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Description of Research:

Dr. Xanthakos' primary research focus is to identify the biologic determinants of non-alcoholic steatohepatitis (NASH), including potential gene-environment interactions with dietary intake during childhood and adolescence. Dr. Xanthakos recently characterized the histologic spectrum of non-alcoholic fatty liver disease (NAFLD) in morbidly obese adolescents undergoing bariatric surgery at Cincinnati Children's Hospital Medical Center in a collaborative study with Dr. Thomas Inge. These studies revealed that the histologic spectrum of NASH in morbidly obese adolescents differs considerably from the features of NASH described in adults, with more portal inflammation and fibrosis than is seen in adults. The etiology of the difference in histologic pattern between children and adults is not known. Importantly, *nearly 20%* of morbidly obese adolescents *do not* develop NASH, despite similar degrees of morbid obesity and insulin resistance. Long-term research goals include 1) determining the biological factors that regulate hepatic susceptibility to inflammation and fibrosis in response to obesity, 2) analyzing how genetic polymorphisms in key cytokines and adipokines alter the expression of genes that regulate inflammation and fibrogenesis, 3) identifying dietary factors that may predispose genetically-susceptible individuals to develop the NASH and 4) developing and applying mechanistically based therapies for NASH in childhood and adolescence.

Collaborations:

Dr. Xanthakos collaborates with Dr. Thomas Inge studying the determinants of inflammation and fibrogenesis in morbidly obese subjects. As a new member, Dr. Xanthakos has not used DHC cores.

Representative Data:

Table 2. Subject Characteristics Across Histologic Subtypes^a

	Normal	Steatosis	Steatosis with isolated fibrosis	Nonspecific NAFLD	NASH	P value ^b
Number (%)	7 (17)	10 (24)	3 (7)	13 (32)	8 (20)	—
Age (y)	17.0 ± 1.3	15.8 ± 1.5	16.3 ± 2.9	16.2 ± 1.6	16.6 ± 2.0	NS
Gender (%)						
Male	4 (57)	6 (60)	0	5 (38)	1 (12)	.15
Female	3 (43)	4 (40)	3 (100)	8 (62)	7 (88)	
Race (%)						
Non-Hispanic white	5 (71)	7 (70)	3 (100)	11 (85)	8 (100)	NS
Black	2 (29)	3 (30)	0	2 (15)	0	
BMI (kg/m ²)	59.7 ± 11.9	63.7 ± 14.1	53.2 ± 8.3	56.3 ± 6.4	58.9 ± 9.4	NS
ALT (IU/L)	26 ± 8.2	45 ± 32	37 ± 12	28 ± 16	56 ± 38	.11
Abnormal ALT (%)	0	4 (40)	1 (33)	1 (8)	4 (50)	.05
AST (IU/L)	25 ± 7	33 ± 14	36 ± 11	31 ± 13	49 ± 23	.04
Abnormal AST (%)	1 (14)	3 (30)	2 (67)	3 (23)	7 (87)	.01
HDL (mg/dL)	35 ± 9	38 ± 8	39 ± 6	35 ± 7	41 ± 5	NS
Abnormal HDL (%)	6 (85)	8 (80)	1 (33)	10 (77)	3 (38)	NS
Triglyceride (mg/dL)	132 ± 83	137 ± 55	157 ± 73	155 ± 78	192 ± 48	NS
Abnormal triglyceride (%)	1 (14)	5 (50)	2 (67)	6 (46)	6 (75)	.20
Insulin (μU/mL)	34.9 ± 20.4	44.9 ± 20.9	46.6 ± 12.9	41.5 ± 19.7	50.1 ± 20.1	NS
HOMA-IR	8.6 ± 5.3	10.6 ± 4.7	10.1 ± 2.9	9.8 ± 4.8	15.5 ± 8.9	NS
Waist circumference (cm)	134.6 ± 10.8	147.5 ± 22.2	131.1 ± 3.3	136.9 ± 11.2	141.0 ± 13.2	NS
Fasting glucose	94 ± 11	97 ± 6	88 ± 6	92 ± 10	118 ± 39	.05
Impaired fasting glucose (%)	2 (29)	3 (30)	0	2 (15)	4 (50)	NS
Hypertension (%)	1 (14)	1 (10)	0	7 (54)	2 (25)	NS
Metabolic syndrome [≥3 Adult Treatment Plan III criteria] (%)	4 (57)	7 (70)	2 (67)	9 (69)	8 (100)	NS

^aPresented as means ± standard deviations or number of subjects (%) when appropriate.

^bP value less than .05 indicates significance for comparisons between histologic subtypes (analysis of variance or Fisher exact test when appropriate).

Table 2 from Clin Gastroenterol Hepatol, 2006; 4:226–232