To conclude, the data that are presented in this thesis indicate that:

1. The assessment of RLP-C is essential in assessing the atherogenic lipoprotein phenotype.
2. RLP possess atherogenic properties, such as oxidizability and foam cell formation.
3. The metabolism of fasting and postprandial RLP-C in AGHD is disturbed and postprandial RLP-C profile is improved during GH therapy. These disturbances in RLP metabolism may be partly responsible for the high susceptibility to premature atherosclerosis in AGHD.
4. Endothelial dysfunction in AGHD patients improves during GH therapy.
5. The postprandial RLP-C profile is related to a pro-inflammatory response.
6. In heterozygous FH patients, increased fasting plasma RLP-C levels are part of the atherogenic lipid phenotype (independent from plasma LDL-cholesterol levels). Simvastatin (80 mg) reduces RLP-C levels to within the normal range in a quarter of FH patients.
7. Postprandial RLP-C response in heterozygous FH patients decreases during Simvastatin therapy.
8. Plasma RLP-C levels in heterozygous FH patients are associated with an increased carotid IMT, but not independent of plasma LDL-cholesterol.
9. The fasting and postprandial RLP-C profile is disturbed, not only in GH deficiency, but also in acromegaly, due to a decreased insulin sensitivity and decreased LPL activity.
10. Insulin secretion in adult healthy subjects is related to the IGF system through plasma IGF-II.
11. Baseline plasma IGF-I levels in AGHD patients determine the decline in insulin sensitivity during GH therapy.
12. The contribution of GNG in AGHD patients increase with pyruvate as major GNG precursor.
13. In addition to insulin secretion capacity of adult pancreatic b-cells, plasma IGF-II levels are inversely associated with the amount of GNG. The adult plasma levels of IGF-II, which is mostly genetically determined, therefore link two major features of the insulin resistance syndrome.
14. Severe dysfunction of the left ventricle in acromegaly is reversible, and is closely related to plasma GH levels.

Prospectives
Clinical features that are related to disturbances in the GH axis/IGF system (such as disturbed lipoprotein remnant metabolism, endothelial dysfunction, increased visceral fat with obesity, hypertension, relation with insulin secretion and gluconeogenesis) resemble closely to the entity syndrome X or the plurimetabolic syndrome. Analysis of the GH axis/IGF system will therefore teach us more about insulin resistance, unravel the plurimetabolic syndrome, and may give rise to novel therapeutic approaches.
References


49. Hodis HN, Mack WJ, Arzen SP et al. Triglyceride-rich and cholesterol-rich lipoproteins have a differential effect on mild/moderate and severe lesion progression as assessed by quantitative coronary angiography in a controlled trial of lovastatin. Circulation 1994; 90:42-49.
68. Twickler TB, Prinsen HC, Vries WRd, Koppeschaar HPF, Sain-van der Velden MG. Analysis of the separate secretion of very-low-density lipoprotein (VLDL)-1 and VLDL-2 by the liver will be a principal factor in resolving the proatherogenic lipoprotein profile in hypopituitarism. J Clin Endocrinol Metab 2002; 87:1907.