Introductions and aims of the day

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Overview

Introduction to the microbiome: The gut microbiome and food safety

6. **Professor Gant (UK Health Security Agency)** introduced his talk by acknowledging the previous work of the COT in this area, which is available on the COT website (Statement on interactions between xenobiotics and the human microbiota and their potential toxicological implications.pdf).

7. The speaker then provided an overview of the gut microbiome in relation to toxicology and food safety.

8. The community of bacterial, viral and fungi microorganisms (called symbionts) is classed into three categories: mutualists (benefit themselves and the host), commensals (benefit themselves but not the host (but do not harm the host)), and pathogens (benefitting themselves but harming the host).

9. In addition to the alimentary canal, such communities are found on any body surface that has a connection with the environment and particularly where conditions are favourable to microbial growth: skin, oral cavity, vagina, lungs.

10. The total diversity of the microbiome is probably about 100 trillion organisms of which we have identified about 1% or less. The gene pool far exceeds that of the host.

11. There are approximately 10^{12} bacteria in 1g of human faeces. The human gut microbiome is thought to be about 8% viral sequences with about 10^{11} viruses per 1g of stool.

12. The number of bacteria in the body is actually of the same order as the number of human cells, and their total mass is about 0.2 kg (Sender et al., 2016). Previously, a ratio of 1:10 for human cells to bacterial cells has been widely reported. New calculations suggest equal bacterial cells to human cells in all of us (approximately $3x10^{13}$ cells).

13. Therefore, it has been suggested that the number of all organisms in the gut exceeds that of human cells in the whole body (Sender et al., 2016), and that this number can be affected by the host's diet and other factors such as age, lifestyle and intake of therapeutics. The type of symbionts present can also change, leading to an unbalanced gut microbiota or dysbiosis.

14. It was noted that the gut microbiome interacts with other organs such as the brain and liver i.e. forming a gut/brain axis and gut/liver axis. Examples of metabolic reactions by the gut microbiome were briefly introduced, some of which are specific to the gut microbiome. These specific reactions can have great importance to risk assessments and can often influence adverse outcome pathways (AOP).

15. The speaker concluded by posing some questions:

- How does our environment affect our microbiome?
- How do genetics affect the microbiome?
- How does the microbiome affect phenotype?

Microbiome manipulation- Government Office (GO) for Science UK Government Review

16. **Dr Chrysi Sergaki (Medicines and Healthcare products Regulatory Agency)** presented on the outcome of the GO Science UK Government Review roundtable discussion held in April 2024 on Microbiome Manipulation via diet, pre-/pro-biotic and other interventions including research gaps.

17. An overview was given highlighting that we are only half human, having more microbial cells than human cells in the body, and cells in the gut are associated with many functions of the human body. Where the balance in the gut microbiome is disturbed, it has been associated with many serious diseases and conditions, such as Parkinson's disease, as well as musculoskeletal, digestive and pulmonary conditions.

18. The presentation then moved on to interventions, which included the discussion at the roundtable that acknowledged the microbiome is highly complex and varied between individuals. It was discussed that we are not able to define "healthy" and "unhealthy" microbiomes as these can look different across different people and gut microbiome compositions. However, it is known that a "healthy" microbiome should be well balanced (both in terms of diversity and co-existence of species) and is associated with the presence of specific bacteria.

19. Pre-biotics and pro-biotics may have different, and sometimes minimal, effects on the gut microbiome due to variability in the microbiome, differences in diet and other characteristics among individuals. There are also variations in biological responses to probiotics among individuals. Actions should be taken to increase public/consumer awareness of these considerations so they can make more informed decisions.

20. It was highlighted as a concern that when the role of the microbiome is discussed in the mainstream media it may not be supported by evidence and public awareness needs to be raised.

21. It was stated that bacteria that are considered to be beneficial can also have negative impacts on health. However, these rare negative impacts should be

weighed against the many positive cases of improved health and reduced disease.

22. It was suggested we need to move towards studying the microbiome and its function / interaction in the body rather than focussing on just taxonomy.

23. The presentation moved on to products with pre- and pro-biotic effects that are currently on the market, however, these can have different effects on different people with varying biological responses. Fermented foods are newly available products, but the literature is sparse and there is concern over antimicrobial resistance (AMR) burden. Not one size fits all, so these products can have different effects depending on an individual's characteristics and differences in diet. The effects can vary with the number of microbial organisms in probiotics and once intervention is stopped the microbiome can go back to its original state.

24. When administered responsibly, faecal microbiota transplantation (FMT) has been shown to help reinstate diversity in the gut microbiome. Use of FMT is regulated in the UK but more research is needed to increase its range of applications.

25. It was noted that knowledge on the microbiome and its importance to human health has been available for over 15 years so why do we not have more products? One of the main issues faced is the lack of consistency in testing/studies which limits the validity of claims, so standardisation is needed. Studies focus mostly on the United States (US) population or other western populations so there is a need for other populations to be included.

26. The research gaps were discussed, and these included the need to define the baseline microbiome e.g. what does the microbiome look like before any interventions to the core diet. Clinical studies have been inconsistently recorded, metabolites and other biomarkers can be used but it is difficult to take accurate measurements, methods for retrieving samples also need improving as currently they are invasive or based on stool samples, while animal studies do not translate well to humans, especially when looking at mechanisms of action.

27. The presentation concluded with current regulatory considerations and what can be done to help to facilitate innovation in the field and to enable translation to products. Suggestions included the need for clear clinical research guidance, especially for dietary pro-biotic and pre-biotic interventions. There are currently a few grey areas when it comes to some products e.g. the borderline between medicine and food and sometimes these products can potentially be covered by two different agencies (MHRA for medicine and Food Standards Agency (FSA) for

food), so clarity is needed.