COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Statement on interactions between xenobiotics and the human microbiota and their potential toxicological implications -Lay Summary

Introduction

1 The human body hosts a wide range of microbes such as bacteria, fungi and viruses (sometimes collectively called the microbiota or the microbiome) , the majority of which are present in the digestive system, largely in the appendix and large intestine. More scientific work has been carried out on the bacteria in the digestive tract than on the other types of organisms, so this paper concentrates on these (and the term microbiota will sometimes be used). Most of the bacteria found in the digestive tract have evolved to live there and we co-exist with them from an early age.

2 Many of the bacetria are beneficial, digesting food and producing vitamins and other essential substances that humans cannot make for themselves, but sometimes they can cause disease. The microbiota are also important because they interact chemically with cells lining the gut to prevent inflammation and the absorption of toxic substances. The gut bacteria and the immune system work together to prevent invasion by disease-causing organisms. Food and the general environment contain chemicals (such as pesticides and heavy metals) that are swallowed, and there is concern that some of these may affect the population balance of the bacteria, killing some types and allowing others to grow more than usual. This effect is called dysbiosis (“dis-by-oh-sis”) . However, assessing the effect of changes caused by chemicals can be difficult since changes can also occur in diseases such as Crohn’s disease, naturally as animals and people age, and with diet, and they may not in all cases be directly associated with any harm to the host.

3 Drugs and other substances (also known as xenobiotics) (“zen-oh-by-otics”) that are deliberately or unknowingly swallowed may affect the gut microbes or be affected by them. For example, antibiotics used to treat bacterial infections elsewhere in the body also kill or affect the growth of the gut bacteria and other drugs may become less effective or more toxic as a result of changes to them caused by the bacteria.

4 These concerns prompted the COT to examine the effects of chemicals from food and the environment on the gut bacteria and the effects of gut bacteria on these

chemicals, and to consider how the risk assessments used to assess the safety of chemicals to consumers address these interactions.

5 Many studies on the effects of chemicals on the gut bacteria have been carried out using mice or rats because the experiments would not be possible or ethical to perform on humans. Experimental animals can be bred and housed in such a way that they are “germ free” and have no gut bacteria. Human bacteria can then be transplanted into their digestive tracts and experiments can be carried out to look at changes in bacteria in live animals (“in vivo”) rather than just grown in the laboratory (“in vitro”). This is as close as animal experiments can get to simulating human gut bacteria, but it is still a “model” rather than a real situation. Differences exist between the animals and humans that make it difficult to draw clear conclusions about the consequences to humans.

6 Experiments in animals have shown that heavy metals (such as lead, arsenic and cadmium), pesticides (such as insecticides and herbicides), antibiotics (such as penicillins and tetracyclines) and a variety of food additives and other substances (such as sweeteners, alcohol and environmental pollutants) can alter the make-up of the bacterial community when consumed at relatively high doses, but how many of these changes might be seen at human dietary levels of the chemicals is unclear.

7 Studies have been carried out to test the effects of chemicals on the bacteria found in humans grown in vitro or have looked at the bacteria in samples of faeces from people exposed to, or treated with, a particular chemical or drug.

8 Faecal samples from people suffering from diseases such as irritable bowel syndrome, diabetes or Crohn’s disease have also been investigated. Changes in the bacterial communities have been noted, but several points need to be taken into account when accessing the significance of the findings:

- A “model” made up of known bacteria is not the same as a whole natural bacterial community, so not all possible effects would be seen and some of the effects may not occur in the whole community;
- Some bacteria cannot be cultured outside the body because they need precise conditions or are “fed” by other species
- Not all of the types of bacteria in the gut come out in the faeces
- It is difficult to decide whether changes seen in a disease are a cause or an effect of the disease, or of any medication taken to treat that disease.
- It is also difficult to determine if a change seen after exposure to a drug or some other substance is an effect that would cause harm to

the host of the bacteria or whether the bacteria have just adjusted to its presence.

9 Although the range of species and number of bacteria in the gut may be affected by exposure to chemicals, there is often sufficient overlap in the functions they perform in an individual that the change in the population may have no ill effect on health.

Risk assessment

10 The assessment of risk is further complicated by the fact that even in healthy animals and people the bacterial population present in the body varies widely between individuals. Using germ-free animals to study the effect of different chemicals on known bacteria allows for some risk assessment but is not easy and, as described above, has its own limitations.

11 New methods are available, such as the so-called “gut on a chip”, which attempts to simulate the conditions found in the digestive system in the lab by growing human cells and bacteria together to create a “3-D” biological model. Here all of the cell types in the gut interact with each other in a similar way to that in a living animal or human. Chemicals can then be added and their effects determined. However, these models are still at a relatively early stage.

12 There is a current trend towards personalised treatment in medicine but there is presently insufficient concrete information about what changes in the gut bacteria constitute a risk to health and which are compensation for chemically-induced stress to enable risk assessment of the effects of a given chemical on an individual via the gut bacteria.

13 The Committee recognises that research is constantly increasing the knowledge and understanding of the gut microbiota and how they relate to human health. It will keep the subject under review, particularly where it applies to chemical risk assessment.