Concluding Remarks

There are number of ingredients to a successful conference which, I hope you will agree with me, existed over the last 3 days, so that a number of concepts have been clarified. We need to thank the organizers, particularly *Philippe Steenhout* and *Wolf Endres*, for putting on a very good conference, particularly under the extremely stressful conditions of having to change the venue within the last 2 weeks. I would also like to thank our speakers for providing very provocative presentations and the participants for very stimulating discussion. The format of providing a short overview followed by extensive discussions is the best way to address the complex topics we considered in this week's conference. *Erika Isolaure* summarized what was discussed today and, if you allow me, I just want to make a couple of observations about the sessions we held on Monday and Tuesday.

In our first session on clinical aspects and definitions, we heard about the changing and increasing incidence of food allergy and I heard a term which I had not heard before, 'the allergic march', which is, I understand, a progression of symptoms over a period of the child's early life after an initial sensitization. From the allergy perspective, we have also learned the complexity of defining allergy and atopy, and that symptoms of allergy, such as dermatitis and asthma, may not necessarily be caused by an IgE-mediated effect, it could be non-IgE-mediated as perhaps it is not even immunologically based, so this is still an area of confusion. We had a particularly insightful presentation by *David Hill* on the prevalence and clinical profile of food allergy and some of his concepts were extremely remarkable. Others suggested that there has been an increase in allergy over the last decade, but he stressed that symptoms need to be carefully documented and defined as allergic in nature, particularly those that are related to the gastrointestinal tract. Of interest and very important, was his showing that eosinophilia and pH probes overlap and may not necessarily prove disease. The other point that *Dr. Hill* made is that it is very important to carefully document disease in your own clinical setting and treat objectively based on the patients seen, in his case in Australia. You can't necessarily generalize to other areas. This concept is very important.

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In the second session on environmental factors we had an excellent description of the 'hygiene hypothesis' and its refinement by one of the originators of the hypothesis. He emphasized the importance of a balance between Th1 and Th2 responses, and that early balance seems to be an important component to a healthy lifestyle as opposed to an allergic lifestyle. There was a very enthusiastic discussion of allergy as an IgE-mediated Th2 response which may be balanced by factors that affect Th1 responsiveness. Finally in this environmental factor session we heard that worm infestation, which is a typical Th2 stimulus, may also protect against allergy. Thus we need to think in terms of other ways that allergy, at least symptomatic responses, can be prevented through counter-regulatory mechanisms with cytokines released, such as IL-10.

In session 3 on oral tolerance, we had a review of the mechanisms of non-responsiveness and some of the experimental observations regarding the counter-regulatory cytokine IL-10 and its effect on IL-13 blocking the actual production of specific IgE instead of symptoms, again in a worm-infested model. We also heard of the importance of innate immunity, not only in producing an appropriate immune response but also oral tolerance. We then had a discussion on gut maturation where regulatory cytokines, such as IL-10 and TGF- β , were very important in modulating the development of appropriate host defense. The fact of establishing oral tolerance in infancy as a developmentally regulated process requires stimulation by actual colonization and an important component of this is how the antigen-presenting cell functions. A very salient point was made that the timing of exposure to antigens may be a very important means of preventing the so-called 'allergic march'.

Finally, in the session on microbial-gut interaction it was emphasized that there is a need for early appropriate colonization for normal development of host defense, and that with inappropriate colonization under conditions of an immature gut it may result in an adverse effect which leads to disease. Then, as a substitute for the original speaker, we had a lecture emphasizing that the means by which we measure intestinal flora as a reflection of the microbiota that colonize the gut appears to cover only a fraction of what actually exists within the gut. Stool cultures really don't tell you the whole story of colonization, so we need to find new ways of quantifying bacteria. We need also to utilize some of the new molecular techniques in identifying bacteria to get a better sense of where we stand. This was addressed in the context of colonizing bacteria which may be different in atopic compared to nonatopic patients, and that colonizing bacteria differ less than they used to with regard to formula versus breast-feeding. A very interesting observation that hydrolysate seems to produce colonization that is more similar to breast milk was made. However, the bottom line is we need more research.

Again I would like to thank everyone for participating. This has been a very fruitful and well-discussed conference and hopefully we now have some 'food for thought' for additional studies. Thank you.

Allan Walker

It is a great pleasure to see you here at the closure of this conference and, although I was not able to attend last week, it is clear that this has been a successful conference because most of you are still awake and sitting straight, which are usually good signs. I thank you for your flexibility in the change of venue from such a nice location in Malaysia to Switzerland, and I hope you have not been too disappointed by the weather and the surroundings here. I am sure you have not been disappointed here at the laboratory.

I have worked here myself for a year and half, and every day I walk into the building with a smile on my face because without a doubt it is the most beautiful laboratory in the world. In addition, as you have noticed this is a very nice room and the kitchen staff is also one of the best in Switzerland. So I take this opportunity to give you two messages to convince you of the fact that, scientifically speaking, we are perhaps not the best but among the best in the world and certainly the most complete laboratory when it comes to nutrition.

The first message I have to give you is that we are not alone. This is the R of the Nestlé R&D system. So research takes place here and, as you can see, the map contains many dots which stand for our polytechnology centers, the research centers that are individually devoted to a product category: there is one for water in Vittel for instance, one for dairy in Konolfingen here, coffee in Orbe, and so on all around the world. The second set of dots are R&D centers where we adapt our products to the local conditions of a country or the local conditions of a whole part of the world. We also do the opposite: we try to obtain local knowledge, local experts who we use all over the world. So the dot here is our laboratory in Singapore for instance, and this one our laboratory in Shanghai which is growing very rapidly.

Here in Vevey there are about 570 people, and I should say we are not here alone. We also have active collaborations outside with the scientific community at various universities and institutions all over the world, and to be able to do that we also have to provide very good science. Last year with these 300 scientists, we had more than 200 scientific publications, and this is a level that we keep up regularly in addition to all the work that we don't publish and keep secret.

The second message is what do we do here. All 570 of us work on various aspects of nutrition. We have a very large department of food science in which we work on things like texture, structure, how the ingredients behave, how we can keep them stable. Food safety of course is a very important

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aspect and we have about 100 people working on this with special emphasis on new solutions. When we eat food, when food meets the consumer, the consumer can be a human, can be a pet, but the food has to be tasteful and the consumer must take pleasure from eating it. So we have a large group of people looking into flavor in terms of molecules, receptors for tasting, and how these signals reach the brain. The same group of people then look at the responses from the consumer. Another topic is satiety: how can we stop people from eating too much, and how can we increase their appetite if they don't eat enough.

And then of course, human nutrition itself. I will take very big steps to where we see our targets in the future. Firstly we look at bioavailability, indisposition, and it is amazing how many common nutrients, ingredients there are. We don't know how well they are absorbed and where indisposition takes place. Secondly if we think about Nestlé as a food company, ingredients are usually preparatory to the point at which they reach the alimentary canal. When they cross the gastrointestinal barrier they are anybody's ingredients. Up to this point they can be ours, and bioavailability is one way of providing some preparatoriness to our products. Thirdly, of course, health effects and their biomarkers are very important, and here we have the newest techniques available today, we work with genomics.

The last point, one that I very much believe in, is individual variation in the future. We are all different as we sit here and of course we all have different needs for certain ingredients. So although it may seem far away to talk about a passport for everybody to show how much they need to eat, this can sometimes be very dangerous by providing different frozen meals for women or for men. So this is where we see the future developing.

I should thank several people in particular for bringing you here: in the first place *Pierre Guesry* who you already met, *Barbara Marchesini*, and *Sylvie Helfer* and her people. So thank you all once again and have a nice dinner and then a good trip home. Thank you very much.

Peter Van Bladeren