients with IBD need to address lifestyle factors. In particular, diet, smoking, psychosocial factors, and physical activity levels are considered modifiable factors with the potential to transform patient outcomes.

Doten highlighted research involving approximately 500,000 patients over 12 years that revealed how genetic and lifestyle factors are independently associated with susceptibility to Crohn's disease and ulcerative colitis. The study also demonstrated that adherence to a favourable lifestyle, such as one that doesn't include smoking, but has a diet rich in fruit, vegetables, and fibre, is associated with a nearly 50% reduction in risk of Crohn's disease and ulcerative colitis, even among those high genetic risk.[6]

Adherence to a favourable lifestyle, such as one that doesn't include smoking, but has a diet rich in fruit, vegetables, and fibre, is associated with a nearly 50% reduction in risk of Crohn's disease and ulcerative colitis

Additionally, a diet high in ultra-processed foods has been associated with an increased risk of Crohn's disease, but not ulcerative colitis, she noted.[7] In another study, researchers explored the

profiles of beneficial versus pathogenic microbiome clusters in first-degree relatives of patients with Crohn's disease. Following a Mediterranean-like diet, there were notable alterations in their microbiome, with decreased levels of *Ruminococcin* and *Dorea,* and increased levels of *Faecalibacterium*.[8] Additionally, the Mediterranean-like diet was linked to reduced subclinical gut inflammation, as indicated by lower faecal calprotectin levels.

Doten acknowledged the growing awareness around food avoidance and explained that despite what patients may have been told 10 years ago, being overly restrictive can harm social interactions, lead to nutrient deficiencies, altered microbial composition, fatigue, and impaired quality of life. Instead, clinicians should promote a healthy and diverse Mediterranean diet; one that is evidence-based and avoids unnecessary restrictions.

CONCLUSION

To conclude the session, Doten offered some practical recommendations: adhering to a Mediterranean diet, minimising processed foods, screening for food restrictions and nutritional deficiencies, quitting smoking, increasing physical activity to at least 150 minutes per week, and addressing psychological comorbidities. Stating that many clinicians often overlook these modifiable factors, she advocated for the development of an effective, scalable, long-term lifestyle intervention strategy to potentially alter disease risk and progression.

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