THE 260 HF DIET, IDEAL FOR STUDYING OBESITY AND ITS COMPLICATIONS

Dr A. Géloën (alain.geloen@insa-lyon.fr) and V. Pierre - Research Laboratory into the Cardiovascular system, Metabolism, Diabetology and Nutrition. INSERM U.1060/University of Lyon1/INRA U. 1235/INSA of Lyon/Lyon Civil Hospices (France)

The increase in obesity in westernised countries, that is to say, those that have fallen victim to fast food, continues to rise all the time, despite the campaigns aimed at informing the populace and raising awareness. Obesity is not just an aesthetical matter, since the excess fat provokes a wide range of pathologies: type II diabetes, hypertension, cancers, etc. It is absolutely essential, in order to study the mechanisms of these pathologies, to have efficient and reproducible models at one's disposal. In order to induce obesity and to study the pathologies associated with obesity, we need a nutritional diet which is rich in calories (hypercalorific) and in lipids (hyperlipidic). A hyperlipidic hypercalorific diet exists, made by a North–American company, but at the time of launching our trials, supply was stopped for reasons unknown to us. Being acquainted with the SAFE company, we enquired of Mr Martel as to the feasibility of such a diet. Over several telephone exchanges, a diet was put together, but would it prove effective for rats and mice?

There is no mystery to it: if you eat too much and too many fatty things without increasing your expenditure of energy, you get fat. Rats are no exception to the rule. When the diet is administered to young Wistar rats, their body mass increases by 14 % in four weeks, 25 % in eight weeks and 32 % in twelve weeks, when compared to that of rats nourished with a standard AO4 diet containing 4 % lipids (see Figure 1). The mass of the main adipose tissue increases by 300 % after a month on a hyperlipidic hypercalorific diet. This increase levels off at around +250 % of the fatty mass after 8 and 12 weeks. The rats subjected to the 260HF diet quickly put on weight, when compared to the control group, but, equally, their glucose tolerance deteriorates rapidly. Effectively, if one carries out a glucose tolerance test by having the animals drink a certain quantity of glucose solution and by measuring the development of glycaemia, one notes that glycaemia in rats subjected to the 260HF diet increases more than that of the control group and, above all, takes longer to recover to the base value (Figure 2).

This intolerance to glucose signals the beginning of type II diabetes, which is associated with obesity.

Until recently, adipose cells were considered as merely cells whose size increased or diminished in relation to the greater or lesser intake of calories regarding energy expenditure. Nobody showed any especial interest in these cells. It is only of recent date that it has become apparent that these cells secrete proteins, freed into the body's circulation and which act on other organs. This is the very definition of a hormone. Adipose cells have, then taken on the status of endocrinal cells. Effectively, they produce hormones that are extremely important, such as leptins, which inform the brain as to the quantity of adipose tissue present. Another important hormone is adiponectine, which enhances the sensitivity to insulin. Today, adiponectine is the best metabolic link between obesity and resistance to insulin. It is, then, essential that we understand the mechanisms that govern the secretion of these adipose hormones (called adipokines) in order to prevent the metabolic complications stemming from an excess of fat. As may be observed in the inserts of Figure 1, the size of the adipose cells increases with the body mass in animals fed with the standard diet, but this increase in the diameter of the adipocytes is much greater in animals fed with 260HF. Our conjecture is that the size of the adipose conditions their hormone production. This is a conjecture which we are able to put to the test, thanks to the 260HF diet (SAFE).

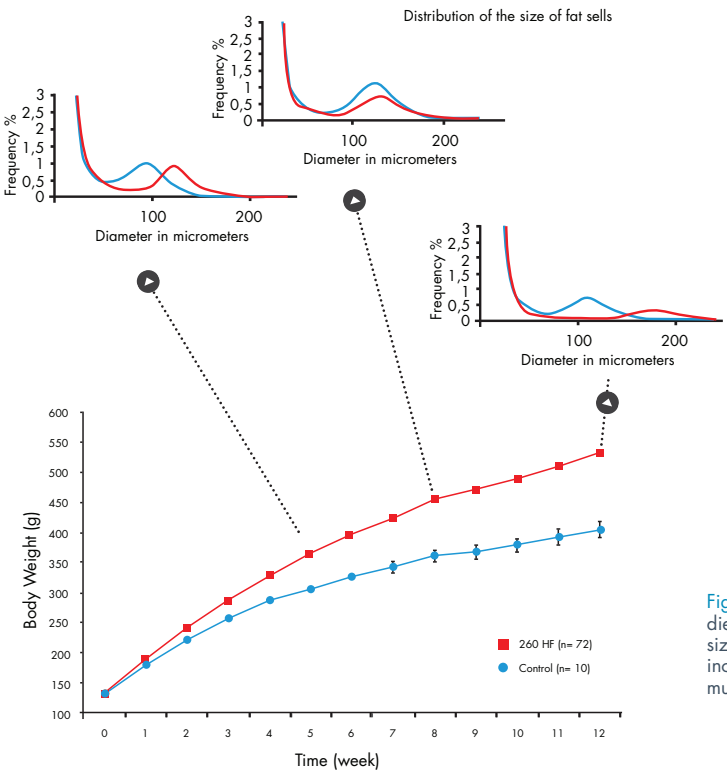

Figure 1: Development of the body mass in male rats from the Wistar strain fed on the control diet (black) or else the 260HF diet (red). The inserts represent the spread in the frequency of size of adipose cells in retroperitoneal tissue. One should note that the diameter of the adipocytes increases greatly in the adipocytes of animals fed with the 260HF diet (red curves), in all events, much greater than those of the adipocytes of rats fed with the standard diet (black curve).

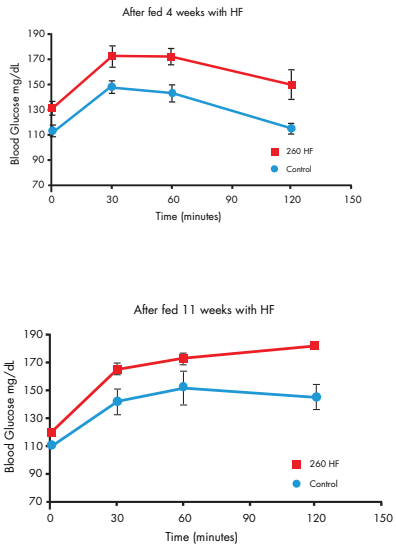

Figure 2:

Glucose tolerance tests, carried out after 4 and 11 weeks on the diets. Four weeks into the diet, the glucose tolerance deteriorated heavily in those animals fed on the 260HF diet, compared to that of the control group.