OBESITY AND THE ADIPOCYTE

Regional adipocity in man

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Introduction

It has become increasingly apparent that body fat distribution rather than total body fat correlates with the metabolic and cardiovascular complications of being overweight, at least in cases of non-massive obesity (Kissebah & Krakower 1994). This review focuses on the epidemiological and metabolic aspects of regional fat distribution in man.

Distribution of body fat

Fat is not uniformly distributed in the body (Table 1). The major adipose depot is subcutaneous (about 80% of all body fat). In the obese and non-obese states there are characteristic gender differences in the distribution of subcutaneous fat. Non-obese women have relatively more subcutaneous fat in the gluteofemoral area than in other subcutaneous regions, whereas in non-obese men the subcutaneous fat is distributed in a uniform fashion. The general differences are further pronounced in obesity. Obese men usually accumulate fat in the subcutaneous abdominal area. This male obesity is called central, upper-body, android or 'apple-shaped' obesity. Obese woman usually accumulate subcutaneous fat in the lower part of the abdominal wall and the gluteofemoral region. This female type of obesity is called peripheral, gynoid or 'pear-shaped' obesity. The link between gender and regional obesity is not absolute. There are many obese men who have peripheral fat distribution, and the other way around.

Table 1 Body fat distribution

	Remarks
Depot	
Subcutaneous	About 80% of all body fat. Can functionally be divided into abdominal and gluteofemoral
Visceral	Drained by the portal vein. Anatomically divided into omental and mesenteric fat
Other	Retroperitoneal, perirenal and orbital

Table 2 Regional differences in lipolysis

	Action on lipolysis	Regional differences
Hormone		
Catecholamines	Stimulating	visc>sc>abd>sc glf
Insulin	Inhibiting	sc>visc
Prostaglandins	Inhibiting	sc>visc
Adenosine	Inhibiting	sc>visc

visc=visceral, abd=abdominal, sc=subcutaneous, glf=gluteofemoral.

As regards the visceral and retroperitoneal fat depots inside the abdominal cavity, there are relatively small differences between non-obese woman and men in the size of these depots. However, obese men – in particular those with upper-body obesity – usually have much more visceral and retroperitoneal fat than obese woman.

Regional fat metabolism

It has been known since the first investigations were made on human fat more than 30 years ago that adipose tissue is a heterogenous metabolic organ (Abate & Garg 1995). The metabolic activity is lowest in the subcutaneous gluteofemoral area, followed by the abdominal subcutaneous area, and highest in the visceral region. These regional differences might be of physiological importance. Only the visceral fat has direct access to the liver by the portal vein. In situations where there is a need for rapid energy supply, such as during physical activity, more fat is mobilized from the visceral fat in comparison to the other regions in relative terms. Some fat depots might be reserved for utilization during a particular situation. For example, the metabolic activity of gluteofemoral fat is activated in lactating mothers.

The mechanisms behind regional differences in metabolism are partly elucidated, at least as regards lipid mobilization through lipolysis in fat cells (Table 2). The lipolytic hormones (i.e. catecholamines) are most active in the visceral fat, followed by abdominal subcutaneous fat, which, in turn, is more active than gluteofemoral subcutaneous fat. The anti-lipolytic hormones and parahormones (i.e. insulin, prostaglandins and adenosine) have a more pronounced inhibitory effect on lipolysis in subcutaneous

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compared to visceral fat cells. When the hormone effects are taken together it appears that elevation of the concentration of any of the lipolysis-regulating hormones will result in a more rapid lipid mobilization from visceral as compared to subcutaneous fat (Arner 1995).

Regional adipocity and complications in the overweight

There is convincing epidemiological evidence that upper-body obesity is associated with the development of a number of obesity-associated complications (diabetes, hypertension, cardiovascular disorders, dyslipidemia) (Lemieux & Despres 1994), whereas peripheral obesity is less harmful in this respect. The earliest epidemiological evidence came from studies in Gothenburg, Sweden. Those investigations showed that men and women with a high waist-to-hip ratio (indicating central fat accumulation) had increased risk of developing diabetes, hypertension and cardiovascular disorders compared to those with a low ratio (indicating peripheral fat distribution). Later on, techniques were developed which allowed a direct quantification of various fat regions based on computerized tomography or nuclear magnetic resonance imaging. A number of studies using these methods have shown that the amount of visceral fat rather than the amount of abdominal subcutaneous fat correlates with the above mentioned obesity complications.

A disease entity has been described, including among other things non-insulin-dependent diabetes mellitus, dyslipidemia, hypertension, coagulation abnormalities, rnicroalbuminuria, atherosclerotic cardiovascular disorders, obesity, hyperinsulinemia and insulin resistance. When several of these abnormalities co-exist a metabolic or insulin-resistance syndrome is likely. Insulin resistance is believed to be the most important factor that links these abnormalities. However, it could just as well be body fat that is the central factor in the syndrome, since most of the patients are upper-body obese or at least non-obese with an upper-body distribution. Anthropometric data suggest that it is the accumulation of visceral fat that is responsible for the correlation between fat accumulation and the insulin-resistance (metabolic) syndrome.

Why is visceral obesity dangerous?

The mechanisms linking visceral fat to metabolic and cardiovascular disorders are not elucidated (Bjorntorp 1994). A common theory is that visceral obesity leads to accelerated mobilization of fatty acids to the portal system because of increased rate of lipolysis in visceral fat cells in combination with an enlargement of the visceral fat depot (mass effect). Elevated 'portal' free fatty acids concentrations can have a number of undesirable effects on the liver (Table 3), as discussed (Frayn *et al.* 1996). These alterations in liver function may cause glucose intolerance, dyslipidemia, and hyperinsulinemia. Direct studies of visceral fat cells in upper-obese subjects have demonstrated a number of abnormalities in the hormonal regulation of lipolysis. These changes are, above all, located at the level of receptor–signal transduction. Decreased functions of insulin receptors and alpha$_2$-adrenoceptors plus increased action of beta$_3$-adrenoceptors have been demonstrated in visceral fat cells of upper-body obese subjects.

Table 3 Consequences for the liver of increased portal fatty acid concentration

Effect	Consequences
Increased glucose production	Glucose intolerance
Decreased insulin breakdown	Hyperinsulinemia
Increased production of triglycerides	Dyslipidemia

Conclusions

Epidemiological studies clearly show that upper-body obesity, in particular visceral obesity, has a close association with most of the metabolic and cardiovascular complications that accompany obesity. Peripheral obesity is much less harmful in this respect. The mechanisms by which visceral obesity leads to complications are not known. It is, however, possible that increased delivery of free fatty acids to the portal vein through increased rate of lipolysis in visceral fat cells is a major pathophysiological factor. Elevated 'portal' fatty acids may cause glucose intolerance, hyperinsulinemia, and dyslipidemia. The mechanisms for increased visceral fat mobilization in upper-body obesity appear to reside at the receptors for the major lipolysis-regulating hormones – catecholamines and insulin.

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