Simerdip Kaur takes a look at the latest ophthalmology-related news stories and asks which are based on facts and which are 'fake news'.

Does a gut-eye axis exist?

Over a decade ago, the Human Microbiome Project was launched by the National Institute of Health in the United States of America following growing interest in the influence of the human microbiome on health and disease. Since then, evidence has shown a correlation between liver and inflammatory bowel disease and colorectal cancers, and gut dysbiosis [1]. It is easy to comprehend the potential association between gut microbe populations and gastrointestinal disease, however, could an organ anatomically as remote as the eye be affected by the gut microbes and if so how?

The microbiome refers to a collection of microbes and their genes within an organism. This includes not only bacteria but also viruses, protozoa and fungi. However, most research has focused predominantly on the bacterial component. The predominant bacterial phylum consists of the Firmicutes and Bacteroidetes species forming over 90% of the population in distal gut. Typically, the human gut is composed of a high ratio of Bacteroidetes to Firmicutes. Bacteroides play a significant role in carbohydrate fermentation and production of short chain fatty acids (SCFA) including butyrate which acts to suppress inflammation. Others include Actinobacteria and Proteobacteria to a much lesser extent, of which the latter is associated with pro-inflammatory states [1].

Gut dysbiosis refers to pathologic transformation in types and populations of microbes leading to adverse interaction of their metabolic products with the host immune system. Consequently, intestinal permeability is heightened – a process often referred to as the 'leaky gut' which allows translocation of bacteria and their metabolic products such as lipopolysaccharides and other pathogen-associated molecular pattern molecules into the blood stream resulting in endotoxaemia [2]. These substances subsequently increase the production of pro-inflammatory cytokines through activation of pattern recognition receptors of the innate immune system cells and ultimately a chronic low grade systemic inflammation manifests [2].

In the field of ophthalmology, Andriessen et al. proved that the incidence of choroidal neovascular membrane (CNV) in predisposed obesity states due to high fat diet intake is associated with altered gut microbiota [2]. In their study, test mice were fed either a regular or high fat diet. At 11 weeks the mice were subjected to laser induced photocoagulation aimed at perforating Bruch's membrane to initiate subretinal blood vessel proliferation from the choroid to mimic neovascular age-related macular degeneration (NV AMD). They observed a 60% increase in incidence of CNV formation in the high fat diet group. They concluded that this was due to dysbiosis resulting from an increase in the ratio of Firmicutes and pro-inflammatory Proteobacteria to Bacteroidetes. Additionally, the high fat diet group demonstrated twice the number of microglia and macrophages at sites of CNV lesions in the retina due to a three-fold increase in intestinal permeability. The presence of these mononuclear phagocytes has been linked to NV AMD disease progression [2].

Besides posterior segment disease, gut microbial dysbiosis can also affect the ocular surface. Researchers from Texas, USA subjected a group of test mice to dessicating stress and a separate group to antibiotic treatment prior to dessicating stress to assess its effects on the intestinal microbiome [3]. The latter group had worse ocular surface disease resembling Sjogren's syndrome (SS) with a reduction of conjunctival Goblet cells, disruption of cornea barrier function and increased expression of inflammatory cytokines, implying a relationship between gut microbiota modification and mucosal surface immunity. They also found that humans with SS have altered diversity in oral and intestinal microbiome, in particular a 50% reduction in Faecalibacterium prausnitzii – of the Firmicutes phylum, another species of a healthy stool microbiome that produces SCFA [3].

Similarly, researchers in Hyderabad, India have demonstrated a difference in the gut bacterial microbiomes of patients with fungal keratitis compared to healthy controls [4]. They analysed fungal and bacterial populations in stool samples of 32 patients with microbiologically-proven fungal keratitis and 31 normal test subjects. No difference was observed in fungal populations between the two groups of patients, however, fungal keratitis patients harboured an increase in pro-inflammatory bacteria such as Enterobacteria, Shigella and Treponema species. As some of the patients with fungal keratitis were on oral anti-fungal and anti-bacterial treatment, further analysis was undertaken to account for this. There was no difference observed in the results, suggesting that gut dysbiosis is linked to the inflammatory process in fungal keratitis patients [4].

It is apparent from mounting evidence that gut dysbiosis contributes to the pathophysiology of various diseases, especially of the eye. However, most data from human microbiome studies are derived from faecal samples used as a proxy for gut microbes. This represents colonic microbes predominantly and less so of the small intestine [1]. Moreover, these studies are not exempt from confounding factors such as the genetic backgrounds and nutritional habits of patients, which unmistakably influences disease prevalence through geographic and corresponding ethnic variation in microbe population and diversity [5]. Similarly, the majority of the research is undertaken in Europe and North America with less representation of the populations in other parts of the world like Asia and Africa for instance [1].

Therapeutic interventions to modify gut microbes via the use of pre and pro-biotics have been trialled. However, there is insufficient evidence of their ability to positively influence gut microbiota in human studies despite some successes in animal models. Furthermore, the use of antibiotics to modulate the intestinal microbiota is not a reasonable option given the risk of microbial resistance [6].

Human microbiome research is undeniably vital in expanding our knowledge and understanding of diseases which will result in a major shift in how we treat our patients in the future.

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SECTION EDITOR

Simerdip Kaur,

Ophthalmology Specialty Trainee Year 3,
KSS Deanery, UK.

E: simerdip.kaur@hotmail.com