Adipose Tissue Development
From Animal Models to Clinical Conditions
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Volume Editors

Claire Levy-Marchal  Paris
Luc Pénicaud  Dijon

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Preface

Adipose tissue has been looked at with a new interest for the past years. Previously seen as a storage organ involved only in fuel metabolism, it is now regarded as an actual endocrine organ. The discovery of a number of adipokines secreted by adipose tissue and involved in the regulation of energy balance, fuel and lipid metabolism, and insulin sensitivity makes it an organ of major interest for new physiological concepts and a major target in the prevention and treatment of a number of clinical conditions. However, little is known today with respect to the interplay between adipocytes and the stromal components of adipose tissue, not only in terms of physiology in the mature tissue, but also in terms of development.

Thanks to the endeavor of the European Society for Pediatric Endocrinology, a seminar dedicated to junior physicians and scientists was held in Paris in March 2009 on the topic of development of adipose tissue. This seminar gathered about 35 young members of the Society from all over Europe to listen to and debate with distinguished international investigators and scientists in the field.

This book encompasses the proceedings of the conferences covering basic knowledge and approaches as well as clinical investigations and experiences.

Adipocytes arise from mesenchymal stem cells by a sequential pathway of differentiation. White adipocytes differentiate from various types of vascular cell types, probably located within the white adipose tissue itself. Brown adipocytes arise from myogenic precursors. The differentiation between white adipocyte and brown adipocyte lineages occurs in the earliest steps of fetal development, and both phenotypes are acquired independently. A better knowledge of these differentiation pathways is crucial for the development, among others, of new drugs in the fight against obesity and the metabolic consequences.

These proceedings cover the importance of nervous regulation of both white and brown adipose tissue mass with a review of the different physiological parameters which are regulated such as metabolism (lipolysis and thermogeneis) and secretory activity (leptin and other adipokines), but also the plasticity of adipose tissues (proliferation differentiation and apoptosis) showing the presence of a
neural feedback loop between adipose tissues and the brain which plays a major role in the regulation of energy homeostasis.

The discovery of leptin has clearly demonstrated a relationship between body fat and the neuroendocrine axis since leptin influences appetite and the reproductive axis. Since adipose tissue is a primary source of leptin, adipose tissue is no longer considered as simply a depot to store fat. Recent findings demonstrate that numerous other genes, i.e. neuropeptides, interleukins and other cytokines, and biologically active substances such as leptin and insulin-like growth factors I and II are also produced by adipose tissue, which could influence appetite and the reproductive axis. Targets of leptin in the hypothalamus include neuropeptide Y, proopiomelanocortin and kisspeptin. These few lines depict the complexity of the cross-talk between the brain and adipose tissue as far as the reproductive function is concerned.

A more recent observation is the relation between obesity and cancer. In addition to diabetes and cardiovascular diseases, epidemiological evidence demonstrates that people who are obese or overweight are at increased risk of developing cancer – colon, breast (in postmenopausal women), endometrial or kidney cancer being among the most frequent. In addition to the increase in tumor occurrence, obesity also affects tumor prognosis, especially in breast and prostate cancers. In breast cancer, obesity is associated with reduced survival and increased recurrence independent of menopausal status. Host factors seem to contribute to the occurrence of tumors exhibiting an aggressive biology defined by advanced stages and high grade. Mature adipocytes are part of the breast cancer tissue and as highly endocrine cells are susceptible to profoundly modify breast cancer cell behavior.

It was demonstrated more than 10 years ago that the development of obesity is determined as early as during fetal life and early infancy. The epidemiological evidence is reviewed here. Early puberty and age at menarche are consequences of rapid infant weight gain and childhood overweight, and in turn these adolescent traits are predictive for obesity, diabetes, hypertension and cardiovascular disease events in later life. An understanding of the nutritional, parental and wider determinants of rapid infant weight gain is important for the development of obesity prevention strategies starting in early life.

A clinical model of the development of fat mass early in life following fetal growth restriction is proposed with respect to the development of insulin resistance and to the metabolic syndrome. Over the last 15 years a number of long-term health risks associated with reduced fetal growth have been identified, including cardiovascular diseases, hypertension, dyslipidemia, and type 2 diabetes. A common feature of these conditions is insulin resistance, which is thought to play a pathogenic role. However, despite abundant data in the literature, it is still difficult to trace the pathway by which fetal events, environmental or not, may lead to the increased morbidity later in life. To explain this association, several hypotheses
have been proposed pointing to the role of either a detrimental fetal environment or a genetic susceptibility or an interaction between the two and of the particular dynamic changes in adiposity that occur during catch-up growth.

The metabolic syndrome defines the clustering of cardiovascular risk factors and is driven by peripheral insulin resistance. The 'driving force' of the syndrome, i.e. insulin resistance, develops mainly in obese children due to a specific pattern of lipid partitioning characterized by increased deposition of fat in the visceral compartment as well as in insulin-responsive tissues, such as muscle and liver. Such a lipid deposition pattern results in peripheral insulin resistance and a compensatory hyperinsulinemia. The definition of the syndrome in childhood suffers from many limitations related to different ethnic characteristics as well as age and development dependency of some of the components. Despite these limitations, the clustering of risk factors characteristic of the syndrome in childhood is associated with accelerated atherogenesis in adulthood. These complications are one of the major future concerns of public health with the rising incidence of overweight and obesity in the youth.

Human lipodystrophies represent a heterogeneous group of diseases characterized by generalized or partial fat loss, with fat hypertrophy in other depots when partial. Insulin resistance, dyslipidemia and diabetes are generally associated with leading to early complications. Whereas genetic forms are rare and represent a unique clinical model for the development of adipose tissue, acquired forms are often iatrogenic.

This splendid collection of investigation data and reviews will with no doubt serve as a reference for all pediatricians and scientists interested by obesity, endocrinology and development.

*Claire Levy-Marchal, Paris*