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George A. Bray

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Lessons from Animal Models of Obesity

David A. York

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Obesity in animals may result from genetic, dietary, or neuroendocrine perturbations. Study of these models has identified the central systems that regulate food intake and energy expenditure and identified the interdependence of feeding behavior, the autonomic nervous system, and adrenal glucocorticoids in the development of obesity. The animal models of obesity have been influential in showing that adipose tissue is an important secretory tissue. The recent identification of five genes that cause obesity will provide new insight into the physiologic systems that regulate energy balance.

Genetics of Obesity in Humans and Animal Models

David B. West

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Obesity has a genetic component that accounts for a significant percentage of the risk for this disorder. Studies are underway in humans and animal models to identify the genetic mechanisms controlling risk for the development of obesity. Identification of these genes will facilitate diagnosis and perhaps lead to new behavioral or pharmacologic approaches to prevent and treat obesity.

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The control of food intake as a physiologically complex, motivated behavioral system is examined. During the past four decades, considerable progress has been made in understanding signals for hunger, satiation, and satiety. The putative physiologic controls of food intake discussed include positive and negative sensory feedback; gastric and intestinal distension; effects of nutrients, nutrient reserves, and metabolism in producing signals to the liver or brain; and peptides and hormones released in the gastrointestinal tract or the brain.

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The methodology to measure components of energy expenditure and the role each component may have in the cause of obesity are reviewed. Although energy expenditure has been studied for more than 100 years, the role that individual components of energy expenditure have in the cause of obesity remains unclear. Reasons for this uncertainty are mainly caused by less than adequate techniques for measuring physical activity, the most variable component of total daily energy expenditure, and the fact that differences in energy metabolism are difficult to detect in a static comparison. Using a combination of the techniques available today, each component can be studied reliably, and the role that each component has in the development of obesity can be ascertained.

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The adipocyte is a metabolically active cell that functions to store energy for times of energy deprivation or enhanced need. Obesity is characterized by increased lipid accumulation and turnover compared with the nonobese state. Both triglyceride synthesis and lipolysis are regulated metabolic processes in the adipocyte. Current research on the metabolic activities of the human adipocyte focus on plasma triglyceride hydrolysis and uptake of fatty acids by LPL, esterification of these fatty acids, and the subsequent triglyceride breakdown by hormone-sensitive lipase in response to stimulation of adrenergic receptors. These topics are discussed in relationship to the development of obesity.

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David W. Harsha and George A. Bray	

Underwater weighing has been the gold standard for the measurement of body composition in humans; however, the two

formulas widely used, the Siri and Bronze, were developed using young adult white males. The development of newer techniques in the past 20 years has greatly expanded the accuracy and ease of measuring body composition. These methods have improved the ability to model relationships between body compartments. This article reviews the compartmental models and then critiques the methods available to measure body composition.

Prevalence of Obesity

Theodore B. VanItallie

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Numerical values for prevalence of obesity are highly dependent on the criteria used to identify the condition and its gradations of severity. Prevalence is also affected by the makeup of the surveyed population. Recently, national surveys of prevalence of obesity in the United States and some European countries have been reported in terms of criteria that permit direct comparison of the findings. When the prevalence of a body mass index is 30 kg/m² or more in US adults is compared with findings in adults in the United Kingdom, France, the Netherlands, and Italy, the differences are striking, with prevalence ratios ranging from approximately 1.5 (US versus UK) to 3.0 (US versus France).

Health Hazards of Obesity

George A. Bray

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Several health hazards and social disabilities are associated with obesity. Increased mortality is associated with increased body weight. A high rate of mortality results from heart disease, diabetes mellitus, gallbladder disease, high blood pressure, and cancer. Physiologic cardiovascular changes occur, leading to left ventricular hypertrophy and lipid abnormalities. Hypertension, stroke, and venous stasis are increased. Pulmonary abnormalities include obstructive sleep apnea, which can be associated with secondary polycythemia and right ventricular hypertrophy. Gallstones, gallbladder disease, and accumulation of fat on the liver are significantly increased. Gout and reproductive abnormalities in women are common. Osteoarthritis of the knees and spine occur, although osteoporosis is rare. Risk for endometrial and breast cancer is increased, particularly in the presence of increased central fat. Changes in the skin include stretch marks, acanthosis nigricans, hirsutism, intertrigo, and multiple papillomas. Impaired psychosocial function is manifested as social isolation, loss of job mobility, increased employee absenteeism, and economic and social discrimination.

The Endocrinology of Obesity

Steven R. Smith

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The endocrine alterations associated with obesity are numerous. Most of these alterations must be considered simply associated

and not causative. They are, however, potentially involved in the pathogenesis of the complications of obesity. The discovery of new endocrine peptides, such as leptin, that signal body fat content open a new era in the understanding of the adipocyte as an endocrine organ.

Behavioral Therapy for Obesity

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Donald A. Williamson and Lori A. Perrin

The research literature pertaining to behavior therapy for obesity is reviewed. Procedures used in behavioral treatment programs are described, and treatment outcome research is reviewed. During the past 30 years, average weight loss has increased, but the problem of regaining body weight following treatment has persisted. It was concluded that obesity should be treated as a chronic health problem and that behavior therapy may have an important role in assisting some obese persons to maintain weight loss if they are enrolled in very long-term treatment programs.

Role of Nutrition Planning in the Treatment for Obesity

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Richard L. Atkinson

Obese people have a chronic disease requiring lifelong differences in eating habits. Low-calorie and very low-calorie diets can be used only temporarily for weight loss. The most sensible eating plans are those that involve a wide selection of natural foods with a modest percentage of kcal as fat. A team of physician and nutrition educators can help obese patients choose the series of dietary compromises compatible with an acceptable quality of life.

Exercise as Treatment for Obesity

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Jeffrey J. Zachwieja

In recent times, our society has become less physically active, which undoubtedly has contributed to the increased incidence of obesity. Exercise training can reduce body weight of overweight individuals, but in many cases the changes produced are small. A combination of regular physical activity, modest caloric intake, and reduced calories from fat leads to slow but continuous weight loss and improves the potential for maintenance of weight loss. Regular physical exercise helps to prevent the development of diabetes, heart disease, and hypertension in overweight individuals even if body weight is not completely normalized. Further research is needed to identify the optimal amount, type, and intensity of exercise for the maintenance of ideal body weight.

Medicating the Obese Patient

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Donna H. Ryan

The acceptance of medication as a legitimate adjunct to diet and behavior modification in the treatment for obesity is an emerging

phenomenon spurred by advances in understanding the biologic basis of body weight regulation and by the demonstration of safe and effective chronic maintenance of weight loss using a pharmacobehavioral approach. The decision to medicate for obesity depends on good clinical judgment based on such considerations as body mass index; body composition; body fat dissociation; age; sex; and comorbid conditions, such as diabetes and hypertension. Several nonadrenergic agents and a serotonergic agent have FDA-approved indications for weight loss. Phenylpropanolamine is available over the counter. Clinical trials support the efficacy of fluoxetine and ephedrine or caffeine in producing weight loss, although these agents do not have FDA-approved indications for treatment for obesity. In addition, new agents are being developed or are anticipated for approval. The use of existing agents in combination and their use adjunctive to diet and behavioral approaches to obesity treatment are fertile areas for research. The expectant attention to this subject is demanded by the imperative that the health in one in three people in the United States is adversely affected by obesity.

Surgery for Obesity

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Frank L. Greenway

The medical risks of obesity increase exponentially as weight increases, and these risks are reduced by sustained weight loss. Behavior modification and dieting provide an approximately 6% loss of body weight at 1 year. Fenfluramine provides an approximately 8% weight loss at 1 year, which can be doubled to 16% when a drug such as phentermine, which works through a different biochemical mechanism, is added to it. This amount of weight loss is insufficient for many severely obese individuals. It was with these facts in mind that the National Institutes of Health Consensus Conference in 1992 recommended that obesity surgery is an appropriate treatment for patients with a body mass index greater than 40 kg/m² who had failed in attempts at medical treatment and for patients with a body mass index greater than 35 kg/m² with severe complications of obesity. Vertically banded gastroplasty and Roux-en-Y gastric bypass are the two operations presently recommended because of their relative safety and effectiveness. This article reviews previous procedures that have provided insight into the mechanisms by which these surgeries cause weight loss. The presently used surgeries and their results also are reviewed because until medical therapy improves substantially, surgery remains the most reasonable treatment option for most morbidly obese patients.

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