Obesity related phenotypes in families selected for extreme obesity and leanness

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BACKGROUND: Obesity is a multigenic trait, and special methods and sampling designs are needed for gene identification.

OBJECTIVE: To describe characteristics of families selected to increase information for genetic linkage studies of obesity.

DESIGN: Families having extremely obese siblings with a lean parent and sibling.

SUBJECTS: 594 members of 94 Caucasian families.

MEASUREMENTS: Measured height and weight, bioelectric impedance, skinfolds, circumferences and questionnaires. RESULTS: Families have an extreme range of obesity phenotypes, which are bimodally distributed. The obese individuals are predominantly women with an onset of obesity early in life. Obesity onset age was negatively correlated with level of obesity, and onset ages were correlated among family members. Individual obesity measures were highly correlated. The extreme range of phenotypes within families increases family variability and presumably gene segregation.

CONCLUSION: Sampling families through extremely obese sibling pairs with a lean parent and sibling results in families with an extreme range of obesity and leanness. The large within-family variance and early age of onset should make these families highly informative for gene mapping and gene identification studies.

Keywords: obesity: leanness; body mass index; percent fat; skinfolds; linkage; association; genetic; gene mapping; age at onset; childhood obesity

Introduction

Obesity is a complex trait influenced by multiple genes and non-family environment. A number of family, twin and adoption studies have established that obesity is heritable in humans, 1-4 and adoption studies consistently show that family environment has minimal influence on adult obesity. 1-4-5 Studies in humans and animals have demonstrated that this heritable pattern is due to multiple genes.

Identifying genes for complex traits requires special analytic methods and sampling procedures. In general, these methods focus on estimating linkage between a phenotype and genetic loci by evaluating identity (by state or by descent) of marker alleles shared by pairs of relatives. Preferential transmission of particular marker alleles from heterozygous parents to affected offspring indicates a genetic association. At present, linkage studies are used to localize susceptibility genes, and association studies are used for fine mapping and for tests of candidate genes. Future studies may use association methods for large scale genome scans as well.

The ability to identify genes for complex traits depends on the genetic heritability of the trait, the population and familial risk, and the proportion of variance accounted for by each specific gene. Risch10 has shown that the ratio of familial to population risk is an indicator of whether a gene is likely to be identifiable. Generally, a risk ratio of at least two is thought to be needed for detection, but higher values are probably needed to assure gene identification. For example, Risch and Merikangas" recently argued that it may be difficult to identify genes with risk ratios below four. Allison et al11 demonstrated that risk ratios for normal levels of body fat are very low and suggested that it will be necessary to sample more extreme phenotypes. Recently, our group demonstrated that families selected through individuals with a body mass index (BMI, kg/m2) ≥ 40 give risk ratios of at least five.12 Therefore, sampling families with extreme obesity should provide substantial power for identifying genes for human obesity.

Below we report on the nature of obesity and leanness in a new cohort of families selected through extremely obese individuals (BMI ≥ 40). In addition, we discuss issues related to the restrictive eligibility criteria we have imposed on our study design. This sampling design meets many of the requirements for mapping and identifying genes for a complex trait such as obesity.

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Obesity Leanness

Derek J. Chadwick, Gail Cardew

Obesity Leanness:

Obesity and Leanness Michael Stock, Nancy Rothwell, 1982 **Leanness in Domestic Birds** B. Leclercq, C. C. Whitehead, 2014-05-20 Leanness in Domestic Birds Genetic Metabolic and Hormonal Aspects is a proceeding of a symposium held in Tours France from 4 to 6 August 1987 Said symposium was concerned with genetic and metabolic factors associated with leanness of poultry and accounts of research in these areas The book is divided into six parts Part I covers studies that involve genetics in the selection of meat leanness Part II deals with the relationship of feed intake and metabolism to the leanness of poultry Part III discusses the lipid metabolism in birds and its related factors and effects Part IV talks about the use of hormones such as insulin thyroid hormones and corticosteroids in the control of fatness in birds Part V covers studies involving amino acid metabolism and its relation to leanness in poultry and Part VI talks about the applications of the studies in commercial use The text is recommended for zoologists agriculturists and poultry farmers who would like to know more about the different factors that affect the leanness of domestic birds and its implications Diet Related to Killer **Diseases, II: Obesity** United States. Congress. Senate. Select Committee on Nutrition and Human Needs, 1977 Debasis Bagchi, Harry G. Preuss, 2012-07-06 The World Health Organization WHO has declared obesity a global epidemic Its prevalence has more than doubled since 1980 causing a myriad of health problems for children and adults Obesity Epidemiology Pathophysiology and Prevention Second Edition explores the molecular mechanisms and pathophysiology Handbook of Obesity George A. Bray, Claude Bouchard, 2003-12-09 Offering leading to obesity and metabolic disord perspectives on the history prevalence and genetics of obesity this book examines the origins and etiology of obesity It considers the relationship between behavioural neuroscience and obesity Diet Related to Killer Diseases United States. Congress. Senate. Select Committee on Nutrition and Human Needs, 1976 Diet Related to Killer Diseases, II United States. Congress. Senate. Select Committee on Nutrition and Human Needs, 1976 **Animal Models of Obesity** Michael F.W. Festing.1979-06-17 Hearings, Reports and Prints of the Senate Select Committee on Nutrition and Human Needs United States. Congress. Senate. Select Committee on Nutrition and Human Needs, 1977 Statistics for Clinicians Andrew Owen, 2023-07-04 This book provides clinical medicine readers with a detailed explanation of statistical concepts using non technical terms This allows clinicians and others without specialist statistical knowledge to understand the medical literature where such concepts are used Many examples from the medical literature are used to exemplify how these concepts are used in practice Current books written for clinicians fall into two broad categories Simple texts that are not designed to cover many important statistical concepts used in the medical literature Comprehensive texts which cover many statistical principles in detail including statistical theory but which are more challenging to read and do not always cover many important statistical techniques used in the medical literature This book assists in the understanding of these techniques Statistics for Clinicians covers such topics in a robust non technical manner accessible to clinicians and is

intended for hospital consultants junior doctors and general practitioners Undergraduates in biomedical sciences and medicine may also find some sections valuable Clinical Obesity in Adults and Children Peter G. Kopelman, Ian D. Caterson, William H. Dietz, 2008-04-15 Highly Commended in the 2006 British Medical Association Book Awards Endocrinology This Second Edition brings together more than 20 internationally recognized experts in the field to provide a timely review of current knowledge. The text remains an invaluable resource for all healthcare professionals involved in the care of patients who areobese New features of this Second Edition include Addition of two new co editors Professor Bill Dietz USA and Professor Ian Caterson Australia Increased number of contributors from around the globe providing a truly international perspective Includes new information about the causes of obesity its complications and new and novel methods of prevention and treatment Reorganized into sections that address obesity and its social and cultural aspects biology associated diseases life stages pediatric and adult management and environmental and policyapproaches **Obesity** Karine Clement, Thorkild I. A. Sorensen, 2007-09-12 This book comprehensively accounts the current understanding of genetic mechanisms of obesity by analyzing obesity phenotypes and genotypes and gene polymorphisms and mutations and current results from animal model research and genetic studies in human models By presenting the impact of genetic factors in the development of obesity and key molec The Origins and Consequences of Obesity Derek J. Chadwick, Gail Cardew, 2008-04-30 This volume examines obesity disorders which can lead to diabetes hypertension and hyperlipidaemia It offers an interdisciplinary and international look at all aspects of the origins consequences and treatment of obesity

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and the 4th edition of Volume 2 both published in 2014 In recent years we ve developed a much better grasp of the factors
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