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International Conference on Health Benefits of Mediterranean diet

Obesity and Type II Diabetes Prevention

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EGEA

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International Conference on Health Benefits of Mediterranean diet

Obesity and Type II Diabetes Prevention

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Preface

Over the years, researchers and public health authorities throughout the world have sought to identify food, nutritional or behavioural factors that are likely to play a role as either risk factors, or protective factors in the determinism of illness and health quality. Several studies developed on cellular, organ, healthy and unhealthy subject, or population models have been carried out during the last 30 years. If, in several cases, the existence of a link between "nutritional" exposure and certain illnesses cannot (for the moment) be asserted by the available arguments, in other cases, on the contrary, the convergence of arguments is such that a consensus can be reached.

The possible health benefits associated with a Mediterranean diet, based on epidemiological studies, were raised more than 15 years ago. Thus, in relation to cardiovascular conditions, the famous Keys international study (1986) on 16 cohorts, throughout 7 countries, highlighted a lower cholesterol level and a lower cardiovascular mortality rate in Mediterranean countries compared with countries in Northern Europe and America. The prospective MONICA study (1994) has shown a lower incidence of coronary conditions in the South of France and in the region of Barcelona (Catalonia, Spain). In relation to cancer, descriptive studies of mortality or incidence rates have also found lower rates in Mediterranean countries, notably in the case of colon cancer and breast cancer. Other conditions seem to benefit from food and nutrients contained in Mediterranean diets: osteoporosis, cataract, deterioration in cognitive functions as part of ageing… Finally, if one considers life expectancy beyond 65 years of age, 4 countries from Southern Europe are grouped together just behind Sweden, which benefits from high social standards: France, Greece, Italy and Spain.

The EGEA International Conference, organised this year in the beautiful city of Perpignan, is taking stock of the situation in relation to certain aspects of the health benefits associated with Mediterranean diet, by specifically taking an interest in obesity and diabetes, which also constitute a major public health problem. The world's best specialists, from mechanistic research to epidemiological studies, have pooled together to paint a very comprehensive assessment of scientific knowledge in these domains, justifying the recommended basis that provides, or will provide, the platform for developed nutritional policy in several countries.

Above all, this Conference demonstrates that we now have at our disposal, a wealth of scientific data highlighting the fact that Mediterranean diet constitutes a set of balanced practices and behaviours that are very favourable to personal health, and which have the extraordinary advantage of associating health, pleasure and conviviality. A useful and superb model for public health managers !

Serge HERCBERG
Director of the U557 INSERM (UMR Inserm/Inra/Cnam) : Nutritional Epidemiology, and of the Monitiring and Nutritional Epidemiology Unit (InVS/Cnam) (Paris, France) and Vice-Chairman of the Strategic Committee in charge of the French National Program "Nutrition and Health" (PNNS) (2001-2005)

An official opening talk was held prior to the scientific lectures
on Wednesday, May 12th, 2004, featuring :

Mr Laurent Damiens, Director of Aprifel
and Ms Saida Barnat, Head of the Scientific Department of Aprifel,
who welcomed their distinguished guests before giving the floor to :
Mr Jean Sales, a vegetable producer in Perpignan city and President
of the French National Fruits, vegetables and horticulture board (ONIFLHOR)
and Ms Gisèle Rossat-Mignot, councillor of Mr Hervé Gaymard,
Ministry of Agriculture, in the field of food and sanitary safety

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Obesity and type II diabetes prevention : What has been done ? Where do we stand ?

Philippe VAGUE
Department of Nutrition-Endocrinology-Metabolic Diseases, University Hospital of Timone, Marseille, France

The first EGEAconference focused on the possible effects of the Mediterranean diet in terms of cardiovascular diseases and cancer prevention. This time, it will look into health benefits of Mediterranean diets for obesity and type II diabetes prevention. Adam Drewnowski has previously presented nutritional aspects of the issue. I would like to talk about issues brought about by the rise of type II diabetes, obesity and its prevention over the world.

According to the International Federation for Diabetes, 2003, there were 189 million people living with diabetes in 2003, and it is estimated that this figure should increase by 72 % in 20 years, to reach 324 millions. This increase should vary from one region to another: it is expected to reach 58 % in North America, even more in South America, much less in Europe, much more In Africa, the Middle-East (as defined by the International Federation for Diabetes), Australia and Asia. Why? Obviously because there is less obesity in some developed or rich countries than others. There will be a smaller number of obese people and thus a smaller incidence of diabetes. Other countries will access a higher standard of living and more low-cost food, which will result in a higher number of obese people and diabetics. In fact, we know that type II diabetes depends on weight and obesity on the one hand, and a more sedentary way of life on the other hand, which is due to mechanization all over the world and its adverse effect on physical activity.

Type II diabetes is an important issue that grows bigger with time. If no appropriate action is undertaken to stop the dramatic increase, this is what is going to happen. Yet we are capable of action. If we work to promote global public health through proper economic and political actions, we should be able to avoid such evolution. As I said, the prevalence of diabetes (and consecutive cardiovascular mortality) will grow in the future mostly because of the growing importance of obesity all over the world, with differences from one country to another. I am stressing this aspect because political and economic differences among countries and health systems prove determining in the fight against those phenomena. Actually, genetics does not vary much from a country to another. In the 20th century, human beings adapt to their environment more or less in the same way everywhere. Differences among countries are due to discrepancies among economic bases, i.e. levels of development and financial standards as well as health systems.

In this introduction, I would like to show you the importance of obesity through a French study that discriminates men and women. The prevalence of obesity increases with age. In France, over 10 % of men over 60 are obese with a BMI above 30. The figures are very similar between 1980 and 1991: the prevalence of obesity has not increased for men. As for women, results are quite similar, except for younger women (age 20-40) whose obesity rates have almost doubled between 1980 and 1991. The prevalence of obesity remains significant in France as elsewhere. We can notice a geographical discrepancy in overweight. In France, if we compare the regions of Haute-Garonne (South-West), Lille (North) and Bas-Rhin (North-East), there is a lower prevalence of overweight in the Southwest than in other regions. This has many causes. Firstly, financial resources are higher in the South than in the North and perhaps also Northeast. Besides, nutritional habits are different: Southwestern diets are closer to the traditional Mediterranean diet.

There are also great discrepancies within Europe, as shown in the comparison of the UK, Finland, former GDR (German Democratic Republic), the Netherlands and France. As for women, the prevalence of obesity remains moderate in the Netherlands: it has not increased between 1987 and 1995. In the UK, it has almost doubled during the period. In Finland and former GDR, it remained stable. As far as men are concerned, figures are quite similar. Examining the evolution of obesity prevalence in several countries may help to adapt public health measures. Between 1975 and 1995, the prevalence of obesity (BMI >30) in men and women dramatically increased in the USAand Germany. On the contrary, in the Netherlands, France and Sweden, the trend slightly drops down. This allows forecasting that the epidemic of obesity may spread quickly in Germany, the UK and the USA but much more slowly in the other countries. It will therefore be easier to take efficient public health measures in those countries. Nevertheless, such measures will prove much more necessary in the USAand Germany.

These observations (global evolution of dietary trends, obvious connections between nutritional habits, income and body weight, worrying yet variable prevalence of type II diabetes and obesity over the world) will guide us through this three-day conference and its six sessions. Tomorrow morning, we will focus on obesity and type II diabetes, multi-factorial diseases, in order to understand why a person becomes obese and possibly diabetic. During the second session, we will tackle Mediterranean diet and the role of fruit and vegetables in body weight management and obesity prevention. In the third session, we will concentrate on child obesity and type II diabetes prevention. I would like to comment shortly on this point: a few years ago, we used to think that childhood diabetes was a regular type I insulin-dependent diabetes, called juvenile diabetes. Obese diabetes, type II diabetes, was called adult diabetes. This distinction is no longer valid: we know that many children suffer from type II diabetes today, since there are more and more obese children. Prevention of children obesity plays an extremely important role in the protection against long-term diseases. It is therefore crucial to focus carefully on children, from the side of therapists as well as public health specialists. During the fourth session we will handle overweight and obesity, and the ways to avoid obesity in overweight people. We will conclude by setting nutritional recommendations on how to adapt the so-called traditional Mediterranean diet to our modern lifestyle.

I hope that, in the coming days, we will contribute to better identify ways to solve the issues we are all already aware of.

Global dietary trends and the nutrition transition

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My talk has to do with global dietary trends and the nutrition transition. As I have mentioned, we are in the middle of a global obesity crisis, which is much more severe in the United States than it is elsewhere. There are a number of socio-economic factors to this crisis, which I will deal with in due course. What I want to show you in this slide is the relationship between incomes and overweight.

What you see here, is a slide from the World Bank showing the distribution of incomes. Of course, the European Union, United States, Canada, and Australia are the richest nations, and the poorest nations are in the Indian sub-continent and Africa. Notice that incomes are related to higher obesity rates. What you see are decreasing rates of underweight in developed nations, higher rates of overweight and the highest rates of obesity.

But there is a paradox. Within poorer nations, it is the richer people who are obese; within the richer nations, it is the poor. The burden of obesity in the United States – and in France and elsewhere – falls disproportionately on ethnic minorities and the working poor. We therefore have a paradox: on the one hand we have developing nations increasing both longevity and the rate of chronic disease, which is hitting the richer sub-groups within them, and on the other hand we have the rich nations, where the problem of obesity resides with the poor.

Let me explain very briefly what we mean by the term 'nutrition transition.' Nutrition transition occurs if incomes rise and populations become more urban. It reflects the shift from an agricultural society to a more urbanised, industrial society. At the same time as the nutrition transition occurs, demographic shifts take place: life expectancy increases and fertility rates drop.

The epidemiological transition means that disease rates shift from infectious disease towards higher rates of diet-associated chronic disease – mainly obesity, cardio-vascular disease and some forms of cancer. So there is clearly a connection between diet and disease rates, which is a part of the nutrition transition. What happens is that the proportion of income that is spent on food decreases very sharply. That relationship is known as Engel's Law. It is a fundamental law of economics and was formulated in 1857.

What also happens to make the diet cheaper is that diet composition changes and starchy staple foods are gradually abandoned in favour of more animal foods, more added sugar, and more added fat. At the same time, physical activity declines and we have higher rates of chronic disease, of which obesity is the most common and the most important right now and, in the long term, the most dangerous.

How do we handle this issue ? How can we promote healthier diets ? There are two ways, and you will be hearing more about those during the congress. One approach is through advertising behavioural change, nutrition education, motivation, and other strategies that have to do with behavioural change at the individual level. This is very important.

For example – and here I quote my colleague Barry Popkin, who was part of the WHO and World Bank Nutrition Consultancy – the final state of nutrition transition, this utopie alimentaire, or the idea of healthy diets for everybody, is based on dietary and behavioural change. He said it begins with a thriving economy and the awakening of the importance of sound nutrition and exercise. At this point, healthy diets and life-styles are 'in', they have become fashionable, and the challenge is to find the triggers to promote a voluntary shift towards healthier diets in a population. This approach has been applied over the past several years and it continues to be applied. You will hear more about it during the conference.

I want to suggest something different. First of all, in the United States we no longer have a thriving economy and we rely less than before on individual behavioural change. We are moving in the direction of environmental and policy change and in order to insure healthy diets for everybody, we may need to look toward agricultural policies and economic measures.

The existing behavioural and educational measures need to be supplemented with economic and policy measures and, in some cases, political action. Right now, the push towards healthier diets, which we are certainly promoting in the United States (notice here the various headlines and covers of journals, dietary guidelines, and so on), actually is not really working. This was the ideal; here is the reality that we are faced with.

One of the points I would like to make is that there is a huge differential in cost between healthy and unhealthy foods. We really need to come to grips with the fact that healthier diets may, in fact, cost more. I am not saying that this is a bad thing; I am saying that even if healthier diets do cost more, it is worth it, in the long term, for the consumer. It is worth consuming a more nutritious diet even if it is more expensive. At the same time, however, the consumer has his or her own economic limitations and will gravitate towards the cheaper food options.

What went wrong ? How did Americans become the fattest people in the world? Is it the shape of things to come ? What can be done about this, first of all in the United States, and then globally ?

I would like to draw your attention to some new books on the subject, some of which may be coming out in a French translation, but you can also get them in English. Eric Schlosser's best seller "Fast Food Nation" accuses the food industry, specifically McDonald's, of privatising profits and socialising costs. He says that the food industry has made profits by passing the health-care costs along to other groups in society. Greg Critser, in "Fat Land", places the beginning of the obesity epidemic at a precise afternoon in 1973, when Earl Butz, who was the Secretary of Agriculture in the Nixon administration, signed a bill authorizing price supports for corn. As a result, we got corn syrup and corn oil at an incredibly cheap cost. This is a bit of journalistic license but, according to Greg Critser, the obesity epidemic can be pinpointed to that afternoon.

Marion Nestle, in her book, talks about the role of the food industry in promoting the creation and marketing of cheap foods, especially to children and adolescents. Kelly Brownell, in his latest book "Food Fight", places the blame equally on just about everybody.

So, right now, the food industry in the United States is under attack and people are talking in terms of fast foods being the tobacco of the 21st Century.

I take a slightly different view-point because I think that the food industry has been providing low-cost food to low-income people, and it becomes a much more complicated situation. One point that I do want to make is that obesity in the United States is very much a socio-economic issue and it has absolutely everything to do with access to healthy diets and, therefore, the costs of healthy diets. Those things really cannot be separated.

We are looking at the possibility that the relation between poverty and obesity is actually linked with the very low cost of energy-dense foods, and is reinforced by the good taste and palatability of sugar and fat.

There is a new focus on the cost of diets. An editorial in a British medical journal, the Lancet, published at the end of January of this year, stated that high-fat energy-dense foods are the cheapest option to the consumer. It specifically noted that as long as a meal of grilled chicken, broccoli and fresh fruit costs more and is less convenient than a burger and fries, then the battle against obesity will be lost.

This is why we need to have economic action and make sure that healthy foods are equally affordable and accessible to all. We are really moving beyond issues of education and information, we are moving into the realm of state-driven agricultural policy to promote the consumption, production and accessibility of vegetables and fruit.

Many of the same points were actually mentioned in the most recent Strategic Plan for Obesity Research, published by the National Institutes of Health (which is the equivalent of Inserm), saying that genetic factors clearly play an important role, but despite their importance, the dramatic rise in obesity rates can only be due to changes in the food environment. Again, the National Institutes of Health specified that the food environment now includes abundant choices of relatively inexpensive calorie-dense foods that are convenient and taste good.

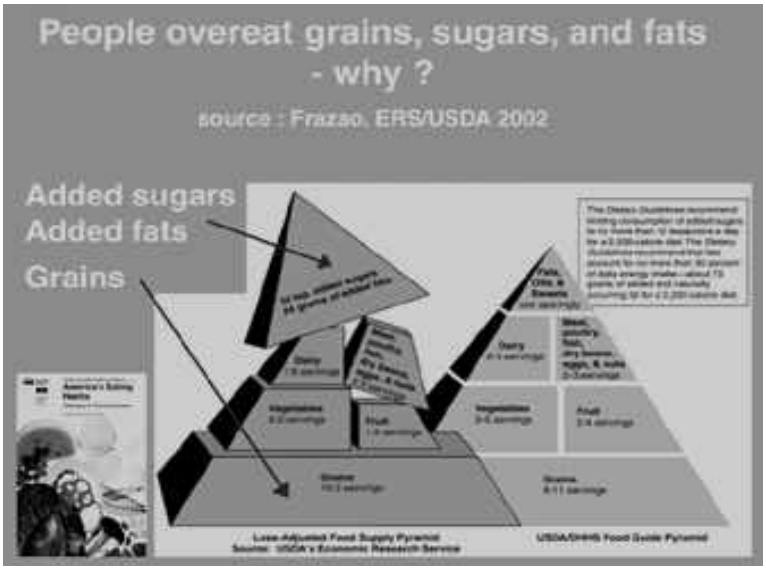
Let us briefly examine the current dietary trends in the United States. I can tell you that very similar trends occur here, in France. I have looked at some of the data from both Credoc and Inserm. I will not present them here but the American data can give you some idea.

First of all, we have the food guide pyramid, which you have seen in its various incarnations. There is now even a Mediterranean diet pyramid, as you will know, constructed by some of my colleagues from Harvard.

This USDA pyramid shows you the contrast between the ideal diet, what people ought to consume, on the right, and the realistic diet, which is what people actually consume, on the left. You see that American consumers eat from the bottom of the pyramid and the top of the pyramid. The bottom of the pyramid is grains, mostly refined grains, and the top of the pyramid is added sugar and added fat. Notice that the consumption of vegetables, and especially fruit, is much lower than it ought to be. Ideally, we would like to increase it to several servings per day. It is not there right now – the space at the tip of the pyramid is taken up by added sugars and fat.

In the past 20 years, the composition of the American diet has changed. We consume 300 more calories per day than we did 20 years ago. Those extra calories come from refined grains, added sugar and added fat. About 8% come from fruit and vegetables, and the consumption of dairy products and meat actually declines in terms of those additional calories.

Basically, the American diet has increased in terms of calories because people consume more of the less expensive foods. Notice that on this slide, it is the consumption of grains that has gone up more than the consumption of either added sugar or added fat. Notice also that the consumption of grains, sugar and fat is in the order of 400 pounds per person per year. Given that soft drinks in the United States are sweetened using high-fructose corn syrup, corn sweeteners have replaced cane and sugar beet sweeteners. As a result, the American diet has more fructose than it used to have.

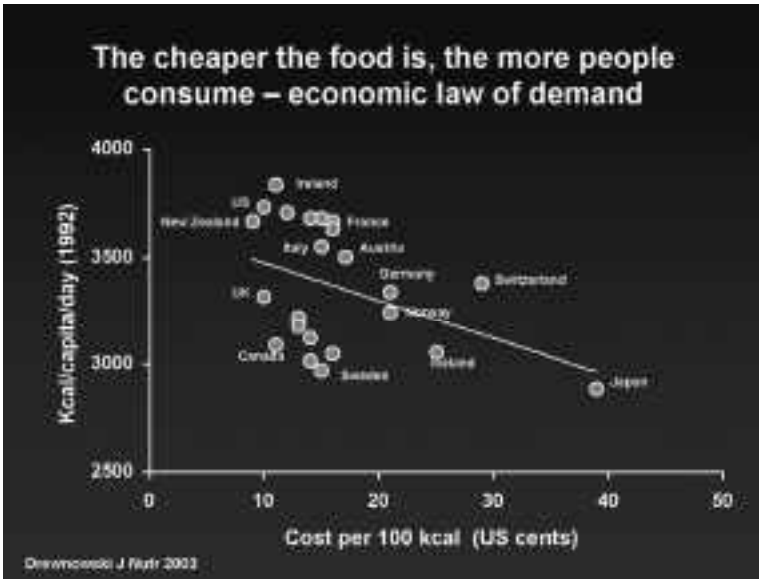


I want to point out something that people always forget. The high fructose corn syrup in soft drinks is not pure fructose : it is 55% fructose and 45% glucose, and, of course, sucrose is 50% fructose and 50% glucose. Right now, I believe that soft

drinks in France are sweetened with sucrose, but all the drinks in the United States are sweetened with high fructose corn syrup.

The consumption of meat, eggs, poultry and fish has been constant. However, the consumption of beef has dropped and is increasing slowly, and consumption of poultry has gone up fairly fast. Fish is a very small part of the nutritional regime in the United States. Notice here that the consumption of fruit is surprisingly monotonous. In the United States, three types of fruit – oranges, apples and bananas – account for 50% of all fruit servings. That means we do not have the diversity in fruit consumption that we ought to have, and that apple juice, orange juice, oranges, apples and imported bananas pretty much account for half of the fruit that is consumed.

Among vegetables, iceberg lettuce, frozen potatoes (meaning French fries) and potato chips account for a third of vegetable servings. Again, there is little variety in vegetable consumption. When you look at the leafy green vegetables plotted on the same scale, which is on the next slide, you will see that their consumption is really very low. These are the vegetables we are promoting, these are the vegetables which are critical to health and their consumption is either stagnant or not increasing, and certainly much lower than the consumption of the lower cost produce.



So, for the average American family, fruit and vegetables pretty much mean potatoes, orange juice, apples, and maybe lettuce. There is a lot of work to be done in terms of education, motivation and awareness, but there is also the economic factor because the fruit and vegetables that are consumed are in fact the ones that cost the least.

How is obesity linked with the nutrition transition ? Is it possible that the obesity epidemic can be explained through the laws of economics ? In my presentation, I will look at some of the common laws of economics and see how they apply to obesity, given that we have a very strong socio-economic gradient with obesity and type 2 diabetes.

The first issue is Engel's Law, which states that as incomes rise, the proportion of income spent on food declines. So that the wealthier countries spend a lower percentage of income on food, and wealthier families spend a lower percentage of income on food. Looking at it on a global scale, you see that poor countries, especially those in Africa and Asia, spend up to 60% or 70% of disposable income on food in some cases. On the other hand, developed nations over here spend anything between 7% to about 21% of disposable income on food consumed at home.

In the United States, we spend the lowest proportion in the world on food consumed at home, representing only 7% of disposable income. In France, consumers spend double that – 15% - which is one reason why their produce and diet are of higher quality. In Japan, consumers spend triple that – 21% of disposable income – on food consumed at home. So the range can be anywhere between 7% and 21%, and notice that the less people spend, the cheaper the diet seems to be.

Here we have data from the United States Department of Agriculture estimating the average cost of the American diet in terms of cents/100 calories. According to those data, the diets in the United States, Ireland, New Zealand and the UK, are among the cheapest in the world: you can get 2 000 calories for approximately 2 $.

These are very low figures, and notice again here that the cheaper the diet, the more people eat. That is the economic law of demand: as the diet becomes more affordable, more of it is consumed. There is a relationship between the cost of the diet and total daily intakes. My argument today is that there are ways to make diets cheaper and those ways involve grains, sugar and fat.

These are data from the United States (there are identical data available from Credoc) showing that the proportion of income in the United States has been declining from 1929 until now. We spend 7% of disposable income on food consumed at home, and 4% of disposable income on food consumed away from home. Altogether, food and beverages account for 12% of disposable income. The French data are much the same: they show a decline in personal expenditure on food.

The amount spent per person per day has been the subject of a number of economic studies. In the United States, the average person spends approximately 7$ per person per day. Inserm's estimate of the amount of money spent by French consumers is in the order of 5¤ per person per day. So when you think of the relationship between diet quality and diet costs, bear in mind that 5¤ has to get you approximately 2 000 calories per day .

Food has become cheaper. These are data from The Economist showing that of all the various market segments, only food and clothing have become cheaper, whereas things like telecommunications, cell-phones and so on, are relatively more expensive. Hence, as consumers devote their resources to other market segments, food and clothing seem to suffer because less money is spent on food.

Now, the clothing industry has achieved a number of savings in a number of ways, detailed in a book called "No Logo" by Naomi Klein. Among the ways to achieve those savings were moving jobs offshore and cheap imports form other nations. Again, the food industry is cutting costs by using cheaper ingredients.
How did this happen ? How did the typical American diet become so inexpensive ? Did some diet components become cheaper than others ?

Generally, in economics, you have a positive relationship between incomes and diet composition. As countries become richer, they consume more fat, mostly animal fat from meat. They consume more sugar, and protein shifts from vegetable

protein to animal protein. These are all components of the nutrition transition: more animal products, more animal protein, more sugar, less vegetable protein, and less staple carbohydrate.

Here you have the data for the consumption of carbohydrate in Cambodia, Vietnam, Laos and Asia, and here you have consumption of carbohydrates in the United States. When you look at this relationship between staple carbohydrates and income, there is another economic law, called Bennett's law, which says that there is an inverse relationship between the percentage of energy developed derived from staple cereals and per capita income.

You can see on this slide how it plays in Asian nations. The poor Asian nations consume close to 90% of energy from carbohydrates, but as they become richer, carbohydrates drop, sugar increases, and the amount of fat goes up. So there was a classic relationship between diet composition and wealth: as nations became wealthier, they consumed more animal products. Those classic relationships have now been uncoupled, and those economic laws no longer hold.

What happened was increased production of extremely cheap vegetable oils. These data were first published in a paper that I published with Barry Popkin in 1997. They show the relationship of the wealth of a nation, from the very poor to the very rich, showing that the amount of animal fat went up as a function of income. However, what happened here was that the consumption of vegetable oils went up. Vegetable oils are so inexpensive that even the poorest nations can have a diet which is 25-30% fat.

Vegetable oils are extremely cheap and this relationship was recently cited by the Food and Agriculture Organization of the United Nations, showing that as incomes rise, even the poorest nations have access to diets which are relatively high in fat. This has to do with the fact that as vegetable fats have become inexpensive, the consumption of vegetable fats has gone up, and that consumption is independent of incomes. Further, in the past, higher degree of urbanization was linked to greater wealth. Right now, we have huge urban agglomerates in South and Latin America and in Asia, which are in reality poor. So you have 10 or 20 million people living under fairly primitive conditions in various areas of developing nations. The one type of food which is delivered reliably and cheaply and that does not spoil is sugar. This means that developing nations will be consuming an ever-increasing proportion of sugar so that, according to economic analysis, urbanization does actually drive sugar consumption, again independent of income.

These are very recent data form Barry Popkin, showing that the increase in sugar consumption between 1962 and 2000 has not actually been in the richest, but in the poorest nations. This means that obesity and type 2 diabetes are a crisis waiting to happen in the developing areas of the world.

We are already seeing that it is the poor in developing countries who consume more sugar. What you are seeing then is an inverse gradient between sugar consumption and incomes among the urban poor in Brazil. You can see quite clearly that the percentage of energy from fruit and vegetables goes up with income and the percentage of energy from sugar goes down with income. It is actually lowest among the richest groups. In economic terms, this makes sugar what is called an "inferior good" because its consumption goes up as incomes decline.

It looks to me as though obesity is linked to the consumption of energy-dense, low-cost diets. We are thus already seeing higher rates of obesity among low-income women in both the United States and Brazil.
These two women are fruit-pickers in the Central Valley of California. They were featured in an article in a Californian newspaper, which stated that they only made money during the fruit season, and then they ate well. However, off-season, the only thing they could afford was added sugar and added fat, with predictable consequences. Thus, there were seasons when they could cook and eat produce and have a healthy diet, but there were also seasons when they could not. As a result, obesity in this group is very much linked to socio-economic status, and it is very largely mediated by food costs.

I have been using this model to look at how people make food choices. This model emphasizes the factors of taste, cost, energy-density, convenience, health and variety. When it comes to taste, it can be fat, sugar and salt. When it comes to cost, it is grains, added sugar and added fat which are least expensive. When it comes to energy density, it is again cereals and fat which are the most energy-dense. When it comes to convenience, we have packaged foods, which are high in fat, sugar and salt. When it comes to health and variety, there at the end you have fruit and vegetables. We need to change this system to make healthier foods more affordable for everybody.

According to our model recently published in the American Journal of Clinical Nutrition, we actually suggest that saving on food and trying to save on food costs will push the consumer towards more energy-dense foods. Energy-dense foods may have a lower satiating power, so there is a greater potential for passive over-eating or excess energy intake. In other words, you consume more than you intended. The point is that the forces that drive people to that are not necessarily physiological, they may be economic.

Research has suggested that we are driven to consume sugar and fat because of genetic factors, natural predispositions, genetic mutations and learned preferences, and all of this is true. However, there is also the possibility that we are driven to consume them because of economic circumstances. Some of us have a choice of healthier diets, but many of us do not. Is it then possible that economic factors coupled with physiology and behaviour are the forces driving the obesity epidemic ? Here, we are saying that trying to constrain food costs and spending less may in fact result in eating more.

Let me show you briefly just how inexpensive sugar and fat really are. At world market prices, sugar costs approximately 9 cents per pound, which means that you can obtain 20 000 calories for one dollar, or just under one euro. For added fats, the market price is approximately 20 cents per pound, which means another 20 000 calories can be purchased for one dollar. Nutritionists generally equate 3 500 calories with one pound of body weight, and here, you can get 40 000 calories for 2 dollars. The cost differential between healthier foods and added sugar and fat is enormous.

People have said that added fat and sugar are evil or bad, or should be curtailed. I am saying that they are not evil, they are merely inexpensive. It is really an issue of economics.

When you start looking at diets, again you can see that starches, sweets and fat give you more calories for less money. These are analyses conducted by Nicole Darmon from unit 557 at Inserm in Paris. Nicole is dealing with obesity and poverty as part of an Inserm research study.

Here, she looked at data form a Val de Marne study, conducted by Serge Hercberg, and concluded that meats, fruits and vegetables were more expensive in terms of the calories they contained. On the other hand, grains, sweets and fats provided more calories at a lower cost. Of course, this is just calories; meat, fruit and vegetables provide nutrients and if you were to re-do this scale in terms of nutrients per dollar or per calorie, it would come out differently. In the United States, we are now

looking at a nutrient-rich score, a naturally nutrient-rich scale per thousand calories, to find out which foods pack the most nutrients in a smaller caloric package.

We had a meeting about this very topic on 16th March in Washington, and you will be pleased to know that fruit and vegetables came right at the very top of the list. We are about to publish this data. The range of the nutrient-density scores runs all the way from soda to spinach, which is exactly what your mother told you. The new nutrient-density score pretty much replicates what we have all known all along.

This is another economic problem. When we look at inflation and rising costs, sugar and fat hold their price, so that prices in the United States for fruit and vegetables have gone up fairly substantially since 1983. On the other hand, sugar, soda, sweetened foods, chocolate – the energy-dense foods – have held their price. There are many economic reasons for this but I cannot list them all. One thing I would like you to go away with is that there are some economic factors at play here.

As a result, about 40% of dietary energy in the United States comes from just two ingredients: added sugar and added fat. Our diet is becoming progressively more reliant on the cheapest ingredients and many consumers are being driven by circumstances towards sugar and fat. This has consequences for the obesity epidemic.

I am sure you have all seen the map of the United States showing which states are the most obese. Right now, a number of states have crossed obesity rates of 25%, which means one in four adults is obese and defined by a body mass index of 30 and above. Those states are Texas, Louisiana, Mississippi, Alabama, South Carolina and West Virginia. You will have seen the map on the left because it has been published everywhere, including in the Journal of the American Medical Association. You will not have seen the map of this relationship here on the right, which is my own calculation of the relationship between obesity rates and income by state. Mississippi, Alabama, South Carolina and West Virginia are the poorest states. You have the highest rates of obesity in the poorest states.

This is not just in the United States; you see the same exact relationship for Canada. I got rates of overweight (body mass index 25) and medium income by province. Again, Newfoundland, Prince Edward Island, Nova Scotia and New Brunswick are the lowest income and the fattest provinces. The least obese group is going to be down here in British Columbia and Quebec: Quebec, possibly because of genetics; British Columbia, perhaps because of climate and opportunities for physical exercise, but the same relationship holds.

The same relationship holds for France – these are data published in the Figaro – and again, you have highest rates up in the North of France, in the Pas-de-Calais, and lowest rates exactly where we are. Except – and this is worrying – the growth is actually highest in this area of France: you have both the lowest rate and, unfortunately, the fastest rate of growth in obesity. In the United States we have a very strong relationship between obesity and income. It is absolutely linear for women; it is blunted for low-income men. There is a relationship for both income and education, which holds for women but not so much for men, except that wealthier men are less likely to be obese.

Of course, the wealthy do a number of things differently. First of all, they have more opportunity to exercise. These are data from centres for disease control showing that recommended exercise goes in relation to education level. That is to say that lower income groups and groups with less than high-school education, lower than Baccalaureat, are least likely to engage in leisure time physical activity. Of course, the wealthier people eat better foods and have healthier diets.

The Healthy-Eating Index is a global measure of diet-quality developed by the United States Department of Agriculture. I believe that one of the speakers at this conference will be speaking about this in a day or two from now. Here you see that healthy-eating index scores go up as a function of income and also of education. You see that the wealthier groups have more opportunity for physical activity, they have better diets, and they have more food choices. My point here is that we need to make those choices equal to all.

These are the latest data from the International Obesity Task-force showing that the highest proportion of obese children was actually, paradoxically, in the Mediterranean countries: Italy, Greece and Spain. This is a menu photographed by a French epidemiologist, Marie-Françoise Cachera, who went on holiday to Greece. The children's menu always shows: hamburgers; spaghetti, French fries, soft drink, and ice-cream. The significant thing here is that this menu costs only 3 euros – all the sugar and fat you can eat for 3 euros. There are two things: one is education concerning healthy diets; the other is economics, and we would like those foods to be available to all.

Obesity and diabetes are becoming a global public health crisis. We already have a crisis in the United States and it is spreading globally. My position is that, to a very large extent, obesity is an economic phenomenon. Many people are obese because they are poor. It is quite possible that obesity is the hidden price we are paying for globalization. There are many provocative arguments one can draw on for or against this theory but what we need are economic policies to ensure healthy diets for all.

Intoduction

Eveline ESCHWEGE
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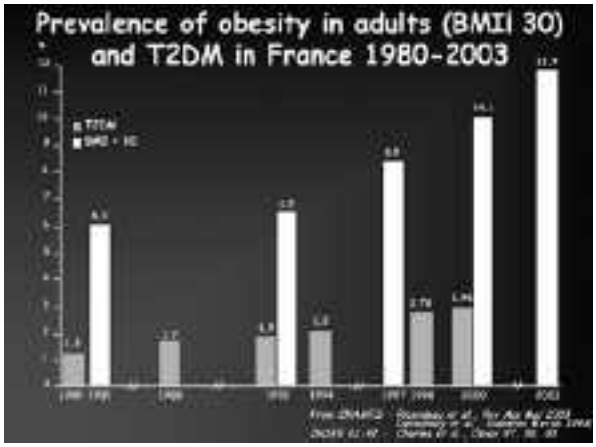
Together with Pr. Philippe Vague, I have the pleasure to chair this first session on "Obesity and diabetes : two multi-factorial diseases".
We will have six presentations. From global epidemiological situation of obesity and diabetes to a closer view of the rising prevalence of these diseases, we will progressively try and understand their constitutive mechanisms and means of prevention. I will show you two slides that Philippe Vague already presented yesterday. The first one is a bit more up-to-date than the one you saw yesterday for France (in white on the graph). USAappears as the "champion of obesity", with a steady increase since the 1970 s. Germany and Finland follow. The UK shows a fast growth in the 1980s, as is the case for Spain, France and the Netherlands from the mid-90s. These countries are undergoing a rapid evolution and may catch up on the USA someday.

The next graph shows very recent data from the International Federation for Diabetes. Paul Zimmet published it last year in Diabetic Medicine. The number of diabetic subjects has grown from 135 million in 1995 to 155 million in 2000 and 189 million in 2003. Forecast for 2025 is 324 million (against 300 million forecasted in 2000 for the year 2025). The most affected regions are Africa, the Middle East and Asia. Obesity in Europe seems not to grow as much for it might have reached a stabilisation stage. This is doubtful though, since population aging tends to magnify the phenomenon.

The share of diabetes caused by weight gain in subjects aged 30+ varies from 25 to 85 % depending on country and gender. As for women, this share represents 80 to 85 % in North America, Europe and Latin America, and much less in Asia and the Pacific (Australia, Japan, China and Vietnam). Taking into consideration the dangerous connection between weight gain and diabetes, weight gain has to be closely monitored.

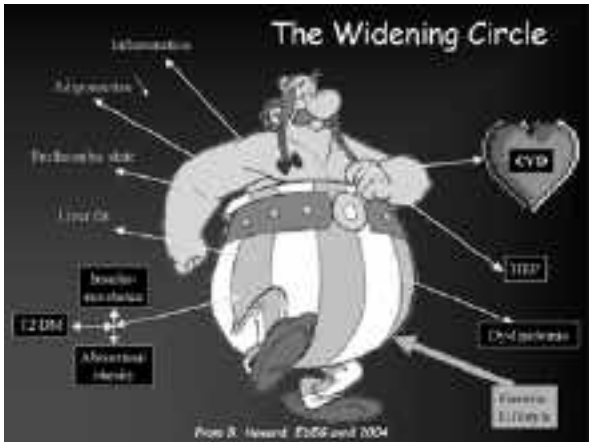
As far as France is concerned, we have relatively recent data. You can see the prevalence of diabetes and obesity according to reliable studies in terms of methodology. The pink histogram shows obesity. Data for 1980 and 1991 come from INSEE decennial surveys on medical goods consumption. Next data were taken from OBEPI surveys. Fundamental characteristics are similar for both types of surveys: it makes sense to compare these studies. Figures should not be taken for granted, since these surveys are based on individual declarations. When you ask people about their weight, they actually tend to minimise it: these figures thus stand for minima. We can see that obesity has grown from 6.1 % in the 1980s to 6.5 % in 1991, 8.5 % in 1997 and 10.1 % in 2000. Almost 12 % of the participants in 2003 have a BMI that exceeds 30.

In parallel, diabetes is shown on the blue histogram. 1980 data come from an INSEE survey asking, "do you have diabetes ?" (1.3 % answered yes) and "what type of treatment are you on ?". For 1988, 1992, 1994, 1998 and 2000, data were taken from surveys made by the CNAM (Caisse Nationale d'Assurance Maladie), either among randomly picked samples the whole population covered by the National Insurance System in 1998 and 2000. The number of diabetic subjects has grown from 1.3 % in 1980 to 2.96 % in 2000, and to more than 3 % nowadays. These figures encompass only type II diabetes, treated with oral hypoglycemic agents. They do not give any indication on diet, since information is based on prescriptions. Since diabetes is treated with specific medicines, we can assume the disease's prevalence thanks to reimbursement records. If we take into account the number of diabetic subjects treated with appropriate diet or insulin, the rate of prevalence amounts to nearly 3.5 %.



This is what is happening in France. There is an obvious parallelism between obesity and diabetes' evolution, notwithstanding the influence of population aging on the evolution of the rate of diabetes.

In a study targeting Northern American health professionals, subjects with a normal BMI (<22) were compared with obese subjects (BMI over 35). Results show that obesity essentially increases the risk of diabetes (odd ratio of 40 for men, 30 for women). For other diseases, such as vesicular calculus, hypertension, coronary diseases, hazard increases by 2 to 4 times.



I would like to conclude with a "national" slide that will introduce the debate on diseases and their interrelations. It is about Obelix asking "What is wrong with my weight anyways ?". Obelix is growing bigger and heavier: this has to do with genetics as much as with lifestyle (physical activity and diet). The way we eat and what we eat intervene in all biological pathologies associated with android obesity, which is at the crossroad of cardiovascular diseases (main cause of death in our countries), hypertension, dyslipidemia and diabetes. Obesity, notably the android type, may be the first noticeable sign associated with insulin-resistance.

The global pandemic of "diobesity"

Jacob C. SEIDELL
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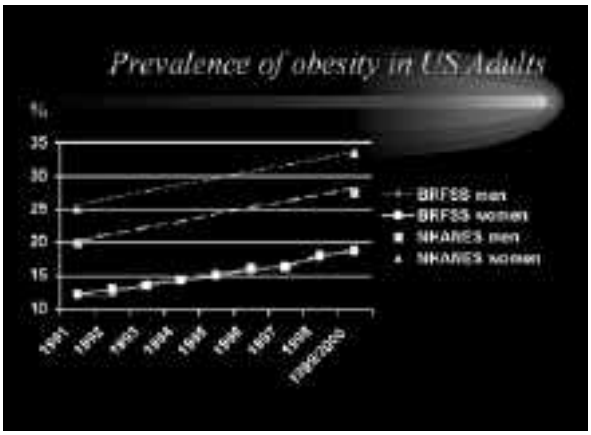
Thank you for inviting me and for the very nice introduction to this morning's session. You will probably see some of the slides again, but maybe in a slightly different context. I will talk about the prevalence of diabetes and obesity, but because they are so tightly linked, people have coined different names for the association between the two. "Diabesity" was coined in the 1980s. People now think that because obesity is the principal thing, "diabesity" might be the correct term to use for this cluster. It all happens because of our change in lifestyle from the early ages to the present day. You have all seen these kinds of figures before; it is our evolution into very strong and muscular men.

In terms of an obesity epidemic, there is certainly an epidemic of media attention to this problem. This is just a recent three-month period and we see there are a number of media stories about obesity in the general media. It is quite clear that there is overwhelming attention to this problem. There is not much more news here compared to here, but increasing attention is certainly being paid not only by the media but by politicians, the European Union, the WHO, FAO and other organisations.

This is to show you what we know about obesity, the prevalence of obesity and how little we know. This is just an example. These are data from the United States, which most of you have seen, and they are two nationally representative studies. One is the survey on the behavioural risk factor in men and women from the United States, where you can clearly see that there is an increase in obesity. These data were presented by Professor Eschwege.



These are telephone surveys, where people reported their height and weight. The other ones are the national health and nutrition examination surveys, which are now continuous. You can see here that these are also nationally representative but here, people have measured the weight and height of responders in the survey. There is an enormous gap between the two estimates. You can see first of all that there is much more obesity in women: 25% in 1991 compared to 12% in the self-reported heights and weights. In early 2000, almost one in three American adult women were obese when you measure heights and weights. This tells us that a lot of the surveys we have been using in Europe to estimate the prevalence of obesity are probably wrong. We do not know how wrong they are, but it could be very serious in underestimating the problem of obesity.

This is to show you what a country could do. The United Kingdom has the best prevalence data in Europe on obesity. They have annual surveys of large numbers of nationally representative responders, and they measure heights and weights in people's homes. They first did this every five years or so, but now they do this annually and you can see this epidemic unfolding. The prevalence of obesity in the United Kingdom is presently somewhere around 25%, which is much higher than any of the other surveys have ever shown it to be. If you look at the surveys of reported heights and weights, you will see that the prevalence of obesity in the UK would be somewhere between 10-15%. So surveys are a bit useless for looking at this epidemic. Maybe it is useful to look at trends, but it is certainly difficult to compare countries and it is very difficult to have exact estimates of obesity. What I am saying here is that we probably grossly underestimate the prevalence of obesity. I have tried to see how many countries actually have good data on this and we have tried to improve them also.

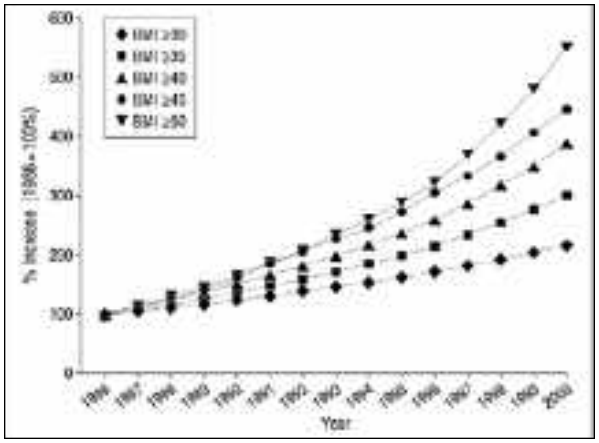
We have done this in the Netherlands. One of the slides that Professor Eschwege showed you is that the Netherlands has the lowest prevalence of obesity in Europe. Well, I am not sure if that is true. These are self-reported heights and weights, and we clearly have a prevalence here of around 10%, which is similar to France, I think. Here, however, we have measured heights and weights in 5000 of the people that were asked to report their height and weight annually, and we know that we have to add at least 3% or 4% in men and women to have the actual prevalence. So we probably have a prevalence close to 15% rather than under 10%. It is just an example of how misleading these self-reported heights and weights can be. This is especially true because obesity is also an increasingly lower social class problem.

These are again data from the Netherlands, but they are shown almost everywhere in Europe. What we have seen from analysis of the Monica study, in which they have repeated surveys of obesity and educational level over time, is that the gap between lower and higher social and economic classes is widening over time. So it becomes an increasingly lower social class problem with increasing problems of underreporting.

Another thing that is usually not shown in these data is that we have cut-off points, like 25 and 30, above which we look at the prevalence of obesity. What is happening is that the BMI distributions are changing over time. How large the increase will be depends on what cut-off point you take.

This is to show you data from the Netherlands, these are measured heights and weights and you can clearly see that if you look at the median BMI, there is not much change, but the biggest change is there in the higher percentiles of BMI. This is more clearly shown here in the United States, where they have used the behaviour risk factor survey studies, and if you look at the BMI over 30 you can see a doubling over time from 1986 to 2000. However, when you use higher cut-off points, the percentage of increase will be much higher. For instance, when you use a BMI over 50, you have an almost a five to six-fold increase in the prevalence of obesity. So it really depends where you take the cut-off point in terms of the increase. What you see is that with every doubling of the prevalence of obesity – and the doubling of the prevalence of obesity say from 10% to 20% is possible by a two-unit increase in average BMI – there is a six-fold increase in massive obesity. This is leading to all kinds of problems, especially in the United States. This is from CNN

where they recently showed that the health-care system is unable to cope with these massive increases in grossly obese people because the medical system is unable to work with them: the CT scans do not fit, the blood pressure devices are not large enough, the nurses are not strong enough to lift patients, the stretchers are not strong enough to carry these obese people and there are all kinds of problems. Because there is such a rapid increase in massively obese people, the health care system is undergoing very serious problems indeed.



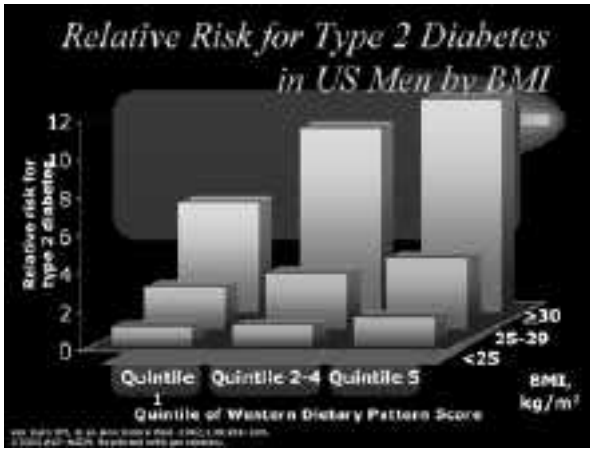
I am talking about the global prevalence of obesity: this is not just an isolated problem, we see it almost everywhere. This is data from the most recent studies in Australia and they all show that there has been an escalating increase in the prevalence of obesity over time. This is also shown almost everywhere in Europe. There has been a sort of levelling off in Finland, but here also you can see that the actual prevalence, as opposed to what we have seen from the survey data, is actually close to 20% of the adult population. This is eastern Finland, where they have measured heights and weights, but self-reported heights and weights from the rest of Finland are very similar, so it is very likely that these are real prevalences for the rest of the country. Germany also has a prevalence close to 20-25%, so one in four Germans are obese. There has been some sort of emancipation, I would say, from east to west. They have grown together. Eastern Europe used to have much higher prevalences than Western Europe but they are now very similar, probably thanks to the reunification.

What you generally see across the world is a rapid shift from underweight problems, as you see here, to overweight problems in countries that are still considered to be developing countries or countries undergoing economic transition. You will hear much more about this during this conference.
Take another example of obesity. Obesity in children in China is doubling every three years. These countries are experiencing a very rapid escalation of the problem of obesity. This is not obesity, but overweight, but here you can also clearly see there are increases in both rural and urban China. These are old data, but it is clearly also the result of rapidly changing lifestyles: these are the same streets just fifteen years apart.

If we want to understand something about these differences in prevalence, we can of course look at nutritional data. They are very difficult to compare, they are unreliable and not systematic, but there are some data that can really be expressed very confidently. Some of these have to do with transportation. These are actually good data. These are all the trips of 10 kilometres and less, and you can see that almost half of these are done by walking and cycling in the Netherlands. It is much less in the UK, and almost nobody cycles in cities in the US, unless you are suicidal, and very few people walk. We have these data from almost every country in Europe because transportation is something that is measured very precisely and time used for transportation is also measured very precisely. You can actually explain almost all the differences between countries in Europe. There are also other things to consider, of course.

I am skipping this slide because we have already seen that diabetes is also going to be the massive problem in the rest of the world.

These are also self-reported data from the United States. Here you see the low prevalences in the 1980s and the very high prevalences in 2001, and exactly the same is happening with type II diabetes. These epidemics are unfolding in a very similar way and almost at the same time when you look across countries. This is because of the very tight correlation between obesity and diabetes. These are the nurses' health study and health professional studies with different follow-ups. It seems that men and women have very different risks, but they are very similar when you actually take the same follow-up. When you take the women here the BMI/diabetes relationship is very rapidly increasing. As epidemiologists, we are always very happy to look at relative risks of about two or three, which we think are high, but here you can see that compared to BMIs of under 22, a relative risk of somebody with a BMI of 25 is already ten times higher compared to the one with a lower BMI. This is escalating very rapidly and coming up with relative risks around 100 when you have reached BMIs over 35. Remember that this is the group of people that is increasing most rapidly.



This is to show you that we are also seeing this in the Netherlands. These are BMIs under 25. These are people age 55 and older in a representative sample of a population in a city, Hoorn, north of Amsterdam, which is actually quite representative of the rest of the Netherlands in terms of socioeconomic class. Here also you can see that if you look at impaired glucose tolerance and diabetes and you add these two together, the percentage of people with a normal glucose tolerance is actually much reduced in those with obesity. This is the attributable risk of obesity, the percentage of diabetes that could be prevented if people did not have the risk factor. For instance, about 40% of diabetes could be prevented if nobody had a BMI over 35. If you add all of these up, you can actually come to very high estimates of the attributable risk.

This is from the Harvard study – maybe you will hear more about this on Saturday, I am not sure. If you have people who are eating healthily, are not overweight, are exercising, are non-smokers and drink moderately, then actually 90% of the cases of type II diabetes could theoretically be prevented. You can see that they have only a tenth of the risk compared to people who do not have these characteristics. Unfortunately, and this is quite clear in the US but it is probably the same here, only less than four percent of all of the women in the nurses' health study

adhere to all of these five risk factors. This is clearly a very powerful way of looking at this.

Apart from obesity, of course, we will be looking at many of the dietary risk factors in this conference. There is much more to type II diabetes than obesity, of course. The point to be made is that this is just our average, middle-aged European man. We see that there is not just diabesity, obesity in diabetes, but there is more. There is insulin resistance in type II diabetes, and also dyslipidaemia and hypertension and low-grade inflammation, and of course this will end in cardiovascular disease.

We need to look at metabolic syndrome, as we will hear more about it in this conference. We have tried to calculate all the different definitions, because when we find something interesting, a lot of people make different definitions. There is the American Heart Association definition of metabolic syndrome, the World Health Organization definition of metabolic syndrome, the European Group for the Study of Insulin Resistance (EGIR), and there are a couple more now. They are all different in terms of how you define metabolic syndrome. It makes a big difference. In this population study, we looked at the prevalence of people who have metabolic syndrome according to these different definitions, and they vary from 19-32% in men, and 16-26% in women. You can see here that most of the men have this syndrome, but here it is the lowest prevalence. This is of course a problem, but it is also a problem if it predicts heart disease differently, and clearly that is the case. If you compare, for instance, the relative risk of all cardiovascular disease, it is quite clear that the American Heart Association gives different risk estimates for cardiovascular disease compared to the WHO and the EGIR definitions.

My summary is that obesity is rapidly increasing in most parts of the world – the only exception is Sub-Saharan Africa, as far as we know – but we underestimate the problem in Europe enormously by using questionnaire data of very poor quality: low response rates, self-reported heights and weights, etc. Diabetes incidence is closely related to this, rapidly following the obesity epidemic, and diabesity has a marked effect on global health.

Thank you very much for your attention.

Questions

Member of the audience
When you showed the slide from the Harvard study with the main characteristics of avoiding the risk of diabetes, you talked about moderate consumption of alcohol. However, your slide shows "above or equal to five grams a day" for alcohol. I ask this question because the consumption of alcohol as wine here is a great problem. I am wondering if your moderate alcohol consumption is above five grams a day or if it was a mistake.

Jacob C. SEIDELL
No, it is above five grams a day, but five grams a day is very little. This is due to the nature of the Nurses'Health Study. Generally we say one or two drinks a day, which I think is equivalent to the European way of saying this. In the nurses'health study, alcohol consumption was very low, so these are people in the highest quintiles and the upper 20% of the intake was over five grams a day. This is very low. Intakes of over two glasses a day were almost non-existent.

Member of the audience
Yes, I agree with that but if you write "above five grams a day", where is the limit?

Jacob C. SEIDELL
Yes, I should add that moderate alcohol intake means between 5-15 grams or so.

Member of the audience
Thank you. You have some very alarming statistics. Can I ask you about the data you showed on walking and cycling in the European countries and in the US, which are very revealing. You made the statement at the end that the differences in the number of journeys taken by foot or by bike could account for most of the differences in obesity between countries. Do you stand by that statement? Is it the case that dietary intake is less important?

Jacob C. SEIDELL
No, I am not saying it is less important. When you look at all of the differences, and also the time trends in transportation and television watching for instance, they are extremely important in terms of energy balance. I am saying this because the surveys never usually include walking and cycling and things like that as being physical activity. They focus on sports participation and all kinds of strenuous physical activities. These are data calculated for 365 days of the year on average, so this is a continuous thing. If you see how many trips of 10 km and less are made over the year and you calculate this in terms of energy balance, then it is clear the gap between most of the European countries and the US is disappearing very rapidly. Between the UK and the Netherlands, it is almost gone when you correct for potential effects on energy balance by transportation. I am just saying that this is an ignored field as a determinant of obesity and we are staring at poorly measured dietary quality data across Europe and trying to find the determinants of obesity while there might be other completely explanations.

Member of the audience
I have a question. You have nicely shown that the prevalence of obesity is increasing in every country, but of course we are referring to the adult population. Is it the same in children? Because the preventive strategy is not the same if obesity begins in childhood as it is if it begins in adulthood,.

Jacob C. SEIDELL
Absolutely. I have not shown them here because I thought they would be shown elsewhere during the programme, but the childhood obesity figures are even more alarming because they are escalating even more rapidly than in adults. In terms of the social gradient, we see that it is also increasing much more, the gap there is widening earlier in children than it is in adults. We can project from this that we will not see the end of the epidemic in adults for a long time in any of these countries, because there is tracking of obesity by age during the course of their lives. The strongest increase is in children who are now between 6 and 12. In adolescence, the increase is less steep than in younger children. So the steepest increase is in children aged 6-12 years, of primary school age. They will be adults in 20 years'time and we will see the impact of that on the prevalence in adults also.
(…)

Jacob C. SEIDELL
If I understand you correctly, what you are saying is that obesity and diabetes have the same causes in diet and physical activity. Of course this is true. It is impossible to look at the impact of obesity while maintaining a constant physical activity and diet. That would be nice. There have been experiments in trying to overfeed people to see how diabetes develops independently of changes in behaviour, but it is impossible. Lifestyle and obesity are so tightly linked that it is impossible to correct for this. You are absolutely right in that there is the common soil hypothesis that it is the underlying lifestyles which are related to both. In addition, obesity is contributing on top of that, independently, to the occurrence of diabetes.

From obesity to type 2 diabetes : the interplay between insulin resistance and impaired insulin secretion

André J. SCHEEN

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Thank you, Mr. Chairman. I would like to thank you for inviting me to participate in this interesting symposium. I have been asked to make a presentation about the very close relationship between obesity and type 2 diabetes, and to share some elements of pathophysiology with you which are particularly useful in providing an answer to the last question asked by our colleague : why does obesity predispose to type 2 diabetes ?

Following a brief introduction, I propose to divide my presentation into two main parts. The first part will concentrate on mechanistic issues, and will attempt to explain the reasons why an excess of fat tissue can contribute towards type 2 diabetes, as a result of the so-called "lipotoxicity". As the concept of lipotoxicity is becoming more and more complex, I will divide this first part into three sub-sections. The role of non-esterified fatty acids, whose importance has been stressed for many years, will be discussed as well as the emergence of two new paradigms over the last two or three years : the excess of triglycerides stored in places other than in the adipose tissue (in the liver, in the skeletal muscles and in the beta cells of the pancreatic islets), and the important and now acknowledged role of adipocytes as endocrine cells, prone to release a series of adipokines or adipocytokines which can interfere with the metabolism of glucose.

The second part of my presentation will be devoted to the very close relationship between insulin secretion and insulin resistance. It is well known that type 2 diabetes is a disease combining these two abnormalities, and it will be shown that there is a very close link between them. This part of my presentation will also be divided into three sub-sections. I will first discuss the so-called "Starling curve" of the beta cell, which was emphasized by De Fronzo, and reconsidered by several authors over the last few years. Afterwards, I will discuss the hyperbolic relationship between early insulin secretion and insulin action. Finally, I will end my presentation by describing how to influence the natural history of type 2 diabetes.

This slide was already shown by Professor Seidell a few minutes ago: it underlines the extremely strong relationship between the prevalence of type 2 diabetes in men and women, on one hand, and the body mass index (BMI), on the other hand. As demonstrated by our Co-President, Ms Eschwege, in her introduction there is not a shadow of a doubt that amongst all the co-morbidities associated with obesity, diabetes presents the greatest relative risk. In addition to the BMI, there is another parameter that should be considered, namely the distribution of fat mass. For a long time, this has been evaluated by the well-known waist to hip ratio. This study, completed in Scandinavia almost twenty years ago, was carried out on men who were followed over a period of 13 years. It demonstrated that the risk of developing diabetes increases according to both the BMI and the distribution of fat tissue. The highest risk was found in men who became overweight and also in whom the excess fat tissue was mainly distributed in the abdominal region (increased waist to hip ratio).

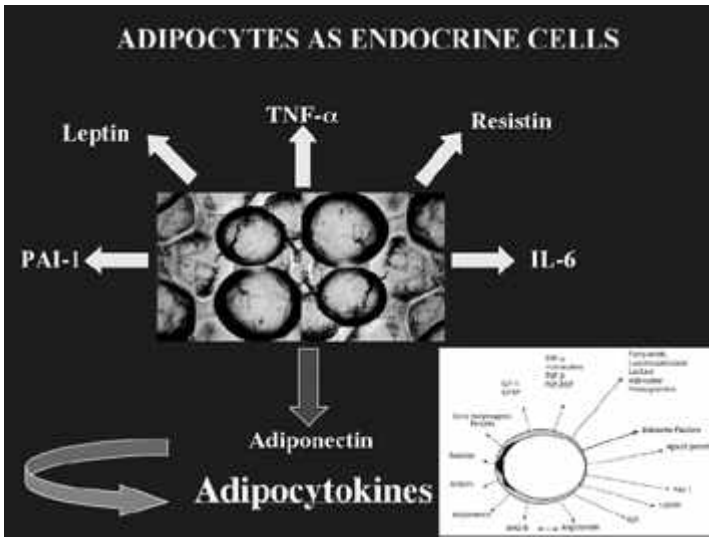
Perhaps younger participants to this symposium are not aware that it was Professor Jean Vague, father of our current President, who back in 1956, was one of the first to draw our attention to the extremely close relationship that exists between android obesity and other risks that are now acknowledged in the metabolic syndrome : gout (corresponding to an increase of uric acid levels), diabetes mellitus, and cardiovascular disease. At that time, he probably did not suspect that the so-called metabolic syndrome, closely linked to abdominal obesity, would become a major public health problem 50 years later. It is no longer the waist-hip ratio that is taken to be the most representative parameter of this relationship with the distribution of fat tissue, but rather the waist circumference, which bears a closer link to the distribution of intra-abdominal (perivisceral) fat tissue as assessed with a sagittal plane scan. Male and female subjects with waist circumferences of greater than 100 cm and 90 cm, respectively, are at a very high risk of developing type 2 diabetes, metabolic syndrome, and also cardiovascular diseases.

It is my task to try to explain how obesity can predispose to type 2 diabetes. Obesity is partially triggered by genetic factors, but it also depends on obvious environmental factors. The relationship between obesity and type 2 diabetes occurs through insulin resistance, since obesity is clearly associated with decreased insulin sensitivity. Fortunately, type 2 diabetes does not occur in all obese people, even if they are massively insulin-resistant. In order for them to develop type 2 diabetes, there has to be a second abnormality, namely a defective insulin secretion. It is the combination of these two abnormalities, insulin resistance and deficiency of insulin secretion, which contributes towards type 2 diabetes. As obesity, type 2 diabetes involves a genetic predisposition (clearly shown by a family history) in addition to environmental factors (poor lifestyle habits). All clinicians know that type 2 diabetes is a disease that evolves over time: there is a vicious circle that is aggravated by glucotoxicity. Hyperglycaemia in itself enhances insulin resistance and desensitizes B-cell to glucose. Such phenomenon has also been documented over the last few years as far as lipotoxicity is concerned, a more recent concept which I am going to discuss in further detail over the next few minutes.

Type 2 diabetes is a disease which, unlike type 1 diabetes, has an extremely complex pathophysiology. It may be considered as a bipolar disease, which combines two defects: a partial defect in insulin secretion (insulin secretion still occurs but it is defective as far as both kinetics and total release are considered) and insulin resistance at different tissue levels (in the liver, muscles and adipose tissue). Confronted to insulin resistance, the beta cells should be able to secrete more insulin, but they are no able to do so because of genetically impaired function in predisposed subjects : type 2 diabetes develops progressively from this moment on. The graph on the right hand side of the slide shows the presence of insulin resistance early in the natural history of the disease. At first, the beta cell is capable of compensating for it, maintaining a secretion that is adapted and remains more or less within the normal limits or is even increased. Once it has started to weaken, hyperglycaemia will occur, generally between 40 and 50 years of age. Unfortunately, given the early obesity in children and infants, American paediatricians are seeing even more adolescents

with type 2 diabetes than with type 1 diabetes, and we will come back to this point later in this symposium. This observation would have been absolutely incredible about twenty years ago.

Following that introduction, we are now going to focus on the issue of lipotoxicity. Given the time that I have been allowed, we will address three problems, one by one: the role of non-esterified fatty acids, the role of ectopic fat stores, i.e. the storage of triglycerides in areas other than in the usual place which is in the adipose tissue, and issues related to adipocytokines. Pathophysiology has been dominated over the last two decades by the fact that when there is an excessive amount of adipose tissue, an excessive release of fatty acids will occur. These fatty acids are able to compete with glucose at the level of the skeletal muscle, as emphasized in the famous Randle theory : if the muscle is confronted with a lot of fatty acids, it will use these substrates as energy fuel and use less glucose. Similarly, if the liver receives a large amount of fatty acids and glycerol coming from lipolysis, it stimulates certain metabolic pathways, in particular gluconeogenesis, and increases its glucose production. This creates a situation where there is excessive production of glucose by the liver and a decrease in uptake of glucose by the muscle: both factors obviously can lead to hyperglycaemia. The excess of fatty tissue leads to the release of excessive amounts of fatty acids. More particularly, it is the visceral fatty tissue, which is very sensitive to lipolytic hormones, which releases these fatty acids. Thus, on one hand, these fatty acids cause reduced peripheral utilisation of glucose by the muscle, and on the other, increased hepatic production of glucose by the liver. However, in addition to these well-known processes, a third effect has been described more recently as it was shown that the chronic excess of circulating fatty acids leads to toxicity at the level of the beta cell and reduce insulin secretion. Therefore, excess free fatty acids may contribute to explain three main abnormalities that initiate and aggravate type 2 diabetes, a concept known as lipotoxicity.



There is a second concept, in addition to that of the increase in fatty acids, which has just been put forward. In an obese subject who has a positive energy balance, the excess calories will be stored as triglycerides, especially in the adipose tissue, but also in other tissues which were not originally intended for the storage of triglycerides: the skeletal muscles, the liver and the pancreas. This famous triumvirate has already been mentioned. The accumulation of triglycerides aggravates insulin resistance at the level of the muscles and the liver, and also contributes to the perturbation of the beta cell. We now know that these triglycerides significantly disrupt the function of these organs and contribute towards insulin resistance and beta cell impairment.

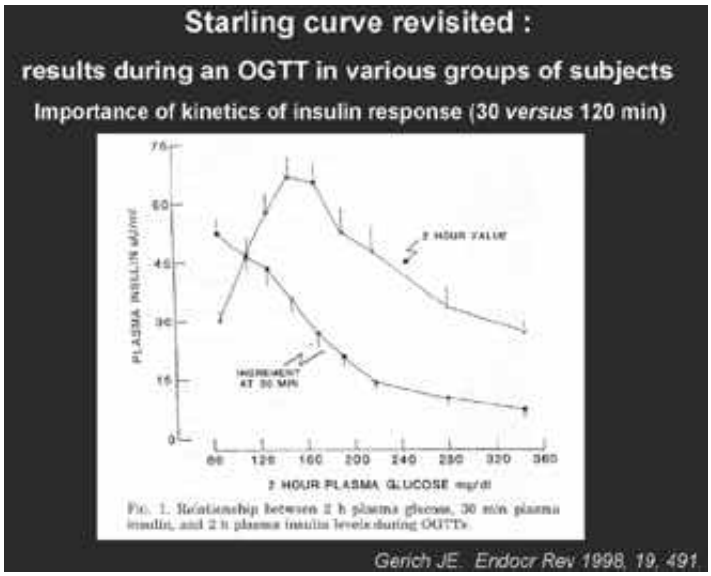
The third paradigm, which appears more and more important, concerns the secretory capacity of the adipocytes. Adipose tissue is not only an organ for storing triglycerides in case of energy excess, but is capable of secreting a multitude of various factors (hormones, cytokines, and inflammatory factors). The role of adipocytokines has been well-demonstrated over the course of the last few years. Leptin is a well-known adipocytokine, but its role in relation to type 2 diabetes is not yet fully understood. In any case, it would seem to be less important than we expected almost a few years ago, at least in humans. Other cytokines seem to play a more important role: TNF alpha (and possibly resistin), which is secreted in excessive amount in the obese subject, and adiponectin, a cytokine whose secretion is decreased when adipocytes are enlarged as in obese subjects. Adiponectin has become a very popular topic over the last two or three years, and there are now dozens of papers published every month about adiponectin. When adipocytes are filled with high amounts of triglycerides, they secrete less adiponectin. It is acknowledged that adiponectin can play an important metabolic role: for example, it is effectively capable of stimulating the muscle to utilise glucose. If an adipocyte secretes less adiponectin, the uptake of glucose by the muscle, and therefore muscular sensitivity, is reduced. This is what happens in the obese subject. Conversely, TNF alpha, a cytokine which usually inhibits the utilisation of glucose by the muscle, is over-expressed in the obese individual. Therefore, these two cytokines interplay in a manner that is extremely disturbing for the glucose metabolism, as the obese subject has less adiponectin and more TNF alpha: these conditions are ideal to induce a resistance to glucose utilisation, especially in the muscles. The same dynamic occurs at the level of the liver, especially with regard to the production of very-low-density lipoproteins (VLDL) and triglycerides.

We can conclude this first part of my presentation by saying that lipotoxicity is becoming a very hot topic. It has moved from a quite simple issue (increased free fatty acids) towards a much greater complexity (ectopic fat stores and disturbed secretion of adipokines). What so ever, increases in the amount of fat tissue set a series of factors in motion, which are fundamentally disturbing to the glucose metabolism. These factors particularly disrupt insulin secretion and insulin action. During the second half of my presentation, I will explain the close interrelation between these two parameters.

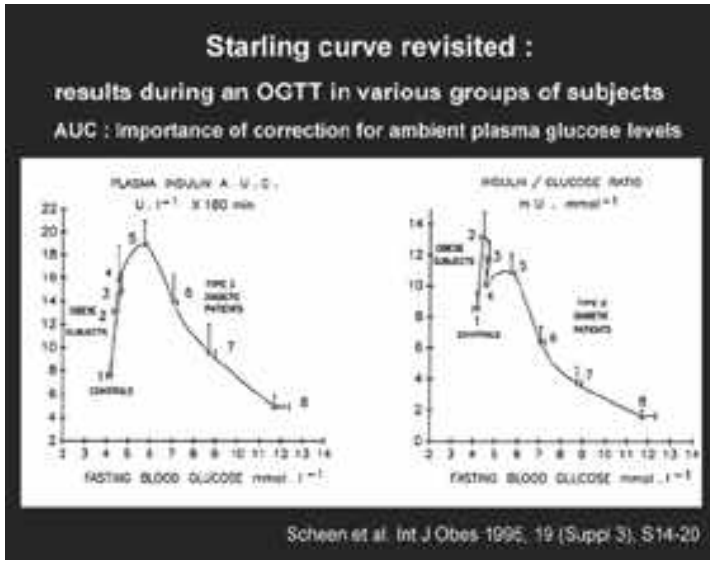
We have already seen that type 2 diabetes is a bipolar disease : it cannot be explained, interpreted, and treated unless two abnormalities are taken into account, one of which is at the level of the beta cell in the pancreas, and the other, relating to the tissues at the peripheral level. Robert Turner convincingly demonstrated 25 years ago that hyperglycaemia in the diabetic subject had to be interpreted according to the level of insulin resistance and the level of beta cell deficiency. Individuals with maximum levels of both insulin resistance and beta cell deficiency have the most severe hyperglycaemia.

Again, this second part of my presentation will be divided into three sections. In the first section, I will discuss the Starling curve, as originally proposed by De Fronzo. De Fronzo studied glucose and insulin responses during oral glucose tolerance tests performed in a range of different subjects (normal lean non diabetic obese subjects, obese subjects with impaired glucose tolerance, diabetic obese subjects, etc.). These subjects demonstrated a progressive increase in glycaemia in the fasting state according to the degree of severity of the diabetes. When measuring the uptake of glucose during a euglycaemic hyperinsulinaemic glucose clamp, the glucose mass taken up by the skeletal muscles progressively decreased as fasting glycaemia

increased, suggesting a progressive decrease in insulin action. When analysing insulin responses (assessed as the area under the curve during the first 180 min after the glucose load), there was an excessive production of insulin in obese subjects with normal glucose tolerance, with impaired glucose tolerance and even with mild diabetes mellitus. Insulin secretion deficiency only developed much later when obvious hyperglycaemia is already present. This is what De Fronzo called the Starling curve of the B cell, drawing a parallel with the Starling curve described for heart function : at first, an adaptation mechanism can be observed, which is followed by decompensation. For a long time, this curve was interpreted to support the statement that type 2 diabetes is first and foremost an insulin resistance disease, and that the failure of insulin secretion is only a secondary and late event. However, this curve needs to be re-examined, as De Fronzo's interpretation, now approximately twenty years old, is oversimplified as it did not take into account the kinetics of insulin secretion.



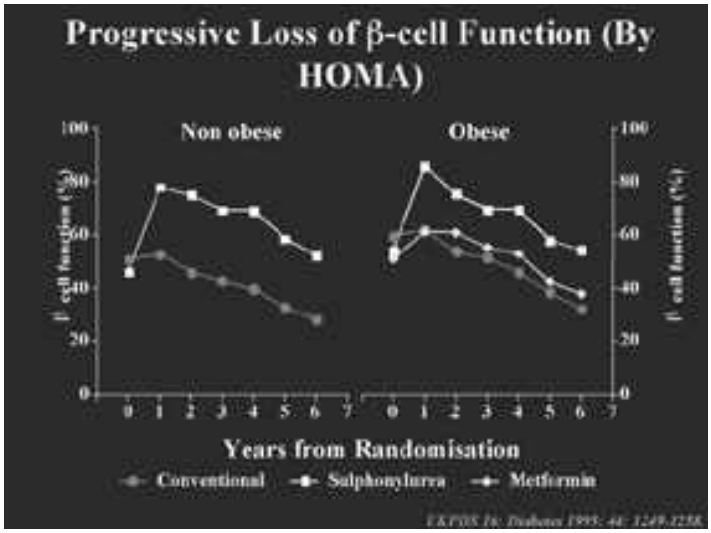
Here are presented personal data, which show exactly the same phenomenon as described by De Fronzo : the area under the insulin curve (AUC) during 180 minutes of an OGTT was measured in a range of subjects (thin, obese with normal glucose tolerance, obese with impaired glucose tolerance, diabetic patients with various severity classified according to fasting glucose levels). Again, the Starling curve is perfectly apparent, but this mode of presentation does not take the corresponding glycaemia into account. If a simple correction is made by dividing the insulin AUC by corresponding glucose AUC over 180 minutes, it can be seen that the obese subjects with normal glucose tolerance are, in fact, the only individuals capable of compensating completely, but obese subjects with impaired glucose tolerance already showed an early beta cell failure. Thus, a simple correction of the area under the insulin curve/area under the glucose curve, allows this early failure of the beta cell to be evidenced.



Moreover, Gerich, another famous investigator in the field of insulin resistance, demonstrated that it is very important to study the dynamics of the beta cell response. On examination of the insulin response at the 120th minute of the OGTT, the Starling curve, as proposed by De Fronzo, is clearly visible. But when examining the early response in insulin, measured at the 30th minute of the OGTT, it can be seen that as soon as the glycaemia increases, there is an immediate failure of the beta cell. The beta cell is incapable of exhibiting an early-phase insulin response. This early insulin secretory defect can be, at least partially, compensated for if the beta cell is stimulated by hyperglycaemia, but it can easily be detected when appropriate correction for ambient glycaemia is performed as already mentioned. De Fronzo now acknowledges this approach, and just last week published in the journal "Diabetologia", in collaboration with the group of Ferrannini, the same type of relationship, although they went even a little further in the correction. Indeed, they divided the so-called insulinogenic index (delta insulin/delta glucose in the first 30 min of the OGTT) by the corresponding individual insulin resistance index measured in each subject during a glucose clamp. When the relationship between the insulin secretion in the OGTT and the resistance is examined, as the fasting glycaemia or the glycaemia two hours after a glucose load increases, there is a linear reduction in the insulin secretion, again demonstrating an early failure of B cell.

This brings us to the second half of the presentation, namely the hyperbolic relationship between insulin secretion and insulin sensitivity. You have already understood that it is impossible to analyse insulin secretion without taking into account the sensitivity of the tissues to insulin in parallel. Richard Bergman and Steve Kahn definitely proved that there is a hyperbolic relationship between these two parameters. By measuring the sensitivity to insulin during a glucose clamp or by using the SI index derived from the intravenous glucose tolerance test (IVGTT), a hyperbolic relationship becomes apparent between the acute insulin response (AIR : measured during the first 10 min of the IVGTT) and the insulin sensitivity index (SI). Amongst lean and non diabetic subjects, there are subjects who are hypersensitive to insulin (sportsmen/thin women), and these people maintain a normal glucose tolerance level with a relatively weak insulin secretion. Because of a genetic abnormality, some subjects are more or less insulin resistant, but are perfectly capable of stimulating insulin secretion, and thus they maintain a normal level of glucose tolerance. Obese non diabetic subjects are known to be insulin resistant, but are capable of secreting large amounts of insulin to compensate for such insulin resistance. In contrast, obese subjects who develop type 2 diabetes are insulin resistant but are not able anymore to adjust their insulin secretion, and the beta cell will be partially defective relative to obvious insulin resistance.

This hyperbolic relationship between AIR and insulin sensitivity was emphasized by Steven Kahn in a recent review published in the journal "Diabetologia" : normal subjects are distributed on a curve between percentiles 25 and 75 % (normal range). Non hyperglycaemic first-degree relatives of subjects with type 2 diabetes have already an inappropriately low insulin secretion, Subjects with impaired glucose tolerance are also insulin deficient relative to insulin resistance, as are women with a polycystic ovary syndrome or having formerly had gestational diabetes, and also elderly subjects. Among all these subgroups, the subjects with type 2 diabetes are the most insulin deficient: they are located the furthest to the left and at the bottom of the hyperbolic curve.



This phenomenon has been described in a longitudinal study performed in Pima Indians from Arizona, where the subjects who will not, in spite of their obesity, develop type 2 diabetes are the ones whose AIR increases along the hyperbolic curve. The more that they are insulin resistant, the more they are capable of adapting their beta cells by secreting more insulin and thus maintaining normal glucose tolerance. Conversely, the beta cells of subjects who will develop a reduction in glucose tolerance and then type 2 diabetes are not capable of adapting insulin secretion with regard to this insulin resistance, most probably for genetic reasons. Thus, the beta cell defect plays a major role in the development of type 2 diabetes. Most of you are certainly aware of the UKPDS study, carried out in Great Britain. At the present time, it is the only extensive prospective study concerning type 2 diabetes. The study followed both obese and non obese subjects with newly diagnosed type 2 diabetes for about 10 years. The function of the beta cell was measured annually using the HOMA model in patients treated by diet only, or by various pharmacological agents (sulphonylureas, metformin or insulin). Gradually over the years of surveillance following discovery of type 2 diabetes, the function of the beta cell progressively worsened, irrespective of the treatment administered. The progressive dysfunction of the beta cell largely explains the deterioration of blood glucose control as assessed by the progressive increase in glycated haemoglobin, whatever the treatment considered. Everyone now agrees upon the fact that this metabolic breakdown can be attributed to the deterioration of the beta cell rather than to a worsening of tissue insulin resistance.

I would like to finish this lecture by sharing with you some personal data. We carried out a glucagon test by injecting 1 mg of glucagon intravenously, and we determined the concentration of plasma C-Peptide at baseline and after stimulation, i.e. 6 minutes after the glucagon injection, as a measure of insulin secretion. In addition, we measured the insulin sensitivity of each subject using a euglycaemic hyperinsulinaemic clamp, the gold standard method to quantify insulin resistance (essentially at the muscular level where it is expressed by a significant reduction in the insulin-mediated glucose uptake). Healthy lean subjects secrete sufficient amount of insulin to adapt perfectly to their insulin sensitivity : they are plotted above the dotted lines which represent subjects with normal glucose tolerance. Obese subjects with normal glucose tolerance are characterized by reduced insulin sensitivity, but they have adapted their insulin secretion perfectly. They secrete more insulin to compensate for insulin resistance and keep normal glucose tolerance. If obese subjects develop non insulin-requiring diabetes (namely, hyperglycaemia is rather well controlled with oral antihyperglycaemic agents), they are much more insulin resistant, and their beta cells should have adapted to compensate for this insulin resistance. However, they are incapable of doing this, and beta-cell exhaustion is already underway: insulin secretion is reduced. Finally, obese type 2 diabetic patients who will require insulin therapy have the same severity of insulin resistance, and this evolution to insulin requirement is almost exclusively caused by the breakdown of insulin secretion. Generally speaking, the same phenomenon is observed in non obese subjects, except that their insulin resistance is lower, and the compensatory insulin secretion is less pronounced as compared to obese subjects.

In summary, the natural history of type 2 diabetes can be summarized in the following way. Both genetic and environmental factors could lead to insulin resistance and secondary mild hyperglycaemia, forcing the beta cell to compensate for in order to maintain normoglycaemia : this results in a paradoxical hyperinsulinaemia which allows to maintain normal glucose tolerance. Even mild failure of beta cell is sufficient to contribute to impaired glucose tolerance and a further defect in insulin secretion results in type 2 diabetes whose severity increases with the progressive failure of beta cell function. However, in some cases, there is probably a genetic defect of the beta cells which can lead to hyperglycaemia even in absence of severe insulin resistance.

What can be done to interfere with this natural history of type 2 diabetes in presence of obesity ? In my final slides, I am going to introduce the topics of the next presentations. Obviously, it is crucial to recommend healthy lifestyle, with limited calorie intake and regular physical exercise, in order to prevent or treat obesity. Professor Vague will show you the results of a few recent studies which demonstrated that lifestyle changes could reduce the incidence of type 2 diabetes by almost 50% in patients with impaired glucose tolerance. If these interventions at the nutritional and life style level are not sufficient, the insulin secretory defect and the insulin resistance can be treated using a series of pharmacological agents. These medicines can be used either to treat type 2 diabetes, or even to prevent type 2 diabetes, and their effectiveness has already been proven in several clinical trials.

It is obvious that modifications in relation to life style, nutrition and physical exercise are the basis of treatment both for obesity and for type 2 diabetes. Lipotoxicity plays an important role, because it can aggravate beta cell dysfunction and insulin resistance, and induces a vicious circle which triggers the metabolic deterioration. In the future, it will be necessary to distinguish the relative roles of insulin resistance and beta cell dysfunction from each other. This may help to correlate these functional abnormalities with genes, thus providing an explanation for this still mysterious disease. It will also allow to design new pharmacological approaches for the treatment and prevention of type 2 diabetes, a disease that is expected to show a pandemic for the next few decades.

Thank you for your attention.

Questions

Philippe VAGUE
I would like to thank you for this brilliant and extremely clear presentation. We can now see that if the link between obesity and diabetes is obvious and the result from the inability of the beta cell to adjust insulin secretion to the increased demand imposed by excessive fat tissue and concomitant insulin resistance, the mechanisms linking all of these phenomena are more and more complex. Does anyone have questions for Mr. Scheen ?

Member of the audience *(Journalist)*
With regard to the risk of diabetes, you set out limits in terms of waist circumference : 90 cm for women, and 100 cm for men. I presume that these are not rigid limits. For example, if a subject is 1.9 meters tall and is 60 years old, a waist circumference of 100 cm is not necessarily associated with a greater risk. Some older women do not have the same waist measurements as a young woman of 20 years of age. Therefore, adipose tissue is less important in this condition, even with a large waist circumference.

André SCHEEN
In fact, the figures that I mentioned (90 cm for women and 100 cm for men) are presented in a summarised form. In general, two thresholds are identified : the first concerns a moderate risk, and has been defined as a waist circumference greater than 80 cm for women and 94 cm for men, and the second threshold relates to a very high risk, defined as a waist circumference greater than 88 cm for women and 102 cm for men. In order to simplify the relationship, some people prefer to round off the figures and indicate that the risk is very high in men with a waist circumference greater than 100 cm and greater than 90 cm for women. These values are easy to remember for students and practitioners. We know that the development of waist size varies according to age: men and women (especially during the menopause) tend to become more portly at the abdominal level as they get older. The data would become extremely complex if it was necessary to develop age ranges by decades. The figures that I have given you apply to all adults, although they may be subject to some adjustment according to ethnicity. They are not valid for children or for adolescents. Perhaps at a later date, it will be necessary to develop categories according to age.

Besides, you emphasised that these figures could also depend on height. In fact, this parameter is not taken into account and waist circumference as a risk factor is apparently not significantly influenced by subject's height.

Eveline ESCHWEGE
I would like to add that we have to compare results of epidemiological research and results of clinical research. With regard to epidemiology, it is much easier to develop clear classifications which make it possible to make comparisons across one or several studies. As far as clinical studies are concerned, things are completely different, and I believe that the latest recommendations of the American Association of Clinical Endocrinologists on the definition of metabolic syndrome are, from this point of view, reasonable, as they provide some very clear limits. For the diagnosis of insulin resistance, they add a certain number of parameters to be left to the doctor's discretion. From a practical point of view, I believe that trust should be placed in the practitioner to decide whether a large waist size corresponds to android obesity with increased risk or not.

Denis LAIRON
You stressed the deleterious role of lipids. Would you be able to say a few words on the possible deleterious role of carbohydrates and of hyperglycaemia on insulin resistance syndrome and of compensation defects?

André SCHEEN
Concerning the role of glucotoxicity, it is probably possible to distinguish two stages. The first stage consists in the early desensitization of the beta cell to glucose. If the beta cells of type 2 diabetic subjects (or even relatives of patients with type 2 diabetes who are still normoglycaemic) are faced with a glucose challenge, they will not recognise the glucose correctly, whilst they do recognise other stimuli such as sulphonylureas or arginine. For reasons that are not yet understood, it seems that the beta cells are early "blind" to the stimulation by glucose. Hyperglycaemia appears in several stages. The first stage is called post prandial hyperglycaemia : if the fasting glycaemia is measured, it registers as normal. However, after each meal, the subject will be subject to mild post prandial hyperglycaemia : this is rarely recognised because it is not measured. It can be checked using an oral glucose tolerance test. We know that we spend 8 to 12 hours or more in a post prandial phase over 24 hours. If the subject is systematically hyperglycaemic during this period, the beta cell and other tissues will be faced with a hyperglycaemia that is asymptomatic but still exerts deleterious effects, by reducing insulin sensitivity – via diverse mechanisms at the level of the insulin receptor or insulin signalling cascade, and by increasing oxidative stress at the levels of the beta cell. The function of beta cell is disturbed when it has to face to chronic hyperglycaemia : it will progressively secrete less insulin.

This is an important point, because it helps to explain the reversibility of metabolic control in a diabetic subject. The diabetologists in this room have certainly encountered patients with chronic severe hyperglycaemia, with significant dampening of insulin secretion. When these patients are treated with exogenous insulin for several days or weeks, sustained normoglycaemia can be reached and insulin secretion is going better : the beta cells which were "anaesthetized" by the chronic hyperglycaemia are reactivated when this hyperglycaemia is suppressed. The mechanisms involved are diverse, for instance a reduction in the number of glucose transporters (GLUT2) at the level of the beta cell, or other, even more complex intracellular mechanisms.

Philippe VAGUE
You have demonstrated that adipose tissue must be considered as an endocrine organ and that it secretes many substances, most of which are cytokines. Adiponectin is one of these cytokines. Given that adiponectin is secreted by the adipocytes, it is difficult to understand why the amount of adiponectin decreases if there is an increase in adipose tissue. Even if adiponectin acts as a insulin sensitizer, how can you explain that the production of this protein decreases when the producing tissue mass increases? What mechanisms regulate this phenomenon?

André SCHEEN
To date, no one knows the precise answer to that question. One can only hypothesize that the adipose tissue secretes another substance which could exert a negative control over the adiponectin by blocking its secretion. This substance could function according to an autocrine mechanism, or could even act upon the genic expression of adiponectin. These are the interpretations that are currently proposed, but we do know neither what the genic effect is, nor what the potential intermediary substance might be. However, it seems to be the only plausible explanation in mechanistic terms.

Member of the audience
With regard to glycation of the insulin itself, when glucotoxicity is caused by the glucose, the insulin is glycated and is therefore less effective. Secondly, articles suggest that the final stage consists in apoptosis of the beta cells, and it is presumed that this apoptosis is caused by glucotoxicity. I have not read anything concerning lipotoxicity inducing apoptosis of the beta cells. This apoptosis of the beta cells would be the final stage and would thus be irreversible. I would like to thank you for your presentation, and I imagine that everyone else would like to do the same.

André SCHEEN
Apoptosis is a very important phenomenon in both type 1 and type 2 diabetes. In type 2 diabetes, we know that final impairment results in cellular death by apoptosis, and lipotoxicity plays an important role in this process. The accumulation of triglycerides in the beta cell poisons this cell and causes apoptosis. It is now believed that glitazones (thiazolidinediones, namely rosiglitazone and pioglitazone), which have a positive effect on glucose metabolism, could also exert a protective effect on the beta cell, as has been proven through a series of studies carried out in animals. One of the proposed mechanisms is the reduction in beta cell apoptosis, possibly due to a reduced intracellular accumulation of free fatty acids and triglycerides, as also shown in the hepatocytes.

Member of the audience
Based on your last slide, I think the question of responsibility is very interesting, whether it is the responsibility of the patient or the doctor. I think we just have to be careful that we do not leave the patient alone and say that everyone is responsible for his or her lifestyle. You have to see the environment and society, etc. I think we have to be careful not to blame obese subjects, but make public health improvements and so on.

André SCHEEN
I agree. We have to remind people that type 2 diabetes is a silent disease and the patient does not suffer from anything at the time he begins to be diabetic. It is quite difficult to motivate patients to adopt lifestyle intervention, except in some cases. I agree with you.

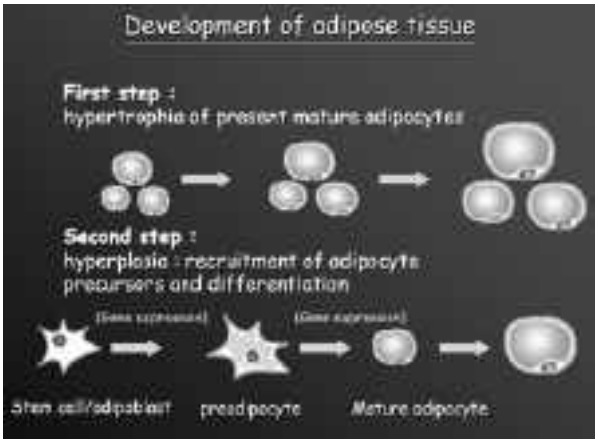
Diet-genotype interactions in obesity development

Denis LAIRON
INSERM UMR-Unit 476, Human Nutrition and Lipids, Faculty of Medicine, 27 Bd Jean Moulin, 13385 Marseille cedex 05, France

I will try and address a very complex issue: interactions between genotype and environment in the development of obesity. W.H.O. defines obesity as an abnormal accumulation of fat tissues, indicated by a criterion called Body Mass Index. A BMI exceeding 25 is the sign of overweight; from 25 to 30 and over, we talk of obesity. Waist circumference is another determining indicator. Excessively high values (over 100 cm for men and 90 cm for women) reveal an abdominal obesity, which clearly appears as the form of obesity with the most hazardous consequences in terms of diseases. Allow me to remind you that when the body weight increases by 10 kg, 7 kg consist of body fat, and 3 kg of muscles (except for body building adepts)…

The prevalence of overweight and obesity is widely spread in all industrialised countries. It is growing quickly in developing countries, with high discrepancies among countries. There is a clear variability in the prevalence of obesity that we cannot completely explain yet.

Interestingly, a comparison of obese subjects and thin ones shows an increase of energy spending in obese subjects, in terms of basal metabolism as well as postprandial thermogenesis and exercise. With a little bit of irony, we could think that obesity is an adaptation response (indeed, a costly one) that allows us to reach a new metabolic equilibrium in order to adapt to excessive food intake (as compared with energy spending). We have been looking for the "key point" of obesity for decades, and have not found it yet.



It is worth reminding you of the mechanisms of adipose tissues: there are two ways to increase fat storage in fat tissues, which are related to the characteristics of fat cells or adipocytes. The first one, which is the simplest, is increasing the size of fat cells, just as you pump a ball. Adipocytes have very little cytoplasm around their core and a droplet of stored fat. The ball thus grows to reach its maximum size. The second way is much more complex: it recruits new cells to increase the total number of cells. These new cells are stem cells, which will quickly turn into adipoblasts. A genetic program develops inside the cell, leading to the expression of new coding genes for new proteins and new functions for the cell. This allows pre-adipocytes to start storing fat. The new program of expression of specific genes leads to the creation of mature adipocytes that have all the functionalities of adult adipocytes, and can as well increase its size by storing fat.

Both ways of "becoming obese" are concomitant. The first method is quite easily reversible: when you have big adipocytes, you can easily reduce their size. This is not the case with the second method: when you recruit new adipocytes, it is impossible to make them disappear, as far as we know for now. The situation is thus complex.

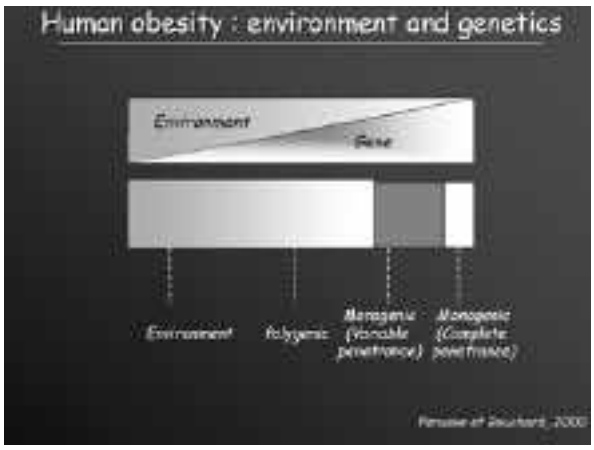
It is also important to understand how an adipocyte gets filled up. In a fasting state, the level of insulin is usually low, while very few triglycerides rich lipoproteins can be found in blood. A hormone-sensitive lipase, located in adipose tissue, constantly hydrolyses stored triglycerides and releases them into the blood as free fatty acids which will serve as a fuel for other tissues, like muscles in particular.

On the other hand, after a meal comprising fat, digestion will release large amounts of lipoproteins rich in triglycerides coming from the intestine or the liver, as well as carbohydrates leading to an increase of blood insulin: this will inhibit the activity of the fat tissue's lipase. Triglycerides of the adipocyte are no longer being hydrolysed and the flow coming out of adipose tissues drops down considerably. At the same time, another enzyme called lipoprotein lipase, located on the capillaries on muscles or fat tissues, hydrolyses triglycerides that stem from the meal's digestion. The fatty acids coming from these triglycerides enter the adipose tissue to re-synthesise triglycerides. It is thus obvious that obesity is a post-prandial phenomenon: you fill up your adipose tissue after eating meals, while you tend to empty it between meals. So there is clearly a cause-effect relation between food consumption and fat storage.

Let us focus on today's topic: what interactions actually exist between genotype and diet? I think the scheme published a few years ago by our colleagues from Quebec, Pérusse and Bouchard, in American Journal of Clinical Nutrition is very simple and eloquent. Today, everybody admits that obesity is due to both environmental and genetic factors, which can vary a lot from one person to another. In some cases, there is a monogenic pathology, which concerns mutation of one specific gene. If penetrance of this genetic feature is complete, pathology will be very patent. Even when only one gene is affected, the pathological effect will be moderate if penetrance is only moderate. In other cases, a number of genes are implied, and interact with environmental factors: this is the most common situation as far as obesity is concerned. At last, in other cases, some subjects have no genetic predisposition, but find themselves under such a strong environmental pressure, in terms of diet, that they will end up obese.

It is worth taking a look at ancient history of mankind: among our 30,000 genes, recently identified within the Human Genome programme, 98.4% are also to be found in primates. This selection was made 7 million years ago, when diet and physical activity had nothing to do with today's world. According to recent findings, primates and humans' evolution diverged 6 or 7 million years ago. Taking a look at today's differences, this means that there has been one gene change between primates and humans every 10,000 years. This low frequency cannot explain most recent evolutions. We have nevertheless undergone major lifestyle changes over the last 7 million years, of course, and all the more over the last century.

To get back to the different determining factors of human obesity, we can see that there are strictly genetic forms, which imply a number of coding gene mutations for some proteins – I will give you two examples later. During foetal life or just after birth, malnutrition or over-nutrition may induce obesity syndromes. There also are behavioural forms: stress, particularly in women, is a major factor of obesity development, which becomes stronger in the case of a settled way of life. In fact, most cases of obesity result from interactions between behavioural aspects (you need to eat too much to get fat), diet (excessive food quantities and unbalanced diet quality) and a genetic tendency.



In trying to understand the role of genes, we can consider that they facilitate fat storage at several levels: either by stimulating food over-consumption, or by diminishing nutrients oxidation in the body (which helps storage), or even by increasing storage in adipose tissues directly. Although these three ways can be found simultaneously in a subject, one isolated factor is enough to create unbalance. We are well aware of the role of family factors in obesity development: for example, 70% of the obese population have at least one obese parent. This relates not only to genetic factors, but also to family pressure, in terms of diet culture and physical activity habits. The figure hence suggests but does not demonstrate clearly a role for genes in obesity.

On the other hand, other data directly target genetic "inheritability". For BMI, or subcutaneous fat deposits, we find inheritability of 5 to 10%. If your parents have a BMI over 30, you statistically have two times the chance to get a BMI over 30. If the parents' BMI exceeds 40, this probability reaches 5 to 8 times. Inheritability is above 25% in average as far as total fat mass and fat tissue distribution (either in the abdomen or elsewhere in the body) are concerned. Inheritability equals 40% for basal energy spending or post-prandial thermogenesis. Clearly, there is a genetic inheritability, which may vary from a parameter to another. It never reaches 100%, and is only one factor among others.

Studies on twins helped better analyse the role of genes. Twins are either of homozygote (strictly alike) or heterozygote (slightly different) type. Usual correlation between parents and children reaches 0.15 and 0.25, which confirms what has been said earlier and marks an existing yet not so strong relation. Taking a look at homogeneity between two fraternal twins, correlation reaches 0.4 to 0.5: there is almost a half-similarity between fraternal twins. For identical twins, similarity is almost perfect. This shows that, depending on the level of genetic connection, genes are a more or less determining factor. It also explains why metabolic studies were done on twins, who are a remarkable model for studies. I would like to mention a study referenced by Pérusse and Bouchard. Identical twins with no obesity history were either given a food surplus during 100 days in order to make them fat, or had to do intense physical activity during 93 days, in order to make them lose weight. This aimed at examining how variations would take place. Looking at correlation between twin brothers/sisters, we can witness a very high correlation upon weight gain and loss. Among pairs of twins, there are much more differences, as some twins lose or gain a lot of weight and others do not. This shows that the genes that are very important in twins clearly discriminate among the ones who are part of the pair and the ones who are not.

I will give one more example. Even for identical twins and despite strong similarities, genetic differences sometimes exist, for instance different mutations on a specific gene with specific functions in one of the twins. In the example of lipase - an enzyme that hydrolyses blood triglycerides to make them enter adipose tissue – a Single Nucleotide Polymorphism (SNIP) was identified. One of the twins may bear the mutation while the other does not. This becomes obvious when twins get overfed. Mutation bearers gain more weight and fat than the ones who do not bear mutation. You can thus have a very determining genetic background (2 identical twins) with variations due to limited genetic mutations influencing one particular metabolic way. This also works with "non –twins".

To get back to monogenic forms of human obesity, which prove to be of so much of interest to the media and researchers, we can see that these pathologies concern very few families over the world. Five families have a leptin deficit, due to a mutation on the gene of leptin, three families have a mutation on the leptin receptor, and twenty families on the melanocortine receptor. In all cases, these mutations are linked with strong forms of obesity, because genetics mutations concern key-proteins: these are true genetic diseases.

Let us take the example of melanocortine receptor 4, located in the hypothalamus and involved in food consumption regulation. Thanks to molecular biology techniques, we can investigate in vitro deleterious effects and functional side effects of a coding gene mutation on this receptor. The frequency of such mutations happens to be higher for severely obese subjects than moderately or non- obese ones. However, penetrance of this genetic feature is only incomplete, hence a variable expression that will cause different types/levels of obesity. This case touches very few families over the world.

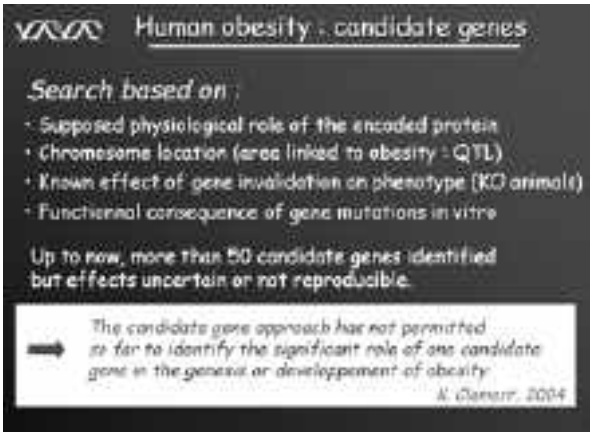
As for the famous case of leptin, it touches only five families in the world. In these families, obese teenagers bear a limited mutation on the promoter of the leptin gene, which causes a decrease in leptin level as compared with control subjects with similar body weight. The mutation can in part explain their obesity. In leptin-deficient families, heterozygote children have lower leptin levels and more body fat. This shows the relation between mutation and obesity.
These human monogenic diseases have been well investigated thanks to animal models that have recently been discovered to be linked to leptin. ObOb mouse, which quickly gets obese on a non-standard diet, has a similar mutation, i.e. a failure on the gene of leptin, which causes hyperphagy and leads to obesity and insulin-resistance. This is an interesting model but there are few equivalent in humans. A similar situation occurs in the case of a mutation on leptin receptor. Db/db rats have been used as a model for over 10 years: they bear a genetic failure of leptin receptor, and develop massive hyperphagy, obesity and insulin-resistance. Then again, the model concerns a small number of human cases over the world.

Another animal model was thought to be interesting but hardly has human equivalent. A mutation leads to protein expression in several tissues, which interferes with regulation of food consumption and leads to hyperphagy and obesity. We are also starting to work with transgenic models. After having identified

major genes that might be involved in obesity development, we make them over-expressed ? in animals, in order to investigate their role in vivo.

Monogenic diseases are not our main issue in the context of obesity epidemics. We are more interested in predisposition genes, specifically so-called economy genes, which constitute the current basis of major concepts in the relation between genes and obesity. We may consider these "economy genes" as the result of a long-term adaptation to extremely hostile circumstances (agriculture and supermarkets have not always existed), such as famines. This explains why the survivors we are have adapted and developed the best storage capacity in order to overcome food shortages. It helps looking at obesity from a new angle, regarding it as a natural disease, due to the process of adaptation to extremely hard circumstances. However, for most of us, today's environment is not as hard anymore, and we are no longer adapted.

In this regard, there essentially are two options for polygenic diseases. We can either assume that a large number of genes are implied in the syndrome, and have very little influence individually. Or we consider that only a few genes are concerned, but that they have great susceptibility and importance in the syndrome development. Both options are hypotheses, but none of them indicate a genetic disease: only environmental factors, i.e. diet, may turn genetic susceptibility into an obesity phenotype. For the moment, as established by Karine Clément recently, we cannot tell which one of the above-mentioned hypotheses is the most valid.



Research is being prolific in trying to determine which "economy genes" may explain inclination for obesity. Based on several experimental laboratorial approaches, researchers try to identify proteins that can help develop or reduce obesity. They also look at chromosomal localisation of some of these genes, since several chromosomal regions may be particularly involved in obesity. Thanks to transgenic animal models, they can understand functional effects of several genes mutations, over-expression or deficiency. Functional consequences of some mutations may also be investigated in vitro. When all elements are gathered, relevant genes can be identified: as far as we know today, over 50 candidate genes might be involved in obesity development, according to latest studies.

The problem is that there is little consistency among conclusions resulting from different studies and experimental approaches, despite fashionable and optimistic discourses about genetics. For now, we do not know which candidate genes are involved in human obesity.

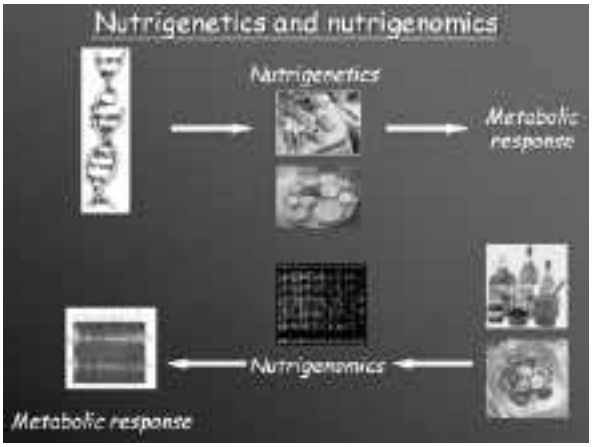
Despite shortcomings of our knowledge in terms of genetics, the epidemic of obesity has indeed started. The prevalence of obesity and overweight is increasing quickly. Children are also concerned. Quick variations over 10, 15 or 20 years allow us to say that genetics alone will not explain the whole phenomenon. Of course, we are not equal in terms of hazard. We have been working with models of food obesity in laboratories for years. We know how to make animals obese.

The most classical way is the model of the so-called "cafeteria rat": you replace normal diet (vegetable-based concentrate with little flavour) with sweet and fatty foods. The rat spontaneously becomes hyperphagic and overeats, just as some of our fellow citizens do when you give them flavourful food to eat. Since they spend more time eating, they get more sedentary and gain weight. They will develop all symptoms of overweight and obesity and will end-up being insulin-resistant. The phenomenon remains reversible as long as the obesity installation phase develops. When obesity is installed, reversibility becomes more difficult.

The other way is called "stressed rat". When you regularly pressure a rat, while giving it access to food, it proves hyperphagic and stressed out, and also gains weight. The importance of stress on obesity development, particularly in women, is well known.

Besides, other factors related to diet promote human obesity development: purchasing power, food accessibility, in terms of quantity and quality (diversity is an appetence criterion), advertisement for energetic foods (carbohydrates and fat), breaking of traditional eating habits, snacking in particular, urban lifestyle (settled way of life and heating systems that reduce overall energy spending). An unbalance of 1% per day in the energy balance represents around 25 kcal/day, the equivalent of a very small piece of bread. If the excess occurs daily, it reaches 10,000 kcal per year, that is to say one more kilogramme of fat in adipose tissue. Regulation of the energy balance is very subtle and can easily be distorted.

In this context, all foods are not alike, since food energy density may vary a lot. It is linked with lipid and water content. In both cases, fruits and vegetables are the least energetic foods, whereas cheese and other fatty or concentrated foods are the most energetic ones.



New trends in this regard are as follows: the nutrigenetic approach aims at investigating the influence of genes variability on our metabolic response to food, and nutrigenomics looks at the way food modifies genes and proteins expression in our tissues, that is to say at our metabolic response. If we can study both aspects further, we will be able to better understand interactions between genes and environment. In that sense, we absolutely need to develop bio-data processing tools which are represent our main frontier today. We need to lead intervention

studies on a broad scale, in order to study interactions between genetic variability of different subjects and their response to diet. We are therefore involved in a multilateral programme in 8 European countries (LIPGENE) starting this year, in order to investigate interaction between dietary fat, metabolic syndrome development associated with obesity and susceptibility genes. We also need good studies on the way food and nutrients can regulate genes expression in tissues.

In order to be able to prevent obesity, we all would like to know whether and to what extent one is more likely to become obese. This kind of evaluation might become realistic in the next decade, to certain conditions. First, we will need to increase our own knowledge, particularly on linkages between genes mutations and their related risks. We will also need to take into account ethical and psychological issues raised by genetic evaluation. Lastly, we will need to have the capacity to offer counselling and treatment, in order to make all this useful. We may be able to do this, but is it really worth it anyway? Prevention is indeed crucial for adults and children, in industrialised and developing countries alike, as a response to the quick evolution of the epidemics. That is to say primary and secondary prevention as well as complications. I will mention the example of the French National Plan for Health and Nutrition (PNNS, Plan National Nutrition Santé), whose priority goal is the reduction of obesity and which needs strong involvement of all partners.

Questions

Eveline ESCHWEGE
Thank you Mr. Lairon for highlighting the fact that genetics is not the only point in this issue. I would like to stress the fact that a surplus of 25 kcal a day leads to a weight gain of 1 kg a year, and that a weight gain of 10 kg consists of 7 kg of fat. Is this assessment reversible? If you reduce food consumption by 25 kcal per day, can you loose 1 kg in one year? Will you loose more fat or more muscle?

Denis LAIRON
It is clear that these assessments can prove valid both ways: reducing energy consumption makes you lose weight, except if you are already so obese that your situation cannot be reversed. In most cases however, reducing food intake is enough to achieve weight loss. In this case, you start by losing a bit of water, then quickly you lose fat. Working out at the same time helps losing fat while preserving muscles. The ideal weight loss situation starts with food intake reduction (especially highly energetic foods) and physical activity, for better body fat reduction and muscle conservation. Very often, when people go on restrictive diets, they lose fat and muscle: physical activity is an easy way to preserve and develop muscles.

Member of the audience
I have a candid question : are there laboratory rats that would not respond to stress by developing hyperphagy, but on the contrary by losing weight under pressure? Some people do respond to stress this way.

Denis LAIRON
I really cannot answer your question. This may be. We have mentioned genetic variability in humans, but it is also valid as far as rats are concerned. When you work with a group of 10 rats and put them on a diet, you usually witness noticeable variations (a factor 2). This clearly means that rats are not equal either. It is thus very likely that rats under stress do not gain weight and may even lose weight. Such a model would be quite an interesting one, in that men, as opposed to women, often eat less and lose weight under stress. Men and women often manage stress in different ways.

Member of the audience
My question refers to a study I read this week: it showed that when you give an animal the choice between two types of food, one containing nutrients and the other nutrients-free, the animal chooses the meal which contains nutrients and pays no attention to the other. It seems that humans have lost this ability. When we consume "empty" calories, aren't we encouraged to eat more of them for our body to get the number of nutrients it needs?

Denis LAIRON
This is an interesting concept. Clearly, the regulation of food intake is a very complex issue, which is not exclusively defined by overall energy supply. The latter is only a sum of different energy supplies (proteins, lipids and sugars). Our food contains many other nutrients that have several functions, including on genes expression. I think the concept is right, but we lack knowledge to understand relations between nutrients and behaviour. Of course, if you only drink sweetened fizzy water all day, you are less likely to meet your needs in terms of micronutrients, and more likely to look around for nutrients or binge on other foods.

Prevention of type II diabetes

Philippe VAGUE
Department of Nutrition-Endocrinology-Metabolic Diseases, University Hospital of Timone, Marseille, France

I will handle type II diabetes in a pragmatic way, i.e. relying on so-called "evidence based medicine", based on actual facts leading to scientific conclusions. The facts I will use come from observation studies and prospective studies on cohorts, as well as prevention trials. I will only base my examples on trials that have been completed and given scientifically valid results.

The first observation study regards the association of physical activity and diabetes in Pima Indians. Pima Indians stem from a tribe that crossed the straits of Bering from Asia a long time ago and settled in Arizona, a desert area with frequent droughts. The ones who survived were the ones with an economy genotype, who were capable of storing fat during drought and had a tendency to become obese when food was available. Nowadays, Native Americans who live in camps hardly exceed 4 hours of physical activity per week. They tend to eat a lot, since they receive subventions. They are obese: average BMI equals 34. 38 % have diabetes, 10 % prove glucose-intolerant. Half the population has a sugar-tolerance trouble.

On the other hand, another fraction of the original tribe, with the same genetic background did not settle in Arizona but went on across Rio Grande. It settled in the Mexican mountains, and its descendants now live there as mountain farmers. This occupation takes a lot of energy, as they work 57 hours a week in average, that is to say more than the average citizen. They also eat less than their cousins from Arizona and have a normal body weight in average. There are few subjects living with diabetes or glucose-intolerance; ratios are close to the ones we notice for Mexicans living in the same conditions with a different genetic background.

Regarding this first study, we can say that, with a similar genetic background, excessive food intake, lack of physical activity and obesity are strongly associated with one another and may lead to great prevalence of diabetes.

All physical activities are not alike. The second observation studies targets high-level athletes from Finland (engaged in international competitions between 1920 and 1965), who were checked again 20 years later. The prevalence of obesity, diabetes, hypertension and coronary diseases proves different depending on the type of sport they practiced. Twenty years later, there are no obese subjects among those who practiced endurance sports (running, marathon…). They may have gone on with their activity. There is neither diabetes nor hypertension, and very few cardiovascular diseases. On the contrary, many of the athletes who used to practice power sports (such as weight lifting) have gotten obese, although they are former sportsmen. 9 % suffer from diabetes, hypertension and some of them also have cardiovascular diseases. The impact of physical activity varies from one subject to another. If you are an international athlete, you probably do not have the same genetic features as a weight lifter. This makes interpretation of observation studies very difficult.

In another study, 8,600 men were followed on a 7-years period: 149 men got diabetes. This number was put in relation with alcohol intake. Five quintiles were established, from abstinence to significant consumption. There are less diabetic people among the ones who drink little alcohol (13 g a day, two small glasses of wine). There are more diabetic people among men who do not drink at all, and even more among big drinkers. Moderation is associated with less diabetes susceptibility. Similarly, as far as antioxidants consumption is concerned, specifically vitamin E, a poor vitamin E blood concentration is related to higher diabetes exposure.

The last study targets American nurses. 85,000 nurses were followed during 15 years. Mr Hu identified a low-risk group with the following characteristics: normal body weight, at least 30 minutes of daily physical activity, non-smoker, diet rich in fibre and polyunsaturated fatty acids, and a drink every two days. Only 3.4 % of the cohort presented these characteristics, and their diabetes risk reaches only 9 % as compared to the others. This means they also have 10 times less chance to get diabetes. As to conclude that 90 % of diabetes cases could be avoided thanks to good living habits, I think it would be a bit exaggerated. Nevertheless, the relation between this lifestyle and low diabetes risk has to be taken into account. Let me stress that lifestyle often has to do with specific genetic, cultural and psychological background.

To sum up three follow-up studies on prospective cohorts that were conducted by Dr Hu's team and recently published. Diabetes risk is low when diet proves rich in vegetables, fruits, fish, poultry and non-refined cereals. It is high when diet contains a lot of red meat, fries, fatty dairy products, refined cereals, desserts and sweets. Observation studies teach us many things, but only underline associations without showing causal relations.

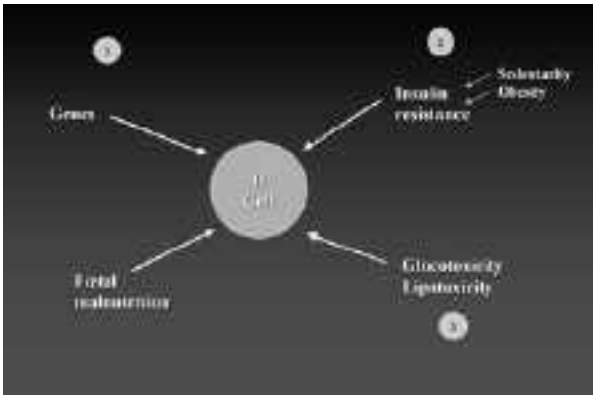
Let us consider prevention trials – I will only mention completed, reliable trials. Many new trials are underway, which we may want to mention in some years time in another edition of EGEA. The first trials targeted lifestyle changes: increasing physical activity and a controlling diet to try and lose weight. The three trials I will introduce are: a Chinese trial in the city of Da Quing, the Finnish "Diabetes Prevention Study", and a North American trial carried out within the framework of a "Diabetes Prevention Program". The trials targeted at risk subjects with glucose intolerance, in order to investigate the role of lifestyle changes on the conversion of glucose intolerance into diabetes. Body weight of subjects before the study must be noted: Chinese subjects had a BMI of 26 (which, according to our Western standards corresponds to a BMI of 29, taking into

account the average stature of Chinese people), Finnish and American subjects had a BMI of respectively 31 and 34 (severely obese). Researchers also indicated the number of subjects, duration of follow-up (6 years, 3 years and 3 years) and differentiated members of the control group (randomly selected subjects that were given lifestyle tips) and members of the intervention group (strongly managed intervention). In average, 10 % of the control group members transformed their glucose intolerance into real diabetes. In the intervention group, there was less than half the number of diabetes incidence (-42 %, -58 % and –58 %). Lifestyle modifications thus help reduce diabetes risk by half, at least during the period of the study. We will talk about these modifications later on.

Some trials also included anti-diabetes medicines, mainly two drugs that increase insulin sensitivity. Pr. Sheen said earlier that type II diabetes touches predisposed subjects, but that there is insulin resistance. If you manage to erase the resistance, you may expect that diabetes does not develop. In the DPP trial with metformin, subjects had glucose intolerance. In the Tripod trial with troglitazon, subjects had developed gestational diabetes. Lastly, in the "Stop NIDDM" trial with acarbose, which slows down the absorption of sugars by affecting sugars hydrolyse in the bowel thus reducing post-prandial hyperglycemias, subjects had glucose intolerance and diabetes was part of their family background. According to their body weight, subjects were obese. Researchers also indicated number of subjects, period of study and number of cases of diabetes that occurred within the control group: over 10 %. Benefits of medicine use are up to 31 % with metformin. Metformin is an effective anti-diabetes drug. Metformin was then stopped, and a check-up was done after 15 days: the figure had dropped from 31 to 25 %. One quarter of diabetes cases can thus be avoided through metformin, one half with troglitazon and one quarter with acarbose. Medical treatment is therefore effective, yet probably less effective than lifestyle changes.

Other trials used non anti-diabetes drugs. The main goal of such studies was to prevent hypertension, cholesterol or cardiovascular diseases, and not specifically diabetes. Trials have been conducted with anti-obesity medicines (Orlista, Exindose). In the Orlista trial, we notice a reduction of diabetes occurrence by 37 % in the treatment group, with additional weight loss of 2.8 kg as compared with the non-treatment group. Results are significant but weight loss remains moderate. Other trials were conducted with IEC or ACE inhibitors, i.e. inhibitors of the rennin-angiotensine system (sartan). Again, we notice reverse effects between the beta-blockers group and the placebo group. With statins, results are variable. Some trials have shown a protective effect against diabetes, while others have not (Sinvastatin, Atorvastatin). Last, with menopausal women (among whom many had had coronary disease): randomly selected women were given hormone replacement treatment, in order to assess effects of such treatment on coronary thrombosis recurrence. The treatment may slow down visceral fat accumulation, which is a consequence of aging and oestrogen deprivation. It is therefore protective against diabetes.

Let us discuss these documents. First, when we take action, do we prevent diabetes or simply delay it ? One of the speakers showed a graph from the UKPDS study, the famous British study on type II diabetes, which asserts that, whatever you do, diabetes slowly grows more and more severe, with gradual loss of insulin secretion functions. You can only slow down the loss of such functions. In the American DPPtrial, the evolution of glycaemia or glycated haemoglobin progressively increases within the placebo group: some subjects will get diabetes and other will not. As for treatment group subjects, these parameters go down but then increase again after some time (in smaller proportions though). Such data may make us optimistic (diabetes may be prevented) as well as pessimistic (the evolution occurs anyways).



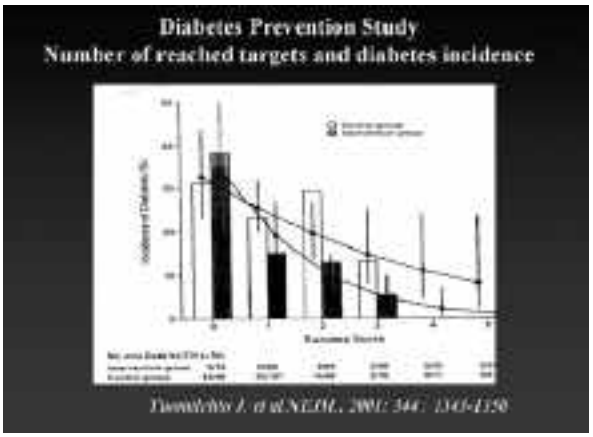
We still are not sure whether treatments prevent or push back the disease. Troglitazons have been proven to protect against diabetes even after the end of the treatment period. Yet, these are only preliminary results and do not encompass enough subjects. But these drugs may protect the ß-cell from failures that we used to consider inevitable. Most trials were meant to diminish insulin resistance. You probably remember that two elements are involved in diabetes breakthrough : ß-cells cannot produce enough insulin, which can be due to genetic defects, or foetal malnutrition among others. Our ß-cells grow older with time, and insulin-resistance adds up to this. Diminishing insulin-resistance allows protecting ß-cells, which may then produce enough insulin. Most trials were lead to reduce insulin resistance.

Yet we still do not know how to increase ß-cells capacity: trials are underway. Thanks to the Da Quing study, interesting results were presented last August in the International Congress of Diabetes, but have not been published yet. I will only talk about what has been presented verbally. Researchers classified predisposed subjects into two categories: especially insulin-resistant subjects and subjects with insulin secretion failure. This can be determined through a simple analysis based on the Oma model. It was thus asserted that very insulin-resistant subjects with small insulin secretion failure could halve their risk of diabetes by using metformin or pioglitazon. Oppositely, diet and physical exercise seemed more effective in subjects with low insulin resistance and severe insulin secretion failure. I cannot be more specific, since those results have not been published yet.

When the risk is high, treatment proves all the more effective. In the trials presented, all subjects were more or less similarly at risk, so this does not really show. It becomes more obvious with observation studies. In this example, 6000 students at the University of Pennsylvania were followed and contacted years later. Diabetes occurrence was estimated according to physical activity habits between 1962 and 1976. The subjects were classified in three groups : low physical activity, moderate physical activity and high physical activity level. An indicator shows the number of subjects with diabetes for 10,000/year. In high-risk subjects with no physical activity, 47 persons a year in 10,000 would grow diabetic, while high-risk subjects with good physical activity levels had half the risk. On the other hand, low-risk subjects with good physical activity levels had an indicator of 11 persons / year. Physical activity does not bring down the risk to zero. We can thus assess that prevention measures are most effective in high-risk subjects.

Although they are difficult to obtain, (even mild) lifestyle changes are very effective. You can see diagrams from the Finnish DPS study, which classified subjects according to their ability to meet the five recommended goals: eat less, lose weight, eat different (more unsaturated fat), exercise more… A comparison of the control group and the intervention group

was made. The intervention group was given lots of guidance and advice. In opposition to the control group, very few subjects met no goal at all in the intervention group. But 4 “control” subjects met the five goals, against 24 “intervention” subjects. Intervention was thus effective in terms of meeting the goals. How about its effect on diabetes breakthrough? Among those who did not achieve any of the goals, 30 to 40 % developed diabetes. But none of the subjects who achieved 4 to 5 goals (both from the intervention and control groups) developed diabetes. This means that for those who met proper lifestyle change objectives, diabetes did not breakthrough during the period. We may hope that this protective effect will last beyond the study if the goals keep being achieved. Lifestyle modifications are thus very effective for populations with glucose intolerance and obesity.



Let us take a look at weight loss in the different trials. Chinese subjects were moderately overweight and lost 2.5 kg for the intervention group. Finnish subjects were obese and lost 3.4 kg. American subjects were severely obese and lost 5.5 kg. Subjects of the Xendos study were very obese and lost 2.8 kg as compared to the ones who got counselling and no drugs. A man with a BMI of 34 weighs around 95 kg: losing 5 kg does not represent much but allows to avoid half the cases of diabetes. This leads to the conclusion that when an obese person loses 1 kg, they reduce risk of diabetes by 15 %. It is thus worth it.

Why ? As I already mentioned, if you are obese and get diabetic, the evolution is due to the fact that you have too much fat that provoke insulin resistance. The most dangerous fat is intra-abdominal visceral fat. In this study, obese women were trained to lose about 6 kg and visceral fat mass was then compared to the initial values. Under skin fat was also traced. Women with a lot of visceral fat lost a lot of it. The ones who had little visceral fat did not lose as much. On the other hand, there is no correlation between the quantity of initial under-skin fat and the quantity that was lost. This can be interpreted as follows: visceral fat is the most mobile; you lose it when you start losing weight. This explains why subjects at risk for diabetes in our trials (who are mostly of the android type) lost 3 kg of visceral fat. This also may be the reason why this weight loss is so effective.

What is better to prevent diabetes ? Change lifestyle or take drugs ? When have seen that medicines are almost as effective as lifestyle modifications. Physical activity is doable: everyone can lose some kilograms and work out if it is worth it. Taking one pill everyday is not very complicated either. There is no risk in changing lifestyle, provided that you get proper cardiovascular watch. Drugs may not be as safe. Some statins were recently prohibited for they proved dangerous. In the DPP trial, the control group was compared to the physical activity group, the metformin group and the glitazon group. Since glitazon proved toxic on the liver, researchers had to interrupt follow-up of this group. Any effective medicine has more or less significant side effects.

Does this influence cardiovascular risk factors ? Just as physical exercise, drugs may, indeed, influence cardiovascular risk. I will mention the Canadian study “Stop NIDDM and cardiovascular risks”. We have seen that acarbose slows down sugars absorption and reduces the risk of diabetes by 25 %. Jean-Louis Chasson, main investigator of this study, showed that the acarbose group reduced the occurrence of new hypertension cases by 34 %, of cardiovascular failures by 48%, of coronary thrombosis and silent coronary ischemia by 90 %, as compared with the control group. All this is not necessary significant, but we may assume that, for mechanisms I will not mention now, acarbose-based treatment reduces cardiovascular risk.

The last issue regards individual responsibility. We are talking about preventing a disease, not curing it. Prevention needs to take into account the ethical/political side: should subjects be given everything or should they make some sort of effort on their own ? To what extent should they get a sense of responsibility ? In lifestyle modifications, there is great individual responsibility, and less responsibility on the side of the physician. On the contrary, drug prescriptions tend to decrease individual sense of responsibility and increase pressure on the physician since side effects may always occur. This is quite schematic but has to be borne in mind.

As a conclusion, I will quote a Jewish physician from Andalusia, who learned medicine in Fez and practiced in Cairo in the 12th century : one of his aphorisms says “a disease that can be cured through diet should not be cured by other means”. Yet this was asserted 850 years ago, and science has been moving forward: we now have efficient drugs that did not exist at that time.
Thank you very much.

Questions

André SCHEEN
I would like to comment on the last table, in which we could insert a row on the cost/efficiency ratio (which is so fashionable). This was done in the DPP study. If you compare cost/efficiency ratios of lifestyle intervention and metformin use, taking into account the low cost of metformin and the difficulty to impose "life time modifications", it appears that metformin has the best cost/efficiency ratio. This is different with thiazolinediones which are much more expensive. Lifestyle modifications do involve the subject, but you need to provide them with some kind of management. And this follow-up costs money.

Philippe VAGUE
This relevant comment can be transposed to many other things. To give statin to cure hypercholesterolemia does not cost too much. But to change your diet drastically is not always easy or doable and requires a lot of energy on the side of the physician. I, as a physician, think that it depends on the person's ability to take their own responsibilities, socially, culturally and psychologically speaking. Being self-responsible creates a feeling of well-being. But some people, for some reason (cleverness, family background…) may not be able to prove self-responsible and can be better cured through medicines. I tend to see the problem through the eyes of a physician, not a national decision-maker.

Eveline ESCHWEGE
We could take the example of tobacco. We have achieved tremendous changes in tobacco-use habits around the world (especially in the USA and Europe), thanks to multiple means. If we act early in life and make a national and constant effort, we may manage to get an interesting cost/efficiency ratio.

Member of the audience *(from Algeria)*
Mr. Vague, your conference was very positive: while others tend to worry us, you reassure us. In our countries, this would have a great impact since access to drugs is quite difficult and the poor tend to be the most affected. From an ethical viewpoint, it is more gratifying to try and create self-responsibility than to pressure physicians.

Denis LAIRON
I did not mean to worry you and will try and reassure you. Together with Philippe Vague, we have conducted a study over the last few years in order to investigate on how two dietary models (Mediterranean diet or classic diet poor in lipid and cholesterol) could reduce risk factors. We have been working on a population of 200 at-risk subjects, among whom 2/3 were overweight or obese. After 3 months, by changing people's diet, we managed to reduce almost all cardiovascular risk factors and subjects lost some pounds. This came together with an amelioration of insulin and glycaemia status, as well as of the lipid parameter. This type of intervention proves very effective, while subjects are given minimum responsibility in following recommendations.

Diet and lifestyle in relation to obesity : Lessons from observational cohort studies

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Mr. Chairman, ladies and gentlemen, I would to thank you for the invitation and for the opportunity to give this talk today.

Obesity is a major risk factor for several chronic diseases, including type 2 diabetes, cardiovascular disease, and cancer. The prevalence of obesity is increasing worldwide. In the United States, the prevalence of obesity was around 10% or less in 1991, but increased substantially during the past years to between 20% and 25% as of today (1). This rising epidemic is not restricted to individual states, but is observed across the entire country.

Currently, heart disease, cancer, and stroke are the major leading causes of death in the United States. However, looking at the actual origins, recent data suggest that poor diet and physical inactivity which lead to obesity are second only to tobacco smoking as the actual cause of death (2).

On a simplistic level, obesity is an imbalance between energy intake and energy expenditure, where obesity develops when energy intake is increased or energy expenditure is decreased. However, there is probably a complex interaction between genetic and environmental factors. Although genetic factors may determine which individuals within a population become obese, environmental factors, such as diet and physical inactivity, clearly contribute to the current high rate of obesity.

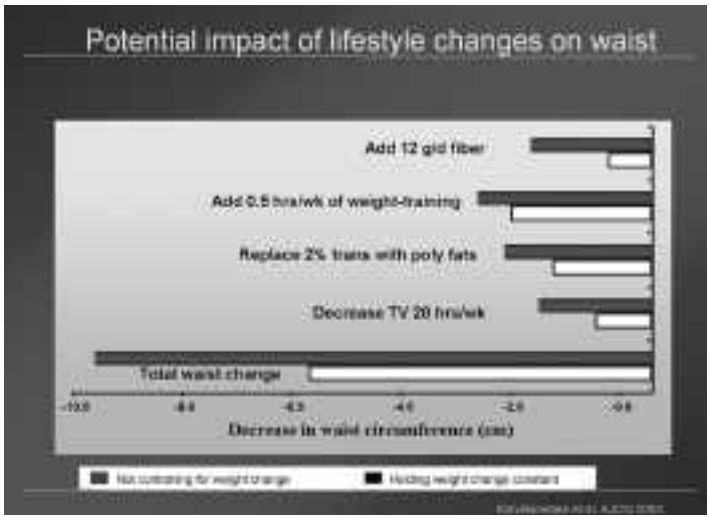
Recent data published by the Centers for Disease Control show that energy intake increased over the last 30 years in men and in women; an increase that was seen across all age groups (3).

Among macronutrients, relative carbohydrate intake, expressed as percentage of energy, increased over the past 30 years, while relative fat consumption decreased during this period (3). However, keeping in mind that during the same period energy intake increased, this translates into absolute increases in carbohydrate and fat intake during the past three decades.

Looking at the current trends in obesity, one would assume not only that energy intake increased, but also that energy expenditure and physical activity decreased. In contrast, recent data released by the Centers for Disease Control show that the proportion of subjects who report no engagement in physical activity actually decreased over the last ten years (4). However, the question of whether or not a person engages in physical activity does not take into account its intensity. Indeed, the intensity of physical activity may be a key determinant of obesity.

Beyond body mass index the fat distribution pattern is an even more important measure of obesity. Obesity can be classified into peripheral and abdominal obesity, where abdominal or central obesity is characterized by an increase in waist circumference and visceral adipose tissue, whereas peripheral obesity is characterized by an increase in hip circumference and subcutaneous adipose tissue (5). It is known that visceral adipose tissue is metabolically more active, and that abdominal obesity confers a higher risk of chronic disease than peripheral obesity. Thus, measurement of waist circumference provides additional information beyond the body mass index about a subject's risk of developing chronic diseases. Abdominal obesity is defined as a waist circumference greater than 102 centimeters in men and greater than 88 centimeters in women (5).

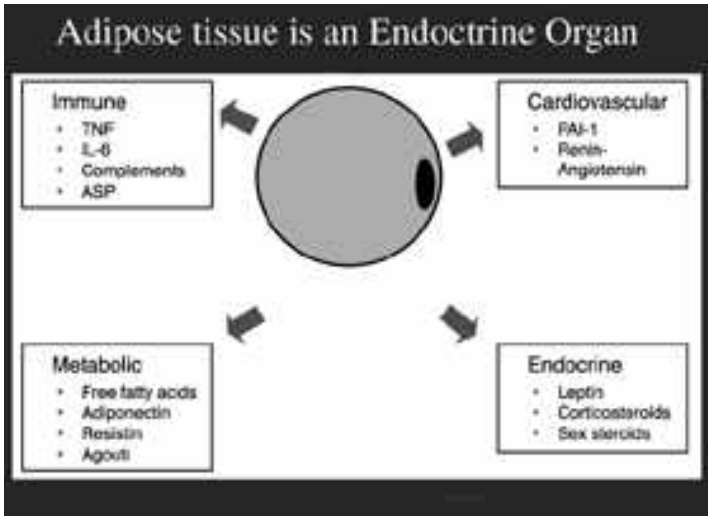
High energy intake and physical inactivity determine body weight gain; however, little is known about diet and lifestyle factors that specifically predict waist gain or an increase in visceral fat tissue mass. This raises the question as to whether there are specific factors that predict the fat distribution pattern.



Koh-Banerjee et al. (6) recently examined the association between dietary and lifestyle factors in relation to waist change in the Health Professionals' Follow-up Study, which is an ongoing cohort study that was started in 1986 with inclusion of about 50,000 participants. Information about diet and lifestyle is assessed every four years, and information about disease incidence and anthropometry every two years. In 1987 and in 1996, waist circumference was measured, so we were able to determine predictors of waist change over a nine-year period in about 16,000 subjects.

Within all age groups body mass index increased over time: about 1 kilogram per square meter in those aged 40 to 50 years, and a little less in subjects older than 50 years. There was also an increase in waist circumference over time: about 4 cm in the younger age groups, and slightly less in the older age groups. The question is: Are there dietary or lifestyle behaviours that predict these changes?

The results of the analysis showed that there was a significant association between changes in dietary fat intake and changes in waist circumference (6): People who increased their fat intake by 5% of energy over 9 years had an increase in waist circumference of 27 mm. However, this increase was attenuated and no longer significant when the model was adjusted for concomitant changes in body mass index. Thus, although fat intake may predict waist gain, it does not predict changes in the fat distribution pattern. In contrast, looking at specific types of fat, trans-fatty acids predicted waist gain even after adjustment for changes in body mass index. Thus, consumption of trans-fatty acids is not only related to an increase in waist circumference in general, but it also predicts the fat distribution pattern, indicating an accumulation of visceral fat tissue.



The results were similar whether carbohydrates were replaced with trans-fatty acids, or whether polyunsaturated fatty acids were replaced with trans-fatty acids. An increase of trans-fatty acid intake by 2% of energy was related to an increase of 52 mm in waist circumference. In contrast, fibre intake was associated with a decrease in waist circumference, which was independent of changes in body weight. Thus, if a man increases his total fibre consumption by 12 grams per day he can expect not only less waist gain in general, but specifically that his waist circumference may become smaller and that his body fat distribution pattern may change.

Vigorous physical activities, such as jogging, running, swimming or cycling, were associated with a decrease in waist circumference – again, independent of general changes in body weight. Interestingly, weight training, which is a non-vigorous resistance-type of physical activity, was also negatively related to waist gain: Men who increased their weight training by half an hour per week had a significant decrease in waist circumference.

Walking in general was not significantly associated with changes in waist circumference; however, walking pace, which is an indicator of intensity of physical activity, was related to a decrease in waist circumference. Thus, people who increase their walking pace may decrease their waist circumference.

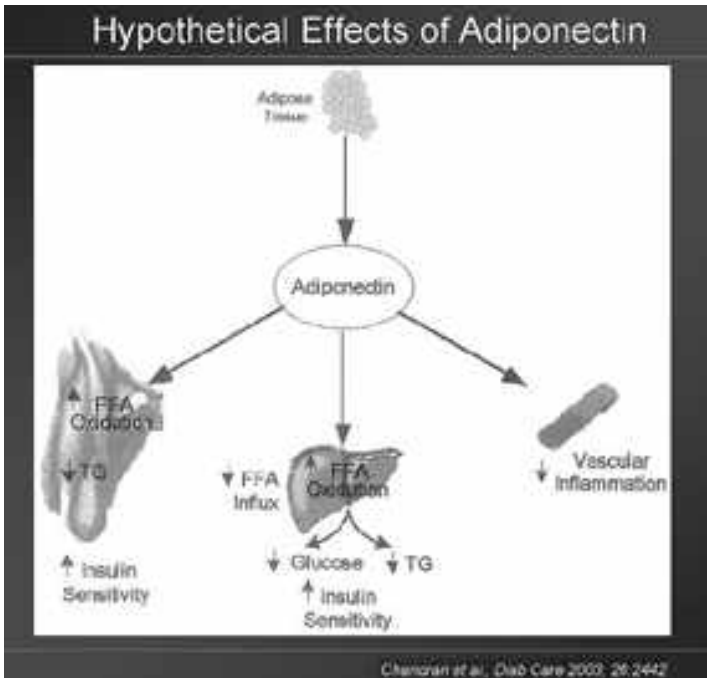
An increase in television watching time was associated with waist gain, independently of changes in physical activity. Thus, TVwatching time may add waist circumference beyond physical inactivity. Activity here refers to leisure time physical activity; this does not take into account occupational activities.
If everything is added up, what can be predicted ? If a man adds 12 grams of fibre per day to his diet, if he has half an hour of weight training per week, if he eats 2 % of daily energy in the form of polyunsaturated fatty acids instead of trans-fatty acids, and if he decreases his TV consumption during the week by 20 hours, than he can expect a substantial decrease in waist circumference of about 6 cm, which is even beyond changes in overall body weight.

Diet and lifestyle factors are related to obesity and disease incidence. What are the mechanisms that link obesity with chronic diseases like type 2 diabetes and coronary heart disease? Not every obese person will necessarily develop a chronic disease. Finding relevant mediators might help identify subjects at risk of disease incidence. Furthermore, studying the relationship between diet and lifestyle with these mediators can also provide information about the prevention of diseases.

Over the past years it was shown that the adipose tissue produces pro-inflammatory cytokines like interleukin-6 and tumor necrosis factor. These cytokines in turn are inducing acute phase proteins, such as C-reactive protein, in the liver, and are implicated in the pathophysiology of obesity-related chronic diseases, like type 2 diabetes and coronary heart disease. Chronic inflammation is an important risk factors for coronary heart disease. In fact, it was shown in a recent report coming from the Women's Health Study that CRP is almost as good as LDL-cholesterol in predicting cardiovascular events (7). In this report (7), women were divided into quintiles based on their CRP and LDL-cholesterol level. The prediction of cardiovascular event-free survival according to the women's CRP or LDL-cholesterol levels was of similar magnitude, which highlights the importance of measuring inflammatory markers for risk prediction. It also underscores the importance to investigate whether inflammation may be a modifiable risk factor to prevent coronary heart disease.

Is there an association between diet and inflammation? In a recently published study (8) we examined the association between trans-fatty acid intake and inflammation in women in the Nurses' Health Study. We found that there was a positive association between trans-fatty acid intake and inflammatory markers. Women in the highest percentile of trans-fatty acid intake had significantly higher levels of soluble tumor necrosis factor receptors, which are indicators of inflammation. Since trans-fatty acid intake has been linked to coronary heart disease risk, our findings suggest that inflammation may be a potential mediator between diet and heart disease. Tumor necrosis factor is involved in the development of insulin resistance. We speculate whether increased trans-fatty acid intake related to increased tumor necrosis factor levels may promote insulin

resistance, leading to hyperinsulinaemia, and, possibly, gain in visceral adipose tissue, which would explain our observation that trans-fatty acids predict waist gain.



It is well established that polyunsaturated fatty acids are involved in inflammatory pathways. Omega 6 and omega 3 fatty acids are precursors of eicosanoids, like thromboxane, prostaglandins, and leukotrienes. Eicosanoids, derived from omega 6 fatty acids are generally considered pro-inflammatory biomarkers, while those derived from omega-3 fatty acids are considered to have anti-inflammatory properties. Alpha-linolenic acid, which is an omega-3 fatty acid, is converted to EPA, and EPA in turn to thromboxane, prostaglandins, and leukotrienes. This conversion is performed by the same enzymes as for the omega-6 fatty acids, suggesting that there is a balance between these two types of fatty acids. Our question was: are these polyunsaturated fatty acids related to inflammatory marker levels in humans?

We analyzed the relationship between polyunsaturated fatty acids and inflammatory markers in men and women with similar results (9). We found a significant inverse association between the long-chain omega-3 fatty acids, EPA and DHA, and inflammatory markers. In contrast, we found no significant association for alpha-linolenic acid or for the omega-6 fatty acid linoleic acid.

It has been argued that omega-6 fatty acid intake in our diet may be too high and needs to be reduced. Interestingly, in our analysis we found a significant interaction between the two types of fatty acids (9). At low levels of omega-6 fatty acid intake, we found no association between omega-3 intake and inflammation. However, at a very high intake of omega-6 fatty acids we found an inverse association. Subjects who had the highest intake of omega-3 and the highest intake of omega-6 fatty acids had the lowest levels of inflammation, whereas subjects with low omega-3 intake and high omega-6 intake had the highest levels of inflammation. This significant interaction was seen for soluble TNF receptor 1 and soluble TNF receptor 2.

We also found an inverse association between inflammatory markers and physical activity (10). Thus, an increase in physical activity level by 20 MET-hours a week, which corresponds to running twice a week for about one and a half hours, relates to up to 10% lower inflammatory marker levels. We also specifically addressed the question of whether this relation might be explained by adipose tissue mass; therefore, we adjusted our analysis for body mass index, and also for leptin levels as a surrogate for fat mass. For some of the inflammatory markers this association was substantially attenuated, indicating that the reduced inflammation associated with physical activity may be explained by less adipose tissue in these people.

The adipose tissue is considered to be an endocrine organ and secretes several mediators that are involved in inflammatory pathways, like TNF or interleukin-6 (11). Some of these mediators, like PAI-1 and hormones of the renin-angiotensin system, are also involved in cardiovascular disease. The adipose tissue also secretes hormones that are involved in endocrine pathways, like leptin and corticosteroids; and hormones that are involved in metabolic functions like free fatty acids and adiponectin. In the past, we have particularly examined the role of adiponectin in human health and disease in our cohorts.

In contrast to other adipose-derived hormones, like leptin, plasma adiponectin levels are inversely associated with body mass index. Obese subjects have significantly lower adiponectin levels compared to non-obese subjects. Adiponectin has been hypothesized to be involved in several metabolic pathways, mainly based on experimental settings in cell cultures or animals (12). Adiponectin increases free fatty acid oxidation in the muscle and in the liver. Furthermore, it decreases triglyceride accumulation in the muscle and inhibits gluconeogenesis in the liver, resulting in improvement of insulin sensitivity. It has already been shown in humans that high plasma adiponectin levels indicate a lower risk of developing type 2 diabetes (13). Furthermore, adiponectin is also related to inflammation. In cell cultures, adiponectin modulates inflammatory pathways, and animal trials have also shown that adiponectin has anti-atherogenic effects. Our question was whether adiponectin – as an adipose-derived hormone – may be related to coronary heart disease risk.

We studied this association in the Health Professionals' Follow-up Study in a nested case control design (14). In 1994, a blood sample was obtained from all subjects without cardiovascular disease. During six years of follow-up, we identified 266 new cases of myocardial infarction. These were matched with 532 control subjects who did not develop any cardiovascular disease during the same period and we then analyzed the biomarkers obtained at baseline. We found that those men who developed myocardial infarction during follow-up had significantly lower plasma adiponectin levels at baseline compared to the control subjects (14).

We also adjusted our analysis for other cardiovascular risk factors, like body mass index, family history of myocardial infarction, hypertension, diabetes, alcohol intake, physical activity , and LDL and HDL-cholesterol levels and found that the association between adiponectin and risk of coronary heart disease was independent of these factors (14). When we categorized subjects into quintiles those subjects in the highest compared with the lowest quintile of plasma adiponectin levels had about a 40% reduced risk of coronary heart disease. When we further adjusted for other potential intermediate variables, like triglycerides, HbA1c or CRP levels, the relative risk was not substantially changed. These findings suggest that adiponectin may be independently association with coronary heart disease.

Our next question was: What is the relationship between dietary factors and lifestyle behaviours and adiponectin levels ? We analysed this in our dataset cross-sectionally and found significant relations of adiponectin with dietary factors, indicating that adiponectin may indeed be related to diet.

In conclusion, we can learn from these observational cohort studies that dietary and lifestyle factors, such as trans-fatty acids consumption and physical activity, may not only predict body weight gain, but may also specifically predict the fat distribution pattern; in other words a gain in visceral adiposity. Dietary and lifestyle factors are also related to obesity-related inflammatory markers, like TNF, IL-6 and CRP, and to chronic disease incidence. Adiponectin is a relatively newly identified protein that is exclusively secreted by the adipose tissue. Our study shows that high adiponectin levels predict a lower incidence of coronary heart disease. Furthermore, given its potential association with macronutrient intake, adiponectin may be a novel mediator which links diet, lifestyle and obesity to chronic diseases, like type 2 diabetes and coronary heart disease.

Current research aims to further examine the association of lifestyle and diet with obesity and obesity-related mediators. In this context, observational cohort studies are a cornerstone to help gain a better understanding of the pathophysiology of obesity and to find possibilities for prevention and treatment.

I would like to thank my colleagues, especially Pauline Koh-Banerjee, who provided and published the analysis of changes in waist circumference; Eric Rimm, whom I had the privilege of working with during the last two and a half years, and Walter Willett, Gokhan Hotamisligil, Susan Hankinson, Frank Hu, Meir Stampfer, Cynthia Girman, and Nader Rifai for their contributions and support of these projects.

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Questions

Member of the audience
An excellent presentation, thank you very much. Did you find any correlation between trans-fatty acids and adiponectin levels ?

Tobias PISCHON
The association between adiponectin and individual fatty acids is an interesting question, because in cell cultures and experimental settings, polyunsaturated fatty acids may specifically affect PPAR-gamma, and PPAR-gamma in turn may affect adiponectin levels. However, types of polyunsaturated fatty acid in our diet are highly correlated with each other; it is therefore very difficult to tease out associations for individual fatty acids. This would require a larger sample size than our study.

Member of the audience
It is probably closely related to the transcription factor regulation.

Tobias PISCHON
Yes

Member of the audience
What are the trends for the intake of trans-fatty acids in the United States, for example? Do they eat more and more trans-fatty acids or less and less ?

Tobias PISCHON
Currently there is an increase in trans-fatty acids. In our data, trans-fatty acids contributed to about 4-5% of total fat and about 1% of energy intake. In the United States, it is now mandatory to indicate the amount of trans-fatty acids on the nutrition labels. I assume that trans-fatty intake probably starts to decrease in the near future.

André SHEEN
I was very interested by this association between adiponectin levels and dietary factors. Can you comment further about this? I am concerned about reconciling such large epidemiological data with correlation even after multi-variable adjustments and pathophysiological or mechanistic processes. Can you speculate what the mechanism would be? What is your explanation, because correlation of cause is not an explanation ?

Tobias PISCHON
Adiponectin levels show only a small degree of short-term variability. There is a slight circadian variability with a small increase during the day and a small decrease at night, but this seems negligible.. There is also no effect of acute meal intake on adiponectin levels. Less is known about long-term effects. Our cross-sectional analysis between dietary factors and adiponectin levels can only show associations; it cannot tease out what is cause and what is effect. Further studies are needed to determine the causal role of adiponectin.

CONCLUSION

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To conclude, I will underline a few facts that struck me. First, on Dr. Seidell's communication about the pandemics of obesity and diabetes: although average body weight of individuals within a given population has not changed, there are twice as many obese subjects with BMI>30 and four times as many massively obese people. This means that obesity, as a disease, has been developing, notably massive obesity. Regarding Pr. Sheen's intervention on relationships between diabetes and obesity, I would like to stress that, beside Rodbell's 40 year-old classical theories – that are true and maybe a bit simplistic – in which excess fatty acids released by adipose tissues are the cause of insulin resistance, we may now consider that adipose tissues influence insulin resistance through many other mechanisms: First, through ectopic fat deposits in muscles and the liver, perhaps also the pancreas; second, through several fat tissue secretions (hormones or cytokines). Denis Lairon has shown relationships between genes and nutrition in obesity development: I will only underline inequalities among human beings in terms of dietary overload or energy spending. To complete the same amount of activity, some of us use a lot of calories, while others do not. Those who do naturally burn a lot of calories tend not to gain weight, while others tend to gain weight. This is a crucial point. I would also like to revert on the last slide: nutrigenetics is the way our genes allow us to use nutrients, and nutrigenomics is the way nutrients act on our genes.

As far as Dr. Pischon's last communication, I will comment on two or three aspects. As years go by, when you grow 10 years older between 30 and 60, even if your body weight remains unchanged, you waist measurement increases by 3 cm. This can be managed through physical activity, i.e. fast walking and through dietary control, i.e. eating less trans-hydrogenated fat. That is it for this interesting morning session, which allowed us to go from fundamental mechanisms to practical issues

Introduction

Ambroise MARTIN
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We have had some very interesting lectures this morning. From the manager's point of view, two points emerge. First, obesity is a major public health concern. This is clear and it is scientifically proven. Secondly, nutrition is a very important issue in this problem. For the managers, and I speak from my recent experience in the French food safety agency (AFSSA), how can we translate this sound scientific background into practical actions ? This afternoon's workshop is clearly in line with the morning's presentations and will give a further opportunity to present the results of scientific research to support practical actions in the field. It is very important to have a sound scientific background to manage the problem. For example, from my experience, not only in AFSSA but also in the French National Food Council, we are now thinking clearly about the development of a food policy – not just a nutrition policy, not just an agricultural policy, but a food policy that can fill the huge gap between the two existing policies; an agricultural policy devoted to the improvement of production and so on, and a nutrition policy devoted to the health of the population. The objectives of these policies are clearly divergent and are often very contradictory. So we need to develop a food policy and for that, we need a very sound scientific background.

I am not a specialist on obesity but I would like to emphasize some points from my experience. The subject of the workshop is the role of fruits and vegetables in weight management and obesity prevention. It is important for biological sciences, clinical sciences and epidemiology to provide very strong evidence, because beyond this evidence, a lot of scientific research has to be done with the view of putting the results of the scientific work into practice at the population level. For example, in the area of fruits and vegetables, there are four very important points that are divergent and also contradictory and which deserve a scientific approach. It is clear that not enough research has been done in these areas, especially in France.

The first one is taste. The evolution of the economic background of the organization of the food chain has not had the best results in this field. The development of the big distribution chains and the need for convenience for this type of distribution is clearly against the maintenance of good taste or the organoleptic properties of fruits. That is important to consider also.

The second topic is the nutritional quality of foods. The development of new varieties, new species and new processes of fruits and vegetables in the past was clearly based solely on technological properties and productivity. Together with the Academy of Agriculture, we have developed some ideas about the introduction of nutritional criteria in the development of new species and varieties of fruits and vegetables. It seems difficult to implement for the moment but it is important to make the first step in this direction.

The third is about price. Yesterday, Mr. Drewnowski clearly demonstrated the importance of price. It is clearly divergent from the other topics but it too illustrates the importance of the development of a food policy.

The last topic of concern for me in AFSSA relates to food safety. In the context of the recurrent food crises in recent years – BSE, then dioxin and PCBs, and so on – the emerging problem concerns pesticide residues in fruits and vegetables. We need better collaboration between nutritionists and toxicologists. Perhaps that is a dream, but it could perhaps become a reality in the future if we want. There are many studies in nutrition on the link between nutrients, nutrition and foods with health. On the other hand, we have many problems concerning food contaminants and we need the tools to assess the risks linked to food contaminants correctly. The contamination of foods by pesticide residues and other contaminants is clearly of concern for the consumer.

The two assessments, nutritional benefits on the one hand, and risks linked to toxicological problems on the other hand, are not connected now. Everyone would benefit from having a better connection between the two and I think that nutritional epidemiology could provide much valuable data in order to improve risk assessment in these areas. My best wish is that there is a better link between the two in the future.

Obviously, in the studies demonstrating the benefits of a high consumption of fruits and vegetables, the fruits and vegetables are consumed as produced – they are consumed with their contaminants. However, for the food policy managers to be convinced, the ratio between the benefits and the risks needs to be assessed better and there is also a need to be able to communicate with consumers about these types of problems. How, for example, do we manage the risk between pesticide residues and, if we do not use these types of products, the increased consumption of mycotoxins, for example? We clearly need to develop such tools. This is a very important issue for basic science showing the benefits of fruits and vegetables, and it is of great concern for the managers.

I will end my presentation now so that we have enough time for the scientific presentations, but I think it is important for everybody to keep all these problems in mind.

Mediterranean diet and obesity

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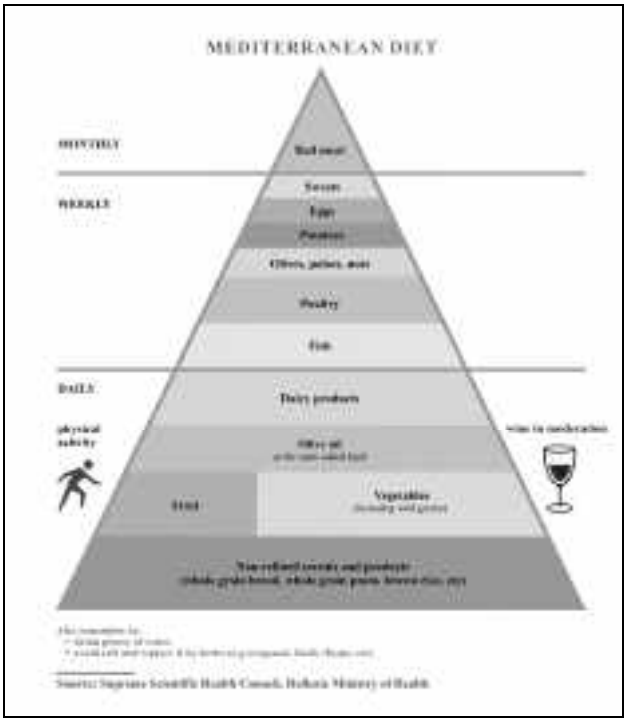
Thank you Mr. Chairman. Ladies and gentlemen, dear colleagues and friends, it is a privilege for me to be here in a Mediterranean city, Perpignan, to talk about the role of diet and lipids on obesity in the context of the Mediterranean diet. I wish to thank again the organisers for giving me this opportunity.

It has been repeatedly mentioned since yesterday that the rise of obesity has reached epidemic proportions and has escalated to become a worldwide problem. I think it is time, as our Chairman mentioned before, to formulate nutrition policies to battle the problem. Messages need to be developed and dietary guidelines have to be proposed, documented and promoted.

Up to now, the existing guidelines, as developed by several organisations in several countries, have been interpreted mainly as targeting a reduction of "fat" intake. Thus, people are advised that fat has to be reduced for obesity to be reduced. The question arises, especially from Mediterranean people: What is meant by fat, because fat has different meaning in different populations. For the Mediterranean populations "fat", it is mainly olive oil. In the northern European countries, it is mainly animal fat – milk, cheese and meat. So these linguistic details may have great influences especially for populations that have not developed their own guidelines and adopt the guidelines of other countries or international organisations.



Fats and oils are distinct categories in the broad group of lipids. Some of us have been advocating for years that instead of using the term "fat" we should be using the term "dietary lipids." Thus the differentiation of the type of "fat" is feasible. There is substantial evidence indicating beneficial effects for health from some types of dietary "fat". This is why in the Greek dietary guidelines, which are based on the Mediterranean dietary pattern, the fraction of energy intake that can be derived from dietary lipids is not specified. It is only mentioned that the main added lipid should be olive oil. It is important to mention that in Greece and most of the Mediterranean countries, olive oil also promotes a high vegetable consumption. Reduction of "fat" in the Mediterranean countries would automatically be associated with reduction in vegetable intake. It should also be stressed that vegetables in Mediterranean Countries are frequently consumed as a main dish as well as in the form of salads. Quite often colleagues, especially from the United States, ask me how we manage to consume 500 grams of vegetables a day, on average. The answer is that we do not eat them on their own; we eat them cooked in olive oil with onion, garlic and a lot of herbs, as a main dish.

During the last 25 years several of us have argued that "fat" reduction'could be detrimental for some populations in southern Europe. In Greece, 40% of energy intake comes from "fat". A step in the right direction was the recommendation in the third report of the National Cholesterol Education Program[1]. They recommend 25-35% of total calories from "fat". Some of you will remember that 20% was a common objective only 15 years ago. Yet, as it was mentioned repeatedly this morning, reduction of fat intake in the United States was associated with weight gain. The reduction in physical activity was not large enough to explain this rise in body weight.

Yes, the Greeks too are becoming obese. Some say it is because of our high "fat" intake. I do not think this is true, because even in the 60s when we were lean and had the highest life expectancy in the whole world, even higher than the Japanese, Greeks were consuming a lot of fat: 40% overall and 43% in Crete. At that time, of course, they were walking much more. But today, we are becoming obese. Why is this happening ? It is because the energy intake has increased substantially and energy expenditure has declined dramatically.

I think that we should re-evaluate whether low-fat diets should be the preferred approach to weight reduction. It would be better to focus on total energy intake and physical active and not so much on whether the energy comes from fat or from carbohydrates. Indeed, there are now two schools of thought: one advocates moderate to high-fat diets (but low in carbohydrates) whereas the other advocates low-fat diets.

For the low fat advocates, energy intake is reduced when you are eating less fat: one gram of fat provides 9 calories and one gram of carbohydrates or proteins provides 4 calories. But, energy density should also be considered. If you mix vegetables with olive oil, on the average it is not so energy dense. When we talk about fatty foods, we are really talking about energy-dense foods, like cookies, rich ice cream, pastries etc. In general, for every food you should consider how much energy it provides and to which extent it induces satiety.

An interesting meta-analysis by Astrup in Denmark summarizes the results of controlled trials lasting over two months[2]. If you want to test the success of a diet for reducing obesity, you have to check the adherence and the length of time it was implemented. So, in this meta-analysis, the trials included have lasted more than two months, although generally less than a year.

The results show that a reduction in dietary fat without intentional restriction of energy intake causes weight loss that is most evident in heavier subjects. I underline "without intentional restriction" because when you are comparing high and low-fat diets, you need to assure iso-caloric diets.

On the other hand if we review the randomized trials focusing on reduced fat intake and lasted for more than one year, meaning that we also address the adherence parameter weight reduction varied from none to rather little with an average of about 1kg.

There is a need for a study that evaluates moderate-to-high fat intake and balanced nutrition, that is, diets that can be integrated in our everyday lives because they are acceptable and pleasant. In this way, taste increases long-term adherence. One of these diets is the Mediterranean diet (Figure). Such a study was done by McManus et al[3]. It was a randomized controlled trial of a moderate-fat diet, compared with a low-fat diet, both low-energy among overweight adults. In the study, 101 overweight men and women participated. In the moderate-fat diet, the energy percentage of fat was 35%, and in the low-fat diet it was 20%. Both groups adhered to the diet for the first six months, but by the 18th month most of participants abandoned the low-fat diet. In the Mediterranean part of the world where we are used to moderate to high-fat diet, it is very difficult to do what the Japanese and Chinese are doing. At the end of 18 months, weight loss for the moderate-fat diet was almost 7 kilos, whereas those on the low-fat diet, actually gained weight. People, who diet and fail, gain more weight afterwards.

These data are revealing: weight reduction is very quick in the beginning. The weight reduction on the moderate-fat diet reflects adherence to a diet which is palatable. Those on the moderate-fat diet maintained the weight reduction, whereas those on the low-fat diet largely abandoned it. Thus, the metabolic evidence that the low-fat diet is more efficient than the high-fat diet is not, by itself, persuasive.

It would be an omission if I did not mention the current trend in the United States: the low-carbohydrate diet. Low-fat diets are no longer popular in the United States. People are not concerned about fat, but they are concerned about carbohydrates [4]. Let us be realistic. What does a low-carbohydrate diet mean if it does not mean increase of fat in the diet? What does a low-fat, high-carbohydrate diet mean, other than increasing triglycerides, reducing high-density lipoproteins, increasing the risk of glucose intolerance and metabolic syndrome?

I think we have to think again about guidelines focusing on reduced fat intake. First of all, we have to think of what is meant by "fat" in the Mediterranean and the other western Countries. In a paper on a cohort study in Spain, it was found that consumers of large quantities of olive oil had low saturated fat intake, high vegetable and legume consumption and more adequate vitamin intake[5]. In the Epic Greek cohort, which comprises 28,000 Greeks, we are doing an analysis. These data are not yet published, but we found that a 10 gram increase in olive oil consumption is associated with a 110 gram increase in vegetable consumption. I think the beneficial effects of olive oil are well known and I do not want to be repetitive, but when preparing for this presentation, I found a paper that was published recently and indicated that olive oil may be effective in reducing insulin resistance 6.

Conclusion: the reduction of the percentage of energy from fat causes a short-term reduction in body weight. Data do not support superiority of low-fat diets for weight loss in long-term trials. Alow energy, moderate- to- high lipid intake Mediterranean diet can be a tasty successful approach to long-term weight loss. Additional research is needed for extended periods of time. We need to know how we will transfer the message to our population, because as Hippocrates said, "The obese die faster than the lean." He said that 2500 years ago and I think it still applies today.

Thank you for your attention.

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Questions

Antonia TRICHOPOULOU
There was an unfortunate development in Greece 25 years ago with the invasion of seed oils. People started cutting down the olive trees because it was said that the seed oils reduced cholesterol. We have another problem right now: the enriched margarine problem. Margarine enriched with sterols and stanols. Greeks are eating it with a spoon because it is intensely marketed. They attempt to reduce their cholesterol by eating margarine, and so they are getting extra calories.

Member of the audience
Thank you Antonia. I would just like to make a comment. We are performing an intervention study in Marseilles, the Medi-RIVAGE intervention study, where we are comparing Mediterranean-type diets, with a moderate amount of fat and especially olive oil, with the usual low-fat or low-cholesterol diet. I can confirm what you showed. At first, the confiance was much better after three months. So the intervention was carried out after three months and then one year. When the Mediterranean diet was compared with the low-fat diet, the low-fat diet drop-out rate was double that of the Mediterranean diet.

Secondly, the efficiency in weight reduction was better in the Mediterranean diet as compared to the low-fat diet. I think there is increasing support saying that a moderate-fat diet would not be detrimental and that maybe a high carbohydrate diet, as long as it is poor in fibre and rich in readily-available carbohydrates, could be rather detrimental to body-weight.

Member of the audience
You mentioned a little about some of the changes that are happening in your traditional eating-habits in Greece. Can you say more about what else is going on in changing eating-habits? What else is happening in Greece in terms of the changes from the traditional diet?

Antonia TRICHOPOULOU
In Greece, as everywhere else, we have seen a big change over the last 20 years. I think that the phenomenon is basically societal. I remember 15 years ago, people did not drink wine because they thought they belonged to a higher societal stratum if they drank whisky or beer. Because they were bombarded by television, they did not trust what they heard from the scientific community. They were trying to adapt and imitate.

Secondly, the effect of marketing is pervasive. I worry a lot about the future of the Mediterranean diet in our region. Young children do not have the experience or the taste of the traditional Mediterranean diet. One example concerns the Greek yogurt: in order for it to be marketed in Northern Europe, it has to be sweet, even though Greek yogurt is sour. By making it sweet, yogourt does not hold the same bacterial flora.

So now, Greek children do not like the traditional healthy sour Greek yogurt. So our effort in the Greek Ministry of Health is to focus on the schoolchildren.

Fruits, vegetables and body-weight management

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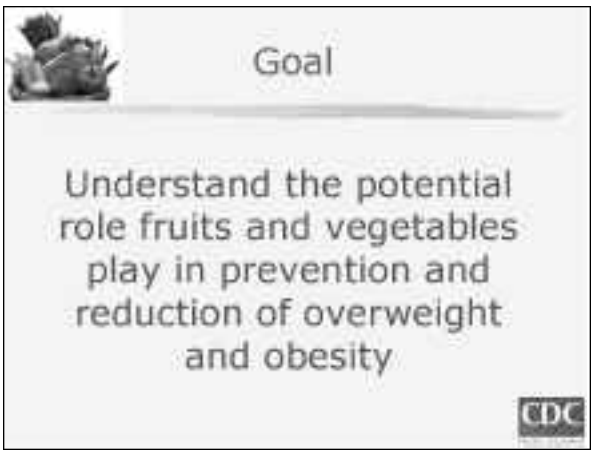
Division of Nutrition and Physical Activity, 4770 Buford Highway MS-K26 Atlanta, GA30341, USA

Good afternoon and thank you so much for having me here today. The title of my talk is "Fruits, vegetables, and body-weight management". The goal today is to have everyone understand the potential role that fruits and vegetables play in the prevention and reduction of overweight and obesity.



I am going to go through a lot of studies that are all covered in these two reviews. The first review was published in January of this year, and the other review that covers the epidemiological studies will hopefully be out this autumn, I am told. I will go quickly through these studies now so that you can refer back to both these papers. They go into much more detail.

My outline for today's talk is going to be :
- Why fruit and vegetables for weight management ?
- What does the research tell us ?
- What can we learn from other evidence ?
- What are some of the caveats when dealing with the relationship of fruit and vegetables consumption and body weight management?

First, why do fruit and vegetables help prevent disease and provide nutrients ? In a recent scientific overview by Diane Hyphon, the conclusion from that paper was that current evidence collectively demonstrates that fruit and vegetable intake is associated with improved health, reduced risk of major diseases, and possibly, the late onset of age-related indicators.

I think that the science is very strong in these areas. These are very popular maps today but since I work for CDC, I still have the right to show these maps. This is the most recent one that you saw earlier today, basically showing that 60% of our population is overweight and 26% of those overweight are defined as obese, with a BMI of 30.

We also know that in the United States, we do not meet our recommended allowance of fruit and vegetables a day: five a day is our goal. The total is 4.2, but if you take out potato crisps and French fries, we drop down to 3.6. Impressive, is it not ? So we know that only one in five adult Americans meets the recommended five a day. Eighty-nine percent of teenage girls and 96% of 2-12 year-olds fall short of eating the recommended 5 a day. There have also been studies showing that obesity levels are lowest among those with the highest fruit and vegetable intake.

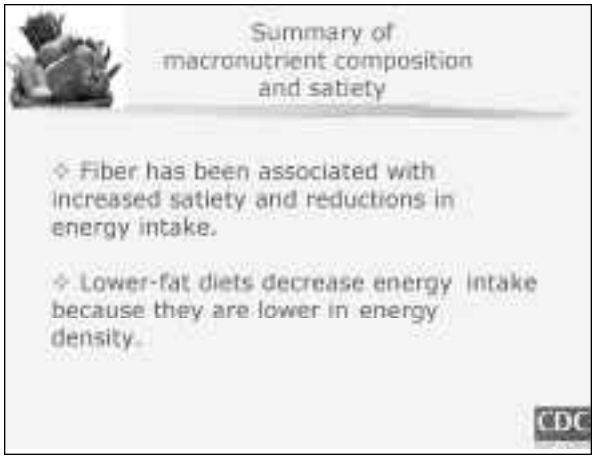
What does the research tell us ? I am going to take you through a series of studies that look at different aspects of eating and food intake. First, we are going to look at satiety studies. Satiety is the effect that food has after a meal has ended. How full do we feel ? Then there is satiation. That process is involved in the termination of a meal. What makes us stop eating ? And then there is energy density, which people have talked about briefly, but that is the relationship of calories to the volume of food. I will go into that in more detail later.

What food properties affect satiety ? There is a whole list of them here, there are sensory properties, and energy density is the main one that I am going to cover. Then there is also volume and physical properties of food.

The first couple of studies that I am going to review look at the addition of vegetables and their effect on satiety. They looked at meals that had added vegetables and equal calories, but they showed that once they had at least 200 grams of added carrots and spinach, it enhanced the fullness, and people felt fuller when there were more vegetables in the meal.

Another group looked at satiety over two hours, of once again iso-caloric foods. They looked at 38 foods, and the highest satiety ratings came from fruit and potatoes, though they did not do a lot of other vegetables, it was mostly potatoes. However, they showed that these foods do enhance fullness.

On satiation, this was by Bell and colleagues. They studied women. They gave them meals for two days and they had low-energy density, medium-energy density, or high-energy density meals. They were told to eat as much as they wanted so it was given to them buffet style. The menus were very similar, except for the addition of vegetables to reduce energy density.



They found that the groups rated the meals as very similar and they tasted good, which we know from our last talk is very important. They ate a similar amount of food, so the amount they were putting on their plate and consuming was the same.

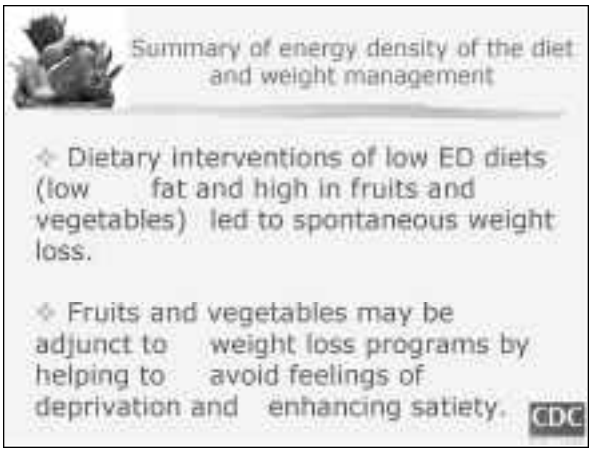
Because some of them were on high-energy density meals, which meant they had more calories, these women ended up consuming an average of 1 800 calories a day. However, for those on the low-energy density diet, it was less than

1 400 calories a day. So they tasted the same and they ate the same amount, but they took in fewer calories. Here it is graphed out. You can see for food intake that they ate the same amount of food over the two days with breakfast, lunch, dinner and snack.

However, the statistical difference shows up in the energy intake because the high-energy density meals had more calories, and the low energy density had fewer calories. Also, on these same diets, the women reported the same amount of hunger across the different diets, and also fullness was the same. So calories did not matter here, it was more the amount of food that they were eating.

Subsequent to that Bell and Rolls did a study in which they looked at energy density in fat content to see if fat content had influenced it. They varied by adding fruit at breakfast and vegetables at lunch and dinner. They found that the energy density affected an energy intake across all fat levels. So it did not matter how much fat was in the diet, it was the energy density that mattered: the lower the energy density; the lower the caloric intake. Once again, the participants ate similar amounts of food, so those in the low-energy density group ate 500 fewer calories a day than the high-energy density.

What happens when we give dietary advice to increase fruit and vegetables ? There is a series of studies where they looked at the AHA (American Heart Association) fat-reduced diets. They wanted one group to increase fruit and vegetables by at least 400 grams a day. This intervention group actually exceeded that goal and got to 575 grams of fruit and vegetables a day and lost at mean of almost 14 pounds after one year of follow-up.



The other group was a fat-reduced diet, but without the added fruit and vegetables. It is important to say that this group did get less dietary counselling, and they got a different message of not emphasizing fruit and vegetables. They ended up losing weight, only about 5 pounds, but they increased their fat and calories over the year, so as they moved away from the intervention, they increased their fat and calories. Here it is graphed out for you, so you can see the difference. The weight loss was more dramatic in the low-fat group with increased levels of fruit and vegetables than in the low-fat group. That is over a year's time.

Shintani and colleagues also did a study in Hawaii of traditional native Hawaiian diets. They let them eat as much as they wanted and it was a diet very rich in the native fruit and vegetables, which Hawaiians have now moved away from. The intervention diet was much lower in energy density and fat than the habitual diet.

After three weeks, they measured reduced energy intake by over 1 000 calories a day, and they lost a mean of 17 pounds. They also reported that the diet was very satiating. I have the graphs to show this. There again, food intake per grams per day was the same from the base line to the intervention, so they ate the same amount of food. Yet, because of the energy density drop, the amount of calories per day went down significantly as did their body weight. There again, you have to remember the study was only for three weeks, so they are impressive results. We would like to see it over a longer period of time.

Again, dietary advice is to increase fruit and vegetables. The Mr. Fit, or the Multiple Risk Factor Intervention Trial, reduced fat and increased fruit and vegetable intake to help lose weight, and the ultimate goal was to improve the blood lipids and blood pressure of the men in the study. They found that this was related to the maintenance of weight loss in those who increased fruit and vegetable intake, so they kept the weight off longer, and the subjects who lost more weight than the rest of the cohorts also showed a greater intake of fruit and vegetables.

In another multidisciplinary weight control programme, they took 213 obese adults and had them eat energy-restricted low-fat high-carbohydrate diets, but again they emphasized unlimited fruit and vegetable consumption. After 7 months, 70% of the subjects had lost an average of 6.3 kilos, and after 25 months of follow-up, 53% of the subjects continued to lose or maintain their weight for a weight loss of 8 kilos over the long term.

One more thing about the previous study was that they did not specifically ask about fruit and vegetable intake. We only know what they advised but we do not know exactly how much fruit and vegetable they took in.

Adietary advice to increase fruit and vegetables was done by Epstein and colleagues on a family level. They wanted to do an intervention in which there was at least one obese parent and a non-obese child in the family. They were randomized to one or two groups. In one group, the message was to increase fruit and vegetable intake, and in the other group it was to decrease high-fat and high-sugar foods. After a year, the fruit and vegetable group lost more weight and actually decreased their intake of high-fat and high-sugar foods. So they lost more weight and had the double message.

If you look here, the yellow line is decreased fat and sugar only, and the green line is increased fruit and vegetable only. So they lost more weight over a year. That was a significant difference. So here a positive message is more effective than a negative message: telling people what they can eat rather than what they cannot.

What do we have in the realm of epidemiologic evidence ? Not much. I am going to highlight three studies. There are more studies out there, but they looked at varied associations only and at chronic disease outcome rather than weight loss and they just happened to include it in their analysis. I am going to look at the studies where it was at least one of the primary focuses.

Kahn and colleagues took the data from cancer prevention studies too. They found an inverse association between a ten-year change in both BMI and waist circumference with vegetable intake, which they defined it as greater than 19 servings per week. This was seen in both men and women. A lot of the epi-studies show it in either one sex or the other, but this study actually showed it in both men and women. It is promising, but they only looked at vegetables, they did not look at fruit, and they included potatoes in this analysis.

With the behavioural risk factor surveillance study, Serdula and colleagues looked at the correlates of fruit and vegetable intake. They found that underweight women consumed more fruit and vegetables than normal weight women, but there was no difference between normal weight and overweight women. So the difference was only seen in the underweight women. There was no difference seen in the men.

In a continuing survey of food intake of individuals, Lin and colleagues took this data and looked at it very precisely. This was the main outcome of the study. They took into account white potatoes and fruit-juice, and they looked at both fruit and vegetables. They found that obese men ate fewer vegetables and more white potatoes. They saw no difference in vegetable or white potato intake among women, however, but they found that both obese men and women ate less fruit compared to the lower BMI categories. They did see the strong relationship with higher fruit consumption and lower BMIs. This was also reflected in the data with children, which I did not present here.

What is the link to energy density with fruit and vegetables? Energy density is the relationship of calories to volume, so it equals calories over grams of food. Water and fibre decrease energy density, while fat increases it. Barbara Rolls, in her book "Volumetrics", came up with four categories of energy density: very low, low, medium, and high.

I will quickly go through very low-energy density foods: fruit and vegetables, skimmed milk, broth-based soups. Low-energy density foods include beans, legumes, oatmeal, packed tuna in water, bananas. Medium-energy density foods include meat, cheese, hard-boiled eggs, jelly, raisins, and also bread products such as bagels, pretzels and popcorn. High-energy density foods include crackers, chips, cookies, nuts, butter and bacon. This is just a sampling of the foods in these categories.

This is to show you a visual on how water affects the energy density. On your right are grapes. This is a $1^{3/4}$ cup of grapes with an energy density of 0.7. On the left is a 1/4 cup of raisins, with an energy density of 3.0. All they did to get raisins was take the water out of the grapes, and both these servings have 110 calories. So you can see how this could make you fuller than the raisins.

Again, comparing water contents, both pretzels and cheese have low water content. Both of these portions have 100 calories and the same energy density for an ounce of food. Now, let us look at this with a sandwich. We eat a lot of sandwiches in the United States. Over here, we have a sandwich that equals 626 calories with an energy density of 3.2. When you take away some of the meat and cheese, use lower fat options, and increase the vegetable content, you bring it down to 429 calories with an energy density of 1.7, and, as you can see, the volume increased.

Then again, we looked at it from a meal standpoint. The meal on your right weighs 320 grams and has the same number of calories, 475, and the meal over here has 700 grams. So you are increasing the volume of food you are eating, but staying at the same calorie and macronutrient percentages. What is also noticeable here is that you can see an increase in vitamins, minerals and phyto-nutrients, just from increasing your intake of fruit and vegetables.

In another study by Stubbs and colleagues, they looked at energy density independent of fat content and influences on the body weight in men. They looked at weight loss over a two-week time period. High-energy density gained weight, medium-energy density stayed about base line, the low-energy density lost weight. They changed energy density by the inclusion of fruit and vegetables. The participants ate a similar amount and weight of food. Energy density was decreased, which spontaneously led to reduced energy intake. This study is another good example showing how fruit and vegetables added into the diet can reduce energy density, and allowing satisfying portions so that people can still eat and yet reduce calories.

What are some of the caveats when we talk about fruit and vegetable consumption and weight management ? The physical form of the food is very important to consider. The preparation methods and how we eat fruit and vegetables. Comfort foods; why we eat.

In some studies that have looked at the physical form of food, researchers have found that when they compare apples to apple purée and apple juice, the apples that had a higher percentage of fibre were associated with higher satiety ratings than the apple purée and fibre-free apple juice. So, eating the whole fruit made you feel fuller than drinking apple juice or eating apple purée. This was found to be true in other studies for oranges versus orange juice and grapes versus grape juice.

Preparation methods: fruit and vegetables in their natural state are low-energy density foods, but the preparation methods may increase energy density. This happens in particular in the United States. Some examples of what we do are adding butter and brown sugar onto sweet potato, which is a very healthy low-energy density food by itself; we add salad dressing, cheese, and croutons on our salad; we bread our vegetables and fry them; we put butter and sour cream on our white potatoes. You can see why that map of the United States is getting fatter and fatter.

Before I go on, I think it is also important is that in epidemiological studies, we do not take into account how people eat food. We will say "Did you eat fruit and vegetables ?" They may respond "Yes", but we did not ask how it was prepared and I think that we are losing some of the research. We could make this point about the relationship between fruit and vegetables and weight stronger.

Why do we eat ? In the United States, we call them comfort foods. We eat to make ourselves feel good. If we are stressed, tired, or lonely, we eat. Alot of times, people eat to overcome fatigue. A lot of people also mistake thirst and hunger. So if they feel they need something, instead of drinking, they will eat. Again, in research studies, we do not normally ask people why they eat; we ask them what they eat. We might get a better feel on defining messages on how to eat fruit and vegetables or a healthy diet if we had a better idea of why and when they eat.

Now for my summary. Fibre has been associated with increased satiety and reductions in energy intakes. Lower fat diets decrease energy intake because they are lower in energy density. Dietary interventions of low-energy density diets, which means they are low in fat but high in fruit and vegetables, led to spontaneous weight loss. Fruit and vegetables can be a part of weight loss programmes by helping to avoid feelings of deprivation so that you feel you are still eating, and yet enhancing satiety and feeling full.

Increasing fruit and vegetables can be a positive message about what can be eaten rather than what cannot be eaten. This has shown to be effective. People can eat low-energy density foods in greater amounts than high-energy dense foods for the same amount of calories. If you remember, a lot of those studies showed that people eat the same amount of food from day to day, so if we can lower the energy density and bring down the calories, but they can see the same amount on their plate, that leads to decreased energy intake and, eventually, weight loss.

Both water and fibre increase the volume of foods, and decrease the energy density. Fruit and vegetables are high in water and fibre, so they can decrease the energy density. And fruit and vegetables in their natural state are good substitutes for high-energy dense foods.

Decreases in dietary energy density, regardless of the macronutrient composition, has also been associated with reductions in energy intake. Choosing foods that are low in energy density enables individuals to consume satisfying portions while reducing energy intake. Finally, we do have some short-term clinical trials that support a role for energy density in weight management.

I would like to acknowledge my colleagues who cannot be here but who have worked on both these review papers with me.
Thank you.

Questions

Member of the audience
I am not a specialist of this topic. Are you aware of studies that are inconclusive or negative ?

Beth CARLTON-TOHILL
Are there studies that show no effect of fruit and vegetables in weight loss ? Yes, there are such studies. They are in the comprehensive review, but most of the epidemiological studies do not show an association. However, we are thinking that that was because of the way the data was collected. It was not the primary outcome of the study; they were looking at chronic disease outcomes. If they had had a more careful assessment of the diet, the subsequent data now says that they may have shown more of an effect. However, some of these studies actually include potato crisps and French fries as a vegetable, so it is going to be harder to see a correlation with lower BMI.

Member of the audience
We can consider that the beneficial role of fruit and vegetables in weight management is generally agreed and is firmly justified. It is important for a matter of public health.

Beth CARLTON-TOHILL
It is very important, and what I set up for you today is the logical progression that fruit and vegetables should lead to weight loss if they are prepared correctly and are not eaten in addition.

Member of the audience
Wendy van Herpen, from Unilateral Health Institute from the Netherlands. Thank you very much for this nice overview. I am looking forward to reading your review papers. I have a question on fruit and vegetable intake. You mentioned that one of the caveats was that the preparation methods are not really known. Do you know if processed fruit and vegetables, such as soups, pasta sauces or pizzas are included in the fruit and vegetable intake ?

Beth CARLTON-TOHILL
In the controlled studies where I showed the data, that was not the case, but in the epidemiological studies, yes. It is most likely that they will include things like pizza sauce and pasta sauce irrespective of how they were consumed. Juice may be considered as a serving of fruit for a day. As I said before, things like potato crisps and French fries can count. Some studies accounted for it and some did not.

Member of the audience
You never mentioned anything about how many meals per day we should divide our calorie intake into. It is very important, especially to me, because it has already been mentioned that obesity is a post-prandial phenomenon. I think it is very important to say that the total calorie intake should be divided into at least five meals a day, and decrease the turnover of fatty acids, and decrease their effect on gene expression and transcription fat. What is your opinion ?

Beth CARLTON-TOHILL
On how much ?

Member of the audience
Yes, on how many meals a day ?

Beth CARLTON-TOHILL
I would say on all meals. If, as long as you are eating more fruit and vegetables, and taking away another calorie source, if you are substituting fruit or vegetables at breakfast, but you take away bread or whatever else you eat normally at breakfast, then I would say you could incorporate it at every meal. The one study shows that the threshold of fat is 200 grams per meal. Then we would be getting close to the Greek data of over 600 grams per day. However, there is no science behind that, as of yet. We only know that 200 grams per meal seems to be a threshold where people feel full for less calories.

Member of the audience
Could you comment, please, on the relationship between energy density and the glycaemic index concept? Are they close? I get the feeling that they are, coming from the diabetes world. I wonder if they have a similar usefulness as a concept for people without diabetes.

Beth CARLTON-TOHILL
I think so, absolutely. Recommending a lower energy density diet would help with that. Is that what you are asking me?

Member of the audience
The connection has been made by people with diabetes, perhaps wrongly, perhaps correctly, that if you eat low glycaemic index foods, concentrating on the sugar increment, they actually help in weight loss. I wonder if that is because of the energy density component as the main mediator of the process of weight loss or weight control.

Beth CARLTON-TOHILL
Probably, because you are getting fewer calories and still getting the fullness feeling. I think you are taking in fewer calories.

Adam DREWNOWSKI
Let me comment on your last point, if I may, on the energy density of foods and diets, which is linked to the water content and pretty much nothing else. Energy dense foods are dry and energy dilute foods are wet: end of story. So, there is no connection to the glycaemic index whatsoever. None. It is linked to fat as well, but water accounts for most of the variance.

The role of fruit and vegetables in the fight against obesity

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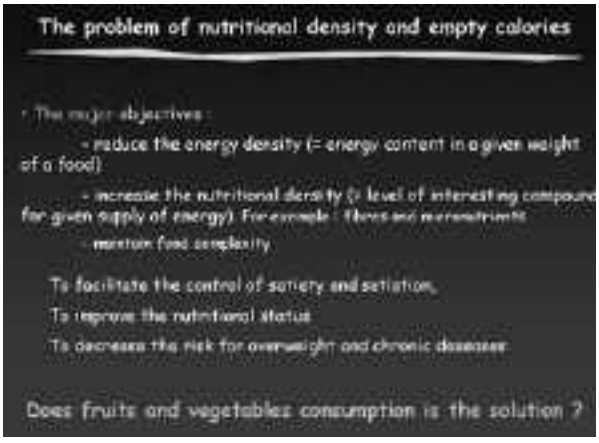
Theix, 63122 St-Genès-Champanelle, France

Obesity prevention has often been handled as a matter of energy and nutrients, while specific effects of food were rather neglected. One of the good points of this conference is that it puts a special emphasis on the role of fruit and vegetables. As you know, over the past fifty years, we have experienced the so-called "nutritional transition", a phrase that understates the dietary upheavals of the second half of the 20th century. Nutritional transition is characterised by a modification in dietary habits, and the substitution of natural product with a wide range of processed foods. This results in higher sugar and fat consumption and overall decrease of fruit, vegetables and fibre consumption. Food supply has thus become prolific in terms of products with low nutritional density.

In this regard, we may think that obesity development is the necessary price to pay for economic development and the modernisation food chain. Obviously, if food supply mainly consists of high energy density products, with inadequate fibres and micronutrients availability, it leads to disorders in appetite control and food intake. With a settled way of life, even a slight energy unbalance may lead to obesity in the long run. In the contemporary world, obesity development is no surprise.

There is a paradox in our nutritional situation: although we use a wide range of processed products and face energy overabundance, we are exposed to micronutrients deficiency. Fibre and micronutrients content of many products have been lowered, to the extent that you can develop overweight and still not meet your nutritional needs. As you know, many factors are involved in nutritional density reduction: intensive use of sugars, refined cereals, fat (we have never used as many oils, margarines and dairy products as we do nowadays), and more recently starch (starch industry is booming). This may be responsible for a total nutritional density loss of about 30 to 50% in common food products available in our supermarkets. Of course, this may also affect appetite control. The importance of fruit and vegetables in food intake regulation has been well underlined by a previous speaker.

It is worth emphasising the necessity to manage nutritional density issues. Everyone knows what energy density means: it is the energy content of a product. But defining nutritional density is a bit more difficult it refers to micronutrients quantity (or other relevant nutritional elements) of any given energy supply. Since fruit and vegetables are poor in calories and rich in micronutrients, their nutritional density is high, while nutritional density of white bread and biscuits is low. Nutritional density of our diet has to be increased in order to improve overall nutritional status and diminish the development of chronic diseases. This also happens to facilitate appetite management, directly, thanks to dietary fibres and indirectly, for a good nutritional status may facilitate regulation of energy intake.



The way to increase fibre supply and nutritional density of diets is to consume more fruit and vegetables, that are low-calorie products. Average energy content of fruit is 55 kcal per 100g. Vegetables have very low calorie content as well. Thanks to volume and water content, they cause an satiety effect. Of course, water and volume alone do not make any food a good one. Actually, vegetables prove naturally rich in micronutrients and minerals: mineral content rises up to 10% in vegetables (in dry extract), which is much more than in ordinary type 55 flour (0.55g per 100g). You may also be aware that fruit and vegetables not only contain ordinary vitamins, but are also rich in phytomicronutrients (antioxidants as polyphenols, carotenoids and many other components with significant health benefits).

How many fruit and vegetables should we eat ? Recommendations are not very specific: in France, average consumption rises up to 150 to 200g of fruit and 150 to 200g of vegetables, which represents 5% of total energy supply. Now, fruit and vegetables consumption should correspond at least to 10% of energy supply, with 300g of fruit and 300g of vegetables a day. I think that eating 1kg of those products per day should help in the fight against overweight. The essential part of energy supply in a balanced diet consists of complex plant produce. It is no longer the case nowadays because of numerous food transformations. Food energy has been extracted from its original plant matrix. Fat production from oleaginous plants has become significant, just as sugar extraction and cereals refinement: this makes us retrieve the energy while eliminating the non-energetic part (fibres, minerals and a wide variety of

micronutrients). All this characterises nutritional transition and has changed food order.

Here are histograms that caricature several dietary behaviours. The first three histograms represent very well balanced behaviours, as subjects eat mostly non-refined cereals, enough potatoes and pulses, fruit and vegetables. In this context, their diet proves adequate even though it is a vegetarian one. Yet eating meat would be even better. With such dietary diversity, subjects should not face nutritional problems. The situation gets more complicated when subjects eat only refined cereals, since they give up on fibres, minerals and vitamins. Ordinarily, people tend to eat less refined cereals and potatoes in order not to gain weight, and to give up on pulses that are difficult to cook, fruit and vegetables that are expensive and hard to peel. They also use many processed foods that are rich in sugars and fat. In this last case, nutritional density of such diets is very low and nutritional deficiencies are likely. We assume that a diet rich in micronutrients helps controlling food intake and vice versa.

What does all this have to do with overweight prevention ? Before answering this question, I would like to present a theoretical comparison of balanced energy supply and balanced micronutrients, fibres and minerals supply. On the side of energy supply, if you reduce the share of complex sugars, increase sugar (empty calories) and fat, you will diminish total micronutrients content. You may also want to reduce fat and sugar content while increasing fruit and vegetables supply in order to in crease total micronutrient content. In this context, food intake proves very rich in micronutrients. This is the type of diet we should recommend in the fight against overweight.

Are fruit and vegetables the right choice to prevent overweight ? They may be, notably for they help controlling appetite, facilitate digestion (in particular in the large intestine), improve nutritional status, cut down hypertension risk (one of the issues of plurimetabolic syndrome), reduce insulin resistance phenomena, manage cholesterol levels, diminish inflammatory processes. It is therefore very valuable to eat fruit and vegetables.
This slide represents the efficiency of fruit and vegetables consumption in satiety status. We should bear in mind that satiation and satiety management is as well linked to digestion quality. It is obvious that a dietary behaviour can get stable only when digestion is normal. In this regard, the large intestine has to get enough fibres, and specifically fibres that help in the development of balanced and symbiotic fermentations. In most fruit and vegetables, fibres are well fermentescible and tolerated. Moreover, these fibres go together with minerals and micronutrients, which has a positive impact on intestinal functions. Fighting overweight by reducing food intake quantity is very difficult; it is therefore crucial to have an abundant yet low-calorie diet. This also facilitates biological functions.

The paradox of current dietary model is that it does not ensure that you meet recommended dietary values. Now, it is crucial to have a good nutritional status. By eating tremendous amounts of fruit and vegetables (1kg a day), you hardly cover 20% of energy needs. However, you will meet 1/3 of calcium needs (with a recommended daily value of 900mg), 50% of vitamin E needs and all your folic acid needs. Fruit and vegetables facilitate coverage of various essential needs.

Fruit and vegetables also are remarkable sources of potassium. This is a key element in the fight against hypertension. The efficiency of potassium supply is reinforced by sodium supply management. Over the nutritional transition, overall potassium intake has been reduced, while excessive sodium supply has been maintained. Large potassium intake helps reducing vascular events. In the same time, it diminishes urinal losses of calcium.

As far as insulin resistance is concerned, this slide shows the negative impact of fatty acids. By reducing sugar and saturated fat and increasing fruit and vegetables consumption, glucose metabolism was facilitated: this will help cut down fatty acids and improve insulin action.

Cardiovascular risk must as well be prevented: fruit and vegetables play again an essential role. Cholesterol is not entirely eliminated through the digestion process: soluble fibres are crucial to inhibit cholesterol absorption and increase faecal elimination of biliary salts. Decreasing energy supply may also help reducing lipogenesis and cholesterogenesis. Fruit and vegetables ensure the supply of antioxidants that prevent lipid peroxidation, which is involved in atherosclerosis development. There is a theory of atherosclerosis prevention, which insists on the status of endothelial vascular functioning. Micronutrients play a role in the prevention of endothelial malfunctions caused by an increase of lipids in blood and post-prandial glycaemia.

Homocysteine levels should also be managed, since homocysteine is a very atherogenic component. I have said that vegetables, in particular foliar vegetables, are remarkable sources of folic acid. Now, this vitamin reduces the level of homocysteine. Greens, as well, prove rich in omega-3, which play a part in reduction of vascular events.

This morning, adipose tissue has been said to be a source of cytokines. Permanent overweight may indeed cause inflammation that leads to chronic diseases development. Obviously, we need to fight these inflammations, by reducing energy intake (since this has been proven to diminish inflammation markers). We may also assume that the effect of fruit and vegetables is reinforced by some fatty acids such as omega-3, which allow to counter type-3 lipidic mediators.

With fat overload, the quantity of free fatty acids increases, which favours lipid peroxidation: obese subjects thus need a better antioxidant protection than ordinary subjects who need to peroxide a smaller quantity of lipid substratum. The equilibrium of oxidative stress is very complex: there is constant production of responsive oxygenated substances related to mitochondrial respiration. Moreover, we are exposed to external sources of free radicals, which may prove very deleterious. We have our own protection against those radicals, but we also need to get antioxidants provided by food: not only vitamin E and C, but also many other antioxidants such as polyphenols and carotenoids, to be found in large quantities in most fruit and vegetables. If your diet does not provide enough antioxidants while you are exposed to free radicals, the risk of oxidative stress increases. Now, such stress contributes to many diseases development. Hence the importance of frequent fruit and vegetables consumption.

Finally, we may start making some recommendations. It is now obvious that excessive produce refinement (in particular cereals) needs to stop, if we want to preserve nutritional density of food. Fruit and vegetables consumption should increase, while excessive consumption of fatty meats and dairy has to be cut down. Consumption of artificial processed foods, sweetened drinks and junk food should be limited.

To my mind, there are two ways to deal with obesity prevention. On the one hand, at the individual level, specifically in the relationship between physicians and patients or within informative and educative health associations. On the other hand, at the level of food production, which should be adapted to our actual needs. In this regard, we could reasonably produce cereals with a good nutritional density, whole-wheat breads, and eat more pulses and potatoes without soaking them with fat. We would also eat more fruit and vegetables, about 300 to 500g a

day of each, according to individual appetite and preferences. We need to moderate animal produce consumption and cut down saturated fat intake and fats with the most unbalanced omega-6 / omega-3 ratio. Finally, we need to avoid the use of totally purified refined products.

The most significant recommendation is to diminish the use of processed foods that are rich in empty calories. Does the current food chain (which is rich in processed food) match the objectives of a global strategy to fight obesity ? I doubt it! I would rather recommend that we build a strategy based on the promotion of complex natural products and sufficient fruit and vegetables consumption. So far, international recommendations (in France or Europe) have not been strong enough to warn consumers against the risks associated with junk food and refined products consumption nor to encourage fruit and vegetables consumption. Food supply of these products, in France and elsewhere, may not be satisfactory enough in terms of quality and costs. Consumers habits cannot be changed easily: there are cultural and know-how barriers. This makes it difficult to have things evolve. The conference should help get such messages heard at the field level, and will step by step gain wider influence.

Thank you.

Questions

Member of the audience
For crudités seasoning, current recommendations seem to favour olive and colza oil, which provide us with omega-3. Yet virgin colza oil is not recommended: I am concerned with omega-3 when oil has been heated up by 200°C. What is your view?

Christian REMESY
I strongly recommend virgin colza oil. Currently, the market is not very developed, but some excellent virgin colza oils with a very typical taste are now available. We should not choose entirely refined colza oils. If consumers push the demand, the supply will follow, since there is nothing wrong with the production of such oils.

Member of the audience
How about daily honey consumption: does it contribute to energy balance without creating any kind of damage ?

Christian REMESY
I did mention this in my pyramid. In particular, fructose, as well as saccharose (which contains only 50% of fructose) are prooxidants. In my laboratory, we have proven that honey is less prooxidant than fructose. When fructose is found in a complex food, fruit or honey, it does not have the prooxidant effects of purified sugars. This was a very comforting finding. Of course we should neither avoid fructose nor systematically look for it (in jams etc). Fructose must be eaten in complex food that are protected by antioxidants and minerals. Honey cannot replace fruit, which comprise other essential elements.

Member of the audience
You recommend a very high level of fruit and vegetables consumption. Is this reliable ?

Christian REMESY
I recommend this in the framework of the fight against overweight. In the day-to-day life, not everyone can eat as many fruit and vegetables, for several reasons: preferences, habits, etc. If you really want to make a difference, i.e. find a strategy that allows the subject to eat as much food as they want while reducing their energy intake, there is no better way than to increase fruit and vegetables consumption. Ordinary people may eat much less: 300g of vegetables and 300g of fruit are a minimum. Even 600g to 1kg is no big deal.

Member of the audience
What do you think of the glycemic index of bananas or grapes? You put them in the fruit and vegetables category: shouldn't you take them out ?

Christian REMESY
Bananas are a source of starch: when ripe, starch gets hydrolysed, which creates maltodextrines, and gives them a sweet taste. In this context, bananas can have a very high glycemic index. If the banana is a bit unripe, this index drops considerably. Other fruit are rich in glucose, fructose or saccharose. Most of the time, there is a good balance between glucose and fructose. In apples, there is a majority of fructose. Saccharose and fructose have a very good glycemic index, because the fructose molecule is absorbed by the liver each time it gets through it. Yet we should not binge on purified sugars just because they have a good index. Glycemic indexes should always be very carefully interpreted.

CONCLUSION

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I am going to conclude this session. I would like to thank my esteemed colleagues and fellow speakers today. I think we went through a lot of important points, from the role of dietary fat and energy density, and nutritional density. We need to think of all these things with fruit and vegetable intake, and all its benefits.

I really liked the point that we need to watch the message of low fat, and what that means in certain regions of the world, and how to define that better. As we saw from some of the data, is low fat as effective as low-energy density? I also think that your point on how we need a global strategy to combat obesity is extremely important. We can adapt it for certain regions, but the fact that we all have a common goal means that we have the same common recommendations, fruit and vegetables being a very important part of that. It is difficult to change behaviours but I do not think it is something we cannot overcome.

I would like to thank everyone again, and I will now end our session. Thank you very much.

The relevance of potato as a source of carbohydrates and potassium in a Mediterranean diet

Christian REMESY
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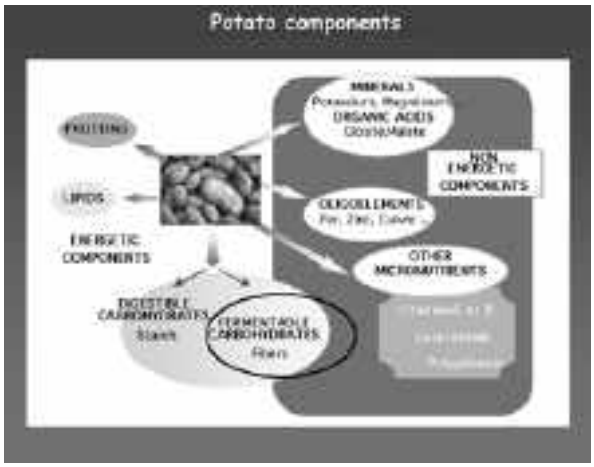
Theix 63122 St-Genès-Champanelle, France

You know that potatoes have a very bad reputation, just because they are associated with specific typologies: fries, overweight…This is not very fair for this tubercle that has helped humanity in so many ways. Potatoes can be inserted in the ordinary strategy of a balanced food pyramid. We need a lot of sugars: quantity depends on individual needs, lifestyle, activity and likeliness to gain weight. We need to have complex sugars that provide us with starch: potatoes perfectly complement pulses and cereals supply.



There is an energetic fraction in potatoes that is very rich in starch, and poor in proteins and lipids. However, there also is a non-energetic fraction which comprises dietary fibres, minerals (potassium), micronutrients, vitamin C that is not eliminated by the cooking process, polyphenols, and carotenoids as well if consumers would not always choose white potatoes. In Peru there are varieties that are as rich in carotenoids as sweet potatoes and carrots. Potatoes could thus be richer in micronutrients than it is now.

If you examine the composition of a plateful of potatoes, pasta or rice, with comparable water levels, there are no major differences among sugar supplies. Of course, potatoes are not a good source of proteins, but neither is rice. Nevertheless, potassium supply is much more significant with potatoes than with pasta or purified rice. Potatoes also provide vitamin B and C, and should therefore not be neglected among starchy produce.

What are the potential roles of potatoes ? These are complex. Potatoes contribute to smooth digestion. Thanks to their dietary fibres, they facilitate cholesterol elimination. They also may have a good glycemic index. Their potassium content makes them a good ally against salty products (potatoes often go together with salted ham). They also are a good source of antioxidants and micronutrients.

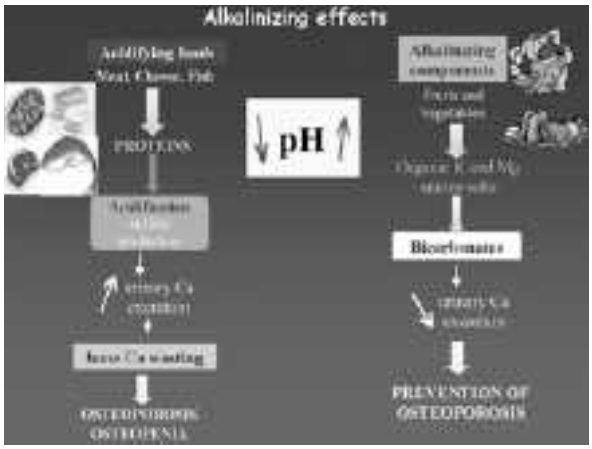
As far as digestion is concerned, potatoes provide soluble and non-soluble dietary fibres, and everything goes fine. Digestion of potatoes does not usually cause any trouble, as opposed to whole-wheat bread. These dietary fibres allow the large intestine to function normally. The production of short-chains fatty acids has a trophic effect on the digestive surface. It also may play a key role in cholesterol and biliary salts evacuation.

Usually, cholesterol has an endogenous and exogenous origin: one part comes from animal produce and the other part is produced essentially by the liver. This cholesterol is eliminated under the form of neutral sterols and biliary salts. Several mechanisms (inhibition of cholesterol and biliary salts absorption in the intestine, insolubilisation of these steroids in the large intestine), facilitate faecal evacuation of steroids. As a response, hepatic cholesterogenesis is stimulated. This increased cholesterogenesis helps the recycling of lipoproteins. Potatoes, as many other plants, contributes to cholesterol homeostasis. When rats are given a potato-based diet, their blood cholesterol decreases notably, as does their hepatic cholesterol. Very few foods have such obvious effects.

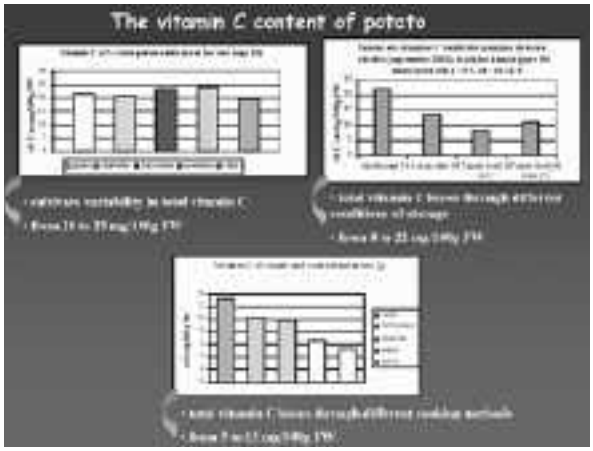
As for glycemic index, we do know that a warm dish of mashed potatoes is quickly assimilated. Mashed potatoes have a good glycemic index. In a complex meal, the index gets even more reasonable than when you eat only mashed potatoes. White bread also has a high glycemic index, while pasta have an excellent index. When you eat chopped potatoes with their peel or slightly browned, the index gets very moderate. You can do even better: put the potato in the fridge for 6 to 8 hours and then add it to a salad or any other meal, and you will get a better index, thanks to starch regression. Nutritionists are currently favouring nutritional density over glycemic index, since nutritional density has a more reliable physiological sense.

Potatoes are one of the richest sources of potassium. Athletes are often told to eat bananas: indeed, tennis players would have a hard time eating a cold potato between two sets! In fact, potatoes are as rich in potassium as bananas. One has to bear in mind that in these foods, potassium is mainly linked to organic acids. These salts of organic acids and potassium play an alkalinising role. Studies have shown that in several potatoes, the proportion of organic acids (citrate or malate) is more important than phosphate content. This makes potassium more related to organic acids than to phosphates. The nature of potassium salts is not the same in all foods: in meats and cereals for instance, there are very few organic acids and a lot of phosphates. Such abundance allows potatoes to have alkalinising effects.

This slide shows how potassium can be an antidote of sodium and play a role in blood pressure. Potassium also reduces urinal losses of calcium. How ? There are two types of food: acidifying foods and alkalinising foods. Acidifying foods are essentially meats and produce rich in proteins: when proteins contain sulphur amino-acids (methionine and cystine), they get metabolised and result in sulphate. This sulphate has to be neutralised in urines, which mobilises calcium. Calcium may even come from the bones, which are a stock of substances for the body. Eating a lot of proteins and/or salt increases urinal calcium losses. It is interesting to note that potassium organic acids have an opposed effect, as was shown with potassium citrate intake. I am not reinventing the meat and potatoes meal: the balance of such an association is obvious, just as meat and vegetables.



Potatoes are a source of vitamin C, which surprises many people. They contain more vitamin C than carrots and apple do: 20mg against 10mg per 100g in apples. At the end of winter, vitamin C content tends to decrease. There also is a variability among potatoes varieties. Vitamin C deceases with time, but is still well preserved. As for cooking ways, steamed and micro-waved potatoes tend to remain richer in vitamin C.



As most plants, potatoes contain polyphenols, in particular chlorogenic acid. There are several tests for antioxidants : in the case presented, trolox was used. You can see that potatoes are rated as well as other vegetables. The next slide shows polyphenol measuring according to the Folin method. We haveinvestigated genetic variability and cooking effects. We can see that it is worth not peeling potatoes, for unpeeled potatoes contain more polyphenols. With time, polyphenol levels in a potato that is kept in a cellar tend to increase. It may synthesise those micronutrients in order to defend against several aggressions. There is thus no reduction of polyphenols with time, as opposed to vitamin C content.

We no longer eat large quantities of potatoes. Potatoes should be integrated to a balanced diet, in particular right food associations with animal produce in order to fight the acidifying effect of some of them. I also indicated that potatoes help balance the sodium/potassium ratio. With salty cheese and ham, you should eat a potato rather than salty bread that contains very few potassium. The association between potatoes and animal produce contributes to reduce glycemic index of the dish.

It also wise to associate potatoes and vegetables. This allows to have moderate energy density meals. Adding potatoes to your veggies helps you meet your energy needs. It is an inexpensive solution and very interesting from the nutritional side. I am convinced that vegetarians who associate pulses and potatoes will tend to live longer: their diet is so balanced.

Potatoes are a part of the Mediterranean culture, as a complementary dish with meats, vegetables: cod and potatoes, basil soups and other potato-pulses-vegetables soups. In Morocco, potatoes are to be found in tajines. Couscous sometimes come with potatoes and other vegetables, with sounds like the right nutritional choice.

Potatoes can therefore be used in many ways, not only as chips and fries, and many examples are to be found in the Mediterranean diet.

Introduction

Marie-Aline CHARLES
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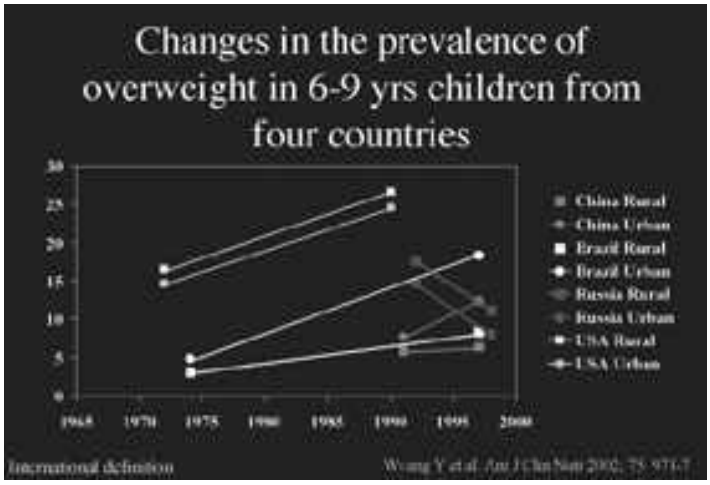
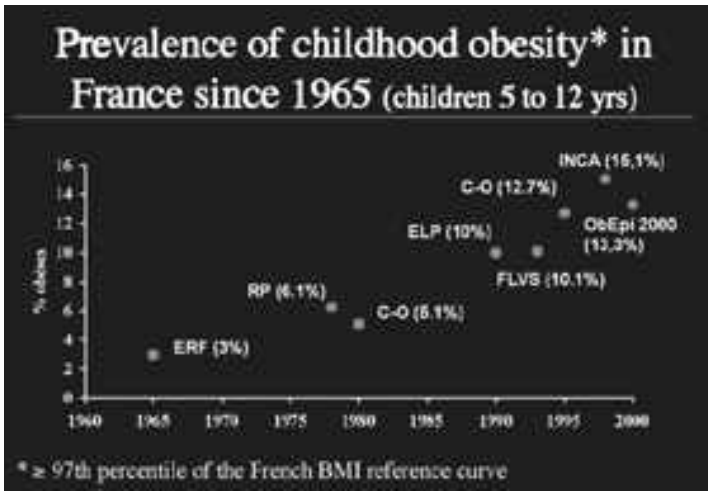
I am an epidemiologist at INSERM, and have been working with Eveline Eschwege on the epidemiology of diabetes and obesity for years. I would like to start this introduction by sharing with you some figures of childhood obesity.
Epidemiologists use a definition of childhood obesity based on BMI. Yet childhood obesity cannot be defined with only one criterion since children's BMI varies with age. We thus use the French reference curves designed by Marie-Françoise Rolland-Cachera to define obesity. We used in France to define obesity as a BMI greater than the 97th percentile. Since 2000, an international definition of obesity has been agreed upon, which was based on relevant data from 7 countries. The definition looks into percentiles that result in overweight (over 25kg/ m2) and obesity (over 30kg/ m2) at age 18. These levels correspond to the definition of adults'overweight and obesity, which allows to connect both definitions.

I am going to use some data based on old studies, i.e. on the 97th percentile of the French BMI reference curve. Between age 6 and 16, this threshold happens to be very close to the international definition of overweight. Here are some figures on evolution trends of childhood obesity. I selected this slide because it brings together several key points of the epidemics of childhood obesity. It shows overweight (according to the international definition) in children from 6 to 9 in four different countries.

There is a general increase in industrialised countries (the USA) and developing countries as Brazil or China. Besides, the increase of obesity in developing countries proves particularly fast in urban areas: this is true for Brazil and China. Urbanisation is a key factor of the epidemics, for children as well as adults. Urbanisation is associated with an increase of food availability, changes of diet type (see Mr Drewnowski's presentation), i.e. with more foods rich in sugar and fat, and reduction of time spent in transfers. Moreover, children living in urban areas may attend school more frequently than rural children who tend to work more. All these factors are related to a very obvious increase of childhood obesity. In industrialised countries as the USA, there is no actual difference between urban and rural areas. We may thus say that obesity development comes together with socio-economic development: if you take a look at Russia's figures, you may see that intense upheavals of the 1990s have resulted in a general decrease of standards of living as well as a reduction of the prevalence of obesity in children and adults.





Let us have a look at French data ranging from 1965 to 2000. Most of our old references come from regional samples, while the most recent are based on national samples. Many of them were conducted by M.F Rolland-Cachera, who was almost the only French expert concerned with the issue. In France, the increase of the prevalence of obesity (that corresponds to overweight according to international references) has proven very gradual and constant since the 1970s. This does not match available data on the evolution of adult obesity. According to relevant national data, the prevalence of adult obesity was more or less stable between 1980 and 1990. It started to increase only in the 1990s. Evolution over the latest period (1997 and 2003) is clearly ascending. There seems to be a gap between adults and children overweight, as childhood obesity (in France) has been increasing for a longer time than adult obesity.

Which social, demographic and family factors can be associated with childhood obesity ? A national survey has quantified the prevalence of overweight and obesity according to age (international references). Parents were requested to weigh and measure their children and then get back to us with the data. I was somewhat surprised by the curve: the prevalence of childhood overweight and obesity rises very quickly in the early years, until it reaches a plateau by the age of 7/8 years old. Yesterday, Pr. Seidell already mentioned this very fast obesity development in the early years. An American study (NHANES) has stressed the same point. Prevalence of overweight reaches a maximum between age 6 and 11: it no longer increases in adolescents. The phenomenon may be partly explained by the fact that the epidemic is launched. 6 to 11 year-old children might become

more obese in their teens. However, about 15% of children are already overweight by age 7. Childhood overweight and obesity sometimes develop during the very first years of life.

Recent data from a French national study underline another factor: family income and education level, that are constantly associated with childhood and adult obesity. The prevalence of overweight in children decreases with the growth of the family's average income. Another crucial factor of childhood obesity is the presence of obese adults: the graph shows the prevalence of childhood obesity when there is at least one obese adult in the family unit, and when there is none. In the first case, the prevalence is multiplied by five. Yesterday, Pr. Lairon asked whether genetic screening of obesity may become doable or ethical someday. As far as children are concerned, no sophisticated genetic screening is needed: parents obesity already allows to identify subjects with genetic and environmental predispositions to obesity.

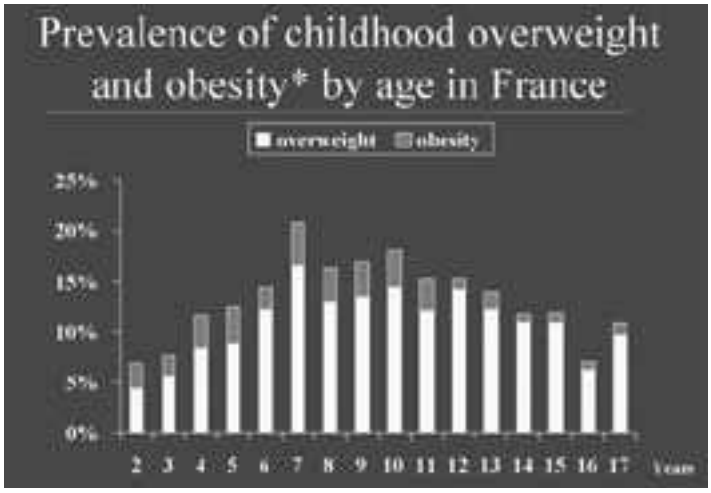
Shall we care about childhood obesity ? Some children seem to develop obesity quite early in life: will these children remain overweight or obese ? So far, we have asserted that early obesity would not necessarily lead to adult obesity. Yet, taking into account the growth of the obesity epidemics in children, I think that this is worth reconsidering.

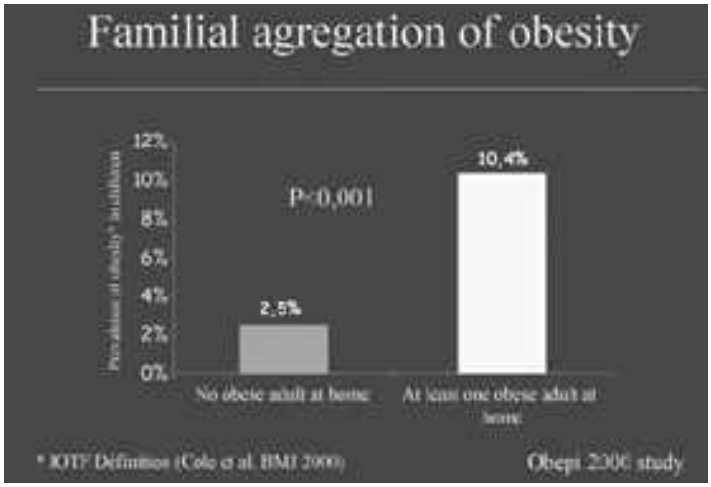
Here are some recent data on childhood obesity, gathered in French junior high-schools among a national sample of 13/14-year-old children. Subjects' BMI when they were 5 years old were classified in three groups (normal, overweight and obese). Most of the children who had a normal BMI also have a normal BMI in their early teens. About 50% of those who were overweight at age 5 also are overweight or obese now. And 70% of the obese 5-year-old children have remained overweight, among which 50% have remained obese. There is thus a persistence ("tracking") of early overweight and obesity.

Some epidemiological studies help us estimate the long-run risk of children overweight. I have gathered a number of studies in that used different definitions of childhood overweight (from obesity with clinical follow-up, to BMI exceeding 30). Mortality risk has been evaluated: all studies find that children or adolescent obesity is associated with a relative mortality risk of about 1.5, without discriminating among causes. As for cardiovascular mortality, overweight children and adolescents have two times the risk to die from cardiovascular issues. Most studies that have looked into gender differences have shown that boys are the most exposed to this increased mortality risk, in particular to cardiovascular mortality related to early overweight. We thus have epidemiological data that show an increased mortality risk for people with early obesity.

I have underlined that the prevalence of childhood obesity has been increasing and that it is linked to urbanisation and economic development. However, the prevalence is still growing within industrialised countries, and prevails among underprivileged sections of the populations. There is strong family aggregation, and a part of these obesity cases develop very early in life. This should encourage us to investigate on possible early determining factors that favour obesity development in children. The probability of early obesity persistence proves significant. We do have available data on long run consequences. We are used to saying that children obesity has no immediate consequences and that it proves dangerous only in the long run. Yet we should ask to what extent such effects can be regarded as "long run" consequences.

Anne Fagot-Campagna is going to talk about the emergence of type II diabetes in adolescents, which is nothing but an immediate risk related to childhood obesity. Most experts think that prevention really is the key to the issue. We should learn from the experience of cardiovascular prevention in children: Hanna Lagström will present one of these trials. Based on lessons learned, we shall be able to tackle childhood obesity prevention. Thank you.





The emergence of type II diabetes in children and adolescents as a consequence of the obesity epidemic in childhood

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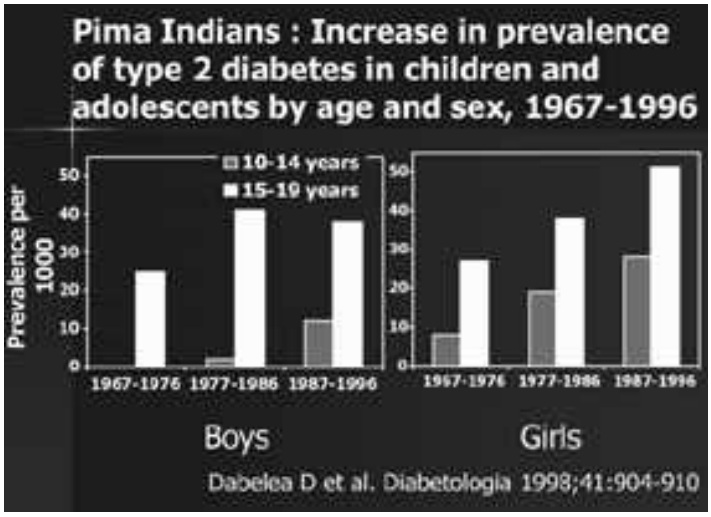
I will talk about the epidemiology of type 2 diabetes in children, i.e. the disease's appearance, history, its prevalence, incidence and current trends. We will then handle its characteristics and complications.

What happened ? A few years ago, children diabetes was called juvenile diabetes or type 1 diabetes. Type 2 diabetes, which is mainly related to obesity and insulin resistance, as well as a the associated failure of responsive insulin secretion, actually affected mainly overweight 50-year-old subjects. Over 20 years ago, we have witnessed the first cases of children type II diabetes. These actually occurred within a group of native Americans called Pima. Now, today, in the Pima society of Arizona, half the population lives with diabetes: this would concern the very subjects who are the most genetically exposed to such risk.

A bit later, we have seen the first cases of type 2 diabetes in native American adolescents from Canada. Then endocrinologists in the USAdiagnosed some children with type 2 diabetes: they were mainly adolescents with various ethnic backgrounds. By the end of the 1990s, papers were published. An official acknowledgement and consensus statement on the disease's existence and development was published in 2000 by the American Diabetes Association and the American Academy of Pediatrics.

The phenomenon is not limited to Northern America: it started in 1990 as for Japan, where there definitely is an epidemic of children type 2 diabetes nowadays. The first publications come out all around the world. The phenomenon affects children from the most at-risk populations (Australian Aborigines, New-Zealand Maoris, Native Americans) as well as children from England, France or Germany. These series actually appear today in Europe, just as they did 20 years ago in the USAwithin high-risk populations.

Let us look at prevalence data. Of course, the most reliable data regards Native Americans: it is based on population studies, with systematic screening since these are at-risk people. In New Mexico, Arizona, Manitoba and Montana, in several groups (Navajo, Pima, Cree and other tribes) and several age groups, the prevalence is very high. The highest one concerns Pima adolescents from Arizona, with a 51 per 1000 or a 5% prevalence. This value is close to the prevalence of type 1 diabetes in the general American population. The lowest prevalence has been reported in Montana and Wyoming, but the method was essentially based of cases review from a hospital data, not on a systematic screening among populations. The increase of prevalence in Native American groups has been very well documented from 1967 to 1996, in boys and girls at age 10 to 14 and 15 to 19. With boys, there is a significant increase of the prevalence of diabetes over time. This may be the highest-risk ethnic group for this disease. Data from the Indian Health Service regards the South-West area and the increase of the number of diabetes cases recorded by Indian health centres. The administrative data also comprises some type 1 diabetes cases since both types cannot be sorted out. Type 1 diabetes is relatively rare for Native Americans, whereas type 2 proves more frequent.



How about other ethnic groups in the USA ?We may look at the share of type 2 diabetes among all diabetes cases in children. Now, this share is increasing. In the case of Montana and Wyoming, it is up to 70%, which shows that type 2 is much more prevalent than type 1 for Native Americans. In several population, type 2 diabetes in children represents between 8 and 45% of newly-diagnosed diabetes cases within American paediatric centres. The variation is due to discrepancies among age groups, ethnic backgrounds, years, surveys and geographic situation. We were able to get a figure of diabetes incidence for some places: in Montana, incidence is high, with 23 per 100,000 /year. In the USA, the incidence of type 2 diabetes is up to twice the incidence of type 1 diabetes in children. In Cincinnati, within a population of White and Black children, the incidence rises up to half the prevalence of type 1 diabetes. In Chicago, for the Black and Hispanic population, there is an incidence of 3.8, but the age basis is wider. In California, the Kaiser Permanente group has investigated an African, Hispanic and White population and reported a very high incidence, over 9 per 100,000.

Type 1 diabetes records are based on the fact that the child needs insulin treatment. They actually found out that children with type 2 diabetes were also included in those records for they needed insulin at the beginning of their treatment. The records of Alleghany, Pennsylvania and the ones of Chicago show an increase of incidence in Black adolescents between 1980 and 1994. Such an increase does not appear for White children, which suggests that those are type 2 diabetes cases. In the Chicago record, there is a high incidence for Black adolescents, with an increase in Hispanic adolescents over the past few years.

When the Chicago record was reviewed, it appeared thatchildren did not necessarily need insulin treatment, did not have all immune characteristics of a type 1 diabetes and were often overweight, which seems to characterise type 2 diabetes.

This is not limited to North America though. We have extraordinary and very worrying data from Japan, which shows incidence increase between 1976 and 1990 and 1991-95. For both age groups, 6-12 and 12-15, there is a great increase of diabetes incidence, as the level exceeds the type 1 incidence in European and American populations. In Japan, there is a systematic screening programme for diabetic nephropathy in schools. Children with a positive urinary glucose level have been systematically tested through glucose stimulation.

We have similar data for France. A Parisian paediatrics centre reviewed all cases on a 5-year period for children under 16. 370 files were thus reviewed: most children suffered from type 1 diabetes, 4 children had type 2 diabetes. When they reviewed data in 2001, there were 5 new cases over one year only. Which makes it 4 cases in 5 years and most recently 5 cases in 1 year.

According to an American case review, the average age of affected children is 12 to 14, which corresponds to puberty. Some puberty-related factors, such as the rise of growth hormones, may favour the emergence of the disease. More girls are diagnosed with type 2 diabetes. Most of these children come from ethnic minorities, but not all of them. Most children have a strong type 2 diabetes family history. Most of them also have a clinical lesion called acanthosis nigricans, which typifies both obesity and insulin resistance. When diagnosed, these children often present symptoms, which is the reason why they underwent screening. Glycosylated haemoglobin proves very high, which means that we have data on children with a quite evolutional disease, and no data for other children.

As for risk factors symptoms, children may present weight loss or even acidosis (considered as typical for type 1 diabetes), which means that these children could have been classified as type 1 diabetics. Average BMI is very high and hypertension and dyslipidemia may also occur. Those factors are commonly associated with diabetes.

Complications are a crucial point. Data comes from the Black American community under 20. Acidosis may occur, as well as hyperglycaemic hyperosmolar status, and 9 cases of deadly coma have been reported. These concern children who were not diagnosed with type 2 diabetes and died from hyperosmolar coma at the beginning or before a treatment could be implemented. We also have data on chronic complications, that appear in high-risk groups. One hundred Pima children who were diagnosed during childhood were reviewed between 20 and 30 : half of them had positive microalbuminuria, 16% had a macroalbuminuria. This means that these young adults were quite at risk for kidney failure and would probably need dialysis before age 40. We already witnessed this among Canadian Indian children who were reviewed before age 33. Five young women had undergone dialysis, two of them had died during dialysis, one had had a toe amputation and another one had become blind. These are isolated yet tragic cases. Twenty years ago, we used to think that type 2 diabetes was not really breaking through for it affected only high-risk populations. But complications later appeared.

What risk factors exist and which studies are underway ? Marie-Aline Charles has shown the prevalence of obesity and its increase. I will present the American data for several age groups. The tragic obesity epidemic goes on in the USA: something may have happened in the 1980s, since the emergence of type 2 diabetes appeared in the late 1980s – early 90s. There is thus a link between obesity and type 2 diabetes in children, which has been shown in several populations, such as Pima Indians. The situation is clearly evolving. Who knows what will happen next ?

USA-Canada : Emergence of complications among youth diagnosed with type 2 diabetes as children

Studies	Populations	Complications
Pinhas Hamiel Diabetes care 1997 Morales J Pediatr 2004	African-Amer. At diagnosis Age 10-21	- Keto-acidosis 25% - Hyperosmolar 4% - 9 Fatal hyperosmolar
Fagot-Campagna Diabetes 1998	100 Pimas FU =5 years Age 20-29	-Microalbuminuria 58% -Macroalbuminuria 16%
Dean Diabetes 2002	79 First Nations FU 1-15ans Age 18-33	- 5 Dialysis (2 deaths) - 1 toe amputation - 1 blindness

Allow me to mention the Eisenmann review of insulin-resistance-related factors, which shows that the epidemic is increasing in children and that type 2 diabetes is developing. However, as far as risk factors of the epidemic are concerned, it gets somewhat more confusing. Cholesterol data show HDL decrease, which is not a good sign. There also seems to be a mild increase of caloric intake, and we have no clear data on physical activity. All this is based on big American or Canadian studies, and we know how difficult it is to measure physical activity in children: reliable and accurate tools cannot easily be found. In this review, Mr Eisenmann underlines the possible role of stress and psychological factors. We know that there are more antidepressant prescriptions and suicide attempts in the USA and that children tend to get fewer hours of sleep. This may play a role in the obesity epidemic within insulin resistance factors.

As far as calorie supply is concerned, data is not always consistent. Yet there is a clear element: the soda consumption increase in boys and girls over time. When children watch TV over 3 hours a day, they tend to get lots of food advertisements for junk food rather than fruit and vegetables. They also tend to eat more junk food than an apple or a banana while they watch TV.

David Pettitt and Dana Dabella have shown another factor in Pima Indians: the vicious circle of diabetes during pregnancy. A mother who has diabetes will give birth to a child who has been exposed to diabetes in utero, and who has thus more chances to get diabetes when it grows up, passing it on to her on child (in the case of a baby girl). When the mother does not have diabetes, the prevalence of diabetes in the child is relatively low. When the mother gets diabetes only after pregnancy, prevalence in children is also quite low whatever the child's age. But when the mother has diabetes upon pregnancy, the prevalence is very high later in life. There is a clear in utero effect of the mother's diabetes on her child.

Here is a classic picture for diabetes specialists. We often tend to represent insulin resistance as an iceberg, which may also characterize type 2 diabetes in children. The visible part of the iceberg is very small and may match diagnosed type 1 diabetes characteristics. Non diagnosed diabetes is not visible but probably represents a greater concealed part. Lastly, there is the invisible part, that favours diabetes and cardiovascular troubles development: moderate hyperglycaemia on an empty stomach, glucose intolerance, insulin resistance. As for insulin resistance in children and adolescents, a recent review has present four studies showing the prevalence of insulin resistance syndrome on a 1000 basis. In adults from the USA, the prevalence exceeds 20% according to the definition that you use. In children, the prevalence is low, i.e. 3 to 4%, except in overweight children. Once again, this reinforces the invisible role of obesity on the insulin resistance iceberg and type 2 diabetes development.

This slide illustrates the influence of ethnic background, gender and age. You may witness small differences in terms of glycosylated haemoglobin in non-diabetic children whether they are Black, Mexican or White, and these differences prove significant in such a sample, with a peak around puberty.

Regarding the Search study that was lead by the CDC and supported by the NIH NIDDK, it gathered data from 6 centres on a 5-year period and 5 million children, and aimed at estimating the prevalence of children diabetes incidence, through diabetes algorithms and characterisation of children with diabetes. The first results actually confirm that it is difficult to classify type 1 and type 2 diabetes and suggest that there might be double diabetes in some children : children with a predisposition to type 1, and also to type 2, in which obesity, absence of physical activity or dietary habits may have supported very early type 2 diabetes development.

The "Stop type 2 diabetes" study by the NIH regards a given population and aims at influencing physical activity, diet and behaviour in the framework of studies that use school as a randomisation place. The "TODAY treatment" study (Treatment Options for type 2 Diabetes in Adolescence and Youth) suggests several treatment for diabetic children. Its main goal is to reach an accurate glycaemia management, and then study the very mechanisms, risks and benefits of an optimal treatment in children. The study has three aspects: metformin, metformin with lifestyle modification, metformin with rosiglitazone. A few years ago, only insulin was considered a treatment against type 2 diabetes in children. But things have changed and treatments have been developed.

As a conclusion, we may discriminate among countries with a high prevalence of type 2 diabetes in children (the USA, Canada, Japan) and other countries (European countries notably). Incidence and prevalence date is very well documented in the first group, whereas the disease is developing within the second group. I am sorry to tell you that this prevalence will increase in the coming years in our countries.

We also witness an increase of complications in high prevalence countries, which will probably appear in the next 10, 15 or 20 years in our countries. Obesity, nutrition and absence of physical activity are strong accelerators of the phenomenon. These children should have developed diabetes later in life, and such an early development will have tragic effects on complications, since the latter are linked to diabetes duration.

In low prevalence countries, the epidemic of obesity will accelerate the process. We will learn from high prevalence countries in terms of epidemiology and secondary prevention. These countries are trying to prevent obesity: this is an emergency for them. We have to watch out for type 2 diabetes development in children and closely monitor it on the epidemiological side, as was done in England in order to have a starting point. I think we currently have the means to act quickly in terms of obesity prevention, and we should learn from other countries'experience.

"Let's put our minds together and see what kind of life we can make for children", says Sitting Bull. I hope we will be able to take action on our own lifestyles and learn from past experiences.

Questions

Member of the audience
Some studies reported that women who had gone on a diet tend to have their children develop diabetes. What is your view ?

AnneFAGOT-CAMPAGNA
I do not know these studies very well. Women who control their glycaemia balance and follow the right diet during pregnancy tend to help prevent their children from bad in utero exposure.

Member of the audience
What do you think of epigenetic transmission in type 2 diabetes evolution? May acquired features explain the evolution ?

AnneFAGOT-CAMPAGNA
Genes may explain in part this evolution, as we can see in the case of Pima Indians. But there also is a strong environmental factor that favors early diabetes development. The Search study will try and investigate the genes component further and better typify type 2 diabetes.

Member of the audience
Since we are suspicious on the role of sugar and sodas in children diabetes development, the authorities should perhaps implement strong prevention measures to prohibit such products? According to your assessments, the situation proves quite alarming and should urge us to react.

AnneFAGOT-CAMPAGNA
A relevant policy in schools and for vending machines should be implemented. We also need family measures: each parent should encourage children to drink water, not sodas.

Member of the audience
What used to be the common diet of Pima Indians ?

AnneFAGOT-CAMPAGNA
Pima Indians are to be found in Arizona and in Mexico, and both groups have evolved in quite different ways. The "thrifty genotype" hypothesis is based on the fact that this population has undergone abundance and famine cycles: the survivors are the ones who can metabolise more slowly their caloric intake, especially around the abdomen. The survival gene becomes a dangerous gene in our modern society. Yet no diabetes gene has been identified so far.

Overweight and obesity in an atherosclerosis prevention trial starting in early childhood. The STRIP study

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Good morning, Ladies and Gentlemen, and thank you for the invitation. It is very nice to be here in France. As you heard, my name is Hanna Lagström and I am working as the Post doc Research Nutritionist in the STRIP project at the University of Turku.

Today I am going to talk about growth, and more precisely about possible obesity, and also the eating habits of children in an arteriosclerosis prevention trial. I have divided my presentation into four parts. First, I will speak briefly about the background of the STRIP project, and then about what the STRIP project actually is. I will then talk about the study design and about the counseling in our project. I will follow with the results of weight-gain in children participating in the project. Finally, I will say a few words about the eating habits of overweight and normal-weight children in the project.

As we all know, coronary heart disease is a major health problem in Western countries. The first morphological signs of the disease are visible in early childhood even if the symptoms usually appear in middle age. The risk factors of coronary heart disease are also well known and many of them are already present in childhood.

Indeed, most of the risk factors of CHD are based on lifestyle. Thus, any counseling aiming at preventing this disease should start long before any harmful dietary or other lifestyle habits have become ingrained, and I will remind you that this was the situation 15 years ago when we started the project.

We all know that epidemiological studies have given convincing evidence that there are a bunch of CHD risk factors: they are either non modifiable or modifiable to a variable degree. As we all know, the most important acquired risk factors are high-serum, cholesterol-concentration, high blood pressure and obesity, which are all more or less related to diet.

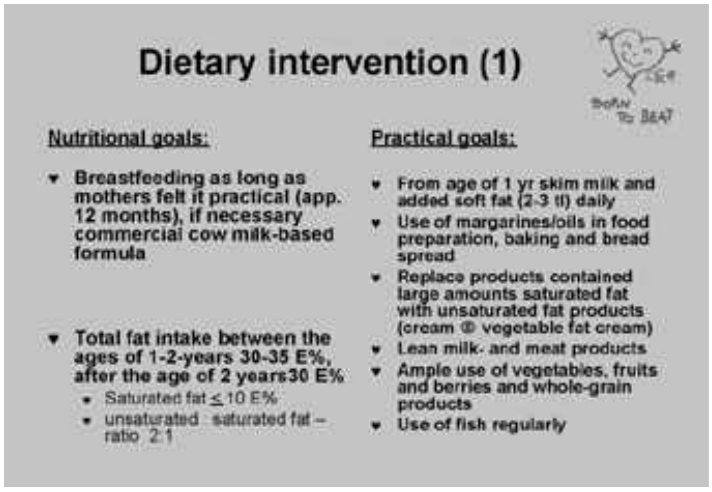
Other risk factors include diabetes, tobacco smoking, physical inactivity, age, genetic factors and male gender. In addition, the quality of human relationships, social environment and recurrent infection might have an impact on the risk of coronary heart disease.

Many of these risk factors are significantly linked with each other. For example, obese children are likely to have a more risk-associated lipid profile than non-obese children. Many of these significant risk factors are already occurring in childhood and adolescence, as we have heard.

Here you can see the main aims of our study. We investigate the possibility of decreasing the number of risk factors through individual counseling starting in early childhood, and we also investigate if intervention can be carried out without disturbing the normal growth and development of children.
We also study the elasticity of children's arteries using a non-invasive ultrasound method. We study the impact of different genetic determinants on dietary intervention, and also how child-based intervention can physically change the parents'risk factor level and that of other family members.

The STRIP study is a prospective randomised trial of infancy onset and is aimed at reducing exposure to arteriosclerosis risk factors. For the population study, families were recruited for the project by nurses at the healthcare centres in the city of Turku. For the trial, 1054 voluntary families with 1062 infants decided to participate. The children and their families were randomised to an intervention group and to a control group. The trial began in the spring 1990 and continued for two years. The oldest children are now fifteen years old and the youngest are about thirteen. We still have over six hundred children with their families in the study.

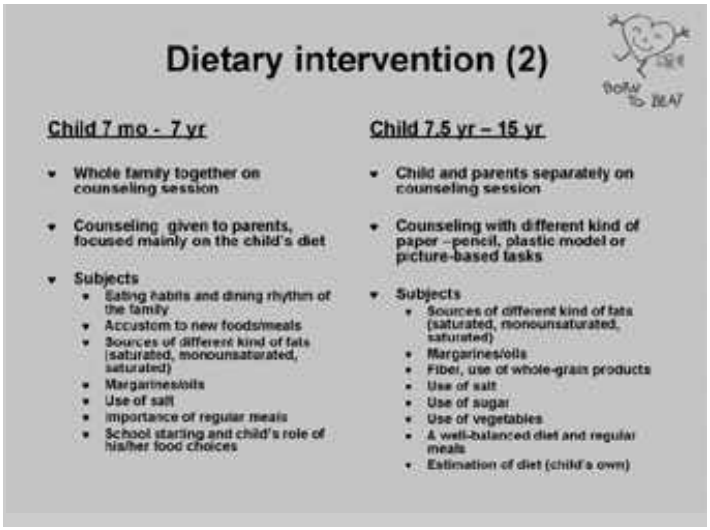
Concerning the study visits, the intervention families visited the study centre at one to three month intervals until two years of age and biannually thereafter. The control families were seen biannually until the child was seven years old and thereafter only once a year. A visit lasted about one hour and the family met the whole counseling team. Dietary counseling lasted about fifteen to 30 minutes.



Now more about the dietary intervention. After the age of seven months, the intervention families received biannual individual dietary counseling focused on a reduction of saturated fats and an increase in unsaturated fats. On the nutritional side, we can say that total fat intake should be between 30 to 35 energy percentage (E%) and about 30 E% after the age of two years. Saturated fat intake should be about 10 E% according to all the nutrition recommendations, and unsaturated fat intake should be about 20 E%. Other energy nutrients follow current recommendations.

With the control group, dietary issues were discussed at twelve-month intervals, as is common in Finnish health care centres. In practice, the mothers were encouraged to continue breastfeeding for as long as they considered feasible, or continue formula feeding until the child was twelve months old. The children in the intervention group were then advised to use skimmed milk as the milk source and add two to three teaspoonfuls of vegetable oil or soft margarine to the food of the child daily until the age of two years.

The aim was to maintain the fat intake at the same level as children who use medium-fat milk. Use of oil or soft margarine instead of butter in food preparation was encouraged. Detailed suggestions were made to replace products containing large amounts of saturated fats with products containing more unsaturated fats. Use of lean-meat products, low-fat cheese and ice cream made with vegetable fats as well as ample use of vegetables was advised, and this was recommended as one of the main meals twice a year after the age of one year. A fixed diet was never ordered but during each visit, suggestions for small changes were made leading to diets of optimal composition. It is important that no foods were prohibited. It is also important that this was a family-based intervention and based on Finnish food culture.



More about dietary intervention today. Until the age of seven years, the whole family were together at counseling sessions. Counseling was given to parents, but focused mainly on the child's diet, and it was based on the previous food habits of the child and his or her family. They were more or less all same for all the families, but the implementation was individualised. The subjects covered were the first eating habits and family dining when the child was very young, introducing new foods or meals for the child, and sources of different kinds of fat in the Finnish diet; using margarine and oils, the use of salt and also the importance of regular meals for the children and I think also for the adults.

When the children grew older and started school, the child's own role and his or her food choices were discussed with the families. From the age of seven and half onwards, the child was alone in the counseling session and we made pencil and paper, plastic model or picture tasks at each visit. The age of the child was taken into consideration when child counseling was implemented. Most of the material used in the counseling was deliberately separated for the project because ready-made counseling materials for children are sparse. The parents were carefully informed each time about the task the child had performed during a counseling session and they were encouraged to further discuss the same food-related topics with the child at home.

Between the biannual visits, one or two letters were sent home to the children to increase their interest in food and nutrition. The letters also contained paper and pencil and cultural tests or food preparation tasks and recipes. The subjects are still mainly the same as earlier. We discuss sources of different kinds of fats –margarines and oils again – fibre and the use of wholegrain products – which we use quite a lot in Finland – salt, sugar and vegetable use and their part in diet, and regular meals, which I think is very important for teenagers. When they are fifteen years old, they plan their own diet and discuss what they think about it, what a healthy diet is and what kind of diet they have. These are the current topics.

Now a few words about methods. The children's weight, height and blood pressure was recorded at each visit. The paediatricians paid special attention to the progress of the physiological and neurological development of the participating children at every visit. Possible cardiovascular disease risk factors in the family, like obesity or elevated blood pressure, tobacco smoking and a positive family history of coronary heart disease were outlined. Also the serum lipids of the child and of the other family members were analysed twice a year. Food consumption was evaluated twice a year using food records that were kept on three to four consecutive days and nutrient intakes were also calculated.

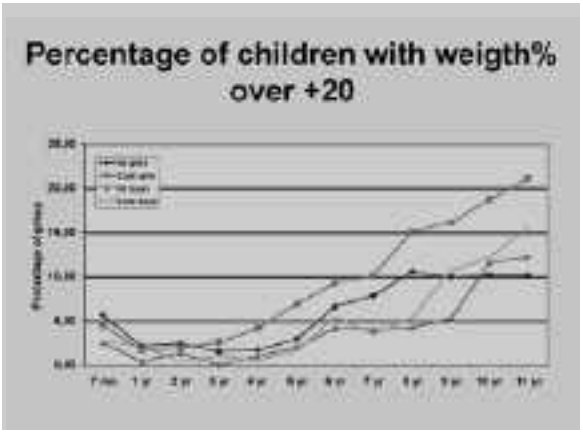
The food records of children in the control families are taken once a year. Blood samples may also be taken once a year, and at the age of 11 and 13 years, the arterial wall structure and elasticity were studied using the ultrasound method. The parents of 13-year-old children were also studied with this ultrasound method.

In Finland, growth charts are based on the follow-up of 1959 and 1971 born groups, and height variation is expressed as relative height which is deviation of height in CD units from the mean height of healthy Finnish children of the same age and the same sex. It should be the straight line that you see here is growing steadily. We also use a relative weight, and the weight variation is expressed as relative weight which is deviation of weight in percentages from the mean weight of healthy Finnish children of the same height and the same sex. This is important; it is not the children's age.

In this presentation, the definition of overweight for children is relative weight, so that the limit for overweight is +20, and +40 for obese. We can also use BMI for children and the BMI values in childhood are based on and compared to the international data. We do not use this in Finland regularly but we have now calculated the BMI values of the STRIPchildren.

We have spoken about the cardiovascular risk factors, about our project and about the methods used in the process. I would like to move forward to the results. Here you can see the relative height of the study children. Throughout the trial, the mean relative heights of the intervention and control girls, and also of the intervention and control boys were closely similar. The relative heights of all groups are above the mean height – I mean the zero line – and this means that the studied children are a little taller than healthy Finnish children of the same age and the same sex. The red line refers to the control children and blue line the intervention children. The same applies to the weight of the studied children: throughout the trial, the relative weight of the intervention and control girls, and also the boys, are very similar. Something happened at the age of 8 or 11 years in girls, but maybe we can understand this later when we go into the weight gain problem more precisely.

As I said, the children are classified as overweight if their relative weight is over +20. Here you see the children from 7 months old to 11 years old who have been overweight. The percentage of control girls here is quite high. Over 20% of control girls can be defined as overweight and other children are about 10 to 15% of their group. Here are the children defined as obese (relative weight over +40) and here also, the intervention girls stand above the other groups. If we group the genders together as a whole, 1.9% of the intervention group and 4.5% of the control children were truly obese. However, the situation is mixed up with the puberty status and we have now tried to analyse the situation onwards but I don't have the results yet.



So these figures are a little different in analysing the weight gain of studied children. The results here are for 3, 7 and 11-year-olds. The solid black lines are the median, which are almost equal for each group. Inside the box is the middle 50% of all observation. Especially at the age of 7, as you can see, in the group of control girls more observations are above of the normal distribution: I mean those open circles and asterisk.
This also means that the control girls are a little different from the other groups.

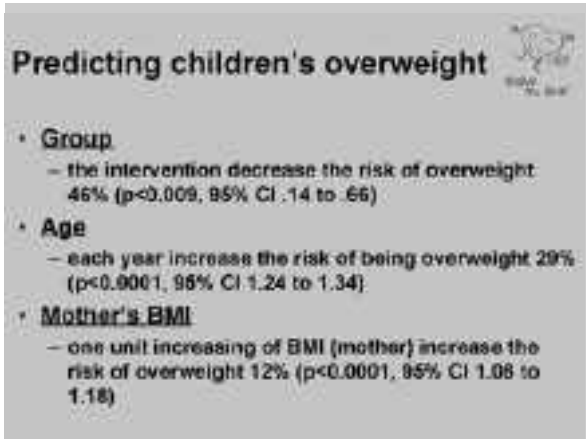
The individual children are here. We drew the weight gain of each child who, once or several times, had had a relative weight of +40 or more, and they had at least 9, and possibly 12, visits during the whole follow-up period. The main point here is that control girls stand out from the rest of the children. The red lines represent those children who are constantly over the +40 level. The green lines represent girls whose weight fluctuates, but who have been over the +40 level once or more.

Here we see the mean values of the BMI of the study children from both the intervention and control girls and boys. They are very similar in both groups. The black line is the international cut-off point for overweight from 2 years old onwards.

These are the figures for 3, 7 and 11-year-old children. The main point here is that at the age of 7, the control girls' values are above the others. I think this only indicates that we can compare these values or definitions of overweight in childhood.

We can also use the relative weight for definition of underweight. In that case, the limit is minus 15. The percentage of slim children is comparable in all groups. At the beginning of the trial, only seven children had a relative weight of minus15 or less. At the age of about 11, about 6% of intervention children and 7% of control children have a relative weight of minus 15 or less –37children in all. In our opinion, this kind of dietary intervention does not increase the amount of thin children. Interestingly, some kind of increase can be seen from the age of eight in all groups. This might be something to do with puberty status, but we do not know yet.

We also tried to find out possible overweight predictors using a statistical mixed model. Children were divided into two groups: relative weight under or over +20. Predictors in this model were sex, the group, birth weight, the mother's BMI, and also energy, fat and protein intake as energy percentages and sucrose intake in grams and calcium intake in milligrams were included. The most powerful protector was the intervention group. The intervention decreased the overweight risk of 46 %. Age and the mother's BMI increased the risk of being overweight. Unfortunately, we have a lot of missing data and the fathers were not included in this model. We normally accompany the whole family but usually, only the mothers are available for the counseling sessions.



Now we have some data about dietary intake. Here is the energy intake, which did not differ between normal-weight and overweight children. However, it is possible that overweight children and their families under-report food consumption. Indeed, there are no differences in energy or nutrients intakes. In the main project, we found that soft fat types were dominant in the intervention group, and you can read about that in the abstract. As we heard, the use of sweet things is increasing and we also studied that kind of thing in overweight and normal-weight children. Here, the blue line is normal-weight children and the red line is overweight children. At the same time, here we can see that sweet and biscuit consumption is more or less increasing. These amounts are not very high – only about 10% of the children's energy intake – but at the same time, fruit and vegetable consumption in both groups is decreasing, I think quite dramatically.

Here we see the daily energy profile in eleven-year-old normal and overweight children: this is normal-weight girls, this is overweight girls, this normal-weight boys and this is overweight boys. We do not know what kind of food they are eating in the evenings, but here, thirty percent of the energy intake comes from some kind of snacks. I think this is important, because we discuss with the families that regular meals – breakfast, lunch and dinner – are most important for the children. This increases with age, so children are eating more snacks as they grow older.

So, I think we can say that the STRIP intervention decreased overweight, and we know that we have had some very good changes in the lipid profile, the nutrient intake profile, and this is also good news.

In conclusion, we can say that overweight increases with age. However, the eating habits of overweight children are very difficult to study because when you look at energy intake, or any nutrient intake, no difference is found, so this is a difficult

situation. I don't have the data here now, but the consumption of soft drinks and sweets increases with age in all groups of children. At the same time, the consumption of fruit and berries – there are no vegetables here – is decreasing. That is why we think that fruit and the berries could be eaten as snacks. We also know from our study that school-age children eat more snacks than real meals.
Thank you.

Questions

Marie-Aline CHARLES
Thank you for your presentation of this interesting trial, which is very special because it started very early in the children's lives and apparently leads to good results in the prevention of overweight.

Maybe I can start with the first question. You did not tell us about the dropout rate. How many families stayed in the program for eleven years ?

Haana LAGSTRÖM
I said we have still about six hundred children remaining in the study and all the children are now fifteen years old. Of course, we have dropouts and I don't have any data about the weight gain of these children. It also happens that families stay away for a while and then come back into the study.

Marie-Aline CHARLES
How about the dropouts ? Did you have a lot of dropouts very early in the study, or do they drop out regularly ?

Haana LAGSTRÖM
Children start school at seven years old in Finland, so most of the dropouts are at that stage. We have the same dropout rate in both the intervention and the control families, so there is no difference in that.

Member of the audience
I would like to know what sort of fat and margarine, you used for your campaign

Haana LAGSTRÖM
In Finland we mostly use rapeseed oil and the margarine is whatever the families like to use. The fat content differs between the margarines but they can use whatever they like.

Member of the audience
Do you check if there are transfatty acids in the margarines ?

Haana LAGSTRÖM
Yes, we do check. We do not have very much transfatty acids in our diet and butter and margarines contain the same amount in Finland.

Member of the audience
Someone has been trying to aggressively deal with the issue of high rates of heart disease now for thirty years. What kind of environmental changes are going on countrywide or from the government to try and continue to bring down the risk factors associated with heart disease and the other chronic diseases we have been talking about ?

Haana LAGSTRÖM
This is a very good question and difficult to answer. The first thing is that these results data have been used in the nutrient recommendations in Finland. As I said earlier, have school lunches are free in Finland so every child can eat at no cost. We were discussing yesterday evening about using milk as a drink and we use a lot of milk products in Finland, but they are mostly skimmed milk or fat-free products in schools. The community can decide but I think they use margarine in schools. These are maybe the easiest things. In Finland, we are discussing these things as a country. We were talking yesterday about soft drinks and vending-machine foods being a big problem in Finland. Even though we have free school lunches, children can skip them – if they do not like it, they do not eat it. They then eat more snacks when they get older. So we also have to do something in this direction.

Marie-Aline CHARLES
I have one other question. The results you showed appear to have a stronger effect with girls than with boys. Do you have any explanation for that ? ou did not really show any differences in the overweight prevalence between the two groups involved.

Haana LAGSTRÖM
This is also a good question. We have the same results for nutrient intake and fat profile for both girls and boys in the intervention group. However, the lipid levels are lower in boys only in the intervention group when compared to the control group. We cannot explain this phenomenon. We also found that the puberty status of girls in the control group is earlier in stage one, so this is also a confusing situation. It seems that in the control group, the number of overweight girls is also decreasing at the age of twelve.

Member of the audience
What are you doing in this project about physical activity and what is the physical activity level of these small children? How much time do they spend watching TV ? What are their physical activities ?

Haana LAGSTRÖM
We do not have the data. We studied the physical activity of only one age of young children (study children), but we have done quite a big study on the thirteen-year olds'physical activity. I do not have any data yet but it is coming.
If I remember correctly, all children, especially the boys, have quite a high physical activity rate. We also have a questionnaire about watching TV and playing on the computer, and these data also are coming.

Potential sensitive targets for the prevention of childhood obesity

Claudio MAFFEIS
Department of Pediatrics, University Hospital, 10 Piazza LAScuro, Verona, I –37134, Italy

Doctor Charles, dear Colleagues, first of all I would like to thank the organisers of this very interesting and exciting meeting on obesity in this wonderful place in France. So, thank you very much for the invitation.

In my lecture, I will try to present some aspects that could be interesting in facing the problem of childhood obesity and, in particular, the prevention of childhood obesity.
I will try to discuss the age at risk of obesity and the risk factors as well as the intervention targets that we could theoretically hit.

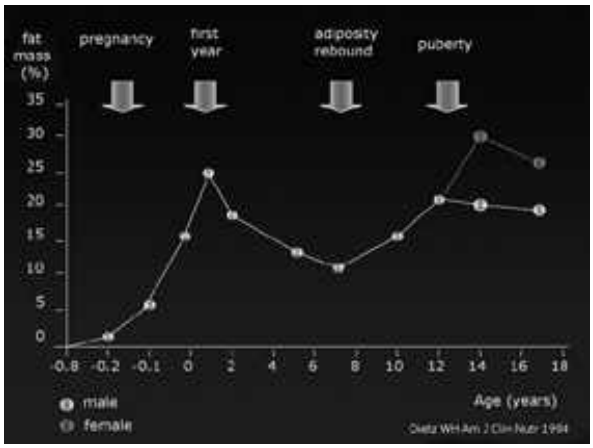
In the previous lecture, we heard that obesity is an epidemic problem. These are data obtained in the USA, where the Authors tried to compare the distribution of BMI collected from different surveys. They found that the average BMI is moving, here on the right of this plot, suggesting that the prevalence of obesity is dramatically increasing. This is true for adults, but it is true for children too. We also have data from Europe. Unfortunately, the highest prevalence of childhood obesity in the Mediterranean area was found in Greece, Spain and Italy. We certainly have to deal with this problem.

However, if the epidemiological data is impressive, the most dramatic problem is that childhood obesity is associated with several adverse effects. First of all, tracking: obese children tend to be obese adults. The second problem is morbidity associated with obesity. Then there are also some relevant psycho-social consequences of obesity and finally, the sensitivity to treatment. We know that the treatment of obesity in adults is very frustrating and most adults treated for obesity failed treatment in the long term. For children, the situation is better. Children seem more sensitive to treatment than adults.

Here, we may look at the results of a study performed by professor Dietz in the USA. He was able to demonstrate that the persistency of obesity into adulthood is associated with the age of the obese child: the older the child, the higher the chance of maintaining obesity into adulthood.

However, in spite off tracking is an important consequence of childhood obesity, I believe that the most relevant problem associated with overweight in early life is its association with morbidity. There are several data in the literature that demonstrate that there is an association between obesity and cardiovascular risk factors. One of the markers of this association is waist circumference: this is a good index for detecting cardiovascular risk factors in the young child.
Insulin resistance is the most common disorder of obesity and it usually precedes the onset of other complications. Yesterday, we had the opportunity to listen in the lecture presented by Professor Scheen that insulin resistance may be considered as a mediator or a predictor of type 2 diabetes. The prevalence and incidence of type 2 diabetes in children is increasing in the USA and in European countries as well. Moreover, insulin resistance is associated with hypertension and other cardiovascular risk factors.

In a perspective of prevention, we should face childhood obesity by looking at the ages at risk. Four different ages in which a potential intervention may be more effective were identified: pregnancy, the first year of life, adipose rebound and puberty.



The importance of pregnancy was forgotten for long, but now more evidences are available. In Pima Indians a relationship between relative weight gain and birth weight was demonstrated: the greater the birth weight, the greater the risk of obesity for the child. This is true not just for Indians, but for Europeans too. If you have a high birth weight, you have a higher risk of becoming obese as a child. Birth weight is the result of intrauterine exposure to maternal nutrition, and so to the mother's potential overfeeding. If you look at the plot of the Pima's data, you can see that there is a sort of U-shaped curve, so there is a relationship with high birth weight and obesity, but there is also a relationship with low birth weight. This is true for the prevalence of type 2 diabetes and not just for obesity. Therefore, extreme conditions in which you have a high birth weight or a low birth weight are both risk factors for morbidity in children.

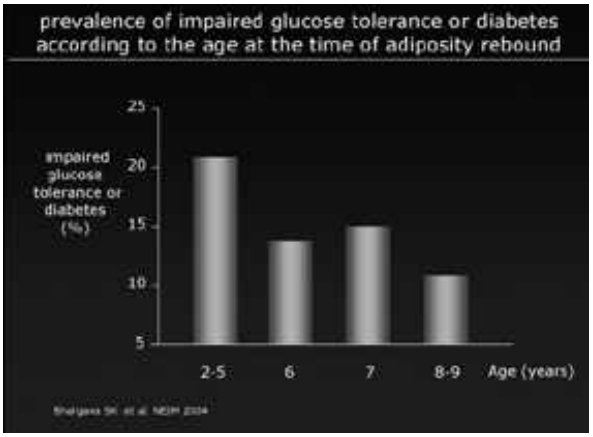
Data published several years ago showed that there was an association between the prevalence of obesity in adulthood in individuals who were born from diabetic mothers. Diabetes during pregnancy is a condition in which the foetus is over-nourished, and this predisposes a metabolic programming for the potential development of obesity later on in childhood. However, you also have the same result with the opposite situation, in which there is exposure to severe under-nourishment in the first or second trimester of pregnancy. Mothers who are undernourished during the first and second trimesters of pregnancy have a higher risk of having children who will suffer from obesity as adults. As you can see here, the prevalence of obesity is much higher in these children than in individuals born from mothers who were not exposed to under-nutrition during pregnancy, or mothers who were only exposed to under-nutrition during the third trimester of pregnancy or post-natally. Exposure to severe under-nutrition is therefore a risk factor.

This is also true for animals. This is a study carried out on animals in which they exposed the experimental animals to under-nutrition in the pre-implantation period. You can see that a severe reduction of protein intake was associated with a significant reduction of the number of cells in the blast cyst.
So, exposure to under-nutrition or malnutrition not only during pregnancy, but also before pregnancy, could be an interesting phenomenon that may explain this kind of output.

If you look at the longitudinal association between growth in children and chronic heart disease, you can see that children born with a low birth weight, or a low ponderal index, are the children with the highest risk of having coronary heart disease in adulthood. Therefore, the extreme of the birth weight curve may be important.

After pregnancy, the infant has the first contact with food. Several studies have tried to look at the relationship between breastfeeding and obesity and there are some contrasting data in the literature. Some studies support the association between the importance and the duration of breastfeeding and obesity risk reduction. However, a very interesting longitudinal study performed in the UK demonstrated that this is not really true. Breastfeeding may protect, in some way, young children from obesity but, later in life, the protective effect of breastfeeding is limited because of several confounding effects that may modulate and reduce the potential preventive effect of breastfeeding. So, I think we cannot conclude anything now on this topic. We need more studies to be conclusive.

Protein intake is also important in the first year of life when the baby is exposed to weaning. The introduction of solid foods in the baby's nutrition is important. Here you see some data that comes mainly from the USA, where the researchers tried to measure the real protein requirement in young infants. They found that the real protein need of infants is very low. However, some epidemiological data demonstrated clearly that - especially in Europe and especially in Italy, unfortunately - we have a very high protein intake during the second trimester of the first year of life, and this seems to be associated with the risk of becoming overweight. So early exposition to high protein intake may be a potential risk factor of fat gain.



Dr. MF Rolland-Cachera very clearly demonstrated that the adipose rebound, or BMI rebound, is an important predictive factor of obesity in children. An early adipose rebound is a risk factor for obesity later in life. This rebound or accelerated growth is interesting because a recent study published in the New England Journal of Medicine demonstrated that the prevalence of type 2 diabetes found in young adults or in adults is associated with the time of the adipose rebound. If you have an early rebound you have a higher risk. This is independent of body weight or birth weight, it is just a rapid weight gain between the ages of two to twelve years, irrespective of the starting weight.

There is another study performed by Nicholas Stettler who demonstrated that rapid weight gain during the first four months of life is an independent obesity risk factor in children.

Why does a child become obese ? This is a gross simplification, but fatness may be considered as a consequence of an increase in fat intake and/or a reduction of fat oxidation, and the balance between the two factors is positive so to maintain or increase adiposity. We will try to analyse the rule of fat intake and fat oxidation.
There is a clear relationship between lipid intake in the diet and fat mass. Several cross-sectional studies conducted on children, adolescents and adults demonstrated this kind of association. However, also longitudinal studies contributed to demonstrate an association between fat intake and obesity in children.

Fatty food is good because it is palatable, but it has also high-energy density and it is less satiating than other nutrients. But fat intake is also associated with a low stimulation of thermogenesis. We compared two different meals with different fat to carbohydrate ratios and we were able to demonstrate that a high-fat intake is associated with a significantly lower thermogenesis. This simple factor is not so important quantitatively, but if you try to calculate the impact of a high fat diet over 24 hours, you can see that 2% of total energy expenditure is reduced if you have a high-fat diet compared with another diet, iso-proteic and iso-caloric, which has a high concentration of carbohydrates and low concentration of fat. This 2% of energy is equal to roughly 2 kg of fat in one year and this is not trivial.

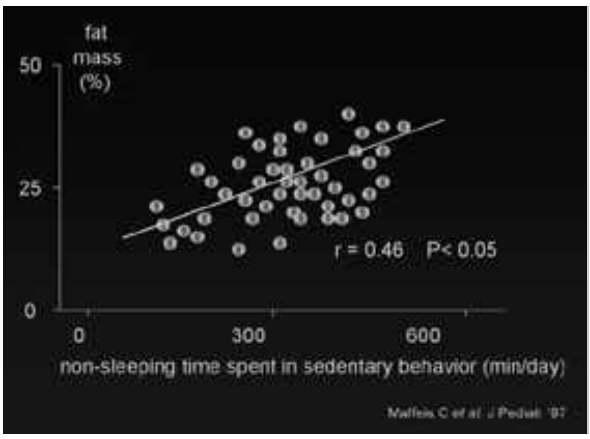
This is a very elegant study conducted in Cambridge, comparing young adults exposed to three different kinds of diets: high-fat, medium-fat and low-fat. They found that an ad libitum food intake covered for the composition of this diet was able to promote fat gain when the subjects were exposed to a high-fat diet. On the contrary, when subjects were exposed to a low-fat diet, a negative fat balance, that promotes a negative energy balance and a decrease of body weight, was demonstrated. This is a clear demonstration that fat in the diet, by itself or via increased diet density, may be an obesity risk factor.

Another important contributing factor is portion size. In this study, researchers tried to demonstrate that portion size is able to induce a higher food intake in children of four years or older. They demonstrated that exposure to high portion size is a stimulating factor for increasing spontaneous food intake in children also at young age.

The second part of the balance equation concerning fat, nutrient or energy, relates to skeletal muscle activity and oxidation.

Fat oxidation is mainly due to skeletal muscle activity. Exercise or physical activity stimulate fat oxidation in the muscle, but fat mass per se is also a stimulating co-factor of fat oxidation in the muscle. Several years ago, we demonstrated that there is a relationship between non-sedentary time spent in sedentary behaviour and adiposity in children. TV viewing is a common sedentary behaviour in children. In Boston, researchers tried to analyse the effect of several variables on the risk of BMI gain over twelve months. They found that video exposure (TV, computer) was the most important predictor. Another independent study showed that each additional hour of TV viewing per day can increase the obesity risk by 6%. The average TV exposure is four hours per day in at least 30% of European children. Others demonstrated that having a TV set in the children's bedroom increases the obesity risk by 31%.
TVviewing is also associated with poor diet composition.

There was an interesting study that tried to prevent or reduce TV viewing time and they succeeded in reducing BMI increase in these children. Therefore, a reduction of time devoted to sedentary behaviours, especially video exposure, may be a good target for intervention.



Skeletal muscle activity is important because the greatest fat oxidation in the body occurs in the muscle. In this study, performed on a group of adults, the change in the nutrient oxidation rate in resting condition, before and after endurance training, was measured. After training, resting fat oxidation rate in significantly increased in these subjects. Interestingly, there was a reduction of plasma-free fatty acid oxidation and a very high increase in non-plasma-free fatty acid oxidation. These fatty acids come from the skeletal muscle tissue.

There was another study, conducted in France, which demonstrated that exposing children to regular physical activity induces in these children different choices in food intake. The carbohydrate intake was higher in children who were performing regular physical activity. Physical activity per se seems to simulate a higher food intake but a better diet composition in children.

Also, a training programme for young children induced a spontaneous increase in physical activity and energy expenditure for non-programme exercise. In this study, the Authors tried to compare the total energy expenditure before and after training in a group of ten-year-old boys. After training, the total energy expenditure was increased. In particular, about 50% of the amount of this difference in energy expenditure was due to the energy cost of training per se, while the remaining was due to the non-programme exercise. So, exercise training stimulated children to be more spontaneously active. I think that this consequence of programmed exercise, if confirmed in obese children, may be potentially important for the prevention as well as the treatment of childhood obesity.

Exercise can also modify body fat distribution. In this study, the Authors measured body fat distribution by MRI. They were able to demonstrate that exercise reduced fat mass but also improved body fat distribution, reducing visceral adipose tissue. We know that visceral adipose tissue is the most dangerous localisation of fat in the body in children too.

This is another study conducted by Michael Goran in the USA. He was able to demonstrate that the most important predictor of weight gain in children among the components of energy expenditure was the VO2 max, the most common index of cardio-respiratory fitness. Regularly trained children improve their fitness and this behaviour is a protective factor against obesity later in childhood. This finding seems very promising for the potential application in the prevention and treatment of obesity.

In the final period of growth, during puberty, the risk of obesity is high. In this slide, you can see the distribution of the physical activity levels of children (i.e. a gross index of physical activity given by the ratio between total energy expenditure and the basal energy expenditure). You can see that there is a reduction of spontaneous physical activity for girls starting at the age of 9-10 years. This is also associated with an increase in fast-food and soft-drink intake. The combination of reduced physical activity, both spontaneous and programmed activity, with the changes in nutritional habits contributes to promote fatness and adiposity at this age.

Coming back to prevention, we have to confess that, unfortunately, we do not have very effective strategies available at the moment. We have little experience and no proofs that our strategies are really effective in the medium, long term. We are now looking for targets and effective strategies for the prevention of obesity in children as clearly reported by the result of a Cochrane database review.

There are a lot of possible variants for childhood obesity preventive intervention. There are programmes focused on the social environment and the community level, and also on the environment per se. Most of the interventions are based on interventions at school and, some of the interventions, at home. Most of the interventions performed at school were able to modify behaviour, but just for a short time. So they may be effective in the short term, but, this kind of intervention does not seem to be really effective in the long term. We need to improve the quality of interventions.

The cost of intervention is another important problem. Funding competition with other primary care problems is high.

In conclusion, on the basis of the multi-factorial aetiology of obesity, I would say that prevention intervention requires that the multiple settings are contemporaneously involved in the programme: we have the family, the school and the community environments. Unfortunately, at present, few models for the prevention of childhood and adolescent obesity have been tested, and generalised conclusions on the effectiveness of obesity prevention programmes cannot be drawn. The need for studies that examine a range of interventions remains a priority, but we have to focus on behavioural changes and nutrition lifestyles. Good evidence exists that diet composition, portion size, distribution of food intake are potential sensitive targets for intervention. The increase in fitness and reduction of video exposure are other potential sensitive targets.

Thank you for your attention.

Questions

Marie-Aline CHARLES
Thank you, Doctor Maffeis, for this review of the potential risk factors for obesity in children. Your conclusions are quite sad. You are saying that what we have done so far, which is mainly the intervention programme at school based on the promotion of nutritional education and physical activity, has not been very successful. Do you have any recommendations? What can we try now that would be more successful than what we have done before?

Claudio MAFFEIS
It is a difficult question. I think that we have to focus on a few targets and try and improve these kinds of behaviour. For example TV viewing is really dangerous. In my country, a lot of families eats dinner all together but they have the TV set on, so they are watching TV really, they are not discussing during the dinner. This is terrible. A lot of children have a TV set in their bedroom and this is not really very good. I think TV watching may be a sensitive target, but it would help if we could replace time devoted to TVwith time devoted to other more attractive activities. More effort and more emphasis were given to the reduction of sedentary time in the research, and that is good. The improvement of the level of fitness in children is very important, because we have data in adults that fitness is potentially a very important predictor of the reduction of mortality per se, independently of bodyweight.
There is an interesting very large epidemiological longitudinal study conducted in the USA, which demonstrated that fitness can reduce the mortality risk, independent of bodyweight or BMI. I think that children who are trained to regularly perform physical activity may reduce their cardiovascular risk factor, first of all. The exposure time to cardiovascular risk factor is a risk factor for morbidity later in adulthood. So, if you reduce the risk exposure, theoretically you may have more chance of a lower morbidity in adulthood. I think we have to reduce sedentary time or substitute activities, and also guarantee a regular physical activity programme for all children, not just obese children.
Then there is the problem of the density of the diet, which is very important. I agree that the consumption of vegetables and fruit has to be promoted as well, but children do not want them. Common experience is that children prefer to eat other foods, so it is very difficult to promote the regular consumption of good foods like fruits and vegetables. I think we need more strategies to promote the consumption of this kind of food in the population.

Member of the audience
I am from the National Cancer Institute in the United States. I just wanted to comment directly on what you just said. In several countries here in Europe and also in the US during the 2002-2003 school year, we had a pilot project in four states to change the environment in the schools with regards to fruit and vegetables. So I want to politely counter what you said. This money was provided by the Congress, we had six million dollars, and the environmental intervention was in a hundred schools and also one Indian reservation, which has the same problems as the Pima Indians. This funding allowed us to provide 97$ per student for the school year to eat at those schools that were in the study: twenty-five schools in each state. The schools could then provide fruits and vegetables that kids wanted to eat as snacks, and they provided them as snacks throughout the day. Basically, a table like that, one of those tables filled with fruits and vegetables that kids could just take and eat as snacks throughout the day. They found many results. One is that in the middle schools and high schools, where the table was filled throughout the day in a central location, the kids were eating three to four servings more per day. Also, they did not ask for the soda machines to be turned on. The school also kept data on how much less money the children spent in the vending machines. The kids then went name and told their parents about buying more fruits and vegetables. There are some data from Norway and Denmark, and there is a study that has just finished in New Zealand. So I think we do have data to suggest that these environmental changes can make a difference and that children like fruits and vegetables, but they have to be available where the kids are.

Claudio MAFFEIS
Yes, I agree with you.

Haana LAGSTRÖM
I have a comment based on our situation and on our project in Finland. We have a healthcare system in Finland where babies are seen about ten times during the first year of life, and then, once a year until the age of 6. They then come under the school healthcare system. In my opinion, if we are discussing prevention, we have to start as early as possible, so that when a woman is pregnant, we can discuss her lifestyle. We can then start prevention early in childhood with a positive lifestyle message. We have trained the healthcare staff to discuss these issues with families so that they can learn a good lifestyle. This could be the key-point, to start as early as possible in the healthcare system.

Claudio MAFFEIS
Yes, I totally agree with you. We are starting the same kind of project and trying to start as early as possible: during pregnancy and in early childhood. We are lucky in our country in that we do not have to pay for the healthcare system, so we have a paediatrician following children from birth, and we may try and start from there.
Then the experience of the school is absolutely excellent. The problem of fruit and vegetables is also the cost for the family. In Europe and in my country, the cost of fruit and vegetables is very high for a family, and so you can also have discrimination on a socio-economic level.

CONCLUSION

Marie-Aline CHARLES
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We have seen that there is a significant increase of childhood obesity and its consequences on adolescents, such as diabetes. This especially shows in very young adults. We also asserted that obesity may start quite early for a certain number of children. So far, we may say that prevention studies have begun too late; we have to take into account that it is possible to modify family habits very early. We can even take action during pregnancy, which might be a new way of prevention. Of course, environmental changes may be achieved through a whole variety of means. Conferences such as EGEA, as well as other types of actions, are currently under way in order to try and modify the environment.

We shall succeed, although this may take some time. You cannot simply “forbid”, since interdiction is a sensitive action. Yet you may be able to progress step by step towards your goal. Before urban environments and schools can be changed, we urgently need to begin specific prevention towards children: this should become researchers and physician’s main priority.

Nutritional transitions : Diet quality and diet cost

Adam DREWNOWSKI
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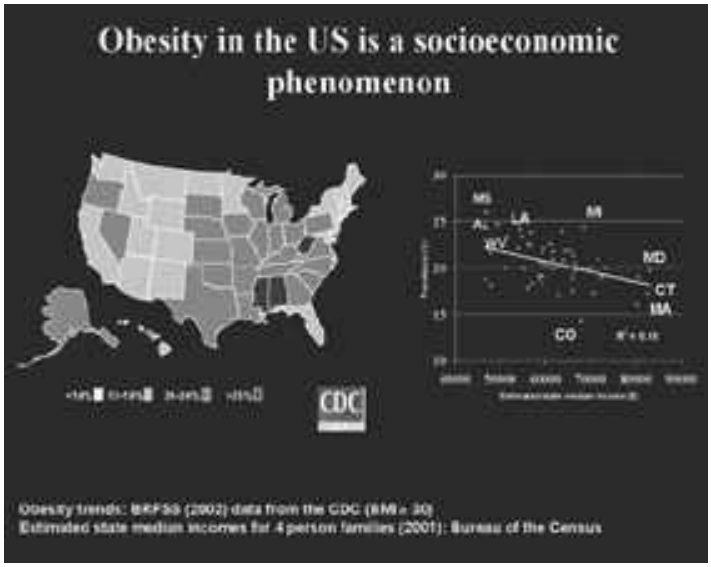
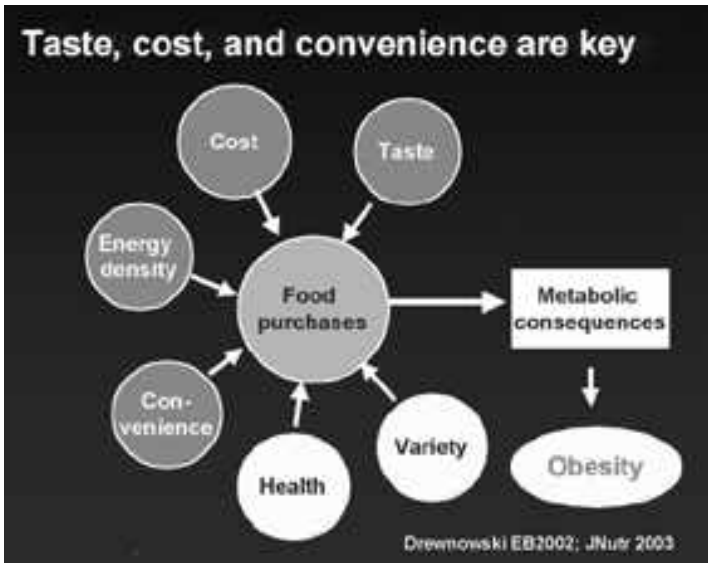
My talk today will deal with the issue of obesity and the relationship between obesity and diet cost. What I have shown you before is a map of the United States linking highest rates of obesity to lower incomes by state, so that the most obese states are also the poorest.

This type of analysis can be extended to neighbourhoods. This is a map of the Los Angeles area in Southern California, and what we see is that the highest rates of obesity are found in the lowest income Los Angeles County, so that would be Central and Eastern Los Angeles. On the other hand, Beverly Hills, Malibu, Huntingdon Beach, Palos Verdes peninsula, Newport Beach, Corona Del Mar and Laguna Beach are relatively obesity-free. So I always say that the best way to lose weight is to move your family to the very expensive Newport Beach.

In other words, obesity may well be influenced by genetics, but it is really predicted by postal code or zip code. There are very strong environmental influences so that those influences have to do with the access to healthy diets – both the cost of the healthy diets and also the relative accessibility of healthy diets, especially fresh produce, in low-income neighbourhoods.

When we look at the model of food choice, we are looking at the critical factors of taste, cost, energy density, convenience, health and variety. I made the point two days ago that taste often equals sugar and fat, cost equals sugar and fat; energy density, still sugar and fat; convenience, sugar fat and salt; and here, we come to vegetables and fruit when it comes to health and variety. What we need to do is to make sure that health and variety are equal to cost in influencing the consumers'food choices.





What I want to show you today is some data on food costs in France and the cost of the French diet. I want to ask a very fundamental question, and that is: do energy-dense foods cost less, and do healthier foods cost more ? The data I want to show you are from the Suvimax study, which is a large-scale study completed only last year, of several thousand French volunteers, both men and women.

We have nine hundred and thirteen foods in the nutrient database. For each of those foods, the French National Institute for Economic Research provided us with mean national food prices. So, in collaboration with Dr Nicole Darmon, and André Briend, Inserm unit 557, we were able to calculate the energy density of foods and link it to cost per calorie.

So let us take a look at the issue of energy density, because this was mentioned both yesterday and today. Energy density of foods is a function of their water content. It can go from 0 (water) to 9 calories per gram, and that is oil. You have oil, butter, margarine and various spreads. The range goes from 0 calories per gram to 9 calories per gram. Here you see it – 900 calories per 100 grams.

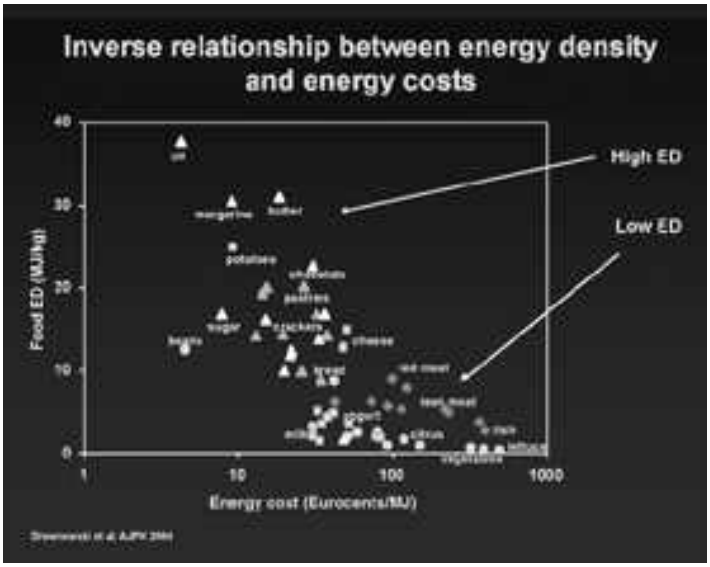
On this scale, you see energy cost in Euros per thousand calories. Notice that this is a logarithmic scale, so each interval is equal to a tenfold differential in cost. These are prices per calorie : 10 Euro cents, 1 Euro, 10 Euros, 100 Euros, 1000 Euros. Notice that this is cheap oil. You can get 1000 calories from inexpensive oil for 10 Euro cents. This is more expensive olive oil and you can still get 1000 calories for under a Euro. What I did here was stratify the foods by various food groups, so here you have sugar, deserts and soft drinks. Sugar at retail prices in France is still relatively inexpensive : notice 4 calories per gram – very low cost (you can get 1000 calories for approximately 5 to 7 Euro cents, you can get 1000 calories from soft drinks for under a Euro). Here you have desserts. Again appreciate that each interval is a tenfold difference in price.

Now you see grains: bread, pasta, crackers and other grain products. Here you have dairy products: cheese, yoghurt, ice cream and milk. Here you have meat products and nuts over here. This is foie gras, so here are the meat products. Here you have fish and shellfish: those are langoustines. Notice that we are moving towards the right and each interval is a tenfold difference in food cost. Here we have vegetables – very low energy density – and a relatively high energy cost. Here you have fruit. And this being France, we couldn't do without the prices of aperitifs, digestives, wine, cognac and so on, so here are wine and alcohol.

Notice the relationship between energy density and diet cost. The energy-dense fats, energy-dense grains and deserts are inexpensive. You have the range of energy-dilute foods, but they become more expensive as you go on. So there is a difference in price between the healthy foods and the unhealthy foods. In a word, the unhealthy foods are much cheaper. The problem is that this price differential is not in the order of 5% or 10%, this price differential is in the order of, in some cases, ten thousand percent. It is just vast.

Here are the fast foods, and notice that the fast foods and the snacks – these are Paris prices – are closer to the snacks and the deserts than they are to the cost of lean meat, fish, vegetables and fruit, which are over here.

The same hierarchy of food prices is obtained in the United States. I want to show you the prices from an American supermarket. We are looking now at energy cost in cents per 10 MJ, again we are looking at a logarithmic scale. Notice that these are oils, shortening, mayonnaise, margarine, cookies and sugar, soft drinks down here, grains, dairy products, meat and fish and nuts, vegetables and fruit. This was Seattle in January, so of course raspberries are way out of season and very expensive.



So we have here this distinction between the healthy foods and the unhealthy foods, and you heard earlier today, and also yesterday, various discussions about the relative healthfulness of those various foods. Previous speakers have mentioned glycaemic index, the high glycaemic load, the hydrogenated fats, the trans-fatty acids, the added sugars, the energy-dense foods, the empty calories, large portions and minimal nutritional value of foods over here. They have also stressed the value and nutritional benefits of foods over here: the anti-oxidants, phyto-chemicals, fibre, vitamins, minerals, nutrient density and so on.

What no-one has really talked about very much is the price differential between those two groups of foods. I would say that we know that the foods over here are healthy and yes, we ought to be consuming them and yes, we ought to assure compliance, but we must also have economic and policy mechanisms in place to make sure that those foods are equally available and accessible to the average consumer. Metabolic and scientific research, behavioural and motivational interventions must be supplemented by economic and policy measures to make sure that those foods are in fact available to all. As I said, the cost differential is in fact vast, going from 100 to 1000 to 10,000 percent, and it is very difficult to bridge that gap by merely encouraging compliance with healthier diets.

Now, you may say that no-one really eats a diet composed entirely of lettuce and that this is just an exaggeration, because a diet will be composed of a number of food groups and perhaps eating more lettuce will not increase the cost of the diet all that much. So, the next studies we did had to do with the cost of the diet. Those studies were based on a more abbreviated data set and this is the data set from the Val de Marne, a study conducted some time ago by Serge Hercberg, the study that preceded the much larger longitudinal cohort of Suvimax.

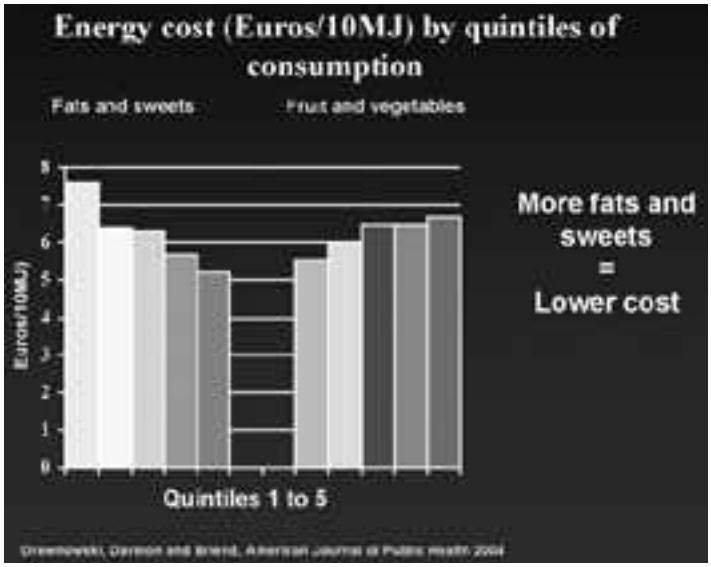
Here we had only 57 foods in the database. We also obtained mean national food prices from the French National Institute for Economic Research. We were able to take those prices, multiply them by the average portion size, and sum over all the foods consumed by a given individual – and we had 837 people in the study – so that we could calculate the estimated cost of each diet. You understand, of course, that this was not what the people paid for the diet, it is merely the estimated cost of what the diet was in fact worth. If they had prepared and consumed everything at home, this is what the raw ingredients would have cost.

This is the price structure for the Val-de-Marne data set. The first conclusion we came to is that the most expensive ingredient in a diet is in fact water. Because water in fish and meat and fresh produce adds to the cost of transport, it makes the produce perishable and as a result, if you want natural water in your diet, be prepared to pay an extra cost.

What we did, of course, was to stratify the consumption by quintiles of consumption: of course, the more you eat, the more you pay. So we need to look at people who eat approximately the same amounts, and then look at the quality of the diet given a constant level of dietary intake. So these are people who approximately consumed 1000 calories per day. Notice that the more hydrated the diet, the more it cost. These are data in Euro cents per day. So you consume 1000 calories, a more hydrated diet is associated with a higher diet cost: 2000 calories, 3000 calories, 4000 calories, 5000 calories, at each level of consumption there is more water in the diet. The more hydrated the diet, the more vegetables and fruit in the diet, the higher the estimated diet cost.

So, for example, the World Health Organisation has recommended reducing the energy density of the diet. Energy density of the diet, as I mentioned the other day, is inversely associated with water content. Our suspicion was that energy-dense diets cost less and energy-dilute diets in fact cost more. These are people who consumed approximately 1000 calories per day. Notice that as the energy density of the diet increases, the cost drops. So eating an energy-dense diet is associated with a decline in diet cost. This is observed at all levels of consumption: 2000 calories, 3000 calories, 4000 calories, 5000 calories. Those data were recently published in Public Health

Nutrition in an article of which Nicole Darmon is the first author, and she in fact conducted these analyses in Paris. Again, notice here that reducing the energy density of the diet – as recommended by the World Health Organisation – is going to involve an increase in diet cost.



So what about energy-dilute vegetables and fruit? What we did here, was to look at fruit and vegetable consumption in grams per day, and associate it with diet costs. Notice that as you go from 200 to 400 to 600 to 800 to 1000 grams per day of fruits and vegetables, costs go up. In fact, costs go up very substantially: each 100 grams are associated with a 0.2 Euros increase, so that ten servings of fruits and vegetables per day would be associated with a higher cost of approximately 2 Euros per day, which works out at 700 Euros per year per person, which is really quite substantial. This also happens at higher level of the consumption – 2000 calories, 3000 calories, 4000 calories, 5000 calories – at each point there is an increase in diet costs.

Of course, when you go to nutrient composition of the diet, for example vitamin C, you see much the same picture: nutrient-dense diets again tend to be more expensive – at every point. Higher vitamin C content in a diet means higher cost. When it comes to fats and sweets, it is the exact reverse: eating added sugar and eating added fat actually results in net savings in diet costs. You eat more snacks and sweets and you actually save money. These are data for consumers: 1000 calories per day, a slight decrease; 2000, 3000, 4000 and 5000 calories, a slight decline in diet costs. We actually figured out much the same relationship for the consumption of sugar. So the more fats and sweets you consume, the less you pay, and the average cost of the diet drops; but the more fruits and vegetables you consume, the more you pay, and the average cost of the diet increases. This has everything to do with the current structure of prices and if we want to change it, we must not only create demand among the consumers, we must also make sure that the supply follows and that the healthy foods are available to the consumer at a reasonably low price.

Interestingly enough, some food groups were neutral with respect to diet costs, specifically dairy products. There was no difference in terms of diet costs looking at the consumption of dairy products in France – notice that those curves are completely flat. Again, for people who consume 1000 calories, 2000, 3000, 4000, 5000, there is absolutely no relationship between the consumption of dairy products and diet costs. That means, interestingly enough, you can increase the consumption of dairy products as a dietary recommendation without the slightest effect on diet cost. That is not true of other segments.

Here we started looking at modelling optimal diets. I will just present you some results about linear programming, again conducted by Nicole Darmon. This is the "programmation linéaire" that Ambroise Martin will talk about tomorrow.

So Nicole was testing this model saying that as you reduce or put a constraint on food costs, you are driven in the direction of more energy-dense foods, perhaps more sugar and fat, less fruit and vegetables. The diets become lower quality, they become more energy-dense, but they do in fact cost less. So the question was whether, by putting a cost constraint and reducing the cost of the diet, energy density of the diet would go up – and yes, it did.

Nicole was using a linear programming model, optimising the quality of the diet, taking into account the usual French eating habits and the usual food preferences. As the cost was reduced from 5 Euros to 4 Euros to 3 Euros to 2 Euros, energy density of the diet went up, both for men and for women. What happened, of course, was that meat, fish, fruits and vegetables dropped out of the diet and were replaced by added fats and sweets and, in some cases, cereals. In other words, if all you spend on your diet per day is 2 or 3 Euros, there are very few options for healthy foods and very few options for vegetables and fruits and this is something that really needs to change.

In the United States, we have been creating similar plans for low-income families, trying to see what kind of foods will fit into a healthy diet at a very low cost. These are some of the solutions obtained using an equivalent linear computer program. These are diets recommended for a family of four, at a cost of only 104 $ per week. This is the equivalent of 26 $ per person for a week, so this is under 4 $ (3 Euros) per person per day. The types of foods you can get for 3 Euros per person per day are really going to be very limited.

The computers of the United States Department of Agriculture came up with this solution: what you see here is again the plot of energy density against energy cost, and the size of the bubble corresponds to the number of calories provided from each of those foods for a family of four. The data show that despite our best intentions, most of the calories for a low-cost diet come from oil, margarine, mayonnaise, sugar, crackers, white bread, beans, potatoes, milk, lemonade, ground beef and ground turkey. In contrast, the amount of calories from lettuce is absolutely minuscule, and the amount of calories from fresh produce is again minuscule.

We very often say that low-income families have made a wrong food choice, that there food choices were perhaps guided by ignorance of nutrition or laziness or something else. What I am saying is that these were the only economic choices possible, and those choices are confirmed by computer-optimisation programs, both in the US and in France. The limiting factor here was diet cost. So again, we ought to change the structure of food prices in order to achieve some meaningful changes in the diet.

However, that is going to be fairly difficult because the same kind of structure of food prices has existed for the past two hundred years. These are data from the year 1887. Wilbur Atwater was working at the time for the American Department of Agriculture. He was concerned with the relative cost of protein, which is still the most expensive nutrient, and he tried to figure out the cost of energy. Here you see energy density and energy cost, with the size of the bubble corresponding to the amount of protein you could obtain for a dollar. Notice that beans, cheese, potatoes and white bread were the cheaper caloric options, beef

liver and beef sirloin were over here, but oysters and oranges were over here. Since then, oranges have become less expensive and oysters have become more expensive, but it is still fat and grains which provide calories at a low cost.

One final thought I want to leave you with is that we should not really behave as though all diets cost the same. Dietary recommendations need to be sensitive to consumer limitations and consumer resources. For example, this is an advertisement for the Atkins diet, which has appeared in many American newspapers. It says ironically, "There is nothing to eat on Atkins except…" and they give you salmon steak, lobster steak, mushrooms, and all kinds of other stuff. Those foods are really quite costly in terms of calories per dollar, though they may be less costly in terms of nutrients per dollar. Then the whole thing changes around. We are looking right now at developing a nutrient density score per dollar. As I said before, that nutrient score will come out with fruits and vegetables on top, because you get lots of nutrients for fewer calories.

The newspaper US Today recently priced the Atkins diet: it came out at 15 $ per person per day. So if an average low-income family spends 3 to 4 dollars per person per day, the Atkins slimming diet costs three to four times as much. Again notice that it is the low-income families that tend to be the most obese, and following the Atkins diet for them is not really an option. We have had a number of idealised perfect diets – pyramids – some of them are created by my esteemed colleagues from Harvard. My position is that some of those pyramids do not take the limitations of the working poor into account. We need to be aware of economic elitism and we need to make sure that all groups of society have equal access to healthy foods.

My final model is that the obesity epidemic in the United States and worldwide is driven to a degree by the very low cost of energy-dense foods. That, in turn, depends on economic resources. The ways to intervene need to include policy and political interventions.

To conclude, obesity in the United States and, increasingly, globally, is a socio-economic phenomenon. As we have seen repeatedly, the highest rates of obesity are observed among the working poor. On the other hand, many of the current strategies for weight control are very middle-class and we need new environmental, economic and policy approaches to make healthier diets available to all. However, that may require a change in food and nutrition policies as well as behavioural and nutritional interventions. Thank you.

Questions

Member of the audience
One of the basic theories that Joan holds very dear is that everyone should grow some of their own food. Even if you have very little land, even if you have none at all, you can plant some pots with tomatoes, you can plant window boxes, you can grow things like carrot tops in the kitchen that are really very nutritious. So, just for a starter, I will put that out.

Adam DREWNOWSKI
Joan Gussow has an estate on the Hudson which is worth millions. She does have a garden, but a lot of us are not quite so privileged.

INTRODUCTION

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I would like to thank the organisers and Pr. Vague for inviting me to participate in this meeting as a " local " endocrinologist and metabolism specialist.

I would like to share some remarks on obesity before leaving the floor to a round table. When you talk about obesity, you are talking about paradoxes.

The first paradox is an economic one: I am quite astonished by the fact that half the world population is starving while the other half is making the wrong nutritional choices, which will lead them to obesity. We should bear this reality in mind. I have worked many times with the NGO “Médecins du Monde” in countries where life is not as easy as it is here, and this reality always struck me.

The second paradox regards the way obesity is being taken on: so far, we have handled genetic context, dietary mistakes, but hardly mentioned the role of medias pressure. Now this is a determining element in obesity development. Pressure by the food-processing industry has not been handled either, although it does play a role in the induction of obesity through information. TV advertisements also participate in this nutritional misinformation. I am quite frightened by the tremendous mistakes that ads sometimes convey. I understand that this is a sensitive topic and I d not know whether we should talk about it.

There is another paradox in the fact that although we try and encourage people to have good nutritional habits (this meeting is a good example), make conferences in hospitals, schools… we face indeed great difficulties in trying to avoid snacking in general, especially when it helps collecting money to fund school trips. Upon several conferences in schools, I have been told that this cannot be removed. Hospitals are constantly requested to make efforts, but on the other hand vending machines are to be found in every hospital hall. We want to have nutritional courses in high-schools, while Mc Donald’s restaurants settle across the street. Are we controlling the situation? I think that the issue should not be taken on in an isolated and ad-hoc manner. We should have a global approach, i.e. go beyond the medical and dietetic framework. This project reaches out toward the whole society, and not only the individual, for individual projects end up failing in the long run, probably because of external factors.

Another paradox lies in the individuals’ level of awareness. According to statistics, there are 80,000 people living with diabetes among 2.5 million inhabitants of the region of Languedoc-Roussillon; among these diabetics, 70 % are obese. In 2002, annual cost of diabetes for the region was up to 230 million euros. On a national scale, this cost represents 3 to 4 billion euros (including hospital costs etc.). You may want to think about it. This appears as a paradox when you know that being aware of these realities is enough. We do know that a better diet and moderate physical activity allows for risk factors reduction. If you drop 7 kg of body mass, your risk of getting type II diabetes also drops by 40 %. This is a public health issue, which is a great opportunity. Why are we unable to have people realise this? Perhaps external pressures are too strong. Knowing what diabetes-related complications are (cardiovascular risk, morbidity…) should be enough to make us want to move on. After 30 years, I still cannot understand why we are not moving forward.

Besides, when an adult is being diagnosed with diabetes, 20 % of the subjects already have diabetic retinopathy. This means we have a 7 to 10 % delay in diagnoses. In the context of this disease, such a tremendous delay turns into a real public health problem.

I have been thinking of all this for years, yet I still have no answer to these questions. Of course, obesity does not occur from scratch, there is a continuum between normal weight, overweight and obesity. Each status has its specificities in terms of care and treatment: Ms Gerber has been working for years on nutritional care in the case of cancer. She will talk about transitions between overweight and obesity. Then Mr Gibault will handle athletes dietetics, and the possible differences among individuals in terms of treatment at several stages of the disease (overweight, obesity). With Ms Liégeois, we will take an inside look of the day-by-day life of overweight, obese, and normal people, since we all are at risk. A debate will follow.

Overweight and obesity factors in a Mediterranean population

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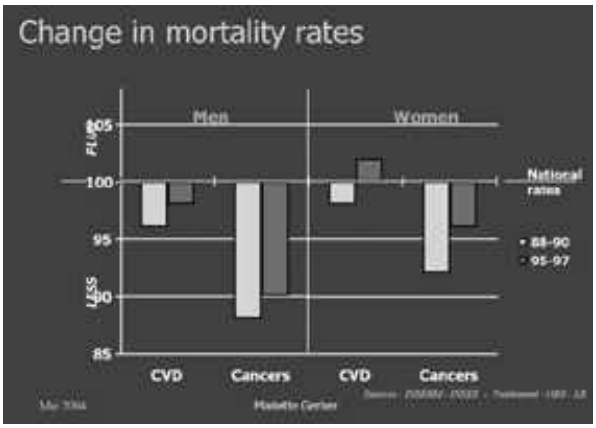
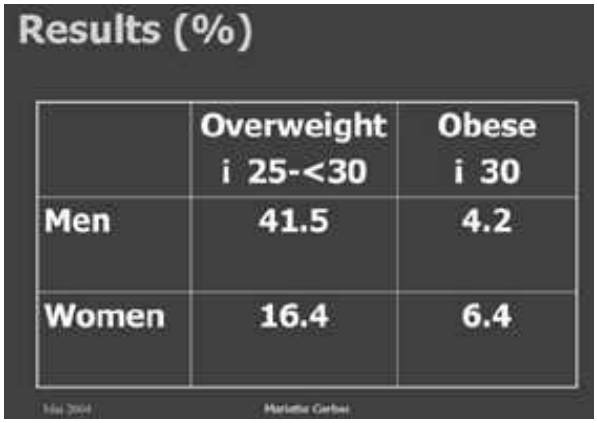
Obesity has become an epidemics, and represents a risk factor for cardiovascular diseases, cancers and diabetes. In France, with the lowest proportion of overweight and obesity (next are Sweden and the Netherlands), we were so far not really at risk. The study E3N showed that women in Southern France have a lower BMI than women in Northern France. However, a study that was lead among young recruits in the army showed that obesity was increasing in exponential proportions in the Mediterranean areas of France: Languedoc-Roussillon and Provence Alpes Côtes d'Azur.



This comes together with mortality rates modifications in our region. If you take the national standard as a 100% basis, in the years 1988-90, men had a lower mortality rate from cardiovascular diseases and cancers. Ten or fifteen years later, we are loosing this advantage. For women, the evolution is even worse: not only have they lost their 1980 advantage, but they also are now above the national standard in the Languedoc Roussillon region. This goes with a loss of the Mediterranean diet in the area. If you compare the Languedoc Roussillon situation to the 100% archetype of the Mediterranean diet as defined by Antonia Trichopoulou, you may see that we still eat a lot of vegetables, much less legumes, fair amounts of fruit and nuts, but way too much meat and dairy, not enough cereals, and the mono-insaturated / saturated ratio is very low, while olive oil consumption is still relatively weak.

Such data is alarming, we have to try and reverse the trend that leads to Mediterranean diet loss and bad health indicators, as well as understand why obesity is increasing. We have tried to look into social and economic factors, as well as dietary factors associated with overweight and obesity in the population, all this in a population sample from the South of France and Languedoc Roussillon. We interviewed 1,169 subjects (578 women, 552 men) between 30 and 77 years old, randomly selected from poll lists. 30 years old was the bottom line because there happened to be very few overweight and obesity cases before this age (our sample was 20 at least). Subjects were directly interviewed, based on a consumption frequency questionnaire with 162 variables. We then distributed BMI data into three categories according to the relevant factors to be studied. Then a multiple regression analysis was lead to test individual independence of each one of these factors. Lastly, we went through a factorial analysis of correspondence. This allows to separate or associate the various factors.



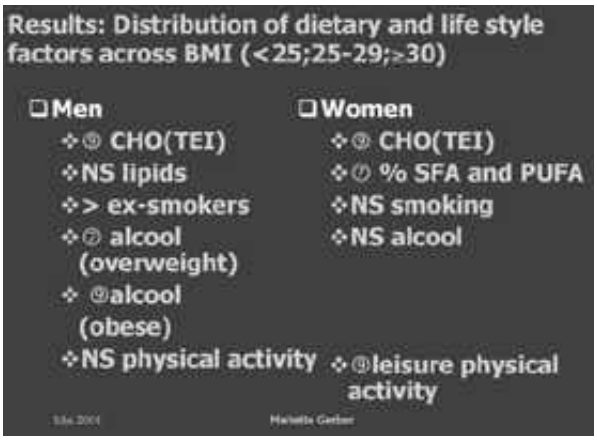
The first results show a large proportion of overweight in men (41.5%) and relatively few obese people in this category. For women, there is less overweight and more obesity. BMI increases with age, both in men and womenBMI are also higher in lower social and lower education level classes for both men and women. From there, effects are different with respect to sex.

While marital status is associated to overweight for men, there is no effect in women. Being an ex-smoker comes together with an increased BMI in men, not in women. There is a strong association with reproductive life events for women. BMI increases with menopause and hormones replacement treatments, and decreases with oral contraceptives. I would like to bring your attention on the fact that menopause age, hormonal treatments and contraception are strongly associated with age: we thus have precise if these factors are independent.

As far as diet and lifestyle are concerned, there are very few dietary factors. BMI increases with lower carbohydrates consumption (expressed as a proportion of total energy intake) in men and women. For lipids, there is a BMI increase in women when they consume more saturated and polyunsaturated fats. This relationship is not shown in men. There also is an increase in body weight for former smokers and no-smokers. As far as alcohol consumption is concerned, overweight people tend to drink more, whereas obese people drink less. There is no such relationship for women. We find no relation with physical activity in men, whereas this relation appears significant for women.

Testing each factor alone leads to associations that may end up in confounding. In order to discrimuinate the independent effect of each factor, we have applied a multivariate analysis. Both for men and women, the highest coefficient regards age. Age is thus the factor that is the most related to overweight. Then, other factors significantly related to BMI were inverse association with carbohydrate as a percentage of total energy intake s and for men, marital status. Having a low level of education, being a former smoker then play a role, before protein consumption and daily physical activity, which have a relatively weak influence. Each one of these factors has an independent and significant impact. Nevertheless, there is a broad fringe that remains unexplained as for men obesity.

For women, age and education level, as well as first menstruation age are important factors. Thanks to a cohort study by Françoise Clavel (E3N), we now know that French young females get their first menstruation earlier and earlier, which may be linked to diet. This also is a risk factor of cancer. A reverse relation with carbohydrate consumption, as well as oral contraception intake seems to reduce obesity risk.



We were quite disappointed by these results since we had very few elements to explain obesity risks. We thus wondered whether we had chosen the right factors, or whether dietary factors, not being measured as precisely as socio-economic/lifestyle factors, could conceal them. Another explanation lies in the fact that there is no linear relation between these factors and BMI. In other words, there might be, at some point, a gap between both categories of obesity.

In order to verify this hypothesis, we applied a factorial analysis of correspondence. For men, axis 1 represents 77% of the explanation, whereas obesity is represented on both axes. Axis 2 represents 22% of the explanation and is the less significant. Age is strongly associated with overweight, as well as low carbohydrates consumption, low education level, former smoker status, manual worker occupation. The situation is reversed in young men who eat less than 2500 calories, over 42% of carbohydrates as total energy intake, with a high education level and are single.

Only one factor is clearly associated with obesity: no alcohol consumption... Other positively associated factors of obesity are, being single and an energy intake over 2500 calories.

For women, there are more factors associated with overweight. The explanation rate of axis 1 is very high (88%), while axis 2 has 11%. Obesity can be found between both axis, while overweight is mainly associated to axis 1. All age-related factors can be found there (early menopause, hormone replacement treatment etc). First menstruation age also influences obesity and overweight. Having a higher level job is inversely associated with overweight but with a lower strength. Leisure physical activity (<1.7 MET/day) is the unique factor positively associated with obesity:.. On the contrary, over this threshold, it is inversely associated with obesity. To sum up, more factors appear in the case of overweight, but some of them are confounded because the factorial analysis of correspondence does not dissociated independent factors.

Thus, factors positively associated with overweight in women are age, low education level, unemployment, manual worker or wife of a manual worker (which is negatively associated with obesity), menopause, hormone treatment, no oral contraception intake, early menstruation (which is also related to obesity). Parity is a bit less significant, as well as calories supply over 2500. Factors that are inversely associated with overweight are: young age, high education, pre-menopause, oral contraception, cigarettes (which should not be said to women who want to loose weight though!) and physical activity at the workplace.

As for women obesity, the most significant factor is low leisure physical activity, as well as early menstruation and, negatively, manual jobs. It thus appears that when you are a manual worker or the wife of a manual worker, this is associated with overweight, but inversely related to obesity. We may explain this result, thanks to a previous study: in our region, manual workers are the ones who preserved the Mediterranean diet best. If this diet is eaten within an energy excess, it may be associated with overweight, but it may also reduce obesity risk.

As a conclusion, age appears as a significant risk factor for overweight in both sexes. Former male smokers are overweighted and smoker women tend to be thinner. Reproductive factors play a crucial role for women. Are dietary factors not that determinent, or is it because we are able to measure other variables better that we do not unravel their effect? A good illustration is the example of manual worker confounding a specific dietary profile. Caloric intake seems to be more important for men; howeverit is well known that women tend to underreport their actual food intake.

As for obesity, it is difficult to identify all factors. Physical activity is extremely important in women. Psycho-social factors, such as being single or not drinking alcohol, reflect social life issues for men. These results regarding psycho-social factors contradict what has been said by Denis Lairon yesterday, who asserted that stress was rather linked to obesity in women: we found out that it was rather associated with men obesity.

As far as medical care is concerned, therapeutic approaches should be different for overweight and obesity, and for men and women. Diet may be more important in overweight development, whereas individual factors and social environment seem to play a major role in obesity problems. Physical activity plays a significant role in the prevention of women obesity as well as reproductive life events.

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From being overweight to obesity : what treatment(s) ?

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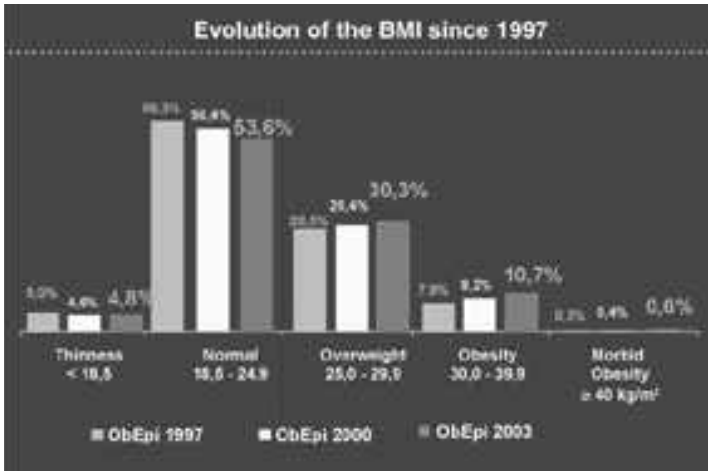
We have been saying that obesity is fastly growing and that we do not really know how to stop it. I will try and give you a physician's viewpoint on the matter. We can help overweight and obese people loose weight. This may contribute to public health improvement.

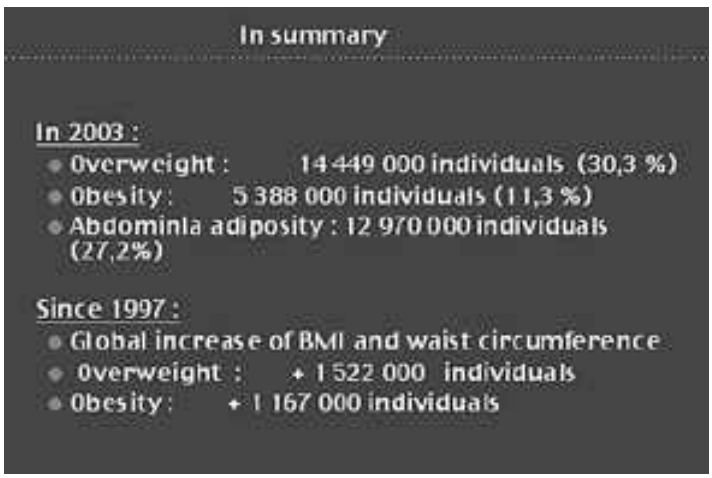
I would like to share with you the results of a very interesting survey that gives an evolution profile of overweight and obesity in the French population. It is the OBEPI survey, lead by INSERM, SOFRES, Roche and Hôtel-Dieu. It aims at investigating the prevalence of obesity within the adult population, and evaluate evolutions over time, since it is repeated every 3 years. It also looks into all risk factors associated with obesity: cardiovascular troubles, diabetes etc. It is lead through questionnaires: data is reported by patients and may thus often be understated. In fact, when you ask someone their weight, they tend to minimise it. Nevertheless, since this study is repeated over time, we may measure the evolution of prevalence. Each survey is lead on a 25,000 sample among adults over 15, with the same methodology. This allows for comparisons among 3 data groups (1997, 2000, 2003).

Today, we may see that although 60% of French adults have no weight issue, 30% have a BMI over 25 and that obesity affects 11.3% of the French population. In most cases (9% out of 11.3%) obesity is moderate, i.e. with a BMI under 35. The BMI evolution since 1997 deserves to be analysed though.

Since the first study, the share of "normal" people has been decreasing. The share of overweight people has grown from 28% in 1997 to 30% in 2003. Meanwhile, there is a growth of development from 8% to over 11% today. In average, this evolution reveals a 5% growth per year. The number of obese people has increased in 7 years: from 3.5 to over 5 million people.

Regional distribution is also very interesting, since we know that some are less affected than others. Now we can see that those privileged regions are the ones with the highest obesity prevalence. In the Parisian area for example, obese people have grown from 6.7% in 1997 to 11.4% today. In Languedoc-Roussillon, this share has increased from 7.5% to 11%. There seems to be a homogenisation of regional discrepancies: all areas tend to be affected.





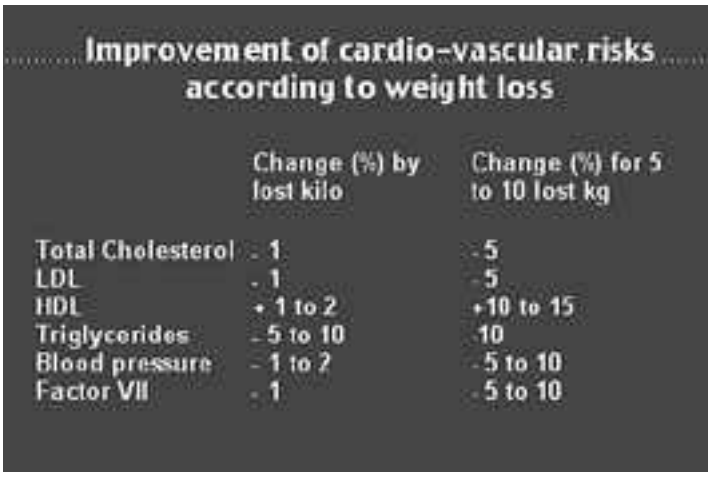
Moreover, we can see that the average waist measurement has also increased. 23% of the French population have a waist measurement over 90cm and 12% over 1 meter. Our abdomen has become larger by 1.6cm in 3 years, which increases the risk of metabolic syndrome.

To sum it up, you may say that 30% of the French are overweight, 11% are obese, and abdominal adiposity (with its consequences in terms of insulin resistance and metabolic syndrome) affect almost 27% of the population.

If this trend goes on, we may reach the 20% threshold of the USApopulation within 15 years time.

What can we do for our patients, as endocrinologists, diabetes specialists, nutritionists ?
The question of a different treatment for overweight or obesity can be answered by yes or no. I think medical care does not depend on the level of overweight, but rather on the patients themselves, as we know that risk factors considerably vary from one person to the other. We take our patients' waist measurement very often, with the threshold values of 88 cm or 90 cm for women, and 100 or 102 cm for men, over which obesity presents cardiovascular risks. According to the OBEPI data, which is mildly underestimated, abdominal adiposity concerns 38% of men and 30% of 45-year-old women.

I will not talk about consequences. We all know that abdominal adiposity is associated with some cardiovascular risks, blood pressure issues, insulin resistance, glucose intolerance, diabetes etc, that constitute the so-called metabolic syndrome I already mentioned.



Obesity has other functional consequences: lumbagos, oedemas, hernias, breath failures etc. All these complications tend to get much better with moderate weight loss. We now consider that loosing weight is not as important as keeping it off. A moderate but durable weight loss is the goal for any overweight or obese patient. The goal is not to loose as many kilos as possible but to keep those off and get stable.

BMI increases with time, and even more when you are obese. The goal may thus vary according to the situation you are confronted with. You may want to stabilise your weight, but patients do not always understand that. With obese persons who have failed in trying to loose weight, the most beneficial message is that they should not try to loose weight but rather to get stable. You may also loose little weight through dietary habits and lifestyle modifications. The goals is to have a moderate weight loss (10 to 15%) which results in a significant decrease of complications. Exceptionally, you may reach a weight "normalisation", or get back to your previous weight.

The core message is that you should not loose a lot of weight quickly, but rather try to loose little weight and keep it off longer. The problem is that the notion of durability is not always well perceived.
There is a consensus on the fact that 10 to 15% is a reasonable objective, and that long term weight management is crucial. All this is intended to avoid a situation in which, while trying to loose weight, patients actually get a greater BMI over time. Meanwhile, they have increased their food restrictions, modified their body composition, decreased their basal metabolism and end up being obese, and under food restriction.

The moderate weight loss objective is explained by the fact that most consequences of obesity respond quickly to weight loss. Reducing body weight by 10kg allows to correct the symptoms, which are of more interest for the patients than risk factors themselves: back pain, breath troubles, perspiration, which also are motivation factors for obese people. Of course they care about managing their diabetes or hypertension, but they are even more motivated by the fact that they may feel better, raise their self-esteem, have a better social life…These are elements we can work with in practice.

Functional signs are the first ones to be corrected by moderate weight loss. Then come lumbagos, polyuria and polydipsia, gonalgies, knees pain, anginas, snoring, PMS, ovulation troubles, urinary troubles etc.
Most significant symptoms in grade 3 obese people (BMI>40) are: apnoeas, oedemas, hormonal deregulation in women. We know that risk factors of a patient who looses weight get better with that weight loss. A 5kg reduction allows for a 5% reduction of cholesterol level or LDL, as well as triglycerides reduction and coagulation factors regulation or blood pressure lowering.

In fact, medical care is based on the idea that a patient should loose about 500g to 1kg per week on a 3 to 6 months period. Frequently, after 6 months, weight loss reaches a plateau, which should be explained to the patient who does not manage to loose weight anymore.

Calorie restriction is not always necessary. In some overly restricted patients, we may want to balance the metabolic situation by increasing energy intake. Patients with good diet habits should be asked to reduce their intake moderately (500 to 1000 calories a day) to reach a 5 to 20kg final weight loss. The main criterion is the absence of weight gain, which is defined by a consecutive weight gain of less than 3 kg after 2 years. These figures are hardly reached in clinical studies, notwithstanding the fact that everything depends on individual factors, on the side of the patient as well as the physician. The more medical follow-up the patient is given, the less weight they will get back.

Can we statistically identify at-risk patients? It is obvious that when BMI exceeds 30, the patients is at risk. Overweight people with abdominal adiposity also have a high vascular risk. The association of other factors (tobacco use, diabetes, hypertension etc) should also be taken care of.

Currently, our means prove relatively modest, since we still do not know the mechanisms that control obesity. We thus prescribe lifestyle changes and provide nutritional advice that will be presented by Ms Liégeois. The goal is to reach a negative energy balance, whether you do this through increased energy spending, i.e. physical activity or energy intake reduction (dietary changes).

We are nowadays talking about the "fight against settled lifestyle", and encouraging people to increase their general level of physical activity, which is a good thing. Asking them to play sports does not work.
As obesity also is a behavioural pathology, cognitive and behavioural therapies prove extremely useful in the case of obesity management. Medicines are relatively rare. We have Orlistat and Sibutramin. Stomach surgery can also be a solution to extreme situations. We should define indications for the means we have.

As for diet, we are very well aware that restriction should be moderate in order for the diet to be better followed in the long run. The diet should not include too many constraints or prohibitions. Positive diet messages have much more impact than negative ones. Encouraging a patient to eat more fruit and vegetables tends to motivate them more than if you ask them to decrease fat and carbohydrates consumption.

However, you should have a lipid intake restriction of up to 30 to 35% of total energy intake and rather go for unsaturated fats. We are all aware of the central role of fruit and vegetables, thanks to their nutritional density and satiety effect. In the case of behavioural troubles, we should only teach the patient how to get back to a regular rhythm with balanced meals to avoid food restrictions and inhibitions that lead to compulsion.

To conclude, I would like to say a word on physical activity.We know that regular activity is beneficial, not only in terms of weight management but also in terms of cardiovascular and other diseases. We are trying to make our patients understand that physical activity does not make you loose weight but improves you body composition and prevents you from loosing your muscles upon weight loss, while you also loose fat. It also has a beneficial impact on abdominal distribution of adipose tissues, which makes it a right tool against insulin resistance.

Another essential element is that it allows for limitation of weight gain after the weight loss period. Therefore I often ask my patients to start caring about physical activity only after the weight loss phase. They also tend to be more at ease with their body to meet these requirements. At that point, physical activity becomes a regulation tool to avoid weight gain.
Current recommendations against settled lifestyle are based on very simple advices: walking 30 minutes a day, climbing stairs rather than using the elevator etc (as far as TVis concerned, I am not so sure about the fact that targeting a settled lifestyle indicator allows to reduce it).

We should fight overweight and obesity the same way, since there is a continuum between both situations. The objectives are similar: they should not depend on BMI. Of course they depend on clinical situation, but a moderate weight loss is the right goal. All means based on lifestyle modifications are similar. Regarding medicines and surgery, responses may vary.

Dietician's practice : what are the solutions ?

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I have been working for 12 years as a dietician and I can say that my patients have changed. I would like to tell you more about the diversity of requests we get, and the way we adapt our recommendations to the different profiles.

Who comes to see a dietician ? We see patients of all age and weight groups. Overweight and obese people of course, but also people with normal BMI who want to get back to their personal weight since they are not comfortable with their body anymore. We see very healthy people as well as people with metabolic complications.

What has changed is that more and more people seem to be aware that changing their eating habits will help them get healthier, and they'd rather change their lifestyle that go through heavy treatments. Many physicians also tend to send us patients before they are diagnosed with diabetes, simply because their tests prove not very good and they have been gaining weight over time.

As far as I am concerned, I have an office in Coulommiers, which is a very rural area: my patients are between 40 and 65 (plus children) with traditional type diets. There are many farmers and shopkeepers. They often have garden yards with vegetable plants, and eat structured meals that are close to the traditional French model. I also have an office in Marne-la-Vallée, next to Eurodisney, where I tend to see young people between 20 and 30, among whom many are foreigners who work at Eurodisney's (Canadians, Americans, Italians, Spaniards). They often have unusual working hours, starting early in the morning and ending late at night, their days off are constantly changed. From a dietary point of view, they are totally different from my main office patients.

Yet all patients express the same type of request. When you go the dietician's, you make a very personal move. Besides, it costs money, which is not refunded. Either people come on their own, or they are sent by their physician, gynaecologist, cardiologist etc – this happens more and more frequently.

All patients are looking for individual follow-up. They do not want a diet that will make them loose weight fast but will not help them get rid of their nutritional issues. I think the general public understands that dieticians may help them design a long term food strategy. Of course, such changes do not happen easily, and this is what we are here for: help them implement their own food habits changes. Individual motivation is very strong as well. We can see that some people are ready to achieve anything (eat better, exercise etc).

Of course, people who come to see us expect short term results as well. Besides, "measurable" results keep their motivation up. Benefits may be evaluated in several ways: weight loss, centimetres loss, better biological check-ups etc.

They also expect you to adapt the diet to their very profile, notably by taking into account their job constraints. It also appears that the "punishment food" craze in over: when you want to change your diet forever, you have to keep the pleasure of eating out, with family and friends without being totally excluded because you are on a diet. France is a country where people like to eat and cook. Even when they go on a diet, patients want to preserve this conviviality.

Of course, we can feel other issues behind such requests. Our patients are often very uncomfortable with their body, under pressure, and have relationship problems. Weight loss alone will not remove these issues, but you have to take them into account to have a confident relationship.

Health and nutrition also create great anxiety. The general public is much more aware of diabetes and obesity consequences. We are afraid of getting older, of diseases, and we seek ways of solution in our diet.

There also is female anxiety when women tend to think that they are not feeding their family well, since they have no time to cook. The meals they manage to cook hardly meet their actual expectations. We must be able to come up with simple solutions that are compatible with their schedule, so that they can feel better as "nourishing mothers".

The "fitness" and "performance" dimension also appears for the young population I see in Marne-la-Vallée. You want to eat better to get your energy back and be fit. Professional pressure plays a role in such reactions.

Rather than solutions, I like to talk of "ways of reflection". First of all, it is very important to define possible objectives in terms of weight, time and meal composition during the interview. During the first consultations, patients tend to be very motivated (I am going to start cooking, shop better etc") but this does not last much. The diet should be realistic and the objectives must be accessible.

We have a major role in terms of active listening: we have to help the patient to find ways of solutions, not come up with ready-to-use answers. Diet is extremely personal; the patient should learn to clarify his/her needs and understand what he/she can do and how he/she can do it.

Whatever type of weight loss, people suffer the same: even when they have only 2kg to loose, the people I see are exhausted, have low self-esteem, have troubles sleeping, cannot dress as they want to etc. Their request is thus similar to me in terms of the efforts they will need to make to achieve their goals.

From a strictly dietary viewpoint, it is crucial to preserve a balanced diet. For years, people have gone on very low-fat or low-carb diets. There was not much to eat, you couldn't cook, food wasn't tasty. We have realised that it is very important to keep a balanced diet in terms of macronutrients in order for it to last. The protein supply must remain close to the norms. Lipids supply may be slightly under the norm, around 35% of total intake, provided that you select the right types of fat. Low-carbohydrates diets prove very effective in the short term: you loose weight fast, but you take it back as soon as you eat carbohydrates again. Everybody knows that now.

Yet patients tend to reduce consumption of some foods although we do not ask them to: bread, pasta, fruit still tend to worry people, just because they have been banished from diets for years.

Great intake restrictions should be avoided: 800 or 900 calories diets have totally disappeared. In some cases, when people have repeatedly failed on a diet, spontaneous intakes are so low that it would be dangerous to reduce them further. Caloric intake is thus not always reduced. It more about finding a balance to your diet and over the day. With the same basis caloric intake, but with a bigger breakfast and a smaller dinner, you actually manage to make people loose weight. The benefit of moderate restriction is that it allows for macronutrients proportions maintenance. Even with a 1400 or 1600 calories diet, 15% of proteins intake allows to preserve muscles.

Dietician's practice : what are the solutions ?

- ❑ The basis : fruit and vegetables, without useless forbidding
- ❑ Starchy foods to balance and to easily stabilize the weight (low GI)
- ❑ Meat, and dairy product, without excess, favoring fish (lipidic balance)
- ❑ Variety of fats
- ❑ Drinking enough water

Fruit and some vegetables still convey some taboos. We often hear patients claim that they should not eat bananas, grapes or cherries. And carrots are considered too sweet. This makes no sense. You should rather diversify. All products may be integrated into a diversified diet. Fruit and vegetables are low energy foods but great sources of protective micronutrients. They allow to cook tasty meals that differ from one season to the other.

In order to preserve a good carbohydrates intake, you should keep starchy foods: bread, potatoes, pasta, legumes etc. Once again, patients often prove reluctant to eat such products. But you have to teach them how to select these foods, in particular legumes.

Animal products (meat and dairy) should remain in the daily diet. You should go for raw, low fat products. As far as fish is concerned, its consumption is a bit more problematic in the area I work in. My patients eat fish once a week, as access to these products is not easy.

As for fat, you should favour seasoning fats that are good for the lipid balance and allow to cook. A no-fat diet is a diet that does not allow you to cook anymore: it takes taste off, which is unnecessary, especially in France.

Of course, water is the ideal drink (1.5 La day) but patients tend to drink excessive quantities, which is not a good idea.

All these elements should be adapted to individual profiles, in particular in the case of metabolic troubles. Such advice is close to the Mediterranean diet model, as well as the recommendations of the PNNS and Daily Values in the context of cancer prevention. There is thus a consensus in terms of dietary recommendations, which facilitates the work we do and our patients'life.

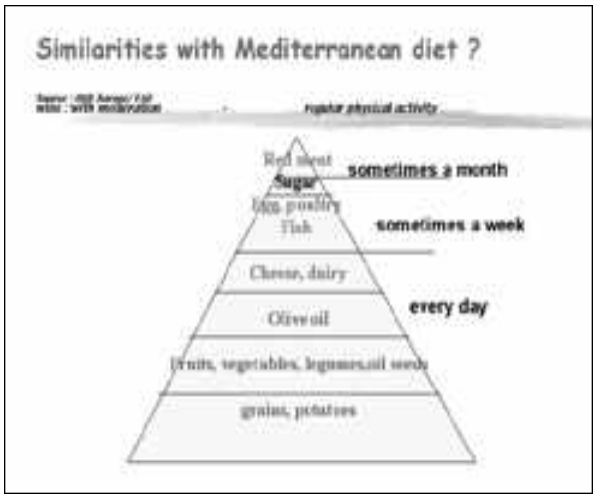
Other advice regards the identification of "empty calories". Eating a plain yogurt with a teaspoon of sugar or honey is the simplest habit and proves less expensive than all the products you find in our supermarkets. We have to teach patients to make the right choices, i.e. this kind of choices, in order not to depend on the industry supply and be able to reach a good nutritional quality.

Dietician's practice : what are the solutions ?

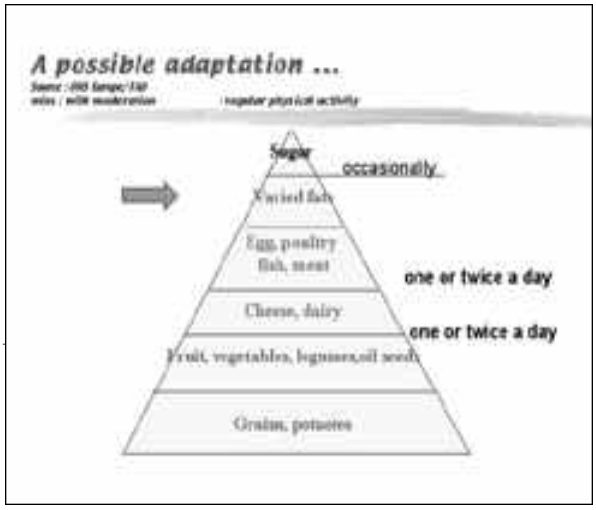
- ❑ Avoiding "empty calories" (purified factory feedstuffs)
- ❑ Choosing simple, fresh and crude foods cooked in a simple way
- ❑ Choosing traditional recipes and modes of cooking when possible (braised, furnace, jumped,...)
- ❑ Knowing how to leave the diet without excess

Cooking meals is a determining aspect. By inventing light versions of traditional recipes, you may have very good and healthy meals. This is very important for women, especially in the context of traditional cultures and habits.

Sometimes you also need to be flexible with your diet. Patients often tend to be more rigid than professionals, because they are afraid of failures. This is a worrying behaviour because it may lead to all kinds of mistakes after the diet is complete. It may be beneficial to have a couple of treats over the weekend when you have very strict weeks. In the long run, this allows for better acceptance of the diet and prevents the patient from being frustrated.



Regarding the Mediterranean diet: since olive oil is very important in this diet's pyramid, this is not the ideal diet for people who want to loose weight. Yet the predominance of a vegetable basis (cereals, potatoes, fruit and vegetables) and the low consumption of animal products and sugar may easily be transposed. I have made an adaptation of the diet by raising fats onto the top of the pyramid: I would also tend to diversify fats. In terms of meals, I would like to show you two possible adaptations :



The first one is based on a traditional meal: charcuterie as an appetizer, cooked meat and potatoes, salad, brie cheese and apples. This may be improved by removing charcuterie, reducing the share of proteins and cooking fats, and adding a vegetable to your potatoes. In order to eat less cheese without removing it, you may serve a smaller portion with salad. You should of course keep bread and fruit, and this becomes a perfect meal.

The second one is based on a more modern type of diet, which is less balanced actually. My younger patients eat lots of pasta and pizza, that they have delivered to their door. They have lunch at the fast-food restaurant and tend to skip breakfast. Their dietary habits are not structured and they have too many sodas and sweet desserts. By adding some fruit and vegetables, reducing desserts and going for more simple products, you may reach a balance with a meal you like. Eating pasta is not a problem, but you should add crudités to it and fruit and vegetables, even if you do not cook them. Sweet food may be eaten from times to times.

We thus tend to offer our patients balanced diets that are rich in micronutrients and resembles Mediterranean diets a lot. It is easy to adapt to several culinary traditions and prevents people from feeling deprived, which makes them more comfortable and less compulsive. The most important point is that this concept of preventive dietary habits has health benefits on the short and long term.

Introduction

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Nutrition, health and chronic diseases are of major interest, especially in the framework of research and public health perspectives. A lot of work still needs to be done, in order to investigate further on these issues, as well as be able to prevent most common diseases, in particular in elder populations: cardiovascular affections, diabetes and cancer.

The question of the Mediterranean diet and ideal dietary recommendations proves very relevant today. We do have doubts regarding the type of diet that should be promoted. Some magazine articles ironically underline contradictions among studies' results. In fact, this is an intrinsic aspect of scientific research. Thanks to this whole range of results, we are able to formulate public health recommendations.

Today's session especially targets the transition from scientific knowledge to public health realities. What should be recommended according to what we know? The Mediterranean diet seems to bring significant answers to this question.

Is there one Mediterranean diet yet, or are there many forms of Mediterranean diets ? I will try and answer this question in my presentation.

We will start with a debate on the food pyramid. Pr Willet will notably tackle the ideal balance in terms of food consumption. We will then compare French and Finnish nutritional recommendations. The debate on general prevention and specific prevention will also be handled. Our conclusion will focus on individual recommendations: to what extent does the target individual get the message ?

This quite busy morning will end with a debate on several conclusions, with regards to current knowledge, previous interventions and elements gathered since Wednesday: we should bear in mind that we need to come up with reasonable and global recommendations.

Dietary patterns in Europe : The results from the EPIC study

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I will introduce this session by showing you some of the results of our investigations on diet in European countries. In Europe we have a study called EPIC, which stands for European Prospective Investigation on Cancer, of which I am the initiator and coordinator. It started some twelve years ago when in different European countries we started collecting data on lifestyle and diet from samples of the general population – with some exceptions, but generally from the general population. The study was progressively enlarged to include ten European countries. This is currently one of the largest prospective core studies on nutrition, lifestyle and health existing in the world. We have data for half a million subjects and we have collected blood samples from close to four hundred thousand subjects.

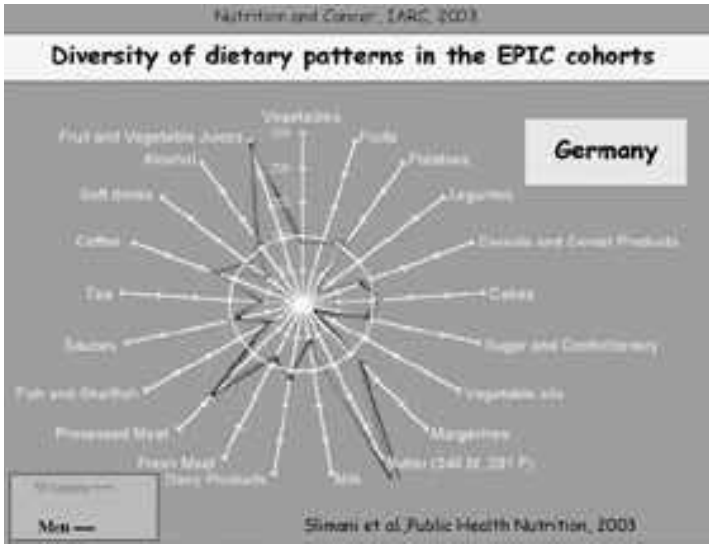
EPIC is classical in design – it is not classical at all for everything else – but it is a classical prospective cohort study where you first collect baseline information: you want to know what people eat, their lifestyle and others characteristics. Depending on the hypothesis you are going to investigate, you do then a follow-up. You identify the subjects with cancer or other diseases, such as myocardial infarction, and then you link the outcome, the occurrence of the disease, with the baseline information and eventually with biomarkers based on blood samples collected and stored.

In the EPIC study, we collected information on diet, tobacco, alcohol, reproductive history and many other lifestyle factors possibly associated with the occurrence of chronic diseases. We also measured anthropometric characteristics and requested information on physical activity.

Regarding diet, data were collected through dietary questionnaires which were adapted to the tradition, language and food habits of each population. The aim was to know what the surveyed subjects usually eat. In addition, in a very large sub-sample of thirty-two thousand subjects, we collected a second very detailed set of data based on an extremely detailed computerised 24-hour questionnaire on what people actually ate in a particular day: over three thousand foods per country, over seven hundred recipes – this is the level of detail.

The second measurement does not provide an accurate measure of what a given subject usually eats , but provides a good average of what a population eat. In addition, we collected blood samples and stored them and these are extremely helpful for studies using diet biomarkers.

We recently published a supplement in the Public Health Nutrition Journal which is entirely devoted to food consumption and lifestyle in the ten European countries based on the EPIC data. I am going to show you six slides which give an interesting picture of the relative balance of what people eat in different countries, in particular what are the major differences between non-Mediterranean and Mediterranean countries. First, I will tell you how to read these drawings in this example from a non-Mediterranean country like Germany. For each food, the yellow circle is a reference and indicates the average of the ten European populations studied in EPIC. The red and blue lines indicate in percentage, how much the consumption in that country diverges from the average of populations participating in EPIC. In Germany, for example, the consumption of butter is about 250% higher than the EPIC average, and the consumption of vegetable oils is about 70% lower than the EPIC average. I would like to emphazise that this is a percentage and should not be read as grams. It reflects the deviation from a common average in ten European populations.



As I mentioned before, in Germany, the consumption of butter is extremely high and the consumption of vegetable oils is extremely low as compared with the average. Processed meat is high, it is actually the highest in EPIC, while fresh meat is close to the average, legumes consumption is very low and cereal consumption is a bit lower than average. Tea is very low and coffee is a bit higher than average. Alcohol consumption is similar to the average.

You can also see something very interesting: the UK participants have the highest average consumption of soft drinks and the highest intake of cakes of all the European populations we investigated, a very high intake of milk and butter and a relatively average intake of vegetables. The intake of margarine is as the average, but the consumption of vegetable oils is much lower.

In EPIC, we included thirty-five thousand subjects who were all volunteers selected from vegetarian and non-meat eaters' associations in the UK, so we have the possibility of comparing

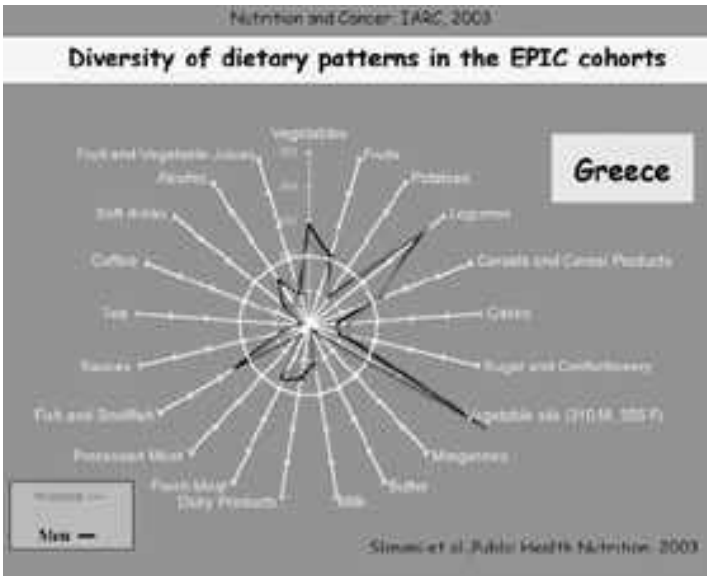
Slimani et al. Diversity of diettary patterns observed in the European Prospective Investigation into Cancer and Nutrition (EPIC) project. Public Health Nutrition 2004 ;5(6B) :1311-1328.

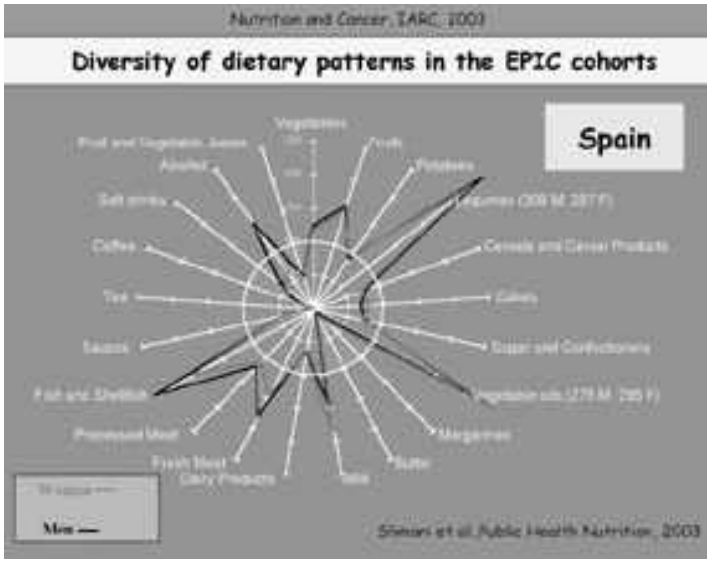
the general population with a population which made the choice of being either strictly vegetarian or consumed less meat than average. We call this population "healthy conscious UK". What is amazing is that in this healthy conscious population, the consumption of cakes is still higher than the average, the consumption of soft drinks is higher than average, tea intake is high (but that was to be expected) and, obviously, the consumption of fresh meat, processed meat and fish is very low. Consumption of butter and margarine are higher than average, whereas vegetable oils are lower. You would probably expect a health-conscious population to lean more towards high vegetable oil consumption, but they do not.

In Greece, a definitely Mediterranean population, the picture is completely different: you see a big spike in the drawing indicating a very high consumption of olive oil in Greece and an almost trivial intake of margarine and butter. Thus, the fat intake is completely reversed compared with the UK – that is a major difference. Consumption of legumes is very high indeed, consumption of coffee and tea is low, and this fits very nicely with the FAO food consumption data. Fish is a little higher than average, and processed meat consumption is very low in Greece – it is actually the lowest of all the European countries we investigated.

If you look at the results for the Spain cohort, you will be surprised. It is also a European Mediterranean country but consumption of fresh meat is among the highest in all of European populations in EPIC: consumption of veal in particular has been very high in the past twenty years, maybe contrary to common belief. Processed meat is relatively high, and fish is the highest observed in EPIC Milk consumption is high and this results are consistent with what we found in a survey of diet and health in Spain in 1978. At that moment, milk consumption was already the highest out of the different European countries we investigated. Vegetable oil is as high almost as in Greece, and it is obviously olive oil. Legume consumption is the highest of any European population, whereas consumption of cakes and sugar is low, coffee is very moderate, tea is trivial (in Spain they say that they only drink tea when they are ill), so can see a very different pattern compared to other European populations.

In Italy, we see yet another pattern: you see that cereals replace legumes. If we compare Spain with Italy, we can say that legumes in Spain are the same as cereals in Italy. In Italy, there is high consumption of olive oil, very low consumption of margarine, but a slightly higher consumption of butter than in the other two Mediterranean countries, mainly in the North of Italy. Milk intake is moderate, such as dairy foods, fresh meat is average, processed meat is low , although the consumption of processed meat varies regionally. Fish is low in Italy and coffee intake is low. Based on the FAO statistics, coffee consumption in Italy expressed as kg/year per inhabitant is only 20% compared with coffee consumption in Denmark and Norway, because Italians drink strong coffee very frequently, but in very small amounts.

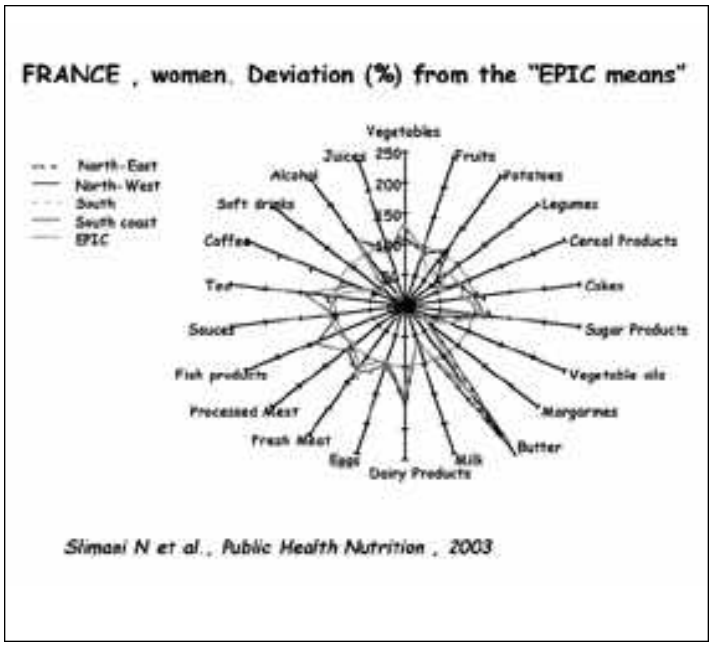




In France, we separated the French population (our study only included women) into the north-east region (close to the German border), north-west region (towards the Atlantic Ocean) and the south coast. It is quite interesting in that we see the same gradient for butter within France that we see in Europe, so the highest consumption is in the north and the lowest consumption is in the south. For vegetables, the highest consumption is in the south, for tea, it is in the north, and for fish, it is in the north near the ocean, which is reasonable because all the fisheries are based there. We see gradients within France which are quite interesting.

These patterns are based on the information provided by the subjects about how they eat. But, is the information provided by questionnaires correct ? I will show you some examples on how biomarkers – which in this case means nutrients measured from blood samples – can corroborate and validate the information provided by questionnaires. For example, lycopene measured in blood. Lycopene, as you know, is a carotenoid, which is of particular interest for its possible preventive effect on prostate cancer. The main source of lycopene are the tomatoes, particularly tomato sauce. The average concentration of lycopene in blood – each column in the graphic represents about 100 subjects –is much higher in Italy than in northern countries such as Denmark or Germany. The difference is striking: the lowest quintile level in Sicily is higher than the highest quintile level in Sweden. We see from this gradient that there is a real difference in consumption of fruit and vegetables. If we look at fish, however, we find the opposite gradient. We find that the Nordic countries, where the consumption of fatty fish is common and frequent, have much higher levels of eicosapentaenoic acid, or omega-3 fatty acids, which is a very good biomarker of fish intake and a clear indicator of fatty-fish consumption. You

see that Denmark is at the top, then followed by Sweden, Cambridge ! And the north of Spain, where there is an important fishing market. Now, why is Spain lower than Denmark in eicosapentaenoic acid ? It is because they eat much more white and lean fish than in Northern Europe. The Italians reported the lowest consumption of fish in Europe, and they did indeed have the lowest concentration of eicosapentaenoic acid. The UK healthy conscious, who have an extremely low level of omega-3 to the point that omega-3 deficiency is considered to be a potential health risk factor for strict vegetarians. Much more data about this study can be found on IARC website at www.IARC.fr.



I will now introduce the next speaker who, I dare say, does not need an introduction: Professor Walter Willett from Harvard University, Chair of the Department of Nutrition at the Harvard Medical School, a pioneer of research on nutrition, cancer and cardiovascular diseases. He is also a friend and the master from whom we learnt at the very beginning, in the eighties, how to set up a large prospective core study to investigate diet and health.

The healthy eating pyramid : empirical assessments of validity

Walter C. WILLETT
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Thank you very much Elio, and also the organisers of this meeting. It is a great pleasure to be here for the first time in Southern France and talk about a topic that is, of course, of interest to all of us, in particular how the Mediterranean diet can be an important way to keep us healthy in the long run.

I am going to talk about the pyramid that has been produced by the United States'Department of Agriculture and that has served as the major guide for dietary advice in the United States since 1991. For better or worse, this has been very influential because many other countries have adopted this pyramid, almost without changing it, as their guide to dietary advice. I was in Iran a few months ago and I was surprised to see that their dietary pyramid was virtually identical to ours except that the words were in Farsi. That is just one example of how influential this pyramid has been.

Of course, the main advice about the dietary pyramid, or other dietary pyramids, has been that all fat is bad. Up at the top, the pyramid says that fats and oils are to be used sparingly, without any distinction amongst the different types of fat. Of course, if we are not going to eat fat, we have to eat something. That, by default, means that we will be eating large amounts of carbohydrates. So the bottom of the USDApyramid emphasizes large amounts of things like white bread and cereals and rolls and crackers, and we are supposed to eat up to eleven servings a day of these foods. As if that was not enough starch in a diet, the US pyramid puts potatoes as a vegetable, so you can have thirteen servings of starch in a day. The question is whether that is really good for our long-term health, and I will discuss that a little.

Another area that has concerned us quite a lot is the so-called meat group, which combines red meat, poultry, fish, nuts, legumes and eggs without any distinction. We are supposed to eat two to three servings a day of those. That turns out to be very convenient because the meat industry can say, eat red meat three times a day, that is supported by the US Government, or the poultry industry can say, eat poultry three times a day. I will talk a little bit on the fact that it actually makes a big differences which of these sources of protein we use in terms of our long-term health.

There is another very interesting issue that I am not going to spend much time on today, but scientifically it is very complex and the data are still somewhat conflicting, and that is the issue of dairy consumption. The dairy industry is very powerful in the United States and we are told that we should have two to three servings of dairy produce every day. Whether that is really optimal for long-term good health is a very interesting question and we are just starting to have data on this issue.

In fairness to the USDA, however, it was not only that organisation that was pushing this idea that all fat is bad. This really reflected the general consensus of nutritionists in the US and in Europe during the 1990s. For example, this is an informational brochure from the American Heart Association, and their number-one advice was to use non-fat products. We were told to eat things like butter-flavoured granules (of course, any French person would be aghast at butter-flavoured granules), non-fat yoghurt, non-fat salad dressings, angel fruit cake because it is low in fat, fat-free cookies and crackers – everything was anti-fat or fat-free. We were not supposed to use any type of butter or margarine, regular yoghurt, regular salad dressing, high-fat cookies and crackers. This was really the major dietary advice and the food industry quickly realised that this was an opportunity because you could make almost anything in a fat-free version and it actually cost less to make, because sugar is cheaper than fat. These almost always had the same number of calories, but were fat-free, they cost less and you could sell them for more because they were special "healthier" products. So the grocery stores became filled with these products which are fat-free: fat-free cookies and cakes, even salad dressing was widely available and widely consumed as a fat-free product. But was that really healthier for us?

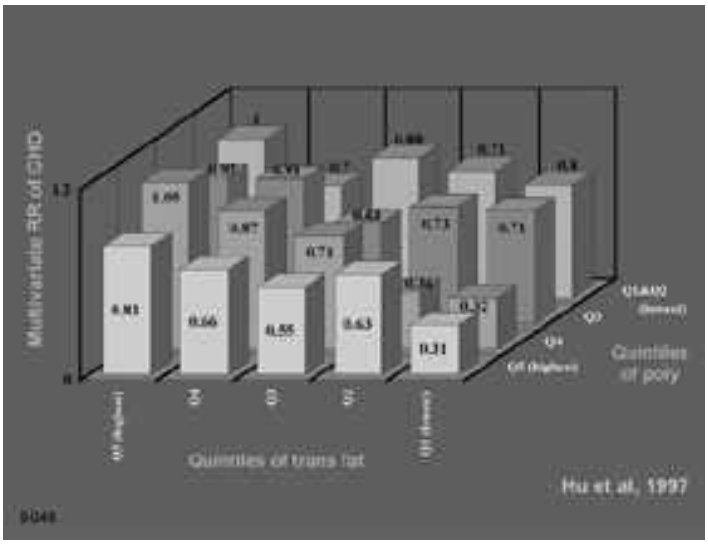
Much of the literature has looked at the consequences of what we eat and what diet does to blood lipids, with the ultimate interest, of course, being prevention of coronary heart disease, which is the number one cause of death. We have seen that that has become potentially misleading and certainly provides an incomplete part of the process by which diet may affect our risk of heart disease. We know now that the effects of diet can be mediated not just by blood lipids – and even here we have to look at blood lipid fractions, not just total cholesterol – we have to look at what diet does to blood pressure, thrombotic tendency, insulin resistance, oxidation or antioxidant function, homocysteine, which is now recognized to be a risk factor for coronary heart disease, inflammation and endothelial dysfunction, which is now recognised as part of the process leading to coronary heart disease, and ventricular arrhythmia, which really reflects the likelihood of sudden death.

The important point here is that if we look at just the effects of diet on each one of these mechanisms at a time, we could become misled because the effects of diet might be different, might be antagonistic or might be synergistic with some of the other factors. So in addition to looking at these intermediate variables, it is important for us to look directly at the relationship between diet and coronary heart disease, because that represents the combination, the synthesis of all of these different pathways. For that reason, we set up the kind of study that Professor Riboli described: several large cohort studies to look at the relationship between diet and heart disease, cancer and other health outcomes.

The first was the Nurses' Health Study. Frank Speizer started this study in 1976 to look at diet as it relates to coronary heart disease in particular. We added diet in 1980, and in this study we continue to repeat our dietary measurements every four years, which we have found to be very important because individuals change their diets and also the food supply is changing. It was in this period, for example, that all these low-fat products entered the food supply, so if we were not taking into account these changes over time, we would be badly out of date.

The Nurses'Health Study concerned women only, so we added fifty-two thousand men in 1986, again to look at diet and risks of major diseases repeated over time. The Nurses'Health Study II, which was started in 1989, is very important too, but this was different because these women were younger, they were aged 25

to 42 when we enrolled them. So this is giving us a special look at diet during earlier years, which is turning out to be somewhat different. I have mentioned a few of my close collaborators in these large projects but many more people have contributed and I will mention a few of their names as we go along.



When we first looked at diet and heart disease – Frank Hu did these analyses – this was after fourteen years of follow-up in the Nurses' Health Study. By that time, about a thousand women had developed a myocardial infarction or died of coronary heart disease. We found that total fat as a percentage of calories was not related to risk of heart disease. That was because some types of fat were bad, and trans fat in particular was by far the worst type of fat. On the other hand, unsaturated fats, particularly polyunsaturated fats, were related to lower risk of heart disease. These women who had high trans fat and low polyunsaturated fat in the diet actually had about three times the risk of women with low trans fat and high-polyunsaturated fat. So the type of fat used is very important. Again, the total fat was not related to the risk of heart disease. This is actually what would be predicted on the basis of the effects of these types of fat on the total cholesterol to HDLratio in the blood.

Here are some examples of how the public was really being misled. The public was told to avoid nuts because they are high in fat. Well, we actually found that women who consumed more nuts in their diet had lower risks of heart disease. For example, these women, who had nuts on most days a week, had about 30% lower risk of heart disease compared to women who had almost never consumed nuts. A number of other studies have confirmed this now. I should add that full-fat salad dressing was another factor that we saw to be related to lower risk of coronary heart disease, whereas the American Heart Association was telling people to avoid full-fat salad dressing. It, of course, is based on unsaturated fats that reduce the risk of heart disease.

We also came to appreciate that many other factors in the diet, besides the type of fat, influence the risk of coronary heart disease. For example, fruit and vegetable consumption was inversely related to the risk of coronary heart disease, and women who consumed eight or more servings a day had about 20 to 30% lower risk of heart disease compared to low consumption of fruits and vegetables. Of course, fruits and vegetables contain many protective factors and one that is often overlooked is simple old potassium, and this is going to be the major source of potassium in most people's diet. Higher potassium, we know now, reduces blood pressure, and blood pressure itself is an important risk factor for heart disease of course.

So, potassium is one component that seems to be important, but many other factors are probably contributing. Folic acid, which comes from fruits and vegetables, seems to be another very important factor which helps to reduce the risk of cardiovascular disease by lowering homocysteine levels in the blood.

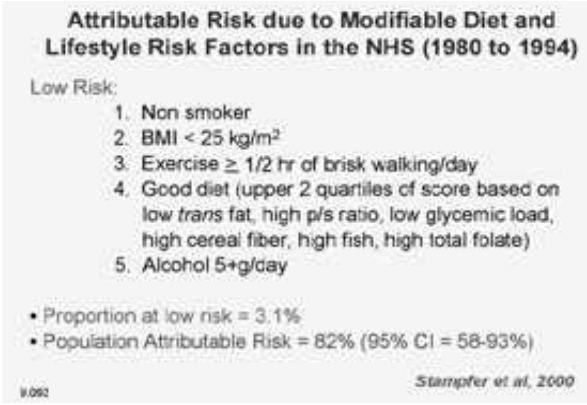
There are probably many other factors contributing to this beneficial relationship with higher fruit and vegetable consumption. We have also come to appreciate that the type of carbohydrate, just as the type of fat, is important in relation to the risk of cardiovascular disease. For a while, we really just considered fibre, or so-called complex carbohydrates, to be beneficial, but it seems that that is quite an incomplete depiction of the role of carbohydrates. For example, a higher intake of cereal fibre from wholegrain products is related to about a 30% lower risk of heart disease. There are about ten studies which consistently show that higher amounts of wholegrain products are beneficial. However, there is more to fibre than that. It looks like high intakes of glycaemic load are related to both increased risk of heart disease and type 2 diabetes as well. I understand you talked about the glycaemic index and glycaemic load yesterday so I am not going to go into detail. However, looking at the risk of type 2 diabetes in the Nurses' Health Study, we see that a higher intake of glycaemic load increases the risk. That would be people who eat high amounts of white bread and potatoes primarily, with high amounts of sugar also contributing to this, but the majority is actually refined starch in the form of bread and potatoes.

Thus, a higher amount of glycaemic load increases risk, and a higher intake of cereal fibre, are both related to lower risk of type 2 diabetes. This inverse relationship of high-cereal fibre with regards to rates of type 2 diabetes is a very consistent finding; of course this is controlled for body mass index, physical activity and family history. Women consuming diets with high glycemic load and low cereal fiber have about two and half times the risk of diabetes compared to women with low intakes of glycaemic load and high intakes of cereal fibre. Why did these women have those kinds of diets ? They were basically following the US Food Guide Pyramid by eating these large amounts of starch in the diet, but unfortunately it was actually putting them at high risk.

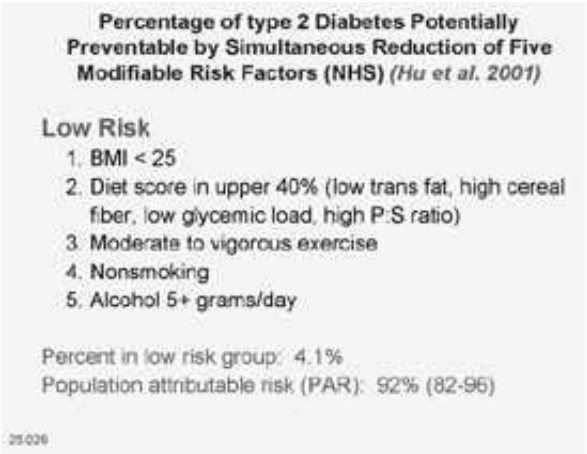
We have also done some analyses recently looking at the question of how much heart disease, diabetes, or various cancers we could prevent if we did everything right, and the results are quite striking. Doctor Meir Stampfer did these analyses, looking at the attributable risk of myocardial infarction, or coronary heart disease, in the Nurses' Health Study. What we first did was to define a low-risk group. Of course, that would be a non-smoker, someone who is not overweight with a body mass index below 25, and who exercises. We said just half an hour per day of brisk walking – we know that more would be better, but almost anyone can do this. Then we said, a good diet. Again we were quite lenient. We said, just be in the upper 50th percentile of a score based on low trans fat, high-polyunsaturated to saturated fat ratio, low glycaemic load, high cereal fibre intake, high fish, meaning twice a week or more, high total folic intake, just getting the RDA [recommended daily allowance], and that could be either from fruits and vegetables or from supplements.

We cannot directly study a Mediterranean diet in our population, mainly because the consumption of olive oil is still too low – it has gone up quite a bit but it is still too low to study. However, I think you will appreciate that this diet, what we call here a "good diet", is quite consistent with what a Mediterranean diet: there would be lots of fruits and vegetables, low red-meat

consumption, certainly low processed-fat consumption with a higher intake of healthy forms of fat – meaning vegetable oils. Most of it, again, is not olive oil in our population but other kinds of vegetable oils, and moderate amounts of fish intake. Alcohol is optional, of course, but this is just half a drink a day, which is very modest.



What we found first of all, to our surprise, was that only 3.1% of our population fell into this low-risk group, which we thought was very easy to do because these are all very modest lifestyle modifications. Based on 14 years of follow up, we could calculate that if everyone had fallen into the low risk, it would have prevented over 80% of coronary heart disease, which people find surprising. It should not be surprising, however, because we have known that populations living in Greece, parts of Spain, and southern France and Italy have coronary heart disease rates of about one tenth of the United States rates. What we are describing here is that within the United States, we also see that you can have extremely low coronary heart disease rates within a modern lifestyle with very modest diet and lifestyle changes. We have also looked at this in relation to the risk of type 2 diabetes and found that over 90% of type 2 diabetes is potentially preventable by a similar set of diet and lifestyle factors.



We have gone back to the USDApyramid and looked at the data, which suggest major deficiencies in the USDA Food Guide Pyramid. Again, the type of fat is not distinguished, the form of carbohydrate is not distinguished, and the source of protein is not distinguished. We have gone on to look at whether people who have followed the Food Guide Pyramid actually do better in the long run in terms of the major risk of disease. This is work that Dr. Marjorie McCullough as a doctoral student. Fortunately, the US Department of Agriculture created something called a "healthy eating index". This is a way of rating diets as to whether they comply with the Food Guide Pyramid. They created a ten-variable score and included things like more grains: if you ate more white bread, you got a higher score; if you ate more vegetables, including potatoes, you got a higher score; if you get more meat, you got a higher score; but if you ate low fat, you got a higher score without regarding the type of fat, and so on.

Some of these made sense: you did get more points in your score for eating more vegetables and more fruits, but some of these other things did not really make much sense given what we had been seeing in our data. Nevertheless, we could go back to our computers and calculate the score for each person based on this healthy eating index, and then follow people over time. As the endpoint, we used something called major chronic disease, which meant any new myocardial infarctions, stroke or cancer, or any other cause of death excluding those due to trauma.

In the Nurses'Health Study with twelve years of follow-up, from 1984 to 1996, about seven thousand women had developed a major chronic disease. If we just look at the age-adjusted data, we saw that women who had a higher healthy eating index score actually did have lower risk of major chronic disease, but of course, the problem is that women who were doing what they were told about their diets were also doing what they were told about physical activity, smoking and other factors. So when we adjusted for smoking only, most of that benefit of diet went away, and when we adjusted for physical activity and other factors, there was essentially no relationship between the healthy eating index score and the risk of major chronic disease – meaning that the Food Guide Pyramid was essentially worthless.

We looked at this in men as well, and there was a very similar relationship after adjusting other factors: there was essentially no significant benefit for being in a higher healthy eating index score. So the Food Guide Pyramid was just not providing the information that would be helpful. Therefore, we thought it would be useful to try creating a revised healthy eating index. This was just our first attempt to do so and I am sure it can be improved further. We took into account the type of carbohydrate, whether it was high-fibre wholegrain; the form of the fat – you got more points for unsaturated vegetable oils but you got fewer points for high trans fat and high-saturated fat intake. We also gave more points for eating fish and nuts and legumes compared to red meat, which did not give you extra points. This did actually more strongly predict major chronic disease risk. After adjusting for all the other factors I mentioned earlier, a higher score of our revised healthy eating index showed a strong benefit for cardiovascular disease. Interestingly, though, for cancer, even this revised healthy eating index was not related to the risk of cancer. For women, cancer largely means mainly breast cancer in this period of life, and that is a little bit sobering.

What we do see is that physical activity and a healthy bodyweight are important in reducing the cancer risk for women, but the types of dietary choices during midlife were not so important. What we are seeing from the Nurses'Health Study II, if we look earlier in life at ages of 20, 30, 40, is that their high animal fat consumption is related to a higher risk of breast cancer, but in women in midlife and later, that does not seem to be so important.

For men, and for men, cardiovascular disease is a more important contributor to overall chronic disease, and we saw a very important inverse relationship between the revised healthy eating index, which again, is representing something close to the Mediterranean diet, and cardiovascular disease. Again, for cancer, we still do not see much benefit for the dietary choices, whereas weight and physical activity are important for cancer risk. This does indicate that we still have more work to do to find diets that are optimised for the risk of cancer.

I have summarised a lot of this information in a book (Eat, Drink, and Be Healthy: The Harvard Medical School Guide to Healthy Eating) that is meant to be for the general public. I apologise for this blatant commercial, and if you buy these books and you find that they are not very useful, there is no money back – but they do each contain ninety grams of fibre! So, if you buy these books and you decide that they are not useful to read, you could put them through your food processor, and if you have some good fresh basil and some healthy oil, you can sauté them and they are really not too bad!

Thank you very much.

Questions

Elio RIBOLI
Thank you very much, Walter, and also for the funny slides on the alternative use for the books.
We are going to have a discussion at the end but if there are any specific questions, we do have a few minutes.

Member of the audience
Did you make any comparison between the Mediterranean score raised by Antonia Trichopoulou and your revised healthy eating score? It would be interesting to compare the scores.

Walter C. WILLETT
Yes, we are looking at the Mediterranean score by Professor Antonia Trichopoulou right now, but I am afraid we cannot use that exact score because she gives a lot of points to olive oil and we just do not have enough olive oil consumption to look at that. We have started to look at that and we have done some analyses using a modified Mediterranean dietary score looking not at major chronic disease yet, we will, but looking at a number of biochemical parameters, and we do see some interesting results. We see inflammatory markers in the blood are substantially lower with a higher Mediterranean dietary score, which I think is indicating a very interesting metabolic pathway whereby, independent of blood lipids, the Mediterranean dietary score maybe beneficial.

Member of the audience
Doctor Lorelei Di Sogra from the National Cancer Institute. My question is a two-part question about women and fruit and vegetable consumption from your study. You recommended more than eight daily servings of fruit and vegetables for women. Is that what you would still recommend ? Is there a higher number ? I am particularly interested in women and also what your data would suggest for African-American women.

Walter C. WILLETT
In terms of fruit and vegetable consumption, it is interesting that when we look at overall cancer specifically, we really do not see much of a relationship. The benefits seem to be mainly mediated by cardiovascular disease. It does appear that substantially higher amounts are beneficial, although we could not look much beyond eight servings a day. However, as you saw, that is where the maximum benefits seem to be. It seems to be fairly dose-response related. When we look at cancer, if anything, there may be a little bit of an increase below two or three servings a day, but very low intakes of fruits and vegetables, but then it is flat and a lot of other recent studies are showing that now. However, quite high amounts do seem to be beneficial for cardiovascular disease.
As for different ethnic groups, we really do not have enough to look at clinical endpoints separately, so I do not think there is any reason why that would be expected to be different.

John E. BLUNDELL
Using your revised healthy index score, do you find any reduction in the relative risk of obesity or diabetes ?

Walter C. WILLETT
We have not actually done those analyses using our revised score but it is quite close to the series of factors where we did see a reduction in the risk of type 2 diabetes. Interestingly, for type 2 diabetes, the type of fat is very important and the form of carbohydrate is very important. We are just doing some analyses now looking at fruits and vegetables and at first glance, we do not see that much of a relationship between type 2 diabetes and fruits and vegetables in general. The form of carbohydrate and the form of fat is looking very important. Neither have we really seen much relationship with weight in our analyses. Parts of that score may be important but parts of it do not seem to be too important. For weight, what we have seen is that a higher intake of fibre is related to less long-term weight gain. We have seen that as well in other studies. The type of fat does not seem to be terribly important overall – certainly, the percentage of calories and fat has not been related to the likelihood of long-term weight in our study. Interestingly, the one dietary factor that has shown up for a long-term weight gain has been transfatty acids. That is turning out to be quite interesting because it does look like trans fats increase insulin resistance. Many different metabolic parameters suggest that there is an increase in insulin resistance with a high intake of transfatty acids.

French nutritional recommendations

Ambroise MARTIN
AFSSA/ DERNS (Direction for Risk Assessment for Nutrition and Food Safety, French Food Safety Agency),
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The first French recommendations were initiated in 1997, when France proposed to have nutrition become the bottom line of a European public health policy. The French Ministry of Health thus looked into the definition of such a policy, before issuing a report to define what could be done and what was at stake in terms of public health policy. The latter was finally supported by the Prime Minister, Mr Lionel Jospin and lead to a declaration and the official launch of a nutrition policy in January 2001.

The slide shows the report's cover and the related logo "National Program of Health and Nutrition". Health costs helped get the mobilization of policy-makers since they are tremendously high and projections prove even more dramatic.

Data on dietary habits evolution over the past decades show many variations, some of which may be considered as positive (access to a wider variety of food, reduction of risk factors etc) and other may not (decrease of fruit and vegetables consumption, tremendous increase of sweet products: sodas, ice-creams, sweets etc).

Among the public health objectives that were then defined, five regard food or nutrients, risk indicators, but also physical activity. The following objectives were defined quantitatively in order to be measured at the beginning and the end of the program :
- reduction of the number of small fruit and vegetables consumers
- reduction of the number of small calcium consumers
- increase of complex carbohydrates and fibers consumption
- limitation or reduction of simple carbohydrates consumption
- modification of the ratio of consumption of several types of fat

In order to achieve these goals, a consistent program has been designed around 6 strategic guidelines that focus on information and education, health system, dietary environment, food processing industry implication, monitoring and research. Some specific responses were also defined towards population subgroups, notably elder people, allergic people and pregnant women.

The first axis regards information and resulted in several campaigns, notably on fruit and vegetables, and, more recently, on physical activity with subway messages. The national institute for health education and prevention will very soon publish a leaflet titled "Moving to get healthy", which will provide simple advice on how to avoid sleepers, TV and sofas.

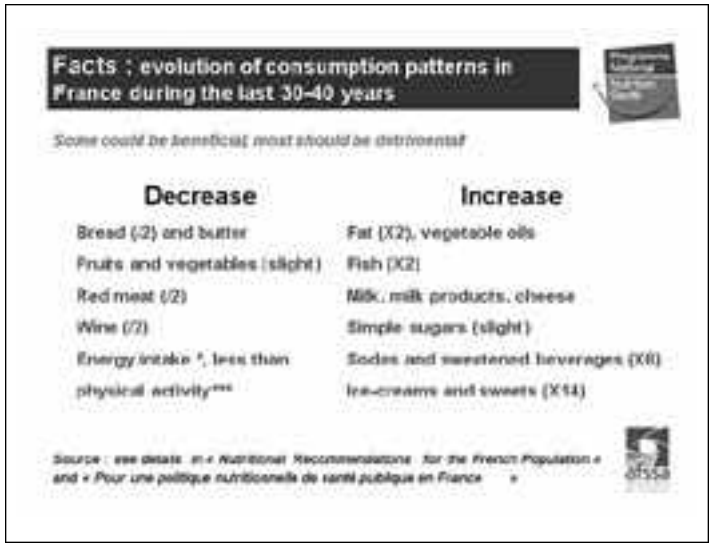
Regarding health system, some measures have been taken , such as awareness campaign directed at physicians for early screening of obesity in children. Through a well-known tool and a simple leaflet, we have given physicians the means to detect early adiposity pick up and to take it on.

As for environment, significant efforts have been made by the Ministry of Education, in terms of school restaurants and program design. Nutrition will be better handled and regarded as directly linked to children's day-by-day life. School medical care authorities are also implementing a prevention and education program which takes nutrition into account. More recently, the French agency for food sanitary safety (AFSSA) has issued a very strong decision against the traditional morning snack in schools.

We are very closely following current discussions within the Parliament in the framework of the preparation and vote of the public health law, particularly as far as food advertisement regulation is concerned as well as the presence of vending machines in schools, which provide only sweet drinks and junk food.

As for scientific aspects, I will present some of the data we have been using to base our recommendations. As I was coordinating the revision of Daily Values for the French population, I thought the recommendations should include such references (i.e. recommended nutrients consumption).

Although we do not have wide epidemiological studies in France, we may be able to use data from Suvimax to reset our recommendations and get a more accurate view of the links between actual diet and health. At that time though, we used the available data.



Since I am not a nutrition expert, it was not obvious to me that a balanced and diverse diet provides everything you need to be healthy. I thus asked such questions as : are values and recommendations realistic in the context of French diets ? are they accessible? Can we validate recommendations that are based on specific foods?

Several methodologies were used according to available data, notably the INCA survey (a national individual survey on food consumptions) . The first methodology regards food typologies and their relation to diversity and daily values observation. The second handles food recommendations modeling. The third one regards linear programming.

Well-known statistical methods allow to stress several consumers groups within the French population because they take into account a food consumption that has been reduced to 44 food

categories and automatic classifications. These groups are characterized by their dietary habits, which are very different and relatively stable over time: they can be found in the 1994 survey as well as the 1998-99 one.
In the middle, you can find "standard eaters". I will mainly focus on the extremes, which provide lots of information.
The first group is the biggest consumer of fruit, vegetables, tea, soups, water, etc, and has a diet which resembles the Mediterranean diet. On the opposite side, the group which is the biggest fast-food and soda consumer is the most "Westernized". A third group represents the traditional North and East of France diet, and tends to eat lots of charcuterie, meat and cheese, and gets 20% of its daily energy from alcohol. The first two groups are quite interesting. They are mainly composed of women (up to 80% and 70% respectively), and the average age varies a lot: from 40 to 65 years old for the "Mediterranean" and from 18 to 35 for the "busy eaters".

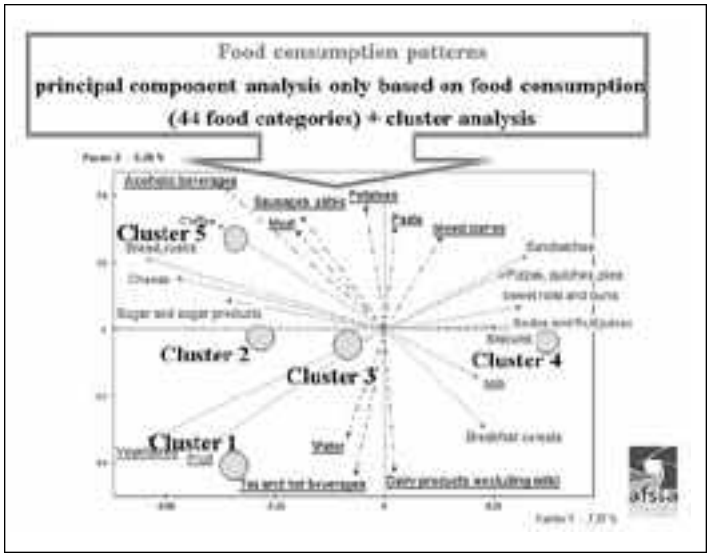
Nutrients distribution for these groups shows a similar carbohydrates and lipids intake, about 40% in value. Of course, lipids are not similar: for the "Mediterranean group", the main lipid vector is salads and crudités. In the "traditional eaters" group, it is fries and butter.

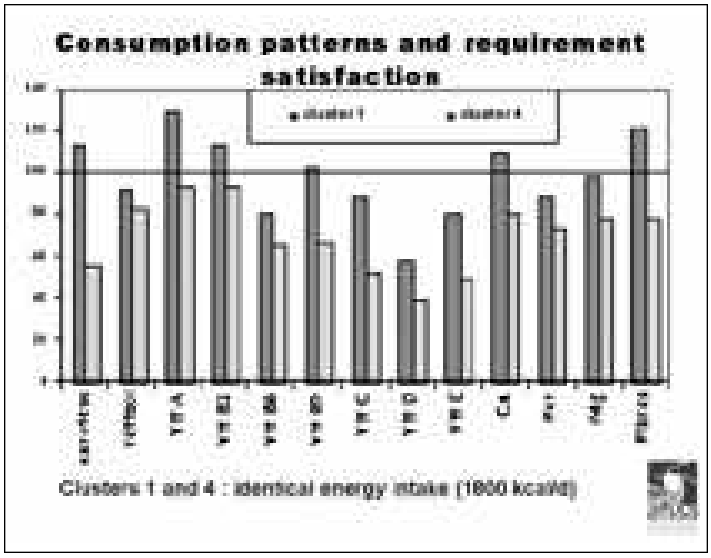
These groups appear very different from a diversity index viewpoint, which is used by the American department of agriculture to determine daily consumption of 5 groups of products. Food diversity reaches a maximum in the "Mediterranean group": everyday, 70% of these women have at least one food from one of the 5 groups. On the contrary, "big eaters" (90% of which are men) have a very lowest food diversity. When you look at diet energy density, you may witness great gaps between the "Mediterranean" and the "traditional" groups, in which energy density tends to be very high.

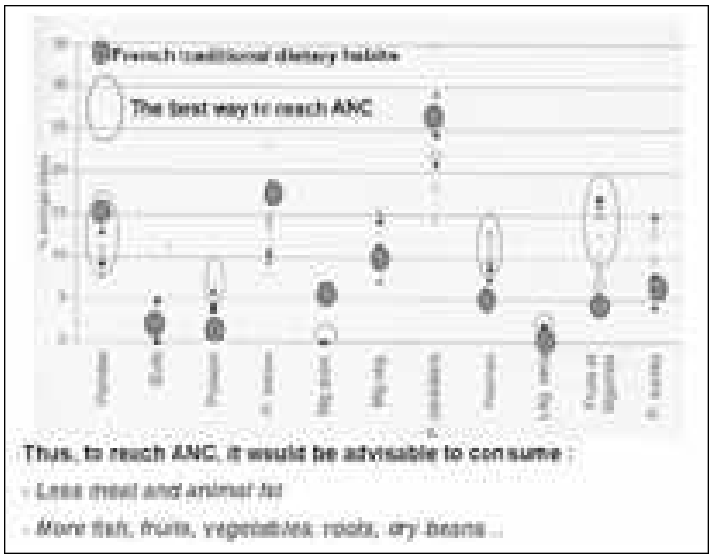
Although this is no epidemiological study but a transversal one, you may see that the share of obesity varies considerably from one group to the other. The "Westernized" group comprises a low share of obese people despite a high energy density. This may be explained by the fact that it is mostly composed of young and active women.

Regarding daily values, it appears that "Mediterranean" women and "busy eaters", although they have the same daily energy intake (around 1800 calories a day), do not meet the requirements in the same way: the "Mediterranean" group tends to meet their nutrients needs better than the other group. Nevertheless, there are common problems that affect all groups, notably regarding vitamin D. As an example, fruit and vegetables consumption varies from 3 to 1 between the "diversified eaters" group and the "busy eaters" one, as fast food products vary from 1 to 2 and fish from 2 to 1.

Regarding nutritional recommendations modeling : the group of experts of the Ministry of Health had suggested to include a recommendation of three dairy products a day, and this has been agreed upon. This "average dairy" contains a certain amount of whole milk, skimmed milk, yogurt, cheese etc, and may thus be modeled according to regular quantities. By doing this for all recommendations, we can have a theoretical approach of all nutrients. This leads to the conclusion that no major problem occurs, except maybe for vitamin D. It is clear that recommendations may evolve though, notably as far as vitamin C or E are concerned, which reach only respectively 100 mg and 9 mg.







The third methodology is linear programming, which is the computer modeling of a diet, according to a database of food composition and with respect to several constraints. We had to meet the daily values, food diversity and maintain reasonable quantities according to French habits. We also included a financial dimension which allowed us to show that meeting the daily values obviously has a cost, which ranges between 2.7¤ a day (if you do not exactly follow French habits) and 5¤ (if you try and stick to these habits).
Linear programming shows that daily values may be met and even exceeded. Some nutrients are always limitative, and if you meet the recommended values, the rest of the diet is no problem at all: these are mainly iron, zinc, vitamin B12.

Yet the trouble we have in meeting the requirements makes us ask whether these are correctly set up. What should be done to facilitate their consumption?

When you go from nutrients to food, diet composition may be compared with average consumption habits. In order for the French to better meet the daily values, they should eat less meat or animal fat, more fish and vegetables (roots and legumes) and more fruit.

These findings were translated into consumption references within the French recommendations, that are no definitive norms, but rather guidelines. These references are the principal food categories, as well as salt and physical activity, which is always underlined.

These recommendations were published in food guides, which were our 2003 best-sellers, with 300,000 books sold and over 1.5 million distributed. There are two versions of these guides, one for the general public and the other directed at health professionals. They are original because they do not provide general recommendations but specific recommendations that are translated into a variety of profiles that people may identify with. For instance, there is a special portrait for people who want to be healthy on a budget, and another profile for people who are afraid of food crises (dioxin, GMO etc). This guide should be soon complemented with a book directed at children and teenagers. The teenagers version will be distributed in high-schools as soon as it is ready. It will come together with version for teachers, which should help relate theoretical biological facts to everyday diets.

Of course, we should closely monitor the implementation and interpretation of these recommendations. The INCAsurvey will thus be re-conducted next year. The new session's results will allow to adjust recommendations if necessary.
I personally insisted a lot at AFSSAin order to improve our food composition tables. We are working together with food processing professionals (fish, cereals, meat) to get more data. We have launched several projects on specific nutrients that still lack in our tables, such as polyphenols, phytosterols or conjugated linoleic acids. Of course, we participate in the design of the European food consumption table in the framework of the EPIC project.

In terms of public health, our approach is slightly different from the one of Aprifel: we think that frozen foods should be taken into consideration, since modern techniques preserve their nutritional qualities.

Questions

Member of the audience
As a dietician, I have the responsibility to help in the implementation of the PNNS. I think that the objectives are quite relevant, but there is a gap between available human resources and these ambitious objectives.

I would also like to mention the fact that children obesity screening is not a problem per se, but once children have been diagnosed, we do not have any structure, network or specific professional to provide them with medical care. Maybe we should implement regional networks or big city micro-networks to allow for a general follow-up of overweight and obese children. What are the means that will be implemented in schools and high schools to have effective nutritional education projects with results in the long run ?

Ambroise MARTIN
Clearly, we need to change our work methods and find innovative ways to interact among categories of professionals. I am hopeful that the political will is going to be sustainable enough to help achieve our public health objectives. We have to try and design a food policy that would allow to harmonize our nutritional policy and our agriculture policy, which have been too contradictory so far.

Member of the audience
As for recommendations, I think that three dairy products a day is not quite appropriate, notably in the context of saturated fatty acids management and overweight monitoring. This should be revised in the 2005 plan.

Ambroise MARTIN
Actually, we favor low-fat dairy products. But I take your point in saying that we need to monitor the way the population will understand this recommendation.

The Finnish recommendations and their application to prevention of type 2 diabetes

Jaana LINDSTRÖM
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Thank you. Mr Chairman, Ladies and Gentlemen, during the past few days we have heard about the increasing epidemic of type 2 diabetes. The situation in Finland is similar to the progress in other European countries. There has been an increasing trend in drug treated type 2 diabetes over the last three decades in both men and women. The increase in type 2 diabetes is mainly caused by changes in lifestyle, namely diet and physical activity.

If we go back in history a little, the consumption of cereals at the beginning of the twentieth century was extremely high: it yielded half of the energy in the typical Finnish diet. During the twentieth century, there was a steady decrease in cereal intake which was accompanied by increases in butter and sugar consumption. At around 1970, the intake of saturated fat was extremely high – the average intake being over 20% of total energy – and at the same time, the serum total cholesterol concentrations in both men and women were almost 7 millimols per litre. Also at the beginning of the 1970s, the coronary heart-disease mortality rate in Finland was the highest in the world and it was especially high in the North Karelia district, which is the eastern part of Finland.

In 1972, the North Karelia project, a community-based programme for the prevention of cardiovascular disease through lifestyle and risk-factor changes, was launched. It turned out to be a success story: a steady decrease in mortality was seen and the gap between the North Karelia province and other parts of Finland was narrowed.

Half of the reduction in heart-disease mortality can be attributed to the reduction of about 1 mmol/l in serum cholesterol levels over twenty years. There was also a reduction in saturated fat intake from 21 to 16% of energy, and a reduction in total fat. Because of these early observations from 1970, some writers still seem to think of Finland as an example of an exceptionally high intake of saturated fat and a low intake of vegetables, but as you can see from this picture, these Finnish school children seem to enjoy vegetables.

Even though a large community programme like the North Karelian project had been completed, the first official Finnish dietary recommendations were launched as late as 1981. Before that, when recommendations were needed, the Nordic nutrition recommendations were used. The most recent Finnish recommendations are from 1998. The aims of the nutrition recommendations are to define the appropriate nutrient intake for population groups; to evaluate the goals for improving public health; to be base for food and nutrition policy and planning mass catering and to be material for nutrition education.

The National Nutritional Council has recommended some changes in the Finnish diet to improve and maintain good health: balanced nutrient intake; balance between energy intake and expenditure, increased proportion of carbohydrates, decreased intake of hard fat, decreased sodium intake and moderate alcohol consumption. Variety and colour; appropriate and adequate; and unhurried enjoyment are the key issues pointed out by the National Nutritional Council.

Cereal products form the basis of the recommended food pyramid. Vegetables, berries and fruit can be eaten in abundance, fish consumption is recommended, low-fat meat, moderate fat consumption, and sugar sparingly. Specific recommendations for amounts of certain products are not given since a healthy diet can be composed in so many different ways. When specific figures for energy and nutrients are needed, they are given as follows: 55 to 60% from carbohydrates, around 30% from total fat, less than 10% from hard fat, protein 10-15% of energy, or 15 to 20% if energy requirement is low, and dietary fibres 25 to 35 grams per day.

Even though a lot of good things have been happening in the Finnish diet over the past decades, we still have problems. We have the same problem as we have heard from other countries over these last few days: the proportion of overweight people has been increasing and at the moment, more than half of Finns are overweight. A good thing is that engagement in leisure-time exercise has increased but, at the same time, commuting exercise has decreased. As a net effect, energy intake is higher than expenditure.

In the beginning of the 1990s, it became clear that the burden of type 2 diabetes was going to be unbearable for the healthcare system, and that was when we started the Finish Diabetes Prevention Study. The main aim of the study was to see if we could prevent or delay type 2 diabetes in high-risk individuals by means of intensive lifestyle intervention. The idea was to see if we could do the same thing with type 2 diabetes that had been done with coronary heart disease.

We recruited 522 men and women who had impaired glucose tolerance in two oral glucose tolerance tests. They were middle aged and their body mass index had to be over 25, so they really had a high risk of getting diabetes. Two-thirds of the study subjects were women, the mean age in the beginning was 55, the mean body mass index was over 31, and the mean waist circumference was over 1 m, so these people were really quite overweight. The study subjects were randomly allocated either to the intensive lifestyle intervention group or to the control group. At the beginning of the study, the control group subjects got general advice on healthy diet, exercise habits and how they could reduce the risk of getting diabetes, but their counselling was not individualised.

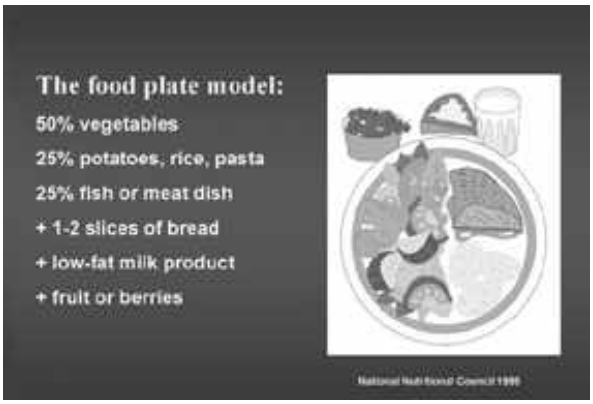
The intervention group subjects completed a 3-day food diary before their intervention sessions, and the recommended changes in the diet were based on the food diaries. They were offered an opportunity to use a gym free-of charge and they had seven dietary counselling sessions during the first year of the intervention, and every three months thereafter.

Obesity is probably the greatest risk factor for type 2 diabetes and weight reduction was also the primary goal in the DPS. Based on their food diaries, we advised the study subjects to substitute energy-dense food items with lower-energy ones and to have a regular meal pattern, avoiding both too long intervals between meals and frequent snacking. They were also, of course, advised to increase all kinds of physical activity, whether it was incorporated in the normal lifestyle or recreational or sports.

The saturated fat goal was <10% of energy. The people were advised to use low-fat dairy products, meat, and meat products, and prepare meals by low-fat methods.

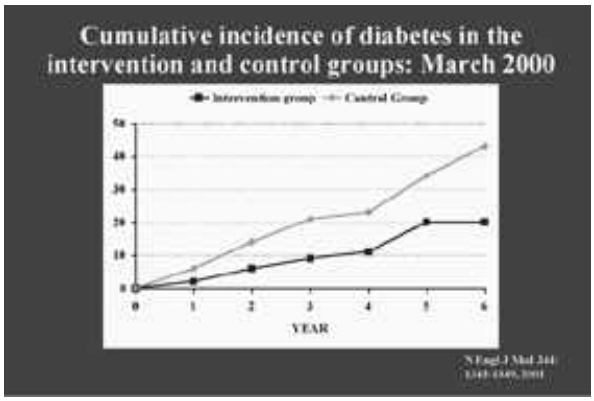
The fat intake goal was <30% of energy, which is not actually a low-fat diet, but rather a moderate-fat diet. If the intake of saturated fat is cut down, then intake of total fat will go down as well. As we already knew in the beginning of the DPS that unsaturated fat is beneficial for glucose tolerance, we advised our subjects to use soft rapeseed-oil based margarine and rapeseed-oil-based salad dressing. Regular consumption of fish was also recommended. The fibre intake goal was 15 grams per 1000 Kcal or more. We recommended wholegrain, especially rye bread and other wholegrain products, and daily consumption of fruit, berries and vegetables was highly recommended. So as you can see, our dietary goals were actually the same goals that are recommended by the National Nutritional Council for the whole population.

Physical activity is important in weight control and it also has an independent effect on glucose tolerance. We therefore advocated all kinds of physical activity and offered a supervised resistance training programme for everyone. We did not ask people to count calories or measure the weight of the food items, we asked them instead to use the food plate model when they were having their meals. If half of the plate is filled with vegetables, there is not too much room for more energy-dense foods items and the energy intake will go down in natural way.



Our intervention was not too demanding for the study subjects, since the drop-out rate was quite low: it was 8% during the whole follow-up and it was similar in both our study groups. The average carbohydrate intake was quite low: 43% of total energy in the beginning, 36-37% of total energy came from total fat, 16-17% from saturated fat, and fibre intake was 12 grams per 1000 Kcal. Their intensive lifestyle intervention did indeed induce changes in diet. In the intervention group, we saw an increase in carbohydrates and fibre and a decrease in total fat and saturated fat. Most of these changes were still prevalent after three years of intervention, even though the first year of intervention was the most intensive one.

We also achieved a moderate weight reduction and the difference between the intervention group and the control group remained during the whole follow up. You have probably seen the main results of our study: cumulative incidence of type 2 diabetes was 58% lower in the intervention group, and the difference between the groups was statistically significant already after two years. However, even though the reduction in diabetes risk was remarkable, not all of our study subjects were able to achieve the lifestyle goals: 6% of the intervention group did not achieve any of these goals, neither did 20% of the control group. On the other hand, 21% of the intervention group subjects were able to meet four or five of the goals, and also there were people in the control group who, after the mini-intervention given to them at the beginning of the study, were able to change their lifestyle. The risk of getting diabetes was directly related to the magnitude of lifestyle changes. Here in the zero-success group, the proportion of those who got diabetes was about 30%, but among those individuals who achieved 4 or 5 of these goals, we had no cases of diabetes at all during the follow-up.



Most importantly, the difference between the two study groups seems to have been maintained even though this intervention period has stopped. We still invite all our study subjects to an annual oral glucose tolerance test and the average follow-up time at the moment is almost six years. The difference in diabetes incidence between the groups seems to remain the same during the follow-up.

The DPS has shown that in high-risk individuals, lifestyle intervention can produce beneficial changes in diet and physical activity. The incidence of type 2 diabetes can be reduced by lifestyle intervention. Most importantly, the lifestyle changes do not have to be extreme: the diet and physical activity recommended for all Finnish people is sufficient to significantly reduce the risk of developing type 2 diabetes.

The next logical step is to try and find out whether we can do this same thing in 'real life'. Finland is probably the first country in the world which has developed a national programme for diabetes prevention and care. Diabetes care is not very successful at the moment, and it also has been estimated that 30% of diabetics in Finland do not know that they have the disease. The population-based strategy of the national programme is aimed at health promotion and more effective lifestyle counselling, and the prevention of overweight and obesity. The high-risk strategy is aimed at preventing or postponing diabetes in those at risk – and this is what we did in the DPS – and the early diagnosis and treatments strategy is aimed at the prevention of complications of type 2 diabetes.

The pilot phase of this programme has been launched in four hospital districts which have 1.3 million inhabitants. The intervention goals are set as in the DPS and they are implemented by multi-professional pilot groups which consist of local healthcare workers. Training, data collecting and evaluation are integral parts of this programme.

How can we reach the people who would benefit from this kind of intensified lifestyle intervention? Opportunistic screening can be done in connection with normal health checks. High body mass index, hypertension, dyslipidaemia, gestational diabetes, and family history are risk factors for type 2 diabetes. We have also developed a diabetes risk test, which is a very simple score that people can do themselves to estimate their risk of getting diabetes in the next ten years. The risk test has been distributed in the media, pharmacies and physicians' waiting rooms. It can also be done on the Internet, and there is an English version of it if you would like to take a look (http://www.diabetes.fi/english/risktest/).

The Finnish diet is not a Mediterranean diet, but I think there are many features in the Finnish lifestyle that are protective against type 2 diabetes. For example, Finnish people like to swim in the lakes – some of us all year round; we like to dance in the dance halls near the lakes in the summertime; Nordic walking has become extremely popular in Finland over the past few years; we have our traditional rye bread; and the Finnish woods are filled with berries in the autumn, which some of us start to pick at a very early age.

Thank you for your attention.

Questions

Elio RIBOLI
Thank you very much. I have a specific question. I wonder whether in the analyses of the data from your intervention study you have been able to separate the effect of losing weight from the effect of changing diet ? Could you estimate, to some extent, whether the main improvement in reducing the risk of the development of diabetes comes from losing weight, or whether there is also an independent contribution of a changing diet for the same weight change ?

Jaana LINDSTRÖM
That is an important and frequently asked question. In this kind of intervention, it is very difficult to discriminate between the effects of the different components of the intervention. Of course, weight loss probably is the most important - we have done an analysis on that – but on the other hand, you cannot achieve weight loss without making changes in your diet.

Elio RIBOLI
I appreciate the answer and you obviously also appreciate the importance. There has also been much debate about other intervention trials where many factors have been changed all at once. While this is extremely important for getting information on a global approach from a public point of view, when you want to derive information from the point of view of the aetiology, which is really important, then you need to separate the major components of weight change, physical activity and diet composition compared to total energy intake. Maybe we can come back to that later.

Ambroise MARTIN
Thank you for your interesting presentation. In line with the question I was asked, what about dairy products ?
The relationship of some peptides in dairy products to the risk of diabetes seems to be an important issue now, so what about dairy products ?

Jaana LINDSTRÖM
Yes, dairy products have been debated, especially in type 1 diabetes. In Finland, we recommend the use of low-fat and fat-free dairy products and we also have a large variety of those in the shops. Dairy products are an integral part of the Finnish diet. If they are low-fat or fat-free, I cannot see that they would increase the risk of getting type 2 diabetes.
There have been some studies indicating that consumption of dairy products would have an effect on weight control.

Nutritional recommendations : population-wide or directed at high-risk individuals ?

Pierre MENETON
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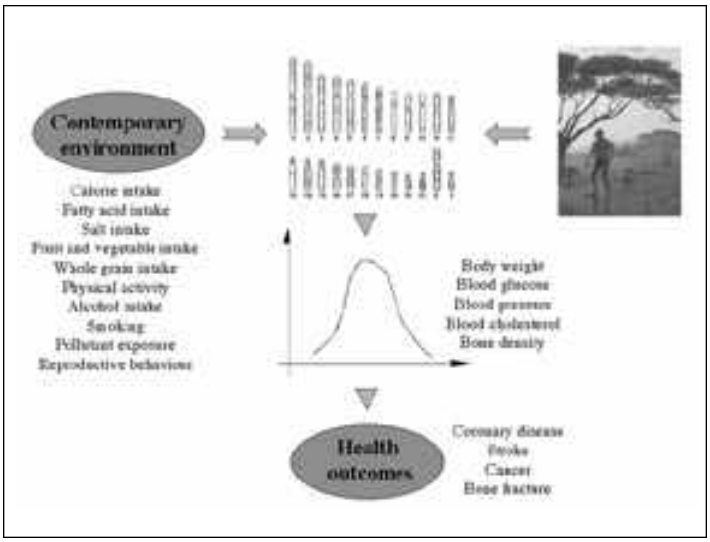
Nutritional recommendations raise a crucial question in terms of public health: should we target high-risk individuals only or the whole population?

According to George Pickering, a population should be taken as a whole for there is a continuity between the healthy people majority and the chunk of "ill" people. Ancel Keys also insists on the fact that there are "healthy populations" and populations living with a disease. According to Geoffrey Rose, when a large number of people are exposed to small individual risk, then a higher number of pathologic cases may occur than in a small population of high-risk individuals. More recently, researchers as Malcolm Law or Nicolas Wald have asserted that the objective is not only to normalise risk factors, but also reduce them.

Cardiovascular diseases, cancers, bone fractures, among other pathologies, result from a blend of environmental and behavioural factors. These factors also interact with your genetic background, which results from a long-term evolution and adaptation process. Analysing "intermediary phenotypes" has a double advantage upon study of such pathologies:
- They allow to look into many environmental and genetic factors through only a few number of easy-to-measure parameters (body weight, glycaemia, blood pressure, cholesterol, bone density etc.)
- They are not regarded as pathologies, even for deviant values, but are good indicators of individual's risk to develop various pathologies.

Between the level of exposition to intermediary phenotype (blood pressure, blood glucose or blood cholesterol…) and the likeliness to develop a disease, identified relationships can present thresholds of increased risk. Some examples can be found in the relationship between body weight and cardiovascular mortality, or between intraocular pressure and glaucoma. There also are linear relationships, such as tobacco use and lung cancer. However, for most pathologies that are of interest to us, the link with related intermediary phenotypes is an exponential one. When you present it as a semi-logarithm, it appears as a straight line that shows an essential point: the definition of ill or at-risk people with respect to normal people can only be arbitrary, since there is no obvious threshold between the risk to develop the disease and intermediary phenotype of those people.



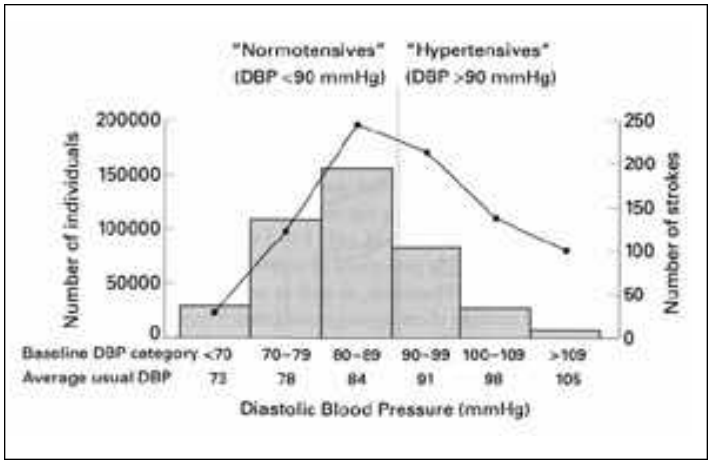
Let us take the example of blood pressure. Current arbitrary definition of hypertension is as follows: systolic pressure over 140mm of mercury and/or diastolic pressure over 90mm of mercury. There are several categories of people with hypertension: moderate, low or severe hypertension, according to blood pressure level and cardiovascular risk. Nevertheless, the crucial point is that all these people are given medical care, whether it is under the form of treatment prescription or nutritional or behavioural counselling.

The problem is that people with levels of systolic and diastolic pressure under the above-mentioned thresholds are not given any medical care. According to their cardiovascular risk, these people with "normal pressure" can be classified into several categories (optimal, normal or middle-high pressure). It is clearly possible to further reduce cardiovascular risk under the current threshold of hypertension. The risk increases substantially (2.5 times in women, 1.6 times in men) from people with optimal blood pressure to people with middle-high pressure.
As a consequence, as patients with systolic pressure close to 130mm of mercury are not given any medical care, we deprive ourselves from a real gain in terms of cardiovascular risk reduction.

The issue gets even more tragic when you compare the number of people with so-called "normal pressure" and the ones with hypertension in a population. Currently, in France, the USA and other Western countries, there are many more people with normal tension than with hypertension. Although the latter have a higher individual risk, "normal" people tend to develop almost as many cardiovascular and brain accidents, because they are more numerous than the other group. This is an illustration of the fact that a large number of people with small individual risk can generate as many cases as - if not more cases than – a small number of people with high individual risk.

Similarly, with blood cholesterol, the higher the level, the higher the coronary thrombosis risk. Most individuals have a moderate level of cholesterol and low thrombosis risk. People with high levels of blood cholesterol and associated risk are proportionally less numerous. As a result, most coronary thrombosis cases actually occur in people with low level of cholesterol and moderate risk, not in high-risk people.

This is a general situation for the type of pathologies we are interested in today (coronary thrombosis, type 2 diabetes, bone fractures etc). The 10% of people with highest blood pressure and cholesterol levels, BMI or bone density contribute to these pathologies by 20-25% only.



The distribution of intermediary phenotypes is thus distorted on highest or lowest values. Such effects have been noted in the case of migrations and fast industrialisation or urbanisation over the 20th century, as well as in countries (Finland, Japan) where national prevention campaigns were lead.

Upon such actions, the distribution curves of blood pressure, cholesterol and BMI tend to be distorted toward extreme values. This leads to quantitative changes:
- reduction of average value of the intermediary phenotype in the population
- reduction of the share of people with the highest blood pressure, cholesterol and overweight levels in the population

In other words, this approach leads to the same results as a strategy that focuses on high-risk people.

Besides, the effect may be extremely significant even if the average value is only mildly modified. For instance, reducing systolic pressure by only 4mm of mercury allows to reduce the number of hypertension cases by 25%. From an individual viewpoint, a blood pressure reduction of 4mm appears as quite trivial. But from a population-wide point of view, the public health impact gets tremendous.

Similarly, with body weight, when a population drops 1kg in average, this has a major impact on its health status. Actually, all intermediary phenotypes present the same characteristics.

In terms of fight against coronary thrombosis or cerebral vascular troubles, when you compare pharmacological actions on high-risk people with prevention actions directed at a whole population, you may see that:
- treatments are extremely efficient to reduce blood pressure levels, but only high-risk people actually benefit from medical care. The impact is thus quite obvious but limited to a small proportion of the population
- On the contrary, a population-wide approach allows to have a more moderate impact but theoretically targets all individuals. In terms of mortality, results prove quite similar, if not superior to the ones of the pharmacological approach.

Another examples lies in the compared impacts of a pharmacologic treatment to reduce cholesterol levels in high-risk people by 325 to 190 mg/dl and a dietetic measure directed at the whole population that reduces cholesterol levels by 263 to 190 mg/dl. Associated reduction of cardiovascular events is much more important in the case of the generalised dietetic measure, even for intermediary reductions of cholesterol levels.

The problem is that this is a theoretical judgement, which implies that we manage to implement effective strategies, either with medical treatments or population-wide measures.

In fact, so far, pharmacological approaches have proven more effective than population strategies, as they allow for a 4 to 5 times increase of healthy life years gain.

Why are population-wide approach so hard to implement ? This has several causes. The first one has to do with motivation: in a pharmacological approach, the patient and the physician are both motivated thanks to the treatment's significant effect. On the contrary, with a population-wide approach, the individual impact proves relatively mild and this decreases the patient's and physician's motivation. Economic factors also play a role: the development of the pharmaceutical industry participates in the economic growth, whereas population strategies often tend to question common habits and products. They are thus perceived as a threat by some lobbies, which makes them even more difficult to implement. It is nevertheless obvious that pharmacologic approaches prove much more expensive, for two main reasons: screening costs and treatment costs.

In a population approach, if you want to shift the distribution curve of an intermediary phenotype towards more physiological values, you may ask what optimum threshold should be reached in a human population. Over the 20th century, a certain number of "traditional" populations of the 5 continents were studied, which allowed to gather tremendously important values that we may use nowadays.

If you compare the systolic pressure curves of 50 year-old London male civil servants and 50 year-old Kenyan nomads, you may witness great differences. Compiling blood pressure data from several traditional population allows to assert that the level does not exceed 110 to 120mm of mercury whatever the age, and never reaches 140mm of mercury. On the contrary, data from industrialised countries for 50+ year-old subjects mostly exceeds 140mm of mercury.

Similar observations can be made for other intermediary phenotypes. In terms of plasmatic cholesterol, values for traditional populations range between 100 and 150 mg/dl, which is quite inferior to our usual "normal" values, between 190 and 200 mg.
This type of data seems very significant for the assessment of optimal values and optimal distribution of intermediary phenotypes in a human population. In industrialised countries, only a small share of the population proves under the average values of traditional populations (from 1 to 5% according to intermediary phenotypes). The reason why many of us are ill is that we are ill populations.

We know that genetic parameters are combined with environmental factors to determine who will get hypertension, obesity etc.

According to your age, the prevalence of extreme intermediary phenotypes and associated diseases increases. Almost nobody is affected by the age of 20. But half the population may be affected at age 50.

Some would like to identify the very genetic factors that explain why some get a diseases while other do not. This would help detect at-risk individuals and limit prevention actions toward these people. To meet this objective, we would have to know which genes participate in hypertension, diabetes, obesity, osteoporosis development…But these are multifactor and complex phenotypes that cannot be easily analysed. They may not be explained by mutations on one specific gene, but result from the combined action of many genes, environmental factors and risky behaviours. Moreover, the genes cannot be easily identified since they have typically mild effects. Such difficulties may explain why most studies end up with quite inconsistent results from one population to another.

In other words, because of cost and scientific feasibility issues, it is very unlikely that systematic individual screening of diabetes or hypertension risk will replace population-wide public health policies in the near future.

The population-wide approach should not be perceived as a challenge to the strategy directed at high-risk individuals: it is rather a complement. Today, the medicine approach is the only one we use. Health policies must develop population-wide strategies if they want to significantly reduce the number of coronary thrombosis, cancers, bone fractures cases in our countries.

Questions

Member of the audience
You have shown the difference between average level of cardiovascular risk factors in traditional populations and industrialised countries. Do these elements take into account the average age of these population, since we have a great population aging and that risk factors increase significantly with aging ?

Pierre MENETON
Aging has no impact since comparisons are lead within the same age categories. Individuals are the same age anyways: there is no survival bias. You question allows to underline another point: such diseases as cancer, cardiovascular diseases etc, are not related to aging but to environmental and behavioural factors we are exposed to. Aging allows for their development. At age 60, in some populations, no one suffers from hypertension. Not in our countries though.

Member of the audience
Regarding the survival bias: 60 or 69-year-old people from a traditional population are not comparable to the people who are that age in our industrialised societies.

Pierre MENETON
Traditional populations and modern ones have been genetically investigated. The main differences are stressed within the population, not between two types of societies. You may witness the same gaps, within each group, among the people who are the same age. There is thus no scientific or medical reason to think that there are individual, i.e. genetic differences among 60 year-old people from a traditional population and a modern one.

Member of the audience
Your intervention reminds me of a quotation by Dr Knock "every healthy human being is a sick person that does not know about it". Dr Knock was right…

Pierre MENETON
No, he was not. For a traditional population, where no hypertension, cholesterol and very few cardiovascular events occur, his phrase is totally wrong. In a modern society, he is only partially right, since not 100% of the people get one of the diseases.

Member of the audience
Are traditional populations immortal ?

Pierre MENETON
Of course not. I am not comparing life expectancy of both groups, but results in terms of certain diseases. Traditional populations have a lower life expectancy than modern ones, mainly because of natal mortality (both for babies and women) and infectious diseases. But cancer-related, cardiovascular, bone fractures mortality is clearly inferior to ours.

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Of course not. I am not comparing life expectancy of both groups, but results in terms of certain diseases. Traditional populations have a lower life expectancy than modern ones, mainly because of natal mortality (both for babies and women) and infectious diseases. But cancer-related, cardiovascular, bone fractures mortality is clearly inferior to ours.

Elio RIBOLI
This is also true with colon cancer. 25 or 30 years ago, Japan had the lowest frequency for this type of cancer. This lead to a debate on the fact that Japanese people might be genetically "protected" against this cancer. Many studies were lead to investigate on this. By looking at Japanese populations in Hawaii, we then found out that the younger generation tended to have a higher frequency of colon cancer than Caucasian populations. Today, the Japanese of Hawaii have the islands' highest incidence for this pathology. Now, genes have not been modified in 30 years…

Pierre MENETON
Some studies on migrations show that migrants adapt to their environment by adjusting their lifestyle after some months or years, which changes their levels of blood pressure, glycaemia, cholesterol etc. There is therefore no difference among people.

Elio RIBOLI
I think there are totally wrong concepts in medical assumptions, as has been shown by behavioural and physiological studies 20 or 30 years ago. Let us presume that we can measure American citizens'anthropometry and do a body weight, height and BMI distribution. Do you think that considering most frequent results as "normal" would reflect the physiological norm ? Transposing statistic frequency in terms of physiological normality raises enormous debates, and I would like to thank Pierre Meneton for presenting a concept that we should think about further.

Can individuals implement nutritional recommendations ? Mechanisms for change or mission impossible ?

John E. BLUNDELL
School of Psychology, University of Leeds, Leeds LS2 9JT, UK

Thank you. I shall be speaking in English and as a point of continuity between the previous talk and my talk, I might ask you to consider that obesity is a condition which is also age-related and if we are thinking of treating obesity, then should we treat the whole population or just the high-risk individuals ? If the latter, can we identify the high-risk individuals ?

I might also comment at the start that I do believe that obesity is an end-point that is different from the end-point of cancer, cardiovascular disease, stroke and osteoporosis in that obesity rises from disregulated system. Obesity may result when there is no inherent fault in the system.

I should say before I start my talk that I hope it will not be as controversial as the last one, and I want to thank the organisers for giving me the honour of being on the scientific advisory committee for this excellent conference, and also for giving me the honour of speaking in a presentation where there are so many eminent speakers. I do not think I actually have any special knowledge that will contribute anything that has not been said before, but I may say it in a rather different way. Now, I am a psycho-biologist and my talk will concentrate on features of individuals as much as possible.

The psychologist in me leads me to consider strongly what people think and do, and individual behaviour at the point at which they make contact with the diet or with the nutritional recommendations. The biologist in me leads me to be interested in variability, because biological variability is simply a fact of all species including humans. Now I will concentrate on obesity and diabetes, but I am not an expert on diabetes – and some people think I am not an expert on obesity either – but I certainly know something about it, and for a number of years we have been focusing on people who are either susceptible or resistant to weight gain. The questions I pose here are: Is it possible for people to change their dietary habits, and can people reduce their body weight ?

We do know that many people want to do both of these, and many people are really trying hard, but many people cannot do it. So why is this ? There are three reasons that I think make it difficult for people to achieve those goals. One is biological susceptibility. We might also call it psychological susceptibility: reasons why people cannot implement what they know to be beneficial. Behaviour is resistant to change, and the cultural values, to put it very mildly, are not helpful – in fact, they are extremely unhelpful. I am not trying to be cynical or very clever here, but I have looked closely at the literature, and what I infer from the tremendous efforts that have been made with strategic interventions whether they are community-based, targeted on the schools, colleges, universities, in the work place, catering outlets, supermarkets, or levels of primary care, a huge amount of organisation and effort has to be invested, often for rather small adjustments in behaviour. I am really not being cynical about that and I think that all of those efforts are worthwhile and definitely should continue, but the output often is small. One exception, I believe, was the Finnish diabetes intervention study we heard about this morning, and the causes for what happens in Finland may come up in the discussion later. One feature that arises from all of these interventions is that it is easier to change awareness and intention than it is to change behaviour. This is exemplified by something called the theory of planned behaviour, something that socio-psychologists have been working with for a number of years, in which there is a relationship between attitude (the belief that you have), the intention (what you want to do), and behaviour.

There is normally a very good correlation between attitude and intention – I believe this; I want to do that – but there is a rather weak correlation between 'I want to do that'and actually doing it. This is called the intention-behaviour gap. Possessing a healthy eating attitude – for example, 'I want to eat more vegetables,' believing it is very good to do that – is not a good predictor of actually doing it. So the first thing is that behaviour at the individual level is more difficult to change than attitude. That is because the behaviour that we express is structured into habits which are rather crystallised as an expression of what we do. As psychologists know very well, the best guide to future behaviour is past behaviour. Habitual patterns are very difficult to adjust, particularly when these habitual patterns are reinforced by something which gives pleasure, by hedonic processes. This is not a carefully guarded secret, but eating is a source of great pleasure in peoples'lives, and the pleasure reinforces the act of eating.

Now, I am often saying to people that eating is the cheapest form of pleasure that they have on a daily basis – I will just pause for a moment to let that sink in – when you consider whether it really is cheaper than the other behaviour that most of you are thinking about, which is probably reading.

Professor Martin earlier today spoke about the nutritional recommendations in France, and in the UK, I think we have probably got a very diluted version in English. What I took from the French recommendations was a clear statement about pleasure and eating in which there are statements like "individual food choice is a free act." In addition to the biological purpose of eating, it has strong social, cultural and psychological aspects and the French guidelines speak about eating as being a moment of pure pleasure which they want to assist. They also say, "Must we from now on," in order to treat obesity, "sacrifice the gentle principle of pleasure to the all-powerful precautionary principle, stopping getting pleasure from the process and doing what we know is good for us, in which eating is plunged into anguish and confusion ?" The guidelines suggest that what is needed is an environment favourable for freedom of choice, and I think that this is a big challenge. Can we provide an environment that provides people with the freedom of choice, and yet still allows them to control their bodyweight ? For me, there is a puzzle in this. I work with overweight and obese people much of my time and I also talk to other people. I know people who exercise great control and effectiveness over many parts of their lives by being disciplined and highly motivated. These people, who are extremely successful individuals, find it impossible to control the amount, frequency and content of what they eat, which suggests

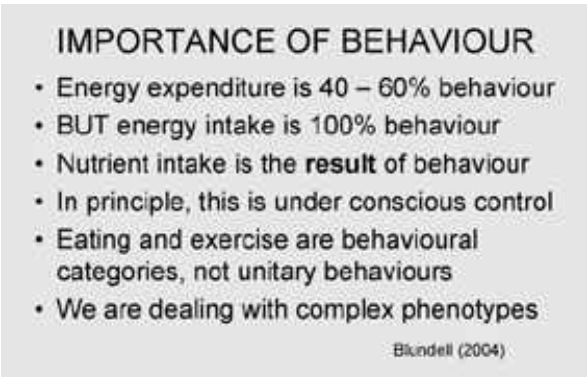
to me that eating is a different end-point from many of the other targets that we set ourselves in our lives. I would suggest that people are actually better able to control sexual and aggressive impulses than they are to control impulses related to food. The reason for that is that eating, unlike many other behaviours, is part of a regulated homeostatic system, and when we eat or do not eat, the system recognises that and adjusts itself accordingly.

Many people, including myself, work within a simple energy balance system to look at the control of food intake, and there are a number of features of this simple relationship between energy expenditure and energy intake. The first is that we are dealing with a regulated system. The second thing is that many of these features of energy expenditure are controlled by our biological predispositions and even our genes and we can do very little about them. Physical activity is discretionary or optional, it is behavioural and we should be able to moderate it either upwards or downwards. There are a number of features of this very simple energy-balance equation and one is that it only takes a very tiny amount of imbalance to lead to weight gain over a long period of time – even 5 to 10 to 20 calories per day over a number of years is sufficient to lead to weight gain, and that could easily come about by eating a little bit too much or decreasing activity just by a tiny amount. And we could never measure those amounts which theoretically are sufficient for weight gain, because we don't have the tools with the appropriate sensitivity.

The system forgives or permits increases in energy intake but defends itself very strongly against reductions in energy intake. So this is very unfair, but the system operates asymmetrically: overeating, over-consumption can occur passively; under-eating must be an active process and the system defends itself. These are a number of the reasons why trying to adjust energy intake in a downward direction is difficult because the system resists it.

Another feature has to do with measuring, because our tools for measuring energy intake in the natural environment are actually very poor. Although we have heard about some of them during the last few days, they are sufficiently good when you have huge numbers of people and you are looking at proportions of intake in different countries or across different groups. The measures that we have for measuring energy intake in the population are quite insufficient for using those data in an energy-balance equation and we have to be very careful, therefore, about accepting data collected on masses of people that speak about total energy intake. I do not want this to turn into a sermon and I am certainly not a cynic, because all the time in much of my career I am trying to find out what it is this that people habitually do eat – and I can tell you, it is extremely difficult.

The second feature of all of this is the importance of behaviour. Whereas maybe 20 to 40 to 60 to 80% of energy expenditure is behaviour, when we come to the other side, 100% of energy intake is behaviour, and nutrient intake is the result of behaviour: nutrition is not behaviour itself; nutrition is the result of behaviour.



There is another issue here for me, because in principle this behaviour is under conscious control: eating means reaching out with hands to grasp food and bring it to the mouth and in principle, I can control my arms and my hands to do this. Everybody can do that, in principle. In practice, we know that it is very difficult for some people to control these very simple actions and I do not think that can be easily brushed aside. It is a feature that we have to confront on a daily and momentary basis.

We are dealing here with behaviours which are actually difficult to control, even though they are under conscious control. The behaviours are not simple units, there are complex categories of behaviour and both eating and exercise constitute complex phenotypes. For this little control paradox, I ask myself why, if human beings represent the most intelligent life form on the plant, do we find it so difficult to make small adjustments in behaviour that on a day-to-day basis we calculate would halt the continuing rise in obesity ? It may be understandable why people cannot make massive changes in their lifestyle, but why is it that people cannot make the small changes ? Of course, this is a rhetorical question just to try and stimulate my mind to think of better ideas to help people.

One message is that behavioural habits are very resistant to change whatever the unit of behaviour we work with, even in one-to-one therapeutic situations. Marketing approaches know that you have to put a lot effort into advertising and selling to get changes. Coercive policies by legislation and prohibition may help. The psychological issue, I believe, is that one size does not fit all. Because of the biological and psychological variability, one method does not suit everybody. So what is happening more and more now is that it is becoming possible to tailor strategies to the individual making use of technology, internet-based approaches and computer tailoring of health messages.

We might just go back a step and ask what determines the food that people eat. Cultural values, obviously. If you want to know what anyone in the world is eating at a particular moment in time, the most important bit of information is what culture they belong to, and that information will give you the most information about what they are eating. Environment is important, there are biological dispositions and there are psychological processes, including the free choices we make, and learning and adaptation.

At another level, thinking of implementing nutritional recommendations, which means altering choices, is it biology or the environment that can control the choices that we make for particular foods ? Biology involves various categories – taste and texture of food, certain drives, satiety signalling – and we know that the environment is obesogenic and pathological. It seems very unlikely that we can intervene on a mass level in biology so we obviously have to intervene in the environment.

There are three lessons that I want to mention. I know this may sound a little like a sermon but it is not intended to be so – these lessons are really for me, I would say. Lesson one comes from a study that was carried out in my own city, the Leeds School project, for which I have a lot of admiration. It involved ten schools: five intervention schools, five control schools, and children from seven to eleven years of age. Over one year, the project was designed to influence their diet and physical activity, not just the knowledge but what they did. It involved parents, teachers, catering staff, school meal plans, daily activities, and a project team provided training for all of these individuals.

What was the outcome after one year ? There was no difference at all in bodyweight between intervention and control schoolchildren. There was an increase in awareness and understanding, so it is easy to achieve that, and an increase in basic knowledge, but sadly and for some unknown reason, sedentary

behaviour actually increased in the overweight children. There was a third of a portion increase in vegetables per child, which seems small but it represents about a 30% increase over what they were consuming before, but it is still a small outcome for huge effort.

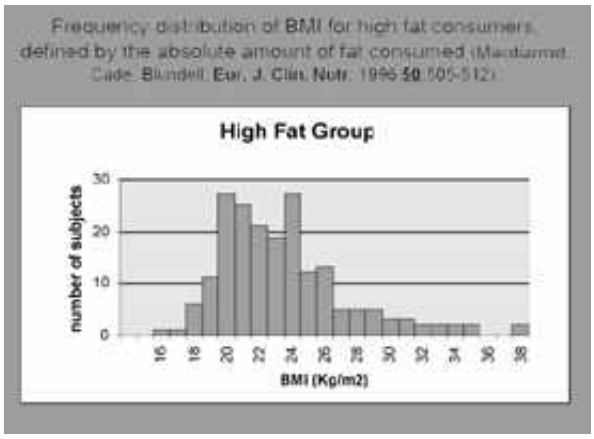
We have heard about the second lesson already, the North Karelia project, and you have heard about the outcome: there is a fantastic fall in heart disease from 700 to 200 per 100,000. However, despite the dietary intervention producing this superb healthy outcome, obesity still continued to increase. So what I learned from that is that dietary habit can be changed. It requires massive effort and organisation on a national scale. Changing dietary pattern may take a generation, but change in food selection itself is not sufficient to reduce obesity, you need something extra, as is recognised in the recent projects which are built on that and now include physical activity and attempts to reduce overall energy intake.

Lesson three comes from a study I heard about very recently at a meeting, which is why it has to be anonymous. It reported information on a structured meal replacement plan that was applied to a group of individuals for ten years. So this group of people are eating a structured meal plan with a meal replacement for ten years. After ten years, they had lost five pounds, or about 2.5 kg. The loss had been ten pounds after five years, but there had been some regression after ten years. That is success: this meal plan had reduced bodyweight by five pounds after ten years. More success: the control population that did not have this structured meal plan day by day, week by week, month by month, had gained 28 pounds, so the difference between the two is 33 pounds – a great success. I am not being cynical here, I am reporting what is an accomplishment.

However, if you look at what the structured meal plan group was doing, they were in energy deficit over ten years by 5 calories per day. Is that success ? It is success, it prevents weight gain and it may be reality; but you have to put in that amount of effort over that period of time and give up all of the natural eating patterns in order to achieve prevention of weight gain. Well, that is my interpretation – people may have other interpretations – but it suggests to me how difficult it is to achieve even prevention of weight gain over a long period of time.

Of course, we can reconfigure this in a different way and think that the way in which people eat and the food that they choose, the ones which they prefer and don't prefer, represents biological traits which constrain their preferences and predispose them to eat certain foods rather than others. A widely held view is that the natural energy you get from sweet and fatty foods has always been evolutionally and biologically useful and these traits are still available to support those, but now in a different environment, they are not useful any more, but we still have the traits.

My point of contact with the last speaker is this European programme. I was actually going to get try and get through this presentation without referring to any of my own work, but I decided I would sneak a little of it in because we have been involved for four years in this European programme which has been designed to examine dietary and genetic influences on susceptibility and resistance to weight gain in Europe – that is the name of the programme. We are looking at similar features to those which Professor Meneton is looking at for his end-points: what constitutes susceptibility to weight gain and what constitutes resistance ? The research objective is to try and find if it is possible to define characteristics of weight gain in people by examining various aspects of what they do. This is designed to link behaviour with genetics, attitudes, and with diet.



The starting point for this was a study conducted over a number of years in Leeds more than ten years ago in which we were looking in the population for people who consistently consumed a high-fat diet and those who consumed a low-fat diet. We would compare those two. These data were taken from the national database, which is usually regarded as the gold standard for generating energy intake – the Seven-Day Weighed Food Diary. These people here, taken from the national database, are all high-fat consumers consuming more than 43% fat. My belief was that high-fat consumption leads to weight gain. However, what is clearly shown here is that the relationship between fat consumption and weight gain is not a biological inevitability. All of these people are high-fat consumers and yet you can see that there is a range of body mass indices here that goes from underweight to overweight. There certainly are more people in the overweight category than in the underweight, but there are many people down at this end who are eating a high-fat diet.

There are two features worth remembering about these data. First of all, whenever you collect information from people about what they are eating, most people find it extremely difficult to disclose accurately what they are doing. There is, however, a calculation, an algorithm – the energy intake to resting metabolic ratio – which allows you to separate the plausible from the implausible food records. These data represent only the plausible food records: that is, only those records in which people reported to us energy intakes which were realistic. For many people in this audience this is just abc, I know that, and you will be familiar with the idea that when people report their eating habits to you, they sometimes report energy intakes which are below even their resting metabolic rate, so that clearly cannot be true.

These are the best records, the ones which are plausible. The implausible ones are taken out. However, since we know that obese people contribute a large percentage of the implausible records, the obese people are actually left out of these data. That is the price you pay for working with the best data.

The second thing to know about this distribution is that the people on the right hand are ten years older than the people on the left hand side. Age, as we know, is the best predictor of body mass index and obesity is an age-related condition, so it may take ten years for people to work their way across this distribution. Therefore, in comparing these people here, who are susceptible to weight gain on a high-fait diet, with these down here, who are resistant, you obviously have to match for age, and you therefore match for the degree of exposure. That is what has been done here: these people are the resistant, and these are the susceptible on a high-fat diet. They are similar ages, they obviously have different weights and different BMI, but these are obese, they are susceptible, they have different body fat, and so on. When we measure all of their features regarding fat consumption and calories using special instruments, there is a similarity for the

intakes of fat and for energy but there is a big difference in bodyweight.

I will just draw your attention to this feature here, the daily energy intake, which, for these people, despite the fact that they are much heavier (they have a BMI of 34 rather than a BMI of 21), they actually report to us that they are consuming fewer calories. That can hardly be true because we know that they require more calories on a day-to-day basis just to be in energy balance. First of all, when they receive low-fat foods for one day and high-fat foods randomly allocated on an alternate day, they eat much more energy with high-fat foods than with low-fat foods. I know that is not very profound because these high-fat foods are obviously more energy-dense, but it does demonstrate a phenomenon called passive over-consumption: people passively over-consume when they are exposed to high-fat food.

The second thing is that the susceptible people now show that they are eating significantly more when we can measure accurately what they do eat, whereas when they report to us what they eat, they actually tell us they are eating less. You can decide which is the most valid measure: what people say they do, or what you accurately measure they do.

This is not a criticism of people taking part in studies because I know that all the time, individuals are trying to do the best, trying to report what is best for them and for us, but they simply find it very difficult to do it.

As a final feature, I would mention that we have also undertaken some qualitative analysis. I talk about this rather than the genetics because I think that it is more relevant for what we are speaking about here.

The qualitative analysis uses semi-structured interviews to ask people to talk about the foods that they consume. We prompt the discussion with certain key references and then the transcripts are analysed and evaluated. In this particular analysis, we have used the resistant individuals eating a high-fat diet, the susceptible eating a high-fat diet, and the low-fat lean. What do we find ? If you at the low-fat lean individuals, first of all, enjoyment of food is not really a major issue for them: they prioritise health over taste and enjoyment, they eat variety but it is related to health. So these people are sad boring people and, needless to say, I am one of these: I am a low-fat lean person, my body mass index is no secret – low-fat diet, lots of exercise, sad and boring person.

However, when we look at the high-fat consumers, the ones who are freely eating yet remaining lean, they prioritise taste and enjoyment: for them getting pleasure from food is important and it is more important than health. These people are eating to enjoy themselves and they enjoy high-fat foods. They do mention that when they are sad or upset, they eat less, but they also say they can eat what they want and they do not gain weight. In fact, this was one of the primary stimuli for us undertaking this research: the idea that we had heard for a long time of the fact that there are people who appear to eat what they want but they do not gain weight. Some people do not believe that these individuals exist. I think they do exist. They are the resistant individuals, and some of them are actually trying to gain eight but they cannot, so I think that sort of person does exist. The contrast between these two descriptions is interesting.

When we come to the susceptible people, they elevate this phenomenon to an extra level. They select food for enjoyment, specifically for its tastiness, and their enjoyment comes from the taste of food. They use very strong descriptions, as you can see here: I just love this; I've got to have more of that. They even enjoy eating large amounts of food, it is not just the taste that gives them the enjoyment, is it the large quantity of food, which they do admit when you have a conversation with them. It would be very hard to get these data from some sort of objective quantitative test. They are aware of their eating habits and their relationship to weight gain. They also say that they eat more when they are depressed or sad.

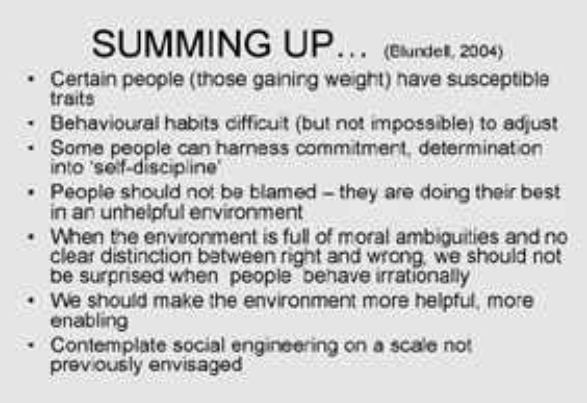
So the differences between the susceptible and resistant individuals does not just reside in their biological traits, it is also in their psychological relationship with food. I can mention that we do believe that it is allelic variation among the population that creates these psychological dispositions, but I do not have time to convince you with data.

This is probably a little controversial but I take the view that Europe is different, at least different from America. So I ask if we can learn anything from America. I am tempted to say no, but because I have great respect for American colleagues, I think the answer is yes. One of the issues that I think very interesting comes from a study of the characteristics of people who have successfully maintained a weight loss. These people are enrolled in something called the weight-control registry, people who have lost a significant amount of weight and maintained it for a year. There are lots of individuals with a high average weight loss and a change in body mass index.

What characteristics do these people demonstrate, as far as they can be divulged from analysis ? Well, they have a low-fat intake, less than 30%, and more than a third of them eat less than 20% fat in their diet. They also have a regular meal pattern, at least five eating episodes a day, and a high level of physical activity, much higher than normal recommendations of, say, 30 minutes per day, as they are moving 28 miles a week, which is obviously equivalent to a marathon. They apply very close and detailed self-monitoring to what they do, so they are watching themselves all the time – what they eat, when they eat and their activity. I am one of these sad boring people myself, I am afraid.

All of this is much more than just implementing nutritional recommendations, it is going way beyond that. It may be that you need to go way beyond that to achieve significant weight loss. I come back to the title of the talk: Is it mission impossible, or can we implement nutritional recommendations ? Linking this with previous talks, individual variability and susceptibility to weight gain, I think, is a key factor in peoples'capacity to implement the behavioural change, even though all want to. Some people will find it much more difficult because of their traits and their dispositions. There is a need to change societal values, this is not easy, of course it is fantastically difficult, but an achievable target might be prevention of further weight gain, and that I think would be a major success. To lower the target to prevention of further weight gain rather than creation of weight loss, that might be achievable. So in summing up, certain people, those gaining weight, have susceptible traits and the habits underlying those traits are difficult to adjust. Some people seem to be able to harness that commitment and determination into self-discipline. As a psychologist, or someone who is psychologically trained, I do not quite like the term "self-discipline" – it seems to be too militaristic and not sufficiently sophisticated or technical – but I think it probably describes what these people can do.

I do believe that people should not be blamed for failing to implement nutritional implementations – many people are trying to. They are trying to do their best in, for the most part, a very unhelpful environment. The view I have is that when the current environment is full of moral ambiguities and moral ambivalence and there is no clear distinction between right and wrong, and it is difficult to predict whether exercising self-denial is going to lead to a better life and if that is the morally correct thing to do, we can forgive people in this morally ambiguous environment for acting emotionally and irrationally.



Of course, this is a political and ideological framework for the environment in which people live but obviously, being obese exists within such a socio-political framework and it can't be brushed aside. So when the environment is so ambiguous and ambivalent, so many mixed messages, people will ask yourselves: If I spend years in my life controlling my bodyweight, will I still get to heaven ? Or is there a guarantee that at the end of it, I am going to be happy ? So we have to make the environment more helpful and more enabling. It may be that in creating an environment like that, we have to contemplate social engineering on a scale not previously envisaged. I do think that if we are serious about dealing with the problem of obesity at a public health level, we have to contemplate social engineering on a massive scale, which has not been achieved so far.

I am not a cynic in this; I remain an optimist and a very positive person. I think that everything that we are all doing, we should continue to do to encourage people to eat healthily and their health will benefit, but we will probably have to be satisfied with rather small achievements. If we want to achieve the goal of eliminating obesity, or significantly reducing it, then we have to create a coercive and socially engineered environment, which means taking away a certain amount of personal freedom and choice.

So I come back to the guidelines from the Ministry of Health in France: do we have to sacrifice this principle of pleasure to the precautionary principle ? Possibly we do, if we are really serious about dealing with the problem, but of course in practice I think it is impossible to do that. We have to try and create an environment that is favourable for freedom of choice, and keep doing what we are all doing to make life better for people with healthy food choices, but be satisfied with small gains because I do think that people are doing their best in a very difficult environment for them.

Thank you.

Questions

Member of the audience
I think the social image of what an ideal body is has changed a lot in the last thirty years. I think there is now a very strong social ideal of a thin body, very fit, with possibly a good tan. In other periods of history, the social ideal was very different. You see this in different ways on TV and also in everyday things. For example, many people who are not obese, but maybe overweight, have real problems finding clothes they like in their size. I think that for many people, this creates a feeling of social pressure that this is unfair, and I think that some people almost feel excluded from society in certain respects. Do you think that this can create a kind of psychological resistance ?

Also, as you said, susceptibilities are very different and some people have been trying to lose weight for twenty years with not very good results. At the end of the day, they can become a little tired of all this and they give up. I just wanted to comment on this.

John E. BLUNDELL
You have actually made an interesting analysis – it is hardly a question, but a very interesting analysis – and I think you are probably correct. When the social ideals create aspirations which are too difficult for people to achieve, then they give up. So you need a social image with aspirations that are attainable for people and giving them the possibility. So, I don't disagree with your analysis. I think the image that we have created for people is far too difficult for most.

FINAL DISCUSSION

Elio RIBOLI
I think Professor Blundell's presentation paves the way very nicely for a more general discussion on what is scientifically supported and what the implications are in terms of policy and behaviour. As a closure to this conference, we will have to invite all this morning's speakers to join me here at the table, and I would like to invite the audience to make general comments and questions. Professor Ambroise Martin will also help me with the conclusions as I was not here for the previous two days. So, the invitation to ask questions is extended to all the speakers.

Personally, I found that Professor's Blundell's presentation, which was neither sad nor boring, was extremely stimulating because I think you put the issue of changes, in the sense of changes towards a better diet and better energy-balance, into the social context, which is extremely important. I think there is too much pressure put on individuals in the social and environmental contexts which actually seems to have been designed to achieve the opposite goal. Everybody knows that the availability of cars has a great effect on how our new urban environment has been designed. Obviously, if you have people working 20 or 50 km from where they live and there is no public transportation, there are no sidewalks and the only way to go to work is by car, then obviously you sit in the car because there is no choice. So the issue of the environment is extremely important. That is my comment.

Member of the audience
Professor Blundell, regarding the prescription of physical activity in the two groups susceptible to resistance, are there different prescriptions for physical activity ?

John E. BLUNDELL
It is certainly clear that physical activity is absolutely vital to introduce into the equation. Trying to change the diet will probably not be sufficient on its own, so physical activity has to be a component. It may be easier to change the physical activity patterns of children than it is to change their diets. However, I think we should still be clear about the amount of physical activity that is required. The recommendations that come from various bodies are in fact rather on the low side: even 30 minutes of walking a day is not excessive and it has actually been calculated that an obese person who has reduced weight requires 80 minutes of physical activity per day at moderate level in order to prevent further weight gain. So I think the recommendations for engaging physical activity have to be elevated to another higher level, they have to be of greater duration, and we are presently configuring.

Member of the audience
I am a Dietician in Béziers, France, a city involved in the EPODE campaign for the prevention of child obesity. This five-year period campaign consists of various interventions targeting pupils and families and promoting physical activity. Since nobody mentioned this programme in the last three days, I would like to hear your view on this.

Ambroise MARTIN
It is true that we have not talked much about physical activity, including as far as the Mediterranean model is concerned, although obviously the people who went fishing or were busy with the goats had a significant level of physical activity.
During the drafting of the PNNS, I insisted on the fact that physical activity and the "energy spending" aspect had to be part of the programme. These have been considered important enough to be promoted by the second media campaign, since the first one had been focusing on fruits and vegetables.

Walter C. WILLETT
I think that it is worth talking a little bit more about some of those issues like weight control and diet, particularly given the context of the conference which is about Mediterranean diet. I think one of the problems has really been the nutrition community which has been pushing this idea that low-fat diets are important and lo-fat diets contribute to weight control and weight loss. Certainly, our national experience in the United States has been that when we went on this low-fat campaign, that is when we really had this explosion in obesity. Now that does not mean too much in itself because there are lots of other things happening at the same time, but I have reviewed all of the randomised trials that have looked at low-fat diets and weight loss, and what happens is that you lose a kilogram or two over a few months, but over the longer term, people find it extremely difficult to stay on these diets, but even those people who do stay on the diet do regain their weight. I did a little analysis on these randomised trials that had been conducted for one year or more, and there was absolutely no benefit to the low-fat diets in influencing reduction in weight. The Cochran collaborative did a similar analysis looking at low-fat diets and weight loss and they also found no benefit. In fact, a number of these trials are now showing that a reduction in the glycaemic load probably does have some benefit on weight control. There are other types of studies that have looked at this. Group of studies looking at very low carbohydrate diets, the Atkin's type of diet, compared to low-fat diets. Despite what nutritionists would like to believe, actually people have tended to do better on the very low-carbohydrate diets than on the low-fat diets. That is not to say that those are optimal diets for overall health in the long run, but it does show that by reducing refined carbohydrates and sugar in particular, many people are able to control their weight better.

Of course, there are other possible ways of changing carbohydrate intake. Doctor David Ludwig has done a randomised trial reducing glycaemic load both by reducing carbohydrate and allowing higher fat intake and also reducing the glycaemic index of the carbohydrates. It is still a small study, but there was significant weight reduction in obese adolescents with a low-glycaemic load diet at one year. There is also the very relevant study of Kathy Mc Manus and Franck Sacks which used a 35% energy, Mediterranean-type diet versus a low-fat diet. There was a major difference in body weight in favour of the Mediterranean-type diet after 18 months and much higher compliance with that than with the low-fat diet. This was a type of diet that people could stay with, enjoy, and find pleasurable at the same time this was helping them control their total caloric intake.

I would like to go back and talk about the National Weight Registry, which was really a completely uncontrolled study. I think the problem in that kind of uncontrolled study is that the same people who had a lot of self-discipline, as was mentioned, were the same people who did what they were told when the recommendation was to go on low-fat diets. So there is serious confounding between self-discipline and low fat-diets. Interestingly, the Consumers'Union recently did a similar type of study to identify people with long-term maintained weight loss. In the more recent data, they were almost all Atkins-type diets – very low carbohydrate diets – that were succeeding in this way. However, a common factor was a high level of physical activity, and I am absolutely sure that is true. That was consistent no matter what type of diet. It appears that some people with high self-discipline will maintain their weight loss better on almost any kind of diet. However, it does seem that the randomised trials clearly show that reduction of fatty intake per se is not useful, and that has caused a lot of confusion.

I also do not want to leave everyone with the idea that these school interventions are hopeless, but we do need to be very careful. I am sure we will improve the interventions over time. However, there are two factors that consistently show up in studies of childhood obesity as being most important. One is number of hours of TV watched per week, and the other is high consumption of soda beverages. There are now about eight randomised trials showing that reductions in TVwatching will help reduce obesity and control body weight. There was also a very impressive study in the British Medical Journal about two weeks ago on school-based randomised intervention trials. The only factor that they changed was reduction in soda consumption, and there was a 7% reduction in the prevalence of obesity just by focusing on soda consumption. I think these are two factors where the evidence is very strong and very clear: we need to get soda consumption out of schools -it is a huge source of calories in children, and in many adults as well – and we also really need to focus on TV watching. This is one of the primary targets as well.

Pierre MENETON
If we look at the traditional populations which, as we mentioned earlier, have very low rates of obesity and diabetes, we notice an average physical activity of 12 to 14 km of walking a day. This type of physical activity is similar to the physical activity of all species of superior primates.

John E. BLUNDELL
Yes. This is developing into quite an interesting discussion and I would like to make a couple of points following Professor Willett's comments. One is that we might make a distinction between creating weight loss, or producing weight reduction, and preventing weight gain. I would not disagree that introducing a low-fat diet will produce rather small gains in weight loss, but that is typical of most single manipulations of the diet whatever they are.

That is not the same thing as saying that a low-fat diet will prevent weight gain, and in most of the data that I know people who have habitually consumed a low-fat diet find it extremely difficult to reach obesity. So I do think that a habitual low-fat diet is protective. That is very different from saying that introducing a low-fat diet will produce a reduction of weight. A problem arose when people were encouraged to introduce low-fat foods or went for high-carbohydrate foods. What almost certainly happened is that they left their fat intake too high - at more than 30%, perhaps 31 or 32%, and added the carbohydrates on top of that. That was probably the very worst thing you could ever do because that produced an extra energy surplus with an insulinogenic diet and a load of carbohydrates that would be oxidised in preference to the large amount of fats that were being consumed. This is quite a complex issue, but when people move their diet from one type to another, we have to be very sure that they are doing it to a degree that is going to be truly effective.

I would argue also for considering the findings from the weight loss registry, even though it may be a rather uncontrolled population. However, it does show that you need a portfolio of factors in order to bring about serious weight reduction – not just a change in diet, but also strong control over your behaviour and a large and substantial increase in physical activity.

Walter C. WILLETT
I think I would disagree that the evidence all shows that people, even starting off on a low-fat diet, do not gain weight. What is happening around the world now is we are seeing explosions of obesity in country after country. That usually tends to be in the lower socio-economic strata of those countries where they are still consuming very low-fat diets of around 20% of calories. They have access to food in ways they did not: food is plentiful now and they can afford to buy all the starch that they want, even if they're still rather poor. So in Latin America, Asia and Africa, poor urban populations sometimes now have a prevalence of obesity as high as the United States – on 20% of calories from fat.

The biggest recent randomised trial, of course, is the Women's Health Initiative, with about 50,000 people randomised to a low-fat diet and running for seven years. So here we are really looking at weight gain over time, because that is a long enough period to gain weight, and there is no weight benefit in terms of low-fat diets – they are gaining weight essentially at the same rate as people on high-fat diets.

I have not seen any good evidence that the biology is different for weight loss or weight gain. It is very true that we should be putting our emphasis on prevention of weight gain and obesity because it is clear that once someone is overweight, it is very difficult to maintain long-term weight loss. That is very clear.

Member of the audience
Just a clarification on something that Professor Blundell said: when you mentioned the 80 minutes exercise in obese people, is this in the face of them continuing with their normal calorific load or in addition to reducing their intake ?

John E. BLUNDELL
I think I got the question: it is whether introducing physical activity can be effective whilst maintaining the normal diet.

Member of the audience
Is the 80 minutes recommended for obesity ? You mentioned 80 minutes exercise for the obese persons, is that while they maintain their calorific intake, or reducing it as well ?

John E. BLUNDELL

These data come from the work of Dale Schoeller, who has carried out stable isotope (double labelled water) studies and energy balance work on individuals who have reduced weight, so these figures are quite accurate. We are working with quantitative estimates here. The people concerned were able to eat freely, but not extravagantly – just maintaining what was a judicious diet. On top of that, just in order to prevent weight gain, they had to have the additional eighty minutes physical exercise. I think it is important that we recognise that taking energy in is very rapid and very easy. Getting rid of energy from the body is a much more time-consuming process and people often overestimate how much energy they have used up for a small amount of activity. For example when people start to perspire, and the legs feel a bit tired, they may have used 100 or only 200 calories, but they feel they have used a lot more. So it is important to get the quantitative estimates of energy balance appropriate.

Elio RIBOLI

I would like to add a comment. I think that here we have a discussion on very fundamental issues, which is the relative importance of what I would call diet composition: the type of food you eat within a given level of energy intake, and then the issue of the relationship between energy intake and energy expenditure. If I just can add what is in my area of competence, my personal reading of the literature on cardiovascular diseases and cancer is that composition has an effect on developing some of these diseases. So, for a given weight more or less within a normal range, and for a given energy intake where the diet is completely unbalanced – too rich in, for example, red meat, processed meat and saturated fat – that is a risk.

Then, there is the issue of the relationship between what we eat and energy expenditure. It is quite interesting to see that in Europe today, the populations which have the healthiest diet composition – southern Spain, southern Italy and Greece – have the highest prevalence of obesity in Europe. There is a very clear North to South gradient. However, if you go to southern Spain in regions like Murcia and Granada, you will find the lowest incidence of cancer that you can find in a western population. In Murcia in the past decade, the incidence of cancer was around 1,300-1,400 new cases per million inhabitants, compared to 350 in Scotland and compared to 140 –150 in Rulag, India. So southern Spain, with the highest prevalence of obesity – particularly in women – still has the lowest incidence of cancer in the western world – at least in Western Europe. It is almost as low as India. So, there is clearly an issue that diet composition, in a population where fruit and vegetables consumption is extremely high, fat from dairies is extremely low and olive oil is the only oil used in cooking, must have an impact.

If we take the other axis, there is the issue of energy intake and energy expenditure. If you go to a population like India or rural China, where you have a very low intake of fat, which means a very high intake of carbohydrates, then the obvious consideration is that traditionally, the carbohydrate is not the sugar you find in a western supermarket, it is actually vegetables and legumes as they are: unprocessed or minimally processed. That brings in another interesting consideration: looking at nutrients and big categories like carbohydrates is probably not very helpful. It may be more helpful to look at the food people have on their plates – or maybe in their hands, if you are in India. It is probably completely different when you have a very high intake of vegetables, fruit and legumes, than when you have a high intake of highly processed and refined carbohydrates. So if you replace fat with sugar, it is not the same as if you replace fat with vegetables. I think that is an important issue in my opinion.

Member of the audience

This question is for any member of the panel who might have investigated it, and it is on exercise and comments on walking. What about the benefits of swimming and other forms of exercise ?

Elio RIBOLI

The issue is leisure-time exercise, sports activity, compared to just daily routine walking and so on.

Ambroise MARTIN

For the revision of their data recommendations, the French did some very detailed work on the values of physical activity and the influence of different physical activities on total energy expenditure. In general, it appeared that sports activity as the only physical activity has little influence on the total general level of energy expenditure. For example, if you do thirty minutes relaxed walking per day, it has exactly the same effect and the same increase in the level of energy expenditure as two or three hours of swimming, or another sport, once a week. So we do not insist on sport in France, but on daily physical activity: to take the stairs instead of the escalator, and so on. It seems very important and it can be demonstrated because we have calculated the energy cost of more than 100 physical activities, sports, and so on, and it is clearly most effective on a daily basis.

Elio RIBOLI

This is clearly a very important point. There is a question over there.

Member of the audience

C*hanging behaviors can prove difficult, but it is sometimes easier to change the environment. How about coercive measures regarding salt content of processed foods, notably bread ?*

Elio RIBOLI

Allow me to comment on the issue of salt. I think it is rarely appreciated that one of the major historical changes in our diet has been the huge decrease in salt consumption which has occurred over the last century. Until the mid 19th century, the most common cancer in Europe was stomach cancer – hypertension was actually very common already – and salt-preserved food is clearly strongly associated with the risk of developing stomach cancer, as has been shown in plenty of studies. In Europe, there has been a major decrease in the consumption of salt as a food-preserving agent over the last century. I would just like to say that my personal perception is that the food industry, which has contributed substantially to this decrease by changing food-preservation methods, is often seen as being responsible for the salt intake. There are some foods with a high salt content, but the fact that natural antioxidants are now used to replace salt in preserving foods in the cold chain is a major positive fact.

Ambroise MARTIN

As far as salt is concerned, Pierre Meneton is certainly more qualified than I am to answer the question.
Following the proposals and the engagements made by industrials on the reduction of salt content, the AFSSA (French Agency of sanitary security for food), together with a consumers association, have implemented a surveillance programme concerning more than 400 foods, with an extremely deepened reflexion on the sampling.
The first campaign of the programme was launched at the end of last year, and will be reconducted at the beginning of 2005. Depending on the results, it will perhaps prove necessary to shift to more coercitive measures.
The second type of work regards possible benefits of mediatization of the debates. Analysis of 6000 families' purchases (which constitutes the French standard database) showed an undeniable decrease of salt purchase from July 2002 onwards. These nonetheless represent only a fraction of the actual salt intake, as Elio Riboli stressed earlier. However, this result shows that such a message can be heard and put into practice. Taking into account salt content of manufactured products, consumers who wish to reduce their salt intake end up absorbing almost as much salt as those consumers who don't pay attention to the issue.
It is thus necessary to achieve changes in the environment. But I'm personally convinced, as Pr.Blundell said, that wide-scaled social engineering is not easy to achieve.

Pierre MENETON

I'd like to bring about some additional facts concerning this topic. I agree, with Elio Riboli, on the fact that the salt content of several foods has decreased during the 20th century, thanks to improved preservation techniques and the cold chain. However, this trend has unfortunately been reversed since 1970. Salt consumption has been increasing eversince in most industrial countries (of more than 30 % in the USA). This is due to an increased intake of processed foods (sandwiches, quiches, croissants…) which contain a lot of salt.
My other point regards populations. When talking about an average consumption of 8 to 10g of salt for the French population, we shouldn't neglect the fact that these figures reflect situations that vary from 2 g to more than 25 g per person. People are usually not aware of this dramatic difference. This still raises crucial questions.

Walter C. WILLETT

It is quite admirable that the French Government is willing to consider these issues. It is an interesting example which I think it will require some social engineering as you describe. Any one company that wants to reduce salt intake on its own will be in trouble, because their food will taste different if other companies do not do it at the same time. So this is the way it has to be done.

We have a government with an interesting political philosophy at the moment: they can interfere in destroying any government around the world but they will not interfere with the salt content of American food products. It is a really serious problem because some of these manufactured products have huge amounts of salt. Elio is right and there has been some reduction overall, but some snacks for children have the full daily allowance of salt in one serving. Unless there is some control over that, there will be many people whose salt intake is far too high.

On the other hand, if one really is eating in the way we would like to encourage people to do, by eating very few processed foods, having lots of fruits, vegetables, wholegrain, nuts and legumes, all those inherently have very little salt intake and so if you are really following that kind of diet, almost automatically you will have a low-salt intake.

Christian REMESY

I'd like to refocus the debate on fruits and vegetables. First, fruits and vegetables consumption not only decreases the energetic intake and increases micronutrients intake, but also results in a modification of nutritional behaviors, that, to my mind, have not been tackled enough in our discussion. Cooking and adding vegetables to your plate, totally changes your nutritional behavior and we should insist on this point, beyond caloric balance and evident issues of physical activity.

Ambroise MARTIN

It is true that we focused a lot on biology, physiology and clinical aspects, while elaborating less on psychological factors, except for the intervention of Pr.Blundell. Sociological and economic aspects would also take another whole conference to be tackled...
Several speeches remind me of a study led by French sociologists on two simple axes: modern type of diet vs. traditional diet. The researchers looked at two elements, attitudes and actual behavior, breaking down the population into 4 categories: consistent attitudes (behavior matches attitude) for both groups and inconsistent ones (when behavior and attitude don't match) for both sides.
The study showed that the risk of obesity was higher for both inconsistent groups, since the discrepancy between attitude and actual behavior caused anxiety.
I think there's a lot to be done regarding these aspects: social engineering has to be taken into account, bearing in mind that this requires a certain level of consensus on actions to be taken and recommendations to be made, i.e. products that should be promoted through economic measures.

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The first four best posters have been selected by EGEA Scientific Committee for an oral presentation on Friday, May 14th , 2004.

Reduction of risk factors in overweight subjects of the Medi-RIVAGE study , benefit of a Mediterranean diet

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Objective : Medi-RIVAGE (Vincent et al,. 2004) was a primary intervention study undertaken with a Mediterranean diet-based nutritional approach. We present here the benefit of such a diet (MED) versus a low fat-low cholesterol diet: CDPA/AHA) in 150 overweight subjects.

Methodology : Beside a BMI>25 these volunteers presented at least another one risk factor (e.g; moderate untreated cholesterolemia, moderate hypertriglyceridemia…).

Different parameters were measured at baseline and after 3 months dietary intervention.

Results : Surveys and nutritional markers allowed observation of an increase in % carbohydrates and decrease in % lipids along with higher MUFA (+1.5% TEI, $p<0.05$) and PUFA (+0.8% TEI, $p<0.05$) but lower SFA (-4.6% TEI, $p<0.05$) in MED arm. The same pattern was observed in CDPA/AHAarm except for MUFA (-0.8% TEI, p=NS).
Numerous nutrients and plasma fatty acids were also quantified to evaluate the good adherence to the diets. We observed an increase in total fibre intake (+11.9%, $p<0.05$ in MED arm vs +4.7%, p=NS in CDPA/AHAarm) and an increase in EPA and DHA(+50.0%, $p<0.05$ and +24.0%, $p<0.05$ respectively in MED arm vs +22.2%, p=0.07 and +11.5%, $p<0.05$ respectively in CDPA/AHAarm).
After 3 months diet and adjustment for age, sex and tobacco, BMI fell off 6% ($p<0.05$) in MED arm (vs 4.5%, $p<0.05$ in CDPA/AHA arm) and we observed beneficial effects of both diets on biological parameters such as total cholesterol (-6.1% vs –2.5% in MED and CDPA/AHA diets respectively), LDL-cholesterol (-8.1% vs –3.3% respectively), triglycerides (-11.7% vs –2.7% respectively), insulin (-19.3% vs –18.1% respectively), glucose (-3.8% in both diets).

Conclusion : In obese or overweight subjects, weight loss has to be associated with a reduction of risk factors commonly present, it seems that the Mediterranean diet followed by the overweight subjects of our study has improved essential metabolic parameters. The amplitude of these beneficial changes is less marked after a low fat-low cholesterol diet.

Vincent S, Gerber M, Bernard M C, Defoort C, Loundou A, Portugal H, Planells R, Juhan-Vague I, Charpiot P, Grolier P, Amiot-Carlin M J, Vague P and Lairon D. The Medi-RIVAGE study: Mediterranean Diet, Cardiovascular Risks and Gene Polymorphisms. Rationale, recruitment, design, dietary intervention and baseline participants characteristics. (In press, Public Health Nutrition).

Individual changes in fruit and vegetable consumption between 2 and 16 years of age

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Introduction : to investigate the relationships between food (fruit and vegetable) consumed in early and late childhood.

Methodology : prospective cohort study conducted in healthy French children recruited among a population consulting for clinical examination in Public Health Centres for Children in Paris. Examinations were offered free of charge. The main motivation of families was to obtain a free check-up. From 1985, the dietician of the research team recorded nutritional intakes in children aged 10 months, 2 and 4 years using the dietary history method. When children were 6 year-old, the families were contacted to continue the follow up at home. At the age of 16 years, 92 children were still participating in the study.

Results : Table 1 shows changes in consumption of fruits and vegetables according to age and gender. In both sexes, the highest values were recorded at the age of 10 years. After the age of 14 years, girls ingested more fruit and vegetables than boys. This difference in consumption is consistent with differences in preferences. More girls than boys quoted fruits (32 vs 4%) or vegetables (43% vs 13%) as their favourite food. Correlation between consumption recorded at 2 year interval was high (Table 2). Between the ages of 2 and 16 years, the correlation is significant (r=0.26; p=0.02), mainly due to the contribution of fruit intake.

Conclusion : Fruit and vegetable consumption varies according to age and gender. Ahigh consumption of fruits in early childhood is associated with a high consumption in late childhood. As fruits and vegetables provide vitamins and fibres, this observation suggests that their consumption should be promoted early in life in order to maintain good habits.

Table 1 : Fruit and vegetable consumption (g) in the same children by sex and age

Ages (years)	Boys (n=54)	Girls (n=38)	p
2	164 ± 66	168 ± 87	0.81
4	274 ± 86	278 ± 110	0.86
6	273 ± 100	264 ± 108	0.67
8	280 ± 102	276 ± 107	0.85
10	298 ± 117	294 ± 90	0.86
14	236 ± 106	286 ± 139	0.06
16	233 ± 115	289 ± 118	0.03

Table 2 : Cor relation between food consumption (fruit and vegetable) recorded at different ages (n=92)

Correlation between ages (years)	r	p
2 and 4	0.47	<0.001
4 and 6	0.38	<0.001
6 and 8	0.55	<0.001
8 and 10	0.56	<0.001
10 and 14	0.52	<0.001
14 and 16	0.25	0.03
2 and 16	0.26	0.02

Food habits and adherence to nutritional recommendations in older diabetics

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Context : The risks associated with ill-balanced diabetes are particularly important in the elderly, increasing their risk of morbidity and mortality. This balance requires an adapted diet.

Objective : To describe food habits of diabetic subjects aged 65 and over, comparatively to non-diabetic subjects of the same age, and to evaluate their adherence to the French nutritional recommendations emitted by the ANAES organization (Agence Nationale d'Accréditation et d'Evaluation en Santé) for diabetic patients.
Methods : Data resulted from the epidemiological " 3Cités-Bordeaux " study, in which a nutritional survey was carried out by dieticians at home. This investigation included a food frequency questionnaire and a 24-hour recall of food consumption. The subjects were considered as diabetics if they reported diabetes and / or if they used hypoglycemic agents.

Results : 157 diabetic subjects and 1381 non-diabetic subjects took part in this study. The proportion of men was greater in the diabetic group than in the non-diabetic one; mean age did not differ between groups. The body mass index (BMI) was significantly increased in the diabetic group, with an average BMI of 28.6 for the diabetics and of 26 for the non-diabetics. According to the 24-hour recall, we estimated that the amount of calories consumed per day was lower in the diabetic group than in the non-diabetic one, but significantly only for women. In proportion of total energy intake, diabetics ingested less carbohydrates than the non-diabetics, men compensating by an increase in proportion of proteins and lipids, and women only by an increase in proportion of proteins. Compared to the recommendation for diabetics to consume 50% carbohydrates, 35% lipids and 15% proteins, diabetics in our study consumed on average 44.4% carbohydrates, 34.6% lipids and 21% proteins. According to the food frequency questionnaire, fruit consumption did not differ between diabetics and non-diabetics; 15 diabetics (9.6%) ate less than one fruit per day on average (less than 5 fruits per week). Diabetics ate vegetables as often as non-diabetics, with an average frequency of 3 vegetables eaten per day. Fish consumption did not differ between the 2 groups with a mean frequency of fish consumption of twice a week. However, diabetics consumed more often meat than non-diabetics. Nibbling was relatively frequent in the diabetic group, since 32 of them (20.4%) reported nibbling sweets between meals at least 5 times per week.

Conclusion : these first results showed that the food behaviors of the old diabetics differed partly from those of non-diabetic subjects of the same age. Some discrepancies with the French nutritional recommendations for diabetics are highlighted.

Characteristics of compliers and non-compliers with population goals for fruit and vegetables (≥ 400 g) and dietary fibre (> 25 g) intakes in Irish adults

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The intakes of fruit, vegetables and dietary fibre (DF) are low in Ireland (Galvin et al, 2001; O'Brien et al, 2003). Characteristics of compliers and non-compliers with both of the population goals for fruit and vegetables (≥ 400g) and DF (>25g) intakes were examined including anthropometric measurements, supplement use, smoking status, recreational physical activity and TV viewing. This study used data from the North/South Ireland Food Consumption Survey (Irish Universities Nutrition Alliance, 2001), which estimated habitual food intake using a 7-day food diary in a randomly selected representative sample of Irish adults (n = 1379) aged 18-64 years.

	Compliers (%)		Non-Compliers (%)	
	Men (n = 328)	Women (n = 293)	Men (n = 89)	Women (n = 224)
BMI Categor y				
Normal 18.5-24.9 kg/m2	35.5	52.0	34.6	50.9
Overweight 25-29.9 kg/m2	45.1	31.7	40.7	30.6
Obese ≥ 30 kg/m2	19.4	16.4	24.7	18.5
Waist Action Level*				
Below Action Level	54.8	51.4	44.3	53.1
Action Level 1 ≥ 94 (80) cm	25.4	25.3	31.1	18.4
Action Level 2 ≥ 102 (88) cm	19.8	23.3	24.6	28.6
Waist Hip Ratio Risk*				
Normal Risk < 0.95 (0.8)	21.0	39.8	19.7	46.9
Increased Risk ≥ 0.95 (0.8)	79.0	60.2	80.3	53.1
Supplement User	19.8	40.3	10.1	24.6
Cur rent Smoker	23.6	19.0	49.4	47.1
Takes part in recreational fitness				
≥ 5.0 MET	87.0	90.2	88.5	72.7
TV viewing > 4 hours per day	14.6	10.5	25.3	24.1

* Risk of development of CVD risk factors, values in parenthesis are for women.
MET = Metabolic equivalents.

Forty-five percent of Irish adults (53% men and 47% women) were compliers with both goals for fruit and vegetables (≥400g) and DF (>25g) intakes, while 23% (28% men and 72% women) were non-compliers. The mean BMI and waist circumference were 26.3 kg/m2 and 87.5 cm respectively in compliers and 26.5 kg/m2 and 85 cm respectively in non-compliers. Compliers were significantly ($p<0.001$) more physically active in recreational pursuits than non-compliers (31.2 MET v 21.8 MET), while non-compliers spent significantly ($p<0.001$) more time watching TVthan compliers (19.8 hr v 17.4 hr), particularly in women. A significantly higher ($p<0.001$) proportion of compliers were supplement users and a significantly lower proportion ($p<0.001$) were smokers than non-compliers.
In this study, more time spent in recreational physical activity and less time watching TV was associated with compliance. Weight status (as BMI, waist circumference or waist to hip ratio) has no affect on compliance with the population goals for fruit and vegetables and DF intakes.

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The Mediterranean Eating in Scotland Experience (MESE) project: Use of the Mediterranean diet score to evaluate dietary change in an internet-based, tailored intervention

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Background : Tailored dietary and psychosocial interventions have proved to be effective in motivating dietary change and internet-technology interventions have shown promising results in encouraging weight loss and physical activity.

Objective : To evaluate the effectiveness of an internet-based nutrition intervention promoting the Mediterranean Diet using the Mediterranean Diet Score (MDS), a composite score based on median intakes of nine components of the traditional Greek diet.

Methodology : Intervention trial using a quasi-experimental design. Subjects received either tailored dietary and psychosocial feedback and internet nutrition information (intervention group, n=53) or minimal dietary feedback and general healthy eating brochures (control group, n=19). All subjects were recruited from the University of Glasgow (intervention) and Glasgow Caledonian University (control), and were all healthy female volunteers. Feedback provided to both groups was delivered via electronic mail. Dietary advice provided to intervention subjects via an innovative Mediterranean Eating Website focused on increased consumption of four components of the Mediterranean diet, namely vegetables, fruit, legumes and MUFA/SFAratio. Subjects completed a 7d-estimated food diary at baseline and 6 months and intakes were energy adjusted to 2000 kcal. Dietary data were analysed to calculate the MDS for these four components and a score of 1 or 0 was given for each component depending on whether the cut-off point (median intake) was met or not.

Results : Forty one subjects in the intervention group and fourteen subjects in the control group completed both the baseline and 6-month dietary assessment. At the end of the 6-month intervention, the proportion of subjects in the intervention group achieving a score of 1 increased for 6 of the 8 dietary components and the increase was statistically significant for the legumes (p=.012) and MUFA/SFA ratio (p=.039) components. The proportion of subjects in the control group achieving a score of 1 increased for 4 components but these increases did not reach statistical significance. There was no significant difference in the proportion of subjects achieving a high MDS (≥4) at baseline compared to 6 months for either group. There was, however, a post-intervention significant increase in the mean MDS for the intervention (p=.019).

Conclusions : The MDS was able to detect dietary improvements in this group of healthy female volunteers. As information technology systems improve and general access to computers has increased, internet-based, tailored interventions that promote healthy eating in the context of the traditional Mediterranean diet have the potential to encourage greater consumption of plant foods in Scotland, in agreement with current dietary recommendations for health promotion and disease prevention.

The project was funded by the Greek State Scholarships Foundation.

Physiological effects of the potassium organic anions present in fruits and vegetables

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Organic anions are chiefly supplied by plant foods, especially fruits and vegetables, as partially neutralized K salts such as K citrate, K malate and to a lesser extent oxalate or tartarate salts. Animal products are also liable to supply K anions, essentially as phosphate. Failure to neutralise acidity generated by protein catabolism leads to low-grade metabolic acidosis, with possible long term deleterious effects on bone Ca status and protein status (since acidosis promotes Ca mobilization and proteolysis). This situation seems quite frequent with western diets and it may account for the relatively high incidence of osteoporosis and muscle protein wasting observed in ageing people. Providing a sufficient supply of K organic anions through fruit and vegetable intake (at least 3-4 g K daily) is recommanded, fostering the actual incitative campaigns ('5-10 per day') launched to promote intake of plant foods rich in complex carbohydrates and various micronutrients.
To further document this topic, we have designed a rat model of low-grade acidosis of nutritional origin and tested the impact of alkalinizing K salts (KHCO3 or K malate) vs. KCl. Urine pH (near 5 in rats fed the basal or KCl diets) rose up to 8 with the KHCO3 or K malate diets and, in parallel, Mg and Ca excretion were markedly reduced. Citraturia, practically nil with the acidogenic diets, was dramatically increased with the KHCO3 or K malate diets. Thus K malate (abundant in fruits and vegetables) appears as least as effective as KHCO3 to reequilibrate acidogenic western diet.
We studied thereafter the effectiveness of organic anions with different carbohydrates supply (starch or sugars, namely fructose/glucose/sucrose). Sugars elicited a slightly greater excretion of urea, Ca, Mg and sulfate than starch. K citrate strongly reduced Ca, Mg excretion and to a lesser extent urea excretion and it restored citraturia (together with 2-ketoglutarate excretion). It appears thus that sucrose tends to slightly worsen the effects of an acidogenic diet, but alkalinizing K salts turned out very effective to counteract acidosis effects with starch as well as with sugars. This observations may thus be relevant for fruits.
In a third set of experiments, we have investigated the potency of K organic anions with two dietary protein levels : normal (13%) or hyperproteic (26%). In our rat model, it appears that acidic urine (pH around 5.5) was found with both dietary levels, suggesting that the lack of alkalinizing anions in the mineral moiety of the basal diets is an important factor of acidification. Logically, urea excretion was greater with the 26% than with the 13% protein diet, but K citrate elicited as large increase in urea excretion with both dietary protein levels and practically abolished ammonia excretion. Sulfate excretion was also slightly greater with the high-protein diets and is was not depressed by K citrate, whereas this salt markedly reduced the Mg and Ca excretion elicited by acidosis.
These experiments indicate that K malate or citrate, present in fruits and vegetable, are quite effective to counteract low grade metabolic acidosis. Several points deserve further investigations, such as the actual impact of K organic anions on amino acid catabolism (especially sulfur amino acids) and on various consequences of low K/acidifying diets on antioxidant protection or glucose tolerance for example. The possible interactions between K organic anions and fibers should also be examined.

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Effect of preferences for, and consumption of, vegetables on lipid profile and some anthropometric parameters in women -preliminary study

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Objective : The aim of the study was to determine the preferences in vegetable consumption and their effect on some anthropometric and biochemical parameters in peri-menopausal women.

Material and methods : The study was carried out in 2003-2004 among 50, 39-59 y.o. women from the province of Warmia and Mazury. The body composition was determined based on anthropometric parameters measured, including: body weight (kg), height (cm), thickness of four skin-fat folds (mm), waist (cm) and hip circumference (cm) and the resulting indices, including: BMI (kg/m2), body fat contents (%FM, %) and WHR index. The biochemical examination included the measurement of the total cholesterol - TChol, HDL and LDL fractions and triglyceride (TG) concentrations. The experimental women expressed their preferences of consumption of 30 selected vegetables with the use of a 5-point scale: "I hate it", "I dislike it", I am indifferent", "I like it" and "I like it very much". An average value of these vegetable preferences was calculated. Consumption frequency was determined for the same 30 vegetables: "I don't eat it at all", "Seldom", "1-2 times a week", "3-4 times a week", "Every day" and an average consumption frequency was calculated. Based on the average values, two categories of vegetable consumption were determined: "average" and "high" and three categories of consumption frequency: "sporadically", "quite often" and "often". The analysed biochemical and anthropometric parameters between the experimental women with different vegetable preferences and consumption frequencies were compared with the use of the U Mann-Whitney test. Statistical analysis was carried out with the use of STATISTICA6.0 PLsoftware package at a significance level of p£0.05.

Results and conclusions : The completed statistical analysis did not indicate differences in the majority of the analysed anthropometric parameters and lipid indices between the women with different vegetable preferences and consumption frequencies excluding the level of triglycerides. Evaluation of the lipid parameters in different preference categories and different consumption frequencies indicates that the entire population of the women had increased levels of total cholesterol, LDLand atherogenicity index HDL/Tchol and low level of HDL, which can be disturbing with respect to health risk [1]. The preliminary study is the first phase of further, more detailed studies.

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The work was accomplished within the KBN research subject no. 3 P06T057 25.

Development and validation of a new questionnaire of habitual physical activity and food consumption for children 7 to 10 years of age

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Objective : To describe the development and assess the reliability and validity of the Childhood Activity and Food Intake Questionnaire (CAFIQ). CAFIQ is a tool designed to collect data about physical activity (PA) and food choices among children 7 to 10 years old.

Subjects : Parents and children (n=69) of one elementary school, in Florianópolis, South of Brazil.

Methods : CAFIQ was developed as a supervised classroom exercise to measure children's physical activities, food groups and foods items choices in a typical day of the week. It is an interviewer-administered structured questionnaire with 6 pages, 50 illustrations, a list of 11 choices of physical activity in three grades of intensities, 5 meals and 16 food groups. Reliability was measured through two rounds of data collection. Reference data for validation of the physical activity section (PAS) was a questionnaire completed by parents and teachers. Food section (FS) was validated against a 24-hour dietary recall administered individually to children. Analyses included intraclass (R) and Spearman correlation (rho), and adjusted kappa statistic (PABAK). Differences were examined using Wilcoxon, McNemar, and Kruskal Wallis tests.

Results : For the PAS, test-retest reliability range from rho=0.46 (transportation to the school) to rho=0.87 (PA attitude). The intraclass correlation was 0.85 for a general measure of PA. Using a proxy measure (parents and teachers report), the children were classified in three groups (low, medium, and high) according to the PA level. Scores obtained using CAFIQ appear to discriminate significantly ($p<0.05$) those groups. Regarding to the FS, the agreement between the two rounds was nearly 80%. None food item presented a PABAK coefficient lower than 0.3, suggesting a moderate to substantial level of reliability. The agreement between data obtained with CAFIQ and the reference method ranged from 42% for bread (afternoon period) to 92% for vegetables (morning). Substantial to moderate agreement was found for 17 food items, while it was poor for 15.

Conclusions : This questionnaire is a useful epidemiologic tool for surveillance, assessing broad intervention effects among groups or providing needs assessment data on selected nutrition and physical activity-related constructs. Despite the limitations of the present study, the results suggest that the questionnaire CAFIQ seems to generate reliable and valid data for both PA and food consumption.

Nutrient intake in a sample of pregnant women in Constantine area (Algeria)

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Food intake in pregnant women should be sufficient to meet energetic and nutritional needs linked to the physiological changes of the mother: increased blood volume and maternal tissues; and normal development of the foetus.
The aim of this study was to investigate the nutrient intake of 142 Algerian pregnant women, using a dietetic interview during prenatal examination.
The quantity of foods was estimated by household units, converted into nutrient intake in order to compare with recommendations.
The frequency of food intake, in decreasing rank order is: cereals products (100%), milk (87,3%), dairy products (70%), animal products (57,1% including fish 25,2%), legumes (56%). Fresh vegetables and fruits consumption differently varied according to the price and season.
The results show a large interindividual variability among women in energetic and nutrient intakes. Energy intake was 2029 kcal. The contribution of starchy carbohydrates was 326.5g / day, of lipids 48.94g / day and of proteins 68,94g / day. Fruit and vegetable intake was rather low. Nutrient deficiency concerned some minerals (iron and Ca) and vitamins (Aand D).

Nutritional models and dietary guidelines realization by the elderly living in North-Eastern Poland

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Objective : The aim of the work was to identify the characteristic nutritional models of the elderly and to compare them with dietary guidelines according to the healthy eating pyramid.

Materials and methods : The research included 354 people (76.9±1.63 years old) living in the North-Eastern Poland. The nutrients intake was specified by means of the 24-hour recall method [1], which, after having included loses, was compared with Poland's RDI at the safe level. For the characteristic nutritional models identification the factor analysis (the main components method) and the cluster analysis (grouping by the k-means method) was applied [2]. The diversity of the food rations nutrient value and products intake of people with different nutritional models was verified on the basis of the single-factor variation analysis (ANOVA) with the use of the STATISTICA v.6.0.

Results : In population 3 nutritional models were identified – low nutritive (LN, 56.5% of population), with the vegetable-fruits and vegetable fats domination (VFVf, 32.2% of population) and dairy-cereal and vegetable fats domination (DCVf, 11.3% of population). The significant differences in the nutrient value and products intake of the identified nutritional models were revealed (p£0.001). The DCVf nutritional model intakes grainy products in the average amount of 10.1 portion/day, vegetables – 2.0 portion/day, fruits – 0.4 portion/day, dairy products – 3.2 portion/day, meat and protein substitutes – 2.1 portion/day, fats and sweets – 4.0 portion/day, the VFVf: 6.3 portion/day, 3.4 portion/day, 0.9 portion/day, 0.9 portion/day, 2.9 portion/day, 3.0 portion/day, respectively, and the LN: 5.2 portion/day, 1.3 portion/day, 0.4 portion/day, 1.2 portion/day, 1.0 portion/day, 1.7 portion/day, respectively.

Conclusions : The significant diversity in the nutrients intake by the elderly was revealed. The identified nutritional models characterized the nutrient value of elderly food well. No nutritional model was compatible with dietary guidelines according to the healthy eating pyramid.

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Effects of calcium supplementations on serum lipoproteins, Apo B-100 and blood pressure in hyperlipidemic obese man

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Objectives : Control of hyperlipidemia and blood Pressure (BP) is vital in obese persons. Limited epidemiologic and experimental data support the possibility that dietary calcium intake play a role in body weight, serum lipoproteins and BP. This study was undertaken
to determine and compare the effects of administration of elemental calcium (EC) on the serum levels of lipoproteins, apo B-100, BP and body weight in obese persons in Iran university of medical sciences, Tehran, Iran from 2003 to 2004.

Methodology : In a double-blind placebo trial of parallel design, 49 hyperlipidemic obese male [total cholesterol (TC) and triglyceride (TG) greater than 200 mg/dl] were randomly assigned to receive 1250 mg of EC or placebo (control) for 8 weeks. Fasting blood samples were collected at the beginning and at the end of the period. TG, TC, LDL-c and HDL-c were measured enzymatically, calcium colorimeterically, apo B-100, immunoturbidometerically. The pattern of food consumption, socio- economic and anthropometric indices were determined by valid questionnares.

Results : There was a significant decrease in serum LDL-c (P=0.003), TC (P=0.001) , apoB (P=0.04), LDL-c / HDL-c (P=0.02), TC/ HDL-c (P = 0.01) and Systolic Boold Pressure (SBP) (P= 0.04) in calcium group compare to control group at the end of study but HDL-c, TG,diastolic blood pressure and body weight had no significant difference between two group at the end of study. There was no significant difference in daily dietary intake between two groups. A significant increase in serum calcium was observed in calcium group compare to control group (P= 0.02).

Conclusion : 1250 mg of EC for 8 weeks had benefical effects on serum LDL-c, TC, apo B-100, LDL-c /HDL-c, TC/HDL-c and SBP in hyperlipidemic obese men and so may reduce the cardiovascular disease risk.

The study of functional characteristics of weighting (loaded) foot in the groupe of obese children and adolescent during reduction of weight

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Objectives : This study is focused on finding the existence of changes in foot proportions and changes in the distribution of force in the sole during reduction of weight in obese children.

Methodology : Along of five-week weight loss courses for 39 children and adolescents (24 girls, 15 boys) between the age of 10 to 19 years, dynamic pressures were measured between the foot and footwear insoles using a Pedar instrument. The foot proportions were measured using the classical method and girth size was analysed the first in loaded and the latter in unloaded position (during sitting and standing). The results were evaluated with NovelWin software, which enables the establishment of maximum pressures at defined locations, the course of maximum force and centres of gravity. The measurement was conducted at the beginning of the course and after its completion.

Results : The average value of weight loss achieved 3.31 ± 1.85 kg (3.22 ± 1.74 kg for girls and 3.51 ± 2.18 kg for boys). From the extensive set of measured data, changes were analysed in values of maximum pressures in the frontal, arch and heel sections on the surface of the foot at the beginning of the experiment and at the end. The determined differences demonstrated that there is the dependence between the weight loss and the selected factors. Most significant was the relationship between the weight loss and girth changes at the metatarsophalangeal joint (toe joint area) (Fig. 1, 2). This determined dependency can be marked as highly significant in regard to the values known to increase the number of foot deformities and disease at the current child population.

Conclusion : The study proves that relatively small changes of weight had significant influence changes in width girth values. The data didn't prove a connection between obesity and foot deformities. A child's foot is evidently able to compensate for weight increases. Also the distribution of pressure on the foot indicates significant changes and this problem should be studied in detail.

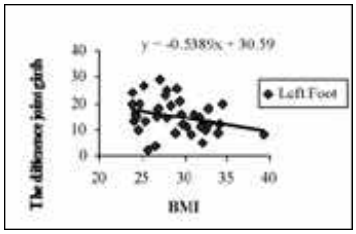

Fig. 1
The difference of joint girth in loaded and unloaded position dependence on BMI by left foot

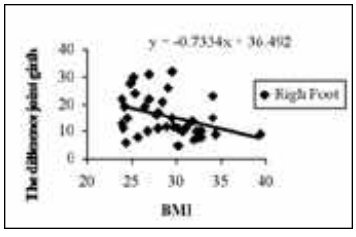

Fig.2
The difference of joint girth in loaded and unloaded position dependence on BMI by right foot

Prevalence of overweight and obesity and associated factors in Languedoc-Roussillon, a French Mediterranean region

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Mediterranean countries are currently observing a rapid increase of overweight and obesity rates among their populations. Several factors including lifestyle and food habit changes seem to be associated with this growing concern.

As part of the National Health Barometer on nutrition conducted in 2002 by the INPES, the prevalence of overweight and obesity were measured, the food consumption and physical activity estimated and knowledge and perceptions assessed. A representative sample of 988 adults (18-75yrs) was interviewed by telephone in Languedoc-Roussillon, a French Mediterranean region. Body mass index (BMI) was calculated, based on declared weight and height. Overweight (OW) was defined as 25£BMI<30 and obesity (OB) as BMI≥30. Dietary assessment was by means of a qualitative 24-hour recall.

The prevalence of overweight was 27,8% and of obesity 6,5%, close to national figures. Men were more likely to be overweight than women (37,3% vs 18,7%, p<0,001) but both were equally concerned by obesity (6,7% vs 6,4%). The prevalence of overweight and obesity increased with age (OW: 14,3% in 18-29yr-olds vs 39,6% in 60-75yr-olds ; OB: 5,1% in 18-29yr-olds vs 9,4% in 60-75yr-olds, p<0,001). Overweight was equally distributed within income or education level, but obesity was more prevalent in the population with low income and low education level: 62,3% of obese individuals had a monthly income <900¤ per consumption unit vs 42% in non obese individuals, p<0,01; 84,1% of obese subjects did not have baccalauréat education vs 55,0% in the non obese group, p<0,001). The number of meals/snacks eaten was the same between BMI groups but obese people ate more quickly than others (for lunch: 32min±21 for OB vs 39min±24 for OWand 37min±21 for others, p<0,05). Whatever their BMI groups, individuals made similar food choices except for a few products. Obese people were more likely to watch TV, doing so longer than others per day (176min±99 for OB, vs 128min±81 for OW and 125min±87 for others, p<0,001). They also practised less sport: only 29,1% of OB vs 40,3% of OW and 48,8% of others (p<0,01) had practised sport at least once during the last two weeks. However, they were more aware of the recommendation concerning daily physical activity: 54,8% of OWand 53,1% of OB vs 44,9% of others (p<0,01) believed they have to practice at least 30 min per day to stay healthy. Furthermore, there were no differences with the knowledge score on nutrition between BMI groups. Obese and overweight individuals did not all have an accurate perception of their weight excess: 26,2% of OW and 4,7% of OB said that they had "the right weight" whereas 7% of OWand 40,6% of OB declared they were "too fat" (p<0,01).

These discrepancies between relatively good knowledge and false perceptions are important to consider when implementing interventions aimed at managing overweight and obesity.

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Obesity and atherosclerosis-possibility of prevention

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Obesity is one of the atherosclerosis risk factor in children beside hypercholesterolemia and hypertensia. Atherosclerosis starts in the early childhood and preventive measure should begin as early as possible.
The purpose of this study was to determine blood pressure, the lipoprotein profile, and total cholesterol/HDL-C (FR), and LDL-C/HDL-C (IA) relation in obese children and in non-obese children.
This study included 758 children aged 6-15 years who came in Cardiologic Counseling Office Health Center Nis. There were 93(12.27%) underweight, 514(67.81%) non-obese, and 151(19.92%) obese, (69(9.10%) with P85<=BMI<=P95 and 82(10.82%) BMI>P95).
Each subjects* height and body weight were measured, and body mass index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters. The data of BMI are those of NHANES I (Am J Clin Nutr. 1991; 53:839-46). Obese children have been considered if BMI>=P85. Two categories have been defined. Children whose BMI are at the 85 the percentile or more, and less than the 95th percentile (P85<=BMI<P95), and children with BMI children with BMI at the 95 th percentile or more for age and sex (BMI>=P95). Children non-obese with P15<BMI<P85).
Systolic and diastolic blood pressures were measured in the right arm after the participant had been sitting for at least five minutes, 3 times in each subject with manometer.
Fasting plasma concentrations of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglyceride were measured. non-HDLcholesterol (non-HDLcholesterol=TC-HDL), total cholesterol/HDL-C (FR), and LDL-C/HDL-C (IA) were calculated.

Results : Systolic and diastolic blood pressures were significantly higher in obese children than in non-obese children (104.57 mmHg, 69.40 mmHg; 98.32 mmHg, 65.14 mmHg; p<0.001), and levels of TC, non-HDL-C, LDL-C, Tg, IA and FR were significantly higher in obese children (4.65 mmol/l; 3.33 mmol/l; 2.86 mmol/l; 1.05 mmol/l; 2.33; 1.31) than in non-obese children (4.35 mmol/l; 2.89 mmol/l; 2.49 mmol/l; 0.88 mmHg; 1.92; 3.24). The average HDL-C level was significantly higher in non-obese children (1.45 mmol/l) than in obese children (1.34 mmol/l)(p<0.01). There was not significant difference between blood pressures and lipoproteines in children with P85<=BMI<P95 and BMI>=P95 (p>0.05). Percentages of increased values TC(>5.17 mmol/l), LDL-C (>3.36 mmol/l) i Tg (>1.14 mmol/l) and percentage of reduced values HDL-C>0.9 mmol/l were in obese children (25.83%; 27.81%; 29.14%; 9.27%) higher than in non-obese children (11.09%; 10.12%; 17.32%; 6.42%).

Conclusion : It is very important to determine body mass index in children and detect obese children. Obese children should be early detected, inspected and controlled, and than they should be included in a diet or medicament treatment. Early discovery of obese children is one of the elements of atherosclerosis prevention.

Iron intake and status in relationship to the body mass index in adult Belgian women

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Objective : To investigate the relationship between body mass index (BMI) and iron intake and iron status in Belgian women at reproductive age.

Population : Adult women (18-39 years) from the region of Ghent (n=726) were examined in the year 2002.

Methods : The iron intake was determined on the basis of a newly developed and validated computer-assisted iron intake assessment tool. The iron status was determined on the basis of the following indicators: haemoglobin, serum ferritin and soluble transferrin receptors (sTfR). Body height and weight were measured in a standardised way. Individuals were divided in 4 groups according to their BMI as follows: 1) BMI <20 (n=113), 2) BMI 20 - <25 (n=406), 3) BMI 25 - <30 (n=146) and 4) BMI ≥30 (n=61). To compare the means in the different groups the Mann-Whitney-U test was used. Spearman's correlation coefficient was determined to investigate the relationship between BMI and iron intake respectively iron status.

Results : The median iron intake (mg/day) in the different BMI categories (1 – 4) was as follows: 10.39, 9.69, 9.93 and 9.40 mg/day. No significant differences between any of the categories were found. Median haemoglobin concentrations in the different BMI categories were: 13.40, 13.50, 13.55 and 13.70 g/dl. The median sTfR values were: 1.11, 1.08, 1.13 and 1.25 mg/l. Finally, for serum ferritin the median values were: 23.00, 26.30, 28.85 and 38.30 ng/ml. Only for sTfR and serum ferritin significant differences were found. Individuals with a low BMI (<20) had a significant lower value for sTfR and for serum ferritin than obese individuals (BMI ≥30). Women with a normal BMI (20 - <25) had also a significant lower value for sTfR and serum ferritin than obese women (BMI ≥30) and also a significant lower value for sTfR, but not for serum ferritin in comparison with overweight individuals (BMI 25 - <30). Finally, individuals with overweight (BMI 25 - <30) had a significant lower value for sTfR than obese persons (BMI ≥30). Spearman's correlation coefficient for BMI and iron intake was –0.031, for BMI and haemoglobin 0.055, for BMI and sTfR 0.075 and for BMI and serum ferritin 0.126.

Conlusions : In general, iron status is considered to be negatively associated with sTfR and positively associated with serum ferritin. Our data suggest that the association between BMI and iron status is difficult to interpret, given that a comparison of different BMI categories results in lower values of sTfR accompanied by lower values of serum ferritin and vice versa. Further analyses are needed to explore these findings in more depth.

Obesity, nutrient intake and the time spent drinking tea in a group of Morrocan Sahraoui women

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Objective : To study relationship between obesity, dietary intake and the length of time spent drinking tea daily.

Methods : Data were obtained on 249 urban women aged 15 and older not pregnant who live in Laayoune a city of Morocco. Only subjects identified as Saharan origin were eligible for this investigation. The following data were collected: Body weight, height, and waist circumference. Intake estimates were based on 24-hour recall interviews. Subjects completed also a questionnaire indicating their activities. This questionnaire served as a basis upon which subjects are grouped according to the time they spent drinking tea: those who spent less than 3h/d (group 1) and those who spent 3 or more h/d (group 2).

Results : The results showed that tea is the beverage most consumed by this population. The mean time spent in drinking tea is 3hours per day. Also Body mass index (BMI), WC and glucose Intake were significantly higher among group 2 than group1. Subject in-group 1 consumed more energy, protein, carbohydrate, Vitamin B1, fibre, Vitamin C, Magnesium and Zinc than those of group 2. Intake of fat is not significantly different in both groups.

Conclusion : The results show that in addition to promoting physical activity, it appears to be necessary also to control the composition of the diet in order to prevent obesity and its complication.

Obesity and central obesity among urban Sahraoui women of South Morocco

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Objective : To study the prevalence of obesity and central obesity in Moroccan Sahraoui women, and to examine the influence of age, calorie intakes, physical activity, marital status, education level and desire to lose weight on obesity.

Methods : We randomly selected 249 urban women aged 15 and older, not pregnant who live in Laayoune city of South Morocco. Only subjects identified as Sahraoui origin were eligible for this investigation. The following data were collected: Body weight, height, circumferences of waist and hip, calorie intakes, physical activity, marital status, education level, and desire to lose weight.

Results : The overall prevalence of overweight and obesity was respectively 30% and 49%. It was already very high at younger age. Central obesity also was very prevalent and increased with age. 68% of women had a WHR >0.85 and 76% had a WC > 88. Energy intake, intake of sugar, and the time spent in traditional sedentary occupation were positively correlated with obesity whereas the time spent in walking activity was negatively correlated with obesity. The prevalence of obesity was higher among married than unmarried women and was not influenced by the education level. Only a very small percentage of the female population expressed a desire to lose weight.

Conclusion : High prevalence of obesity, even in young adults, need immediate attention in terms of prevention and health education in the urban Sahraoui women.

Analysis of problems conected with wearing special prophylactic shoes for diabetics type II

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Objectives : The issue of diabetics footwear wearing has been systematically explored only in the last decade. The most important assertion was found, that the lesion (injury) on a diabetic's foot is related to wearing unsuitable shoes. In The Czech Republic the prophylactic footwear is offered to diabetics with the diabetic foot syndrome. This footwear is partly paid by insurance companies.

Methodology : In the Zlín region (CZ), marketing research was conducted with a focus on understanding the consumer behaviour of diabetics. The research (made by oral questionnaire) was pursued by means of the diabetological clinic with the diabetologist and was also supplemented by controlled interview with diabetics. Questionnaires were given to 158 diabetics of type II of whom 98 were women and 60 men in all age categories. 20 parameters were monitored. The goal was to determine the subconscious of diabetics about prophylactic footwear, how much are diabetics pliable to purchase one pair of shoes in relation to length of diabetes duration and current state of their feet. The investigation lasted 3 months and it hasn't been finished yet. It is presumed that 230 respondents will be addressed.

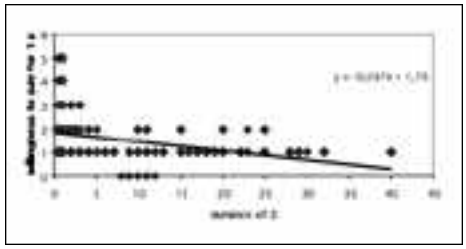

Fig. 1

Results : Sufficient number of respondents allowed us to present following results. More than 76 % of diabetics were older than 50 years. The average length of diabetes durance was 7,25 years. Relatively high quantity of diabetics (63,3 %) is pliable to pay no more than cca. 30 EUR for 1 pair of prophylactic footwear and only 6,4 % took as the acceptable price in range from 43 to 57 EUR. Approximately, every third diabetic (37.6 %) told that they didn't buy prophylactic shoes because they were too expensive. Almost the same count of diabetics (38,6%) knew about prophylactic shoes and knew their advantages, but only 17,7 % of diabetics owned them. The biggest influence that affected diabetic purchase of special shoes was from their physician (41,7 %). Surprisingly, with the increasing length of diabetes mellitus durance the amount of money those diabetics are decided to pay for one pair of the special footwear decreases (fig.1) and the satisfactory with the state of their feet also declines (fig. 2).

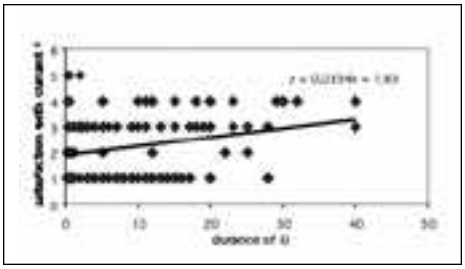

Fig. 2

Conclusion : By this research was found, that the diabetics understanding about the existence and advantages of prophylactic footwear are deficient. Dangerously there are a low number of diabetics that are willingness to protect their feet and to wear prophylactic shoes regularly. Thereafter there was proved that with increasing age the willing of diabetics to participate financially by purchasing of suitable prophylactic shoes declines even if they know that the state of their feet are getting worse.

Paradoxical effect of coronaropathy on n-3 docosahexanoic acid (DHA) levels in erythrocyte from diabetic patients in Marseille

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Background : Recent developments confirm and extend the concept that n-3 (omega 3) fatty acids are beneficial in the prevention of cardiovascular diseases and sudden cardiac death. Many reports have shown inverse positive correlation between n-3 polyunsaturated fatty acids (PUFA) and coronary artery disease (CAD). Our previous study with Mediterranean people (where diabetic patients were excluded) showed association between CAD and a decreased n-3 PUFAlevels in erythrocyte phospholipids. In fact, diabetes is known to profoundly impair the omega 3 levels in practically all tissues but nothing is known about the n-3 PUFAstatus from diabetic patients with CAD.

Objective : To investigate the erythrocyte and plasma fatty acid patterns in diabetic patients with and without angiographic coronary stenosis.

Methods : A total of 20 consecutive patients with diabetes were included between June to august 2003. The erythrocyte membrane fatty acid patterns were analyzed by gas chromatography in 8 diabetic patients without coronary stenosis (Group D) and compared to 12 diabetic patients with coronary stenosis (Group D+CAD).

Results : Mean percentage (SE) of DHA (C22:6 n-3) in erythrocytes was 4.7 (0.3) in D and 6.6 (0.4) in D+CAD (P = 0.003). The values for the most abundant n-6 PUFA (arachidonic acid) in erythrocyte were 17.0 (0.9) in D and 17.7 (0.7) in D+CAD, (P = 0.3). The n-3/n-6 PUFA balance from diabetic patients with CAD is similar to control patients without diabetes or CAD (data not shown). This study shows for the first time that the well known alteration in n-3 PUFA levels induced by diabetes is not found in erythrocytes or plasma from diabetic patients with CAD.

Conclusion : This effect seems a paradox. Explanations of this paradox could be various for example: nutritional changes in consumption habits, increased conversion to long chain PUFA, decreased metabolism of n-3 PUFA, etc...

Improvement of type 2 diabetes and metabolic syndrome after weight loss following bariatric surgery in severely obese subjects

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Background and aims : Obesity is strongly associated with type 2 diabetes mellitus and the metabolic syndrome (especially dyslipidaemia and arterial hypertension). Achieving and maintaining weight loss with life-style changes in severely obese diabetic patients remains a real challenge so that bariatric surgery may be proposed in well-selected patients with severe refractory obesity. We compared the efficacy of two surgical approaches, either gastroplasty (GP : vertical-banded gastroplasty or adjustable silicone banded gastroplasty) or gastric bypass (GB : “Roux en Y” technique)), with the results obtained with classical medical approaches, on body weight loss and related metabolic changes in severely obese patients with type 2 diabetes.

Material and Methods : In a first short-term evaluation, results of weight loss, blood glucose control, lipid profile and blood pressure were compared 29 ± 9 months after medical treatment (n = 14), 28 ± 4 months after GP (n = 24) and 28 ± 14 months after GB (n = 14). In a second long-term evaluation, results were compared 79 ± 30 months after medical treatment (n = 14) and 105 ± 31 months after GP (n = 17) (no available long-term data with GB)..

Results : In the short-term evaluation, no significant changes were observed with medical treatment regarding body weight (body mass index or BMI : from 40.8 to 41.0 kg/m_), as well as fasting blood glucose concentrations, HbA1c levels, lipid parameters and systolic/diastolic blood pressure. In contrast, significant ($p < 0.05$) reductions were observed after GP regarding BMI (from 44.8 to 33.3 kg/m_), fasting glycaemia (from 8.6 to 5.8 mmol/l) and HbA1c (from 8.3 to 5.6 %). Similar results were observed after GB with significant reductions in BMI (from 41.8 to 29.2 kg/m_), fasting glycaemia (from 8.9 to 6.1 mmol/l) and HbA1c (from 8.7 to 6.2 %). Similar reductions in triglycerides (from 2.6 to 1.4 mmol/l with GPand from 3.6 to 1.3 mmol/l with GB) and arterial pressure (from 167/98 to 137/78 mm Hg with GP and from 166/95 to 133/79 mm Hg with GB) were observed with the two surgical methods. In contrast, the decrease in total cholesterol was greater with GB than with GP(- 16 % versus – 6 %, $p < 0.05$), presumably because of partial fat malabsorption associated with GB. In the long term, BMI was almost stable with medical management (BMI from 40.8 to 40.3 kg/m_) and pharmacological treatments should be intensified in order to keep almost similar metabolic control. Interestingly, after GP, BMI significantly decreased from 42.7 to 33.5 kg/m_, fasting glycaemia from 9.4 to 7.8 mmol/l, HbA1c from 8.2 to 6.9 %, total cholesterol from 6.2 to 5.4 mmol/l, triglycerides from 2.9 to 1.8 mmol/l, and arterial pressure from 163/87 to 143/78 mm Hg. In contrast to patients receiving medical treatments, patients treated with GPor GB obtained better metabolic results in both short- and long-term in spite of significant reductions of antidiabetic (insulin, sulfonylureas and/or metformin), antihypertensive and lipid-lowering pharmacological agents. No serious side effects were observed in the two surgical groups throughout the study.

Conclusions : As compared to classical medical treatment, bariatric surgery results in better short-term and long-term control of blood glucose and other cardiovascular risk factors related to the metabolic syndrome in severely obese patients with type 2 diabetes. Because of the poor overall prognosis of such patients, bariatric surgery should be considered as a valuable alternative after failure of medical approaches, but always after a careful initial evaluation and under strict medical supervision by a multidisciplinary tea.

Xylooligosaccharide improves blood glucose independent of BMI in type II diabetic patient

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Xylooligosaccharide is a prebiotic and beneficial to decrease blood lipids and blood pressure. Our previous studies showed xylooligosaccharide alleviated hypertriglyceridemia, prevented postprandial hyperglycemia and decreased body fat in fructose induced endogenous glucose intolerance animal model.

Objectives : This study was to evaluate the effect of xylooligosaccharide supplementation on blood glucose and body mass index in type II diabetic patients.

Methodology : Subjects with type II diabetes were recruited from local clinics. Food frequency questionnaire was finished with the instruction of professional dietitian in the beginning of the study. The diet and medication was maintained as usual except 2g per day xylooligosaccharide were given in the 8 weeks experimental duration. Body mass index, blood glucose, insulin, lipids, blood pressure, and urine were assayed in the beginning and final. Casual blood glucose and urine test were preceded every two weeks. Patient's health status was monitored by physician during the whole experimental period.

Time		Xylooligosaccharides— 2g		
Assay		0 week (%)	8th week (%)	
BMI	BMI<18.5	0.0	0	
	18.5<BMI<24	33.3	16.7	
	24<BMI<27	50.0	66.7	
	BMI>27	16.7	16.7	
HbA1c	< 7 %	0.0	16.7	
	> 7 %	100.0	83.3	
Assay	Time	2nd week (%)	4th week (%)	6th week (%)
Casual	< 200 mg/dl	33.3	33.3	66.7
Plasma Glucose	> 200 mg/dl	66.7	66.7	33.3

Results and conclusions : Xylooligosaccharide 2g per day improves HbA1c and blood glucose independent of BMI in type II diabetic patient.

Procyanidin extract (PE) modulation of Cu/Zn-superoxide dismutase expression in non-diabetic and streptozotocin-induced diabetic rats

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Free radicals and oxidative stress have been implicated in the aetiology of diabetes and its complications. Glucose oxidation is believed to be the main source of free radicals, particularly superoxide anion radicals. Given the powerful antioxidant activity described for PE , we hypothesized that PE supplementation would normalize the changes in oxidative stress markers caused by the hyperglycemic state of diabetes.

This in vivo study has examined whether acute administration of grape seed-derived procyanidin extract (PE) modifies the hepatic gene expression of Cu/Zn-superoxide dismutase (Cu/Zn-SOD), the principal superoxide scavenging enzyme in normal and streptozotocin-induced diabetic rats.

Diabetes was induced in male Wistar rats by a single injection of streptozotocin (70mg/kg body weight) resulting in polyuria, glycosuria and hyperglycemia (ª 20mM) 2-3 days post-induction. All studies were carried out one week after STZ had been injected. Normal and diabetic rats were treated with an oral gavage of PE (250mg/Kg body weight).

Although hyperglucemia-associated diabetes may induce a stress response mechanism, we found no differences in the enzymatic activity of Cu/Zn-SOD between diabetic and non-diabetic control rats. We observed that the effect of PE was similar in diabetic and non-diabetic rats. PE treatment did not change either mRNA or protein levels of Cu/Zn-SOD although the enzyme activity was observed to increase slightly (about +20%) with respect to PE non-treated animals.

This is an agreement with previous results from our group, which showed mainly post-translational regulation of Cu/Zn-SOD by PE in rat hepatoma cells (Fao).

These results support that procyanidins act post-translationally on Cu/Zn-SOD expression to exert their protective effect.

Ef fects of a fructose-enriched diet on antioxidant status and antioxidant enzyme expression in spontaneously hypertensive rats

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Fructose consumption by Wistar and Sprague-Dawley rats induces type 2 diabetes resulting in hyperglycaemia, hyperinsulinaemia and antioxidant status alteration. No similar experiment has ever been carried out with hypertensive rats.

Twenty spontaneously hypertensive rats (SHR) were divided into two groups and fed a 60%-fructose diet or a control diet (60% starch). Blood and liver lipid peroxidation and antioxidant status were studied after 3 months. The Elisa method was used for insulinaemia determination. Whole blood, erythrocytes, plasma and liver antioxidant status was determined by a KRLTM test: red blood cells (RBC) were subjected to free radical generator, RBC antiradical resistance was expressed by the time to reach 50% haemolysis. Lipid peroxidation was measured by thiobarbituric acid-reactive substance (TBARS). The antioxidant enzyme activities [superoxide dismutase (SOD) and glutathione peroxidase (GPx)] were measured with biochemical methods and their expressions were studied by semi-quantitative and Real time PCR.

Compared with the starch diet, the fructose diet induced hyperglycaemia and hyperinsulinaemia. Moreover, the fructose diet diminished the whole blood antioxidant status. This is associated with an increase in plasma TBARS concentrations and a decrease in erythrocyte GPx activity and glutathione concentrations. The fructose diet, however, improved liver antioxidant status by increasing SOD and GPx activities. GPx mRNAin liver tissues in the fructose fed rats showed a decrease, while little changes were observed in SOD mRNAin this organ. These findings suggest that the fructose diet increases peroxidative damage in whole blood and not in liver, and leads to hyperinsulinaemia associated with hyperglycaemia, therefore type 2 diabetes.

Diabetic angiopathy : Structural survey of the aortic atherosclerosis among the diabetic sand rat

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Introduction : the type 2 diabetes mellitus is emerging as a threatening public health problem in Algeria. The toxic effects of chronic hyperglycemia induce a large number of alterations in vascular tissue that potentially promote accelerated atherosclerosis.

The pathogenesis of the diabetic syndrome (DS) is not been yet fully elucidated so a better understanding of its onset and progress to the aorta tissue level of a particularly auspicious animal: 'natural'Psammomys obesus (NPO) can help us to identify some agents likely to inhibit human angiogenesis.

Objectives : Through a study of NPO population our aim is to show a direct relationship between a relatively high energy diet and the DS regardless of any other etiological factor. Then to outline on the morphological and ultrastructural levels any impact of such DS on aorta arterial wall at different development stages of the diabetes.

Material and method : Our study was conducted over 62 NPO of the both sexes, caught in South west of Algeria divided into 2 groups. A first one of 24 was kept as 'witnesses'group and was fed on Sahara halophile plants. As to the second group of 38 animals were on a standard laboratory diet program. The experimentation period lasted 12 months. Animals were regularly followed on both ponderal and biochemical levels throughout the DS development. Sacrifices were done every three months.

Results : The morphological and histo-enzymological aspect showed an alteration of the elastic fibers of the media and enrichment in collagen and in glucosaminoglycans. Enzyme's activity linked to the parietal lipolyse (esterase, cholinesterase) decreased strongly among the diabetics; correlatively the neutral lipids accumulate in the intima and in the internal part of the media. At the ultrastructural level deep changes of the aortic wall were observed: the conjunctive tissue was altered and disorganized, the elastic fibers were thinned, numerous ruptures were observed, and the internal elastic limit was fragmented. The development of the collagen tissue entails a real fibrosis. Deep degenerative changes affected the smooth muscular cells: inflation of the mitochondria's, vacuolization of the cytoplasm and denaturation of the nuclear substance. These cells ended up necrotizing and one could observe many cellular remnants in the affected zones. The arterial lesions were especially frequent to the last stage of the illness where animals became insulin dependant.

Conclusion : It was shown that we could induce a DS on NPO through a relatively strong caloric diet and that a direct relationship exists between diabetes and cardiovascular complications of the aorta regardless of any other etiological factor. This animal is definitely a suitable model for induced diabetes study since its phenotype in case of angiopathy is similar to what is observed on humans. Recent study have come to the same results confirming NPO is a model suitable for research works on angiopathy pathogenesis and for identification of inhibitors of the proteic glycation at the human population.

Phenotypic Frequencies HLA DR and Genetic Risk of Type 1 Diabetes in the Area of Tlemcen (West-Algeria)

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Background : The principal genomic region controlling the predisposition to the Type 1 insulin dependent diabetes (type 1 IDD), is that of the major complex of histocompatibility (HLA) of class II. Besides, the types of HLA associated with it vary according to studied populations. Jointly, we tried to measure the phenotypic frequencies of associations of HLA class II DR3 and/or DR4 antigens, detected by serologic method of microlymphocytotoxicity, in diabetic and nondiabetic (ND) subjects originating from the area of Tlemcen (West-Algeria). Specifically, we tried (aim) to decode HLADR molecules of greater susceptibility to the genetic risk to develop the disease in this area. In this respect, we randomly recruited ninety-one related subjects, thirty-nine type 1 IDD and fifty-two ND controls, at the Board of Internal Medicine of the University Medical Center of Tlemcen (West-Algeria), for a case-control retrospective study.

Results : Singularly, the frequencies of DR3 antigens were comparable between the type 1 IDD and the ND and do not show association with the disease ($p = 0.9180$, OR <1, log OR <0) ($p < 0.05$ was considered significant). But, DR4 and DR3DR4 antigens were associated with susceptibility to the development of type 1 IDD (OR > 1, log OR > 0, that is respectively OR confidence interval 0.73-6.11 and 0.38-4.00, 95% CI) (so, there is susceptibility). No incidence was related to the sex for the frequencies of DR3 ($p = 0.2646$) or DR3DR4 molecules ($p = 0.0699$). However, significant differences in HLA DR4 frequencies were related to the sex between the type 1 IDD and ND ($p = 0.0085$).

Conclusion : Altogether, the strongest association with the Type 1 IDD was noticed in HLADR4 antigens followed by the DR3DR4. This study revealed a ethnic characteristic of the area of Tlemcen that interminably witnesses a history of consanguinity marriages. Irrefutably, the studies of associations between the disease and genetic polymorphisms must be contributed in the absence of consanguinity to eliminate ambiguities in interpretation of the results.

Validation of dairy products intake frequency questionnaire ADOS-Ca used for osteoporosis risk by evaluation of calcium intake and estimation of calcium deficiency risk

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Objective : Validation of dairy products intake frequency questionnaire ADOS-Ca, worked out as a diagnostic test for quantitive calcium intake assessment and estimation of its deficiency risk taking into consideration osteoporosis risk.

Materials and methods : In the work the compatibility of calcium intake estimation obtained according to ADOS-Ca test with the evaluation obtained by 24-hour recall method, repeated for 7 following days [1]. The research was carried out among 90 students aged 21-26. On the basis of the questions included in the questionnaire, concerning the amount and the frequency of 11 dairy products intake during a week and the agreed indices of frequency intake, the mean Ca/person/day intake (x±SEM) was assessed. For comparisons the mean calcium intake from dairy products were used, obtained from the 24-hour recall method, repeated 7 times. In the statistical analysis the T test and tau-Kendall correlation coefficient (r), with p£0,05 were used. Test ADOS-Ca diagnostic accuracy was determined by sensitivity, specificity and Youden ratio [2].

Results : There were no differences in intake of calcium between the value obtained according to diagnostic test and the 24-h recall method (women p=0.156; men p=0.684). The average consumption of calcium assessed by the diagnostic test ADOS-Ca in comparison to that of 24-h recall method amounted for men to 619±54.6mg and stated 92.5% of the calcium amount assessed by means of the 24-hour recall method, and for women 434±33.0mg and 96.4% (r=0.64), respectively. The sensitivity ratio amounted for men to 78% and for women to 90%, the specificity ratio to 74% and 62%, respectively, and the Youden ratio to 64.6% and 70.6%, respectively.

Conclusions : The results permit for a satisfactory evaluation of the diagnostic test as a simple tool for quantitative estimation of calcium intake.

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The work was accomplished within the KBN research subjects no 3 P06T039 22.

A new anti-atherogenic mechanism of plant sterols : the reduction of oxysterols in human plasma

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Objectives : Many studies indicate that an increased level of oxysterols in the serum and in the vascular wall plays a fundamental role in the pathogenesis of atherosclerosis. Moreover, oxysterols may induce the processes of apoptosis, necrosis, and inflammation. So far we have proved that plant sterols contained in fat spreads not only lower LDL-cholesterol, but also reduce the levels of C-reactive protein and anti-ox-LDLantibodies.

Methodology and results : In the present studies we tested the hypothesis that plant sterols may exert an effect on the level of oxysterols in plasma. 42 young male volunteers participated in the experiment. They were randomized to two groups: one consumed margarine supplemented with PUFA omega-6, and the other consumed fat spread enriched with plant sterols. After 4 weeks of the study, in both groups a significant reduction in LDL-cholesterol was found (6,7% in PUFA group and 11% in sterols group), but in the sterols group, significant (ANOVA and TUKEY Test) reductions in hCRPby 23,2% and 7-ketocholesterol levels by 14,3%, and 7b-hydroxycholesterol levels by 15,8% were observed.
In an independent experiment we have also demonstrated that plant sterols significantly inhibit the absorption of oxysterols studied (7-ketocholesterol and 7b-hydroxycholesterol) from egg powder during postprandial lipaemia.

Conclusion : In conclusion, our studies indicate that plant sterol may have also preventive action in cardiovascular disorders by inhibiting the absorption of oxysterols from food.

Six weeks consumption of olive phenols increased urinary phenol concentration without affecting measures of oxidative damage in humans

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Objective : to determine whether 6 weeks consumption of olive oil phenols with or without vitamin E improves measures of oxidative damage in humans.

Methods : In a parallel study design, 60 volunteers aged 45-70y were randomized into four groups of 15 persons. Body weight was equally distributed among the groups. All volunteers consumed daily 30 g of margarine for 6 weeks. The four groups received either a control margarine; a margarine fortified with a phenol rich olive extract (about 100 mg phenols); a fortified margarine with 100 mg of vitamin E or a fortified margarine with a phenol rich olive extract (about 100 mg phenols) plus 100 mg vitamin E. Fasting blood samples were taken before and after the intervention period for analysis of measures for oxidative damage. At the end of the study, 24h urine was collected from the control group and the group receiving the margarine with the phenol-rich olive extract, to measure olive phenols and phenolic metabolites.

Results : Consumption of olive phenols for 6 weeks resulted in increased urinary hydroxytyrosol and its oxidation product 3,4'-dihydroxyphenylacetic acid, but did not affect measurements of oxidative damage. Consumption of vitamin E protected against oxidative stress as demonstrated by an increased lag-time of ex vivo LDL oxidizability, a reduced maximal LDLoxidation rate and a reduced lipid oxidation measured as plasma F2-isoprostane levels.

Conclusion : Six weeks consumption of olive phenols increased phenol concentration without affecting measures of oxidative damage in humans. Consumption of vitamin E, however, reduced lipid oxidation, measured as increased resistance of LDL to oxidation and reduced plasma F2 isoprostane concentration.

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