

## Lipokathexis: A fat paradox

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### Abstract

'Lipokathexis' is derived from the term 'Lipo' meaning fat and 'kathexis' which means retention. We propose this name for describing a clinical situation wherein despite excessive stores of fat are noted in the body but lower levels of circulating lipids are present in the blood. Different disease conditions that express such a phenotype including Tangier's disease, metabolic healthy obesity and those coming under the domain of obesity paradox have been described in this manuscript. This paper will invoke the readers interest on different facets of lipid metabolism in context of metabolic medicine and explore this concept of "Fat Paradox".

**Keywords:** Cholesterol, dyslipidemia, hyperlipidemia, LDL cholesterol, myelokathexis, Tangier's disease.

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### Introduction

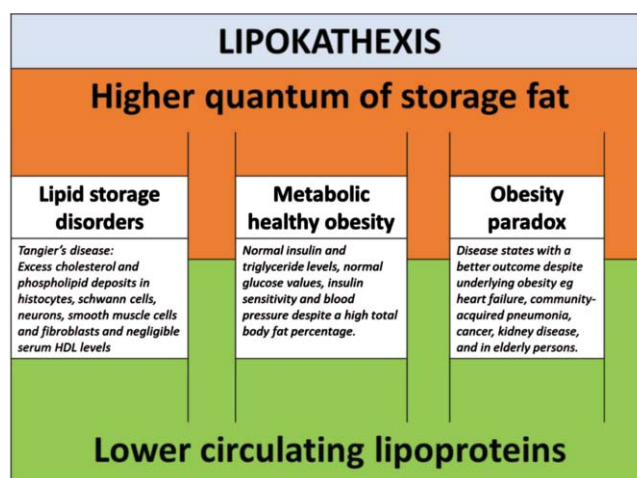
The Greek term 'kathexis' which means 'retention', has lent itself to the naming of the disease myelokathexis. Myelokathexis is characterized by retention of white blood cells in the bone marrow, leading to severe chronic leucopenia.<sup>1</sup> Similar situations are also noted in obesity and lipid metabolism. In this perspective, we propose the concept of lipokathexis, to describe clinical situations characterized by obesity, overweight, or localized lipid accumulation (lipid storage disorders), with low or low-normal levels of circulating lipoproteins. We explore the analogy, and differences, between myelokathexis and lipokathexis, to generate interest in this field of metabolic medicine (Figure).

### Lipid Storage Disorders

Lipid storage disorders or lipidoses, are inherited metabolic disorders due to specific enzyme deficiencies. They are marked by cellular damage due to excessive storage of fat in organs such as the brain, liver, spleen

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**Figure:** Different conditions that may have lipokathexis.

and bone marrow. The phenotypic presentation of various lipidoses is heterogenous, but the lipid levels are not used for diagnosis or monitoring. Tangier's disease, an autosomal recessive inherited alpha lipoproteinaemia, is known for the near or complete absence of HDL (high density lipoproteins), despite of excess cholesterol and phospholipid deposits in histocytes, Schwann cells, neurons, smooth muscle cells and fibroblasts.<sup>2</sup> This is due to mutations in the ABCA 1 (ATP-binding cassette transporter 1), a permease enzyme which maps on chromosome 9q31. This discordance between intracellular lipids and circulating HDL allows Tangier's disease to be classified as a lipokathexis.<sup>3</sup>

### Metabolically Healthy Obesity

A much more common occurrence in clinical medicine is that of obesity. Obesity is frequently associated with elevated serum triglycerides, very low-density lipoprotein (VLDL), apolipoprotein B, and non-HDL cholesterol. While metabolic disorders are well known in normal weight individuals, not all people with obesity exhibit metabolic abnormalities such as dyslipidaemia.<sup>4,5</sup> A subset, termed as metabolically healthy obesity (MHO) does present with obesity, but enjoys freedom from cardiometabolic diseases, have a healthy cardiometabolic phenotype, normal blood pressure, normal insulin triglyceride content, and normal insulin sensitivity.<sup>6,7</sup> If the strict definition, proposed by Smith et al. is to be followed, MHO cannot be termed as

lipokathexis, as the liver lipid content is always not often abnormal in this situation.<sup>6</sup>

### Obesity Paradox

The term 'obesity paradox' has also been used to explain the improved outcomes and survival noted in persons with mild obesity, as compared to those with normal body weight.<sup>8</sup> The obesity paradox has been documented in disease states as varied as heart failure, community-acquired pneumonia, cancer and kidney disease, and in elderly persons. It is possible that a variant of lipokathexis may be at work here, minimizing the release of potentially harmful lipoproteins into the circulation.

Adipose tissue topography, or distribution of fat, is an important marker of metabolic health. Adipogenic capacity in subcutaneous adipose tissue is greater in MHO than in metabolically unhealthy obesity (MUO). The adipose tissue may act as a reservoir, to create an adaptive lipokathexis of sorts, which functions to prevent metabolic dysfunction. A higher ratio of large to small adipocytes in subcutaneous abdominal fat deposits suggests a healthier homeostasis, with greater insulin resistance.

### Reverse Lipokathexis

A 'reverse lipokathexis' is noted in lipodystrophy syndromes. There are a varied group of disease, where selective absence of adipose tissue, with lack of functional adipocytes, precipitates ectopic steatosis and severe dyslipidaemia. Lipodystrophy can be viewed as a disorder of lipid partitioning.<sup>7</sup> Whether or not a term such as reverse lipokathexis can be used to describe lipoatrophy is debatable. However, one should be aware of the various clinical states where the phenotype and lipid profile are discordant with each other.

### Summary

We have explored the use of the term lipokathexis in the

context of metabolic medicine. The closest analogy to the haemato-oncologic condition myelokathexis is Tangier's disease, in which circulating HDL cholesterol is near absent, though lipid storage is excessive. However, an antilogy can be identified in a subset of obesity, which has been documented as the obesity paradox. Further discussion and debate on the lines of lipokathexis should help uncover important facets of lipid metabolism, which in turn can improve metabolic health in persons with lipid disorders.

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