

21 patents
14 licences
9 European projects
concerning the links
between food and nutrition
and health at INRA *

FOOD, NUTRITION AND HEALTH

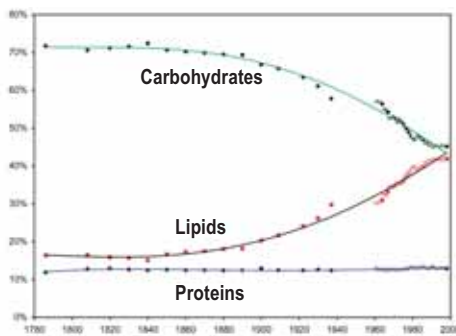


The prolongation of life expectancy in developed countries has been accelerating during recent decades. Advances in hygiene (particularly food-related) and defences against infectious diseases (vaccines and antibiotics) have, in particular, enabled a drastic

reduction in premature (infantile) deaths. However, this trend has given way to other, more chronic conditions, which are often diet-related. The sad quartet of obesity, diabetes, cardiovascular disease and cancer is gathering pace at an alarming rate. The solution seems simple: reduce the amount of food we eat! In fact, analysis of this question reveals intricate relationships between numerous factors: the complexity of foods, their multiple combinations in a varied diet and the complexity of their effects on health as a function of the physiological, genetic or sociological environment of individuals. Understanding this gigantic puzzle has proved to be a major challenge for research. The stakes are high because food and nutrition is undoubtedly the principal – or perhaps the only – lever we can use to act against the growth of these chronic diseases and the costs they imply.

Xavier Leverve
Scientific Director, Human Nutrition
and Food Safety

Dietary changes between 1780 and 2000



(from P. Combris)

From a little-varied, high carbohydrate and low lipid diet, we have moved to a varied diet which contains too many lipids. The National Nutrition and Health Programme recommends a 30% lower calorie intake.

* data 2005

FIGURES FOR FRANCE

In 2004, **life expectancy** exceeded 80 years (76.7 years for men and 83.8 years for women), or 10 months longer than in 2002.

(Source: INED)

14.8%: **the share of food** in household expenditure in 2002 (Source: INSEE 2006).

In 2003, **obesity** affected 11.3% of adults, or 5.4 million obese adults (body mass index >30); 14.4 million adults were overweight (BMI between 25 and 30). (Source: Obépi) Prevalence in children rose from 2.4% in 1990 to 3.9% in 2001.

The direct and indirect costs (disease) of obesity or overweight have been evaluated at between 2% and 7% of the national public health budget. (Source ANC 2005)

INRA-INSERM COLLABORATION IN HUMAN NUTRITION

Arnaud Basdevant, Professor of Nutrition at Hôtel Dieu and advisor to INSERM, is one of the architects of the INRA-INSERM collaboration.

What can be gained by this union of strengths?

Arnaud Basdevant: From the first joint actions to the current ANR (French National Research Agency) research programme on food and nutrition, INRA and INSERM have tried to create cross-disciplinary and inter-agency links to facilitate access to biological and epidemiological resources and enable teams to attain an international reputation; in short, to decompartmentalize! Bridges have thus been created between fundamental, human and social sciences, enabling the confrontation of views between researchers, experts, consumers and industry. This gamble has paid off: networks have been set up and we can now measure the structural effects and impetus achieved.

Research in human nutrition needed this openness and these links between the respective research areas of INSERM and INRA. For example, if we want to determine the consumption of fish by pregnant women, we need to know not only how the consumer perceives contradictory messages concerning the benefits of fish and the risks involved (contamination by heavy metals), and how we can envisage modelling tools and methods to evaluate and manage this public health question. Such projects also require input from experts in toxicology and sociology.

Which areas should be targeted in the future?

A. B.: We need to provide more support for emerging teams and young researchers, to identify more clearly the resources and technological platforms required. In the context of the Centres for Research in Human Nutrition (CRNH), the possibilities for investigation are now considerable. Public/private collaborations can be developed. Openness towards Europe is now a priority. An initial analysis with our European colleagues has shown that the programmes managed by INRA and INSERM are precursors in terms of the level of collaboration between researchers and the advances they have achieved in their thinking on different themes.

GLOSSARY

Allergenicity: sensitivity to a substance (allergen) which determines or favours allergy.

Epigenetics: modifications to the activity of genes which are not coded by the DNA sequence

Epidemiological study: a study performed in a large group of individuals which demonstrates the links existing between diseases and various factors linked to lifestyle, environment, individual characteristics, etc.

New scientific approaches to study the links between food and health

Research on food and nutrition at INRA aims to understand the role of food in maintaining humans in good health, and beyond that to procure well-being. This work has seen considerable development, for several reasons. Dietary behaviours are highly diverse, and it is difficult to evaluate their consequences in the long term. In parallel, it has been seen that the gene pool of each individual influences his or her specific biological response to foods, and the expression of this gene pool is modulated by nutrients, the intestinal flora, intoxications, etc. Without forgetting the fact that scientists find it difficult to extrapolate to man the effects of nutrients proven in animals. Finally, although consumers are globally aware that their health depends on their dietary habits, and although they are acquainted with the main dietary guidelines, this does not suffice to ensure that they apply them.

To be understood, these situations require new tools, new research strategies and new skills. These are gradually, and actively, being developed at INRA. Alongside traditional research, studies are being carried in healthy humans in

“To understand the role of food in maintaining humans in good health, and beyond that to procure well-being”



Patrick Étievant, Head of the Food and Human Nutrition Department at INRA

Centres for Research in Human Nutrition (CRNH), and – thanks to animal genetics – animal models more representative of humans are being employed. In addition to acquiring knowledge on nutrients taken in isolation (lipids, carbohydrates, proteins, micronutrients), the aim is also to analyse the combined effects of these different components in the diet and during meals on the major physiological functions (digestive, motor, cognitive, cardiovascular, etc.), on mood disorders and on gene expression. Finally, it is necessary to observe and measure the long-term effects of different types of dietary behaviour while taking account of individual variations.

A technology platform to study the metabolome

The effect of a nutrient or molecule on the functioning of a cell or organism has traditionally been studied by adopting physiological, metabolic and genetic approaches. Today, research in nutrition can call upon "high-throughput" tools,

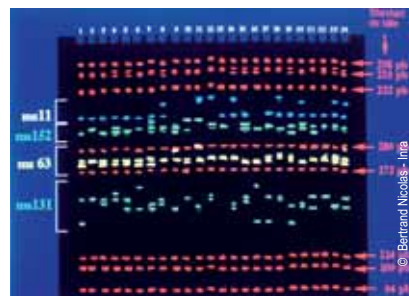


Photo of a display unit showing a DNA sequence

such as metabolomics. This provides a global view (in the blood or urine) of the thousands of molecules which are produced by enzymes as a result of gene activation. This approach enables the identification of all metabolites.

In Clermont-Ferrand, a mass spectrometry platform enables study of this metabolome. The protective effects of micronutrients, and determination of the early signals of obesity and its metabolic dysfunctions, can be analysed. For these approaches to be pertinent, they must be based on major databases, which is made possible by our participation in the European NUGO (European Nutrigenomics Organisation) network.

Jean-Louis Sebedio

Intestinal flora: all bacteria living in the digestive tract.

Metabolite: molecule produced during the chemical and biological transformations which occur within an organism.

Métabolome : ensemble des métabolites produits par les cellules.

Intestinal metagenome: genomes

of all bacteria comprising the intestinal flora.

Nutrigenomics: study of interactions between nutrients and genes.

Nutrient: Product of the digestion of foods or substances that can be directly assimilated by the body.

Oligosaccharide: molecule made up of 2 to 4 simple sugars.

DIETARY BEHAVIOUR



Serge Hercberg
Director of the Ile-de-France Centre
for Research in Human Nutrition

The study of dietary behaviour is a recent scientific approach and is based on the observation that our diet cannot be defined as a sum of nutrients. This work requires a global approach, in which behaviour is a key factor. The aim of the Ile-de-France Centre for Research in Human Nutrition is to analyse dietary behaviour and consumption, to study their determining factors and their effects on nutritional status and health, and to evaluate strategies for prevention, communication and education in nutrition.

This research requires a grouping of skills ranging from epidemiology, clinical research, sociology, economics, physiology, genetics and pedagogics, etc. Several methodological tools are available to carry out these analyses. Epidemiological studies generate databanks on diet and health, such as the Suvimax study which is based on a sample of 13,000 people who have been followed for more than 10 years. Consumer panels enable economic analyses. Finally, clinical studies in healthy volunteers supplement our approaches: the effects of an induced modification to behaviour, or the role of certain determinants (e.g. portion size, eating in front of the television, etc.). The Ile-de-France CRNH works in the context of a study centre for healthy volunteers and an outpatient investigation unit.



THE DIGESTIVE SYSTEM AND WELL-BEING



Jean Fioramonti
Deputy Director of the Food
and Human Nutrition Department,
based at the INRA centre in Toulouse

Our research on the digestive system focuses on the intestinal wall and intestinal flora, the latter constituting the essential vector for a dialogue between food and our bodies. We are studying the interactions between flora, foods and the digestive tract which cause discomfort (stomach ache, distension) or well-being (correction of lactose intolerance, for example). We have noted that some dietary components – in principle neutral – may become harmful or beneficial after they have been transformed by the intestinal flora. Research has received new impetus with the prospect of sequencing the metagenome of intestinal flora.

In Toulouse, my team is working on visceral sensitivity and the immune system. By their very nature, the digestive contents and intestinal flora maintain a latent inflammatory state: 15% to 20% of the population present with digestive function disorders, which mainly cause stomach aches. The aim is to attenuate this sensitivity but without affecting the "silent" sensitivity which is at the origin of major physiological regulatory mechanisms.

At present, our studies are focusing on the neonatal period; digestive disorders during that period of life can have consequences until adulthood.

80% of the immune cells in the body belong to the digestive tract

ALLERGIC PHENOMENA



Sandra Denery
Scientist in the Research Unit
on Biopolymers – Interactions
and Assemblies

With particular regard to wheat, my research team is looking at food allergies using various approaches. One focuses on the identification of allergens. In collaboration with clinical teams, we are analysing the serum of allergic patients using ELISA and cellular tests. By working in a more in vivo context, these tests enable a clearer understanding of allergens. Another approach concerns technological sequences. Some treatments applied during food processing modify proteins and can also diminish or increase the allergenicity of the final product. Based on

knowledge of these allergens, our research is trying to understand and reduce this allergenicity. It is generating opportunities for clinicians to improve the management of patients. In the case of the

apple, for example, we now have sufficient research experience to be able to distinguish between several families of allergens, one of which is destroyed by heat (compote). Researchers in the Netherlands have also bred apples with a low allergen content.

With respect to wheat, our research is more recent. The same approach regarding the identification of allergising proteins has enabled improvements in the diagnosis of dietary allergy to wheat. Furthermore, INRA has launched a breeding programme for wheat varieties which do not contain certain allergens but retain their bread-making potential.

DIET DURING THE PRENATAL AND POSTNATAL PERIODS LEAVES A NUTRITIONAL "FINGERPRINT"



Dominique Darmaun
Director of the INRA-University
of Nantes Joint Research Unit for the
Physiology of Nutritional Adaptations
in Humans

During the last trimester of pregnancy, the weight of the foetus triples; after birth, the baby's weight triples again within one year. This rapid growth reflects the long-acknowledged impact of perinatal nutrition. In recent years, health indicators have also been determined: epidemiological studies have indeed demonstrated a correlation between a low birth weight (a sign of under-nutrition in utero) and an increased risk of obesity, cardiovascular disease, diabetes,

hypertension or cancer during adulthood. Similarly, several studies have suggested that the diet during the first few months of postnatal life influences the subsequent risk of obesity or diabetes. Exposure to certain nutrients (or their deficiency) during the perinatal period leaves a metabolic "fingerprint" which will have consequences upon health during adulthood. The mechanisms involved are not known. An INRA team of neurophysiologists in Nantes is currently studying the possibility of epigenetic modifications to part of our brain (the hypothalamus) which could generate long-term disturbances to the regulation of food intake. Although our early diet affects the maturation of all organs, its effects on the intestine – the key organ in nutrition – remains unclear. These effects are being studied by another team of researchers.

We are initiating experimental and clinical studies in this area thanks to the presence of neonatal specialists in our research unit. In particular, the aims are to measure the consequences of the neonatal intake of several nutrients from breast and artificial milks: firstly, the role of oligosaccharides, which have a major impact on the colon and are specific to breast milk, and secondly, the role of certain proteins, the levels of which are increased in formula milk when compared with breast milk, in order to accelerate growth. And although it is traditional to ensure that low birth-weight infants to make up their growth deficiency as rapidly as possible, scientific controversy is now increasing as to whether this accelerated growth may not have negative, long-term effects on several organs in the future adult.

A RESEARCH UNIT ON CONSUMER BEHAVIOUR



Set up in 1990 as part of the Social Sciences Department (SAE2), the Consumption Research Laboratory (Corela – Ivry-sur-Seine) aims to identify and analyse the factors affecting consumption and dietary practices. The unit contains seven economists, five sociologists and two historians, who combine theoretical thinking, methodological studies and empirical analyses. The problems studied include: analyses of markets and products, dietary practices, standards and policies and the links between social, dietary and health inequalities. Today, research also addresses the public health concerns linked to food safety and the development of chronic diseases of dietary origin. We thus are analysing how information on risks is taken into account in consumer choices, and the effects of nutritional guidelines. In addition, we are studying the behaviour of populations under major stress (precarious living conditions) and the social determinants of obesity. Research also aims to improve the implementation of public health policies, and particularly the national Nutrition and Health Programme. This work is being carried out in the context of the Observatory on Food Consumption at the Ile-de-France Centre for Research in Human Nutrition (CRNH).

France Caillavet, directrice du Corela

POLNUTRITION

The "Polnutrition" research project funded by the ANR (French National Research Agency) is contributing to the implementation of integrated public health policies. It is studying the links between agricultural and nutritional policies in the context of two food sectors: fruits and vegetables on the one hand and sugar on the other. The project is evaluating changes in consumption caused by actions on prices, the nutritional qualities of products and the information available to consumers. The results should enable the compilation of recommendations with respect to government intervention. Corela is a partner in the project, which is being coordinated by Philippe Bontems, Research Director at INRA in Toulouse.

RESEARCH UNITS FOCUSED ON NUTRITION AND HEALTH

INRA Units and Joint Research Units with other agencies



A FEW PROGRAMMES

In the context of the French National Research Agency (ANR)

- **Polnutrition**: impact of government policies and food industry regulations on consumption (coordinated by INRA in Toulouse).
- **TransQual**: comparison between trans fatty acids of natural and technological origins in the dairy food chain (coordinated by INRA in Theix and the University of Clermont).
- **MitHyCal**: effects of a high-calorie diet on mitochondrial activity and implications regarding obesity and metabolic syndrome

(coordinated by INRA-University of Montpellier).

- **Prot Neonat**: effects of high-protein neonatal nutrition on intestinal, renal and hypothalamic maturation and long-term consequences (coordinated by INRA and University of Nantes).
- **Compalimage**: nutritional epidemiology programme on dietary behaviour and the quality of ageing (coordinated by INRA-INSERM and the CNAM Ile-de-France).
- **Nutrisens**: analysis of the impact of dietary imbalances by detecting

nutrients with an effect on the control of dietary intake (coordinated by CNRS in Toulouse).

At a European level

Nugo (European Nutrigenomics Organisation) is a Network of Excellence (Rex) which involves 33 European partners who have committed to integrating their research in nutrigenomics, notably by setting up a common database for their scientific findings (coordinated by the University of Wageningen in the Netherlands, 2004-2009).

A FEW RESULTS

- A leucine-supplemented diet has beneficial effects on muscle mass during ageing.
- Crohn's disease appears to be linked to a reduction in the diversity of intestinal flora.
- The high omega 3 content in fish flesh endows

it with beneficial effects on human health.
- A detector for dietary deficiencies has been discovered in the brain.
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