

# Hormonal Balance

REVISED  
SECOND  
EDITION

## Understanding Hormones, Weight, and Your Metabolism

- Help your body work more efficiently
- Balance your hormones, balance your weight
- Feel better and achieve total wellness



**Scott Isaacs,**  
M.D., F.A.C.P., F.A.C.E.

Preface by  
Neil Shulman, M.D.



# HORMONAL BALANCE

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Understanding Hormones,  
Weight, and Your Metabolism

by Scott Isaacs, M.D., F.A.C.P., F.A.C.E.



BULL PUBLISHING COMPANY  
BOULDER, COLORADO

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ISBN 10: 1-933503-04-1 / ISBN 13: 978-1-933503-04-2

Published by Bull Publishing Company,  
Post Office Box 1377, Boulder, Colorado 80306  
(www.bullpub.com)

**Library of Congress Cataloging-in-Publication Data**

Isaacs, Scott, 1967-

Hormonal balance: understanding hormones, weight, and your metabolism /  
by Scott Isaacs. —2nd ed.

p. cm.

Includes bibliographical references and index.

ISBN 13: 978-1-933503-04-2 / ISBN 10: 1-933503-04-1

1. Hormones—Popular works. 2. Weight loss—Endocrine aspects—Popular works. 3. Endocrine glands—Diseases—Popular works.
4. Metabolism—Popular works. I. Title.

QP571 .I833 2006

612.4'05—dc22 2006028378

2002003824

INTERIOR DESIGN AND TYPOGRAPHY BY DIANNE NELSON,  
SHADOW CANYON GRAPHICS

COVER DESIGN BY LIGHTBOURNE IMAGES

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# CONTENTS

FOREWORD . . . . .	v
INTRODUCTION TO THE SECOND EDITION . . . . .	vii
INTRODUCTION . . . . .	ix
ACKNOWLEDGMENTS . . . . .	xiii
CHAPTER ONE	
<b>HORMONES AND METABOLISM</b> . . . . .	1
CHAPTER TWO	
<b>INSULIN AND FOOD</b> . . . . .	25
CHAPTER THREE	
<b>INSULIN RESISTANCE</b> . . . . .	61
CHAPTER FOUR	
<b>ANDROGENS</b> . . . . .	115
CHAPTER FIVE	
<b>ANDROGEN DISORDERS IN WOMEN</b> . . . . .	155

CHAPTER SIX	
<b>WOMEN'S HORMONES</b> . . . . .	185
CHAPTER SEVEN	
<b>THYROID HORMONE</b> . . . . .	223
CHAPTER EIGHT	
<b>CORTISOL, THE STRESS HORMONE</b> . . . . .	269
CHAPTER NINE	
<b>GROWTH HORMONE</b> . . . . .	297
CHAPTER TEN	
<b>HUNGER HORMONES AND THE FUTURE OF WEIGHT LOSS</b> . . .	321
CHAPTER ELEVEN	
<b>LOSING WEIGHT NOW</b> . . . . .	347
RECIPES FOR THE HORMONAL HEALTH DIET . . . . .	385
FOOD DIARY . . . . .	411
SHOPPING LIST . . . . .	413
HORMONE DISORDERS: A GUIDE TO SYMPTOMS . . . . .	415
BIBLIOGRAPHY . . . . .	423
ABOUT THE AUTHOR . . . . .	447
INDEX . . . . .	449

# FOREWORD

BY NEIL SHULMAN, M.D.

*HORMONAL BALANCE* IS THE ESSENTIAL MANUAL FOR KEEPING YOUR BODY HEALTHY. It gives you the most up-to-date, cutting-edge facts about hormones and how they may be contributing to obesity. This book is a first. The hormone factor has been ignored, but may be critical. Before embarking on a series of diets, alterations in lifestyle, and pill taking, you should determine whether hormones are contributing to your problem.

Only after ruling out hormone problems can you make a rational decision about treatment. If you make a commitment to losing weight, you want to make all your agony worthwhile. For every minute and every dollar you put into losing weight, you want a payoff.

Finally, a physician expert in obesity and hormones is willing to reveal the secrets and intricacies of the hormone-obesity connection in an excellent, comprehensive, easy-to-read format.

Scott Isaacs, M.D., is board-certified in endocrinology, diabetes, and metabolism and has been treating patients, training doctors, and conducting research on hormones, stress, and obesity his entire career. Dr. Isaacs is a caring doctor who listens to his patients and explains things in easy to understand language. This book reflects that philosophy.

I don't eat candy, I don't eat fudge  
Those facts not withstanding, my pudge, won't budge

Not a nudge.

Government concerns about obesity have been sounded,  
But none of my pounds are lost, they're always "founded."  
I give a whole new meaning to the term "well-rounded,"  
Luckily, though, I'm never hounded.

And that for me, is the key.  
Don't lose weight for he,  
Or she,  
But for thee.

—RB



# INTRODUCTION TO THE SECOND EDITION

SINCE THE FIRST EDITION OF *HORMONAL BALANCE* WAS PUBLISHED IN 2002, research on the subject of hormones and obesity has exploded. Literally, thousands of scientific articles have been published on every conceivable aspect of this topic. New discoveries are being made every day.

Despite these scientific breakthroughs, we are still fat.

Government studies estimate that almost 75 percent of Americans are either overweight or obese. If you aren't overweight, you're in the minority. And obesity-related illness, like heart attacks, strokes, high blood pressure, diabetes and even certain cancers have become the number one preventable cause of early death in the U.S.

We continue to see the rise and fall of fad diets. No-fat, No-carb, low-carb, Jenny Craig, Nutri-System, SugarBusters, Atkins, South Beach . . . The more we diet, the fatter we get.

Studies have shown that about 98% of people that lose weight on a diet will regain the weight or even more within 5 years.

Why?

Hormonal imbalance.

**If you want to have permanent weight loss, your hormones have to be balanced. Through hormonal balance, you will be able to lose weight and keep it off forever.**

What is hormonal balance? It really depends on who you ask. If you ask a gynecologist, she'll tell you it's the female hormones—estrogen, progesterone and prolactin. If you ask a urologist, he'll tell you it's all about testosterone. If you ask a diabetologist, he will tell you it's about balancing your insulin, glucagon and blood sugar. An endocrinologist will tell you that hormonal balance is having all your hormones

balanced. This is because all your hormones affect one another. It's one big circle. When one hormone is out of balance, it has profound effects on all your hormones. They are all connected. Hormonal balance means having the perfect amount of every hormone. It means having a body that's healthy and resilient.

Hormonal balance improves just about every aspect of your life. Your body will be lean and efficient. You won't have excessive hunger or cravings and your metabolism will work to keep your body at a healthy weight. You will feel more energetic but without stress or anxiety. Your mood will be elevated. You will have deep, restful, rejuvenating sleep every night. You will have a sharp mind. Hormonal balance means feeling better and living longer.

As you read this book you'll how all your hormones work together to control your appetite, body weight and metabolism. You'll learn about the subtle or not so subtle signs and symptoms of hormonal imbalance and what you can do to get your body's system of communication back on track.

Virtually all of the information that was in the first edition of *Hormonal Balance* still holds true today. You won't see any new philosophies or dieting principles in this edition. The purpose of the second edition of *Hormonal Balance* is to incorporate new research on hormones that affect your body weight, appetite, body composition and metabolism into the existing structure of the first edition. I've also tried to include all the new medications and supplements available to treat the various hormonal conditions. As well as bringing to light some ineffective or even dangerous products that falsely claim to help you lose weight through hormones.

Since the publication of the first edition of *Hormonal Balance*, thousands of people have seen permanent weight loss success following the Hormonal Health Diet. This diet is a balanced and nutritious way of eating that will allow you to lose weight without feeling hungry or deprived. There is a new seven-day meal plan, with delicious new recipes as well. I've also included a sample page from a food diary, to help you track your progress on the Hormonal Health Diet.

You *can* control your hormones. You can control your metabolism. Follow the lessons in this book, and you will be on your way to a lifetime of health and hormonal balance.

# INTRODUCTION

IN MY CAREER AS AN ENDOCRINOLOGIST, I've routinely dealt with people who have trouble losing weight. An overweight patient will come to my office and tell me his or her story. "I've tried everything, doc," the patient will say. "I've followed diet books, I've taken diet pills, I exercise regularly. But nothing works. I'm really not eating that much, but I'm still fat. I can't lose the weight. What's wrong with me?"

What's wrong, I tell these patients, is not simply their diet or exercise regimen—at least, not at the root. The problem, I suggest, may be with their very body chemistry—their hormones.

Sometimes the patients believe me and we get right to work. Sometimes they thank me, leave the office, and go see another doctor—or two, or three—and take diet pills or try yet another diet plan. I wish them well. They may just be treating the symptoms, but not the disease.

You can do all the dieting, exercise, medicating, and thinking you want, but you're not going to lose the weight, keep it off, and live a healthy life unless you address the real problem: hormones.

Hormones are the misunderstood part of our whole weight-obsessed culture. Yes, you can lose weight on a diet—but you might not be healthy, and you'll probably put it all back. The Hormonal Health Diet, found in Chapter 11, is a different type of diet. It is a balanced and nutritious way of eating that will help you balance your hormones and have permanent weight loss without hunger or cravings.

And this book isn't going to give you great buns in 30 days. It may give you great buns in a few months, or a flat stomach in a year, but that won't be because of me. *That will be largely because you learned to understand your hormones.*

Diet and exercise are important, but they aren't the whole story. Underneath all the meal suggestions, exercise programs, and everything else in the dietary lexicon are little messengers within your body, your hormones. Your hormones—and there are hundreds of them—carry messages from your brain to your body and from your body to your brain. When you eat certain foods, some hormones kick in telling you whether you want more food, where that food will go, what effect it will have on the body and on the brain. When you exercise, hormones go to work, directing the body to move energy stores here, consume energy stores there, boost this part of the body, shut down that part. It's a very delicate dance.

And it's very easy to throw off. If one of your glands—the places in your body that produce hormones—shuts down, becomes overactive, or develops a tumor; if your consumption of a particular food throws off your body chemistry; if depression, pregnancy, any kind of emotional, psychological, or physical turmoil occurs—the body goes a little haywire.

Sometimes, it's self-correcting. It might be off for a few minutes or a few days, but pretty soon things return to normal. But sometimes it's a “new normal.” The body has gotten used to its condition and you eat more, or metabolize less, or vary between those two extremes. That's when you start to gain weight.

And, lest we think that “new normal” can be caused only by an “extreme” situation—like tumors or gland failure—consider the aging process. If you could consume pizza and beer every night during your college years without gaining an ounce, you've probably found you can't do that any more.

What's the reason? Hormones. The production of many hormones declines with age, slowing metabolism. It's a fact of nature. But that doesn't mean we have to be captive to weight gain.

The hormonal changes that cause weight gain and occur because of weight gain are complex. The myriad of diet books and hormone books that are currently available are incomplete. Most of these books focus on the hormone *insulin* as the major hormone that makes you fat. Books on other hormones, such as *estrogen*, *thyroid*, and *growth hormone*, are also available, but none of these really get to the heart of the matter. All of your hormones work in concert to control your metabolism, body composition, and body weight. I wrote this book because I became frustrated with the incomplete messages these other books provided.

The information contained in this book is not a bunch of theories I invented myself. This book contains the most up-to-date scientific information about your body's hormones. Most of the topics in this book have been the major focus at national and international medical meetings. There are hundreds of scientific studies to back up this information; many of these are listed in the Bibliography at the end of this book. Some of the information I present in this book is pretty technical, but I have made every effort to walk you through the concepts step by step so that you understand all the variables involved.

My intention with *Hormonal Balance* is to bring hope and some new solutions to overweight people who suffer needlessly because of hormonal imbalance.

*This book is dedicated to my lovely wife, Fiona,  
who has helped me with every aspect of this book,  
especially by giving me the love and support I needed  
to make this book a reality.*

# ACKNOWLEDGMENTS

I WOULD LIKE TO THANK all my patients, past and present, for the knowledge they have given me about the multiple faces of hormonal balance and imbalance, and the privilege of being involved in their care. I would also like to thank my office staff Janet Baldwin, R.N., Jennifer Kotze, Melva Baker, R.N., M.S., F.N.P.B.C., Beth Larker, Andrea Floyd, Shundalyn Vanderhorst, Deborah English, Stacy Wilson, Tamika Slack and Fran Ritter, R.N.

Also, an extra special thanks to Dr. Anthony Karpas, whose insights into the field of endocrinology have been invaluable. I would also like to thank all the nurses in the diabetes units at Northside Hospital and Crawford Long Hospital for taking care of all my patients. I am also thankful to everyone at Bull Publishing, especially Jim Bull, for his faith in me and willingness to publish a book on this topic and his vision to publish this second edition.

I'd like to thank my family Howard Isaacs, Sheryle Isaacs (and special thanks to my mother for delicious new recipes for the Hormonal Health Diet), Fiona Farrelly, Margaret Farrelly, Aaron Farrelly, Joyce Young, Brianna Young, John Little, IV, John Little, Sr., Stephen Gargan, Brenda Gargan, Rebecca Gargan, Laura Gargan, Lori Johns and Chase Johns.

— *Dr. Scott Isaacs*

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# HORMONES AND METABOLISM

AMERICANS ARE FATTER THAN EVER. Our comfortable couches, our reliance on fast food, our speedy cars and our road systems and spread-out cities that mean you never have to touch a foot to the ground—they help make us fat. We spend billions of dollars on diet books; we throw \$50 bills at jars of diet pills; we tear through diet supplements, diet magazines, and turbo-speed weight-loss plans; we sign up for subscriptions at health clubs that we never use, book appointments with diet doctors whom we ignore, and make half-hearted attempts at starting exercise programs that we never finish.

And still we are fat.

Why is this? Why can we not lose the weight? Why can we not be the thin, svelte, sexy, beautiful human beings we picture ourselves to be?

Well, part of it is in our minds. Until we can separate ourselves from our images of what a sexy, beautiful human being ought to be (thin, rapturously muscled, and sleek), we have no chance of getting there. That ideal version of a human being—represented by those actors, athletes, and supermodels you see on television and in magazines—is a trick of the photographer's light, a creation of the makeup artist's pencil. That ideal version of a human being is an impossibility.

But part of the problem, a large part of it, is in our bodies. The human body is a terrifically complex machine. Each piece of the machine has an impact on every other piece of the machine, and the

machine is constantly analyzing input from inside and outside and adjusting itself accordingly. If one part of the machine goes “off,” other parts can follow.

Obesity can be the result of the human machine getting off track. And one purpose of this book is to help you understand why and how it gets off track—forces that are greatly influenced by our hormones. Finally, this book will tell you how to maintain your body so that it doesn’t get off track at all, and your weight remains under safe and healthy control.

### **A NEW WAY OF THINKING ABOUT YOUR WEIGHT**

The statistics are staggering: According to the National Heart, Lung, and Blood Institute, almost 75 percent of Americans are overweight or obese. Forty years ago, the figure was 43 percent. Thirty-five percent of children under the age of 19 are at risk for becoming overweight. Ninety-eight percent of people who lose weight on a diet gain it all back within five years. Some gain more than they lost.

Science has labored to discover the cause of obesity. People try diet after diet, losing some weight only to gain back more, desperately trying any solution they can find. But there is no magic cure. There won’t be one in this book either, so if you’re expecting one, put the book down now and blow \$50 on those “diet pills” over there. If there were a magic cure, you’d know about it. It would not be a secret.

Fortunately, the last few years have brought a change in the way doctors and scientists view obesity. Most have thought of obesity, except in the rarest of patients, as a matter of willpower. Obese people ate too much. They didn’t exercise. They didn’t practice a balanced diet or a regular workout program. They could lose the weight if only they’d have some guts and determination.

Obesity is no longer considered a problem of willpower. It’s a lot more complicated than that.

Obesity used to be considered almost a problem in itself. Now doctors realize it’s more a part of a syndrome. Obesity has passed cigarette smoking as the number one preventable killer because it’s connected with a host of medical problems ranging from heart disease and high blood pressure to diabetes, arthritis, gall bladder problems, and even certain types of cancer. The thing about many of these medical problems

is that they cause other medical problems. Obesity is merely one part of the overall picture.

But think of how we treat these medical problems: individually. Pharmaceutical companies get rich manufacturing the vast array of medications needed to treat these conditions. I'm not putting down medical science; these medications have extended our lives and prevented certain death for many people. But it's a sign of the times that we treat so many individual diseases by using drugs, and not by tackling the root causes of our problems.

In fact, these diseases—which are known as “diseases of civilization”—were almost unheard of generations ago among our lesser-weight ancestors. And doctors have discovered that even a minuscule amount of weight loss—say, 5 or 10 pounds—can reduce our risk for many of these diseases.

The key to that weight loss? Hormonal balance. Hormonal balance can help you achieve the weight loss you need to prevent, alleviate, or even cure many of these conditions.

## **YOUR HORMONES CONTROL YOUR WEIGHT**

Whether you are lean or overweight, your hormones regulate your fat cells or fat tissue. This is a simple fact, as many women already know. For example, when some women gain weight, their menstrual cycles go out of whack.

But the hormones that control the menstrual cycle are only some of the many hormones that regulate your weight. And hormones don't go out of whack in a vacuum. Many overweight people have an intuitive sense that something's wrong in their bodies. Hormones not only regulate weight; mood and emotion, the desire (or lack of desire) for food, and the ability to process that food are all intimately related to hormone levels in the body. Again, it has nothing to do with willpower.

Listen to Dr. Bjorntorp of the University of Goteborg, Sweden:

With visceral fat accumulation multiple endocrine perturbations are found, including elevated cortisol and androgens in women, as well as low growth hormone and, in men, testosterone secretion. These hormonal changes exert profound effects on adipose tissue metabolism and distribution. At the adipocyte (fat cell) level, cortisol and

insulin promote lipid accumulation by expressing lipoprotein lipase (fat cell enzyme) activity, while testosterone and growth hormone and probably estrogens exert opposite effects.

What does this mean? Hormones have powerful interactions with your fat cells and have a major influence on your weight. And insulin is only one of many hormones involved.

And what are hormones? Hormones are as fundamental as life itself. All living creatures, as a matter of fact, have hormones. They are powerful molecules that control your metabolism. Hormones regulate how much fat you have and where you have it; they control your appetite; they affect your energy level; they influence your mood, your emotions, even your desire to exercise. Hormones determine the size and strength of your muscles. And hormones help determine your body weight.

This book will show you that by balancing your hormones, you will improve your metabolism, increase your energy level, lower your appetite, and quite possibly correct your body weight.

## **THE FAT GENE?**

Great strides have been made in determining the genetics of obesity, and many genetic links to obesity will be discussed in this book. Many genes have been attributed to the control of body weight, metabolism, appetite, and body fat distribution. To date, more than 500 genes have been linked to obesity. Because of our genes, our hormonal systems are almost identical to those of our ancient ancestors. Very little has changed over the generations.

Unfortunately for us, our environment has changed even if our hormonal systems have not. No longer do we need to forage for nuts and berries; no longer do we need to kill our dinner or go without. We have McDonald's, Snickers bars, bags of Doritos, Ben and Jerry's, and cars to get us to the restaurant or grocery store. "Becoming obese," says obesity expert Dr. James Hill of the University of Colorado, "is a normal response to the American environment."

It's an environment that was created by the Industrial Revolution. Before the Industrial Revolution, with all its advances in agriculture,

transportation, and processing, granulated sugar was an extravagance. Ice cream was a delicacy. Anything requiring refrigeration was a luxury reserved for the wealthy (or those in very cold climates). It all changed almost overnight, in the time scale of human history: suddenly, high-calorie, high-fat, highly refined sugar foods were inexpensive and readily available.

And we *like* those foods. We want more; and we want more for our money. Think of “super-sizing.” A double cheeseburger for 99 cents! A 48-oz. Coke for only a dime more than a 32-oz. Coke!

Seems like a bargain, right? But does “more” mean “better”? We are paying a price for all that “free” extra food. Sugars and fats bombard our delicate hormonal systems. Our genes can’t keep up with the changes.

Many nutrition experts today recommend that we eat the way our ancestors did thousands of years ago. Dean Ornish, creator of the diet that bears his name, has said that thousands of years ago “it was survival of the fittest.”

But things have changed. Back then the problem was finding enough food to avoid starvation. And different cultures had different diets. The Inuits of northern Canada had (and still have) a high-protein, high-fat diet, the better to insulate their bodies during the long, hard winter (the body burns that fat for heat and keeps itself alive). The ancient tribes of Africa, Mexico, and India adhered to a whole-grain, high-carbohydrate diet. The bottom line was the same: many different diets resulted in hormonal balance and lean physique.

But today we look for a “one size fits all” solution. That’s why so many diet books contradict each other. Different authors select the diet of a particular ancient culture to match the diet they’re writing about. This anthropological basis for dieting falls short due to the fact that it does not take hormones into consideration at all. Obesity today exists because the food of our civilization disrupts the delicate hormonal balance genetically programmed into our bodies.

“Genetics loads the gun. Environment pulls the trigger,” says obesity guru George Bray.

Well, we can’t change our genetics (not yet, anyway). But we can change our hormones. And you can change your hormones without eating like a caveman. This book will show you how.

## HORMONES REGULATE YOUR METABOLISM

**Metabolism** (n.)—The sum of all the chemical and physical changes that take place within the body and enable its continued growth and functioning.

Metabolism is a critical determinant of your weight. Why is it that two people can eat the same amount of food and one gains weight while the other does not? It's metabolism. A fast metabolism will burn off the calories, while a slow metabolism applies them directly to the hips.

And what regulates metabolism? Hormones.

Hormones and metabolic rate help explain the paradox that exists between those who pig out and never gain weight and the calorie counters who gain weight simply by smelling doughnuts.

Think of your body as an engine. Metabolism is the rate at which the engine runs. Hormones are the push on the accelerator. Step on the gas and raise your metabolism.

Most of us have a very efficient metabolism. (Nowadays, this is bad.) This means that the food—the fuel—you eat is efficiently burned, with as much conserved as possible. But unlike a car's engine, where the more efficient the better, an efficient metabolism requires less food to maintain. And what happens to that extra food? It's stored as fat.

Why do most of us have such an efficient metabolism? The answer is genetics. We have been genetically selected for our efficient metabolism. Keep in mind that, until very recently, food was scarce. Many people died of starvation. There was no such thing as a fat caveman. The key to survival was a slow metabolism: save every excess calorie as fat, because you'll need it during the famine.

And times of famine were plentiful. The world revolved around agriculture, and agriculture was far less refined in those days. Any natural event—and, of course, there were no weather forecasts to warn about them—could wipe out a year's crop and influence the crops for years to come.

So only those with an efficient, slow metabolism survived. Those people who would be considered naturally thin in today's society died in the famines.

Some people with inefficient metabolisms survived the centuries. You know these people. These are the ones who eat and eat and never get fat. Their internal processes are so inefficient that they need to take

in as much fuel/food as possible just to keep their bodies going; there is never enough left over to be stored as fat. At one time this was a survival disadvantage, but times have changed. The metabolically inefficient are able to eat large quantities of food and never get fat.

But what about the rest of us? Are we doomed to keep piling fat on until the next famine? Of course not. There is a lot you can do to change your metabolism, and changing your metabolism will improve your health.

If your metabolism is efficient and slow, you are sluggish and tired all the time. When you speed up your metabolism, you burn calories quicker. Your energy levels are raised, and you feel great.

Unfortunately, there is no perfect medication to make this happen. Medications that do claim to accomplish this have side effects: they'll make your heart beat faster or cause your mind to race, both of which put psychological and physiological stress on the body.

Maybe you're thinking you can do the job with exercise alone; after all, if you burn the calories, you'll lose weight, right? Well, yes, but there are limits. Most people exercise one or a maximum of two hours each day. But a revved-up metabolism works 24/7. Take jogging: you'll need to jog about 35 miles to lose just one pound. But boost your metabolism via your hormones, and your weight will come off consistently and stay off the right way.

As you read this book, you'll learn about the various hormone systems in the body and the hormones specific to each one. You'll also learn how the systems work together, how one hormone can influence another (or several others), and how the most efficient system for losing weight is the one that's in balance. Throughout the book, up to and including the end, I'll supply nutritional advice to help you on your way to losing weight—and keeping it off.

## **INSULIN AND BEYOND**

You may be familiar with the hormone insulin and its links to body weight. You also may have heard that too much insulin makes you fat. That's what the experts say, anyway. (They are only partially right.) Dozens of books have been published on the subject of cutting back on insulin. These books offer solutions on how to lower your insulin levels and ultimately lose weight.

This book goes beyond insulin. It describes many more of your body's hormones and their relation to metabolism, hunger, body weight, and body composition. There are many medical conditions that can cause you to be overweight. We will discuss conditions such as hypothyroidism, metabolic syndrome, Cushing's syndrome, polycystic ovary syndrome (PCOS), male hypogonadism, menopause, aging, growth hormone deficiency, insulin resistance, and even stress and depression. All of these conditions can slow your metabolism and make you gain weight.

Insulin is important; I don't mean to question that. But it is not the only hormone that affects your weight.

Human beings can have countless hormonal problems. These can bring about a variety of symptoms, physical conditions, moods, and emotions. And by identifying specific hormonal deficiencies or excesses, you can alter your diet, add certain vitamins or herbal products, or even go on medications to help balance your hormones.

Recent medical breakthroughs have revealed that insulin is only a small part of the complete hormonal picture. Dozens if not hundreds of hormones are involved in the regulation of body weight. Glands such as the adrenal gland, the thyroid gland, the pituitary gland, the ovary, and the testicle all produce hormones that influence your body weight and body composition.

Hormones contribute to obesity, and obesity creates a hormonal imbalance that slows metabolism and perpetuates itself. Here insulin does play a role. Improper insulin action leads to high insulin levels, resulting in hunger and weight gain.

But there's also the thyroid. Low thyroid hormone levels or inefficient processing of thyroid hormone slows metabolism and causes weight gain.

Low androgen and growth hormone levels lead to reduced muscle mass and increased fat mass.

In women, low estrogen levels increase the amount of fat in the belly, but high estrogen levels increase fat in the hips and buttocks.

High cortisol levels increase fat in the belly and can cause tremendous weight gain.

Leptin, resistin, adiponectin, and other hormones are produced by the fat cell itself. "Hunger hormones" have powerful actions on the hunger centers in the brain. Various genetically controlled hunger hormones affect your appetite, metabolism, and body weight.



Also, food affects your hormones. Food is a powerful drug that triggers a vast array of hormonal, chemical, and brain effects.

But you're not hostage to your hormones. You can alter them and achieve hormonal balance. With hormonal balance you will experience weight loss and increased energy, but the benefits do not stop there.

Hormonal balance can dramatically reduce your susceptibility to the medical problems mentioned above and can alleviate a wide variety of complaints. Hormones also have powerful effects on the immune system.

Put simply, hormonal balance can save your life.

The eating principles in this book are not designed specifically for weight loss; they are intended to help you achieve hormonal balance. With hormonal balance, you will optimize your metabolism and you will lose weight. And by learning about the actions of your body's hormones, you can tailor the nutrition plan for yourself and your family members. This book explains how.

## **YOUR HORMONAL IDENTITY**

You are an individual. Your fingerprints are unlike anyone else's fingerprints; your sense of humor is not like anyone else's sense of humor; your tastes in music, clothing, colors, animals, and people differ from everyone else's tastes in those things, and almost any other thing.

So, of course, your hormones are not the same as anyone else's hormones.

But keep in mind that hormones control all facets of life. In addition to body weight and metabolism, hormones control mood, the menstrual cycle, and your biological clock. Hormones are also the key that unlocks the door to a healthy body weight.

Hormonal balance will help you achieve health, wellness, physical and mental well-being, and optimal metabolism. The secret to achieving a healthy body weight is in your hormones.

And *your* hormones, in particular, reflect your internal chemistry. Hormones are the reason some people remain youthful and vital later in life while others quickly deteriorate both mentally and physically.

You may not know what your hormonal identity is, but this book will help you find it. Subtle signals, from physical symptoms to physical

traits, give us clues to our hormonal identity. In addition, hormonal testing, *when done properly*, may also help us discover our hormonal identity.

Each chapter in this book offers methods of determining your status with regard to a particular hormone. Your levels may be too high, too low, or right where you want them—but you can have them right where you want them all of the time.

## **HORMONES CHANGE WITH AGE**

Want to know why you get fatter when you age? Want to know why your muscles droop, your sex drive diminishes, and your sleep gets harder to come by? The answer is your hormones.

Many of our vital hormones are at a fraction of what they were when we were young. These low levels, once considered a normal part of aging, are now considered by many physicians to be abnormal.

Aging is a major focus of this book, because hormones, aging, and metabolism are so closely related. We become older; our metabolism slows; we gain weight. But that need not be the end of the story. This book will show how you can reverse some of the hormonal changes that occur with aging.

Largely due to modern medicine, we no longer accept that aging means falling apart and crawling into that long goodnight. Doctors are now treating hormonal deficiencies, and a new branch of medicine, called anti-aging medicine, has evolved. Anti-aging physicians routinely prescribe hormones as a way of reversing some of the effects of aging. It's a whole new paradigm for medicine. This book discusses not only methods of hormone replacement, but also alternative ways to raise hormone levels using diet and specific vitamins and herbal remedies.

## **FOOD AND YOUR HORMONES**

What's the most powerful drug you take on a regular basis? You might think it's some sort of high-tech medication, and there are many that have profound effects on the body. But in terms of a day-in, day-out regimen, the most powerful drug is food. Food can create or cure illness;

every bite you take affects your hormones. Hormones can even be affected by the *sight or smell* of food.

Powerful stuff, indeed!

Every time you eat, a chemical reaction takes place between your hormones and the food. Hormones control your digestive system, and your digestive system, in turn, produces its own set of hormones. Hormones control your appetite and hormones control your cravings. Carbohydrate cravings, for example, are closely linked to several hormones. (You chocolate lovers will find out that there's a reason you crave chocolate the way you do.)

The hormone most closely linked to food is insulin. But insulin isn't the only hormone affected by food, nor is it necessarily the most important.

Sometimes hormones in food can affect us without our even knowing it. Hormone use in the livestock industry is commonplace, and we ingest those hormones when we eat the cows, pigs, sheep, and chickens that have eaten them. The toxins and chemicals that get into our foods frequently contain substances that mimic hormones.

There is also a positive side to this: Some foods and many common herbs contain natural substances that mimic hormones. These can sometimes be used as alternative forms of hormone replacement.

In this book, we discuss food—carbohydrates, proteins, and fats—and how it affects your hormones. We also discuss food cravings, how hormones control your cravings, and how you can eliminate your cravings by controlling your hormones.

But we'll go beyond that. Specific foods affect specific hormones. Foods contain micronutrients that control the production and processing of hormones. Today's processed foods lack many of the vital nutrients that the body requires for proper hormone production and efficient hormone action.

The eating suggestions in this book are not an attempt to force a rigid system into your life. Rather, we offer simple eating guidelines as a way to help you achieve hormonal balance.

## **THE ENDOCRINE SYSTEM: YOUR BODY'S HORMONES**

The endocrine system is the body's way of communicating and controlling its functions. Virtually every part of the body is regulated by

hormones. The word *hormone* has an interesting etymology: it comes from the Greek *horman*, meaning “to stir up” or “to urge on.” Classically, a hormone is a substance produced by a gland and secreted into the bloodstream to execute its action at a distant location in the body.

We now know that almost all organs, and not just glands, make hormones. Nerve cells, fat cells, intestinal cells, liver cells, and even heart cells and kidney cells all make hormones.

Many of the “classic” hormones are controlled by the pituitary gland—referred to as the “master gland”—in the brain. These include thyroid hormone, androgens, estrogens, cortisol, and growth hormone. The pituitary gland makes its own set of hormones that control these glands. The pituitary gland is controlled by a portion of the brain known as the *hypothalamus*. Higher centers in the brain, influenced by our thoughts, moods, emotions, and hormones, control the hypothalamus.

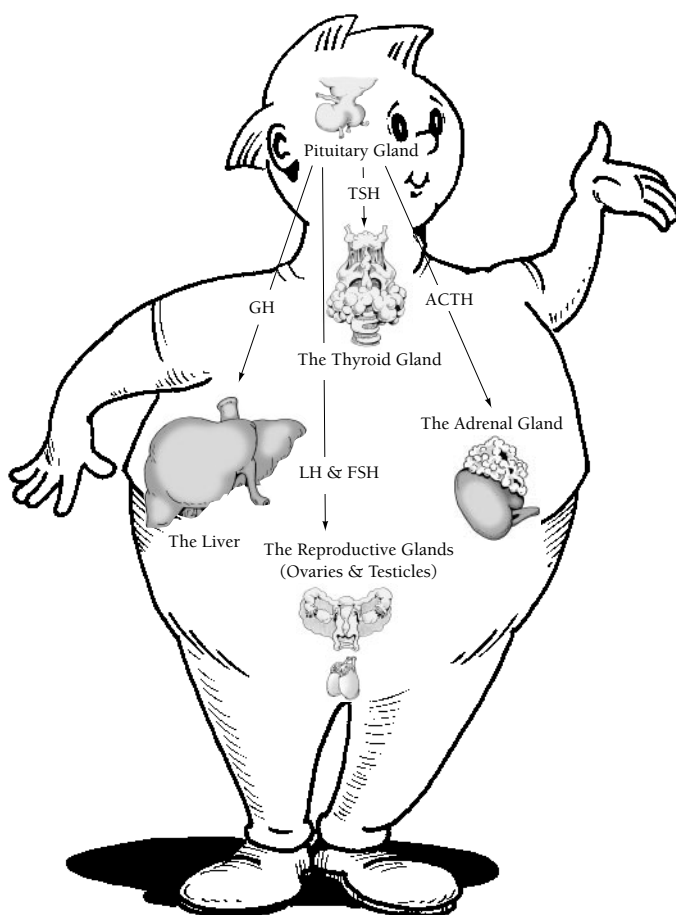
Ultimately, then, your brain controls your hormones. *But* your hormones also control your brain.

Your hormone levels are constantly in a state of flux. They are never steady, always going up or down. Your brain “listens” to your hormones to figure out what to do. High hormone levels feed back to the brain, telling it to shut down production of a particular hormone. Low hormone levels do the opposite, causing brain hormone production to surge.

The rhythms are not always predictable. Some hormones follow a regular 24-hour cycle, known as a circadian rhythm. But those rhythms aren’t in sync. Cortisol, for example, peaks at 7 to 8 a.m. Growth hormone, on the other hand, peaks at about 3 a.m.

Many other hormones are not under the control of the pituitary gland. Insulin is not officially controlled by the pituitary gland, but imbalances of thyroid hormone, growth hormone, cortisol, estrogen, or testosterone can affect insulin. Various other hormones are not regulated by the pituitary gland, such as fat hormones, pancreatic hormones, gut hormones, and other hormones that don’t come from traditional “glands.”

Many things can go wrong with hormones. There can be too much or not enough, the receptors might not work, there might be proteins in the blood binding up specific hormones—the possibilities are endless.



**Figure 1.1**

**THE ENDOCRINE SYSTEM I: Control by the "Master Gland"**

The pituitary gland, also known as the master gland, produces hormones that regulate other glands in the body. Thyroid-stimulating hormone (TSH) regulates hormone production from the thyroid gland. Adrenocorticotropic hormone (ACTH) regulates adrenal gland hormone production including cortisol and dehydroepiandrosterone (DHEA). Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) regulate gonadal (ovaries or testes) hormone production including estrogen, progesterone, testosterone, and androstenedione. Growth hormone (GH) regulates the production of insulin-like growth factor-1 (IGF-1) in the liver. Hormones made by the target glands send signals back to the pituitary gland.

## HOW DO HORMONES WORK?

Think of a lock and a key. The key (hormone) unlocks the lock (receptor), “directing” it to open or close, as the case may be. It changes the lock’s status from locked to unlocked, or vice versa.

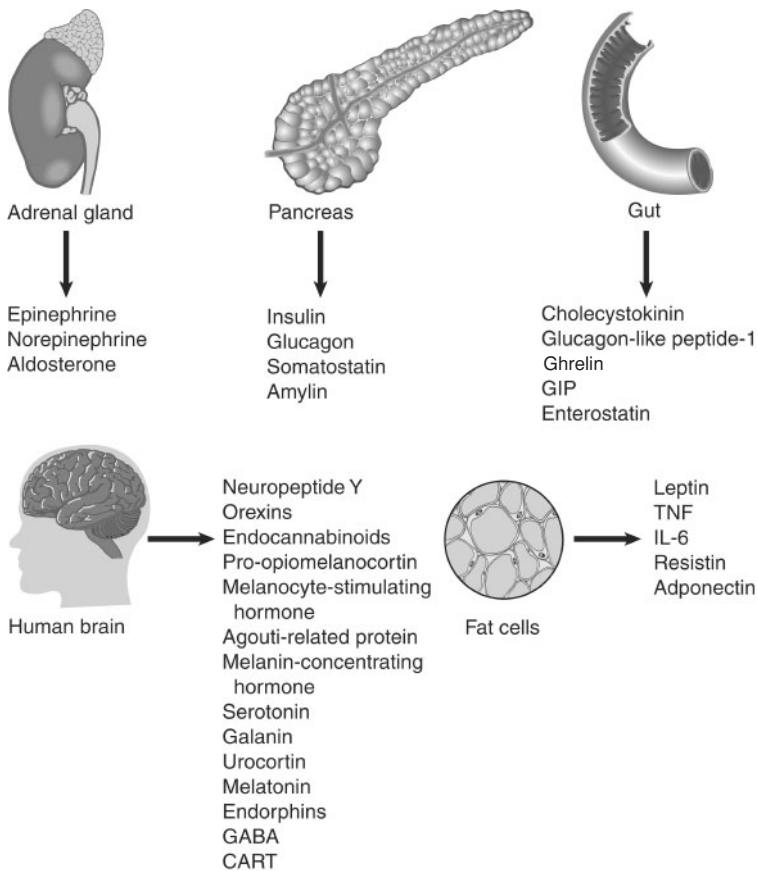
Hormones, in the great scheme of things, are tiny. A single drop of blood contains literally thousands of hormones. The hormones travel through the blood and other bodily fluids, serving as chemical messengers. The message directs the organism at the receiving end—known, appropriately enough, as a “receptor”—to do something. Receptors are special proteins that can recognize and bind a particular hormone, and when hormone and receptor merge in a cell, a chain of events begins. Hormones cause specific genes in the cell to turn on and off. Since hormones work by turning on and off genes, you can fight against your genetic predisposition to being overweight by changing your hormones!

The keys—the hormones—are made by glands. The pituitary gland (also known as the master gland) makes special hormones that control many of the glands (think of the pituitary gland as the CEO of the key company). And the brain makes other hormones that control the pituitary gland (like the chairman of the board). So, ultimately, everything is controlled by the brain. But in keeping with nature’s delicate balance, a system known as “feedback” exists. Hormones made by the glands have reciprocal influences on the brain and pituitary gland. In other words, your brain controls your hormones, and hormones control your brain. The situation works both ways because, as messengers, hormones can tell parts of the body what to do, and then they have to obey a part of the body telling *them* what to do.

After all, every living cell has hormone receptors, and hormones control every living cell. They do so by working through the fundamental component of living beings: DNA. Glands “secrete” hormones into the bloodstream. There they travel to every nook and cranny of your body until they locate their specific receptors. Virtually every cell in the body has receptors for a wide variety of hormones.

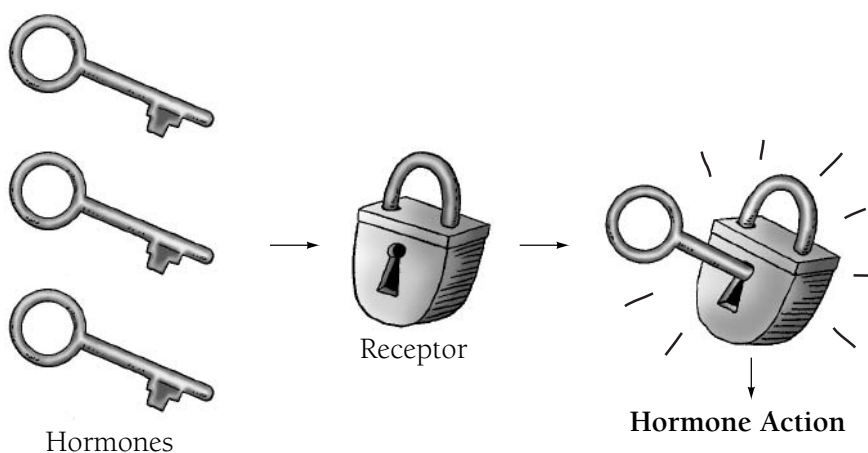
## STRESS DISRUPTS HORMONAL BALANCE

In general, stress means pressure or strain on the body from physical, psychological, or emotional causes. We are living in stressful times.

**Figure 1.2**

**THE ENDOCRINE SYSTEM II: Many Hormones Function  
Independent of the Pituitary Gland.**

Many hormones are not under the control of the pituitary gland. The adrenal gland produces the stress hormones epinephrine and norepinephrine, as well as aldosterone (a steroid hormone that regulates blood pressure). The pancreas produces several important hormones, including insulin, glucagon, somatostatin, and amylin. The stomach and intestines make ghrelin, cholecystokinin (CCK), enterostatin, and glucagon-like peptide-1 (GLP-1). Fat cells make leptin, TNF, IL-6, resistin, and adiponectin. The brain makes many hormones, including orexins, endocannabinoids, neuropeptide Y (NPY), proopiomelanocortin (POMC), melanocyte-stimulating hormone (MSH), Agouti-related protein (AgRP), galanin, endorphins, GABA, melanin-concentrating hormone (MCH), serotonin, urocortin, and melatonin.



**Figure 1.3**

**HORMONES AND RECEPTORS: How Hormones Work**

The specific hormone molecules are like specific “keys.” Only the appropriate hormone corresponds to a receptor (lock). When a hormone and a receptor interact, it sets forth a chain of events that ultimately lead to the actions associated with each specific hormone.

Certainly, many generations have uttered those words, but think of what our generation faces: instantaneous communication, constant availability, “just-in-time” production methods. Even children, once largely free of the stresses of adult life, now make “play-dates.” Our lives have been sped up in ways previous generations never could have imagined.

We cope, or try to. *Allostasis* is the term scientists use to describe how the body copes with stress. We take vacations to get away from it all. But most of the year, there it is, all the stress we live with. And then there are other stresses: the death of a loved one, the heartbreak of a relationship, even the “good-for-you” hunger of a crash diet (which, of course, isn’t really good for you at all).

Usually, two things happen in response to stress. The first is that our body goes into conservation mode. Metabolism slows, and even the normal diet we were adhering to makes us put on weight. The second is that we look to one of the most familiar items in our lives for consolation: food. And often not just food, but chocolate bars, sugary



sodas, and super-sized containers of French fries—“comfort food,” it’s sometimes called.

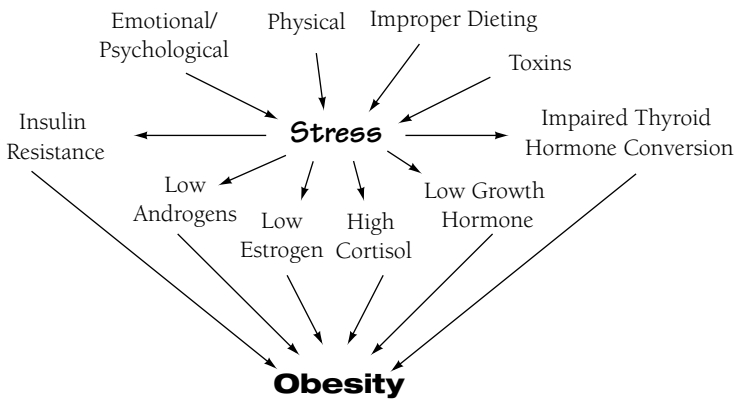
Why do we do this? Because of our hormones. Any kind of stress—whether mental, physical, or emotional—can disrupt the hormonal balance in our bodies in ways that make us gain weight.

Stress causes the brain, pituitary gland, and adrenal glands to pump out stress hormones. These hormones cause the biological reactions we associate with stress, from a rapid heartbeat to a rise in blood sugar to slowed digestion. They prepare us for the “fight or flight” response.

Now, all of us experience stress. Furthermore, our bodies have adapted to handle the normal hormonal surges that occur with stress. Acute, short-term stress does not cause you to gain weight.

Chronic, long-term stress, however, is something else entirely. Too much stress and longer-term elevations of stress hormones cause weight gain.

Many diets make you lose weight in a way that puts a tremendous stress on your body. This is why most diets ultimately fail. Chronic



**Figure 1.4**

#### **HORMONAL CHANGES THAT OCCUR WITH STRESS**

Stress disrupts the body’s hormonal system by creating insulin resistance, lowering sex hormones (estrogen and testosterone), lowering growth hormone, and increasing cortisol levels. Stress also reduces the body’s ability to convert thyroid hormone to an active form. Each one of these hormonal changes slows metabolism and causes weight gain.

stress also causes the body to shift its focus away from its normal activity. Stress causes the immune system to wane, muscles to shrink, and, in general, a lousy feeling throughout your body.

We'll discuss the hormonal effects of stress further in each chapter.

### HOW CHRONIC STRESS AFFECTS YOUR HEALTH

**Digestive system:** Stress causes increased stomach acid production and stomach pain. It causes irritable bowel syndrome, with symptoms such as nausea, diarrhea, or constipation.

**Obesity:** Stress increases appetite and alters hormonal balance.

**Immune system:** Weakening of the immune system makes you more likely to get infections.

**Nervous system:** Stress causes anxiety, depression, insomnia, and an inability to enjoy life. Stress can also impair memory and the ability to make decisions.

**Cardiovascular system:** Stress increases the risk for heart attacks and strokes.

### DIETS CAN WRECK YOUR METABOLISM

When you go on a diet, your metabolism is dramatically altered. When your body is losing weight, it can become “stressed”—causing all the hormonal disruptions that make you stop losing weight. Dieting, ironically, slows your metabolism. This is why 98 percent of diets ultimately fail.

How does this happen? Think of a famine. When you go on a diet, your body doesn't realize that you are doing this for its own good. Your body thinks it is starving. It cannot tell the difference between a diet and a famine. It's all about survival.

Your body slows its metabolism, making it even more efficient. After all, it has no idea when the famine will end. And how is metabolism slowed? Through your hormones, of course.

During dieting, thyroid hormone and androgen levels plunge and cortisol (a hormone that makes you gain weight) surges. Eventually your body succumbs to this hormonal pressure, and your diet ultimately fails.

This book will show you how to prevent this from happening. We will show you how to lose weight consistently, and *you will keep the weight off*. In fact, it is possible to lose weight and maintain—or even increase—your metabolism. It all depends on hormonal balance.

## **HORMONES REGULATE BODY COMPOSITION**

The amount of muscle you have is perhaps the most important determinant of your metabolism. Your hormones, most notably androgens and growth hormone, control your muscle mass.

Think of the bodybuilder on steroids. He eats all day and puts on more and more muscle. Without the boost of “roids,” all that food would become fat. As the old saying goes, “muscle burns fat”—and it’s true. If you want to boost your metabolism, a sure-fire way is to increase your muscle mass.

Now, many of us actually have a normal body weight but a very high percentage of body fat. A person with this condition has been described by Dr. Neil Ruderman as the *metabolically obese, normal-weight individual*, or MONW. But obese or not obese, if you have a high percentage of body fat, you are likely to have hormone problems.

This book makes an effort to explain how hormones affect your body composition and how your body composition affects your hormones.

For example, as we age, our levels of growth hormone and testosterone plunge. Although they once considered this a normal part of aging, doctors have been treating these low levels to get them back to the levels of a 30- or 40-year-old. Why? Growth hormone and testosterone both have an effect on muscle mass. In this book, we will go over the effects of growth hormone, testosterone, and other androgens (testosterone-like hormones).

## **HORMONAL DISORDERS IGNORED BY MANY DOCTORS**

Doctors learn about hormonal disorders in medical school, along with so many other things. But the medical school curriculum stresses that hormonal disorders are usually rare. Not only is this untrue, but it does

a disservice to endocrinologists, who study hormones and hormonal disorders, and to patients, who are told that the problem lies elsewhere. Medical schools teach about hormonal disorders in their extreme cases but fail to teach about less severe cases of the same disorders.

In real life, hormonal disorders can occur across a wide range and can have many causes. Some hormonal disorders are caused by tumors (some cancerous, some not cancerous) of glands, which cause the glands to pump out excessive amounts of a particular hormone. Other hormonal disorders are caused by the complete failure of a gland.

The flaws of medical education don't stop there. In med school, the blood test is emphasized as the be-all and end-all. Symptoms are brushed aside; other test results aren't considered as seriously. But tests can be wrong. Many people with hormonal problems can have normal blood test results.

Medical schools don't teach much about the hormonal disorders caused by a mild overproduction or a minor deficiency of a hormone. They also don't teach much about receptor problems or other ways that a hormone can go haywire. The result: over the years, many doctors don't look for hormonal disorders. Why should they? They've practically been trained to ignore them.

But the consequences can be costly for patients in more ways than one. Many overweight patients seek advice from their physicians. They are usually told that their hormones are normal. "It's not your hormones," the doctor says. "Just eat less and exercise more."

Meanwhile, the doctor may be thinking, "This poor obese patient. I know that the odds are less than 2 percent that this person will ever lose weight, so why even bother to try?" This attitude has become so prevalent that doctors now openly debate the utility of trying to get their patients to lose weight at all.

Sometimes doctors miss extreme hormone problems because they are not in the frame of mind of looking for such disorders. I have seen many examples of this myself. They ignore subtle complaints and attribute your problems to your weight. They fail to consider that your symptoms may be clues to the *cause* of your weight gain, and not the *result* of it.

And although our hormones are affected by food, dieting, stress, and the other factors I've listed, sometimes hormone problems go beyond these factors. Many things can go wrong and cause hormones to be excessive or deficient, or to simply not work properly.

Many hormonal disorders will make you gain weight, and all the dieting in the world will not help until the hormonal disorder is corrected. Maybe a simple blood test won't find them, but other testing methods can—and hormonal testing techniques continue to improve. We can detect hormones in blood, urine, and even saliva. But a well-trained doctor will know what else to look for, because tests can only go so far: They should be given at certain points of the day and focus on certain parts of the body, and address other specifics that many doctors aren't aware of.

This book will discuss the symptoms of various hormonal disorders. Your symptoms will help you determine if you may have a hormonal disorder. This book will also explain various tests and help you to interpret the results.

This book is not meant to be a substitute for your physician. It is simply a guide to help answer questions. It is also intended to increase your awareness of symptoms so that you can make your physician aware of them.

## **HORMONE PROBLEMS CAN BE TREATED**

Hormone treatments cover a wide range. For some people, dietary recommendations are enough. For others, specific vitamins and/or minerals may be helpful. For yet others, medications may be required.

Fortunately, hormones and hormone treatments come in many forms—pills, patches, shots, gels, and creams—and they work in many ways. Some boost the body's natural supply of certain hormones, such as estrogen, while others work by stimulating a particular gland to make more of its hormone.

Treatment with hormones goes back to the nineteenth century, when French physician Charles Edouard Brown-Sequard injected himself with an extract of crushed dog and guinea pig testicles in order to test its efficacy. At the time, the good doctor was 72 years old, and, as with many 72-year-olds, aging had taken a toll on his appetite and sex drive. However, after the injection—to the amazement of his colleagues—the extract was found to have the same effect as modern-day testosterone.

While testosterone medications are derived from different sources nowadays, some hormone medications are still administered in an

animal form processed for human consumption. For example, a popular thyroid hormone medication, Armour Thyroid, consists of ground pig thyroid glands. And a popular estrogen medication is made from the urine of pregnant mares.

But hormones come from a variety of sources, and “natural” is not always better than “synthetic.” Moreover, some hormones work better when taken by mouth; others are digested in the stomach and work only if taken by injection, patch, cream, gel, or other creative delivery device.

In today’s managed-care environment, the average doctor has only about 10 minutes to spend with each patient. Your doctor simply doesn’t have enough time to go into as much detail as this book does. So this book is written as a guide for you and your doctor. It will explain your treatment options in some detail.

This book is also recommended for doctors and other health care providers as a guide to up-to-date treatments for hormonal problems. One of the goals is to help demystify hormone treatments for both patients and professionals. Whether you’re already taking hormones or merely considering it, I believe this book will be very helpful to you.

## **HORMONE WEIGHT-LOSS PRODUCTS AND HORMONE PREPARATIONS**

Health food store shelves are filled with herbal products that claim to affect your hormones and/or your weight. In a clever bit of marketing, herbal products are now referred to as *nutraceuticals*—“functional foods,” including vitamins and minerals, which are available from health food and drug stores without a prescription.

Nutraceuticals are not under the strict regulation used for prescription medications. The quality is highly variable. Many of them have not been properly tested. Prescription medications are held to a much higher standard. This is not to write off nutraceuticals completely; many of them show great promise.

But you should know what you’re getting. Many nutraceuticals are derived from plants, whereas some hormone preparations are made from ground animal glands or brains. The labels can be cryptic (*bovine* means cow, *porcine* means pig) and consumers may end up buying something that—at worst—can hurt, not heal.

Consider this: Many nutraceutical products make weight loss claims. And many of these products claim to affect your metabolism and/or your hormones. The important point is that these products, although considered “natural,” can be just as potent as prescription medications and should be treated as such.

In this book, I will describe many nutraceutical products. Moreover, this book will help you put things into perspective. It will tell you what products are worthwhile, what products are garbage—and what products are dangerous.

This book will also point out specific instances where a common vitamin or mineral affects your hormones. Many of us eat too much processed food that is lacking in vitamins and minerals vital to proper hormonal balance. In addition, many crops are grown in nutrient-poor soil, so that even fresh fruits and vegetables may be lacking in specific vital nutrients. Hormones require specific vitamins and minerals in order to be produced or processed efficiently.

This book will present simple dietary changes you can make to increase the minerals you need to achieve hormonal balance. Vitamins and minerals can come from the foods we eat. You don't always have to “pop a pill.”

## **HORMONAL BALANCE: YOUR GUIDE TO A HEALTHY LIFE**

It all comes down to hormonal balance. Whether you want to lose a significant amount of weight, get in shape, or even reverse the effects of aging, hormonal balance is critical.

How can this be accomplished? It starts with diet. You can tailor your diet to achieve a perfect equilibrium of hormones. The hormones themselves will do the rest of the work.

We've come to assume that once out of control, hormones will remain out of control—that we are powerless to govern these messengers circulating throughout our bodies. That isn't true, even if you've already suffered from a hormonal ailment. You *can* control your hormones. You *can* control your metabolism. Follow the lessons in this book, and you will be on your way to a *healthier, thinner, well-tuned* version of you.

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# INSULIN AND FOOD

EVERY BITE OF FOOD THAT YOU PUT IN YOUR MOUTH AFFECTS YOUR HORMONES. Whether you eat junk food or healthy food, large quantities or small quantities, or even if you starve yourself, your hormones are affected. When it comes to food, one hormone stands out above all the rest: insulin.

You've probably heard of insulin, but you may not have realized that insulin is a hormone. It's the hormone that's responsible for your blood sugar, but insulin does more than that. Insulin problems are the cause of diabetes and metabolic syndrome, and they have been linked to medical problems such as hypertension, heart attacks, strokes, peripheral vascular disease, and early death. When it comes to *hormonal balance*, insulin is critical.

Insulin is one of several hormones made by the pancreas. The pancreas is really two separate organs in one. The *endocrine pancreas*, also known as the islets of Langerhans, consists of cells that produce the hormones responsible for the *metabolism* of food. Special cells, known as beta-cells, make insulin. Other cells in the endocrine pancreas synthesize the important hormones glucagon and somatostatin. Glucagon and somatostatin are discussed in detail in Chapter 10. Hormones produced in the endocrine pancreas are secreted into the blood and act on tissues throughout the body. The *exocrine pancreas* makes enzymes needed for the *digestion* of food. These enzymes are secreted into the intestines. Damage or injury to the pancreas can cause problems involving both hormones and enzymes.

All the pancreatic hormones work together to help regulate your blood sugar, appetite, metabolism, and, ultimately, body weight. When it comes to weight regulation, insulin has a double effect. Insulin is a *hunger hormone*, stimulating appetite centers in the brain. Insulin is also a *fat storage hormone*, telling the body to store food as fat, instead of burning it as energy. In Chapter 3 I'll talk about *insulin resistance*, a condition where insulin does not function properly and higher insulin levels are necessary to keep blood sugar under control. Even if you don't have insulin resistance, the wrong foods can cause your body to produce extra insulin. When insulin levels are high, weight loss is more difficult.

Insulin itself is one of the body's most important hormones, if not *the* most important. It affects every cell and every organ. Insulin instructs the liver to stop making glucose. This prevents the breakdown of muscle and fat. Insulin also causes these tissues to transport glucose out of the blood and into the cell, a process known as "glucose uptake." Together, these actions of insulin result in lowered blood glucose and the build-up of muscle and fat.

In this section, I will focus on how food affects insulin and how the Hormonal Health Diet helps you lose weight, in part by keeping insulin (and appetite) low. I'll discuss the three basic building blocks of food—carbohydrates, proteins, and fats—and how they affect insulin. I'll also explain the *glycemic index* and *glycemic load*, a controversial rating system for different types of carbohydrates. I'll explain how some carbohydrates can cause unstable blood sugar levels, giving rise to problems such as hypoglycemia, carbohydrate cravings, afternoon or nighttime hunger episodes, polyphagia (extreme hunger), and fatigue.

## THE TRUTH ABOUT CARBOHYDRATES

Scientifically, carbohydrates, or "carbs," are compounds that feature hydrogen and oxygen—the elements of water—combined with carbon. They are the most common organic compounds found in nature and are the substances produced by green plants during photosynthesis. Your body requires insulin to properly metabolize carbohydrates.

Carbohydrates in one way or another are the focus of many fad diets. For most of these plans, breads, pasta, sugary foods, and grains

are off-limits; the idea is to keep insulin production low. The upshot is that high insulin levels will make you fat. Many “low-carb” or “no-carb” diets have helped people shed pounds. The problem is that these diets are almost impossible to stay on forever. Once the diet is stopped, the weight that was lost (or even more) is regained very quickly. The truth is that all foods—carbohydrates, proteins, and fats—affect insulin, not just carbohydrates.

## CARBOHYDRATES: A QUICK GUIDE

Carbohydrates are often referred to as coming in two kinds: simple and complex. Simple carbohydrates are usually sugars; complex carbohydrates are usually starches. Regardless of what kind they are, carbohydrates—in the form of sugar, wheat, rice, grains, fruit, and vegetables—are the principal components of almost every human’s diet, and the primary source of energy in our diet.

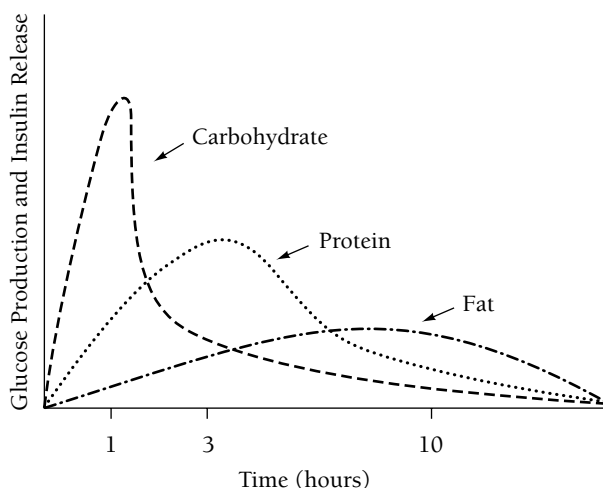
Though many fad diets emphasize low- or no carbohydrate intake, carbohydrates are an important part of your diet and are necessary for *hormonal balance*. When you are losing weight, it is essential that your body get ample supplies of carbohydrate in order to prevent muscle breakdown. Too much or the wrong kind of carbohydrate, however, can cause problems with insulin spiking and unstable blood sugar levels, which leads to hypoglycemia and carbohydrate cravings.

The terms “sugar” and “starch” are very nonspecific. I’d like to provide a more detailed, scientific description of carbohydrates to help you understand exactly what a carbohydrate is and how sugars and starches are all made up of the same building blocks. (Those of you who got an A in high school science can skip to the next section.)

- **Monosaccharides** are the building blocks of all carbohydrates, just as amino acids are the building blocks of protein. *All carbohydrates are made up of these three simple sugars:*

**Glucose:** The most abundant monosaccharide. It has the strongest effect in stimulating the production of insulin. In general, the terms “blood sugar” and “blood glucose” are interchangeable.

**Fructose:** Constituting half of what we know as table sugar, fructose is best known as the primary sugar found in fruit. Fruit provides only mild insulin stimulation, which is why it’s an



**Figure 2.1**  
**GLUCOSE AND INSULIN RELEASE WITH**  
**CARBOHYDRATES, PROTEIN, AND FAT**

Various nutrients have different effects on glucose production and insulin release. Carbohydrates cause rapid spiking of insulin. Protein and fat also cause insulin release that is longer lasting but has less spiking.

essential element to hormonal balance. The Hormonal Health Diet recommends that you consume at least 5 servings of fruit every day (see Chapter 11).

**Galactose:** No, this is not the kind of sugar they use on *Star Trek*, but a form of sugar found only in milk and milk products.

- **Disaccharides** result when two monosaccharides come together to form a simple sugar. During digestion, disaccharides are broken down into monosaccharides by special enzymes in the intestine. The two primary disaccharides are:

**Sucrose:** Made of equal parts of glucose and fructose, sucrose is found in fruits and table sugar.

**Lactose:** Made of equal parts of galactose and glucose, lactose is found only in milk and milk products. Lactose is digested using the enzyme lactase. People with *lactase deficiency* have problems digesting milk.

- **Polysaccharides** are created by the linking of many monosaccharides in very complex arrays. However, they're still nothing more than a string of monosaccharides. Polysaccharides are also known as **starches** or **complex carbohydrates**.

## DIGESTION AND METABOLISM OF CARBOHYDRATES

What actually happens when you eat carbohydrates? It's a seemingly complex process, but it takes only a matter of hours to occur—sometimes less. Let's run through it step by step.

Carbohydrates are broken down in the intestines to their most basic form, monosaccharides (glucose, fructose, and galactose), by pancreatic enzymes. Monosaccharides are small enough to be transported through the intestinal lining into the bloodstream. This blood flows to the liver through a vein known as the portal vein. This is very important, because the liver does not treat all monosaccharides the same. Glucose zips straight through the liver, but fructose and galactose must be converted by the liver to glucose before moving on. So foods like fruits, vegetables, whole grains, and dairy products, which have fructose and galactose, are ultimately converted to glucose by the liver, but this takes time. The result is that these foods cause less spiking of blood sugar than other carbohydrates.

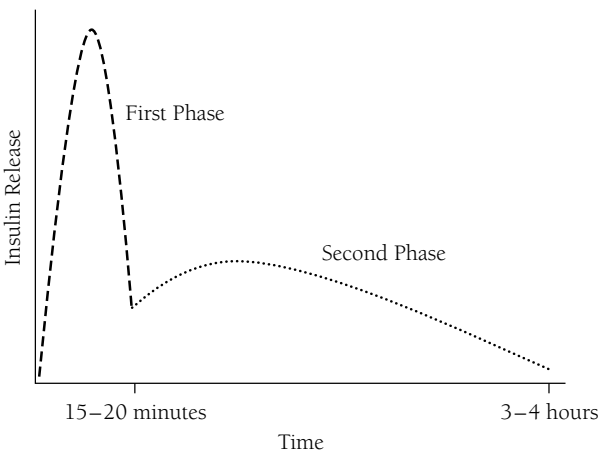
Glucose is detected by the beta-cells of the pancreas, which respond by pumping out insulin. There are two phases of insulin release. The immediate (first) phase is the release of pre-made insulin and is a set quantity. The later (second) insulin release phase comes as new insulin is produced and is a variable amount that depends on the body's needs.

## DO CARBOHYDRATES MAKE YOU GAIN WEIGHT?

For the past several decades, there has been great public interest in the composition of the American diet. The high calorie and fat content of the typical diet has been linked to a wide variety of diseases, including cardiovascular disease (heart attacks and strokes), diabetes, liver disease, kidney disease, and cancer. In their fervor to cut back on calories

from fat, many people end up increasing their consumption of carbohydrates. Diet experts continue to debate the perfect balance of carbohydrates, protein, and fat. My belief—and the belief of many other physicians and nutrition experts—is that a diet should feature a healthy balance of carbohydrates, protein, and fat. Exact percentages aren’t critical, however.

The average American now consumes over 20 teaspoons of sugar every day. Sweeteners make up as much as *one-third* of the carbohydrate content of the typical American diet. Think about that: *thirty-three percent* of everything the average American consumes is simply sugar. Thirty-three percent! That’s the brown sugar in your “fat-free” “whole grain” muffin, the sugar added to the “mango salsa” on your “heart-healthy” grilled grouper, the sugar in that “energy” bar. That’s the sugar in soft drinks, gourmet coffees, ketchup, snack cakes, and even salad dressings. And if you don’t think you’re eating so much sugar, check the labels of some of your favorite products.



**Figure 2.2**

**THE TWO PHASES OF INSULIN RELEASE**

Insulin is released in two phases. The first phase occurs in the first 30 minutes and represents pre-made insulin that is stored in the pancreas. The second phase of insulin release occurs over the next 3 hours and represents the production of new insulin.

Many low-fat or no-fat products have hit the shelves in recent years: fat-free chips, fat-free ice cream, and even fat-free chocolate cookies. But these foods aren't calorie free; in fact, because they are so much higher in carbs, some fat-free or low-fat foods have a higher caloric content than their fat-full counterparts.

## **VEGETABLES AND FRUITS**

Vegetables and fruits are by far the best carbohydrates that you can eat. If there is such a thing as a "miracle food" for weight loss, vegetables and fruits are just that. The Hormonal Health Diet allows you to have unlimited amounts of most fruits and vegetables. Why? Pound for pound, vegetables and, to a lesser extent, fruits are extremely low in calories. Fresh vegetables and fruits are high in fiber and health-promoting phytonutrients and antioxidants. In fact, many studies have been published proving the effects of vegetable and fruit consumption on the reduction of cancer, heart disease, and strokes, among other ailments. These benefits have not been replicated by the use of vitamin pills.

I strongly encourage you to consume at least 5 servings of vegetables and 5 servings of fruits every day. I consider these numbers minimums. As far as vegetables and fruits go, more is better! If you are hungry, vegetables and fruits are the first thing you should eat. It is better if you have only fresh vegetables and fruits (although frozen or canned fruit in unsweetened juice is also acceptable). Dried fruits, sweetened canned fruits, and fruit juices are high in calories and are like other "processed" carbohydrates. Processed fruits should be consumed only in very limited quantities. Grapes, watermelon, bananas, pineapple, and other tropical fruits are higher in sugar and are not off-limits, but should not exceed 5 to 7 servings in a given day.

If you are not used to eating vegetables and fruits, you may have trouble eating 5 servings of each on a daily basis. I encourage you to stick with it. Eventually you will begin to feel bad if you do not get your 10 servings of vegetables and fruits each day. When you fill your belly with these healthy foods, you will feel less hunger for the bad foods. See Chapter 11 for more information on vegetables and fruits.

## COMPLEX CARBOHYDRATES

In their most basic form, complex carbohydrates, or starches, are strings of simple sugars that come in many different arrangements. Ounce for ounce, all carbohydrates have the same number of calories. They differ, however, in the speed at which they are digested. This has profound effects on blood sugar and insulin production. All carbohydrates are eventually converted by the body to glucose. “Healthy” carbohydrates are digested and broken down slowly, providing a more gradual source of sugar to the body. “Unhealthy” carbohydrates, on the other hand, are rapidly digested and cause huge sugar and insulin spikes. In order for you to achieve *hormonal balance*, most of the carbohydrates you eat should be healthy carbohydrates.

The complex carbohydrates found in beans are very good because they are encased in a “lattice” of protein. To digest this super-healthy starch, your body must first disrupt the protein latticework. Beans provide a stable, constant source of energy that can last many hours.

Other factors that affect the digestibility of carbohydrates are cooking, processing, chewing, and digestive enzymes.

- *Cooking.* The more a carbohydrate is cooked—heated—the more easily its chemical bonds are broken down and the more quickly it is digested. Interestingly, however, there’s a flip side to cooking called *retrogradation*. When food is heated, then cooled, then heated again, the process can actually modify starches and make them harder to digest. So if you bake a potato, place it in the refrigerator overnight, and then reheat it the next day, it will be digested more slowly than it was after first being baked. Leftovers, in other words, are a *good* thing.
- *Processing.* Grinding grains makes them easier to digest, so finely milled flour is digested more quickly than whole wheat flour or simple cracked wheat. In general, the more processing something undergoes, the less healthy it is.
- *Chewing.* Back in the 1800s, many families followed the teachings of clergyman Sylvester Graham. Today, Graham would be considered prescient in many ways. A vegetarian, he encouraged his followers to eat fruits and vegetables and to avoid fried foods, and he invented an unsifted wheat flour that has taken his name (as has a



**Table 2.1**  
**FAT-FREE VERSUS REGULAR FOOD CALORIE COMPARISON**

Whether it comes from carbohydrate or fat, a calorie is still a calorie. Any food eaten in excess can cause insulin surges and can lead to weight gain.

<b>Fat-Free or Reduced Fat</b>	<b>Calories</b>	<b>Regular</b>	<b>Calories</b>
Reduced-fat peanut butter (2 Tbsp)	190	Regular peanut butter	190
Reduced-fat cookie	128	Regular cookie	136
Fat-free fig cookie	70	Fig cookie	50
Nonfat frozen yogurt (½ cup)	190	Ice cream (½ cup)	180
Fat-free caramel topping (2 Tbsp)	130	Caramel topping (½ Tbsp)	130
Reduced-fat granola cereal (¼ cup)	110	Granola cereal (¼ cup)	130
Reduced-fat croissant roll	110	Regular croissant roll	130
Baked tortilla chips (1 oz)	110	Regular tortilla chips (1 oz)	130
Reduced-fat breakfast bar	140	Regular breakfast bar	130

**Source:** *The Practical Guide to the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*. National Institutes of Health, September 1998, p. 31.

cracker made from that flour). But one of his pronouncements was dead wrong. He believed, rightly so, that Americans ate too fast. His solution, however, was that one should chew food at least 32 times (one chew for each tooth) before swallowing, and many more times than that if possible. This process, and some of the philosophy behind it, became known as *Fletcherism*, after one of Graham's followers.

Unfortunately, excessive chewing liquefies and almost completely digests the food while it's in your mouth. Saliva contains an enzyme, *salivary amylase*, that breaks down carbohydrates, so we actually start to digest sugars and starches before we swallow. By the time the overchewed food hits the stomach and intestines, it's ready to be instantly absorbed into the bloodstream—creating a huge insulin surge. (And, as nineteenth-century Americans found out, excessive chewing also leads to colossally boring meals. When do you get a chance to talk?)

- *Enzymes.* Many of the enzymes needed to digest certain types of carbohydrates come from the pancreas, as do enzymes that digest proteins and fats. The main one for starches, *pancreatic amylase*, is essentially the same enzyme found in saliva.

The thing is, it doesn't matter how many enzymes you have participating in the process. Our bodies come equipped with these enzymes far in excess of what we need; if you ate three-quarters of a pound of pure starch, you'd still have plenty of enzymes around to digest the starch. Moreover, nothing can change the digestibility of the starch you just ate. You can down a half-gallon of water after that serving of pure starch; you can chow down on other food groups; you can even throw some enzyme supplements into your system. It doesn't matter. The enzymes are going to do their job at their own pace.

Interestingly, many "fad" diets promote certain combinations of foods to "enhance" digestion. *Any diet that combines specific foods for the purposes of enhancing digestion is, at its heart, fundamentally flawed.* Slower digestion is beneficial. It produces a more gradual supply of energy to the body. If the digestion of starches is sped up, the energy load comes hard and strong and all at once, and you get an insulin surge. The insulin surge causes energy to be converted to fat,

instead of being burned as fuel, and results in a rapid lowering of blood sugar, causing symptoms of hypoglycemia. So beware of diets that base their food combinations on “enhancing digestion”: all they’re doing is enlarging your waistline.

## THE GLYCEMIC INDEX AND GLYCEMIC LOAD

The glycemic index dates back to 1981, when Dr. David Jenkins and Dr. Thomas M. S. Wolever published a paper detailing the concept that not all carbohydrates are created equal. Today, many “fad” diets are based on the glycemic index, although experts still debate its significance. The glycemic index and glycemic load (which is derived from the glycemic index) are still considered controversial because they can be misleading. When used in the proper context, however, the glycemic index and glycemic load are helpful to rate different carbohydrates more precisely than just “simple” or “complex.”

The glycemic index is a number that is determined by measuring blood sugar levels in healthy volunteer subjects who have been fasting and who then eat a portion of food that contains 50 grams of carbohydrate. The amount of food can vary, as long as it contains this constant amount of carbohydrate. The average blood sugar levels from a group of volunteers are compared to those associated with a standard high-carbohydrate food (typically a pure-glucose beverage or white bread, which is assigned a score of 100). Carbohydrates that are digested quickly cause a rapid rise in blood glucose level and have a high glycemic index. Carbohydrates that are digested slowly release glucose into the bloodstream slowly and thus have a low glycemic index. Foods with a glycemic index of 70 or above are considered to be high, scores between 56 and 69 are moderate, and scores of 55 or less are considered low.

Computation of the glycemic index is different from the measurement of the calorie. Calories are measured in a laboratory, not in real people. A food is placed in a device known as a *bomb calorimeter* and literally burned to a crisp. The amount of heat produced by the food is measured as calories. A true calorie is the amount of heat required to raise the temperature of 1 cubic centimeter of water by 1 degree Celsius; the calories we’re familiar with, the ones listed in the nutrition

information box found on every supermarket food product, are actually kilocalories—1,000 calories. Either way, what’s being determined is simply a measure of energy—not the effect a food has on the body.

The glycemic index measures glucose in the blood, but what we are really interested in is insulin. Scientists make a giant leap of faith and assume that the response of insulin parallels that of glucose. Measuring blood glucose is not the same thing as measuring insulin response. However, the two are closely related, so it can be assumed that they work in conjunction. The body requires less insulin to process low-glycemic index foods. Some have suggested the development of an *insulinemic index* as a true measure of the body’s insulin response to food.

The glycemic index can be affected by a number of variables. Acidity lowers the glycemic index; so does a high amount of fiber. The way in which foods are cooked also affects the glycemic index. The glycemic index is based on eating one food at a time, and eating foods in conjunction with each other—as we do in real life—affects the overall glycemic index.

Many experts and professional organizations do not support the use of the glycemic index. The criticisms of the glycemic index include variability in testing as well as the fact that we have no idea what these foods do in a “real-life” meal situation. The glycemic index is based not on a typical serving, but on the amount required to get those 50 grams of carbohydrate. For some foods, the portion is so huge that it is not a realistic serving size. On the other hand, the portion of another food may be unrealistically small. Many fruits and vegetables, for example, have a high glycemic index, but to get the predicted blood sugar spike you would have to eat huge quantities.

The glycemic load was developed to correct for the serving size problem with the glycemic index. The glycemic load measurement gives a rating of the blood glucose response to the amount of carbohydrate in a “typical” serving of food. A glycemic load of 20 or more is considered high, between 11 and 19 is moderate, and 10 or below is considered low.

	Glycemic index	Glycemic load
High	Above 70	Above 20
Moderate	56–69	11–19
Low	Below 55	Below 10

The experts do agree on some things. Slowly digested carbohydrates are more beneficial than quickly digested carbohydrates: beans and lentils are better than mashed potatoes and white rice, for example. Fruits are also an excellent form of carbohydrate because they're high in fiber and have fructose as their source of sugar. Studies have shown that low-glycemic foods improve blood sugar levels and reduce the risk of diabetes, improve cholesterol, and increase "fecal bulk"—the size of the stool, a known factor in the risk of colon cancer.

Table 2.2 (pages 38–45) shows the glycemic index and the glycemic load of selected foods. The glycemic index represents the impact that various carbohydrates have on blood sugar levels and insulin response. The higher the glycemic index, the greater the glucose and insulin responses. Foods with a glycemic index greater than 70 are considered high, 55–70 is considered intermediate, and less than 55 is characteristic of a low-glycemic index food. The glycemic load is calculated from the glycemic index and a typical serving size of the particular food. Foods with a glycemic load of 20 or above are considered high, 11–19 is considered intermediate, and 10 or below is typical of a low-glycemic load food.

### **SPREAD YOUR CARBOHYDRATES THROUGHOUT THE DAY**

Nibbling or eating small, frequent meals throughout the day is a great way to balance your blood sugar and insulin levels because you don't overwhelm your body with nutrients. Eating a huge portion of a so-called healthy food, such as beans or lentils, can prompt an insulin surge as easily as a Twinkie can. So if you eat frequently throughout the day, you will provide a constant source of energy to your body. The body becomes *accustomed* to receiving a constant supply of energy, and this increases your metabolism. On the other hand, if you starve the body by skipping meals and then gorge on a huge meal once or twice a day, the body freaks out. It thinks it's starving and does everything it can to store the food.

What happens then? Metabolism is slowed, you get sleepy after the meal, and the insulin surge created by the huge meal allows the meal to be stored as fat rather than being burned as energy. Big meals make you sleepy *because* your metabolic rate is slowed. The body is conserving

**Table 2.2**  
**GLYCEMIC INDEX AND GLYCEMIC LOAD OF SELECTED FOODS**

From the *International Table of Glycemic Index* and from *Overcoming Metabolic Syndrome* (Addicus Books)

	Glycemic Index	Glycemic Load
<b>Breads</b>		
Bagel, white, frozen	72	25
Baguette, white, frozen	95	15
Bread stuffing	74	16
Barley kernel bread, 50% barley flour	46	9
Barley flour bread, 100% barley flour	67	9
Coarse whole wheat bread	52	10
Hamburger bun	61	9
Melba toast	70	16
Gluten-free white bread (gluten-free wheat starch)	76	11
Oat bran bread	47	9
Rye kernel (pumpernickel) bread	50	6
Whole meal rye bread	58	8
White wheat flour bread	70	10
Pita bread	57	10

**Table 2.2**  
**GLYCEMIC INDEX AND GLYCEMIC LOAD OF SELECTED FOODS**

	Glycemic Index	Glycemic Load
<b><i>Crackers</i></b>		
Breton wheat crackers	64	10
Puffed rice cakes	78	17
Rye crackers	64	11
Stoned wheat crackers	67	12
Soda crackers	74	12
<b><i>Breakfast Cereals</i></b>		
All-Bran	42	9
Bran Buds	58	7
Bran flakes	74	13
Cheerios	74	15
XXX Bran	75	15
Corn flakes	81	21
Cream of Wheat	66	17
Golden Grahams	71	18
Grapenuts	71	15
Mini Wheats, whole wheat	58	12
Muesli	49	10
Nutrigrain	66	10

**Table 2.2**  
**GLYCEMIC INDEX AND GLYCEMIC LOAD OF SELECTED FOODS**

	Glycemic Index	Glycemic Load
<i><b>Breakfast Cereals (cont'd)</b></i>		
Oat bran	67	9
Quick Oats	66	17
Puffed wheat	67	13
Raisin bran	61	12
Rice Krispies	82	21
Shredded wheat	75	15
Total	76	13
Wheat biscuits (plain flaked wheat)	70	13
<i><b>Cereal Grains</b></i>		
Pearl barley	25	7
Buckwheat	54	16
Cornmeal	69	9
Sweet corn	53	17
Couscous	65	23
Millet	71	25
Rice, white	64	23
Rice, brown	55	18
Instant, puffed rice	69	29



**Table 2.2**  
**GLYCEMIC INDEX AND GLYCEMIC LOAD OF SELECTED FOODS**

	Glycemic Index	Glycemic Load
<b><i>Pastas</i></b>		
Fettucine	40	18
Linguine	46	22
Mung bean noodles	33	15
Macaroni	47	23
Spaghetti, white, boiled	42	20
Vermicelli, white, boiled	35	16
<b><i>Fruits</i></b>		
Apples, raw	38	6
Apple juice	41	11
Apricots, raw	57	5
Apricots, canned in light syrup	64	12
Apricots, dried	30	16
Banana, raw	51	13
Cherries, raw	22	3
Cranberry juice	68	16
Dates, dried	103	42
Figs, dried	61	16
Grapefruit juice, unsweetened	48	9

**Table 2.2**  
**GLYCEMIC INDEX AND GLYCEMIC LOAD OF SELECTED FOODS**

	Glycemic Index	Glycemic Load
<i>Fruits (cont'd)</i>		
Grapes, raw	59	11
Kiwi fruit, raw	53	6
Lychee, canned in syrup and drained	79	16
Mango, raw	51	8
Oranges, raw	42	5
Orange juice	52	12
Pawpaw/papaya, raw	59	7
Peaches	42	5
Pears	38	4
Pineapple	59	7
Pineapple juice, unsweetened	46	15
Plums	39	5
Prunes, pitted	29	10
Raisins	64	28
Cantaloupe	65	4
Strawberries	40	1
Tomato juice	38	4
Watermelon, raw	72	4

**Table 2.2**  
**GLYCEMIC INDEX AND GLYCEMIC LOAD OF SELECTED FOODS**

	Glycemic Index	Glycemic Load
<b><i>Vegetables</i></b>		
Green peas	54	4
Pumpkin	75	3
Sweet corn	62	11
Carrots	47	3
Parsnips	97	12
Boiled potato	50	14
French fries	75	22
Mashed potato	91	18
Sweet potato	61	17
Tapioca	70	12
Taro	55	4
Yam	37	13
<b><i>Legumes</i></b>		
Baked beans	48	7
Beans, dried, boiled	29	9
Black-eyed peas	42	13
Butter beans	31	6

**Table 2.2**  
**GLYCEMIC INDEX AND GLYCEMIC LOAD OF SELECTED FOODS**

	Glycemic Index	Glycemic Load
<i><b>Legumes (cont'd)</b></i>		
Chickpeas (garbanzo beans, Bengal gram), boiled	28	8
Navy beans	38	12
Kidney beans	28	7
Lentils	29	5
Lima beans	32	10
Mung beans	31	5
Peas, dried, boiled	22	2
Pinto beans	39	10
Soybeans	18	1
Split peas	32	6
<i><b>Beverages</b></i>		
Coca-Cola	58	15
Apple juice	40	12
Carrot juice	43	11
Cranberry juice cocktail	56	16
Grapefruit juice, unsweetened	48	11
Orange juice	50	13

**Table 2.2**  
**GLYCEMIC INDEX AND GLYCEMIC LOAD OF SELECTED FOODS**

	Glycemic Index	Glycemic Load
<b><i>Beverages (cont'd)</i></b>		
Pineapple juice, unsweetened	46	16
Tomato juice	38	4
Gatorade	78	12
Hot chocolate mix	51	11
Water	0	0
<b><i>Dairy Products</i></b>		
Custard	38	6
Ice cream, regular	61	8
Ice cream, reduced- or low-fat	39	5
Ice cream, premium	38	3
Milk, full-fat	27	3
Milk, skim	32	4
Chocolate milk	34	9
Pudding	44	7
Yogurt	36	3
Yogurt, low-fat with aspartame	14	2
<b><i>Nuts</i></b>		
Cashews	22	3
Peanuts	14	1

energy because even though it just got a huge meal, it is still in starvation mode and doesn't know when the next meal is coming. When you provide a continuous source of calories to the body in the form of small, frequent meals, the body relaxes: it goes out of starvation mode and starts using the calories instead of storing them. The result is less hunger, more energy, and weight loss.

### ***Faith's Story***

*Faith didn't like diets. A New York attorney with a large firm, she couldn't stick to them: too much to remember, too many schedules to keep. Besides, she usually worked right through lunch anyway, and dinner had to wait until she could take the subway to Grand Central Terminal, catch a 6:32 to Westchester, and get home from the local train station. She usually didn't eat until 7:30 at the earliest, weary and cranky. She was also carrying 160 pounds on her five-foot, five-inch frame—at least 30 pounds too much.*

*Ironically, considering her work habits, Faith would have been a good subject for a nibbling diet. She could have kept carrot sticks and fruit in the office refrigerator; or she could even have taken a bagel from the snack cart in the morning, eating half then and half in the afternoon. Exercise could have been easy, too: instead of the elevator, she could have taken the stairs to her seventh-floor office, or she could have walked 11 blocks from Grand Central to her midtown Manhattan office instead of taking the subway.*

*Faith decided, however, that she was just going to skip meals: no lunch, no mid-morning or mid-afternoon snack, no protein bar at the newsstand before boarding the commuter train. Her food intake would consist solely of a light breakfast, usually coffee and cereal, and a dinner of high-protein, low-carbohydrate foods, such as chicken and fish.*

*This worked well in the beginning. Faith dropped 5 pounds the first week; she attributed her fatigue and short temper to the diet, and she told people that. But after a few more weeks the weight stopped coming off, yet Faith remained tired and irritated. She snapped at co-workers; her memory was foggy; her work suffered.*

*Her body had fallen into starvation mode. Even though Faith still weighed over 150 pounds, her body was trying to conserve energy, not use it.*

*Faith eventually figured out that her starvation diet wasn't doing the trick. She started following the Hormonal Health Diet, eating six small meals each day and adding physical activity to the mix, and the pounds gradually came off. More important, Faith felt better.*

Small, frequent meals are a proven treatment for hypoglycemia. Patients with hypoglycemia are instructed to avoid high-glycemic index foods and to eat six small meals a day. Doing so prevents the insulin surge that comes with larger meals or high-glycemic foods, which in turn prevents blood sugar from dropping in response to the insulin surge.

When you think about our evolution, this all makes sense. Our ancient hunter-gatherer ancestors lived from moment to moment, often off whatever nuts and berries they came across in their daily search for food. A big meal was a treat! It's only in modern times, when even our agricultural workers are governed by the time clock, that we've focused on eating three big meals a day—allowing us the morning and the afternoon to reserve for work.

The bottom line is that nibbling is good. By nibbling, you are supplying the body with its nutrients in a gradual fashion—the way it handles them best. The concept matches that of the glycemic index and glycemic load: with low-glycemic foods, the natural digestive process allows for the gradual release of glucose into the bloodstream, just as nibbling does. Either way, no foods are forbidden. If you eat high-glycemic foods, simply eat them in small quantities. Calories do count.

## **THE PROBLEM WITH SKIPPING BREAKFAST**

Have you ever seen a sumo wrestler? These Japanese titans often weigh well over 400 pounds, a handy size to be when you're trying to force your opponent out of the ring—or simply knock him down.

But do you know how a sumo wrestler gains all that weight? Sumo wrestlers don't eat breakfast. They wake up, exercise and practice their

technique all morning (for big men, sumo wrestlers can be quite nimble), and have a big lunch. It's a healthy lunch—the Japanese have notably healthy diets, high in seafood and low in fat—but it's also loaded with starch in the form of white rice, a high-glycemic food. After that lunch, they sleep for several hours. As noted earlier, metabolism slows after a big meal, and sleep slows metabolism (and digestion) even more. Sumo wrestlers become very fat.

Interestingly, during their careers, at least, they're not in terrible shape. They exercise frequently, so the fat tends to form under the skin (subcutaneously) and not in the stomach (visceral fat). The incidence of diabetes and cholesterol is very low among sumo wrestlers.

But once they retire, health-related problems hit with a vengeance. Suddenly fat shifts to the belly, and the incidence of high cholesterol and diabetes shoots way up. All of the weight they carry around becomes a burden, not an advantage.

Several studies have linked obesity to skipping breakfast. In fact, the *more* meals you have per day, the *less* likely you are to be overweight.

Many of my patients have told me that they simply aren't hungry for breakfast. I have found that the most common reason for not being hungry for breakfast is overeating the night before. It is a vicious cycle. Skip breakfast and get too hungry for lunch and dinner. Overeat at night and feel full the next morning. The cycle repeats itself. If you follow the Hormonal Health Diet, you will become hungry for breakfast.

You should always have protein with breakfast. Protein at breakfast has been shown to reduce hunger and cravings throughout the day. In fact, if you have protein with your breakfast, you will be less likely to overeat at both lunch and dinner. There are many ways to enjoy protein in the morning. My personal favorite is an egg white omelet packed with fresh vegetables and a slice of fat-free cheese. For more suggestions on healthy breakfasts, see Chapter 11.

## **FIBER KEEPS INSULIN LOW**

If you want to lower your insulin levels, fiber is the way to go. Fiber is a polysaccharide, like starch, but with one major difference: The body cannot digest fiber. That's bad, right? Nope. It's a good thing.



Fiber lowers the glycemic index of food by delaying digestion. This, in turn, lowers insulin levels. Fiber also plays a major role in maintaining good health in a variety of other ways:

- Fiber makes you feel full. Soluble fibers swell in the stomach and bowels, reducing feelings of hunger and making you feel full. Soluble fibers also slow gastric emptying, keeping other food in the stomach longer. And since the body cannot digest fiber, the fiber harmlessly makes its way through the digestive system, eventually passed out into the stool.
- Fiber nourishes your “colonic mucosa,” the innermost layer of the large intestine, and has a role in the prevention of colon cancer, constipation, and other colonic diseases.
- A high-fiber diet reduces LDL (bad) cholesterol by as much as 10 percent.
- Fiber lowers the glycemic index of foods.
- High-fiber diets help people lose weight.

Not all fiber is created equal. Soluble fibers are foods like beans and oats, and also psyllium (Metamucil), as well as pectin, found in apples. Insoluble fibers are foods like whole wheat or bran, foods often found in certain cereal grains.

You need 25 to 35 grams of fiber each day, minimum, in your diet. At the least, it keeps you regular, reduces the risk of colon cancer, and promotes good digestion; at best, it can help you lose weight—partly because it helps you feel “full,” partly because of its glycemic index—lowering and insulin-lowering properties.

The best way to get fiber in your diet is to eat lots of fresh vegetables and fruits. More is better when it comes to vegetables and fruits. Yes, vegetables and fruits have calories, but it is difficult to overeat these items. For more information, see Chapter 11.

## **PROTEIN**

Protein is an essential part of a balanced diet. Proteins, you may recall from high school biology, are made up of molecules called amino acids. Amino acids can be easily converted by the body into glucose

and fat. The body can also use amino acids as the building blocks for potent hormones and neurotransmitters. (Neurotransmitters are the chemical signals that the nervous system's cells—neurons—use to communicate with one another.) Protein tells the body to release hormones like cholecystokinin (see Chapter 10 for more on cholecystokinin), a hormone that reduces appetite and makes you feel satisfied.

I recommend that you eat about 0.4 grams of protein each day for every pound you weigh. So a 150-pound person should consume about 55–60 grams of protein each day. However, this formula isn't perfect, since it doesn't take into account body composition. The Hormonal Health Diet provides for limited amounts of most proteins but unlimited quantities of egg whites (which are pure protein). In theory, this could lead to eating too much protein; however, most people find it difficult to eat too many egg whites. If you have kidney problems, you should consume much less protein. It pays to be careful and cautious. If you have any doubts, see your doctor.

You should spread your protein throughout the day, but in particular, you need protein at breakfast. Many people are accustomed to a breakfast consisting entirely (or mostly) of carbohydrates, such as juice and toast, cereal and skim milk (which has minimal protein), pancakes or waffles and syrup. High-carbohydrate breakfasts cause glucose and insulin spiking and result in hunger, sleepiness, and carbohydrate cravings (usually in that order) later in the day. In fact, these symptoms are so common that they cause many people to skip breakfast. Unfortunately, skipping breakfast leads to problems with insulin. The answer: protein at breakfast. Protein at breakfast will help control hunger and cravings for the entire day. You will eat less at lunch and dinner. Protein at breakfast will also supply your body with a source of long-lasting glucose that will give you energy and prevent fatigue associated with glucose crashing (hypoglycemia). See Chapter 11 for more information.

## **FAT**

Fat has become the most maligned of the nutrients and is blamed for causing obesity, cardiovascular disease, and other health problems. Ounce for ounce, fat is more than twice as high in calories as protein

or carbohydrates. But fat is an essential part of our diet, and the right kinds of fats are necessary for *hormonal balance*. A *balanced* diet means a healthy blend of carbohydrates, protein, and fat. A diet that is very low in fat is not considered a healthy diet.

Most experts recommend that your diet include about 25–35 percent fat. Fat has a number of benefits. Fat is what makes food more flavorful. It also makes the texture creamier. We like the taste of food when fat is in it. Fat can also help to slow down the rate at which the entire meal hits the bloodstream, thus slowing digestion. And fat causes the body to produce hormones—such as cholecystokinin, leptin, glucagon-like peptide-1, and others—that tell your brain that it's time to stop eating. It's the fat that makes you feel full. Healthy fats are an important part of the Hormonal Health Diet.

The best fats are known as *unsaturated fats*. Nuts, olives, seeds, and avocados are good sources of unsaturated fat. These foods also contribute vitamins, minerals, and dietary fiber. Fish is an excellent source of unsaturated fat. Chicken breast meat has primarily unsaturated fat, but chicken skin and thigh meat are higher in saturated fat. Grass-fed beef and meat from other grazing animals (like buffalo, elk, and deer) have a higher amount of unsaturated fat than grain-fed beef, which is very high in saturated fat. Most vegetable cooking oils are unsaturated fat, but olive oil, peanut oil, sunflower oil, and canola oil are the best. Remember, all fats, whether good or bad, are high in calories, and calories always count, so you still need to limit them.

Unhealthy fats are *trans fats* and *saturated fats*. These fats contribute to cholesterol problems and are linked to cardiovascular disease and other health problems. Unhealthy fats almost always come from one of three sources: animal products, tropical oils (like palm oil or coconut oil), and processed oils (like margarine or partially hydrogenated vegetable oil). Unsaturated fats are converted to saturated fats by a process called hydrogenation—literally, bubbling hydrogen gas through the oil. As hydrogen is added to the fat, it “saturates” the oil with hydrogen, changing its chemical makeup. This process also creates a particularly dangerous form of unsaturated fat known as trans fat. So even though trans fat is technically an unsaturated fat, it is even more toxic than saturated fat.

The best fat for your cholesterol is unsaturated fat; the worst are trans fats and saturated fats. Unsaturated fats can actually have a beneficial

effect, raising good-cholesterol levels and lowering bad-cholesterol levels. Trans fat and saturated fat have the opposite effect.

Cholesterol-lowering products containing healthy fats are being made in the form of margarines, salad dressings, and other foods (examples are Benecol and Take Control) and are a good option for people with cholesterol problems. These products contain compounds known as *hydrogenated sterols* or *plant stanol esters*, which are recommended by cholesterol experts as part of a heart-healthy diet. Although effective for cholesterol, these products have the same number of calories as the regular products and do not help you lose weight.

All fats—whether saturated, trans, unsaturated, or a combination of the three—have the same caloric content: 9 calories per gram. Proteins and carbohydrates have about 4 calories per gram, so fat is more than twice as caloric as an equivalent amount of protein or carbohydrate.

Certain fats are, indeed, vital to our well-being. These are known as *essential fatty acids* (EFAs). Two EFAs, *linoleic acid* and *lenolenic acid*, are chief among the body's requirements. Linoleic acid is an omega-3 fatty acid; lenolenic acid an omega-6 fatty acid. Without EFAs, we fall victim to a variety of symptoms of *essential fatty acid deficiency*, including dry, flaking skin; hair loss; arthritis; weakness; incoordination of muscles; and numbness and tingling of the hands and feet.

Fish, especially fish that live in cold water (sardines, mackerel, herring, lake trout, and salmon), are very high in omega-3 fatty acids. Flax, soybeans, sunflower seeds, sesame seeds, peanuts, and walnuts are also good sources of this beneficial fat. Omega-3-enriched eggs and other omega-3-enhanced products are now available. Omega-3 fatty acids play a role in lowering insulin levels and reducing insulin resistance (see Chapter 3). By lowering blood triglycerides, these beneficial fats also reduce your risk of heart disease.

The heart-healthy benefits of omega-3 fatty acids have prompted the American Heart Association to recommend that everyone eat two 3-ounce servings of fish each week. But the fish oils sold in capsules should be used with caution. Many over-the-counter products have inconsistent amounts of omega-3 fatty acids. Some products have been

found to be contaminated with mercury. Prescription omega-3 fatty acids are more reliable. Omega-3 fatty acid overdoses have been linked to impaired immune function, elevations of vitamins A and D to toxic levels, and aggravation of diabetes.

### **Fat Substitutes**

Olestra, also marketed under the name Olean, is essentially a fat that the body cannot absorb, so it's passed through the digestive system without entering the body. In large amounts, it has been shown to trigger diarrhea and gastrointestinal pain. On the plus side, it adds virtually no calories to products. There is a concern that fat substitutes can leach vital nutrients from your body. For the prevention of vitamin deficiencies, the Food and Drug Administration has mandated that the fat-soluble vitamins A, D, E, and K be added to these products. Replacement of these four vitamins may not be enough, however. In general, I recommend you use these products sparingly, if at all.

### **Fat Blockers**

Orlistat, marketed under the brand name Xenical or Alli, works by blocking the digestion and absorption of some of the fat you eat. This medication does work; however, orlistat, coupled with too much fat consumption, can overload your intestinal tract with fat and cause gastrointestinal problems, including diarrhea and leakage of oily stool. It has been said that if you take orlistat and "cheat" on your diet, you will be "punished" by these side effects; thus, it helps to keep you eating healthy. There is concern about deficiencies of vitamins A, D, E, and K with the use of orlistat; therefore, it is recommended that if you use this product, you also take a multivitamin.

Natural-foods partisans have their own obesity product, chitosan. Chitosan is made from crustacean shells and is supposed to block fat absorption. However, chitosan in fact blocks *zero* of the fat in your diet. The next time you see one of those infomercials for chitosan, don't be tempted. It's just a come-on and a rip-off. Another product, nopal cactus, claims to have the same effect as chitosan but has not been proven.

## HYPOGLYCEMIA

Glucose is the body's main fuel. In a good diet, the idea is to keep the level of glucose more or less constant, increasing it at times when you need more energy and letting it wane when you need less—but usually not to the point where it causes a negative reaction.

Of course, almost none of us do that. Think about it: Have you ever eaten a huge meal? Have you ever ordered a rich dessert, often in an oversized serving, in a fine restaurant? Have you ever gotten home late at night, tired but not sleepy, and had a comforting bowl of ice cream? Have you ever quenched your afternoon carb craving with a bag of potato chips or a candy bar?

All of these actions spike your blood sugar. That in itself isn't terrible; our bodies are well equipped to deal with spikes in blood sugar, and the worst thing that usually happens is that we gain weight.

But some people are afflicted with a condition called hypoglycemia. Literally, hypoglycemia is "low blood sugar." The glucose level in the blood drops below the point where it can fuel the body's activity. This form of hypoglycemia usually occurs after you eat large meals or high-glycemic index foods: the blood sugar rises, the insulin surges, and then—very rapidly—blood sugar levels decline. The hypoglycemia is caused by "undershoot," where blood sugar levels fall below the level that existed *before* you ate. This type of hypoglycemia, known as *reactive hypoglycemia*, invariably occurs as a reaction to food.

When blood sugar drops rapidly, symptoms of hypoglycemia set in. You feel hungry (already!), sleepy, tired, and fatigued; your heart rate picks up, and your sweating increases. All you want to do is take a nap, which is the worst thing you can do; your metabolism slows to a crawl. But you probably can't sleep anyway, even though you feel sleepy; with your heart pounding and the extra sweating, you feel irritated, jazzed up, and annoyed. Eating carbohydrates makes brain serotonin levels surge (see Chapter 10). Serotonin calms you and makes you sleepy, slowing your metabolism. This, of course, leads to weight gain, creating a vicious circle.

As noted earlier, we probably all have these symptoms periodically. We all like to eat, and we don't always eat what's good for us. What we can do is fight the appetite and the urge to sleep: we can take a

walk or engage in some other physical activity. We can do something to maintain or raise our metabolism and level out our blood sugar. Endocrinologists treat people with reactive hypoglycemia by having them eat low-glycemic index carbohydrates in multiple small meals spread out through the day. This type of eating reduces blood glucose surges and the insulin spikes that follow.

### **Brooke's Story**

*Brooke, a 47-year-old financial analyst, came to me with what she thought was a strange collection of symptoms. She'd been gaining weight, she told me, even though she believed her diet hadn't changed much in many years. She also had periods of confusion. She'd forget where she was when out for a walk, or she couldn't keep a list of numbers straight—a disastrous condition, considering her job. She noted that the symptoms came on anytime she went more than two or three hours without eating. She responded to the problem by eating more and more.*

*Her symptom of mental confusion was concerning, as was the weight gain. We performed some tests and determined that she had hypoglycemia. Brooke's hypoglycemia was not the result of eating the wrong types of carbohydrates, though. The cause of her hypoglycemia was an insulinoma—a tumor that causes the production of far more insulin than is needed. Fortunately, the tumor was found on an MRI scan, and Brooke was scheduled for surgery. A tumor about the size of a marble was removed from Brooke's pancreas. After the surgery, her problems with hypoglycemia disappeared. More important, with her lowered insulin levels, Brooke was finally able to lose some weight.*

## **DANGEROUS HYPOGLYCEMIA**

Sometimes hypoglycemia can be a life-threatening condition. Problems with the islet cells in the pancreas can, on rare occasions, cause the production of excessive amounts of insulin, resulting in life-threatening low blood sugar levels. A small tumor in the pancreas, known as an

insulinoma, can cause severely low blood sugar levels. Unlike reactive hypoglycemia, the hypoglycemia caused by an insulinoma almost never occurs after a meal. Instead, this type of hypoglycemia occurs when you have not been eating. Without a constant source of food, blood sugar levels can drop dangerously. Low blood sugar can affect the brain, a condition known as *neuroglycopenia*, causing symptoms such as personality changes, confusion, and seizures or passing out. Once food is consumed, blood sugar rises and the symptoms disappear. The symptoms of an insulinoma can be subtle.

Many patients with insulinomas are not diagnosed for 10 years or more, and they keep getting fat because of the high insulin levels and because they keep eating in an effort to counteract the low blood sugar. They learn that if they do not eat large amounts of food all of the time, they pass out. If you have symptoms of this disorder, you should see an endocrinologist to make sure you're not suffering from this potentially fatal, though rare, problem.

Recently, another type of hypoglycemia has been observed as a complication of gastric bypass surgery. The condition causes abnormal growth of insulin-producing cells of the pancreas, which is known as *nesidioblastosis*. Patients who have had gastric bypass surgery and who experience symptoms of hypoglycemia should discuss the condition with their physicians.

### **Miriam's Story**

*Miriam was a 42-year-old woman with a loving husband, two children, and a secret: a constantly replenished chocolate bar stash, which she kept in a cabinet above the vent for her stove. Miriam wasn't overindulgent with her chocolate craving, at least not at first: in the afternoons, usually after finishing some housework, she would dip into a bag of Hershey Kisses or a similar sweet and eat about 2 ounces' worth. She wasn't terribly overweight, maybe 15 pounds.*

*But Miriam was extremely conscious of her extra weight, and since she didn't exercise much, she frequently tried diets. Most of these were faddish and lasted only a couple weeks. With the recent trend in low-carbohydrate diets, however, Miriam decided to go that route. That, of course, would mean cutting the chocolate bars almost entirely out of her life.*



*It didn't work. The late-afternoon cravings for sweets and other carbohydrates not only killed the diet but also caused Miriam to gain even more weight. (With few carbohydrates in her new diet, her blood sugar levels would spike higher every time she consumed some carb-heavy food, and the fat of the chocolate bars didn't help.) She was hungry all the time, particularly a couple hours after a meal, and generally sleepy in the late afternoon, her craving time. She started going through bags of Hershey Kisses, not just a couple ounces. Miriam needed help.*

*Miriam started the Hormonal Health Diet—eating protein and low-glycemic carbohydrates, spread out throughout the day. She started snacking on lean protein snacks like turkey and tuna. Most important, she started having protein with her breakfast. She stopped tempting herself with bags of chocolate. At first the cravings continued with a vengeance, but this time Miriam did not give up. When her body said, “Eat chocolate,” she ate a chocolate protein bar. Within a couple of weeks, the cravings subsided. Miriam still ate chocolate, but her cravings were controllable. Before she knew it, Miriam had dropped two dress sizes and felt better than ever.*

## **CARBOHYDRATE CRAVINGS**

Typical symptoms of carbohydrate cravings are:

- Feeling hungry all the time, especially two to three hours after a meal
- Feeling sleepy and sluggish in the afternoons
- Anxiety
- A feeling of calmness and satiation when eating sugars, candy, chips, pretzels, and other heavy-carbohydrate foods

This condition is caused by insulin and serotonin. As insulin falls after its normal post-meal rise, a brain chemical known as serotonin is released. You may have heard of serotonin; it's the neurotransmitter whose quantities are increased with the use of anti-depressant drugs,

such as Prozac, Celexa, Lexapro, Zoloft, or Paxil. It makes you feel better, and it also provides a key signal to the brain: I am satisfied; I don't need to eat anymore right now.

If insulin goes too high, serotonin is not released in the brain. As a result, people become anxious, easily irritated, and generally out of sorts. Moreover, the brain hasn't received that key message to stop eating. So people continue stuffing their faces, often with carbohydrate-laden comfort foods, in an effort to bring back that calm, satisfied feeling. See Chapter 10 for more information on serotonin.

How do you avoid carbohydrate cravings? Keep your insulin low. Eat protein with breakfast. Eat small, frequent meals. Eat lots of fruits and vegetables. The diet principles discussed in this book and the Hormonal Health Diet offer the ultimate solution for completely eliminating carbohydrate cravings.

### **HEALTHY EATING GUIDELINES**

- Eat the correct number of calories. The amount of calories you should consume each day depends on your body weight and activity level. In general, men should eat 11–12 calories per pound per day, and women should eat 10–11 calories per pound per day.
- Read food labels. Look for hidden sources of sugar and fat.
- Eat at least five servings of vegetables and five servings of fruits every day. Fruits and vegetables are critical to hormonal balance. If you are hungry, eat more vegetables and fruits instead of stacking on more fattening foods. As far as vegetables and fruits go, more is better! It's tough to overeat vegetables and fruits.
- Maintain a healthy balance of carbohydrates, proteins, and fat. Exact percentages aren't important, as long as you satisfy your protein requirements and do not eat too much fat.
- Eat low-glycemic carbohydrates. If you eat higher-glycemic carbohydrates, do not eat them alone; instead, incorporate them into a meal. Alternatively, nibble on high-glycemic carbohydrates slowly, over several hours. This diminishes the impact on your blood sugar and insulin levels.
- Don't give in to carbohydrate cravings. Eat vegetables and fruits or a protein snack instead.

- 
- Eat multiple small meals each day. Your goal should be 5 or 6 meals per day.
  - Do not skip meals, especially breakfast.
  - Make sure you get enough protein. Minimum protein requirements for healthy adults are 0.4 gram per pound of body weight each day (roughly 55–60 grams of protein per day for a 150-pound adult).
  - Eat protein (egg whites, lean meat, turkey, chicken, fish, or tofu) at breakfast. This will help you eat less at lunch and dinner.
  - Don't eat too much protein. Remember, protein, especially when combined with carbohydrates, can cause insulin spiking. The Hormonal Health Diet provides for unlimited quantities of egg whites because most people find it very difficult to eat huge quantities of this food.
  - Eat foods low in fat. I recommend that your diet be no more than 25–35 percent fat. Despite the benefits of healthy fats, remember that fat is high in calories, and calories still count.
  - Eat healthy fats. Replace saturated fats and trans unsaturated fats in your diet with monounsaturated and polyunsaturated fats. Good sources of healthy fat include olive oil, avocados, nuts, and fish.
  - Avoid fat substitutes.
  - Drink at least eight 8-ounce glasses of water each day.
  - Do not attempt to speed digestion with enzyme supplements or special food combinations. The slower your digestion, the better.

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# INSULIN RESISTANCE

MORE THAN 60 MILLION AMERICANS HAVE INSULIN RESISTANCE, BUT MOST DON'T KNOW IT. It's the most common hormone problem in the world today. Insulin resistance is a complex disorder that is only beginning to be understood. Insulin resistance plays a role in many medical conditions, such as type 2 diabetes, obesity, PCOS, high blood pressure, and cardiovascular disease. Overcoming insulin resistance is an important part of achieving *hormonal balance*.

## WHAT IS INSULIN RESISTANCE?

Insulin resistance has become a buzzword in the dietary community. Chapter 2 described the problems of insulin spikes: unstable blood sugar levels, increased appetite, and fatigue—a process that makes it difficult to lose weight.

The idea of insulin resistance starts with the concept that “receptors” for insulin gradually malfunction. (See Chapter 1 for more on hormones and receptors, how they work, and what can go wrong.) Insulin resistance is a classic type of hormonal problem: the hormone is perfectly fine, but the receptor for the hormone doesn't work properly. The body compensates by making more insulin.

There can be different degrees of insulin resistance. The level of insulin resistance is determined by many factors, including genetics and

overall body weight. Everyone who is overweight has some degree of insulin resistance, and the heavier you are the more insulin resistance you have. If you have obesity or diabetes in your family, it is likely that you have a greater degree of insulin resistance than someone else who is similar to you in height and weight.

Insulin resistance does not affect every part of the body the same way, and although more insulin is required for proper blood sugar regulation, the higher insulin levels overstimulate appetite centers in the brain and encourage the storage of nutrients as fat instead of burning them as energy. People with insulin resistance need extra insulin to maintain proper blood sugar levels, but the consequence is increased appetite, fatigue, and weight gain. Insulin resistance is the primary cause of *metabolic syndrome* and is linked to high blood pressure, cardiovascular disease, and many other health problems. The “end stage” of insulin resistance is when the pancreas can no longer make enough insulin to keep up with the demand. When this happens, blood sugar levels rise, eventually leading to diabetes.

### **WHAT CAUSES INSULIN RESISTANCE?**

There are many factors that contribute to the development of insulin resistance, and the more factors that apply to you, the more severe the insulin resistance.

#### **Excess Weight, Especially in the Belly**

This is the most common cause of insulin resistance. Most individuals become insulin resistant when they grow even slightly overweight. Increased abdominal fat is a telltale sign of insulin resistance.

#### **Genetics**

Genetics determines at what weight you will develop insulin resistance, rather than whether you will develop it. If you have a family history of diabetes or obesity, you are more likely to have insulin resistance.

People with certain ethnic backgrounds (American Indians, African Americans, Hispanics, Asians, and Pacific Islanders) are at increased risk for insulin resistance.

### **Physical Inactivity**

This is a major cause of insulin resistance. Studies have shown that as little as 3 weeks of regular exercise can lessen insulin resistance.

### **Stress**

Stress causes insulin resistance for many reasons. Two hormones secreted when the body is under stress, cortisol and epinephrine, promote insulin resistance. (See Chapter 8 for more on cortisol.) The stress of *poor health* also increases insulin resistance. A person with diabetes who gets a cold, for example, experiences a rise in blood sugar levels because of worsened insulin resistance. This is true for any number of ailments, from infections to mental illness.

### **Infection or Illness**

By stressing the body, infection or illness increases insulin resistance. Illness can cause increased levels of substances known as *inflammatory cytokines* such as *tumor necrosis factor* and *interleukin-6* (see Chapter 10), which make tissues in the body more resistant to the actions of insulin.

### **Mental Illness**

Depression and anxiety have close links to insulin resistance. Treatments for insulin resistance also improve depression and anxiety. The reverse also holds true: treating depression and anxiety can lessen insulin resistance.

## The Pima Indians

The Pima Indians live just south of Phoenix in southern Arizona's Gila River Indian Community. Their North American ancestry goes back countless generations; indeed, they are believed to have been among the first settlers of North America, first moving here 30,000 years ago.

For 2,000 years, the Pimas were a subsistence agricultural people. They grew wheat, beans, squash, and cotton, and were well known for their generosity. But in the late 19th century, their water supply was diverted by Western settlers, and the Pimas suffered from famine and poverty. To maintain their survival, they began eating foodstuffs given them by the U.S. government: lard, white flour, and sugar.

When the United States entered World War II, many Pimas left the reservation and joined the thriving wartime industry in Phoenix and other southwestern cities. Others joined the U.S. military. Both provided the Pimas with greater prosperity; both also prompted a further change in their diet to one similar to that of most Americans.

And, like many Americans, the Pimas started growing fat. But their obesity was on a scale far different from that of the rest of the country: by some indications, the majority of Pima adults were quite overweight.

In 1963, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) did a survey of rheumatoid arthritis among the Pimas and another tribe, the Blackfoot of Montana. They found that the Pima Indians had an extremely high rate of diabetes, far beyond what was considered normal. Two years later, the NIDDK and several other organizations, including the Pima community itself, began another study to find an explanation for this. By figuring out the secret of the Pimas' affliction, they hoped to shine a light on the causes of diabetes as a whole, particularly the reasons why diabetes affects Native Americans, Hispanics, and other non-white North American peoples at a rate 10 times that of Caucasians.

The Pimas provided an excellent scientific sampling, and continue to do so. They have lived in the Gila River region for hundreds of years, and members of the tribe usually marry other members of the tribe and stay on in the area. Families thus have intermingling lineages, and it's easy to trace the transfer of key genetic characteristics. The Pimas have also maintained their agricultural roots, so to speak, for centuries. Even today they are a farming people, cultivating oranges, pistachios, and olives.



So why the high rate of diabetes? The researching organizations turned up a number of causes and indicators:

**History.** Until the late 19th century, the Pima diet contained about 15 percent fat and was high in starch and fiber. Today the Pimas consume about 40 percent fat. Moreover, like most of us, the Pimas don't exercise much. One hundred years ago, their agriculture required more physical labor; today, machines do a lot of the work, and leisure time is spent in sedentary activities. Interestingly, a community of Pima Indians in Mexico—which still adheres to the ancient traditions and diet—has a much lower rate of diabetes and obesity. Diabetes and obesity are, of course, closely related.

**Genetics.** The Pimas have several genetic “markers” that differentiate them from the white population. One gene, known as FABP2, is found more regularly in Pimas than in the general population; it makes an intestinal fatty acid-binding protein using one of two amino acids. The National Institutes of Health scientists who discovered the gene believe it could lead to a higher level of fats in the blood, contributing to insulin resistance. Pimas also seem to have a genetic tendency to retain fat. The “thrifty gene” theory plays a role here. Geneticists believe that populations that underwent continuous cycles of feast and famine developed a gene that causes energy (that is, fat) to be conserved during the fallow times. Today's cornucopia of foods—particularly high-fat foods—makes this gene superfluous, but it's still there, doing its job. In the Pima, it does its job all too well.

**Metabolism.** Studies on the Pima Indians have shown that overweight people, before they gain weight, have a slower metabolic rate compared to people of the same weight. As a result of this, coupled with the Pimas' high-fat diet, the body cannot burn fat fast enough, and weight gain is inevitable.

However, the story doesn't necessarily have an unhappy ending. Both genetics and environment play a role in perpetuating insulin resistance, and health workers have worked with the Pimas to change their diet and their degree of physical activity. The Pimas have cooperated closely with health authorities; in physical and mortal cost, they've seen what diabetes can do. The Pima Indians aren't genetically doomed—and neither are the rest of us.

### **Inflammation**

This is the response of the immune system to fight infection or irritation. Inflammation in the lining of the blood vessels (known as the *endothelium*) is one of the links between insulin resistance, high blood pressure, and cardiovascular disease.

### **Pregnancy**

Pregnancy is a classic insulin-resistant state. The prototypical insulin-resistant person is apple shaped: big stomach, thin arms. Sound familiar? In a pregnant woman, all the weight—in this case, the baby—is concentrated in the stomach; the arms and legs stay thin. In fact, all pregnant women are tested for *gestational diabetes* because insulin resistance makes the condition so common.

### **Aging**

Does aging make people more insulin resistant? There's some controversy about whether aging actually causes insulin resistance. Some experts say it's not aging as much as it is our decreased physical activity and weight gain that cause insulin resistance; others maintain that aging itself has an independent effect. More research needs to be done.

### **Menopause**

The decreased *estradiol* (healthy estrogen; see Chapter 6) levels in menopausal women can promote insulin resistance. The effect of estrogen is small compared to other factors that contribute to insulin resistance.

### **Puberty**

Adolescents have low levels of insulin resistance, but obese adolescents going through puberty have very high levels of insulin resistance. This would seem to correlate with other effects of puberty: some children

lose their baby fat and become strapping young adults, while for others their weight problems just get worse. We are now seeing alarming increases in rates of type 2 diabetes (previously known as *adult-onset* diabetes) because of the epidemic of adolescent obesity.

### **Kidney or Liver Problems**

For a number of reasons, kidney or liver problems may cause insulin resistance. *Hemochromatosis* is a common genetic disorder of iron metabolism that causes liver problems and insulin resistance. (For more on hemochromatosis, see Chapter 4.)

### **Low Potassium (Hypokalemia)**

Potassium is necessary for insulin to work properly. Low potassium levels increase insulin resistance. Diuretic medications, which are commonly used to treat high blood pressure, can cause excessive loss of potassium in the urine. High levels of the adrenal gland hormones cortisol and aldosterone can also lower potassium.

### **Dieting**

Low-fat/high-carbohydrate diets increase insulin resistance. These diets are well known to cause insulin resistance, high triglyceride levels, and—in some cases—overt diabetes.

### **Hormonal Excess**

High levels of many different hormones can cause or worsen insulin resistance. I'll deal with some of these hormones more extensively in later chapters; cortisol, growth hormone, and glucagon, in atypical quantities, can make people insulin resistant. These hormones are considered *counter-insulin hormones* in that they provide checks and balances for insulin. A toxic hormone, *resistin*, has been linked to fat cells and insulin resistance. Resistin, made by *white adipose tissue* (see Chapter 10) makes other tissues, such as muscle and liver, more insulin resistant.

## Smoking

For decades, smoking has been a way for some people to keep their weight down. Nicotine acts as a stimulant, after all, and the buzz of a nicotine high can keep thoughts of eating more food at a distance. (Many smokers suffer a great gain in weight when they quit smoking, or even try to quit: the desire to put something, anything, in one's mouth is overwhelming.) But smoking is also a known cause of insulin resistance. For this reason—as well as many others—it should be avoided.

## Medications

A variety of medications can cause or worsen insulin resistance. For more information, see the section at the end of this chapter.

### ***Laura's Story***

*Laura, a law professor, was living a stress-filled life. She and her husband had recently purchased a large house that cost a little more than Laura had been willing to spend. Her two children were approaching college age, and Laura wondered how she was going to afford their educations. And she had a punishing workload of classes, committees, and consulting sessions.*

*One day, it all came crashing down. Laura suffered a heart attack during class and was rushed to the hospital. It was touch-and-go for a while, but Laura was in reasonably good shape for a woman of 49—she didn't smoke and was only a few pounds overweight—and she pulled through.*

*While she was there, physicians performed several tests. One of them determined that Laura's blood sugar was exceptionally high. This surprised Laura, who had not known she was diabetic.*

*Perhaps, it turns out, this was because she wasn't diabetic. Laura's recovery was slow and arduous: exercise, an improved diet, and—above all—a curtailment of her previous responsibilities. Six months later, she submitted to a new round of tests. This time her blood sugar level was fine and she had no signs of diabetes. The hyperglycemia may have been caused entirely by excessive stress.*

## **CANDIDA (YEAST) INFECTIONS**

I have heard some people say they believe that insulin resistance and blood sugar problems are caused by overgrowth of a type of fungus or yeast known as *Candida albicans*. In fact, some books have made the outrageous claims that Candida overgrowth or toxicity is responsible for many chronic medical conditions, such as chronic fatigue syndrome, fibromyalgia, eczema, psoriasis, scleroderma, lupus, arthritis, attention deficit disorder (ADD), asthma, headaches, irritable bowel syndrome, multiple sclerosis, autism, food allergies, carbohydrate cravings, insulin resistance, and diabetes. Proponents of this theory blame antibiotics, birth control pills, and high-sugar diets for yeast overgrowth. There's even something they call *leaky gut syndrome*, in which, they claim, Candida migrates from the bowels into the body. The yeast in bread is blamed for causing diabetes (I blame the carbohydrates and calories in the bread).

I have seen patients who take heavy-duty antifungal medications to fight what they believe to be Candida overgrowth. My opinion, and the opinion of many of my colleagues, is that Candida has nothing to do with these conditions. All human beings have Candida in their intestines and in their stools as part of what is called the *intestinal flora*. Medical problems that lower the immune system, like AIDS and uncontrolled diabetes, can lead to infections with Candida, primarily vaginal yeast infections and mouth infections (known as thrush). But a yeast infection is a consequence of high blood sugar, not the cause of it. Candida can infect the whole body and get into the bloodstream, but this is seen only in patients who have severe immune system problems, such as AIDS or transplant patients. This condition, known as *systemic candidiasis*, is a life-threatening condition characterized by severe illness and very high fevers. Although Candida infections can be a real medical problem, there is absolutely no truth to the claim that Candida overgrowth is a cause of insulin resistance.

### ***Julia's Story***

*Julia was a woman who came to see me with a diagnosis of systemic Candida infection. She had been undergoing intravenous treatments with a very toxic antifungal medication known as amphotericin B (what doctors call "amphoterrible"). She was also*

*following a special diet to eliminate Candida from her system. She had seen many doctors and had a very long medical record. She pointed out several tests that “proved” she had Candida in her blood. The first was a stool culture that was positive for Candida. This was easily discounted, as all human beings have Candida growing in their stools. Next she showed me a photograph of a drop of her blood under a microscope. There was an arrow pointing to small circular discs next to the red blood cells. The arrow was labeled “Budding Yeast.” The arrow was actually pointing to a platelet, a normal component of blood. Once she was convinced that she did not have systemic Candida infection, she discontinued the amphotericin B. She felt a little better, but she never really found an answer to her chronic complaints.*

## **MEDICAL COMPLICATIONS OF INSULIN RESISTANCE**

Insulin resistance is linked to a variety of medical complications. Treating insulin resistance can treat all of the complications at the same time. When you achieve *hormonal balance*, you minimize your risk of these deadly complications.

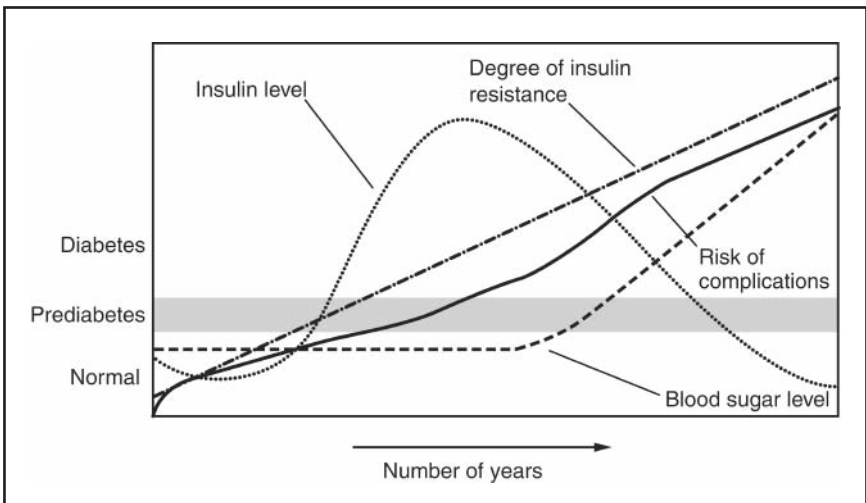
### **Diabetes**

It’s estimated that 15 million Americans have type 2 diabetes. Insulin resistance can result in diabetes, but it takes many years. Insulin resistance alone simply means that more insulin is required to keep your blood sugar levels under control. As long as the pancreas can keep making more and more insulin, you won’t get diabetes. When the pancreas can no longer keep up with the demand, blood sugar levels start to rise. Elevated blood sugars have a deleterious effect on the pancreas, known as *glucotoxicity*, impairing its ability to produce insulin. The pancreas eventually burns out and makes less and less insulin.

So when someone has elevated blood sugars, it means that the pancreas can no longer keep up with the demand from many years of insulin resistance—now the person has *both* insulin resistance and a relative insulin deficiency. The earliest stages of blood sugar elevation are termed *impaired fasting glucose* and *impaired glucose tolerance*,

and are collectively referred to as *prediabetes* (endocrinologists hate the term “borderline diabetes”). Prediabetes means that your pancreas is already starting to show signs of strain, and blood sugar is elevated, but not high enough to qualify for diabetes.

The diagnosis of blood sugar problems is made based on blood sugar levels, not insulin levels. *Insulin levels are not always a reliable test for diabetes or insulin resistance.* If the pancreas is burned out, insulin levels will be low despite a high degree of insulin resistance. Early on, most people don’t show symptoms of elevated blood sugar. If the condition is not diagnosed early, there will eventually be symptoms of *hyperglycemia*—excessive thirst, excessive hunger, frequent urination, and blurred vision. Early diagnosis of blood sugar problems is important because even when blood sugars are minimally elevated, they can cause damage to the heart, blood vessels, eyes, nerves, and kidneys.



**Figure 3.1**  
**THE NATURAL HISTORY OF INSULIN RESISTANCE**  
**AND TYPE 2 DIABETES**

Early on, blood sugar levels are normal because increasing insulin levels are able to overcome insulin resistance. When insulin production can no longer keep up with the demand, blood sugar levels begin to rise. Eventually, insulin-producing cells “burn out” and insulin levels decline, despite an increasing level of insulin resistance. The risk for complications of insulin resistance and diabetes begins many years before blood sugar levels begin to rise.

### **High Blood Pressure (Hypertension)**

More than half of Americans over the age of 50 have hypertension. Hypertension is called the “silent killer” because most people don’t have any symptoms. Hypertension is a major risk factor for serious medical problems like heart failure, kidney failure, blindness, heart attack, stroke, or even sudden death. Insulin resistance has an effect on blood pressure for several reasons. Insulin causes retention of sodium, or salt, in the bloodstream. This increases the volume of blood, leading to a rise in blood pressure. Insulin resistance causes blood vessels to become stiffer or less compliant, which raises blood pressure. Interestingly, people with insulin resistance are at risk for a different type of hormonal hypertension known as *hyperaldosteronism*. Here, the adrenal gland produces excessive amounts of the hormone *aldosterone*. People with hyperaldosteronism have high blood pressure and low potassium levels. And because potassium is required for proper insulin function, the low potassium worsens insulin resistance. If you have high blood pressure and low potassium, or high blood pressure that is very difficult to control, you should be checked for hyperaldosteronism.

### **Unfavorable Lipid Profile (Dyslipidemia)**

Dyslipidemia means abnormal blood fats—low “good” cholesterol, high “bad” cholesterol, and high triglycerides. Cholesterol comes in two basic kinds: *high-density lipoprotein* (HDL), or “good cholesterol,” and *low-density lipoprotein* (LDL), or “bad cholesterol.” *Triglycerides* are not cholesterol, but another type of blood fat that contributes to cardiovascular disease. The term “lipids” refers to all types of cholesterol and triglycerides. Most people know that high LDL is a risk factor for cardiovascular disease, but research has shown that low HDL is an even greater risk factor for the development of heart and blood vessel problems. The dyslipidemia of insulin resistance has a classic pattern of low HDL cholesterol, normal or high LDL cholesterol, and high triglycerides.

High-density lipoprotein (HDL) cholesterol is considered the “good” cholesterol because it removes harmful cholesterol from blood



vessels and brings it to the liver for excretion from the body. This scavenger action of HDL cholesterol prevents the formation of clogged arteries, a condition known as atherosclerosis. Low HDL is a major risk factor for cardiovascular disease. Insulin resistance not only causes low HDL but also decreases its quality, making it less protective.

Low-density lipoprotein (LDL) cholesterol is called “bad cholesterol” because it penetrates blood vessels, causing atherosclerosis. LDL cholesterol elevations are not always caused by insulin resistance. In fact, high LDL cholesterol is usually a genetic condition. Insulin resistance alters the quality of LDL, making it smaller and denser, which in turn makes it more dangerous and more likely to penetrate blood vessel walls.

Triglyceride elevations cause atherosclerosis and cardiovascular disease, just like cholesterol elevations, although triglycerides are considered a non-cholesterol blood fat. Insulin resistance makes triglyceride levels soar. Triglycerides and HDL cholesterol have a powerful effect on each other. High triglycerides cause lower HDL levels, and the reverse is also true: if HDL increases, triglycerides decline. Triglyceride elevations above 1000 mg/dL can cause inflammation of the pancreas, known as *pancreatitis*.

## Cardiovascular Disease

Cardiovascular disease is the number one cause of death among people with insulin resistance. Cardiovascular (*cardio* = heart, *vascular* = blood vessels) disease refers to a disease of the heart and blood vessels caused by *atherosclerosis*, a process in which deposits of cholesterol and fat lead to the build-up of “plaques” in the arteries. High blood pressure, diabetes, and cholesterol problems all contribute to cardiovascular disease. Other factors, such as increased blood clotting and inflammation, also play a role. According to some controversial hypotheses, insulin itself may cause cardiovascular disease. Critics say it’s not the insulin itself; high insulin levels are simply a sign of insulin resistance and merely correlate with—but do not cause—heart disease.

Cardiovascular disease includes heart attacks and strokes, but any organ or any blood vessel can be affected. There are several major forms of cardiovascular disease:

- *Coronary artery disease*, which leads to heart attacks.
- *Carotid artery disease* and *cerebral vascular disease*, which lead to strokes.
- *Peripheral arterial disease*, which is atherosclerosis in the blood vessels of the legs and can lead to an amputation.
- *Renal vascular disease*, which can lead to kidney failure and makes high blood pressure very difficult to control.

### **Increased Blood Clotting**

Insulin resistance causes a *hypercoagulable state*, which means that there is an increased ability for blood to clot. There is also a decreased ability for the body to dissolve blood clots, which is known as *impaired fibrinolysis*. Increased blood clotting plays a role in worsening cardiovascular disease and contributes to heart attacks and strokes. There can also be blood clots in the legs, known as *deep vein thrombosis* (DVT), or a blood clot in the lungs, known as a *pulmonary embolism* (PE).

### **Left Ventricular Hypertrophy (LVH)**

This condition is marked by an abnormal thickening of the heart. Insulin resistance and high blood pressure combine to put strain on the heart. This causes the heart to become overworked, and it enlarges in an abnormal way. Over time the thickened muscle becomes stiff, loses flexibility, and is unable to pump adequate amounts of blood to the body. This is known as *heart failure* or *congestive heart failure* (CHF).

### **Obstructive Sleep Apnea (OSA)**

This is a very common disorder that is often overlooked, but is a serious medical complication of obesity and insulin resistance. Sleep apnea literally means that an individual stops breathing many times during the night. A person with sleep apnea is usually not aware of the condition, except for the symptoms that linger on into the day.

The main symptoms of sleep apnea are severe fatigue and daytime sleepiness. For people with this condition, sleep is very unrestful and it is hard to wake up in the morning. The fatigue and sleepiness can be severe enough to cause one to fall asleep at the wheel while driving. People with sleep apnea commonly say that they are too tired to exercise. People with sleep apnea usually snore loudly or have episodes in which breathing stops, followed by gasping for air. They may also have a condition known as *restless legs syndrome*. Sleep apnea can also be a cause of *attention deficit disorder* (ADD) and memory problems. Headaches, especially in the morning, are common. Sleep apnea is linked to high blood pressure, heart rhythm disturbances, heart attack, stroke, and sudden death.

Sleep apnea is diagnosed using a sleep study, also known as *polysomnography*. The best treatment for sleep apnea is weight loss; but this can be next to impossible because the condition itself slows metabolism, which makes weight loss extremely difficult. Another treatment, known as *continuous positive airway pressure* (CPAP), helps people breathe while they are sleeping by forcing air into the lungs. Once treated with CPAP, many people experience a dramatic improvement in energy level and metabolism, which allows them to finally lose the weight.

### **Insomnia**

Many people with insulin resistance have difficulty falling asleep or staying asleep. Improving insulin resistance often improves sleep. The reverse is also true: improving sleep improves insulin resistance.

### **Fatty Liver Disease**

Also known as *nonalcoholic steatohepatitis* (NASH) or *nonalcoholic fatty liver disease* (NAFLD), this very common but often overlooked condition is caused by excess fat in the liver. It is similar to liver disease seen in alcoholics. Excess fat in the liver can result in inflammation and permanent scarring, known as *cirrhosis* of the liver.

### **Male Hypogonadism**

Men with insulin resistance commonly have low testosterone levels, known as hypogonadism. This condition causes muscle loss, fatigue, depression, and sexual dysfunction. Men with insulin resistance find it very difficult to get motivated to exercise. This makes the insulin resistance worse. For more on hypogonadism, see Chapter 4.

### **Polycystic Ovary Syndrome (PCOS)**

PCOS is a condition that has insulin resistance at its core. It is believed to affect more than 10 million women in the United States. Insulin resistance stimulates the ovaries and adrenal glands to produce excess male hormones, resulting in irregular menstrual cycles, fertility problems, acne, hair loss, and facial hair growth. PCOS dramatically increases a woman's risk for diabetes, cardiovascular disease, and cancer of the uterus. For more on PCOS, see Chapter 5.

### **Gout**

Gout is a painful disorder caused by deposits of a substance known as *uric acid* in the joints, most commonly the big toe. Insulin resistance causes increased levels of uric acid. Increased uric acid levels have also been associated with an increased risk of cardiovascular disease.

### **Skin Problems**

Insulin resistance is associated with a host of skin problems, including acanthosis nigricans, skin tags, acne, stretch marks, and fungal skin infections. Some experts also believe that psoriasis is linked to insulin resistance.

### **Pregnancy Complications**

Insulin resistance is associated with an increased risk for *gestational diabetes* and high blood pressure in pregnancy, known as *preeclampsia*.

### **Kidney Disease**

Insulin resistance causes protein leakage from the kidney, known as *microalbuminuria*. Insulin resistance, combined with high blood pressure and blood sugar elevations, can result in decreased kidney function, known as *chronic renal failure* or *chronic kidney disease* (CKD). CKD worsens insulin resistance, creating a vicious cycle.

### **Gallstones (Cholelithiasis)**

Insulin resistance and obesity increase the risk for gallstones. This can result in inflammation of the gallbladder, known as *cholecystitis*, and the need for gallbladder removal.

### **Cancer**

Insulin resistance increases the risk for many cancers, including pancreatic cancer, colon cancer, breast cancer, uterine cancer, and prostate cancer.

### **Fatigue**

Although fatigue can be caused by many different things, insulin resistance is a major cause of fatigue. Insulin resistance causes the food that you eat to be stored as fat instead of being burned as energy. Treatments for insulin resistance almost always improve energy levels.

### **Psychiatric Problems**

Insulin resistance increases the risk for psychiatric problems such as depression or anxiety.

### **METABOLIC SYNDROME**

Metabolic syndrome is not a single condition, but a clustering of medical problems that are all connected by the common thread of insulin

resistance and increases the risk of diabetes, cardiovascular disease, and early death. It's estimated that 55 million Americans, or 27 percent of the population, have metabolic syndrome. Metabolic syndrome is also known as *insulin resistance syndrome* or *syndrome X*. It is important to recognize that the ailments of metabolic syndrome have a common thread of insulin resistance, but some experts criticize the diagnostic criteria, stating that they are ambiguous or incomplete.

The criteria for metabolic syndrome are listed in Table 3.1.

- **Elevated blood sugar:** Fasting blood glucose of 100 mg/dL or above. This is below the diagnostic cutoff for diabetes. Most experts believe that a fasting blood sugar level above 95 mg/dL is very abnormal and probably high enough to qualify for metabolic syndrome.
- **Increased belly fat:** Waist circumference 35 inches or greater for a woman, 40 inches or greater for a man. Increased belly fat is a key factor in the development of insulin resistance and metabolic syndrome. Expert panels chose waist circumference over body weight as a more accurate criterion.
- **Elevated blood pressure:** Blood pressure of 130/85 mm Hg or higher. This is considered “borderline” high blood pressure, or *prehypertension*, and is overlooked by many physicians.

**Table 3.1**  
**DIAGNOSTIC CRITERIA FOR METABOLIC SYNDROME**

**Three or more of the following:**

- Fasting blood glucose  $\geq$  100 mg/dL
- Waist circumference  $\geq$  35 inches in women,  $\geq$  40 inches in men
- Blood pressure  $\geq$  130/85 mm Hg
- Fasting triglycerides  $\geq$  150 mg/dL
- HDL cholesterol  $\leq$  50 mg/dL in women,  $\leq$  40 mg/dL in men

- **High triglycerides:** Fasting triglyceride level of 150 mg/dL or above. Triglycerides are a non-cholesterol blood fat and increase your risk for heart attacks and strokes.
- **Decreased good cholesterol:** HDL cholesterol of 50 mg/dL or less in women, 40 mg/dL or less in men. Insulin resistance causes low levels of protective cholesterol, increasing your risk of heart attacks and strokes.

For more information, you should read my book *Overcoming Metabolic Syndrome*. The book is a guide to help you better understand and overcome this complex disorder.

### ***Floyd's Story***

*He came into my office one day, a large man with his shirttail untucked, his tie loosened, and his face red from overexertion, even though he had spent some time in the waiting room. He stood five-foot-ten and weighed 320 pounds. His chart told the story: Hypertension. High cholesterol. Diabetes. He also had a touch of angina—no surprise, given his age (46) and his condition.*

*Floyd knew he had to lose weight. His diabetes was of the late-onset variety; with a poor, sugar-filled diet and the excess weight, he had simply pushed his pancreas past its breaking point, and it had stopped doing its job. The diabetes wasn't going to go away with weight loss, but at least he could get into a condition enabling him to live a longer, fuller life. The way things were now, he wouldn't have many years left, and what little time he had was going to be increasingly uncomfortable.*

## **PHYSICAL FEATURES OF INSULIN RESISTANCE**

Physical features are the best way to diagnose insulin resistance. Most of the time, if you have one or more of the physical features, you have a high likelihood of insulin resistance.

### **Body Weight**

People with a body mass index of 25–27 kg/m<sup>2</sup> or greater are at high risk for insulin resistance. The heavier you are, the more likely you are

to have insulin resistance. For more information on how to calculate your body mass index, see Chapter 11.

### Waist Circumference

Excess weight in the abdominal region is a major sign of insulin resistance. A person with *android obesity* or *central obesity* is fat in the middle section with skinny arms and legs—“apple-shaped” obesity. A person with *gynecoid obesity* or *peripheral obesity*, on the other hand, has a large rear end and hips—“pear-shaped” obesity. Think of the two kinds as “gut vs. butt.” (Fat in the gut is worse than fat in the butt.) People with excess fat in the belly are more likely to have insulin resistance.

Men with a waistline of more than 40 inches and women with a waistline of more than 35 inches are classified as having “central obesity.” Here, the fat literally surrounds the organs. This fat is also known as visceral fat (“viscera” is a term for innards) because of its location. The other fat—the fat of love handles, large buttocks, and big hips—is subcutaneous fat. Of the two, visceral fat is bad fat—I would even call it **metabolically evil**. Why? Because visceral adipocytes—the fat cells surrounding internal organs—are the bad boys of insulin resistance. This metabolically active adipose tissue is regulated by a number of hormones, only one of which needs to go out of whack to make it grow. Increased cortisol and decreased growth hormone can cause central obesity; so can decreased testosterone in men and increased testosterone and decreased estrogen in women. Any combination of these hormonal problems, along with insulin resistance, promotes the accumulation of fat in the belly.

### Elevated Blood Pressure

People with blood pressure above 130/85 are at increased risk for having insulin resistance.

### Skin Tags

Skin tags, or small bits of skin projecting from the surrounding skin, is a common sign of insulin resistance.



### **Acanthosis Nigricans**

This skin condition appears as a black, velvety skin rash or dark discoloration in a ring around the neck. Acanthosis nigricans also occurs under the arms, around the belly button, under skin folds, or in the groin. It looks like dirt, but it won't wash off. This condition is caused by insulin resistance and is usually a sign of prediabetes or diabetes. Insulin is a growth factor—and insulin also makes skin grow. In the presence of abnormally high insulin levels, skin grows in very strange ways, making it turn dark. If you have acanthosis nigricans, you are virtually guaranteed of having insulin resistance. But it's not an incurable condition: as you lose weight, the acanthosis nigricans disappears as well. One word of warning, however: in rare cases, acanthosis nigricans is caused not by insulin resistance but by cancer. If you have this condition, by all means see your doctor.

### **Symptoms of Polycystic Ovary Syndrome**

Symptoms of PCOS, such as acne, facial hair growth, infertility, or abnormal menstrual cycle, are common with insulin resistance. For more information, see Chapter 5.

### **TESTING FOR INSULIN RESISTANCE**

There is no absolute criterion for diagnosing insulin resistance. The most reliable way to test for insulin resistance is using a technique known as the *hyperinsulinemic euglycemic clamp*. This test requires simultaneous infusions of glucose and insulin into two different veins (IV catheters are placed in both arms). Blood sugar levels are checked every 5 minutes for 3 hours, and the rate of the glucose going in is adjusted to keep blood sugar levels stable. The amount of glucose required to keep blood sugar in the normal range is used to determine the level of insulin resistance. The euglycemic clamp is difficult to perform, and there is a risk of causing low blood sugar levels. The test is used for medical research but is not used for routine clinical care. The *insulin suppression test* and *deuterated-glucose disposal test*

(<sup>2</sup>H-GDT) are very reliable for diagnosing insulin resistance, but are also used for research purposes only.

**For most people, blood tests to diagnose insulin resistance are not necessary.** If you are overweight or have several physical features of insulin resistance, or if you qualify for metabolic syndrome, you most likely have insulin resistance. Blood tests are still necessary to test for complications of insulin resistance, such as blood sugar or cholesterol problems.

### **Fasting Plasma Glucose**

The fasting plasma glucose test measures the amount of sugar in the blood after an overnight fast. This is a simple yet important test for assessing blood sugar status and diagnosing diabetes or prediabetes. If you have a fasting blood sugar level between 100 and 125 mg/dL, you are classified as having *impaired fasting glucose* (IFG), although most experts believe that a fasting blood sugar above 95 is definitely abnormal. If your level is above 125 mg/dL on two separate occasions, you have diabetes. Any blood sugar elevation above 95 mg/dL indicates that insulin production can no longer keep up with the demand of insulin resistance.

### **Random Plasma Glucose**

The random plasma glucose test can be done at any time without fasting. For this test, a normal blood sugar level is below 140 mg/dL. A diabetic level is more than 200 mg/dL. A random glucose reading between 140 and 199 mg/dL is considered prediabetes.

### **Oral Glucose Tolerance Test (OGTT)**

The oral glucose tolerance test is like a “stress test” for the pancreas. It determines how quickly and efficiently your body can handle a load of glucose. The test is done when you are fasting. First, a fasting (or baseline) blood glucose level is measured. Then the patient is

given a pure glucose beverage to drink, and a second glucose level is measured 2 hours later. The amount of glucose given and the time between blood glucose measurements can vary, but the standard procedure is to give 75 grams of glucose and wait 2 hours to get the second reading. Extension of the testing (for several more hours) will sometimes show a drop in blood sugar levels, which is the result of a delayed but exaggerated response of insulin production. Anyone diagnosed with prediabetes should have a glucose tolerance test. A version of the OGTT is used to screen pregnant women for gestational diabetes.

### **Meal Tolerance Test**

The meal tolerance test, also known as a *postprandial blood glucose test*, is a “real-life” version of the oral glucose tolerance test. Instead of drinking a glucose beverage, you eat a big meal, and the blood glucose level is measured before and 2 hours after. The meal tolerance test is not as reliable as other tests but can be used to diagnose diabetes or prediabetes using the same cutoffs as the random glucose test.

### **Self-Monitored Blood Glucose (SMBG)**

The most accurate way to measure glucose levels is from a sample of blood that is processed in a laboratory. Home glucose monitors (also known as glucometers) that measure blood sugar from a drop of blood (from a prick of the finger) are also helpful, but not as accurate as laboratory testing. Readings from a glucose monitor cannot be used to make a definite diagnosis of diabetes or prediabetes, but are helpful in giving you a general idea of what your blood sugar is doing during different times of the day. It's best to test at different times because blood sugar can be normal at one time but high at another. The highest blood sugar levels usually occur 2 hours after a meal, especially a large meal. People with diabetes should monitor their blood sugar several times a day. People with prediabetes should check their blood sugar a couple of times a week.

**Table 3.2**  
**BLOOD SUGAR LEVELS**

**Fasting Blood Sugar Levels**

Normal: below 95 mg/dL

Impaired fasting glucose: 100–125 mg/dL

Diabetes: above 125 mg/dL

**Random Blood Sugar Levels**

Normal: below 140 mg/dL

Prediabetes: 140–199 mg/dL

Diabetes: above 200 mg/dL

**Two-Hour Stimulated Glucose Levels (75 grams of glucose)**

Normal: below 140 mg/dL

Impaired glucose tolerance: 140–199 mg/dL

Diabetes: above 200 mg/dL

**Hemoglobin A1c**

The *hemoglobin A1c test*, also known as HbA1c or A1c, estimates the average blood sugar level over the last 3 months. Hemoglobin A1c is a protein in red blood cells that bonds with blood sugar. Because red blood cells can live about 90 days, hemoglobin A1c represents the average blood sugar level for this length of time. A reading above 5.7 percent indicates that blood sugar is higher than normal.

In the past, this test was recommended for only those with diabetes. More recently, however, A1c has been recognized as an excellent test for assessing long-term blood sugar levels in people with insulin resistance. Elevated A1c is also an independent risk factor for cardiovascular disease.

### Insulin Levels

It's logical to think that high insulin levels are the best way to diagnose insulin resistance. Most experts do not recommend measuring insulin levels, however, for two reasons. First, laboratory testing methods for insulin are still unreliable and can be inaccurate. Each laboratory uses a slightly different testing method; the results have not been *standardized* against each other, so no one really knows what "normal" is. Second, many people with insulin resistance have normal or even low insulin levels because of glucose toxicity and pancreatic burnout. Nevertheless, some doctors still measure insulin levels to make the diagnosis of insulin resistance. If insulin is measured after an 8-hour fast, a level above 10 to 15  $\mu\text{U/mL}$  is considered high. Insulin is sometimes measured in conjunction with the oral glucose tolerance test; here it is referred to as a *stimulated insulin level*. The fasting insulin level and the insulin level 2 hours after consumption of a glucose beverage are compared. The "area under the curve" for insulin in a 2-hour oral glucose tolerance test uses a mathematical formula to analyze insulin levels after a glucose load. This method is considered a reasonable way to test for insulin resistance.

### Glucose and Insulin Calculations

Researchers have developed ways to estimate insulin resistance based on sophisticated calculations. Calculations are more reliable than simple measurements of glucose and insulin, and correlate very well with the gold standard test, the euglycemic insulin clamp. These calculations have been criticized, however, because they were originally developed as a research tool to study large groups of people. The critics claim that the calculations aren't always accurate for an individual person.

The *homeostatic model assessment of insulin resistance* (HOMA or HOMA-IR) uses the formula

$$\text{HOMA} = \text{insulin } (\mu\text{U/m}) \times [\text{glucose (mmol/L)}/22.5]$$

This formula requires that glucose be converted to the units of  $\text{mmol/L}$ , which is different from the standard unit of  $\text{mg/dL}$ . Patients with a HOMA score of 2.6 or above are considered to have insulin resistance.

The *quantitative insulin sensitivity check index* (QUICKI) uses the formula

$$\text{QUICKI} = 1 / \log \text{ insulin } (\mu\text{U}/\text{m}) + \log \text{ fasting glucose } (\text{mg}/\text{dL})$$

Patients with a QUICKI score of 0.33 or above are considered to have insulin resistance.

### **Breath Testing**

A novel and very accurate way of assessing insulin resistance is with a breath test marketed as Diatest. The test requires that a patient consume a glucose beverage that contains a non-radioactive isotope known as  $^{13}\text{C}$ -glucose. A normal breath of air is exhaled into tubes before and after drinking the beverage. The tubes are analyzed and compared to check for insulin resistance.

### **Urinary Microalbumin**

This test measures microscopic amounts of protein (albumin) in the urine. The microalbumin test is very sensitive and will detect levels of protein much lower than is possible with a traditional urinalysis. People with insulin resistance, diabetes, or high blood pressure can have increased levels of protein in the urine. It is recommended that everyone at risk for insulin resistance be tested for microalbumin once or twice a year.

### **Potassium Level**

Potassium is necessary for proper insulin action. Low potassium levels are an easily treatable cause of insulin resistance. For insulin to function best, the potassium level should be above 4 meq/L. Anyone with a low potassium level should also be evaluated for hyperaldosteronism (see below).

### **Aldosterone and Renin Levels**

If you have high blood pressure and insulin resistance, there's about a 10 percent chance that you have an additional hormonal problem known as *hyperaldosteronism*. Aldosterone is a hormone produced by

the adrenal glands that, when produced in excessive amounts, causes high blood pressure and low potassium levels. Anyone who has both high blood pressure and low potassium (or is taking potassium supplements to keep the potassium level normal) should be tested for hyperaldosteronism. A second hormone, renin, should also be tested during the evaluation. Renin is a hormone produced by the kidney that stimulates the adrenal gland to make aldosterone. Renin is measured by testing what is known as *plasma renin activity* (PRA). In classic cases of hyperaldosteronism (known as *primary hyperaldosteronism*), the plasma renin activity is very low because the adrenal gland is pumping out aldosterone independently of the normal signal from renin. In a classic endocrine fashion, renin levels are lowered in an attempt to lower aldosterone. So a high aldosterone level and low plasma renin activity are indicative of primary hyperaldosteronism. Diagnosis of the hormonal condition is imperative, because the cause could be a tumor in the adrenal gland, which may need to be removed surgically. Even if a tumor is not present, knowing that hyperaldosteronism is present will guide your physician to use more appropriate medications.

### **Lipid Profile**

A *standard lipid profile* includes total cholesterol, calculated LDL, HDL, and triglycerides. Insulin resistance causes a typical pattern of low HDL cholesterol and high triglycerides. This pattern is also an indication of your risk for cardiovascular disease. Total cholesterol is not always a helpful test because it measures both good and bad cholesterol, and does not tell you how much of each is present. It is better to focus on the individual measurements of LDL and HDL cholesterol. In a standard lipid profile, the LDL cholesterol is not actually measured but calculated using the following formula:

$$\text{LDL cholesterol} = \text{Total cholesterol} - [\text{HDL cholesterol} + (\text{Triglycerides}/5)]$$

This formula is not accurate when the triglyceride level is above 400 mg/dL.

**Table 3.3**  
**INDICATORS OF INSULIN RESISTANCE BASED ON**  
**A LIPID PROFILE**

High triglycerides

Low HDL (good) cholesterol

More small-dense LDL (bad) cholesterol

Normal or high LDL (bad) cholesterol

*Direct LDL measurement* is available and is routinely done as part of an *advanced lipid profile*. Advanced lipid testing gives a more detailed measurement of LDL and HDL cholesterol. There are two types of HDL cholesterol, known as HDL<sub>2</sub> and HDL<sub>3</sub>. HDL<sub>2</sub> provides the most protection from cardiovascular disease. There are two types of LDL cholesterol, small dense (known as pattern B) and large fluffy (known as pattern A). Although all LDL cholesterol is bad, the small dense LDL cholesterol is the more dangerous type of LDL cholesterol. Insulin resistance causes lowered HDL<sub>2</sub> levels. Insulin resistance does not always increase LDL cholesterol, but does cause an increase in the more dangerous small dense LDL particles.

HDL and triglyceride levels are frequently used as an indicator of insulin resistance. A person with an HDL level below 40 mg/dL is likely to have insulin resistance. A fasting triglyceride level above 150 mg/dL puts one at risk for insulin resistance. The *ratio of triglycerides to HDL cholesterol* is an excellent way to assess for insulin resistance. A ratio above 3 represents high risk for insulin resistance.

*Advanced lipid testing* can also measure the proteins that carry cholesterol, known as apolipoproteins. *Apolipoprotein A*, or *apo A*, is primarily found in the HDL particle and is a good way of assessing the body's ability to clear cholesterol from the blood. *Apo B*, also known as *apolipoprotein B*, represents LDL cholesterol.



**Table 3.4**  
**CHOLESTEROL LEVELS**

**Total Cholesterol Levels**

Desirable: Less than 200 mg/dL

Borderline high: 200–239 mg/dL

High: Above 240 mg/dL

**HDL Cholesterol Levels**

High: 60 mg/dL (higher is better)

Normal: 40–60 mg/dL

Low: Less than 40 mg/dL

**LDL Cholesterol Levels**

Ideal: Less than 70 mg/dL

Normal: 70–100 mg/dL

Borderline high: 100–130 mg/dL

High: 130–160 mg/dL

Very high: Greater than 160 mg/dL

**LDL Subtypes**

Pattern A: Less dangerous type (large fluffy particles)

Pattern A/B: Intermediate type (combination of particles)

Pattern B: Most dangerous type (small dense particles)

**Triglyceride Levels**

Ideal: Less than 100 mg/dL

Normal: Less than 150 mg/dL

High: 150–199 mg/dL

Very high: 200–499 mg/dL

Extremely high: Greater than 500 mg/dL

Danger of pancreatitis: Greater than 1000 mg/dL

### **Plasminogen Activator Inhibitor-1 (PAI-1)**

PAI-1 is a blood clotting test that is often done in conjunction with advanced lipid testing. Insulin resistance is associated with an increased risk for blood clotting and elevations in PAI-1 levels. PAI-1 elevations are associated with an increased risk of cardiovascular disease. Traditional tests for blood clotting, known as *prothrombin time* (PT) and *partial thromboplastin time* (PTT), are not sensitive enough to pick up the blood clotting abnormalities seen in insulin resistance.

### **Homocysteine**

This toxic amino acid increases the risk of blood clots and cardiovascular disease, even among people who have a normal lipid profile. High homocysteine levels can be the result of a deficiency of vitamin B<sub>6</sub>, folic acid, or vitamin B<sub>12</sub>. People with insulin resistance tend to have high homocysteine levels.

### **C-Reactive Protein (CRP)**

The CRP test is a measure of inflammation, which is a major feature of insulin resistance. CRP levels can be high due to any type of inflammation—when the body experiences injury, infection, or other stress. The CRP test is a very good test to predict future cardiovascular disease in otherwise healthy individuals.

#### **C-Reactive Protein Levels**

Low risk: Less than 1.0 mg/L

Average risk: 1.0 to 3.0 mg/L

High risk: Greater than 3.0 mg/L

### **Sex Hormone Binding Globulin (SHBG)**

SHBG is a blood protein that carries the sex hormones, estrogen and testosterone, in the bloodstream. For reasons that are not fully known, a decreased level of SHBG is associated with an increased risk for insulin resistance. (See Chapters 4 and 6 for more on SHBG.)

### **Insulin-Like Growth Factor-1 (IGF-1) and the Growth Hormone Suppression Test**

Excess growth hormone produced by a tumor of the pituitary gland (known as *acromegaly*) is a cause of insulin resistance. IGF-1 is a hormone produced by the liver that is used as a surrogate marker for growth hormone levels. If the IGF-1 level is high, a growth hormone suppression test should be done to further evaluate growth hormone levels. For more information on growth hormone, see Chapter 9.

### **Immune System Testing**

A rare form of insulin resistance, known as *type B insulin resistance*, is an autoimmune disorder caused by antibodies directed against the insulin receptor. If you have other autoimmune problems, you may have this unusual type of insulin resistance. See Chapter 7 for more information on autoimmune diseases.

### **Sleep Study (Polysomnography)**

Insulin resistance is a major risk factor for sleep apnea. Sleep apnea is diagnosed with a sleep study, also known as *polysomnography*.

### **Ultrasound**

A *liver ultrasound* can detect fatty liver disease. A *pelvic ultrasound* can detect polycystic ovary syndrome. Both of these problems are common in insulin resistance.

## **Cardiovascular Testing**

Because insulin resistance is a major risk factor for cardiovascular disease, it is recommended that testing be done to screen for potential cardiovascular problems. Many tests are available, and the exact tests needed should be determined by your physician. Cardiovascular tests include electrocardiogram (EKG), echocardiogram, treadmill stress test, nuclear cardiac testing, cardiac CT scan, and carotid ultrasound.

## **TREATING INSULIN RESISTANCE**

Reversing insulin resistance is a critical step to achieving *hormonal balance*. Insulin resistance is not incurable. At the beginning of this chapter, we saw how the Pima Indians, despite being genetically disposed to insulin resistance, are still able to avoid obesity, diabetes, and a host of other ailments that surround insulin resistance. The same is true for all of us, particularly since many people become insulin resistant through poor dietary choices and a sedentary lifestyle—which may then be exacerbated by any genetic predisposition. The answer to insulin resistance is a healthy diet and lifestyle. Even modest diet and lifestyle improvements can improve insulin resistance and dramatically lower your risk of getting complications like type 2 diabetes and cardiovascular disease. Although improved nutrition and increased physical activity are the best ways to treat insulin resistance, medications can improve insulin resistance and can treat many of the complications of insulin resistance. Vitamins, minerals, and herbal supplements can also be helpful, but should not be a substitute for a healthy diet and exercise.

## **Weight Loss**

Insulin resistance always improves with weight loss. If you get down to a normal body weight (BMI below 25 kg/m<sup>2</sup>; see Chapter 11), there is a very good chance that insulin resistance can be completely alleviated.

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### **The Hormonal Health Diet**

To counter insulin resistance—and, by no coincidence, to promote balanced nutrition—the Hormonal Health Diet is a higher-protein diet consisting of about 40 percent carbohydrates, 30 percent protein, and 30 percent fat. (Exact percentages aren't critical, as long as you're in the ballpark.) This is a slight deviation from American Diabetic Association (ADA) guidelines, which support a diet containing 20 percent protein and 50 percent carbohydrates. A diet slightly higher in protein actually improves insulin resistance *beyond* what is seen with a traditional ADA diet.

### **Fish High in Omega-3 Fatty Acids**

Omega-3 fatty acids help to reduce insulin resistance. Moreover, fish are a terrific source of both protein and “healthy fat.” Fish oil lowers bad cholesterol and raises good cholesterol, and diets high in fish improve insulin resistance beyond what is seen in diets without fish. The American Heart Association recommends eating fish twice a week. It's OK to take omega-3 fatty acid supplements, but you won't get the benefit of the protein from fish. Table 3.5 lists the omega-3 fatty acid content of fish.

### **Lower-Glycemic Index/Glycemic Load Foods**

As noted in Chapter 2, experts have shown that low-glycemic index and low-glycemic load foods have a variety of positive effects. The body breaks them down slowly, so there are fewer insulin spikes, and the body can absorb the energy from sugar gradually, which has a salutary influence on other body processes.

### **Small, Frequent Meals**

Small, frequent meals are an excellent way to eat. The reverse is also true: don't eat too much at one time. No diet is effective if you overload your body with too many calories; calories do count.

**Table 3.5**  
**OMEGA-3 FATTY ACID CONTENT OF VARIOUS FISH**

Only certain fish, mainly those that live in cold water, contain meaningful amounts of omega-3 fish oils. Measurements are grams of omega-3 fatty acid per 100 grams of raw fish.

Sardines (in their own oil)	21.1 grams
Atlantic mackerel	2.5 grams
Lake trout	1.6 grams
Salmon	1.2 grams
Striped bass	0.8 grams
Tuna	0.5 grams
Pacific halibut	0.4 grams
Channel catfish	0.3 grams
Shrimp	0.3 grams
Dungeness crab	0.3 grams
Swordfish	0.2 grams
Red snapper	0.2 grams
Sole	0.1 gram

**Source:** Christine Gorman, "We Love Fish," *Time*, October 30, 2000.

### **Foods High in Potassium**

Potassium is important for proper insulin action. Foods high in potassium include sweet potatoes, white potatoes, tomatoes, yogurt, clams, fish, carrots, bananas, spinach, watermelon, apricots, cantaloupe, peas, beans, and oranges.

### **Don't Eat Late at Night**

Our bodies secrete hormones cyclically. Growth hormone and cortisol, both counter-insulin hormones that create insulin resistance, are secreted mostly at night, with the peak time between 3 A.M. and 6 A.M.

If you eat during your growth hormone and cortisol peaks, your body will have to pump out more insulin to process your meal to overcome the effects of these hormones. Sleep slows metabolism, so foods eaten during this time will not only take longer to break down, but also won't be burned up as energy.

### **Alcohol, in Moderation**

Moderate alcohol use—one (for women) or two (for men) drinks a day—can be good for your health. Alcohol decreases insulin resistance, a fact that doctors have known for years; but out of fear of encouraging alcoholism, this information hasn't been well promoted. Beer, wine, and hard liquor—any alcoholic beverage—will lower insulin resistance, but beware of calories. And remember moderation: when I say one or two drinks a day, I mean exactly that. You can't save up drinks for the weekend.

### **Physical Activity**

Physical activity is one of the best ways to alleviate insulin resistance. Even without weight loss, exercise can have a dramatic effect on lowering your level of insulin resistance. Physical activity reduces insulin resistance in part because it builds muscle. The more muscle you have, the more tissue you have to take up glucose, and the better your sensitivity to insulin. As the old saying goes, “muscle burns fat.”

Studies have shown that exercise improves insulin resistance even if you *don't* lose weight. Physical activity allows your body to handle blood glucose better. When you exercise, the muscles become not only stronger, but *metabolically stronger*. Exercise allows your body to “dispose” of glucose more easily—it gets into the muscles more easily—and your insulin levels drop. Simply put, given two people of identical body weight, if one exercises and the other doesn't, the one who exercises will have lower insulin levels and less insulin resistance.

Unfortunately, there's no magic pill, no as-seen-on-TV contraption that will take the place of a good, solid workout. I recommend that you set a goal of getting at least 60 minutes of physical activity every day. This can be any type of physical activity, from taking a walk to lifting weights. It's helpful, but not mandatory, to do a variety of types of physical activity over the course of a week.

## **Stress Reduction**

Part of what makes contemporary Americans so susceptible to insulin resistance is our sedentary, comfortable lifestyle. We don't even get up to change the channel on the TV any more; we simply click a button on a remote control. Ironically, though, we're probably working harder than ever. In days past, we were allowed to take time to do our work, and if it didn't get done by the end of the day, we would always have tomorrow. Nowadays, with faxes, e-mail, and other forms of instant communication, not only do we not have to the end of the day to finish our work, we don't even have to the end of the hour! No wonder we're so stressed: we don't exercise, we're trying to get things done yesterday, and it seems like there's more to do than ever.

When your body is physically or emotionally stressed, cortisol—the stress hormone—is released. Cortisol is a counter-insulin hormone and thus can undo much of the positive effects that exercise has on blood sugar.

I'll go into stress and cortisol in much more detail in Chapter 8, but let me leave you with two more words on the subject: hot tubs. *Hot tubs* have been shown to improve insulin resistance. Why? We don't know. But consider: hot tubs improve blood flow. Hot tubs relieve stress. Hot tubs improve sleep. Perhaps it's not so surprising that with all of these positives, they also improve insulin resistance.

## **VITAMINS, MINERALS, AND HERBS FOR INSULIN RESISTANCE**

People with insulin resistance may benefit from supplementation with certain vitamins, minerals, and herbs. The concern, however, is that most of these remedies have not been adequately tested. The quality, purity, and potency of many products may be uncertain since they are not well regulated by the FDA. The most important thing to remember is that vitamins, minerals, and herbs are not a substitute for proper nutrition and physical activity and are usually not as potent as medications.

## **Chromium**

This element—yes, the same one from which “chrome” in automobiles is made—is essential to our health. Without chromium, insulin doesn't



work properly. It is required only in trace amounts in the diet; but without those small amounts, people can suffer from a condition known simply as *chromium deficiency*, which can cause insulin resistance, impaired glucose tolerance, and overt diabetes. Doctors usually don't test for chromium deficiency because testing is unreliable.

Maintaining chromium in the body is difficult. For one thing, we don't consume enough chromium-rich food; for another, chromium is easily passed out of the body in urine and sweat—even more easily if a person has high blood sugar or consumes high-glycemic index foods.

Foods high in chromium include brewer's yeast, beef, mushrooms, wheat germ, broccoli, hard cheese, chicken, shellfish—especially clams—corn oil, molasses, whole grains, and a variety of fruits. I highly recommend incorporating these foods into your diet, but chromium supplements (500–1000 µg daily) can also improve insulin resistance. One word of caution: if you do not have chromium deficiency, chromium supplementation is unlikely to help reduce your insulin resistance.

## Vanadium

Another element, vanadium—ironically—was mistaken for a form of chromium when discovered in the early 19th century. One of the hardest of all metals, it is never found in a pure state, but always in a compound form with other elements.

Scientists still aren't sure about the exact contribution of vanadium to our diet, but *vanadium deficiency* can cause insulin resistance.

Though bodybuilders and people with diabetes have taken a form of vanadium, vanadyl sulfate, to improve the way insulin works, there still is no proof it does this. What vanadium probably does is mimic the action of insulin by turning on the insulin receptor. However, another form of the element, vanadate, is not recommended because of toxic effects, ranging from anemia and green tongue to cataracts and death. Because of those toxic effects, I do not encourage taking vanadium supplements.

Though I don't approve of vanadium supplements, I support eating foods high in vanadium. These include beets, black pepper, buckwheat, carrots, dill, eggs, fish, milk, mushrooms, oats, olive oil, radishes, parsley, shellfish, soybeans, sunflower oil, and whole wheat.

### Other Vitamins and Minerals

Any diet should include a variety of vitamins and minerals, and one to improve insulin resistance—as well as overall health—is no exception. To protect against insulin resistance, I encourage a diet high in zinc, copper, and selenium, as well as vitamins A, C, and E.

- *Selenium.* Selenium-rich foods include meats, poultry, dairy products, and other animal foods. I'll discuss selenium in more detail in Chapter 7. Selenium is key to healthy function of the thyroid gland.
- *Zinc.* Foods high in zinc include oysters, beef, wheat germ, lima beans, and dairy products. Zinc helps insulin work properly; in fact, certain types of insulin used by diabetics contain zinc, which helps the insulin last longer in the body. Zinc is vital for proper leptin action (see Chapter 10).
- *Copper.* Copper-rich foods include oysters, shellfish, nuts, cherries, mushrooms, and beans. A high-fructose diet—that is, one high in fruit—can cause copper deficiency. Copper is needed in exceptionally small quantities in the diet—about 1.5 to 3 micrograms, or about one-tenth the amount of zinc.
- *Vitamins A, C, and E.* These antioxidants may also be beneficial in lowering insulin resistance.

### Omega-3 Fatty Acids

Omega-3 fatty acid supplements can be helpful for insulin resistance but are not the ideal source of this beneficial lipid. It is better to get omega-3 fatty acids from eating cold-water fish. If supplements are required, I recommend taking Omacor (see below), a prescription formulation, which is much more potent and pure than over-the-counter preparations.

### Folic Acid (Vitamin B<sub>9</sub>)

Folic acid helps prevent complications of insulin resistance like heart attacks and strokes by helping the body break down the toxic amino acid homocysteine. Folic acid is found in whole grains, green leafy vegetables,

nuts, avocados, bananas, and oranges. Many physicians recommend supplementation with up to 1000 micrograms (1 milligram) of folic acid every day.

### **Biotin (Vitamin B<sub>7</sub>)**

This water-soluble B vitamin is essential for proper carbohydrate metabolism, as well as cell growth and replication. Eating foods high in biotin, or consuming biotin supplements, enhances insulin sensitivity and increases the activity of enzymes necessary for proper carbohydrate metabolism; conversely, a *biotin deficiency* can cause insulin resistance or diabetes.

Most of us have plenty of biotin in our diets, however. Among the foods that contain biotin are brewer's yeast, egg yolks, whole grains, breads, fish, nuts, beans, meat, dairy products, lentils, peas, peanuts, walnuts, and molasses. Moreover, biotin is a natural product of the bacteria in our intestines. The recommended daily allowance of biotin is 30 to 100 micrograms a day, a relatively minuscule amount.

However, other items in a diet can create the need for more biotin. Egg yolks, as I noted, contain biotin; however, raw egg whites inactivate the vitamin, so people who eat lots of raw egg whites can become biotin deficient. Alcohol raises the biotin requirement, as does estrogen. And food-processing techniques, such as canning and cooking, can destroy biotin.

Like the deficiency of any vitamin, a deficiency in biotin can cause a variety of ailments, not just insulin resistance. Symptoms include hair loss, scaly red rash around the nose and mouth, anemia, high cholesterol, loss of appetite, nausea, depression, sleeplessness, and hallucinations.

Biotin is commonly a component of standard multivitamin tablets; however, if you follow the Hormonal Health Diet, you shouldn't need to take special biotin supplements. But if you've had any of the above-listed symptoms, that might have been the source of your trouble.

### **Niacin (Vitamin B<sub>3</sub>)**

High doses of niacin or a prescription formulation of niacin are used to treat the lipid abnormalities of insulin resistance. Niacin is considered ideal because it simultaneously corrects the three major lipid abnormalities, lowering LDL cholesterol and triglycerides while raising HDL

cholesterol. Unfortunately, niacin can raise blood sugar levels and can worsen insulin resistance. Even though niacin is available over the counter, I recommend that you take it only under the supervision of a physician.

### **Cinnamon**

Studies have found that half a teaspoon of cinnamon a day can reduce blood sugar levels in people with diabetes. The discovery that cinnamon lowers blood sugar levels was made by accident. Researchers at the U.S. Department of Agriculture were looking at the effects of different foods in people with diabetes. They were surprised to learn that apple pie did not affect blood sugar as one might expect. Further research determined that the cinnamon in the pie blunted the effects of the sugar and the fat. Cinnamon has insulin-like properties that can lower blood sugar and may perhaps prevent diabetes. The active ingredient is found in powdered cinnamon, not cinnamon oil. The best way to get cinnamon is to add it to foods you already eat, like coffee, yogurt, or cereal.

### **Garlic**

Garlic has antioxidant properties and helps lower cholesterol. To see any meaningful effect from garlic, you have to eat a huge amount. Garlic pills are an odorless, tasteless formulation that allows you to get enough while avoiding garlic breath.

### **Fiber**

Fiber improves insulin resistance in several ways. It adds volume and bulk to food without adding calories. It helps you feel satisfied and stimulates release of the appetite-suppressing hormone cholecystokinin (see Chapter 10). Fiber also lowers the glycemic index and glycemic load of foods, which slows the rate at which sugar hits your bloodstream. The best sources of fiber are vegetables, fruits, and whole

grains. The Hormonal Health Diet emphasizes foods that are high in fiber. High-fiber cereals and over-the-counter fiber supplements such as Metamucil, Citrucel, and Benefiber are others way to increase fiber in your diet.

## **MEDICATIONS TO TREAT INSULIN RESISTANCE AND ITS COMPLICATIONS**

There are no drugs that are approved by the U.S. Food and Drug Administration for the treatment of insulin resistance. Many medications do alleviate insulin resistance and also treat the manifestations and complications of insulin resistance. There is no perfect medication for insulin resistance. A drug that treats one feature of insulin resistance may make another feature worse. The best way to have *hormonal balance* is to achieve a balance between the benefits offered by a medication and the risk that it could make things worse.

Medications are never a substitute for proper nutrition and physical activity. When doctors use medications for insulin resistance, they have several goals in mind. Some medications can make insulin work more efficiently, lowering blood sugar and insulin levels, and can reduce the risk of diabetes. Medications that have weight loss as a “side effect” are frequently used to treat insulin resistance. Other medications prevent or treat cardiovascular disease, high blood pressure, lipid abnormalities, blood clotting, or inflammation. It’s also important to treat other hormone problems associated with insulin resistance, like PCOS and male hypogonadism.

### **Diabetes Medications**

Because insulin resistance is a cause of type 2 diabetes, it is logical that diabetes medications are first-line treatments.

*Metformin (Glucophage, Glucophage XR, Fortamet, Riomet, and Generics)*

Metformin is the most common medication prescribed for diabetes in the world. It works mostly by reducing the liver’s ability to make sugar

(a process known as *gluconeogenesis*). Metformin does more than just treat diabetes, however. It lowers LDL cholesterol and triglyceride levels. Metformin has weight loss as a “side effect,” but without improved nutrition and physical activity, this effect is minimal. Metformin reduces the risk of cardiovascular disease and the risk of type 2 diabetes. The original, short-acting version of metformin is better for weight loss and treating insulin resistance. The long-acting formulation is still good for treating insulin resistance, can be taken once a day, and has fewer side effects. If the pills are too big to swallow, a liquid form, called Riomet, is available.

The most common side effects of metformin are nausea, diarrhea, and upset stomach, which occur in about one of four people who take it. These side effects are almost always temporary and subside in three or four days, but can last for several weeks. To minimize side effects, start with the 500 mg tablet once a day with breakfast, and gradually increase the daily amount over several months. A fiber supplement can also be helpful for the side effect of diarrhea. The best dose for alleviating insulin resistance is 850 mg three times a day. It's important to take metformin with a substantial meal to minimize side effects. The manufacturer recommends that you do not drink alcohol while taking metformin, but many of my patients have an occasional alcoholic beverage without any problems. Metformin can cause problems in people who drink heavily or have a severe infection, or kidney or liver disease because of a rare but deadly side effect known as lactic acidosis. For the most part, however, metformin is a very safe drug.

*Thiazolidinediones: Rosiglitazone (Avandia) and Pioglitazone (Actos)*

A type of diabetes medication known as thiazolidinediones, “glitazones,” or simply TZDs make cells more sensitive to insulin by regulating genes in the cells. They are excellent at improving insulin resistance and reversing many of its manifestations above and beyond their ability to treat diabetes. Their effects include lowering blood pressure and reducing inflammation and blood clotting. TZDs are ideal for treating the lipid abnormalities of insulin resistance because they decrease triglycerides, raise HDL levels, and can shift LDL from the dangerous “small dense” type to the less dangerous “large fluffy” type. TZDs reverse atherosclerosis, cardiovascular disease, and fatty liver disease. A particularly interesting effect of TZDs is their ability to redistribute body fat, moving it from dangerous areas, such as the belly and vital

organs, to safer areas, such as the hips, buttocks, and under the skin. TZDs can prevent the high-risk people from getting diabetes and are used to treat a variant of insulin resistance seen in HIV patients known as *HIV lipodystrophy*.

The most publicized side effect of TZDs is weight gain, but the truth is that most people gain only a few pounds or none at all. If you follow the Hormonal Health Diet, it is more likely that you will lose weight while taking a TZD. Fluid retention is a more serious side effect, which can result in swelling of the legs and can be responsible for some of the weight gain. Heart failure is a contraindication to the use of TZDs because there can be a worsening of symptoms due to the fluid retention. (Some people with mild heart failure can take low doses of TZDs under close supervision.) The lowest doses (Avandia 2 mg or Actos 15 mg) are better for treating insulin resistance because there is less weight gain and less fluid retention.

*Metformin-TZD Combination Tablets (Avandamet—Rosiglitazone and Metformin; Actoplus Met—Pioglitazone and Metformin)*

These medications are ideal for treating insulin resistance because of their synergistic actions. Metformin negates the weight gain seen when TZDs are used alone. For convenience, the manufacturers have combined them in one pill. Taking the medications as separate pills gives the exact same effect as the combination tablets.

*Miglitol (Glyset) and Acarbose (Precose)*

These diabetes medications work by blocking an enzyme in the intestine that breaks down carbohydrates, known as *alpha-galactosidase*. They slow, but do not prevent, the digestion of food, and foster a mild decrease in the absorption of carbohydrates. Their effect on weight loss is minimal.

*Exenatide (Byetta)*

This is a new hormonal medication that was listed as an experimental drug in the first edition of *Hormonal Balance*. Exenatide is now available and approved by the FDA for the treatment of diabetes. Exenatide imitates the actions of the digestive hormone glucagon-like peptide-1 (GLP-1). (For more information on GLP-1, see Chapter 10.) The medication not only treats diabetes but also improves cholesterol and triglycerides, and has weight loss as a “side effect.” Nausea is also

a side effect because the drug slows down the digestive system, but as with metformin, the nausea is usually temporary. In rare cases, exenatide has been blamed for causing pancreatitis. The medication is given as an injection twice a day.

### *Pramlintide (Symlin)*

Also listed as experimental in the first edition of *Hormonal Balance*, pramlintide is a newly approved hormonal diabetes medication. This drug works by mimicking amylin, a pancreatic hormone that regulates blood glucose. It is not widely used to treat insulin resistance, but can help people who have diabetes. The medication is given as an injection. Nausea, vomiting, low blood sugar, and headache are all possible side effects.

## **Lipid Medications**

Lipid problems are a hallmark of insulin resistance, so it's not surprising that many people with insulin resistance end up taking medications. Combination drugs like Vytorin (a combination of ezetimibe and simvastatin) and Advicor (a combination of long-acting niacin and lovastatin) are convenient and may save on insurance co-pays, but offer no additional advantages to taking the medications as separate pills.

*Statins: Atorvastatin (Lipitor), Pravastatin (Pravachol), Simvastatin (Zocor), Fluvastatin (Lescol, Lescol XL), Lovastatin (Mevacor, Altoprev), and Rosuvastatin (Crestor)*

You can't watch the evening news nowadays without seeing a commercial for a class of drugs known as *statins* or *HMG CoA reductase inhibitors*. Statins work by inhibiting the enzyme HMG CoA reductase, which is needed to produce bad cholesterol. These blockbuster drugs are the most commonly used medications to treat high LDL cholesterol. But the amount of LDL cholesterol is not always the problem in insulin resistance. Insulin resistance causes the quality of LDL to shift to the dangerous "small dense" type. Statins have a small effect in lowering triglycerides and raising HDL levels. Statins help in reducing insulin resistance because they improve the quality of LDL from the "small dense" type to the less dangerous "large fluffy" type. Statins have "antioxidant" properties, decreasing inflammation and blood clotting.



Statins dramatically reduce the risk of cardiovascular disease, and can even reverse it. This is why statins are being prescribed more and more commonly and in higher doses than ever before.

The most common side effect is muscle problems, which can range from mild aches and pains to severe muscle damage. Any muscle pain or weakness should be reported to your physician. A test called CPK or CK can be done to determine if the drug is causing muscle damage. Because statins have such tremendous health benefits, most physicians now recommend that you continue taking the statin if it is causing only mild muscle pain. Inflammation of the liver is an infrequent side effect. Your doctor will need to monitor liver function periodically.

*Fibrates: Fenofibrate (Tricor, Lofibra, Antara, Triglide) and Gemfibrozil (Lopid and Generics)*

Also known as “fibric acid derivatives” or “fibrates,” fenofibrate and the older, less effective gemfibrozil are cousins of the TZDs. Fibrates are a perfect choice for treating insulin resistance because they lower triglycerides and LDL cholesterol while raising HDL cholesterol. Side effects are uncommon, but muscle or liver problems can occur.

*Niacin (Niaspan)*

Also known as nicotinic acid or vitamin B<sub>3</sub>, niacin, in high doses, simultaneously treats multiple lipid abnormalities by lowering triglycerides and LDL cholesterol while raising HDL cholesterol. Regular niacin is available as an over-the-counter supplement but is very hard to take because the doses needed (usually 1000–2000 mg per day) almost always cause side effects of flushing or tingling or redness of the skin. To reduce side effects, start with a low dose and gradually increase the dose over several months. The flushing can also be reduced by taking an aspirin and drinking a full glass of water one hour before taking the niacin. The slow-release prescription formulation of niacin known as Niaspan is easier to take because there are fewer side effects; however, there can still be significant flushing with this product.

A concern with niacin is that it can worsen insulin resistance and can raise blood sugar levels. For many people, the benefits outweigh the risks, and niacin can be beneficial in an overall plan of health and wellness. Even though niacin is available without a prescription, it should be taken only under medical supervision.

*Omega-3 Fatty Acids (Omacor)*

Omacor is a prescription formulation of the omega-3 fatty acids approved for the treatment of high triglyceride levels. This substance, found naturally in cold-water fish, also improves insulin resistance. The prescription formulation is better than over-the-counter preparations because it is purer and more potent.

*Bile Acid Sequestrants: Cholestyramine (Questran, Questran Light), Colestipol (Colestid), and Colesevelam (WelChol)*

These drugs, known as *bile acid sequestrants* or *bile acid resins*, lower LDL cholesterol by pulling it out of digestive juices, allowing it to pass in the stool. Cholestyramine and colestipol come in granular form and in packets or canisters, and are mixed with water for consumption. It is usually taken several times a day. Questran Light is a sugar-free version and is recommended for people with blood sugar problems. WelChol is a tablet taken once or twice a day. Bile acid resins can raise triglyceride levels. The most common side effect is constipation. Fiber supplementation and proper hydration help control this problem.

*Ezetimibe (Zetia)*

This medication lowers LDL cholesterol by blocking absorption of cholesterol from the intestines. Ezetimibe doesn't do much for triglycerides or HDL cholesterol. Side effects are rare, but there can be abdominal pain or diarrhea.

## **Blood Pressure Medications**

High blood pressure is a major feature of insulin resistance that frequently requires treatment with medications. Some of these drugs can improve insulin resistance and can reduce the risk for diabetes and cardiovascular disease. Other blood pressure medications can slow metabolism and worsen insulin resistance.

*ACE Inhibitors: Ramapril (Altace), Perindopril (Aceon), Trandolapril (Mavik), Lisinopril (Zestril), Benazepril (Lotensin), Quinapril (Accupril), Enalapril (Vasotec), and Captopril (Capoten)*

Angiotensin-converting enzyme, or "ACE," inhibitors slow the production of a hormone that raises blood pressure. ACE inhibitors are good

at lowering blood pressure, but the benefits of this class of drugs go far beyond this. ACE inhibitors can improve insulin resistance. They have been shown to reduce the risk for diabetes, kidney disease, and cardiovascular disease. This is why ACE inhibitors are one of the best medications for people with insulin resistance. To obtain the protective effects from an ACE inhibitor, the maximum dose is needed.

One side effect is high potassium levels, so potassium should be monitored a few weeks after starting an ACE inhibitor. Other side effects include dry cough, fatigue, and headache. In rare cases, a serious allergic reaction can cause lip and tongue swelling, with sudden difficulty swallowing or breathing.

*Angiotensin Receptor Blockers (ARBs): Losartan (Cozaar), Valsartan (Diovan), Ibesartan (Avapro), and Candesartan (Atacand), Olmesartan (Benicar), Telmisartan (Micardis), Eprosartan (Teveten)*

ARBs, or angiotensin receptor blockers, operate on the same hormone system as ACE inhibitors but work by blocking the receptor for the same blood pressure-raising hormone. These drugs tend to be better at lowering blood pressure than ACE inhibitors. The beneficial effects of ARBs are similar to those of ACE inhibitors, but these medications don't have the long-term studies to support their use over ACE inhibitors. ARBs are traditionally recommended for patients who can't take ACE inhibitors, but are increasingly being used as first-line therapy. Side effects are unusual, but high potassium levels are sometimes seen.

*Carvedilol (Coreg)*

This medication is a second-generation beta-blocker. Carvedilol is a unique version called an *alpha-beta blocker* that tends to improve insulin resistance, whereas other beta-blocker medications make insulin resistance worse. Side effects include fatigue, slow heartbeat, and difficulty breathing.

*Potassium-Sparing Diuretics: Spironolactone (Aldactone), Amiloride (Midamor), Triamterine (Dyrenium), and Eplerenone (Inspra)*

Low potassium causes insulin resistance, so these mild diuretics help by lowering blood pressure and raising potassium levels. Side effects can include liver problems or elevation of potassium levels. Potassium levels and liver function should be monitored at regular intervals. Eplerenone blocks the adrenal gland hormone aldosterone, which is responsible for raising blood pressure and lowering potassium levels.

## **Weight Loss Medications**

Weight loss medications can be helpful for treating insulin resistance when combined with proper nutrition and physical activity. Studies on weight loss medications show that most patients who lose weight gain it back when the medication is discontinued. There is no perfect medication, and the effects of available medications are mild at best.

### *Orlistat (Xenical, Alli)*

Orlistat works by slowing or blocking the digestion of fat. This results in about one-third of the fat from the diet being passed in the stool. The typical weight loss with orlistat is about 25 pounds in 6 months. The most common side effect is oily diarrhea. This can be minimized by eating a low-fat diet and by taking a fiber supplement. Orlistat has a risk of blocking the absorption of fat-soluble vitamins, A, D, E, and K. I have seen a few patients who developed severe vitamin D deficiency (known as *osteomalacia*) from taking orlistat.

### *Sibutramine (Meridia)*

Sibutramine is an appetite suppressant that works by altering the brain chemicals serotonin, norepinephrine, and dopamine. (See Chapter 10 for more information.) This drug is similar to venlafaxine and duloxetine in the way it achieves its effect. The main way it works is by increasing the feeling of satiety during a meal; it helps you feel full quicker. The average weight loss with sibutramine is 25 pounds in 6 months. High blood pressure, rapid heartbeat, insomnia, and agitation can be side effects. Blood pressure must be monitored regularly while you are taking sibutramine. Cardiovascular disease and uncontrolled blood pressure are contraindications to the use of sibutramine.

### *Phentermine (Adipex)*

Phentermine is a weight loss medication that was one part of the “phen-fen” combination. Phentermine is approved only for short-term use, and people who take it routinely gain back all the weight they lost (or even more) after it is discontinued. Phentermine can cause agitation, insomnia, and elevated heart rate and blood pressure. For all of these reasons, I do not recommend its use.

*Rimonabant (Acomplia)*

Rimonabant has been called “anti-marijuana,” because it acts by blocking the action of brain chemicals that have actions similar to marijuana (cannabis), known as *endocannabinoids*. The drug was developed with the knowledge that marijuana gives people the “munchies”; rimonabant blocks the reception of these hunger signals. Rimonabant causes people to lose these cravings to help prevent overeating. Rimonabant also helps reduce cravings for cigarettes and thus can help you quit smoking. Both smokers and overweight people have overstimulated endocannabinoid systems. The endocannabinoid system is a system of natural brain chemicals that plays a role in maintaining metabolism through the regulation of food intake and energy expenditure. Rimonabant selectively blocks receptors in the endocannabinoid system, which puts the system in proper balance. Nausea, vomiting, and depression are possible side effects of rimonabant.

**Antidepressants**

Most antidepressants affect your weight in one way or another. This is because the brain chemicals related to depression—*serotonin*, *norepinephrine*, and *dopamine*—are the same brain chemicals that help regulate appetite. (See Chapter 10 for more information.) While some antidepressants typically cause weight gain, others can cause weight loss. The effect of antidepressants on weight is variable and may even be the opposite of what is typical for a particular drug. It is thought that antidepressants that improve insulin resistance do so because they make you lose weight. But depression itself raises cortisol levels, which can also cause insulin resistance, so treating the depression improves insulin resistance.

*Venlafaxine (Effexor, Effexor XR) and Duloxetine (Cymbalta)*

These medications alter the same brain chemicals (serotonin, norepinephrine, and dopamine) as the weight loss medication sibutramine (Meridia). The medications can decrease appetite and help with weight loss but may take several weeks to start working. The most common side effects are high blood pressure, rapid heartbeat, and insomnia. It is recommended that you have your blood pressure monitored

regularly while taking these medications. These drugs can create a “withdrawal” syndrome if discontinued abruptly. If you need to stop taking venlafaxine or duloxetine, you should taper the drug slowly, under the supervision of your physician.

*Bupropion (Wellbutrin, Wellbutrin SR, Wellbutrin XL)*

Bupropion is a unique type of antidepressant that affects several brain chemicals, including dopamine and norepinephrine. Bupropion helps with weight loss by decreasing appetite. The weight loss seen with bupropion is similar to that characteristic of weight loss medications. Side effects of bupropion are related to its “stimulant” action and include agitation, insomnia, and in rare cases seizures.

### **Antiseizure/Antimigraine Medications**

*Zonisamide (Zonegran) and Topiramate (Topamax)*

These medications are frequently used to treat seizures, chronic pain, and migraine headaches. They are now being prescribed for weight loss because they can decrease appetite and prevent overeating. The exact way these medications work is unknown. This class of medications is especially helpful in reducing episodes of binge eating and nighttime eating. Higher doses of the medications are more effective for weight loss, but it is recommended that you start with a low dose and slowly increase the dose over several weeks. My experience is that many patients who tried these medications never took a high enough dose to result in any significant weight loss. Unfortunately, although higher doses are more effective for weight loss, they also increase the likelihood of side effects such as tingling of the hands, kidney stones, sedation, and memory problems.

### **Aspirin**

Insulin resistance increases the risk of blood clotting and cardiovascular disease. This is why the current recommendation is that anyone with insulin resistance should take a baby aspirin (81 mg) every day.

### **Testosterone Replacement Therapy**

This therapy is for men only. Testosterone deficiency, known as hypogonadism, is extremely common in men with insulin resistance. As discussed in Chapter 4, testosterone deficiency results in less muscle and more fat in the belly. Testosterone replacement therapy (TRT) improves insulin resistance by increasing muscle and decreasing fat. See Chapter 4 for more information.

### **Growth Hormone Replacement Therapy**

Growth hormone deficiency results in loss of lean body mass, which causes insulin resistance. Growth hormone is considered a *counter-insulin hormone* because it can raise blood sugar, but the long-term effect is to lower insulin resistance. This is because growth hormone replacement therapy increases lean body mass and decreases fat mass. For more information, see Chapter 9.

## **MEDICATIONS THAT WORSEN INSULIN RESISTANCE**

In order to achieve hormonal balance, it's important, whenever possible, to avoid medications that can intensify insulin resistance. Medications can make insulin resistance worse for a variety of reasons.

### **Corticosteroids (Glucocorticoids)**

Common medications including prednisone, hydrocortisone, dexamethasone, and methylprednisolone work by mimicking the action of the hormone cortisol. Excessive cortisol causes severe insulin resistance and massive weight gain and promotes fat accumulation and muscle loss. Corticosteroids can cause diabetes and can increase the risk of cardiovascular disease and other ailments. For more information, see Chapter 8.

**Sulfonylureas: Glyburide (DiaBeta), Glipizide (Glucotrol),  
and Glimepiride (Amaryl)**

This class of drugs treats type 2 diabetes by stimulating the pancreas to produce insulin. They are great for blood sugar but make insulin resistance worse. Weight gain is a common side effect of sulfonylureas.

**Diuretics: Furosemide (Lasix), Torsemide (Demadex),  
Bumetanide (Bumex), Indapamide (Lozol),  
Hydrochlorothiazide (HCTZ, Microzide, Hydrodiuril),  
and Chlorothiazide (Diuril)**

Diuretics cause loss of potassium in the urine. When potassium is deficient from the body, insulin resistance gets worse. If you take diuretics, potassium supplementation is helpful.

**Synthetic Progestins: Medroxyprogesterone (Provera),  
Norethindrone Acetate (Aygestin), Megestrol (Megace),  
Micronor, Nor-QD, Ovrette, Depo-Provera, and Norplant (as  
Well as Birth Control Pills That Contain Levonorgestrel,  
Norgestrel, or Norethindrone)**

Progestins have high androgenic activity and produce side effects such as acne, bloating, weight gain, and elevated blood sugars. See Chapter 6 for more information.

**Beta-Blockers: Propanolol (Inderal), Metoprolol (Toprol),  
and Atenolol (Tenormin)**

Although sometimes necessary to treat conditions like high blood pressure, congestive heart failure, and abnormal heart rhythms, these medications can slow metabolism and worsen insulin resistance.



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**Calcium Channel Blockers: Amlodipine (Norvasc), Nifedipine (Procardia), Verapamil (Calan), and Diltiazem (Cardiazem)**

Calcium channel blockers can sometimes worsen insulin resistance and can increase the risk of diabetes.

**HIV/AIDS Medications: Amprenavir (Agenerase), Tipranavir (Aptivus), Nelfinavir (Viracept), Ritonavir (Norvir), Saquinavir (Invirase, Fortovase), Tipranavir (Aptivus), Indinavir (Crixivan), Fosamprenavir (Lexiva), Atazanavir (Reyataz), Darunavir (Prezista)**

These life-saving drugs, known as *protease inhibitors*, cause severe insulin resistance and diabetes. They also cause a variant of insulin resistance known as *HIV lipodystrophy*, where people develop many of the physical features seen in Cushing's syndrome (see Chapter 8).

**Antidepressants**

Some antidepressants increase appetite and have weight gain as a side effect. The same brain chemicals involved in depression also regulate appetite (see Chapter 10 for more information). Older antidepressants, such as amitriptyline and nortriptyline, frequently cause massive weight gain. Mirtazapine (Remeron) is also notorious for increasing appetite and causing weight gain. Antidepressants such as fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil, Paxil CR), citalopram (Celexa), and escitalopram (Lexipro) have variable effects on weight.

**Antiseizure Medications: Carbamazepine (Tegretol) and Gabapentin (Neurontin)**

These medications can increase insulin resistance and cause weight gain and sedation.

### **Antipsychotic Medications: Olanzapine (Zyprexa), Risperidone (Risperdal), and Quetiapine (Seroquel)**

These drugs can cause massive weight gain, insulin resistance, and diabetes and have been devastating for people with mental illness.

### **Antihistamines**

Older antihistamines, such as diphenhydramine, and other antihistamines that make you sleepy can also worsen insulin resistance and cause weight gain. These antihistamines are a common ingredient in many over-the-counter allergy medications and sleep aids.

# ANDROGENS

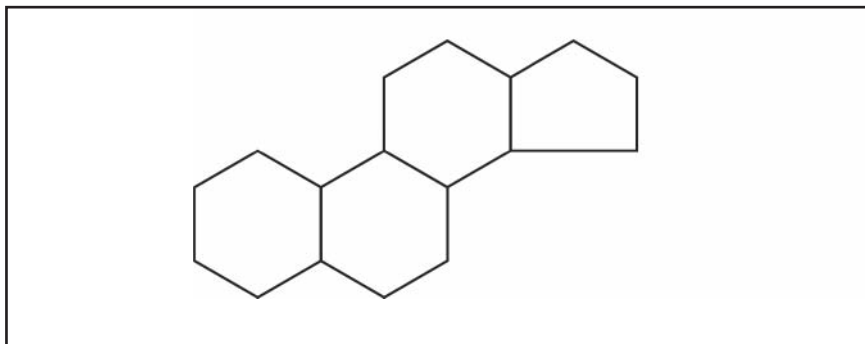
THE TERM “ANDROGEN” COMES FROM THE GREEK *ANDROS*, MEANING “MAN,” AND *GENNAN*, MEANING “TO PRODUCE.” Androgen or androgenic hormones are best known for male sexual characteristics and include hormones such as testosterone, androstenedione, and dehydroepiandrosterone sulfate (DHEA-S). Androgens have potent effects on body weight and body composition. In fact, one of their primary actions is to increase muscle and decrease fat. Androgens have a powerful effect on the brain, influencing mood, sexual desire, desire to exercise, and energy level.

Testosterone is the most important androgen for men. Testosterone is made in special cells in the testicles called Leydig cells. The weaker androgens, androstenedione and DHEA-S, are made in the outer portion of the adrenal gland called the adrenal cortex. Adrenal gland production of androgens is relatively unimportant in men but makes up 50 percent of androgen production in women.

### WHAT IS A STEROID?

A “steroid” hormone is any hormone that, in chemical terms, has a structure derived from cholesterol. Yes, cholesterol—what you thought was bad is also beneficial. All steroids have a common structure that consists of four rings of carbon, which is the backbone of the cholesterol molecule. Cholesterol is modified by special enzymes in a series

of steps to become one of the various steroid hormones. The enzymes present in each gland determine the final hormone produced. Steroid hormones include testosterone, androstenedione, estrogen, aldosterone, DHEA-S, pregnenolone, progesterone, cortisol, and even vitamin D. So the term “steroid” simply describes the chemical structure, not the action of the hormone.



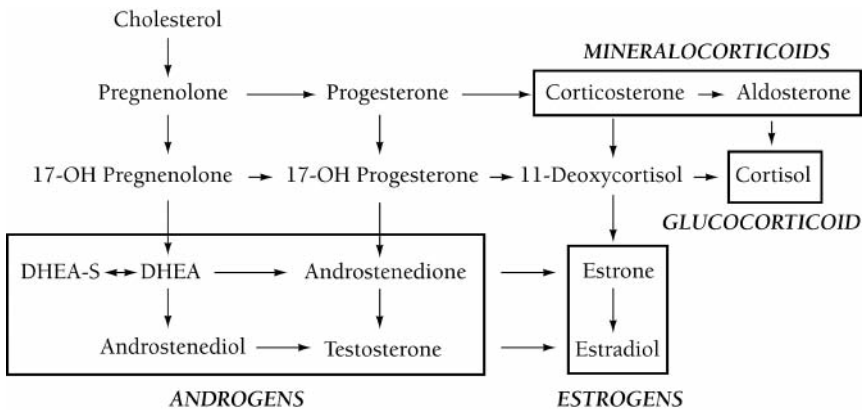
**Figure 4.1**

#### **THE FOUR-RING STRUCTURE OF STEROID HORMONES**

All steroid hormones are derived from cholesterol. The four-carbon ring backbone, known as the *steroid nucleus*, is common to all steroid hormones. The term “steroid” simply refers to the chemical structure, and not the action of the hormone.

Androgen hormones are known as *anabolic steroids*. The term “anabolic” refers to a metabolic process that promotes tissue growth. Anabolic steroids specifically promote the growth of muscle tissue. All steroid hormones exert their action by controlling your genes. Anabolic steroids turn on genes that make muscles grow.

Anabolic steroids were originally developed as medications for cancer patients and victims of starvation. The positive effects of anabolic steroids have made them attractive to people who do not have medical conditions that warrant their use. This is known as *anabolic steroid abuse*. Because of their muscle and strength building qualities, athletes and bodybuilders take them to acquire a competitive edge. The International Olympic Committee, Major League Baseball, and most American team sports for years have banned anabolic steroids, but their

**Figure 4.2****THE STEROID BIOSYNTHESIS PATHWAY**

All steroid hormones are synthesized from a common precursor, cholesterol. The enzymes present in each gland determine the final hormone produced. Steroid hormones can be converted to other steroid hormones.

covert use is widespread. Illicit “designer” androgens help athletes gain an unfair competitive edge while avoiding detection. Anabolic steroid abuse is not a problem only among elite athletes. The epidemic of abuse has spread to local fitness centers as well as college and high school athletes. Even young boys have been caught using anabolic steroids.

**TESTOSTERONE AND YOUR BRAIN**

Androgens affect the brain by controlling the “maleness” in our personalities. The most notable actions of testosterone on mood are increased sex drive and increased aggression. Even women’s personalities are affected by androgens, a subject I’ll get to in Chapter 5. Testosterone is essential for hormonal balance, and men with low testosterone invariably feel depressed, anxious, or just plain tired. They report a decrease in zest for life and don’t feel like being social. Testosterone replacement therapy (TRT) improves many of the psychological symptoms of hypogonadism.

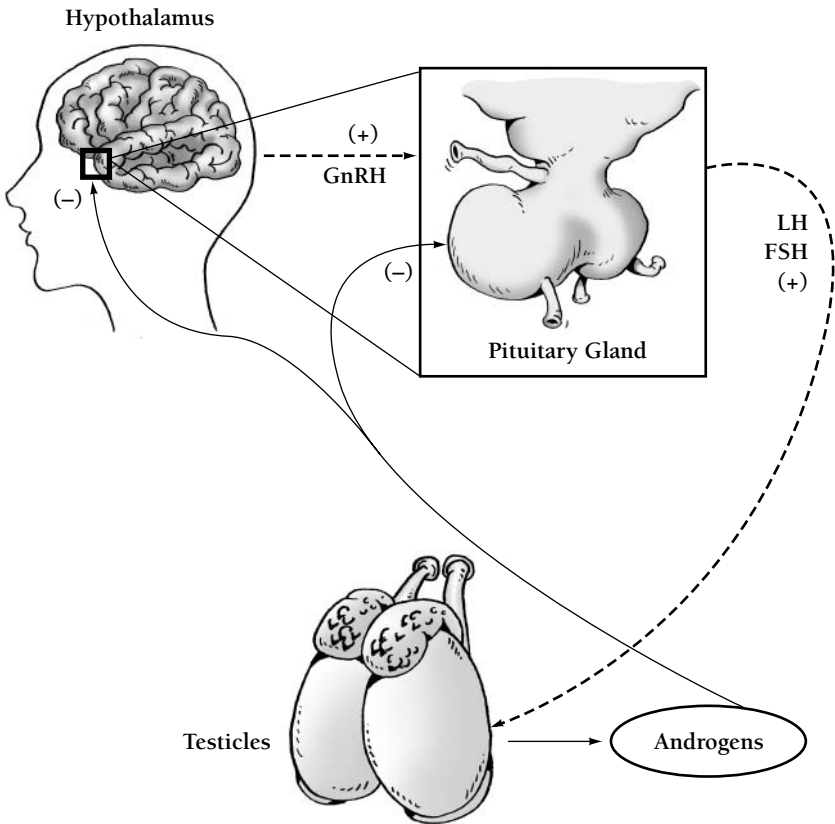
Ironically, however, not only do androgens affect the brain, but the brain affects androgens—by regulating the levels of these substances in our bodies. We have seen how the body is in a constant feedback loop, and how much of the information in this loop comes from the glands. A gland produces a substance, the substance sends a message to the brain, the brain sends a message to a particular part of the body, action in that part of the body increases or decreases, the information gets back to the brain, which sends a message to the gland . . . and on and on and on.

In the case of testosterone, the pituitary gland makes two hormones—*luteinizing hormone* (LH) and *follicle-stimulating hormone* (FSH)—that trigger androgen production (as well as sperm production) in the testicles. In turn, LH and FSH are regulated by another hormone called *gonadotropin-releasing hormone* (GnRH). GnRH comes from a higher level in the brain known as the *hypothalamus*.

GnRH must be released by the hypothalamus in pulses. If a constant level of this hormone is produced, the pituitary will shut down. In fact, doctors use excessive doses of GnRH when they want to deliberately inhibit testosterone production, such as in prostate cancer therapy. The signal from the pituitary gland to the testicle is removed, and the testicle stops making testosterone—fortunately so, since testosterone helps prostate cancer grow. Men with low testosterone levels caused by GnRH deficiency can bring testosterone levels back to normal by using a device similar to an insulin pump that delivers small pulses of GnRH through a catheter under the skin. GnRH can affect testosterone differently according to how it is given: small pulses of GnRH boost testosterone production while a large dose will shut down testosterone production.

In stressful situations, the brain can prompt *more* testosterone production. If it senses that the body needs more—such as before an aggressive event such as a football game or boxing match, or if the testicles are failing—the brain will send the gonadotropin (LH and FSH) signal to the testicles to produce more androgen. The opposite is also true: if the brain, via the pituitary, senses an abundance of testosterone, it will decrease LH and FSH production.

This brings us back to bodybuilders, athletes, and other people who use anabolic steroids. Invariably, they have small testicles. With all that extra testosterone floating around, the brain tells the testes that

**Figure 4.3****ANDROGEN ENDOCRINOLOGY: HORMONE FEEDBACK LOOPS**

Higher centers in the brain send signals to the hypothalamus, which produces pulses of gonadotropin-releasing hormone (GnRH). GnRH pulses stimulate the pituitary gland to make follicle-stimulating hormone (FSH) and luteinizing hormone (LH), collectively known as gonadotropins. Gonadotropins stimulate the testicles (or ovary) to produce androgens. Androgens “feed back” to the hypothalamus and pituitary gland, slowing gonadotropin production. Positive “feed-back” is denoted by (+) and negative “feedback” is denoted by (-).

there is no need to produce more. The family jewels turn soft and shrivel. In endocrine circles it's called the *L-M-N-O-P syndrome*: lots of meat and no potatoes!

Problems with the pituitary gland and other parts of the brain may cause hypogonadism. It's called *central hypogonadism* (for the central nervous system), *secondary hypogonadism*, or *hypogonadotrophic hypogonadism*, because the main problem is deficient production of pituitary gland hormones that regulate the gonads—gonadotropins (LH and FSH). In this case, there may be a problem with the pituitary gland or hypothalamus that is causing the FSH and LH levels to be low, so the testicles don't get the message to produce testosterone.

### ANDROGEN CONVERSION

Steroid hormones can be converted to one another, and testosterone is no exception. A blood enzyme, known as *5-alpha reductase*, can convert testosterone into a form called *dihydrotestosterone*, or DHT. DHT is responsible for two distinctly male characteristics: male-pattern balding and benign growth of the prostate. Alternatively, androgens can be converted to *estrogens* from an enzyme called *aromatase*. Androstenedione is converted to *estrone* and testosterone is converted to *estradiol*. Estrogens are important in men because they are responsible for bone health, but too much estrogen can cause problems. Testosterone can be converted to inactive hormones like *epitestosterone* or *etiocholanolone*.

Finasteride (Proscar) and dutasteride (Avodart) are used to shrink an enlarged prostate gland by blocking the 5-alpha reductase enzyme. Propecia—yes, the hair growth medicine—is also a brand of finasteride. It helps men with male-pattern baldness grow some of their hair back by blocking the actions of DHT in the scalp. Testosterone may make men more virile, but it's also the reason men lose their hair. (No wonder women are more attracted to bald men!)

A class of drugs known as *aromatase inhibitors* block the conversion of testosterone to estrogen. Anastrozole (Arimidex), exemestane (Aromasin), and letrozole (Femara) have become blockbuster medications in the fight against breast cancer. In men, aromatase activity increases with age and with level of obesity. This means that older men



or obese men have lower levels of testosterone and higher levels of estrogen. Aromatase inhibitors are sometimes given to men who take testosterone replacement therapy to boost testosterone levels and prevent its conversion to estrogen.

### TESTOSTERONE RESISTANCE

Testosterone works just like other hormones. To exert its actions, it must bind with a receptor. Think of the “lock and key” concept discussed in Chapter 1. Steroids, like other hormones, have very special and specific receptors. Either the receptor is on the actual DNA, or it binds to the steroid and the steroid-receptor unit then binds to DNA. Either way, the steroid hormone works by turning genes on and off in our cells directly and controlling certain genes, which are known as steroid-responsive genes. Different receptors may have different activity levels or be present in various amounts in different people.

The way testosterone interacts with a receptor varies from person to person. Here’s an extreme example of receptor viability: There’s a condition called *androgen insensitivity syndrome* in which the androgen receptors don’t work at all. The DNA of an individual with this syndrome does not detect androgen even though the levels are sky high. The body keeps making more and more keys—the androgen itself—but the lock—the androgen receptors—is broken. If this happens during fetal development, the result is a baby that has developed as a female, because of the lack of androgen, but is genetically a man, with a Y sex chromosome.

A person with androgen insensitivity syndrome has testicles hidden in the abdomen and a blind vaginal pouch; there’s no uterus or ovaries. But since, to all appearances, this genetic male is a female, the condition often doesn’t make itself known until puberty, when the expected onset of menstruation fails to occur. Some don’t realize they have this condition until they try to get pregnant. Overall, most live their lives as normal women, but they can’t have children. In time, they should see a doctor to have their testicular tissue removed, because it can become cancerous if it remains in its original condition.

I bring up this extreme example because more subtle examples also exist. There are situations where testosterone levels may be normal or

even high, but the testosterone cannot function properly because the receptor is defective. This *testosterone resistance* is similar to other types of hormone resistance, such as insulin resistance (see Chapter 3) and thyroid hormone resistance (see Chapter 7). Spironolactone (Aldactone) and other medications can block the androgen receptor and cause symptoms of hypogonadism.

### **Bob's Story**

*Bob won a copy of Hormonal Balance as a door prize at a charity auction. He wasn't overweight and had kept in great shape his entire life, so he didn't think that the book applied to him. Hormones were for women, he thought. But something had happened lately. Over the past 6 months, he hadn't been feeling like himself. He had a gym at his office building and had been working out three times a week for the last 10 years. He still worked out, but he was getting weaker, not stronger. I'm just getting old, he thought. He also noticed that his libido was reduced, but he blamed stress. He had no problems getting an erection and still had sex with his wife. But he did feel depressed. He read Hormonal Balance, and he realized that the symptoms could indicate hypogonadism. He sent me an email, and I encouraged him to see his PCP and get tested, which he did. Testosterone was low, so he got a shot and started feeling great. Now, he's using T-gel and is back to normal.*

## **Low "T"**

Low "T," or low testosterone production, known as *hypogonadism*, is estimated to affect 4–5 million men in the United States. Hypogonadism, or inadequate functioning of the gonads, can affect men at any age. Baby boys who show irregularities in development may have a genetic condition that affects testosterone production, such as *Klinefelter's syndrome* or *Kallmann's syndrome*. Medical problems like mumps, head injuries, or immune system problems also cause low testosterone and can occur throughout life. But the risk of hypogonadism increases with age. All men experience a gradual decline in androgen levels as they get older, beginning as early as 25 years. By

the age of 70, more than 80 percent of men have testosterone levels below the normal range. How much of this is related to normal aging and how much is a medical problem depends on the individual. Men who are overweight or have other medical problems such as high blood pressure, diabetes, or chronic pain are more likely to have medically significant hypogonadism. Studies have shown that very healthy men show fewer age-related declines in testosterone levels. If you keep yourself healthy, follow the Hormonal Health Diet, exercise, keep the stress down, and stay away from cigarettes and heavy alcohol, you can do a lot to counteract the inevitable decline in androgens as you get older.

Both men and women experience declines in sex hormone levels that are associated with aging. Despite controversy, the treatment of estrogen deficiency in women, especially during the transition to menopause, remains common practice (see Chapter 6). Slowly, doctors are beginning to recognize that testosterone deficiency can cause a host of symptoms in men that may also warrant treatment. Yet many men with hypogonadism are undiagnosed and untreated. Some physicians even say they don't believe in treating men for hormonal deficiencies.

Low testosterone levels are associated with decreased muscle size and strength, increased body fat, sexual dysfunction, thinning of the bones, depression, fatigue, diminished sense of well-being, cholesterol problems, and increased risk for heart disease. Declining androgen levels can occur slowly or abruptly, and the rate varies from person to person. If the symptoms come on abruptly, you may have a more serious form. But at whatever rate it occurs, overtly low testosterone levels are a concern.

## FEATURES OF HYPOGONADISM

One of the challenges in making the diagnosis of hypogonadism is to distinguish between the symptoms of *normal aging* and those of *medically significant hypogonadism*. If someone has other medical problems, what doctors call "overlapping illnesses," it can be even more difficult to make the diagnosis. Many physicians don't even consider the diagnosis of hypogonadism unless the primary symptoms are sexual in nature, like erectile dysfunction or decreased sex drive. But the truth is that symptoms like fatigue, weight gain, decreased quality of life, and even depression are just as common.

## **Erectile Dysfunction or Decreased Sexual Performance**

Sexual problems are the best-known symptom of hypogonadism. Adequate testosterone levels are required for proper sexual functioning; however, most people with hypogonadism still get erections from time to time. Men with hypogonadism complain about the quality of their erections: they are not as strong or as frequent as they used to be or they can't be maintained for as long as they used to. Men with a poor response to medication such as Viagra, Levitra, or Cialis are at risk for having hypogonadism. Some men with hypogonadism have completely normal sexual function, so the absence of this symptom does not exclude the diagnosis of hypogonadism.

## **Decreased Sex Drive (Libido)**

Testosterone exerts its effect on the brain by regulating sex drive. Many men with hypogonadism have decreased libido; however, some men do not. A normal libido does not exclude the possibility of hypogonadism.

## **Weight Gain (Especially around the Middle)**

Hypogonadism is a common cause of weight gain. Typically, there is muscle loss and increased fat, which causes decreased metabolism. Men with hypogonadism have less desire to exercise, which further contributes to the weight gain.

## **Muscle Weakness, Loss of Endurance, or Decreased Muscle Mass**

The normal effect of testosterone is to build muscle, so it's logical that hypogonadism is associated with loss of muscle mass, muscle weakness, or decreased endurance. Some men report deterioration in their ability to play sports.

### **Fatigue**

Low energy is one of the most common complaints in men with hypogonadism. Men frequently report falling asleep after dinner or being too tired to exercise. Decreased muscle strength, poor sleep, depression, and anemia are all contributing factors to the fatigue.

### **Depression or Anxiety**

Men with hypogonadism report changes in mood, such as increased depression, nervousness, diminished sense of well-being, irritability, anger, or negative thinking. Clinical depression is commonly seen. Men with untreated hypogonadism typically have a poor response to antidepressant medications. Many men with hypogonadism just feel terrible. They have completely lost their interest in life. Testosterone replacement therapy reverses these symptoms, but sometimes antidepressant or anti-anxiety medications are also required for complete relief of symptoms.

### **Decreased Quality of Life or Sense of Well-Being**

This is one of the most overlooked symptoms of hypogonadism. Men treated with testosterone replacement therapy report dramatic improvements in their quality of life and sense of well-being.

### **Insomnia**

Insomnia may occur as a symptom of hypogonadism. This can contribute to fatigue.

### **Poor Memory and Lack of Concentration**

It is normal to experience an age-related decline in mental capacity, but the declines seen with hypogonadism are more severe than those seen with normal aging. Many men will report deterioration in their work performance.

### **Premature Aging**

Hypogonadism speeds up the normal aging process. Men with hypogonadism look older and feel older. Testosterone replacement therapy makes a man look younger and feel younger.

### **Male Breast Growth (Gynecomastia)**

Low testosterone can result in the growth of male breast tissue. Gynecomastia is typically more pronounced in obese men, but lean men can also get it. Testosterone replacement therapy can improve gynecomastia, but gynecomastia can also be a side effect of TRT. Some men have permanent breast enlargement even after the hypogonadism is treated. Breast reduction surgery is available for men who have gynecomastia that is bothersome.

### **Bone Problems (Osteoporosis or Osteopenia)**

Thinning of the bones, known as *osteoporosis* or *osteopenia*, is traditionally thought of as a disease that women get after menopause, but bone problems are also very commonly seen in men with hypogonadism. Bone loss is one of the most serious complications of male hypogonadism. Testosterone (because it is converted to estrogen) is required for proper bone health. Mild bone loss, known as osteopenia, can progress to the more severe form, osteoporosis. Bone loss puts men at increased risk of fracturing a bone. The most common bones to be fractured are the hip, wrist, and spine. A fracture of the spine, called a *spinal compression fracture*, can result in loss of height and humping of the back (known as *kyphosis*).

### **Joint Problems**

Hypogonadism increases everyday aches and pains, and the joints are no exception. Men with hypogonadism and arthritis report that the pain from the arthritis gets better when the hypogonadism is treated.

### **High Blood Pressure**

High blood pressure is an infrequent feature of hypogonadism.

### **Hot Flashes or Excessive Sweating**

Sensations of warmth, flushing, or excessive sweating can occur, especially at night. This is a similar symptom to what women experience when they are going through menopause.

### **Anemia**

Anemia means a decreased red blood cell count. Testosterone is one of the factors responsible for red blood cell production. Men with hypogonadism typically have mild anemia that gets better with testosterone replacement therapy.

### **Decreased Frequency of Shaving**

Testosterone is responsible for facial hair growth. Some men with hypogonadism report a decrease in their need to shave.

### **Loss of Body Hair, Chest Hair, Pubic Hair, or Armpit Hair**

Along with facial hair, hair on other parts of the body require testosterone for proper growth. Testosterone deficiency can result in loss of hair in these areas.

### **Skin Problems**

Testosterone regulates the amount of oil produced by the skin. Some men with hypogonadism notice that their skin seems dry, flaky, or thinner than it used to be.

### **Male Infertility**

Testosterone and pituitary gland hormones known as gonadotropins (LH and FSH) are required for normal sperm production. Men with hypogonadism may have a low volume of ejaculate and poor sperm quality, or low sperm count, known as *oligospermia* or *azoospermia*. Testosterone replacement therapy generally does not improve sperm quality or sperm count. Some men with hypogonadism can improve sperm count using GnRH pumps or clomiphene citrate.

### **Shrinking or Softening of the Testicles**

Hypogonadism may result in either shrinking or softening of the testicles.

### **Softening of the Voice**

Low testosterone has effects on the vocal cords that can result in a softer voice.

## **CAUSES OF HYPOGONADISM**

Determining the cause of hypogonadism is very important. Low testosterone can be a result of many different conditions that require additional treatments beyond traditional testosterone replacement therapy. Hypogonadism can be a sign of a more serious medical condition. Anyone with hypogonadism should have a full evaluation to determine the cause.

### **Age-Related Testosterone Decline**

There are many names for this medical condition, which still has not been precisely defined: “male menopause,” “mild testicular failure,” “andropause,” “viropause,” “male climacteric,” “male gonadopause,” “late-onset hypogonadism,” “ADAM syndrome” (androgen deficiency of the aging male), or “PADAM syndrome” (partial androgen deficiency in



the aging male). These names all suggest a phenomenon that parallels female menopause. But this may be the wrong message to be giving men with age-related testosterone decline.

Although 4 to 5 million men in the United States have testosterone deficiency, less than 15 percent are being treated for their disease. Androgen replacement therapy or testosterone replacement therapy is not well accepted for treating normal aging. But some doctors even worry about treating men with medically significant hypogonadism. Critics note that long-term studies on TRT safety have not been done. The concern parallels the controversy that surrounds treating menopausal women with estrogen. *Estrogen replacement therapy* (ERT), once considered the standard of care for menopausal women, has become increasingly controversial because long-term safety studies showed increased risks for blood clots, cardiovascular disease, and breast cancer. Despite this, many women still undergo ERT.

Although all men experience lower testosterone levels as they age, doctors have to make a clinical judgment as to when low testosterone is medically significant and should be treated. The key is to make sure the potential benefits outweigh any potential risks. One of the primary factors in deciding on TRT is the health of a man's bones. If a bone density test shows osteoporosis or osteopenia (thinning of the bones), testosterone replacement therapy is almost always warranted. If someone has symptoms of hypogonadism, especially if it is moderate or more severe, he is also a good candidate for treatment.

### **Trauma or Injury to the Testicles**

Any injury to a gland can result in its dysfunction. I have seen many patients with previously untreated hypogonadism who have a remote history of injury to their testicles. I have also seen many patients with hypogonadism who had one testicle removed years ago and never realized it was a risk for hypogonadism.

### **Urologic Problems**

Urologic conditions like *varicocele*, *hydrocele*, *spermatocele*, and even *testicular cancer* can cause swelling in the testicles, which can cut off

the blood supply to testosterone-producing cells. Not everyone with these conditions gets hypogonadism, but it does increase your risk. A complete examination of the testicles and scrotum followed by a *testicular ultrasound* is a good way to check for these conditions.

### **Vasectomy**

Although the subject is controversial, it is thought that vasectomy can increase your risk for hypogonadism. The surgery may disrupt blood supply to the testicles, causing a decline in function. Unfortunately for some men, the problem is less subtle. Infections and bleeding are complications of vasectomy or vasectomy reversal surgery that can lead to more severe cases of hypogonadism.

### **Head Injury**

Head injuries are a very common cause of pituitary gland dysfunction. Men with head injuries, even from many years ago, may develop low testosterone alone or in combination with other pituitary gland hormone deficiencies. It is very common to see growth hormone deficiency in conjunction with a head injury, and many of the symptoms of growth hormone deficiency overlap with those of hypogonadism (see Chapter 9).

#### ***Richard's Story***

*Richard is a 49-year-old man with a 3-year history of type 2 diabetes. He came to my office because his primary care physician wanted me to help get his blood sugar under control. When first diagnosed with diabetes, he started a healthy diet and began exercising, but he ultimately needed to take the medication metformin (see Chapter 3) to get his blood sugar under control. For the next 2 years he did great. He lost a few pounds and had incorporated a healthy diet and regular physical activity into his lifestyle. But at his last checkup, the A1c test (which estimates the 90-day blood sugar average) had increased unexpectedly. He said he felt fine and had no symptoms of hypogonadism. "I have a great sex life, doc." Those were*

*his exact words. He almost forgot to tell me that he had been taking Viagra for the last 2 years. He didn't really "need" it, but it improved his sex life. He had been told that diabetes can make erections less firm, and he wanted to keep things like they used to be. I measured his testosterone levels and, sure enough, they were low enough to warrant treatment. He started therapy with testosterone gel. His testosterone levels returned to normal almost immediately, but it took several months before he noticed an improvement in his blood sugar levels. After 6 months, he had lost 16 pounds, and his A1c test had returned to the normal range without his having to change diabetes medications. Unfortunately, as part of the standard evaluation for male hypogonadism, he was given a bone density test, which showed that he had osteoporosis. And although his testosterone replacement therapy improves bone density, he has begun taking another medication called Actonel for his bones. As for the Viagra, he still uses it, even though he says he doesn't "need" it.*

## Diabetes

Testosterone deficiency is an extremely common condition in men with diabetes. Men with type 1 diabetes, which is an autoimmune condition, are at risk for hypogonadism caused by immune system destruction of testosterone-producing cells known as Leydig cells. Men with type 2 diabetes are also at very high risk for hypogonadism. It's thought that insulin resistance, high blood sugar, and chronic illness combined with excess weight and age-related androgen decline all play a role. These factors synergize to cause medically significant hypogonadism. Men who have diabetes and untreated hypogonadism gain fat and lose muscle and have difficulty getting their blood sugar under control. Testosterone replacement therapy not only reverses the symptoms of hypogonadism but also improves insulin resistance and improves diabetic control. The reverse can also be true: improving insulin resistance can send testosterone levels back into the normal range. (For more on insulin resistance, see Chapter 3.) Diagnosing testosterone deficiency in men with diabetes can be tricky. Men with diabetes have increased *sex hormone-binding globulin* (SHBG) levels, which cause the *total testosterone* level to appear normal when it may actually be low.

## Obesity

Obesity itself can lower androgen levels for many reasons. Being overweight worsens the age-related decline of androgens. Other hormone signals, such as leptin and cortisol (see Chapters 8 and 10), can lower androgen levels to a significant extent—and these two hormones' levels increase as you gain weight. Fat cells produce hormones (called *inflammatory cytokines* or *adipokines*) that lower testosterone by slowing signals from the hypothalamus and pituitary gland, increasing the risk of hypogonadism in overweight men. Overweight men have increased levels of *aromatase*, the enzyme that converts androgens into estrogens. Low testosterone results in higher estrogen levels and lower growth hormone levels (see Chapter 9), leading to further decreases in muscle mass and increases in body fat.

So it's a vicious cycle: being overweight (or having a high percentage of body fat) disrupts androgen balance and overall hormonal balance, making you lose muscle and gain fat.

Diagnosing and treating hypogonadism in obese men can be challenging, for the same reasons listed above for men with diabetes. Standard testosterone preparations like testosterone gel or testosterone patches may not penetrate the skin adequately in obese men, and alternative therapies may be required.

## Infection

Any infection of the testicles, known as *orchitis*, can result in hypogonadism. *Mumps* is infamous for causing testicular failure. Male hypogonadism is the most common cause of hormone deficiency in men infected with the *HIV virus*. In fact, HIV patients are one of the largest groups of men taking testosterone medications.

### **Frank's Story**

*Frank seemed the very model of a successful, virile male. An executive of a chemical manufacturing firm, he was 46, married with two children, and entering the stage of his life when he could afford to get out and play a little more. And play he did: Frank liked nothing better than escaping from the office on*

*a Friday afternoon and getting in a round of golf with his colleagues.*

*But another form of play—that of sexual intimacy with his wife—wasn't going so well. Frank was having trouble getting and maintaining erections, and his sex life suffered. At the same time, he had put on a few pounds around the middle, his weekly round of exercise notwithstanding, and found himself feeling depressed. "I don't seem to have the same zest for life I used to," he said to me later. When he first experienced the symptoms, he visited his family doctor for a checkup and a prescription for Viagra.*

*Not long after, Frank was on the golf course and tripped while leaving a bunker. The impact broke his wrist. When he went back to his doctor for a more thorough workup, the doctor discovered that Frank was suffering from osteoporosis: thinning and brittle bones.*

*Eventually, Frank came to see me. After a series of tests, I determined that he was suffering from testicular failure; his testicles were simply not producing testosterone anymore. This being an easily treatable condition, I prescribed a testosterone gel. That only solved part of the problem, however. Frank later developed thyroid failure as well. It turned out that the same disease process that had caused antibodies to disable his testicles had also affected his thyroid.*

### **Immune System Problems (Autoimmune Syndromes)**

Along the same lines as type 1 diabetes and autoimmune thyroid disease, these are conditions where antibodies are produced that cause the body to attack itself. Any gland can be a target for attack, and the testicles are no exception. (For more on autoimmune disease, see Chapter 7.)

#### ***Errol's Story***

*Errol was 44 years old and came to see me because he had diabetes and a dreadful fear of needles and was cursed with taking four shots of insulin every day. We got him switched over to*

*an insulin pump, and his diabetes quickly got under good control. During his evaluation he was found to have low T and low LH and FSH, and was diagnosed with central hypogonadism. He also had elevated liver tests, and on further questioning, he said that a lot of relatives on his father's side had HH. We tested him for the HH gene, which was positive. His hemoglobin, hematocrit, ferritin level, and iron level were all very high. He started testosterone replacement therapy and phlebotomy (periodic removal of blood) every month. He is doing much better. He had a liver biopsy, which showed cirrhosis (a complication of HH).*

### **Hereditary Hemochromatosis (HH)**

This is a genetic disease in which the body absorbs too much iron, which is deposited in organs, causing tissue damage. HH frequently causes endocrine dysfunction because of iron deposits in the glands, especially the pancreas and the pituitary gland. Pancreatic dysfunction results in insulin deficiency and a form of type 1 diabetes. Iron deposits in the skin give it a bronze color, so it's sometimes called *bronze diabetes*.

The most common pituitary gland dysfunction seen with HH is hypogonadism. It's called *central* or *hypogonadotropic hypogonadism* because the main problem is deficient production of pituitary gland hormones that regulate the gonads (gonadotropins, LH and FSH).

It's much more common than most doctors realize: one out of every 200 people have HH. It's one of the most common genetic diseases in Caucasians, yet it's hard to diagnose early because the symptoms are so subtle. On average, it takes 10 years from the first symptom to a diagnosis. The most common early symptoms are fatigue, joint aches, and a decreased sex drive; other symptoms include abdominal pain, tanning of the skin (without being out in the sun, the skin will eventually become more and more "bronzed"), and depression.

But early diagnosis is important. If left untreated, hemochromatosis can lead to insulin resistance, diabetes, arthritis, hepatitis, hypogonadism, heart failure, cirrhosis of the liver, or liver cancer. Treatment for

hemochromatosis is a periodic phlebotomy, or removing of the blood. If you have symptoms of hemochromatosis, or a family history of HH, you should discuss this with your physician. Tests for blood counts, iron metabolism, and the HH gene can diagnosis the condition. Because of the high risk of cirrhosis of the liver, most doctors recommend that patients with hemochromatosis have a liver biopsy.

### **Sarcoidosis**

Sarcoidosis is a disorder of unknown cause that is characterized by the formation of substances known as *granulomas*. Granulomas can occur anywhere in the body but are most common in the lungs. When sarcoidosis affects the brain, it is known as *neurosarcoidosis*. Neurosarcoidosis can cause central hypogonadism when it damages the hypothalamus and pituitary gland. Typically, neurosarcoidosis causes multiple deficiencies of pituitary gland hormones. Sarcoidosis is more common in young adults and in African Americans, and it tends to run in families. If you have sarcoidosis and symptoms of hypogonadism, you should discuss this with your physician. An MRI scan of the pituitary gland can be helpful in diagnosing neurosarcoidosis.

### **Toxins, Alcohol, Drugs, and Tobacco**

Believe it or not, one of the most pernicious toxins to the testicle is alcohol. Drinking too much can permanently damage the testicle and inhibit testosterone production. Tobacco smoke, marijuana, cocaine, heroin, and other drugs have a similar effect. Narcotic medications are well known to cause hypogonadism by exerting a toxic effect on the testicles as well as the hypothalamus and pituitary gland.

### **Excess Cortisol**

Whether from corticosteroid medications or abnormal production by the adrenal gland, excess cortisol can lower testosterone levels in men. For more information on cortisol, see Chapter 8.

### **Fluid Retention**

Liver problems, kidney problems, and congestive heart failure can cause fluid retention in the body, and sometimes in the scrotum or testicles. This can cut off the blood supply to androgen-producing cells, decreasing the production of testosterone.

### **Chronic Pain**

Men with chronic pain, especially those on prescription pain medication, are at very high risk for hypogonadism. The relationship between narcotic medications and hypogonadism was noted above. Chronic pain also results in insulin resistance (see Chapter 3) and increased cortisol production (see Chapter 8), which lower testosterone levels.

### **Radiation**

Radiation treatments to the head or pelvis for cancer or other conditions can result in hypogonadism. Hypogonadism may begin many years after radiation therapy.

### **Chemotherapy**

Chemotherapy treatments can cause permanent hypogonadism.

### **Liver Disease**

Liver disease can cause higher levels of female hormones, which in turn lower testosterone levels. High estrogen combined with chronic illness compound to cause medically significant hypogonadism in many men with liver disease. Hereditary hemochromatosis is a genetic condition associated with liver problems and hypogonadism. Liver disease can also cause abnormal SHBG and albumin levels, so testing can be difficult.



## Exposure to Female Hormones

Unintended exposure to female hormones (from a spouse's estrogen cream, for example) can cause male hypogonadism. Rare cases of testicular tumors can produce high amounts of estrogen. *Environmental estrogens* can also lower male hormone levels. (For more information, see Chapter 6.)

## Genetic Conditions

*Kallmann's syndrome*, *Klinefelter's syndrome*, *Del Castillo syndrome*, *hereditary hemochromatosis*, *neurosarcoidosis*, and *polyglandular autoimmune syndromes* are genetic conditions that can result in hypogonadism.

## Problems with the Brain or Pituitary Gland

The brain, pituitary gland, and testicles are intimately connected through hormones. Problems in one area affect the others. When the hypogonadism is caused by brain or pituitary gland problems, it's called *secondary hypogonadism*, *central hypogonadism*, or *hypogonadotropic hypogonadism*. *Head injuries*, even from the remote past, can result in hypogonadism. A tumor of the pituitary gland, known as a *pituitary adenoma*, is a common cause of hypogonadism. One variant of a pituitary tumor, known as a *prolactinoma*, almost always results in hypogonadism. This tumor produces excessive amounts of the hormone *prolactin*, which is responsible for milk production in women. Prolactinomas can cause male breast growth (*gynecomastia*), and in rare cases they have been known to cause breast milk production (*galactorrhea*) in men. (For more on prolactin, see Chapter 6.)

*Hereditary hemochromatosis*, *Kallmann's syndrome*, and *neurosarcoidosis* are causes of central hypogonadism. Obesity and head injuries can cause a form of central hypogonadism with low testosterone levels and inappropriately normal gonadotropin (LH and FSH) levels. Finally, there's *idiopathic hypogonadotropic hypogonadism*, which means we can't figure out why a patient has central hypogonadism.

## THE CHALLENGES OF MEASURING ANDROGENS

Androgen measurement remains one of the great challenges in endocrine laboratory testing. Even with all the advances in the field, diagnosing hypogonadism can be difficult. Tests for androgen levels can be variable and inaccurate for many reasons:

- *Test reliability.* Testosterone is one of the most difficult hormones to measure. Many tests are available, but so far there is no perfect test. Most tests are pretty good at measuring normal or high testosterone levels. The challenge is measuring low levels of testosterone. In today's managed care environment, a particular test may be done because it is cheaper, not because it is better.
- *Lab imperfection.* Doctors are not perfect, and neither are labs. Androgen testing is notorious for being associated with a high degree of variability. I have sometimes taken a blood sample from a patient, divided it in half, and sent the blood to two different labs for the same test. The results were very different. Doctors call this disparity *assay variability*. Endocrinologists will try to minimize this problem by sending all of their hormone tests to a single lab. Even so, there can be problems with quality control and variability. And each lab has its own "reference range"—that is, its own definition of normal—so the normal range also varies from lab to lab.
- *Hormone fluxes.* Testosterone is secreted in cyclic patterns; diurnal rhythms, diet, activity level, and even sun exposure will affect testosterone production. Testosterone usually peaks early in the morning, which is why men often wake up with an erection. This is also why I recommend measuring testosterone levels first thing in the morning. If the level is low, it's a tip-off that there are production problems: after all, this is when production should be at its highest. To control for minute-to-minute hormone fluxes, endocrinologists will sometimes draw three separate blood samples 20 minutes apart, combine the blood, and send the combined samples to the lab for a single test. The complete sample, known as a *pooled sample*, provides a more integrated measure of hormone secretion.
- *Blood proteins.* Ninety-eight percent of testosterone is attached to proteins in the blood. Sex hormone-binding globulin (SHBG)

holds about 60–80 percent of the testosterone. Testosterone bound to SHBG is not biologically active. Twenty to 40 percent of testosterone is bound to another protein, albumin. Albumin-bound testosterone can come free and is biologically active, unlike SHBG-bound testosterone. Total testosterone measures SHBG-bound, albumin-bound, and free testosterone in the aggregate. Variations in SHBG or albumin will cause the total testosterone measurement to be unreliable.

- *Normal?* Testosterone experts still debate what, in fact, a “normal” testosterone level is. Many doctors now agree that the “normal” range is not accurate and should be reevaluated. Some laboratories are now reporting normal values according to how old you are. More research is needed to more precisely identify normal values and to determine what is considered normal for one’s age.

## TESTING FOR HYPOGONADISM

Despite problems with testing, establishing a diagnosis of hypogonadism requires laboratory confirmation of low testosterone levels. Several different types of testosterone measurements may be necessary to fully evaluate someone’s testosterone status. Because there is no perfect test, the diagnosis of hypogonadism can be a judgment call on the part of the physician.

### Total Testosterone

This is the test most commonly used to diagnose hypogonadism, but total testosterone is not always the most accurate measurement. Different laboratories employ different testing methods, so there can be tremendous variation in test results. Total testosterone is a measure of the total amount of testosterone in the blood—both free and bound to proteins, primarily SHBG and albumin. But since up to 60–80 percent of total testosterone is bound to SHBG, this test is highly dependent on SHBG levels. Testosterone that is bound to SHBG is not readily available to the tissues, and is said to be inactive. If SHBG levels are normal, the total testosterone level is usually accurate; but abnormal SHBG

levels will throw the test off. Higher SHBG levels will make the total testosterone level appear normal when it is actually low.

Although the “normal range” is still debated, most laboratories report a reference range for total testosterone of around 260–1000 ng/dL. But many endocrinologists agree that a total testosterone level below 300–500 ng/dL may constitute medically significant hypogonadism. Levels below 300 ng/dL almost always warrant treatment. Testosterone levels between 300 and 500 ng/dL represent a “gray zone” and require further testing. I recommend measuring total testosterone between 7:00 and 10:00 A.M., when levels are at their highest.

The traditional method of measuring total testosterone is *immuno-bistochemical luminescence* or *radioimmunoassay* (RIA). A new laboratory technique called *mass spectrometry* is even more accurate and more reliable than the traditional methods of measuring testosterone. The total testosterone is used to determine free testosterone levels, so if the measurement is inaccurate to start with, the free testosterone level measurement will also be inaccurate.

### **Measured Free Testosterone**

The free testosterone, also known as *dialyzable testosterone*, represents testosterone that is not bound to proteins. This test is desirable because it measures the most active component of testosterone. The free testosterone level is not affected by SHBG levels. In order to measure free testosterone accurately, the total testosterone must be measured as well. The free testosterone level is determined based on the total testosterone and the percentage of testosterone that is removed using a process called *equilibrium dialysis*. If the laboratory is good at measuring total testosterone, the free testosterone measurement will be much more accurate. Inaccurate total testosterone measurements, on the other hand, result in inaccurate free testosterone determinations.

The problem with free testosterone measurements is that most laboratories use testing methodology that is unreliable. They use inexpensive and unreliable procedures to determine total testosterone measurements. Instead of using the preferred *equilibrium dialysis method*, free testosterone measurements can employ an inferior technique using antibodies, called the *analog method*. The analog method is cheap and easy to perform but is not reliable. It is best to have free

testosterone measurements done at a well-known laboratory that performs accurate total testosterone measurements and uses the equilibrium dialysis method to determine free testosterone.

### **Calculated Free Testosterone**

In some situations, the calculated free testosterone can be more reliable than either the total testosterone or the measured free testosterone. This is because it combines the best of both worlds. Technically speaking, the total testosterone is the most reliable test. The free testosterone is calculated using the more accurate total testosterone level but also takes proteins (albumin and SHBG) into consideration. A simple calculation of free testosterone is called the *free testosterone index*. A more sophisticated mathematical equation gives a value for the free testosterone based on total testosterone, albumin, and SHBG levels. The formula for this calculation can be found on the website of the International Society for the Study of the Aging Male at [www.issam.com](http://www.issam.com).

### **Bioavailable Testosterone**

Bioavailable testosterone represents all the testosterone that is readily available to the tissues and includes *free testosterone* and *weakly bound testosterone*. Free testosterone makes up about 2 percent of the total circulating testosterone. Another 20–40 percent of total testosterone is loosely bound to the blood protein albumin. This albumin-bound testosterone can be easily extracted and is said to be a *bioavailable* component. Knowing how much testosterone is tightly bound and how much is bioavailable to the tissues is very important. Bioavailable testosterone is calculated using a variety of measurements, including total and free testosterone as well as albumin and SHBG levels.

### **Salivary Testosterone**

Salivary testosterone levels are not a good way of measuring testosterone levels. The test is not accurate enough, and the normal range

has not been clearly defined. Salivary testosterone measurements hold promise, though, and may become the standard way of measuring testosterone levels in the future.

### **Gonadotropins**

The gonadotropin hormones, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), give doctors information about the pituitary gland and the hypothalamus and their regulation of testosterone. Testosterone follows a traditional endocrine feedback loop with LH and FSH. If the production of testosterone declines, LH and FSH levels increase in an attempt to stimulate the testicle to produce more testosterone. So if testosterone is low and LH and FSH are high, the patient has *primary hypogonadism* or *testicular failure*. If testosterone is low and LH and FSH are also low, the patient is said to have *hypogonadotropic hypogonadism*, *central hypogonadism*, or *secondary hypogonadism*. Sometimes the testosterone level is low but the LH and FSH levels are normal. In this situation, the gonadotropins are said to be *inappropriately normal*, because if the pituitary gland were working properly, levels would be higher. This is also a form of central hypogonadism.

### **Sex Hormone–Binding Globulin (SHBG)**

SHBG is the main protein that carries testosterone in the bloodstream. Sixty to 80 percent of testosterone is bound to SHBG. SHBG binds testosterone very tightly and makes it inactive. SHBG is important because most of the testosterone that is measured in a total testosterone test is bound to SHBG. Yet this form of testosterone is not active in the body. When SHBG levels are normal, total testosterone is a fairly reliable test. But when SHBG is either too high or too low, the total testosterone does not accurately represent the body's testosterone status. It's important to know SHBG levels to determine the reliability of testosterone levels, but abnormal SHBG levels don't necessarily translate to a medical problem. SHBG levels increase with aging. Obesity and diabetes also cause higher SHBG levels. Low SHBG is a risk factor for insulin resistance. Liver problems, kidney problems, genetics, and many medications can affect SHBG levels.

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### **Albumin**

Twenty to 40 percent of testosterone in the body is bound to the blood protein albumin. The testosterone is weakly bound to albumin and can be easily extracted for use in the tissues. Albumin-bound testosterone is said to be *bioavailable*. Abnormal albumin levels are not as common as abnormal SHBG levels, and in the grand scheme of things, albumin is less important than SHBG when it comes to testosterone measurements. Obesity, malnutrition, and liver disease can affect albumin levels. Albumin levels are generally part of a standard blood test called a *complete metabolic panel*.

### **Prolactin**

Elevations of prolactin may indicate a pituitary tumor, a common cause of hypogonadism. All men with low testosterone and especially those with low or normal LH and FSH levels should have their prolactin levels measured.

### **Dihydrotestosterone (DHT)**

DHT is made from testosterone by the enzyme *5-alpha reductase*. DHT levels are sometimes helpful in diagnosing hypogonadism or in monitoring therapy. DHT is primarily responsible for the negative effects of testosterone, such as prostate enlargement and hair loss.

### **Estrogen**

Elevated estrogen levels can be a clue to the cause of hypogonadism. The most common test performed is based on *estradiol*, but *estrone* and *estriol* levels can also be measured. Accidental exposure to estrogen, liver problems, and obesity are all causes of high estrogen levels.

### **GnRH Stimulation Test**

This test is used to determine the ability of the pituitary gland to respond to signals from the hypothalamus. Gonadotropin-releasing

hormone (GnRH) is given by injection, and then LH and FSH as well as estrogen and testosterone are measured.

### **Clomiphene Stimulation Test**

This is another test used to determine the health of the pituitary gland and the hypothalamus. The medication clomiphene is given by mouth, and LH, FSH, and testosterone are measured.

### **Liver Function Tests**

Because liver disease is frequently associated with hypogonadism, liver function tests should be administered periodically. Alanine transaminase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transpeptidase (GGT), alkaline phosphatase, bilirubin, albumin, and prothrombin time (PT) are all tests of liver function.

### **Hemoglobin and Hematocrit**

Hypogonadism causes low red blood cell counts, known as *anemia*, which are measured by the hemoglobin and hematocrit tests. Testosterone replacement therapy increases red blood cell counts but can cause *too* much blood, a side effect known as *polycythemia*. Hemoglobin and hematocrit should be monitored at least every 6 months during testosterone replacement therapy.

### **Prostate Specific Antigen (PSA)**

Testosterone has effects on the prostate gland, and monitoring prostate health is an important part of TRT. PSA should be measured before starting TRT and, if elevated, should be fully evaluated by a urologist before determining if TRT is appropriate. PSA is monitored every 3 months for the first year on TRT and then every 6 months.



## **Bone Density Testing**

Because low testosterone is an important causal factor in thinning of the bones, any man with hypogonadism should undergo bone density testing or have the *bone mineral density* (BMD) test performed. *Dual-energy X-ray absorptiometry* (DEXA) is the most accurate and advanced test available for measuring bone density. The test is quick and painless and gives very important information about the density of bones.

## **Other Tests**

Men with hypogonadism are at increased risk for a variety of medical problems. Blood sugar, cholesterol, and thyroid testing should be done in all men with hypogonadism. Levels of other androgens—including androstenedione and DHEA-S—can be tested. Sometimes it's useful to measure multiple androgen levels, although testosterone is usually the most informative. Women, however, usually must have multiple androgens measured if they are suspected of having an androgen disorder.

## **TESTOSTERONE REPLACEMENT THERAPY (TRT)**

The goal of treating testosterone deficiency is to alleviate the symptoms of hypogonadism and to bring testosterone levels into the normal range. TRT comes in a variety of forms. Testosterone pills should not be used in men, because this form of TRT causes liver toxicity.

## **Testosterone Injections**

*Testosterone enanthate* and *testosterone cypionate* are the two most common types of injectable testosterone. These are long-acting testosterone medications, given as a deep muscle injection. The testosterone is dissolved in oil, and injections are given every one to four weeks.

There are two main problems with testosterone injections. First, the shot is difficult to take. Because testosterone is dissolved in sesame oil (enanthate) or cottonseed oil (cypionate), a large needle must be used,

and the injection is given very deep into the muscle. The testosterone forms a reservoir whose contents are slowly released into the bloodstream. The second problem is that testosterone levels do not remain steady. Hormone levels peak about 24 to 72 hours after an injection and decline over the next several days to weeks, leading to fluctuations in mood, appetite, sex drive, and energy level. To minimize these problems, I recommend taking a lower-dose injection once a week. This gives more stable blood levels and reduces the volume of the injection, allowing the use of a smaller needle that doesn't have to go as deep into the muscle.

### **Androgel**

Androgel has become the number one most prescribed type of TRT. It is an alcohol-based gel that is 1 percent testosterone. The gel is applied to the upper arms, shoulders, or abdomen every morning and dries quickly. It supplies fairly constant levels of testosterone to the blood, eliminating the highs and lows seen with testosterone injections. Androgel comes in 2.5-gram and 5-gram packets with a pump that delivers 1.25 grams per pump depression. If you use testosterone gel, you must be careful not to let wet gel touch the skin of anyone, especially children or your partner. Once the gel is dry, contact is safe. I have found that some men require as much as 10 grams each day (two packets or eight pump depressions) to get their testosterone levels into the normal range. Sometimes even 10 grams of Androgel is not adequate. In these cases, there is usually a problem with the gel penetrating the skin. I recommend trying Testim, which can have better skin penetration. Striant (discussed below) injections are also good options when skin penetration is a problem.

### **Testim**

Testim is a formulation of 1 percent testosterone gel that uses a compound known as *pentadecalactone* as the base for the gel. Pentadecalactone is very good at penetrating the skin, getting more testosterone into the bloodstream. Testim comes in 5-gram tubes that have a screw top. The main problem with Testim is its peculiar odor

(the manufacturers call it a scent). Some people say it smells like musk oil; others say it smells like fishy perfume or body odor. Endocrinologists joke about the smell; they know someone is on Testim the instant they meet him, just by the smell. The gel is sticky or tacky and can feel uncomfortable on the skin. Despite these inconveniences, Testim is the TRT of choice for many men. If there are problems with stickiness or bothersome smell, I recommend the following: rub the gel in for at least 2 minutes. This allows the gel to penetrate the skin, and the stickiness goes away. Apply the gel to the thighs, lower back, and calves. The farther away it is from the nose, the less you will smell it. Apply talcum powder or baking soda after rubbing in the gel. When following these steps, most men do very well with Testim.

### **Striant**

Striant is a testosterone tablet that is not swallowed but placed between the cheek and gum. It's called a *mucoadhesive sustained-release buccal tablet*. The tablet is placed on the upper gum, where it gradually softens into a waxy glob that conforms to the shape of the gum. The usual dose is one 30 mg tablet twice a day, and patients are instructed to wipe the residual portion out of their mouth before applying a new tablet. I have found that some patients do well using the tablet once a day and not wiping out the residual portion. Many men find Striant difficult to get used to, but when used properly, most men achieve normal testosterone levels. Striant is a great choice for obese men, who frequently have problems with the gel penetrating the skin. Striant is also reportedly associated with lower levels of DHT, the testosterone by-product that contributes to prostate enlargement and hair loss.

### **Testosterone Patches (Androderm and Testoderm)**

Testosterone skin patches (or transdermal testosterone patches) come in two varieties. Testoderm is applied to the scrotum. Androderm is applied to the upper arms, back, or abdomen. Skin patches are an effective but not a popular form of TRT. Up to 30 percent of men experience rashes or skin irritation, and up to 12 percent experience blister formation. The patches can be inconvenient and can fall off during exercise.

### **Testosterone Creams**

Some doctors prescribe their own formulations of testosterone creams, which can be prepared by an experienced compounding pharmacist. As with all pharmaceuticals made by compounding pharmacists, the quality of these products can be poor. I have seen a tremendous amount of variability in the testosterone levels of patients who use compounded testosterone creams. I usually don't recommend testosterone cream, but I have seen it work for a few patients.

### **Anastrozole (Arimidex), Exemestane (Aromasin), and Letrozole (Femara)**

This class of drugs, known as *aromatase inhibitors*, works by blocking the conversion of testosterone to estrogen. The drugs are approved for use in women for the treatment of breast cancer, but are increasingly being used as an adjunctive therapy to TRT. Most experts still consider the use of aromatase inhibitors in men very controversial.

### **Oxandrolone (Oxandrin)**

Oxandrolone is a synthetic androgen available in pill form. It's very expensive and not commonly used for male hypogonadism.

### **GnRH Pumps**

Gonadotropin-releasing hormone (GnRH) must be released in small pulses in order to work properly. Men can wear devices similar to insulin pumps that do this for them, stimulating the pituitary gland to make LH and FSH, which tell the testicles to get going. This system is effective only if there is a brain problem but the pituitary gland and testicles are OK. It is a very attractive option for men who want to have children, because it also stimulates sperm production.

### **Clomiphene Citrate (Clomid)**

Approved as a fertility drug in women, clomiphene is also effective for raising testosterone levels. As with the GnRH pump, the pituitary gland and testicle function must be normal for this therapy to be effective.

### **Future Therapies**

New delivery systems for testosterone are always in the works. A nasal spray formulation looks promising. Research is also being done on the injection of microcapsules and a long-acting version of testosterone, *testosterone undecenoate*, which lasts 3 months instead of a few weeks. Synthetic versions of testosterone-like hormones are being developed that may have advantages over traditional TRT.

### **SIDE EFFECTS OF TRT**

Once the correct dose is determined, most men do not have side effects from TRT. The biggest complaint about TRT is the method of delivery since a simple pill is not available. I have heard patients complain about every type of treatment. Some people hate rubbing gel into the skin every day; others can't stand the thought of a shot. The buccal testosterone is gooeey; the patches cause rashes. Testosterone, however, can have more serious side effects that occur with any of the delivery devices. There can be an increase in the level of anger or aggression. Some men get a huge increase in their sex drive, and it's too much for the wife to handle. (TRT has been responsible for many divorces.) There can be breast growth (gynecomastia), acne, testicular shrinkage, liver problems, high blood pressure, fluid retention, headaches, cholesterol problems, prostate enlargement, decreased sperm count, and increased red blood cell count (polycythemia). TRT has also been reported to cause a worsening of sleep apnea, but I have never had a patient with this complication.

There is always the potential for androgen abuse, known as *anabolic steroid abuse*, among men. Some men, in fact, have a psychological condition called BDD—*body dysmorphic disorder*—in which they

become convinced that their body is horribly unattractive. Their concern can be focused on many parts of their body—from their hair to their legs—but for many, it's the physique that's disappointing. They work out, and to help their workout along, they abuse testosterone. Anabolic steroid abuse is associated with testicular shrinkage, permanent sterility, erectile dysfunction, breast tissue growth, psychological problems, cholesterol problems, and premature cardiovascular disease.

To date, there is no evidence that testosterone replacement therapy causes prostate cancer. But it is known that TRT causes existing prostate cancer to grow. Therefore, any man who is planning on starting TRT should be evaluated for prostate cancer with a *prostate-specific antigen* (PSA) test and a *digital rectal examination* (DRE). PSA should be monitored every 3 months for the first year and every 6 months thereafter. TRT can make male breast cancer worse, so this condition is a contraindication to the use of testosterone. There is also the risk of the unknown. No large, long-term prospective trials of TRT have been performed, so the clinical benefits and long-term safety of TRT are unknown.

## ANDROGEN SUPPLEMENTS

Thanks to professional athletes and the birth of *anti-aging medicine*, interest in androgen supplements is high. But do they really work?

### Androstenedione

This hormone, almost identical to testosterone, is available as a dietary supplement without a prescription. Andro, one of the major brands, had more than \$100 million in sales in 1999, thanks in no small part to baseball slugger Mark McGwire's revelation that he took the supplement during his record-setting 1998 season.

It is thought that androstenedione supplements are converted to testosterone and have the effects of increasing muscle mass and reducing fat mass. Studies have failed to show that androstenedione lives up to its claims, however. In fact, it appears that androstenedione tends to raise testosterone *and* estrogen levels, the latter putting men at risk for breast growth. Androstenedione also lowers HDL (good) cholesterol.

In 2004, the U.S. Food and Drug Administration (FDA) issued a warning on products containing androstenedione because they pose

the same risks as long-term anabolic steroid abuse. The consensus among endocrinologists is the same. Other versions of androstenedione, such as androstenediol, 19-norandrostenedione, and 19-norandrosterone, are available as dietary supplements but have not proven to be any safer.

### **Dehydroepiandrosterone (DHEA)**

DHEA is considered a “weak” androgen. DHEA can be converted to androstenedione and testosterone. Unfortunately, DHEA can also be converted to other hormones, such as estrogen. So what happens in your body when you take DHEA? No one really knows.

DHEA is naturally made by the adrenal gland. There’s also more than one kind of DHEA; sometimes you may hear of “DHEAS” or “DHEA-S.” But that isn’t much different from standard DHEA; all the “S” means is that a sulfate is attached to the DHEA, something that occurs naturally in the body.

DHEA has been called the “youth hormone” because its levels peak when people are in their 20s, and then decline dramatically with advancing age. The decline has been given a name, *adrenopause*. Among the claims: it’s anti-aging, increasing lean body mass; it improves insulin resistance; it boosts energy levels and libido; and it improves mood. Yet all of these claims remain unproven.

There are some troubling side effects. The most notable is a theoretical risk of prostate cancer in men and breast cancer in women. Those doctors who do recommend DHEA disagree on dosage levels, which range from 10 mg to as high as 1600 mg per day.

I typically do not recommend DHEA supplements. But sometimes I will prescribe very low doses of DHEA for hypogonadal men who *also* have adrenal gland deficiencies (such as polyglandular autoimmune disease with Addison’s disease).

### **MUSCLE BOOSTING TIPS**

TRT isn’t for everyone, and there are other things you can do to build up your muscle mass. Even if you do take testosterone, these tips may help your hormones to work more effectively.

### **Exercise**

Physical activity of any kind boosts testosterone levels. Exercise makes muscles physically and metabolically stronger. Exercise is an important step in achieving hormonal balance.

### **Weight Training**

To significantly improve your body composition, you must lift weights. There are many different weight lifting techniques. If you have never lifted weights before, I recommend that you start with very low weights and slowly work your way up to higher weights. You may also want to consider two or three sessions with a personal trainer to perfect your technique. Lifters commonly debate which is better, free weights or machines. My answer: both are great. Just remember, if you use free weights, you need to use a spotter. Many weight lifting injuries can be prevented by the use of a spotter.

You should plan on hitting the gym at least twice a week. Consistency is key. A 30-minute weight training session twice a week will have a significant effect on your body composition in as little as 4 weeks. Weight training is the best way to increase muscle mass. Remember, the more muscle you have, the better your metabolism.

### **Stress Relief**

Stress lowers androgen levels by reducing hormonal signals from the brain. Stress has a negative effect on many hormones, creating a hormonal imbalance that slows metabolism. Stress, either psychological or physical, reduces muscle mass and increases fat mass. Suggestions for stress relief are provided in Chapter 8.

### **Vitamin D**

Vitamin D is best known for its beneficial effects on bones, but healthy muscles need vitamin D too. Vitamin D deficiency has been reported



to occur in 36 percent of healthy adults and 60 percent of elderly people. If you have Vitamin D deficiency, your muscles will be tired, flabby, and weak. Vitamin D supplementation at a dose of 800–1000 IU daily can improve muscle strength and muscle size as well as physical endurance.

### **Check Your Growth Hormone**

Growth hormone is another hormone that has a major effect on muscles. Growth hormone deficiency has many of the same symptoms as hypogonadism. For more information, see Chapter 9.

### **Get Plenty of Sleep**

Your hormones are dependent on circadian rhythms. Androgens and growth hormone are both secreted while you sleep. When you don't get enough sleep, these hormones are not made in sufficient quantities.

### **The Hormonal Health Diet**

Stay away from fad muscle-building diets. It is important to get the right number of calories and to have a healthy balance of carbohydrates, protein, and fat.

### **Protein Supplements**

Protein provides the building blocks for healthy muscles. Make sure you get your minimum protein requirements (see Chapter 2). Egg whites, low-fat dairy products, tofu, fish, and lean cuts of meat are excellent sources of protein.

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# ANDROGEN DISORDERS IN WOMEN

ALTHOUGH GENERALLY KNOWN AS “MALE” HORMONES, ANDROGENS ARE JUST AS IMPORTANT FOR WOMEN AS THEY ARE FOR MEN. Androgen hormones like testosterone, androstenedione, and dehydroepiandrosterone sulfate (DHEA-S) play an important role in *hormonal balance* for women. Testosterone and androstenedione are produced primarily in the ovary, and DHEA-S is made in the adrenal gland. The main cause of androgen problems in women is androgen hormone excess, but low androgen may also cause problems for some women. Testosterone is the primary androgen hormone in men, but in women, DHEA-S and androstenedione play equally important roles.

## ANDROGEN EXCESS IN WOMEN

Androgen excess, known as *hyperandrogenism*, is the most common hormonal disorder in young women. Polycystic ovary syndrome (PCOS), also known as *Stein-Leventhal syndrome*, is the most common cause of androgen excess. Insight into the causes and treatment of PCOS has increased significantly in the past 10 years. It's known that insulin resistance is the underlying cause of PCOS because insulin stimulates the body to produce excess androgen hormones. Most treatments for PCOS, in fact, are the same as those for insulin resistance (see Chapter 3).

Other conditions, such as unintended exposure to male hormones, nonclassical congenital adrenal hyperplasia (NCAH), Cushing's syndrome,

acromegaly, pituitary gland tumors, ovarian cancer, and adrenal gland cancer, also cause excess androgens in women. The treatment depends on the cause of the hyperandrogenism, so making the right diagnosis is very important.

Androgen excess can have serious metabolic consequences. Androgen excess and excess weight go hand and hand. Elevated androgens are linked to health problems such as high blood pressure, cholesterol problems, insulin resistance, diabetes, obstructive sleep apnea, cardiovascular disease, and an increased risk for cancer.

### **FEATURES OF ANDROGEN EXCESS**

Androgen excess causes a variety of complications in women, ranging from minor cosmetic concerns to more severe problems. The severity of symptoms usually correlates with the degree of androgen excess. Symptoms such as deepening of the voice, male-pattern balding, or enlargement of the clitoris, known as *virilism*, are signs of a more severe androgen problem, such as cancer of the ovary or adrenal gland.

#### **Weight Gain (Especially around the Middle) or Difficulty Losing Weight**

Because weight gain and insulin resistance are so closely tied, weight gain is a primary feature of hyperandrogenism. If the insulin resistance gets worse, androgen levels go higher. With androgen excess, the location of excess fat is the same as with insulin resistance: usually in the belly. Many women with insulin resistance and androgen excess are unable to lose weight despite valiant dieting attempts. Improving insulin resistance lowers androgen levels and can make weight loss easier.

#### **Facial Hair (Hirsutism) or Excess Body Hair**

Androgen excess causes hair growth on the upper lip, chin, sideburns, neck, chest, arms, nipples, back, buttocks, stomach, shoulders, arms, legs, and inner thighs. Excessive hair growth is not always a sign of an

androgen problem. This can be normal, especially for women of Mediterranean or Middle Eastern heritage, and is known as *benign familial hirsutism*. Hair on the lower back, chest, stomach, shoulders, buttocks, and inner thighs is usually considered abnormal, however, and should be evaluated. If your menstrual cycle is perfectly normal, excess hair growth is unlikely to be a serious problem.

### **Hair Loss (Alopecia)**

Although excess androgen causes hair to grow on the face and body, it can also cause hair loss from the scalp. Some women don't have visible hair loss but report the loss of excessive amounts of hair when they shower or brush their hair. Sometimes the pattern is thinning hair across the entire scalp. Higher androgen levels cause hair loss in a "male pattern," in the form of a receding hairline or hair loss on the top of the scalp (known as the *vertex*). Male-pattern hair loss, also known as *androgenic alopecia*, may be a warning sign of cancer of the adrenal gland or ovary.

### **Acne**

Up to 50 percent of teenagers have acne, so just having acne doesn't mean that you have hyperandrogenism. Persistence of acne into the late teens or 20s, known as *adult acne*, is usually a sign of androgen excess. Adult acne is usually hard to treat with traditional acne medications, but treatments for androgen excess make these medications more effective.

### **Masculinization of the Body**

Although weight gain and excess fat are more common signs, extensive muscle growth and shrinkage of the breasts and hips may be seen with elevated androgen levels. This can be a sign of serious androgen problems, such as cancer of the adrenal gland or ovary.

### **Excessive Body Odor**

Hyperandrogenism increases the production of foul-smelling sweat, especially in the armpits.

### **Acanthosis Nigricans**

A darkening of the skin, usually at the neck and armpits, associated with insulin resistance, is commonly seen in women with androgen excess (see Chapter 3).

### **Menstrual Cycle Problems**

Androgen excess almost always affects the menstrual cycle in one way or another. The most common scenario is skipped periods; however, androgen excess can lead to many different problems, including infrequent cycles (*oligomenorrhea*—fewer than nine cycles per year), light cycles (*hypomenorrhea*), or heavy flow (*hypermenorrhea*), and periods that are either missed, late, or too frequent. Excessive blood loss, also referred to as *dysfunctional uterine bleeding*, can cause *anemia*, which makes you feel tired. Severe *premenstrual cycle syndrome* or excessive cramping with the menstrual cycle (*dysmenorrhea*) may also be seen. I have seen many women with androgen excess that have stopped having a menstrual cycle, a condition known as *amenorrhea*. In general, doctors correlate the menstrual cycle with ovulation, so it is assumed that an abnormal menstrual cycle means a woman is not ovulating. This is known as an *anovulatory cycle*. Menstrual cycle problems, especially amenorrhea, are a risk factor for cancer of the uterus.

### **Infertility**

Primarily because of ovulation problems, women with hyperandrogenism can have difficulty getting pregnant. Treatments for insulin resistance can lower androgen levels and improve fertility.

### **Premature Menarche (Early Puberty)**

Excess androgen can cause a girl to start her menstrual cycle (menarche) earlier than what is considered normal.

### **Psychological Problems**

Androgens have powerful effects on the brain. Androgen excess has been associated with anxiety and depression. Many women with androgen excess also have problems with poor body image, which can lead to feelings of low self-worth and social isolation. Excess androgens can increase irritability, anger, and aggression. Husbands of women with androgen excess may claim that their wives have a “short fuse.”

### **High Blood Pressure**

High blood pressure is usually seen with high androgen levels as a consequence of the underlying condition. Insulin resistance (see Chapter 3), Cushing’s syndrome (see Chapter 8), and acromegaly (see Chapter 9) are causes of both elevated androgens and elevated blood pressure.

### **Abnormal Lipids (Cholesterol and Triglycerides)**

Women with hyperandrogenism have the typical dyslipidemia of insulin resistance, with high triglycerides, low HDL (good) cholesterol, and normal or high LDL (bad) cholesterol. For more information, see Chapter 3.

### **Blood Sugar Problems**

Blood sugar problems related to insulin resistance are common in women with hyperandrogenism. *Prediabetes*, *impaired fasting glucose*, *impaired glucose tolerance*, and *type 2 diabetes* are all commonly seen. For more information on blood sugar problems, see Chapter 3.

### **Cardiovascular Disease**

Androgen excess increases the risk for cardiovascular disease (heart attacks and strokes). Insulin resistance, high blood sugar, abnormal lipids, and high blood pressure contribute to the risk.

### **Deepening of the Voice**

Androgens can cause thickening of the vocal cords, which may cause the voice to deepen. This is considered a very serious sign of hyperandrogenism. Any woman who experiences deepening of the voice should be evaluated for adrenal gland cancer or cancer of the ovary.

### **Enlargement of the Clitoris (Clitoromegaly)**

On rare occasions, high androgen levels can cause the clitoris to become enlarged. Clitoromegaly is defined as a clitoris longer than 1 cm. It may even begin to take on the appearance of a small penis. This is considered a severe manifestation of androgen excess and always warrants an evaluation for cancer of the adrenal gland or ovary.

### **Obstructive Sleep Apnea (OSA)**

Women with excess androgen commonly have sleep apnea. Sleep apnea literally means that you stop breathing many times during the night. A person with sleep apnea is usually not aware of the condition, except for the symptoms that linger into the day. The main symptoms of sleep apnea are fatigue, headache, restless legs, memory problems, snoring, and daytime sleepiness. Sleep apnea is linked to high blood pressure, heart rhythm disturbances, heart attack, stroke, and sudden death. For more information, see Chapter 3.

### **HYPERANDROGENISM CAN BE A SIGN OF CANCER**

If symptoms arise suddenly or are severe, don't even think of hesitating; get right to a doctor. A sudden onset of an androgen disorder is a



warning sign for cancer, of either the adrenal gland or the ovary. Severe androgen excess is also known as *virilism*. Warning signs for cancer include:

- Male-pattern balding
- Excessive body hair growth
- Excessive body odor
- Severe cystic acne
- Cessation of the menstrual cycle
- Deepening of the voice
- Increased musculature
- Loss of breast tissue
- Enlargement of the clitoris
- Low potassium level
- Sudden onset of symptoms

### **Anita's Story**

*Anita was a woman in her early 40s. She came to me full of attitude, very angry and aggressive. Every question I asked had a retort; every comment was met with a glare. (Aggressiveness, as noted earlier, can be a sign of too much testosterone.) She told me that all she needed was her cholesterol checked; why was I wasting time with all these questions?*

*But once I managed to get past her embarrassment, I noticed that Anita had hair on her chin. Intrigued, I asked her about it. She hadn't had the growth long, she told me. She also admitted that she had stopped having periods a few months earlier, but birth control pills had taken care of this. As I asked her about other symptoms of sudden-onset androgen disorder, she nodded her head. She had almost every one.*

*I performed a physical exam and detected a mass in her belly. Anita had a very large adrenal gland cancer. To combat it, we tried every therapy known to science. Still, two years later, she died. It was a long time to live for this kind of cancer, but that's little solace. It's never long enough.*

## CAUSES OF ANDROGEN EXCESS

There are numerous causes of androgen excess. It is important to find out the cause of hyperandrogenism, because this will determine your treatment.

### ***Sally's Story***

*Sally was a 31-year-old fitness competitor who came to see me because she was frustrated with the changes she was seeing in her body. She had taken a break from exercising and in 6 months time had gained 14 pounds. She felt like all the fat was in her belly. Her menstrual cycle was regular, but she was taking birth control pills. She said she started birth control pills at age 13 because of irregular cycles. She also had some acne and facial hair. Her blood tests were "normal," but the LH and FSH tests were "out of balance." The LH level was three times higher than the FSH, a classic sign of androgen excess. After ruling out other conditions, I diagnosed her with PCOS. She started metformin and noticed immediate improvement in her menstrual cycle. She was finally able to start losing weight, but it came off very slowly. At the end of one year, she had lost 10 pounds and was feeling much better.*

## **POLYCYSTIC OVARY SYNDROME (STEIN-LEVENTHAL SYNDROME)**

Polycystic ovary syndrome (PCOS) is the most common hormonal disorder in women. One of every ten women has it. Although first described by Stein and Leventhal in 1935, this condition had been largely ignored by doctors until the last decade or so. PCOS is a combination of two hormonal aberrations—insulin resistance and androgen excess.

Most women with PCOS are overweight or obese, but 25 percent are not overweight. PCOS is a genetic disorder, but a single *PCOS gene* has not been identified. It's known as a *multigenetic disorder* because several genes are thought to be responsible for the different features of PCOS. It's not unusual to have a sister, mother, or aunt with symptoms

of insulin resistance or androgen excess. PCOS can also be transmitted through the father's side. If anyone in your family has insulin resistance or type 2 diabetes, you may have the genetics for PCOS.

Obesity itself is not considered a cause of PCOS, but a factor that makes the symptoms worse. And it's a cycle. Excess weight goes right to the belly, increasing insulin resistance, leading to even more weight gain. Weight loss breaks the cycle and lessens the symptoms of insulin resistance and androgen excess.

Women with PCOS start developing symptoms not long after puberty, but they usually aren't diagnosed for five or more years. The heavier you are, the more likely symptoms will develop at an early age. Excessive androgen can cause a girl to start having menstrual cycles early, known as *premature menarche*. Every attempt should be made to diagnose and treat PCOS as early as possible. PCOS has serious health consequences that go beyond excess weight and excess androgens. Women with the disorder are at high risk for diabetes, high blood pressure, cholesterol problems, sleep apnea, metabolic syndrome (also known as *syndrome X*), cancer of the uterus, and cardiovascular disease. The name *syndrome XX* has been suggested as a sex-specific variant of PCOS with metabolic syndrome.

The symptoms of androgen excess tend to improve when a woman goes into menopause. Insulin resistance and the risk for medical problems get worse with menopause. Sometimes menopausal women still have features of androgen excess. When androgen levels remain high in menopause, a woman is said to have *ovarian hyperthecosis*.

The name PCOS is misleading because it implies that there are multiple cysts in the ovaries. Although this is true for some, up to 30 percent of women do not have cysts in their ovaries. (And many women with cysts in their ovaries do not have PCOS.) Also misleading is the implication of the ovary as the primary source of androgen excess. Women who have had their ovaries removed can still have PCOS. This is because the ovary and adrenal gland are equally responsible for elevated androgen levels. High insulin levels stimulate the production of androgens by both the ovaries and adrenal glands. Insulin resistance lowers the level of sex hormone-binding globulin, which increases the proportion of biologically active *free testosterone*.

PCOS is among the most common causes of infertility. This is because the hallmark of PCOS is a problem with the release of eggs

from the ovary. Insulin resistance causes the walls of the ovary to thicken and form cysts; as a result, eggs cannot be released at their normal time of the month. This condition, known as *anovulation*, is also one of the reasons women with PCOS have menstrual cycle problems and infertility. Facial hair, acne, and hair loss are signs of androgen excess. Darkening of the skin, *acanthosis nigricans*, is common in women with PCOS and is a sign of insulin resistance.

Diagnosing PCOS is challenging. The symptoms of PCOS are different for different women and can vary with time. An exact definition of PCOS has still not been developed. But experts agree that to diagnose a woman with PCOS, all other types of androgen excess must be ruled out. An international committee has proposed that a woman have at least two of the following features to be diagnosed with PCOS: (1) ovulation problems (usually manifest as menstrual cycle problems); (2) hyperandrogenism, which is defined as either skin manifestations of androgen excess (facial hair, body hair, adult acne, or male-pattern hair loss) or high androgen levels; and (3) polycystic ovaries. Polycystic ovaries do not need to be present to make the diagnosis of PCOS, and polycystic ovaries alone do not establish the diagnosis.

### **Diagnostic Criteria For PCOS**

#### **Any two of the following:**

- Menstrual cycle problems
- Hyperandrogenism (skin problems or elevated androgen levels)
- Polycystic ovaries on ultrasound

Other disorders causing hyperandrogenism must also be excluded.

In recent years, the primary treatments for PCOS have shifted from treating androgen excess to treating insulin resistance. Treatments for insulin resistance almost always improve androgen levels and symptoms of androgen excess. Special attention should also be given to the prevention of diabetes, cancer of the uterus, and cardiovascular disease.

### Ovarian Hyperthecosis

It is still unclear if ovarian hyperthecosis is a distinct cause of hyperandrogenism or a variant of PCOS. It is characterized by more severe facial hair growth as well as other manifestations of androgen excess. Most women with ovarian hyperthecosis are overweight or obese. Unlike PCOS, which occurs during the reproductive years, hyperthecosis can occur in women of any age. Some doctors recommend surgical removal of the ovaries because of the associated risk of ovarian cancer.

#### ***Jennifer's Story***

*A secretary-receptionist in (of all places) a doctor's office, Jennifer was 43 years old when she had a heart attack. Jennifer weighed close to 200 pounds; had a diet high in sugars, starches, and fats; and followed an exercise regimen that was limited to walking from her car to wherever she was going. She was also afflicted with PCOS, which didn't help matters any; in addition to being overweight, she was insulin resistant and at strong risk for diabetes. She took metformin, but ignored her doctor's advice on diet and exercise.*

*Jennifer was lucky in one way: her heart attack happened at work, and she was treated immediately. And, of course, she lived. But she knew that unless she changed her lifestyle, she may not be so lucky next time. With encouragement and guidance from her employers, as well as no small amount of willpower on her own, she adopted a regular exercise regimen, cut back on the junk food and added more vegetables and fruit to her diet, and started paying attention to all aspects of her life. She lost 60 pounds and has emerged a healthier, happier person.*

### **Hyperandrogenic Insulin-Resistant Acanthosis Nigricans (HAIRAN) Syndrome**

This is a mouthful, but it refers to a “malignant” form of PCOS. It's everything bad about PCOS magnified, and it's very destructive to the body. Women with HAIRAN syndrome usually are overweight or

obese, and have diabetes or prediabetes, high blood pressure, cholesterol problems, and a high risk for cardiovascular disease.

### ***Patty's Story***

*Patty was a 32-year-old woman who was very athletic and a fitness competitor. (She happened to be a friend of Sally, whose story appeared earlier in this chapter.) She worked out all the time but was gaining weight and had irregular cycles, which was unusual for her; her cycle had always been like clockwork. She had been told that she had PCOS. She tried metformin, but it did not help. I measured her prolactin level, which was high, and an MRI scan showed a small tumor in her pituitary gland. She started a medication called Dostinex, which lowered her prolactin level and shrunk the tumor. Her symptoms of androgen excess improved, but she still had trouble losing weight. Further testing revealed that she also had growth hormone deficiency, another problem commonly seen in people who have pituitary tumors (see Chapter 9). She started growth hormone replacement therapy, and her body weight and body composition improved remarkably. A year later, she won a local fitness competition.*

## **Prolactinoma**

A common variant of a pituitary tumor known as a *prolactinoma* frequently causes androgen excess. This tumor produces excessive amounts of the hormone *prolactin*, which is responsible for breast milk production. High prolactin levels can cause a woman to produce breast milk, even if she is not breastfeeding.

## **Acromegaly**

Acromegaly is a condition caused by a pituitary gland tumor that produces excess growth hormone. Women with acromegaly can have symptoms of androgen excess. Acromegaly is also associated with other pituitary hormone deficiencies, insulin resistance, and diabetes. For more information, see Chapter 9.

### **Excess Cortisol**

Excess cortisol, whether from corticosteroid medications or produced abnormally as a result of Cushing's syndrome, can cause androgen excess. Cortisol has the opposite effect in men, causing low androgen levels. For more information on cortisol, see Chapter 8.

### **Premature Ovarian Failure (Premature Menopause)**

Menopause before the age of 45 is known as *premature ovarian failure*, or POF. POF is usually caused by an overactive immune system, which can attack any gland in the body. Sometimes the immune system destroys estrogen-producing cells in the ovary but does not kill the androgen-producing cells. The result is higher androgen levels and symptoms of androgen excess. Multiple hormone deficiencies known as *autoimmune endocrinopathies* or *polyglandular autoimmune syndrome* can occur in association with premature menopause. Hypothyroidism or hyperthyroidism (see Chapter 7) and Addison's disease (see Chapter 8) may occur at the same time. Symptoms of premature ovarian failure include hot flashes, vaginal dryness, and light or absent periods. For more information see Chapter 6.

### **Hypothyroidism**

When the brain (hypothalamus) detects low thyroid hormone levels, it sends hormonal signals via the pituitary gland to tell the thyroid gland to ramp up production. This hormonal signal can also stimulate production of the hormone *prolactin*. Excess prolactin causes hyperandrogenism. Hypothyroidism causes weight gain, which leads to more insulin resistance. Hypothyroidism is common in women with PCOS. Hypothyroidism may not be the primary cause of excess androgen, but can be a *contributing factor* that makes symptoms worse. See Chapter 7 for more on hypothyroidism.

### **Congenital Adrenal Hyperplasia (CAH)**

Endocrinologists refer to the adult variety of this genetic condition as *21-hydroxylase-deficient nonclassical congenital adrenal hyperplasia*,

or NCAH. The classical form of this disorder presents at birth and causes *ambiguous genitalia*, in which little girls are born with a clitoris so enlarged that it looks like a penis. The milder form, CAH, is responsible for 1 to 2 percent of cases of androgen excess in women. CAH is particularly common in people of Mediterranean descent and the Ashkenazi Jewish population. The source of the excess androgens is the adrenal gland. Doctors (even endocrinologists) commonly miss NCAH because it isn't usually tested for. Standard androgen testing can produce results identical to those of PCOS.

I recommend testing for CAH in any woman with an androgen excess problem. The treatment for CAH is markedly different than that for PCOS. Ask your doctor for the *17-hydroxyprogesterone* (17-OH-P) blood test. However, even this test is not perfect; many CAH patients fall into a gray zone. If this is the case, more sophisticated testing may be needed. There is a genetic test to diagnose this disorder, but, as with most genetic tests, it is rarely covered by insurance.

If the disorder is mild, treatment is not mandatory. Sometimes women shave or use creams or electrolysis to control hair growth. In more severe cases, cortisol medications like dexamethasone (Decadron) or hydrocortisone (Cortef) are used to treat the condition.

### ***Arlene's Story***

*Arlene had NCAH. She had the symptoms: she was overweight and slightly hirsute. But she was never diagnosed with the disorder.*

*Arlene got pregnant. Her child, a girl, was born with full-blown CAH—a genetic condition. (Given the severity of her child's condition, the father must have been a carrier of the gene.) The little girl required extensive plastic surgery to make her vagina appear normal, and she undoubtedly had been subjected to high androgen levels during her fetal development.*

*None of this is the end of the world, of course. But if Arlene had been screened and diagnosed with NCAH, she could have been treated with dexamethasone during her pregnancy, and the baby's problems likely could have been avoided. If you've been told you have PCOS and plan to get pregnant, please get checked for NCAH.*



## **Exposure to Male Hormones**

Unintended exposure to male hormones—from a spouse’s testosterone gel, for example—can cause androgen excess in women.

## **Progestins**

Progestins are synthetic forms of the hormone progesterone. Progestins have androgen properties. Birth control pills that contain *androgenic progestins* (such as *levonorgestrel*, *norgestrel*, or *norethindrone*) or progesterone-only pills, such as *medroxyprogesterone* (Provera), or other progesterone medications, can cause both insulin resistance and androgen excess.

## **Other Medications**

Medications that contain testosterone are an obvious cause of excess androgen, but other medications, such as cyclosporine, valproic acid, minoxidil, or phenytoin, can also cause androgen excess.

## **Cancer**

If the symptoms of an androgen disorder come on suddenly or are severe, it could be an indication of ovarian or adrenal cancer. See a doctor right away.

## **Idiopathic Hirsutism (Benign Familial Hirsutism)**

If the answer “none of the above” fits, doctors use the term *idiopathic*. This is a diagnosis of exclusion after all of the above-mentioned medical conditions are ruled out. To qualify for this diagnosis, a woman must have normal menstrual cycles.

Ironically, in this case it’s not idiopathic at all. It turns out that idiopathic hirsutism is a disorder of the *5-alpha reductase* enzyme, but this

is an enzyme that is in the skin. The rest of the body is normal. In the skin, testosterone is converted at an abnormally high rate to the more active *dihydrotestosterone* (DHT), causing male-pattern hair growth. It's sometimes referred to as *benign familial hirsutism* because it doesn't seem to be associated with any other problems, other than cosmetic issues, and it runs in families.

The condition is genetically transmitted, so if your mother and grandmother are hairy, or the women on your father's side are hairy, you also have a good chance of being hairy. It is more common in women of Mediterranean ancestry.

### TESTING FOR ANDROGEN EXCESS

Someone with features of androgen excess is said to have *hyperandrogenism*. Excess androgen detected in a blood test is known as *hyperandrogenemia*. Several androgen tests are usually done because different androgens give clues to the specific disorder that may be causing the problem. Because so many blood tests are needed to properly diagnose androgen disorders, the evaluation can be very expensive.

If all your tests are perfectly normal, you could still have androgen excess. Why? Because tests are not perfect, and when it comes to measuring androgens, science still has a long way to go. Laboratories are particularly inaccurate at measuring low androgen levels. Even though we're testing for androgen excess, high female androgen levels are still only one-tenth the levels of men. The lower the androgen level, the more difficult it is to measure accurately. The other problem is that the normal range is not clearly defined. Most experts believe that the upper part of the normal range is probably *not* normal, but high. Many women whom I see with symptoms of androgen excess have "normal" levels that are in the upper end of the normal range. If someone has symptoms of hyperandrogenism, I consider these levels high.

Experts agree that if you have features of hyperandrogenism, like menstrual cycle problems, facial hair growth, or adult acne, and have normal lab tests, then you probably still have hyperandrogenism (just not hyperandrogenemia). When it comes to diagnosing hyperandrogenism, symptoms are more important than lab tests. Also critical is a careful physical exam, focusing on signs of androgen excess. Hirsutism can be graded using a scale known as the *Ferriman-Gallwey scale*. Do

not be shocked if your physician requires a pelvic exam or asks to inspect your vulva and clitoris. Tell your doctor if you have a family history of obesity, diabetes, high cholesterol, or high blood pressure.

## Testosterone

Measuring testosterone levels in women can be complicated. For a number of reasons, testosterone levels may be inaccurate or misleading. Test quality and variability, hormonal fluxes, and blood proteins all affect testosterone measurements. The techniques for testosterone measurement in women are the same as for men. For more information on the laboratory evaluation of testosterone, see Chapter 4.

*Total testosterone* measures the total amount of testosterone in the blood—both free and bound to proteins, primarily *sex hormone-binding globulin* (SHBG) and *albumin*. Testosterone that is bound to SHBG is not readily available to the tissues and is said to be inactive. Women with hyperandrogenism frequently also have low SHBG levels, which will make the total testosterone appear lower than it really is. Very high total testosterone levels (above 300 ng/dL) are suggestive of cancer of the ovary or adrenal gland.

The total testosterone test is important because it is used to determine free and bioavailable testosterone. If the total testosterone measurement is not accurate, it makes the other measurements inaccurate as well. The best way to measure testosterone is the *mass spectrometry* technique. This new technique has become available recently but is not always used because it is more expensive than other techniques.

*Free testosterone* represents testosterone that is not bound to proteins. This test is a better test for women with hyperandrogenism because it measures the active component of testosterone. Free testosterone can be measured or calculated; both methods have advantages and disadvantages (see Chapter 4).

*Bioavailable testosterone* represents all the testosterone that is readily available to the tissues and includes *free testosterone* and *weakly bound testosterone*. Free testosterone makes up about 2 percent of the total circulating testosterone. Another 20–40 percent of total testosterone is loosely bound to the blood protein albumin. This albumin-bound testosterone can be easily extracted and is said to be a *bioavailable* component.

### **Dehydroepiandrosterone Sulfate (DHEA-S)**

This hormone is made in the adrenal gland. Very high levels are a tip-off to an adrenal gland problem such as congenital adrenal hyperplasia, Cushing's syndrome, or adrenal gland cancer. Another version of the test, dehydroepiandrosterone (DHEA), without the sulfate, is available but is not as accurate as DHEA-S and is generally not recommended.

### **Androstenedione**

Androstenedione is a lesser-known and weaker androgen that is made primarily by the ovary. Androstenedione can be converted by the body into testosterone or into estrogen. Androstenedione testing is not always required in the evaluation of hyperandrogenism but can be helpful, especially if the ovary is the source of hyperandrogenism.

### **Sex Hormone–Binding Globulin (SHBG)**

SHBG is a blood protein that binds both testosterone and estrogen. Hyperandrogenism, birth control pills, and insulin resistance are among the causes of low SHBG levels. SHBG measurement is important because it helps put the total testosterone test result into perspective.

### **Gonadotropins**

Gonadotropin hormones, *luteinizing hormone* (LH) and *follicle-stimulating hormone* (FSH), give doctors information about the pituitary gland and hypothalamus and their regulation of testosterone and estrogen. These hormones follow a traditional endocrine feedback loop (see Chapter 6). Women with hyperandrogenism usually have gonadotropin levels in the “normal” range, but they can be *out of balance*. Typically, the LH level is at least double the FSH level. This is called an *elevated LH/FSH ratio*. If the LH/FSH ratio is more than 2:1, it is highly suggestive of hyperandrogenism. However, one-third of patients with hyperandrogenism do not have an elevated LH/FSH ratio.

### **Urinary Luteinizing Hormone (LH) and Fertility Monitors**

Urinary LH levels are a good way of testing for the LH “spike,” which is indicative of ovulation. Ovulation problems are a common feature of androgen excess. LH testing kits are available without a prescription for home use. A fertility monitor is an electronic device that tracks the monthly cycle using urinary LH levels and notifies you when it detects the LH spike. Fertility monitors are more accurate and are a more reliable way of knowing that you are ovulating than measuring your daily basal body temperature. For more information on LH and the menstrual cycle, see Chapter 6.

### **Prolactin**

Elevations of prolactin may indicate a pituitary tumor, a common cause of hyperandrogenism. All women with features of hyperandrogenism should have prolactin levels measured.

### **Insulin-like Growth Factor-1 (IGF-1) and the Growth Hormone Suppression Test**

Excess growth hormone produced by a tumor of the pituitary gland (known as acromegaly) is a cause of excess androgen levels. IGF-1 is a hormone produced by the liver that is used as an indicator of growth hormone levels. If the IGF-1 level is high, a *growth hormone suppression test* should be performed to further evaluate growth hormone levels. For more information on growth hormone, see Chapter 9.

### **17-Hydroxyprogesterone (17-OH-P)**

This test is done to check for congenital adrenal hyperplasia, a cause of hyperandrogenism. This test is frequently overlooked but is important because the treatment of congenital adrenal hyperplasia is different from other treatments for hyperandrogenism.

## Progesterone

Progesterone testing is helpful in determining if you are ovulating. Progesterone levels should be measured on day 21 of the cycle. A progesterone level below 2 ng/mL suggests that you are not ovulating. Progesterone measurements during other times of the cycle can be done to help determine what phase of the cycle you are in. For more information on progesterone, see Chapter 6.

## Estrogen

Testing estrogen levels is helpful if there are symptoms of ovarian failure such as hot flashes or vaginal dryness. Estradiol, estrone, or estriol can be measured. For more information, see Chapter 6.

## Glucose Testing

Blood sugar problems and hyperandrogenism are closely linked. Thirty to 40 percent of women with PCOS have blood sugar problems, and 10 percent have full-blown diabetes. All women with hyperandrogenism should undergo glucose testing to check for prediabetes or diabetes. The most basic test uses the *fasting glucose level*. Other tests, including the *hemoglobin A1c test* and the *oral glucose tolerance test* (OGTT), may be necessary. For more on glucose testing, see Chapter 3.

### **Debbie's Story**

*Debbie was a 41-year-old woman with PCOS. She had acne, facial hair growth, and irregular menstrual cycles. She had had a lifelong struggle with her weight. She was taking metformin, which improved her menstrual cycle and helped her lose some weight. After 6 months she had lost 20 pounds but was still overweight, at 190 pounds. During one of her routine follow-up appointments she was found to have a high blood sugar level and was subsequently diagnosed with type 2 diabetes. After the diagnosis, she improved her diet and increased her amount of physical activity and lost another 24 pounds. Her*

*lifestyle improvements were short-lived, however, and she ended up gaining all the weight back. Her diabetes became harder and harder to control with standard diabetes medications, and insulin injections were needed to get her blood sugars into the normal range. Now she's on four shots of insulin a day and has been diagnosed with diabetic kidney disease.*

### **Insulin Testing**

Insulin testing is sometimes done because of the link between hyperandrogenism and insulin resistance. Checking insulin levels is not necessary in someone who is overweight or has other features of insulin resistance. But insulin testing can be helpful in lean women with elevated androgen levels. For more on insulin testing, see Chapter 3.

### **Cholesterol Profile**

High LDL (bad) cholesterol, low HDL (good) cholesterol, and high triglyceride levels are associated with hyperandrogenism. All women with hyperandrogenism should have a *fasting lipid profile*. For more information on cholesterol testing, see Chapter 3.

### **Thyroid Testing**

Thyroid problems, especially low thyroid levels (*hypothyroidism*), commonly occur in women who have androgen excess. Each condition can intensify the symptoms of the other. For more information on thyroid testing, see Chapter 7.

### **Saliva Tests**

Saliva tests are not a good way of measuring androgen levels. The tests are not accurate enough, and the normal range has not been clearly defined. Saliva tests hold promise, though, and in the future may become the standard.

## **Pelvic Ultrasound**

A pelvic ultrasound is useful to check for cancer of the ovary. It also can detect cysts in the ovary. Thirty percent of women with cysts in their ovaries do not have androgen problems, and not all women with androgen problems have detectable ovarian cysts.

## **Endometrial Biopsy**

Androgen excess can cause a build-up of the lining of the uterus, known as *endometrial hyperplasia*, which is a risk factor for cancer of the uterus. An endometrial biopsy should be done to screen for uterine cancer (known as endometrial carcinoma) in women who go more than three months without a menstrual cycle.

## **Sleep Study (Polysomnography)**

Women with androgen excess are at high risk for sleep apnea. Sleep apnea is diagnosed using a sleep study, also known as *polysomnography*.

### ***Natalie's Story***

*Natalie was a 27-year-old woman who went to the emergency room one night with severe pain in the belly. She had an ultrasound and was told there were cysts in her ovaries. The pain ended up being a stomach bug, but she was told to see her gynecologist about the cysts. She was otherwise healthy and had no medical problems. Her gynecologist told her that she had PCOS and started her on the medication metformin. She had a common side effect, nausea, and felt terrible. Three months later she came to see me. She was just miserable, nauseated the entire time and having diarrhea. Her evaluation was essentially normal, with no features of PCOS and normal lab tests. I told her that she didn't have PCOS and she stopped taking the metformin. She had the cysts checked by her gynecologist 6 months later and there was no change. She felt great, had no problems, and went on to lead a normal life.*



## **TREATMENT OF ANDROGEN EXCESS**

Androgen excess can be treated using several different approaches. Androgens can be lowered directly by using androgen blockers, known as *anti-androgen medications*. Birth control pills lower androgen levels, but the synthetic *progestin* component can have undesirable androgen properties. Androgens can also be lowered by treating insulin resistance. Insulin resistance causes both the ovary and the adrenal gland to produce excess androgen hormones. Improving insulin resistance lowers androgen production. Experts feel that treating insulin resistance is the best way to treat androgen excess (especially if you have PCOS) because it treats the source of the problem. If you are overweight, the most important first step to improving insulin resistance is weight loss. The medications that treat insulin resistance work best when combined with a healthy diet and regular physical activity.

### **Nutrition and Physical Activity**

Even though there are medications for PCOS, they are never a substitute for nutrition and physical activity. The Hormonal Health Diet is the ideal diet for PCOS. Weight loss improves insulin resistance, which leads to lower androgen levels and improvement of symptoms. Physical activity helps with weight loss and improves insulin resistance.

### **Self-Confidence**

Many women with PCOS have problems with *poor body image*. The fear of social rejection can make a woman become socially isolated. Poor self-esteem and low self-image can even lead to depression. Work on developing social skills and self-confidence. It is helpful to understand PCOS as a medical/hormone problem. It is not your fault that you have PCOS. Many mental health professionals now specialize in treating body image problems related to PCOS.

## **Treatments for PCOS That Help Insulin Resistance**

All of the treatments for insulin resistance discussed in Chapter 3 can improve the symptoms of androgen excess.

### *Metformin (Glucophage, Glucophage XR, Fortamet, Riomet, and Generics)*

Although metformin is approved by the FDA for the treatment of type 2 diabetes, it is the most prescribed medication for treating PCOS. Metformin attacks the primary cause of PCOS—insulin resistance. Metformin can improve many symptoms of PCOS, including menstrual cycle problems and skin problems, and can help women lose weight. Metformin increases fertility and has been responsible for many “PCOS babies.” For more on metformin, see Chapter 3.

### *Rosiglitazone (Avandia) and Pioglitazone (Actos)*

These medications help alleviate androgen excess by ameliorating insulin resistance. They are approved by the FDA for the treatment of diabetes but have become widely used to treat PCOS. Rosiglitazone and pioglitazone can improve all of the symptoms of androgen excess and can increase fertility and lower the risk for diabetes. For more information, see Chapter 3.

### *Birth Control Pills*

Birth control pills, or oral contraceptive pills (OCPs), are a tried and true way of treating androgen excess. OCPs decrease androgen levels because they shut down androgen production in the ovary as well as increase the production of blood proteins, such as sex hormone-binding globulin (SHBG). SHBG binds to androgens, making them inactive. Birth control pills contain synthetic versions of the hormones estrogen and progesterone. The amount of estrogen and the type of progesterone are what make each pill different.

Synthetic progesterone, called *progestin*, is not exactly like real progesterone. Progestins stimulate both the progesterone receptor and the androgen receptor and are said to have *androgenic activity*. When it comes to PCOS, I recommend birth control pills that have progestins, like *drospirenone*, *desogestrel*, or *norgestimate*. These progestins have the least amount of androgenic activity. The best progestin, drospirenone,

actually blocks the androgen receptor. It was developed specifically for women with androgen excess. Drospirenone is found in the product Yasmin, which is the most frequently prescribed pill for PCOS. It has a chemical structure similar to the androgen-blocking medication spironolactone. It also has mild diuretic properties, so there's less fluid retention and bloating than with other OCPs. Yasmin can also raise potassium levels, which can improve insulin resistance (see Chapter 3). A side effect can be potassium levels that are too high, so regular blood tests are necessary. Because Yasmin and spironolactone have similar actions, it is inadvisable to take both of these medications at the same time.

### **Desirable Birth Control Pills for PCOS**

- Yasmin
- Yaz
- Apri
- Desogen
- Othocept
- Ortho-Cyclin
- Ortho Tri-Cyclen

The progestins *levonorgestrel*, *norgestrel*, and *norethindrone* have high androgenic activity. OCPs with these progestins have side effects including acne, bloating, weight gain, and insulin resistance.

Side effects of all birth control pills include acne, headaches, breast tenderness, nausea, PMS, and depression. OCPs with the androgenic progestins levonorgestrel, norgestrel, and norethindrone can increase insulin resistance, raise blood sugar, and cause weight gain. OCPs with high doses of estrogen may also cause weight gain, but the medium- and low-dose pills do not cause weight gain. Life-threatening blood clots, heart attacks, and strokes are a real risk with birth control pills. The risk is highest if you smoke cigarettes. If you smoke, you should not use birth control pills.

### *Progesterone and Progestins*

Progesterone and progestins (synthetic progesterone) are used in the treatment of PCOS primarily to induce a menstrual cycle. Not having a cycle for 3 months or more is a risk factor for cancer of the uterus. Progesterone is usually given for 10 days every 3 months to induce a menstrual cycle. Other than stimulating a menstrual cycle and lowering the risk of uterine cancer, progesterone does not do much to help PCOS. In fact, progestins with high androgenic activity make PCOS worse. Most physicians prescribe *medroxyprogesterone acetate (Provera)*, which is a highly androgenic progestin that causes side effects like weight gain, bloating, depression, and hot flashes. Androgenic progestins can make insulin resistance worse. If progesterone therapy is necessary, I recommend one of the following products.

*Micronized progesterone (Prometrium)* is natural progesterone that is a good choice for women with androgen excess. The process of micronization allows the tablet to break down into smaller pieces, so that the progesterone dissolves easier and is easily absorbed into the body. This product comes from yams and is dissolved in peanut oil. It causes less weight gain but also makes you sleepy. Take it before you go to bed.

*Progesterone gel (Crinone, Prochieve)* is a vaginal gel made of natural micronized progesterone (also derived from yams). A pre-measured applicator ensures that you get the right amount into the vagina. The progesterone is absorbed through the lining of the uterus and works quite well at protecting the lining. Only about 4 percent of the medication is absorbed into general circulation, so there is much less hunger, fluid retention, and weight gain compared with progesterone taken by mouth.

*Progesterone-containing intrauterine devices (Progestasert and Mirena)* release small amounts of progesterone into the lining of the uterus. Little progesterone is transferred to the rest of the body.

### *Spironolactone (Aldactone)*

Spironolactone has two different effects that work together to improve androgen excess. It is a *potassium-sparing diuretic* medication that also blocks the androgen receptor. The anti-androgenic effect is mild and works best in combination with a birth control pill. As a potassium-sparing diuretic, spironolactone helps the body retain potassium.

Potassium is required for proper insulin action, and low potassium can lead to insulin resistance. Spironolactone can be taken one to four times a day. Blood tests are required to monitor potassium levels and to check for liver problems, which are a rare side effect. Spironolactone can cause birth defects and should not be taken unless a woman is using some form of birth control.

#### *Flutamide (Eulexin)*

Flutamide is a potent androgen-blocking medication that is best for treating excessive facial hair. This drug is not used very often because it can cause liver problems. Like all other androgen blockers, it can cause birth defects.

#### *Finasteride (Proscar, Propecia) and Dutasteride (Avodart)*

Although approved for use in men, these medications are sometimes used to treat androgen excess in women. Finasteride and dutasteride work by blocking the enzyme *5-alpha reductase*, which converts testosterone into the more active form, *dihydrotestosterone* (DHT). Although effective, these medications can cause birth defects and should be used only with careful supervision.

#### *Clomiphene Citrate (Clomid)*

A medication usually used as a fertility drug, clomiphene citrate is an effective treatment for PCOS in women who want to get pregnant.

## GETTING RID OF EXCESS HAIR

For many women, hirsutism is seen as both cosmetically disfiguring and detrimental to one's emotional and social life. It is important to note that all of the preceding treatments may slow the progression of hirsutism, but may not make the hair go away entirely. The best and most effective ways of doing so are mechanical.

- **Electrolysis** is claimed to permanently remove the hair, but multiple treatments are usually necessary.
- **Shaving** is one of the best ways to remove excess facial hair. (Incidentally, the hair will not grow back thicker; this is a myth.)

- **Plucking** and **waxing** can lead to inflammation and infection in the skin and are not as good as shaving.
- **Bleaching** and **depilating creams** are helpful but can also cause inflammation of the skin.
- **Laser hair removal** has still not been perfected. It's expensive, and the hair tends to grow back with time. In the future, better laser techniques may make this the hair removal therapy of choice.
- **Eflornithine hydrochloride (Vaniqa)** is a cream approved for the treatment of unwanted facial hair. The medication works by inhibiting the biosynthesis of hair proteins. The cream must be applied twice a day for at least 2 months before you will see an effect. Unfortunately, if the cream is stopped, the hair grows back.

### FEMALE LOW-ANDROGEN SYNDROME

Although androgen excess receives more attention, low androgen levels can also be problematic for some women. Up to one-third of all women experience problems with androgen deficiency at some time in their lives. Androgens help maintain muscle mass and determine body fat distribution. Androgens are responsible for the appearance of body hair; they make the skin oilier; and, as in men, they contribute to the sex drive.

Also just as in men, women's androgen levels decline with age. Androgen decline at menopause is considered part of the natural aging process. (The decline actually begins when a woman reaches her 30s.) Estrogen medications suppress testosterone production by the ovary, so women on estrogen replacement therapy or birth control pills usually have low androgen levels. Symptoms of androgen decline include loss of sexual desire (libido), weight gain (or sometimes weight loss), increased fat in the belly, loss of muscle, tiredness, lack of energy, decreased sense of well-being, depression, loss of shine in the hair, dry skin, lack of mental clarity, anemia, urinary incontinence (from loss of muscle tone in the pelvis and the bladder), and osteoporosis.

Androgen therapy for women is considered controversial by most endocrinologists. The only androgen products approved for use in women are *Estratest* and *Estratest HS* (a "half-strength" version), which combine conjugated estrogens and testosterone (*methyltestosterone*).

These products are used as *hormone replacement therapy* for women who have symptoms of menopause that are not completely relieved by estrogen alone.

Testosterone gels (*Androgel*, *Testim*) are approved for use in men but are being prescribed more and more for female low-androgen syndrome. The dose is one-tenth that for a man. Dosing is difficult because of the way testosterone gels come packaged. A 2.5-gram Androgel packet should last 5 to 10 days, but once opened, the gel dries out in a few days. The Androgel pump dispenses a pre-measured amount, so it's hard to get the right amount for a woman. Testim comes in 5-gram tubes with a screw top, which makes it more practical for women to use. One tube (which is one day's dose for a man) should be used by a woman over 10 days. Testosterone creams can be made by some compounding pharmacies, and as with other products of this nature, quality control can be variable. A testosterone patch for women holds promise but has had problems getting approval by the FDA.

Androgen therapy can have many side effects. Among the most serious are the risk of birth defects, negative effects on the cholesterol profile, and a possible risk of heart disease. Anyone who takes androgen replacement therapy should do so under the supervision of a qualified physician. Other side effects include acne, hair growth in male areas (face, chest, nipples, and back), voice deepening, overactive sex drive, irregular bleeding, hair loss, and enlargement of the clitoris. For women who take other hormone medications, such as thyroid medication, the dosage may need to be adjusted after initiation of androgen therapy.

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## WOMEN'S HORMONES

THE TERM “FEMALE HORMONES” OR “WOMEN’S HORMONES” REFERS TO ESTROGEN, PROGESTERONE, AND PROLACTIN, BUT THIS IS A VERY LOOSE TERM. The truth is that men and women have each other’s hormones. As we saw in Chapter 5, “men’s hormones,” or androgens, play an important role in female hormonal balance.

The best-known female hormone is estrogen, which takes its name from the Greek term for “mad with desire.” It is estrogen, after all, that helps mold a girl into a woman during puberty. The breasts form; the hips, thighs, and buttocks take their adult shape; and vaginal lubrication increases. (Other changes in puberty—the growth of pubic and underarm hair, skin oiliness, and certain body odors—are due to androgens, hormones more closely associated with males.) Estrogen is responsible for the female body shape—weight gain goes to the hips and buttocks. Estrogen is also responsible for bone health, and that’s one of the reasons men need estrogen too.

Progesterone is known for its effects of fluid retention, bloating, weight gain, and PMS. Its name comes from “gestation,” or preparation for pregnancy. Progesterone works together with estrogen to regulate the menstrual cycle and fertility.

Prolactin is a pituitary gland hormone that is important for breast health and milk production. Estrogen, progesterone, and prolactin work together to regulate many of the basic female biological functions, such as puberty, the menstrual cycle, pregnancy, and menopause.

Recent concern has focused on *environmental estrogens*, also known as *xenoestrogens*. These are chemical compounds that have a structure similar to that of natural estrogen. Like estrogen, they can turn on the estrogen receptor. Many modern chemicals—particularly pesticides—are similar in chemical structure to estrogen and have impacts we’re only beginning to recognize. Plastics and detergents also contain chemicals similar in structure to estrogen. These substances are stored in body fat and are non-biodegradable.

And these do not include just chemicals in the great wide open, but also chemicals where we live. Some tooth fillings have xenoestrogens; so do the linings of cans, meat, and milk products, even marijuana. Some of these estrogens come about as a product of the environmental circle: we spray a field with a pesticide, the cow eats the grass from that field, we drink the milk from the cow, and we thus end up consuming a form of that pesticide. But other estrogens are formed naturally; bacteria in cow intestines, for example, ferment clover to form natural estrogens. And some estrogens, such as those in many plants, are considered healthy.

This chapter will discuss issues related to female hormones and weight—female hormones and the fat cell, weight effects of various birth control methods, hunger, cravings and moodiness of the premenstrual syndrome, bloating and cyclical fluid retention, pituitary tumors, premature ovarian failure, menopause, and hormone replacement therapy.

## **BASIC ENDOCRINOLOGY OF FEMALE HORMONES**

Estrogen, progesterone, and testosterone are more closely related than people think. All three are *steroid hormones*, and they are chemically almost identical to one another. The term “steroid” refers to the chemical structure of the hormone, which is derived from cholesterol. Calling a hormone a “steroid” says nothing about its biological activity. It’s only minor changes in the structure of steroid hormones that make them act differently. Steroid hormones work like all hormones: they bind to receptors, which is like turning on a light switch. Steroid hormones bind with receptors that regulate the DNA of cells. For more information on steroid hormones, see Chapter 4.

There are three major types of estrogen:

- **Estrone** (E1; -one = 1) is produced by fat. Yes, fat makes hormones, just like any other gland. (See Chapter 10 for more on fat as an endocrine organ.) Unlike other types of estrogen, estrone promotes storage of fat in the belly and around the organs. As discussed in Chapter 3, this type of “metabolically evil” fat causes insulin resistance. This is why many doctors refer to estrone as a “bad estrogen.” Young women have low levels of estrone because the ovaries can easily convert estrone to estradiol. After menopause, the ovary loses this ability.
- **Estradiol** (E2; -di = 2) is produced by the ovary and is the predominant estrogen in young women. Estradiol promotes the storage of “healthy” fat around the hips and butt. This fat distribution improves insulin resistance and blood sugar levels. Estradiol is responsible for the majority of the benefits attributed to estrogen and is known as a “good estrogen.” Estradiol is responsible for the “female” body habitus. The fat in the hips and buttocks is “safer fat” compared with fat in the belly. When estradiol is low, fat accumulates in the belly.
- **Estriol** (E3; -tri = 3) is produced by the placenta during pregnancy and is made from other types of estrogen. This is a weaker form of estrogen that has little effect on metabolism.

Each type of estrogen prompts slightly different actions, and each one can be converted to one of the others. That’s why they’re generally thought of simply as estrogens. But, as you can see, all estrogens are not the same. This has led to some of the misunderstandings about estrogen. The estrogen level is not as important as the relative amounts of estrone, estradiol, and estriol. Menopause is associated with a decline in healthy estrogen (estradiol) and a rise in unhealthy estrogen (estrone). Many women have problems with birth control pills and estrogen replacement therapy because they take estrogens that disrupt the normal healthy balance of estradiol and estrone.

Your brain controls estrogen production, and estrogen controls your brain—the feedback loop found with so many hormones and hormone-producing glands. Hormones such as gonadotropin-releasing hormone (GnRH), follicle-stimulating hormone (FSH), and luteinizing

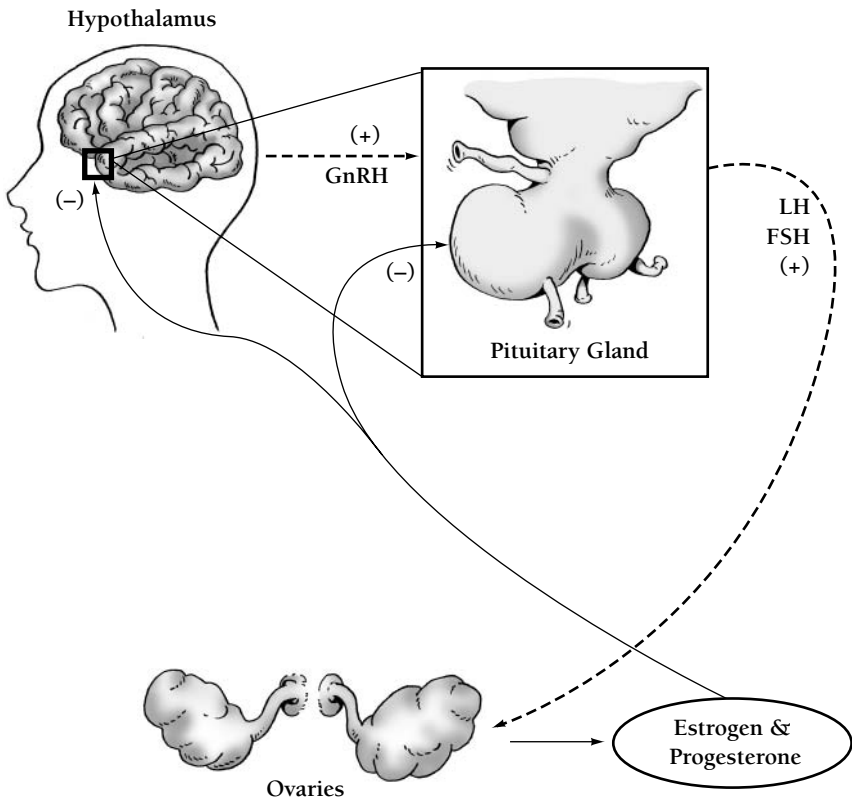
hormone (LH) act on the ovary by means of a traditional endocrine feedback loop. GnRH is produced by the hypothalamus in a pulsatile manner, and the small bursts of this potent hormone stimulate the pituitary gland to make its two hormones—FSH and LH. These hormones work collectively to control the production of hormones from the ovary. Each of these hormones feeds back to the brain in a check-and-balance-type system.

Though thought of as a “male” hormone, testosterone is also made by the ovary. And just as testosterone makes men (and women) more aggressive, improving libido but also creating shorter fuses, estrogen can help prevent mood swings, anxiety, and even depression. For more information on testosterone, see Chapter 5.

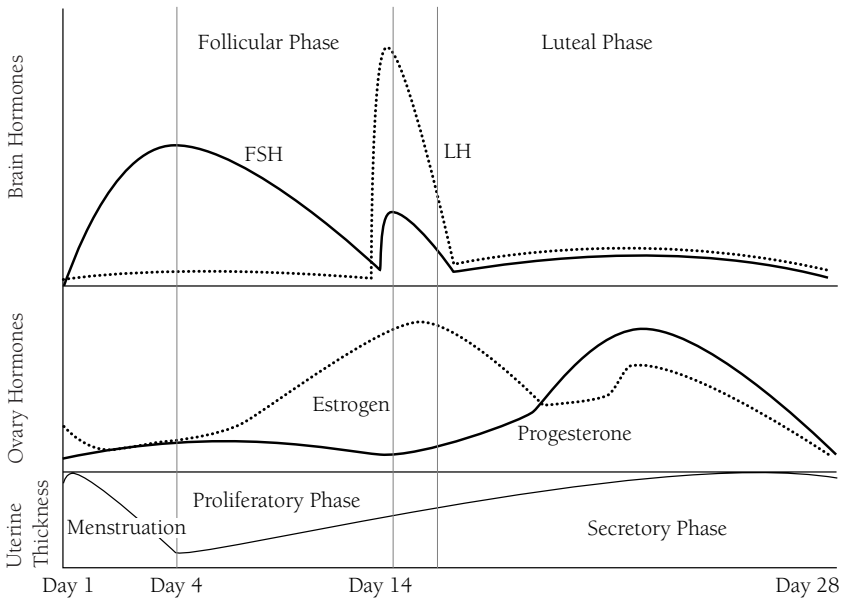
### **FLUID RETENTION AND BLOATING**

It's no secret that the menstrual cycle, with its ebb and flow of estrogen and progesterone, has a marked effect on the rest of the body—particularly fluids, appetite, and mood. Day 1 of the cycle is considered to be the first day of menstrual flow. This starts the first phase of the cycle, known as the *follicular phase*, which is marked by rising estrogen levels and low progesterone levels. About 13 days into the cycle, brain levels of LH and FSH abruptly rise, signaling a critical event in a woman's monthly cycle—*ovulation*. Test results showing a spike in urine LH levels predict that ovulation is hours away. If the egg is fertilized, the lining of the uterus will be healthy and thick, and ready for implantation. If fertilization does not occur, the *luteal phase* begins, where progesterone and estrogen levels drop and the uterus sheds its lining—menstruation. The high progesterone levels just prior to menstruation are responsible for fluid retention, food cravings, mood swings, and premenstrual syndrome.

Why bring all this up? Well, the normal hormonal fluctuations of menstruation represent perhaps the most elegant hormonal systems in the entire human body. The timing of the GnRH pulses from the hypothalamus controls it all like the conductor of a symphony. It helps to understand your hormone fluctuations and, in particular, how they affect cravings and bloating or fluid retention. It's all about the high progesterone levels during the second half of the cycle.

**Figure 6.1****FEMALE HORMONE ENDOCRINOLOGY: HORMONE FEEDBACK LOOPS**

Higher centers in the brain send signals to the hypothalamus, which produces pulses of gonadotropin-releasing hormone (GnRH). GnRH pulses stimulate the pituitary gland to make follicle-stimulating hormone (FSH) and luteinizing hormone (LH), collectively known as gonadotropins. Gonadotropins stimulate the ovaries to produce estrogen and progesterone. Estrogen and progesterone “feed back” to the hypothalamus and pituitary gland, slowing gonadotropin production. Prolactin (PRL) is produced by the pituitary gland and regulates breast health as well as estrogen production. Positive “feedback” is denoted by (+) and negative “feedback” is denoted by (-).



**Figure 6.2**

**HORMONAL CHANGES DURING THE MENSTRUAL CYCLE**

The hormonal rhythms of the menstrual cycle. The graph depicts a 28-day cycle.

The root of the word “menses,” as in “menstrual cycle,” is the same as that for “month”—which, in turn, comes from “moon.” The moon has a 29-day cycle, more or less; the menstrual cycle is 28 days. In ancient times the body was considered a miniature universe, and from what we know now, the ancients weren’t far wrong. After all, life began with water and the chemical reactions of a developing planet, including the cycles of the moon and the tides. Today, we carry around that history in our DNA. Unfortunately for many women, water and the menstrual cycle are still closely related. Many women suffer from fluid retention and bloating, conditions that occur just before menses. Not coincidentally, this is a time of high progesterone levels.

Progesterone causes muscle relaxation, particularly in the smooth muscle—the type of muscle found in the uterus and bowels. The uterus relaxes from the action of progesterone, as does the smooth muscle of

the bowels. During the second half of the menstrual cycle, when progesterone levels are high, the smooth muscle relaxation causes the bowels to expand, stretching the belly and causing the sensation of bloating. The belly sticks out because the muscle tone of the bowels is not as good and cannot keep everything in tight. Bloating is rarely associated with serious disease, incidentally; it is an uncomfortable symptom but is usually not a sign of a serious hormonal disorder. Nevertheless, it is a common concern of women.

Progesterone is also responsible for preparing a woman's body for pregnancy. The same factors are responsible for stimulating appetite and salt cravings. After all, pregnant women need to gain weight.

What can be done about fluid retention and bloating? Here are a few tips:

- *Follow the Hormonal Health Diet.* The eating suggestions I have recommended will lower insulin resistance and help with fluid retention.
- *Avoid salt and prepared foods.* Salt makes you retain water. Do not reduce your water intake, though; this will not help, and it can make you dehydrated.
- *Avoid foods high in fat, especially animal fat.* Fat slows the movement of the intestinal tract and makes bloating worse.
- *Avoid too much fiber.* Although I advocate plenty of fiber, if you have bloating, fiber should be minimized. Fiber swells in the intestines and worsens the sensation of bloating. Beans in particular are high in fiber and also cause gas, which could worsen bloating.
- *Eat small, frequent meals.* Nibbling or "grazing" prevents overdistension of the stomach.
- *Don't skip breakfast.*
- *Eliminate—or at least moderate—caffeine and alcohol consumption.* Both have diuretic effects, and both function as stimulants, which artificially raise the body's levels of various hormones, only to send them crashing when the effect wears off.
- *Exercise.* Progesterone tends to make you sleepy, reducing your activity level. Muscle activity is important for reducing fluid retention. As muscles are worked, they force blood into the heart. Swimming can be very beneficial, because the pressure of the water in the pool forces tissue fluid back into the general circulation, where it can be eliminated by the kidneys.

- *Use a heating pad.* Yes, heating pads may actually reduce bloating, and they're not expensive at all.
- *Lose weight.* All of the above should help you do so, but don't just do these things during "that time of the month." Obesity contributes to fluid retention by increasing pressure inside the abdomen, making it harder for blood to return to the heart.
- *Be careful with diuretics.* Diuretic medications should be used only under the careful supervision of a physician.
- *Get checked by your physician.* Incidentally, fluid retention may not be due to progesterone. *Idiopathic cyclic edema* is an extreme form of menstrual fluid retention. ("Idiopathic" is medical jargon for "we don't know what's causing this.") Severe edema can be a sign of a more serious disease, such as heart failure, blood clotting, or kidney or liver disease.

### **WEIGHT GAIN FROM PREMENSTRUAL SYNDROME**

Progesterone is the primary culprit behind the cravings that come during the second half of the menstrual cycle. And it's progesterone that provokes appetite. Progesterone also makes you sleepy and less likely to want to exercise. Progesterone causes insulin resistance and makes blood sugar levels rise. This can increase weight gain, especially during the second half of the menstrual cycle. Progesterone is a steroid hormone, just like estrogens, androgens, and cortisol. Progesterone is made very early in the steroid synthesis pathway. In fact, most other steroid hormones can be made from progesterone.

Premenstrual syndrome is the subject of jokes—by both men and women—and remains a misunderstood part of women's biology. It's a time when tempers can get short, appetite can increase, depression can set in . . . and it can all fade away after a few days. It's PMS, premenstrual syndrome (aka *premenstrual dysphoric disorder*), and it has been estimated to affect 60 percent of all women.

#### ***Darlene's Story.***

*Darlene is 38, a mother twice over, and a middle manager in a paper company. Every month before her period, she becomes irritable and depressed. She lashes out at her children, her husband,*



*and her pets, and the slightest incident—a dropped glass, a car cutting in front of her on the expressway—is cause for a huge blowup. She has collapsed in tears and practically slugged a co-worker. Sometimes this period can last for more than half of the month.*

*Darlene laughs off the symptoms—after they’ve safely gone away—and calls it PMS. “Oh, you’d better not get near me when I’m PMSing,” she’ll tell others, but she wonders: Is this really PMS? Or is she being affected by something more serious?*

*It doesn’t help that there are physical problems, too. She feels achy. Her breasts swell. She gets occasional panic attacks. And the problem has only become worse as she has gotten older.*

*Is there hope for Darlene? Does she indeed have PMS, or is it something else?*

From a medical standpoint, the problem with PMS is that it’s such a broad designation. There are several common symptoms—food cravings, eating binges, bloating and fluid retention, weight gain, increased hunger, depression, crying spells, anxiety, panic attacks, fatigue, and headaches and migraines. But we’re still not sure what causes PMS. Many physicians blame progesterone, but hormonal theories remain controversial. PMS may be a sign of an androgen disorder (see Chapter 5). What is known is that PMS is a problem of the brain, and it’s caused by the brain’s response to hormones.

The good news is that PMS can be tamed, if not cured:

- Follow the Hormonal Health Diet.
- Exercise and reduce stress.
- Stop smoking.
- Minimize caffeine intake.
- Get plenty of sleep.
- You’re allowed a little chocolate. Just don’t overdo it.
- Take calcium supplements. Calcium is recommended to help prevent osteoporosis, but it also decreases the symptoms of PMS. I recommend you take 1500 mg each day.
- B-complex vitamins, especially vitamin B<sub>6</sub>, increases brain serotonin levels. This helps reduce symptoms of moodiness, irritability, and carbohydrate cravings.

- Be sure to get enough vitamins C and E (fruits and vegetables are an excellent source of both).
- Use SSRI antidepressants, such as Celexa, Lexapro, Prozac (also marketed as Sarafem specifically for PMS), Paxil, Zoloft, and Luvox. These medications are gaining in popularity among physicians for treatment of PMS.
- Evening primrose oil (which contains vitamin E) tends to help with the symptoms of PMS.

### **PROGESTERONE CAUSES INSULIN RESISTANCE AND ANDROGEN EXCESS**

*Progesterone* refers to the hormone produced in the ovary. Progesterone medications are produced from a natural plant source (typically yams) but are chemically identical (*bioidentical*) to human progesterone. In contrast, *progestin* refers to a hormone that is synthetically produced and differs in many ways from natural progesterone. For purposes of classifying medications, the term *progestogen* refers to either natural progesterone or synthetic progestins. Progestins were originally developed because natural progesterone is not easily absorbed in pill form. Progestin pills are absorbed into the blood without trouble. Today, several natural progesterone products have been developed to overcome absorption problems. Despite this, the use of synthetic progestins remains commonplace. In fact, nearly all birth control pills and combination hormone replacement products still contain synthetic progestins.

Progestins do not always act as progesterone does in the tissues. While synthetic progestins may imitate some of progesterone's actions, they can cross-react with receptors for other hormones or cause other unwanted effects. The three main problems caused by synthetic progestins are insulin resistance, effects of androgen excess, and disruption of prolactin balance. Each progestin is slightly different in its ability to cause hormonal imbalance. Too much natural progesterone or unwanted effects from synthetic progestins can disrupt hormonal balance and start a cascade of other hormone problems that have a negative impact on health and body weight.

For reasons still not completely understood, synthetic progestins and, to a lesser extent, natural progesterone increase insulin resistance

and raise blood sugar levels. Synthetic progestins have a more potent effect on insulin sensitivity and have been known to cause diabetes in many cases. Most women who take progestins for long periods of time experience weight gain in the belly. Increased belly fat worsens insulin resistance, raises blood sugars, and increases the risk of developing diabetes. Many common side effects of progestins are thought to be, at least in part, complications of insulin resistance. These include blood clots in the legs and lungs, cholesterol problems, gallbladder problems, liver problems, menstrual cycle problems, fluid retention, insomnia, fatigue, depression, and anxiety.

Progestins can make you hungry, especially in high doses. One medication, *megestrol* (Megace), is used as an appetite stimulant in patients with cancer or AIDS. Progestin medications are known to lower HDL (good) cholesterol and raise LDL (bad) cholesterol. Progestins cause fluid retention, which can be responsible for bloating and cyclical edema.

Progestins can cause depression, irritability, and mood swings. It's thought that the effects of progestins on brain chemicals like *serotonin* and *norepinephrine* compound with insulin resistance to influence mood. Depo-Provera, an injectable progestin, is notorious for causing severe depression in some women.

Other unwanted effects of progestins are features of excess androgens, like facial hair and acne. Progestins have the ability to stimulate the receptor for male hormones—the androgen receptor. The *androgenic potential* varies among progestins, but in general the ones that have the most androgenic effects also have the most detrimental effects on insulin resistance, blood sugar, and cholesterol.

Progestins disrupt the balance of another important female hormone, *prolactin*. Breast tenderness and breast milk production are side effects in some women who take progestins.

The progestins *medroxyprogesterone*, *levonorgestrel*, *norgestrel*, and *norethindrone* are the worst in terms of the effects of excess androgen, insulin resistance, and weight gain.

Natural progesterone and the progestins *desogestrel*, *norgestimate*, and *drospirenone* are less androgenic and cause less insulin resistance. Desogestrel, norgestimate, and drospirenone are available only as combination tablets with estrogen. Most progestin products are birth control pills that combine progestins with synthetic estrogen. *Prefest* is a product used for hormone replacement therapy that combines natural

**Medications That Contain Norethindrone****Pure Norethindrone Products**

Aygestin

Micronor (birth control pill)

Nor QD (birth control pill)

**Combination Norethindrone Products**

Activella (hormone replacement therapy)

Brevicon (hormone replacement therapy)

FemHRT (hormone replacement therapy)

CombiPatch (hormone replacement therapy)

Eurostep Fe (birth control pill)

Loestrin (birth control pill)

Microgestin (birth control pill)

**Medications That Contain Levonorgestrel****Pure Levonorgestrel Products**

Nordette (birth control pill)

Norplant (birth control implant)

Plan B (emergency contraception pill)

**Combination Levonorgestrel Products**

Climara Pro Patch (hormone replacement therapy)

Aviane (birth control pill)

Alesse (birth control pill)

Seasonale (birth control pill)

Lessina (birth control pill)

Levlen (birth control pill)

Levlite (birth control pill)

Levora (birth control pill)

Portia (birth control pill)

Preven (emergency contraception pill)

Mirena (IUD)

## **Medications That Contain Norgestrel**

### **Combination Norgestrel Products**

Lo/Ovral (birth control pill)

Low-Ogestrel (birth control pill)

## **Medications That Contain Medroxyprogesterone**

### **Pure Medroxyprogesterone Products**

Provera

Depo-Provera (injectible)

### **Combination Medroxyprogesterone Products**

Lunelle (birth control pill)

Premphase (hormone replacement therapy)

Prempro (hormone replacement therapy)

estrogen (estradiol) with norgestimate. The products Yasmin and Yaz contain a unique progestin, drospirenone, that blocks some of the effects of androgens. Drospirenone is similar to the medication spironolactone, which blocks testosterone action (known as an *anti-androgen*). Drospirenone is a mild diuretic, which means it is associated with less fluid retention and bloating compared to other progestins.

Breakthroughs in medication delivery technology have produced natural progesterone products that are safe and reliable and have the approval of the FDA. *Prometrium* is a capsule form of progesterone that uses a process called micronization to make very tiny crystals, which are more easily absorbed through the digestive tract. Crinone and Prochieve are products with progesterone in a vaginal gel that is easily absorbed into the bloodstream and gets into the entire body.

**Natural Progesterone Products**

Prometrium (micronized capsules)

Crinone (gel)

Prochieve (gel)

Progestasert (IUD)

**Medications That Contain Desogestrel****Combination Desogestrel Products**

Apri (birth control pill)

Cyclessa (birth control pill)

Desogen (birth control pill)

Kariva (birth control pill)

Mircette (birth control pill)

Ortho-Cept (birth control pill)

**Medications That Contain Norgestimate****Combination Norgestimate Products**

Ortho Tri-Cyclen (birth control pill)

Ortho Tri-Cyclen Lo (birth control pill)

Ortho-Cyclen (birth control pill)

Prefest (hormone replacement therapy)

Natural progesterone is also available in the form of custom-made preparations, such as progesterone creams, from compounding pharmacies. Progesterone creams, extracted from Mexican yams, are a natural alternative reported to be effective in helping relieve the hot flashes of menopause. These creams are made by a variety of local pharmacies, so there is tremendous variability among different preparations. Some creams can be exceptionally potent, 10 to 20 times more potent than pills. I have seen many women gain weight from progesterone creams, and I do not recommend their use.

### ESTROGEN AND THE FAT CELL

Your body contains more than 30 billion fat cells. The fat cell contains the *aromatase* enzyme, which converts androgens to estrogens—primarily estrone. Estrone is the estrogen that gains dominance after menopause, when the ovaries shut down; before that, estradiol is the primary form of estrogen in the body. Given that fat cells convert androgens to estrogen, and that estrogen is primarily estrone, people who are overweight also have—guess what?—a lot more estrone than average. And remember, estrone is the “bad estrogen” that causes insulin resistance.

There's an irony here. The fat cell makes estrogen, but it's also influenced by estrogen. You've probably encountered this theme before in the book—that circle where hormones are made by a certain organ, and that organ is influenced by the hormone it produces. The body is truly one big feedback machine.

(Incidentally, the “metabolically evil” fat in your belly also results in too much cortisol; see Chapter 8.)

In terms of weight gain, women are not alike. Young women tend to gain weight where they already have fat—the buttocks and hips. Older women (and men) tend to gain weight in the belly. The former, the classic pear shape, is thought of as “gynoid”; the latter, the apple shape, is called “android.” So when estradiol production declines and estrone levels rise during and after menopause, fat in women tends to follow the same pattern as fat in men—going to the belly. This shape is associated with a greater risk of insulin resistance, metabolic syndrome, hypertension, diabetes, and cardiovascular disease.

Men and women have about the same number of fat cells, but the enzyme systems of the two sexes have subtle differences. The female fat cell is bigger and has more fat storage enzymes. Estrogen stimulates fat storage enzymes and determines where fat will be stored. It also directs where fat will be lost when a woman diets—making it difficult to lose weight in the places desired. (Every woman knows that hips and thighs can be particularly resistant to weight loss.) And men have more muscle than women: androgens create muscle, and muscle burns fat.

Women's fat cells are also more efficient than men's at storing fat. But consider: fat is protective, a reserve of energy for times of need. Back in prehistoric times, when finding food was a daily gamble, this reserve meant the difference between life and death—between having the support system for fertility and pregnancy and wasting away.

Estrogen, however, does not make you fat. It's more complicated than that. The point I'm trying to make is that there are differences between men and women with respect to the fat cell and how it responds to estrogen.

### **BIRTH CONTROL PILLS, SYNTHETIC ESTROGEN, AND YOUR WEIGHT**

The synthetic estrogen in birth control pills has become a regular part of care for millions of women all over the world. Ten million U.S. women take the pill, and despite 40 years of hand wringing and warnings from anti-birth control forces, it has become an accepted part of the American scene.

The main synthetic estrogen used in birth control pills is *ethinyl estradiol*. It's been blamed for weight gain—but this is due to the synthetic progestins as much as the synthetic estrogen. Synthetic estrogens raise the risk of blood clots, stroke, or heart attack in women over 35, especially those who smoke. There are dozens of brands of birth control pills on the market, containing different types and/or amounts of synthetic estrogen and progestin.

Birth control pills contain synthetic estrogen in varying amounts—low, medium, and high. As far as your weight is concerned, the medium-dose estrogen is the best (30–40 µg ethinyl estradiol). High-dose ethinyl



estradiol (50 µg) can cause nausea, headaches, and weight gain. The low-dose ethinyl estradiol (20–25 µg) also causes problems because it disrupts the balance of estrogen and progesterone.

Birth control pills come in two main classes, *monophasic combination pills* and *multiphasic combination pills*. This distinction is based on the relative doses of estrogen and progesterone. Monophasic pills keep the dose of estrogen and progesterone the same throughout the entire month. Multiphasic pills vary the dose of estrogen and/or progesterin throughout the month. The rationale for multiphasic pills is that they more closely simulate the hormonal fluctuations of a normal menstrual cycle. There is no evidence, however, that there is any advantage to taking a multiphasic over a monophasic pill.

### Medium-Estrogen Birth Control Pills

Apri	Nordette
Brevicon	Norinyl
Demulen 1/35	Norethin 1/35
Desogen	Ortho Tri-Cyclen
Estrostep	Ortho-Cept
Genora 1/35	Ortho-Cyclen
Jenest	Ortho-Novum 1/35
Levlen	Ortho-Novum 10/11
Levora	Ortho-Novum 7/7/7
Lo/Ovral	Ovcon 35
Loestrin 1/30	Tri-Levlen
Low-Ogestrel	Tri-Norinyl
Modicon	Triphasil
Necon 0.5/35	Trivora
Nelova 1/35	Yasmin
Neocon 1/35	Yaz
Neocon 10/11	Zovia 1/35

For most women, I recommend Desogen, Ortho-Cept, Ortho-Cyclen, Ortho Tri-Cyclen, or Yasmin because these birth control pills contain both an ideal level of estrogen and the best progestins.

Side effects of birth control pills include acne, headaches, breast tenderness, nausea, PMS, and depression. OCPs with the androgenic progestins *levonorgestrel*, *norgestrel*, and *norethindrone* can increase insulin resistance, raise blood sugar, and cause weight gain. OCPs with high doses of estrogen may also cause weight gain, but the medium- and low-dose pills do not cause weight gain. Life-threatening blood clots, heart attacks, and strokes are a real risk with birth control pills. The risk is highest if you smoke cigarettes. If you smoke, you should not use birth control pills.

### **TROUBLE LOSING WEIGHT AFTER PREGNANCY**

Women who have trouble losing weight after giving birth may have a thyroid problem known as *postpartum thyroiditis*. Short-term thyroid dysfunction lasting about one year is common after pregnancy. The condition may be misdiagnosed as *postpartum depression* and never be properly treated. Usually, the hypothyroidism gets better by itself and is forgotten. But the afflicted woman, by this time, has been miserable for about a year and may have gained tremendous amounts of weight. This condition occurs in up to 5 percent of American women. For more information on thyroid disorders, see Chapter 7.

### **MENOPAUSE IS NOT THE ONLY CONDITION THAT DISRUPTS FEMALE HORMONAL BALANCE**

Female hormones are under regulation from the brain, hypothalamus, and pituitary gland. Many things can go wrong that disrupt hormonal signals. The immune system can destroy hormone-producing cells in the ovary, resulting in early menopause.

### **Pituitary Gland Tumors**

Studies show that 15–30 percent of women have a tumor in the pituitary gland. Most aren't even aware of it. Tumors are usually very small and

don't cause much trouble. But problems arise if the tumor is a *prolactinoma*, or prolactin-secreting tumor. High prolactin levels shut down production of estrogen and progesterone, causing a woman to have symptoms of menopause. Tumors that cause high prolactin levels are associated with cessation of periods and *galactorrhea* (breast milk production).

Tumors can also cause problems if they grow too large. A large tumor will compress the rest of the pituitary gland, which can result in multiple hormone deficiencies. Sometimes pituitary tumors produce hormones that cause problems in association with other female hormone problems, like Cushing's syndrome (see Chapter 8), acromegaly, or growth hormone deficiency (see Chapter 9).

The following are symptoms of a possible pituitary gland tumor.

- Anger
- Breast milk production
- Depression
- Diabetes
- Facial hair growth
- Fatigue
- Headaches
- High blood pressure
- Infertility
- Insomnia
- Memory loss
- Menstrual cycle problems
- Mood swings
- Sexual dysfunction
- Vision problems
- Weight gain

### **Hypothalamic Amenorrhea**

Problems with female hormones are commonly seen with problems that affect the brain, including brain tumors and head trauma. Starvation and excessive exercise can also shut down female hormone production via the brain. When a woman's body fat drops too low, the brain shuts the ovary down as a form of self-protection. This is the reason many women with *anorexia nervosa*, as well as female athletes, stop having periods.

### **Premature Ovarian Failure**

Menopause is considered normal any time after the age of 45, but some women develop menopause much earlier.

The hallmark of menopause is the cessation of ovary function. Early menopause (also called POF, for *premature ovarian failure*) is usually due to an overactive immune system that destroys the ovaries. POF is associated with other autoimmune conditions like Hashimoto's hypothyroidism and Addison's disease. Smoking is a source of damage to the ovary as well. Women who smoke go through menopause one to two years earlier than women who do not smoke. Hormone replacement therapy is recommended for women who have had premature ovarian failure, at least until the age of 45 to 50.

### **WEIGHT GAIN DURING PERIMENOPAUSE AND MENOPAUSE**

Perimenopause is the time of transition just before a woman enters menopause. It's not always a gentle time. For a while—years for some women—a woman may have alternating periods of low estrogen mixed with surges of very high estrogen levels. Symptoms wax and wane, causing even more problems. This condition is commonly misdiagnosed as a thyroid problem or manic depression.

Perimenopause is also a time when many women gain weight, especially in the belly. Women who have always carried their weight on their hips and butt may experience a shift in the distribution of body fat to the middle section.

When estrogen levels become low, women frequently experience "vasomotor symptoms." The most common of these is called the "hot flash" or "hot flush," the latter term preferred by endocrinologists. Sleep disturbance is one of the most common symptoms of perimenopause. Sleep problems lead to disruption in growth hormone production (see Chapter 9).

Meanwhile, menstrual cycles may become irregular. Estrogen will surge at times, causing episodes of very heavy bleeding. The estrogen surges can contribute to the growth of benign uterine tumors known as *fibroid tumors*, or simply "fibroids" or "fireballs." They almost never cause cancer, but they are one of the most common reasons for the

necessity of a hysterectomy. Some can become quite large. One patient of mine gained 40 pounds when she was in her early 40s. All of the weight was up front, leading her (and many of her friends) to believe she had become pregnant. The truth turned out to be far less joyous: she had a 40-pound fibroid uterine tumor. She underwent a successful operation, and her weight is now back to normal.

Meanwhile, along with the estrogen surges—which cause weight gain and bleeding—come periods of low estrogen levels. It's at this time that women begin to lose the protective effect of estrogen. The risk of heart disease increases, bad cholesterol goes up while good cholesterol tumbles, osteoporosis sets in, and fat distribution begins to change.

Usually, estrogen (especially estradiol) causes fat to go to the hips, butt, and under the skin. But as estradiol levels drop in the early stages of menopause, and estrone takes on increasing importance, fat moves to the belly. This “visceral fat” or “abdominal adiposity” is the metabolically evil fat discussed in earlier chapters. Many women note that their breasts and hips get smaller, but they gain weight in their bellies during this time. When menopause is complete, this effect on weight distribution is even more pronounced.

Menopause is a stressful situation. Stress causes hormonal changes that slow metabolism and promote weight gain, including insulin resistance, low thyroid hormone activity, high cortisol, and low growth hormone.

Other symptoms kick in. Progesterone production declines, followed by erratic estrogen fluctuations. In many women, loss of androgens begins during perimenopause and is associated with symptoms of female low androgen syndrome (see Chapter 5). Menstrual cycles become irregular; hot flashes, sleep disturbances, vaginal dryness, weight gain in the belly, and shrinkage of breasts may occur. The fluctuations in hormones cause emotional instability.

It's at this time that women should carefully consider the risks and benefits of hormone replacement therapy (HRT). This is because changes due to *estrogen deficiency* begin in the body during perimenopause. In particular, this is a time when there is rapid bone loss, leading to *osteopenia* and *osteoporosis*.

The average woman goes through menopause at age 50 and dies at age 80. That's 30 years of post-menopausal life. On average, women

gain about 10 pounds in the first few years after menopause. Moreover, the body shape may change, with more weight going to the belly.

Why this weight gain? Is it the fault of menopause?

Doctors refer to menopause as a state of “estrogen deficiency.” Hormone replacement therapy (HRT) remains controversial and is not without risks. For some it is a smart move, while other women are better off not taking hormones. The biggest concerns about hormone replacement therapy include cardiovascular disease, weight gain, cancer, blood clots, gallbladder problems, and the unknown, all of which have scared women off HRT at one time or another.

In fact, most women do not make use of hormone replacement therapy. It is estimated that only 20 percent of women who could take hormones are given the opportunity to do so by their physicians. And among those who are prescribed HRT, half stop taking the hormones within the first year.

Estrogen has both positive and negative effects on other parts of the body. For the cardiovascular system, the effect is controversial. Early studies indicated that estrogen was good for the heart, but the Women’s Health Initiative and other studies have demonstrated that HRT increases the risk for cardiovascular disease. It is thought that HRT is good for the heart in younger women, but can increase the risk of cardiovascular disease as women get older.

It is known that estrogen improves insulin resistance, but this doesn’t mean that the benefits outweigh the risks. Other studies suggest that estrogen replacement given early on is good for the heart, but if you wait too long, the opposite is true.

Estrogen replacement therapy, when taken in the proper dosage and form, improves insulin resistance and body fat distribution. (The key is “taken in the proper dosage and form”: if estrogen medication is taken in higher dosages or the wrong form, it can *worsen* insulin resistance; and if it is taken via the patch as opposed to pills, the positive effects are diminished.)

The average age of menopause is 51. This hasn’t changed since records were first kept about this life change, about 600 A.D. In the perimenopausal years, estrogen production declined; at menopause the aging ovary shuts down and stops making estrogen entirely. Progesterone deficiency occurs as well, although the significance of this is not as well understood.

One of the most concerning features of estrogen deficiency is bone loss. Osteoporosis—or the milder version, osteopenia—is a painless, silent disease. Unless tested for it, most people have no idea they even have it until they break a bone. And once a bone is broken, the chances of acquiring another illness—such as pneumonia or a blood clot—are greatly increased. Fractures of the spine known as compression fractures make women shorter as they age and give them that all-too-familiar humped back, known as *kyphosis*. Indeed, many women die within a year of their first broken bone from osteoporosis.

The symptoms of menopause include:

- Anger
- Anxiety
- Cardiovascular disease
- Depression
- Dry skin
- Fatigue
- Hot flashes, also known as hot flushes because the woman may become red and flushed
- Irritability
- Memory loss
- Migraine headaches
- Osteoporosis or osteopenia
- Sleeping problems and insomnia
- Urinary tract infections
- Vaginal dryness and pain with intercourse (dyspareunia)
- Weight gain, especially around the belly

### TESTING FOR FEMALE HORMONE PROBLEMS

Most hormone tests aren't the be-all and end-all of diagnoses. So many variables come into play, and so many mistakes can be made, that before you allow the diagnosis to stand, you should always make sure that (1) your doctor is very familiar with your diet and lifestyle and (2) your doctor knows how to properly interpret test results.

In women, there are additional variables. Levels of female hormones undergo tremendous fluctuations over the course of a month,

something that is simply part of the female cycle. Symptoms of menopause—such as vaginal dryness, hot flashes, and a loss of sex drive—in combination with the cessation of menstrual periods, are about as good an indicator as any blood test. Most women do not need, and have never needed, a blood test to tell them they are menopausal. If problems are suspected, female hormones should be tested:

### **Follicle-Stimulating Hormone (FSH)**

As the ovary makes less and less estrogen, the brain responds by increasing FSH levels. Although both LH and FSH are released from the pituitary gland to control the ovary, FSH is the first hormone to increase in menopause. Doctors call this a *monotropic FSH rise*. The elevation of FSH with a normal LH level is a common situation in early menopause. If you are still menstruating, the best time to measure your FSH level is on the second day of the menses. If the FSH level is more than 10 mIU/mL, it means that the ovaries are beginning to fail. An FSH level over 40 mIU/mL suggests menopause, but should be confirmed by a second test. FSH levels fluctuate wildly, so repeat testing often gives very different results. A low FSH level can indicate a problem with the hypothalamus or pituitary gland.

### **Luteinizing Hormone (LH)**

Eventually LH will rise, but elevated FSH is the first indicator. A low LH level can signal a problem with the hypothalamus or pituitary gland.

### **Estrogen Levels**

The most common test performed is measurement of *estradiol*, but *estrone* and *estriol* levels can also be measured. Estradiol is an indicator of “healthy” estrogen levels. Estradiol levels drop in menopause, but estrone (the estrogen made from fat) may actually go up. Estradiol should be checked on day 2 or 3 of your menstrual cycle (follicular phase). An estradiol level less than 80 pg/mL is suggestive of estrogen



deficiency, and levels below 50 pg/mL are highly suggestive of estrogen deficiency. Levels up to 200 pg/mL are considered normal. Estradiol levels can fluctuate wildly during perimenopause.

Estradiol levels can also be used to monitor the adequacy of hormone replacement therapy (HRT). If you are on HRT and are tired, are gaining weight, or have other symptoms of menopause, your dose may be too low. Many women have symptoms of menopause (including weight gain in the middle) when their estradiol levels are below 80 pg/mL.

### **Saliva Tests**

Salivary measurements of female hormones are not considered reliable. Salivary testing is not accurate enough, and the normal range has not been clearly defined. Salivary hormone measurements hold promise, though, and may become the standard method of measuring female hormone levels in the future.

### **Prolactin**

Elevations of prolactin may indicate a pituitary tumor, a common cause of female hormone problems. If you have an elevated prolactin level, you probably need to have an MRI scan to evaluate the pituitary gland.

### **Androgen Testing**

Problems with male hormones, androgens, are a common cause of female hormone problems. For more information, see Chapter 5.

### **Thyroid Testing**

Thyroid problems frequently occur in association with female hormone problems. The risk for thyroid disease increases with age. Up to 15 percent of menopausal women have a thyroid problem. Symptoms of thyroid problems can overlap with those of female hormone problems and can confuse the diagnosis. Estrogen-containing medications can make certain thyroid tests invalid. For more information, see Chapter 7.

### **Liver Function Tests**

Because liver disease can be associated with female hormone problems, liver function should be checked periodically. Alanine transaminase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transpeptidase (GGT), alkaline phosphatase, bilirubin, albumin, and prothrombin time are all tests of liver function.

### **Hemoglobin and Hematocrit**

Heavy menstrual cycles can result in low red blood cell counts, known as *anemia*, which are measured by the hemoglobin and hematocrit tests.

### **Bone Density Testing**

Because low estrogen is an important causal factor in thinning of the bones (*osteopenia* or *osteoporosis*), all women over the age 65 of should have a bone density test or *bone mineral density* (BMD) test performed. *Dual-energy X-ray absorptiometry* (DEXA) is the most accurate and advanced test available for measuring bone density. The test is quick and painless and gives very important information about the density of bones.

### **Other Health Maintenance**

Menopause should be a reminder to make sure you are up to date with regular health maintenance, such as having a mammogram, colonoscopy, EKG, or cardiovascular stress test.

### **HRT AND ALTERNATIVE THERAPIES**

Menopause is frequently associated with weight gain—on average, several pounds. But not all women gain weight, and some women gain quite a lot. Obviously, other factors come into play: heredity, weight distribution, and diet.

Estrogen replacement therapy does not necessarily help women lose weight. It may redistribute fat to the chest and hips, places where it was in more youthful days, instead of the stomach, where it tends to go during and after menopause. And a quarter of women who take estrogen actually gain weight, even if only a couple pounds of fluid retention. This is one of the reasons that only 30 percent of all menopausal women use HRT.

But what estrogen *can* do is improve vitality and insulin resistance, two key factors in battling the bulge. Estrogen can help you feel younger, helping you to maintain a more active lifestyle—as well as more muscle. Although estrogen does not have a major effect on your weight, it does on your body composition. Studies confirm that women who take estrogen have more muscle and less fat than those who do not. Estrogen medications do not cause significant weight gain; however, you may notice an increase in lean tissue (muscle and bone) and a decrease in fat. This may lead to a small increase in weight (but also a smaller body).

Each formulation of HRT has its advantages and disadvantages. Estrogen pills are absorbed through the intestines to the bloodstream and then transported to the liver, where they are metabolized. This is known as the “first-pass effect.” (The liver is an important organ in the insulin resistance game; it’s through the liver that estrogen improves insulin sensitivity.) For the most part, estrogen pills improve insulin resistance. The estrogen patch avoids the liver and has less of an effect on insulin. Estrogen from patches is absorbed through the skin and then transported directly into the general circulation, so the effects on the liver are greatly diminished, though not eliminated. Estrogen pills decrease LDL (bad) cholesterol and increase HDL (good) cholesterol, but the patch’s impact here is, again, diminished. Estrogen pills, ironically, can increase triglycerides, but the patch can lower them. The patch is less likely to cause blood clots as well as perhaps migraine headaches and gallbladder problems than the pill.

HRT has become increasingly controversial in recent years. The standard advice given by many professional organizations is that HRT should be used only to treat the “symptoms of menopause,” primarily hot flashes. It is also recommended that the lowest possible dose of HRT be used for the shortest possible amount of time, usually 3 to 5 years. Nausea and breast tenderness are the most common side effects of estrogen. It usually helps to start at a very low dose and increase it

gradually. Weight gain, vaginal discharge, acne, and headaches may accompany HRT.

Studies such as the Women's Health Initiative have brought estrogen's safety into question. Nevertheless, many women do benefit from HRT. Each woman needs to discuss all the risks and benefits with her physician to determine if HRT is right for her. The risks of HRT include an increased chance of cardiovascular disease, blood clots, breast cancer, gallbladder disease, liver disease, elevated triglyceride levels, high blood pressure, and headaches.

Estrogen benefits include increasing "safe" fat. Without estrogen, metabolically evil belly fat increases, making insulin resistance worse. HRT raises good (HDL) cholesterol and lowers bad (LDL) cholesterol, the pills more so than the patch. Estrogen prevents menopausal bone loss, but this is not the best reason to take HRT, since other medications are available to prevent bone loss. Estrogen's effect on bones also helps women hold on to their teeth. Estrogen helps skin retain collagen and prevents early wrinkling. Although this is considered controversial, estrogen is thought to protect against ovarian cancer and may also protect you from colon cancer. Most women who take HRT feel younger and more vibrant.

A woman's decision to initiate hormone replacement therapy is a personal one. You must look at all the advantages and disadvantages in terms of yourself; everyone is different. For example, if you have a pronounced family history of breast cancer or heart disease, you may be less inclined to take estrogen than someone in the opposite situation. On the other hand, if you are at particular risk for osteoporosis or have side effects from osteoporosis medications, you may be willing to accept the slight risk of breast cancer or cardiovascular disease in return for the positive effects on bones. The bottom line is that each woman has to weigh her own risks and benefits and come to a decision with her physician.

Most estrogens come from natural sources, but natural does not always mean better. Premarin, which is considered a "natural" hormone, is extracted from the urine of pregnant horses and contains estrogens that are foreign to humans. There is no "cookbook" dose of estrogen. In my experience, women usually have to try two or three (or sometimes more) different doses or brands of estrogen until they find the one that suits them. If you've had problems with estrogen in

the past, don't give up; it's likely you'll find a regimen that works for you. I usually start with a low dose of estradiol and increase the dose over the next 6 to 12 months. If this doesn't do the trick, I will switch to a different form of estrogen. As always, a healthy lifestyle is an important aspect of female hormonal balance. Even if you don't take HRT, there are still many things you can do to help balance female hormones. Regular physical activity and the Hormonal Health Diet are as important as medications and enhance the effects of HRT.

### **Bioidentical Hormones**

Bioidentical hormones are also called “natural” hormones because they are identical to the hormones made naturally by the body. They are available as prescription products approved by the FDA and as custom-made products prepared by compounding pharmacies. Bioidentical hormones can be taken as a pill, cream, gel, patch, or injection. As with all hormone products, prescription products are preferred over compounded products because the quality control is much better. There is no scientific proof that bioidentical hormones are safer or more effective than synthetic hormones. Having too much estrogen in the blood, whether natural or synthetic, can cause problems. One advantage to bioidentical hormones is that they can be measured in the blood. This makes treatment easier because you can monitor estrogen levels to tailor the dose.

### **Estradiol**

Pure estradiol in the form of *17-beta estradiol* is available in a variety of formulations. Estradiol (Estrace) is a bioidentical natural hormone that is derived from plant sources. The pills are made using a special manufacturing process called *micronization*, which produces a pill that dissolves into very small pieces. This allows the estradiol to be easily absorbed into the system. Estradiol is called a “natural estrogen” because it is the most abundant form of estrogen in the body during the reproductive years and is responsible for many of the benefits attributed to estrogen.

Estradiol patches, also known as *transdermal estrogen therapy*, has both advantages and disadvantages. The patch has less benefit in terms of insulin resistance and improving cholesterol. On the other hand, the patch is associated with fewer blood clots and triglyceride problems. The blood clot issue makes the patch a better alternative for smokers.

The patch provides the steadiest levels of estrogen. Estrogen levels spike and then fall after taking the pill, but they remain constant with the patch. But there are problems to be aware of: The patch can fall off or irritate the skin. Dosing is inflexible; if you need a value in between the available patch doses, you are out of luck.

### **Estradiol Patches**

Estraderm

Alora

Climara

Vivelle

*Micronized estradiol cream* (Estrace cream) is excellent for its relief of vaginal and urinary symptoms (known as *atrophic vaginitis*). Only small amounts of estrogen enter the general circulation, so the effect remains localized to the vagina. Estring is a flexible, time-release source of estrogen that is inserted into the vagina like a diaphragm. It can be left in place for up to 3 months. As with the cream, not much of the estrogen from the ring is absorbed into the bloodstream, which makes it best for relief of vaginal dryness and urinary problems.

### **Conjugated Equine Estrogens (CEE)**

*Conjugated equine estrogens* (Premarin) are among the most common estrogen products used for HRT. Many think Premarin is a synthetic estrogen, but it is a natural form of estrogen (just not natural to humans). CEE is a collection of estrogens extracted from the urine of pregnant mares (thus “pre-mar-in”). Since it comes from horses, it is

“natural.” The exact components of Premarin have never been completely identified, but the substance contains at least 10 different estrogens. The most abundant of these is estrone. Estrone is the type of estrogen that is associated with insulin resistance and weight gain. Another concern with CEE is that besides estrone, CEE contains other forms of estrogen not natural for humans; these are estrogens for horses known as *equilenin* and *equilin*. *Conjugated estrogen cream* (Premarin cream) is also available to treat vaginal symptoms.

*Conjugated synthetic estrogen* (Cenestin) is a synthetic estrogen product that contains high levels of estrone.

### **Esterified Estrogens**

Estratab and Menest, known as *esterified estrogens*, contain several types of estrogens derived from plants. Estrone is the primary ingredient.

### **Estropipate**

Ogen and Ortho-Est are brands of *estropipate*, which is considered a natural estrogen. This estrogen is very similar in chemical structure to estrone. Estrone is a “bad estrogen” and can contribute to insulin resistance and weight gain, but there is no proof that estropipate, in the proper doses, does this. It’s worth a try if other estrogens have not worked for you. Estropipate cream (Ogen cream) is also available for vaginal symptoms.

### **Estrogen Progesterone Combination Therapy**

Progesterone or synthetic progestins are added to hormone replacement therapy for only one reason: to prevent uterine cancer. If you have had a hysterectomy, there is no reason to add progesterone to your HRT. There are several ways to take progesterone.

With *cyclic dosing*, a larger dose of progesterone is added to the daily estrogen for 5 to 14 days a month. You will continue to have

monthly cycles. The natural hormonal cycles are mimicked in this regime, but the cycle is far from being exactly like the natural hormonal ebb and flow. Expect to have a short and light menstrual period six hours or so after the last dose of the month. The periods will be very regular. This form of HRT can also result in PMS, something most women would like to avoid.

In *continuous dosing*, a smaller dose of progesterone, in combination with estrogen, is taken every day. You may have irregular and unpredictable spotting for up to 6 months, but you should then have no further bleeding. Most women prefer this to the cyclic dosing. Continuous dosing protects against uterine cancer better than cyclic dosing. Twenty percent of women who use cyclic dosing will stop having periods after a while. This is OK: the lining of the uterus has simply become inactive.

A new regimen for HRT is known as *pulsed progestin HRT*. Here the progesterone is given for three days on, followed by three days off. The difference is perhaps fewer side effects and better protection against uterine cancer than with traditional continuous dosing, without the withdrawal bleeding you will have with cyclic dosing. Ortho Prefest is a combination estrogen-progestin product that alternates three days of estradiol alone with three days of estradiol plus the progestin, norgestimate.

Estradiol is available in combination products for hormone replacement therapy. These products all combine natural estrogen with synthetic progesterone. Ortho Prefest contains norgestimate, which is considered a healthier type of synthetic progesterone than norethindrone, which is an ingredient of Activella and FemHRT.

### **HRT Combination Products That Contain Estradiol**

Activella

FemHRT

Prefest

CombiPatch



CombiPatch is a combination patch for HRT that contains estradiol and norethindrone. Prempro and Premphase contain conjugated equine estrogens and medroxyprogesterone. Both of these ingredients have been blamed for causing weight gain.

### **Raloxifene (Evista)**

One new alternative to estrogen is a SERM, or *selective estrogen receptor modulator*, also known as a *designer estrogen*. These products have some of the positive effects of estrogen without some of the negative effects. SERMs may be a consideration if you cannot take estrogen. They have “selective agonist and antagonist properties”—remember the lock and key analogy—and thus stimulate the estrogen receptors in some tissues while blocking the receptors in others. Doctors call this action “tissue specific” or “mixed agonist-antagonist.”

There are some disadvantages to SERMs. They're not quite as good as estrogen for bones, although they remain a great choice. They do not relieve the symptoms of menopause, such as hot flashes, and they may even make the symptoms worse. But the biggest problem is lack of knowledge. The drugs are too new to have any long-term research or patient experience to draw from. The other problem is that there is no “perfect” SERM. The perfect SERM would act like estrogen at the level of the bones, the heart, and the blood vessels, but would block estrogen at the level of the breast and uterus. It would lower breast cancer and uterine cancer risk, prevent osteoporosis, and help the heart and blood vessels. Raloxifene is a good SERM, but better SERMs and more specialized SERMs are in development. Maybe one day a special SERM for women who want to lose weight will be developed.

### **Clonidine (Catapres)**

Clonidine is a widely used medication for high blood pressure, available in both pill and patch forms. It's another potent regulator of body temperature. Clonidine is also commonly used to treat the symptoms of menopause. The main limitation of clonidine is that it can make some women sleepy.

### **Vitamin D**

Menopause is a time when women have bone problems, and although these are usually attributed to estrogen deficiency, vitamin D deficiency (known as *osteomalacia*) is a major cause of bone problems in the United States. Vitamin D is actually a steroid hormone, one that allows your gut to absorb calcium. Without it, most of the calcium you eat passes right into your stool. Most people do not get enough vitamin D from sunlight and dairy products. Vitamin D deficiency can cause bone pain and fatigue. I recommend 800–1000 IU of vitamin D every day.

### **Calcium**

This key mineral becomes even more important to women as they age. If a person suffers from a shortage of calcium, the body will take the differential directly out of the skeleton, leading to bone loss. Studies have also shown that consuming calcium, particularly in the form of low-fat dairy products, can accelerate weight loss. It's thought that calcium somehow enhances the action of fat-burning enzymes in the body.

Physicians recommend, before menopause, a daily minimum of 1000 mg of calcium in food and/or supplements. During and after menopause, at least 1500 mg of calcium is recommended. Keep in mind that the average American consumes less than 800 mg per day.

Calcium should be consumed over the course of the day, not all at once, and always with plenty of water. (All humans should drink plenty of water anyway; not only does it help with absorption, as in the case of calcium, but it flushes the system.) Unfortunately, high-fiber diets prevent the absorption of calcium, so you should take this into consideration when taking calcium supplements. It's better to get your calcium as *part* of such a diet, not *in addition* to it. Calcium itself interferes with the absorption of iron, so iron supplements and calcium supplements should not be taken at the same time.

All calcium preparations contain “elemental calcium” for a simple reason: calcium is an element, number 20 on the periodic table. But it cannot exist alone and must be bound to another atom or molecule to be stable. For this reason, not all calcium supplements are created

equal. Calcium carbonate, for example, has about 40 percent calcium, so the typical 1250 mg tablet has about 600 mg of elemental calcium. Calcium citrate, however, contains only 21 percent calcium—so an equivalent tablet has almost 300 mg less elemental calcium. It's an old saw, but one that holds true: Always read those labels!

Calcium carbonate is the most common calcium preparation available. It's got the highest percentage of calcium and is readily available in sources ranging from oyster shells to antacid tablets. The most common side effect is gas or upset stomach. Calcium citrate is a good alternative for people who have side effects from calcium carbonate. Calcium itself is a mineral in milk, cheese, yogurt, collard greens, kale, broccoli, and sardines.

### **The Hormonal Health Diet**

The Hormonal Health Diet is an important part of achieving female hormonal balance.

### **Physical Activity**

Weight-bearing exercises, such as walking and lifting weights, are ideal for menopausal women because they prevent bone loss. Physical activity helps add lean body mass, aids with fat loss, and improves insulin resistance.

### **Natural Menopause Supplements**

Many of the natural menopause products available in grocery stores, drug stores, and health food stores contain soy isoflavones. Isoflavones are chemicals extracted from plants (like soybeans) that are similar to (but not exactly the same as) estrogen. For the most part, I am hesitant to recommend these products at this time. Concentrations of isoflavones vary tremendously from brand to brand and pill to pill. In addition, because isoflavones are not identical to estrogen, their effects are not identical to those of estrogen. I do recommend consuming foods high in plant estrogens to help with your menopausal symptoms.

### Estrogen and Progesterone in Foods

Natural estrogens and estrogen-like substances found in nature are known as *phytoestrogens* (plant estrogens). More than 300 different plants—including soybeans, lentils, whole grain wheat, whole grain cereals, dried seaweed, rice, dates, flaxseed oil, bean sprouts, pomegranates, cherries, and coffee—have been found to contain estrogen-like substances. A number of herbs contain estrogen. These include parsley, garlic, licorice, red clover, thyme, turmeric, hops, and verbena. Black cohosh (*Cimicifuga racemosa*) and red clover (*Trifolium pratense*) are the best-known herbal sources. Red clover contains a phytoestrogen called *coumestrol*, which is also found in bean sprouts.

At least 20 naturally occurring estrogen-like compounds, with names like *lignans* and *isoflavonic phytoestrogens*, have been identified. They are slightly different in how they stimulate or block the two estrogen receptors. In general, they're weaker than actual estrogen, and they don't build up in tissues like estrogen does. But they seem to have a positive effect against several types of cancer, including breast cancer, uterine cancer, and prostate cancer.

Phytoestrogen usage dates back centuries, even to the time of Hippocrates. It was only when some sheep became sterile, however, that they were recognized as such; the sheep had eaten clover containing the substance.

Interestingly, despite their long history of use, phytoestrogens haven't been studied much, and their effect on weight and various organs remains unknown.

Another common nutrient that has had a positive, estrogen-like effect on women is soy. Soy products may reduce risk of breast cancer, lower cholesterol, and prevent heart disease. (Asian women have traditionally had an easier time with menopause than Western women.) Several soy phytoestrogens have been identified, known as *flavonoids* and *isoflavonoids*. (Among the best known are *diadzen*, *genistein*, *glycitein*, and *coumestrol*.) Many soy isoflavone products are now available in pill form from health food stores and drug stores.

Soy, of course, can be a central part of any diet. Soybean oil, the most commonly used oil in the world, pops up in a number of products, even ones that claim to use "vegetable oil." The catch is that soybean oil has often been hydrogenated in products like margarine and

shortening (see Chapter 2). If possible, avoid products that have been hydrogenated.

Oil isn't the only product that contains soy, of course. There's soy protein, found in cookies, cakes, breads, breakfast cereals, pasta, and processed meat products; soy milk, an excellent source of nutrition for people who are lactose intolerant; soy flour; tofu; miso (soybean paste); and tempeh (soybean cake), used as a meat substitute.

Just as there are *phytoestrogens*, there are *phytoprogesterones*. Mexican yams and yam root generally are the most common sources of progesterone and are contained in the medications discussed previously. The chemical substance *disogenin* is the progesterone-like component of the yam. Other herbs with progesterone properties include oregano, verbena, turmeric, thyme, red clover, and damiana.

### Fruits and Vegetables

Don't forget about fruits and vegetables! These contain many other vitamins and phytochemicals helpful in menopause. The Hormonal Health Diet will help regulate your body weight and hormones. And, as with any good health regimen, sleeping well and exercising are important as well.

### Chocolate

Many women know about the intense craving for food—particularly chocolate and sweets—that hits during the second half of the menstrual cycle, the time before menstruation. After ovulation, estrogen levels drop slightly and progesterone levels rise markedly. Progesterone is produced by the ovary in preparation for possible pregnancy. There are a number of theories about this, but essentially it comes down to one simple fact: *progesterone makes you hungry*.

Why chocolate and sweets? Chocolate—the sweetened, Hershey bar or M&M form we're used to—contains the three most valuable food groups if you're craving food: fat, sugar, and mood-affecting chemicals. Fat, as we know, provides comfort. Sugar offers energy. And the chemicals, which include *phenethylamine* and *theobromine*, have the same

effect on the brain as more expensive antidepressants, offering a rush of *serotonin* along with a calming influence.

Chocolate gets a lot of guff, but it won't get it from me. Not only does it taste great, it's not the major bugaboo that some health authorities would have you believe. Chocolate was considered an aphrodisiac a few hundred years ago (and there are more than a few people who will tell you it's a worthwhile forerunner to sex today). It doesn't necessarily lead to weight gain, either: the French and Swiss, who eat far more chocolate than Americans do, have less obesity than Americans. Chocolate is rich in a substance called *phenolics*, the same chemical found in red wine, and may decrease the risk of heart disease, as wine does. And chocolate cravings may not necessarily be a sign of weakness, but merely a result of *acylethanolamines*, chemicals that may have a similar effect on the brain as marijuana. Marijuana has been known to create a condition known as "the munchies," a sudden craving for food. Chocolate can do the same thing.

On a larger level, women may have carbohydrate cravings just before or after the menstrual period. This is because the second half of the menstrual cycle is associated with altered glucose metabolism. As we've seen in past chapters, a slowdown in metabolism is often answered by a desire for more food, not less—at least until the body exhausts itself. The body wants energy, and the most immediately available form of energy is in sugars and starches. The Hormonal Health Diet will help eliminate food cravings.

# THYROID HORMONE

IT IS A SMALL, BUTTERFLY-SHAPED, BROWNISH-RED ORGAN LOCATED AT THE BASE OF THE THROAT. It weighs only about an ounce, and it contains and secretes relatively small amounts of two hormones. But this small structure, the thyroid gland, and the substances it produces have a wide-ranging impact on your health—an impact that is often misunderstood or ignored.

Millions of Americans suffer because their thyroid hormone levels are too low. It's easy to overlook the effects of a healthy thyroid gland, as easy as overlooking simple good health. The thyroid helps regulate body temperature. The thyroid controls metabolism. The thyroid helps maintain psychological well-being, appetite, energy level, sex drive, and mood.

If you develop thyroid dysfunction, your body systems can go haywire. An underactive thyroid (hypothyroidism) can lower your energy level. Suddenly, your metabolism slows down. You're tired, so you don't feel like exercising. Coupled with the lowered metabolism, this lack of activity promotes depression and anxiety and begins a vicious circle, which—pardon the term—feeds on itself. You become irritable, unhappy, and overweight.

Many people have heard about underactive thyroid as a cause of weight gain. They know an underactive thyroid makes them tired and depressed, makes their hair fall out, and gives them dry skin. But when they go to the doctor, they get a standard “TSH” test and are told

everything is OK—if that. Doctors often overlook the role of the thyroid in this vicious cycle. Nowadays, it's easy enough to suggest psychotherapy and prescribe a pill, such as Prozac or Zoloft, for depression. Certainly, many things can bring on depression, and a capable psychiatrist can help patients come to terms with their issues and thought processes. But this "it's all in your head" diagnosis ignores the importance of the thyroid in affecting mood, appetite, and metabolism.

More and more physicians are becoming aware of underactive thyroid and the role it can play. Endocrinologists, such as myself, are treating milder and milder cases all the time, and scientific data is finally coming out that confirms what clinicians have known all along—that you can have normal thyroid tests and still have thyroid dysfunction. There are many reasons this can occur, ranging from brain tumors to environmental toxins to nutritional problems and even stress.

Given the thyroid's importance to metabolism, any insult to the system—whether it is stress, other hormone problems, improper diet, nutritional or vitamin deficiencies, or toxins—can block the critical conversion of one type of thyroid hormone to another, a conversion that is key to metabolism regulation. Without a diagnosis and treatment that includes the thyroid, many patients who could be well on their way to better health and loss of weight may remain in that vicious cycle for years. And that's something no diet can cure.

This chapter will outline modern thoughts on thyroid dysfunction. I will stress symptoms that may be a clue to a thyroid disorder. This chapter will be helpful if you suspect you have thyroid disease, or if you've been diagnosed with hypothyroidism and are taking medications, but still don't feel well. For more information, please read my book, *A Simple Guide to Thyroid Disorders*, which has more detailed information about thyroid disease.

## **THE FACTS ABOUT THYROID DISEASE**

Thyroid disease is much more common than most people realize. It is estimated that more than 10 million Americans have some form of thyroid disease. (Some estimates put the figure at as many as 1 in 10, or almost 30 million Americans.) Women are 10 times more likely to get thyroid disease than men. And thyroid disease is more likely to affect



you as you get older. Given the current demographic trend of the United States—with more and more of the 75 million person-strong group of baby boomers (persons born between 1946 and 1964) passing age 50 each year—there's a strong possibility that thyroid disease may be on the rise.

But thyroid disease is difficult to pin down. Thyroid problems tend to present themselves in the form of a wide variety of medical complaints. Each person is affected differently: you may have one, two, or many symptoms. Any or all of the body's organ systems may be influenced by changes in the thyroid.

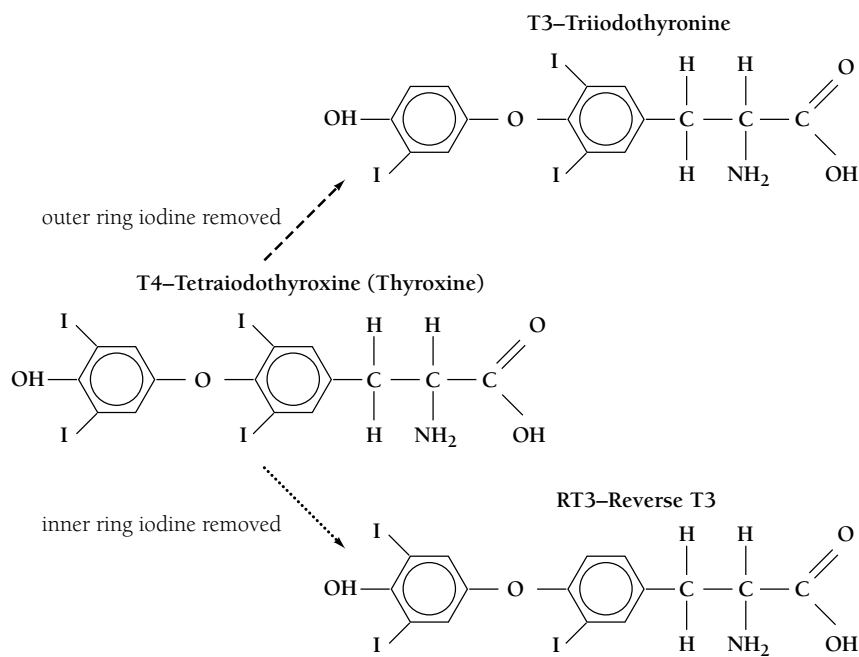
When weight problems begin, many people suspect that the thyroid gland may be at fault. They may have noticed other symptoms, such as a diminished sex drive or simple fatigue. But their doctors tell them that everything is OK; the problem lies elsewhere. This isn't necessarily the physician's fault. Traditional thyroid tests may not detect subtle or even not-so-subtle forms of thyroid disease.

## HOW THYROID HORMONES ARE MADE

Let me take a minute to discuss how thyroid hormones are made. The backbone of thyroid hormone is an amino acid called *tyrosine*. Tyrosine is found naturally in protein (amino acids such as tyrosine are the building blocks of protein) and is also available in capsule or pill form from many health food stores. Two tyrosine molecules are linked together to form a double ring structure.

There two types of thyroid hormone, *triiodothyronine* (T3) and *thyroxine* (T4). The 3 and the 4 refer to the number of iodine molecules attached to the double ring structure. A healthy thyroid gland produces about 80 percent T4 and 20 percent T3.

T4 is considered an "inactive hormone." In order for the T4 hormone to become activated, one of the iodine molecules on the outer ring must be removed by special enzymes. This process is known as T4 to T3 conversion, or *deiodination*. The three-iodine version, triiodothyronine, or T3, is the active and most potent form of thyroid hormone. An inactive form of thyroid hormone, known as *reverse T3*, is created when the iodine molecule is removed from the inner ring instead of the outer ring. Problems with removing iodine, or removing the wrong iodine molecule, can lead to thyroid dysfunction.



**Figure 7.1**  
**THYROID HORMONE STRUCTURES**

Note the similarities among thyroid hormones. T4, thyroxine, is a mostly inactive hormone that is converted by enzymes to its active form, T3 (triiodothyronine), by removing an iodine molecule from the *outer ring*. If an iodine molecule is removed from the *inner ring*, T4 is converted to “reverse T3,” an inactive hormone.

The enzyme responsible for removing this outer-ring iodine from T4 is known as *selenodeiodinase*. Selenodeiodinase is known by that name because it contains the element *selenium*, a trace mineral necessary for the enzyme to function properly. Another trace mineral, *zinc*, is also important for proper enzyme function. A deficiency of selenium or zinc can cause problems with the conversion of inactive T4 to the active T3. Too much copper in the diet can also block the conversion process. Low T3 levels slow metabolism and cause weight gain.

A common blood pressure medication known as propranolol (Inderal) can inhibit the conversion process. Propranolol comes from a

class of drugs known as beta-blockers. Another medication, amiodarone, also causes thyroid hormone conversion problems. Amiodarone is a heart medication currently growing in popularity. Interestingly, amiodarone has been found to cause a variety of thyroid difficulties, including over- and underactivity.

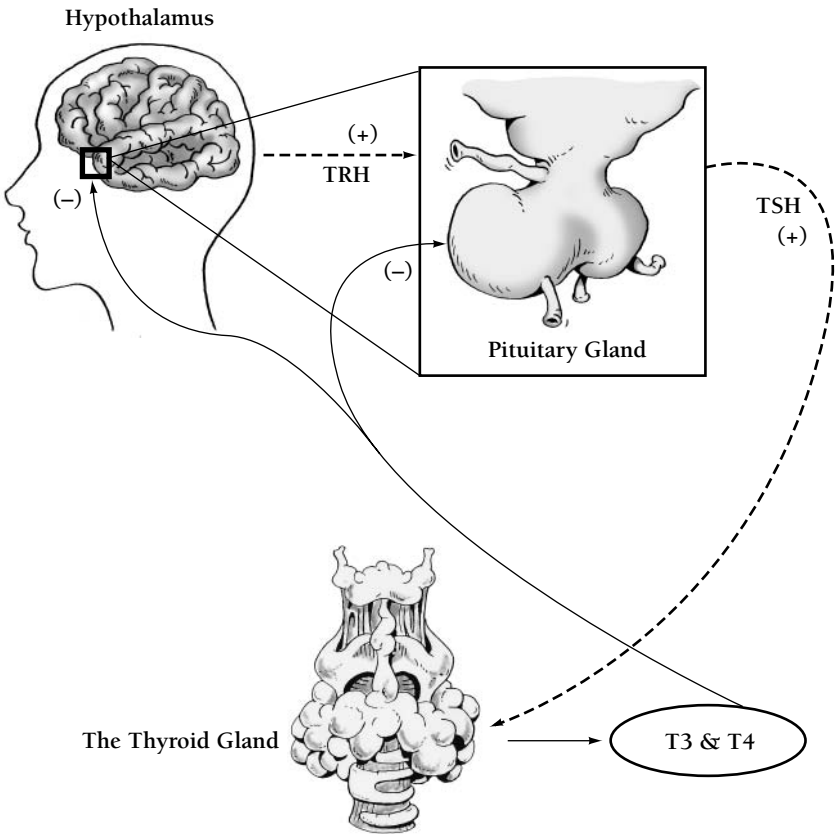
## THE BRAIN REGULATES THYROID HORMONE PRODUCTION

Your body is a collection of systems constantly changing based on the short-term and long-term messages it receives from the brain. As your senses come into contact with new information—as you hear a baby’s coo, for example, or see a car ahead stop short, or even if you simply feel hungry—your brain puts the various systems to work. Because of the hormones it secretes and those hormones’ importance in dealing with stress, the thyroid is a key link in making those systems work.

It starts with signals from the brain. Your body is undergoing a stressful event; the brain immediately starts sending messages to parts of the body in the form of hormones. The hormones originate in the section of the brain known as the hypothalamus, the part of the brain that regulates the internal activities of the body. Along with hormone production, these activities include sexual behavior, emotions, and functions of the autonomic nervous system. The hypothalamus, which is located roughly behind the eyes, is hard-wired to almost the entire nervous system and directs the “fight or flight” impulse that puts such stress on the body.

To get to the thyroid, the hypothalamus sends a message to the pituitary gland in the form of a hormone—TRH, or *thyrotropin-releasing hormone*. The pituitary gland reacts to the influx of TRH by releasing a second hormone—TSH, or *thyroid-stimulating hormone* (aka *thyrotropin*). TSH travels through the bloodstream to the thyroid gland and directs it to produce thyroid hormones. The pituitary is responsible for making sure the level of thyroid hormones in the blood remains constant, so if thyroid hormone levels fall, the pituitary gland increases its production of TSH. Incidentally, TRH can also stimulate production of another pituitary gland hormone, *prolactin*. For more on prolactin, see Chapter 6.

Because of its impact on the thyroid, the pituitary’s production of TSH has a profound effect on the body, particularly in regard to diet.



**Figure 7.2**

**THYROID HORMONE ENDOCRINOLOGY: FEEDBACK LOOPS**

Higher centers in the brain send signals to the hypothalamus, which produces thyrotropin-releasing hormone (TRH). TRH stimulates the pituitary gland to make thyroid-stimulating hormone (TSH). TSH stimulates the thyroid gland to produce thyroid hormones. Thyroid hormones “feed back” to the hypothalamus and pituitary gland, slowing TSH production. Positive “feedback” is denoted by (+) and negative “feedback” is denoted by (-).

If the body is starving, the pituitary produces less TSH, prompting the thyroid to produce less T<sub>4</sub>, slowing metabolism. However, the body doesn't make distinctions about why it's starving; the same decline in T<sub>4</sub> production will happen regardless of whether a person is on a crash diet, suffers from an eating disorder, or is simply malnourished.

### Autoimmune Thyroid Disease

Most cases of thyroid disease are caused by an overactive and misdirected immune system. Autoimmune diseases include a wide range of disorders in which a person's immune system attacks his or her own healthy tissue. They have a genetic link but are not directly passed on from one generation to the next. A combination of genes and environmental factors (such as exposure to certain viruses or environmental toxins) determines who is susceptible to developing an autoimmune disease.

If the immune system causes an underactive thyroid, it is known as *Hashimoto's disease*. If it causes an overactive thyroid, it is known as *Graves' disease*.

Hashimoto's disease is also known as *Hashimoto's thyroiditis* (-itis means inflammation) because the immune system causes chronic inflammation in the thyroid gland. If you have autoimmune thyroid disease, you are at risk for other medical problems associated with an overactive immune system. If you have several autoimmune hormonal deficiencies, you have a condition known as *polyglandular autoimmune syndrome*. *Schmidt's syndrome*, also known as *polyendocrine autoimmune disease, type II*, is fairly common and includes Hashimoto's thyroiditis, Addison's disease, and type 1 diabetes. A rare form of insulin resistance, known as *type B insulin resistance*, is an autoimmune disorder caused by antibodies directed against the insulin receptor. This is a different form of insulin resistance from the type described in Chapter 3.

More than 60 autoimmune disorders have been described. The following are the most common autoimmune disorders seen in patients with autoimmune thyroid disease:

- Addison's disease (see Chapter 8)
- Alopecia areata

- Autoimmune hepatitis
- Celiac disease
- Crohn's disease
- Goodpasture's syndrome
- Hypoparathyroidism
- Idiopathic pulmonary fibrosis
- Male hypogonadism (see Chapter 4)
- Myasthenia gravis
- Pernicious anemia (vitamin B<sub>12</sub> deficiency)
- Premature ovarian failure (see Chapter 6)
- Primary biliary sclerosis
- Raynaud's syndrome
- Rheumatoid arthritis
- Scleroderma
- Systemic lupus erythematosus (also known simply as *lupus*)
- Temporal arteritis / giant cell arteritis
- Thrombocytopenic purpura
- Type 1 diabetes
- Vasculitis
- Vitiligo
- Wegener's granulomatosis

### **Stress and Your Thyroid**

Just as thyroid dysfunction can have an effect on the mind, so the mind can have an effect on the thyroid gland. Stress is a major catalyst in disrupting the normal performance of the thyroid.

When under stress, the body sends messages triggering responses from many hormones. Many of these responses are short-lived and beneficial; the production of adrenaline (epinephrine), for example, provides the extra shot of energy and excitement often needed to get through a stressful situation. (Think of how you feel when making a public speech: the palms sweat, the heart beats faster, you feel very afraid and very alive—all part of the “fight or flight” instinct developed over millions of years.)

But if the stress lasts for a long time, such as the kind you feel after surviving a tragedy or losing a loved one, your endocrine system

becomes overburdened. Naturally, this can lead to health problems. In particular, the immune system becomes dysfunctional, because your brain—using the flood of stress-inspired chemicals as a guide—is focusing its responses elsewhere. With the immune system out of whack, the body is helpless against viruses and other toxins that attack the thyroid. The immune system can become overactive, attacking and destroying the thyroid gland, or stimulating it to produce excessive amounts of thyroid hormone. Autoimmune problems are the most common cause of both an underactive and an overactive thyroid gland.

Moreover, stress isn't just psychological. Weight loss can cause physical stress because the body believes it is starving. The resulting impact, however, is similar: the immune system is weakened and the thyroid comes under attack.

But when the body is under stress, other problems can occur. In one scenario, the wrong iodine—the inner-ring iodine—can be removed from the T4 hormone. This creates a totally inactive form of the hormone called reverse T3. Given the inert state of reverse T3, metabolism is slowed to a crawl.

### ***Sloan's Story***

*Sloan went on a crash diet. She quickly lost 10 pounds, but she also became fatigued, depressed, and discouraged. Moreover, despite her continuing efforts, she was unable to lose any more weight, exacerbating the cycle. Sloan stopped exercising, and whatever positive results she had gained from the diet went by the boards.*

*Sloan visited a doctor for a consultation. The doctor tested her, but all her thyroid hormone levels appeared to be normal.*

*Eventually, Sloan got another diagnosis. Because of the stress of her crash diet, her body was fooled into thinking that it was starving, and it lowered its metabolism—via its thyroid hormones—accordingly to protect itself. This condition, known as sick euthyroid syndrome, is associated with normal thyroid tests in the early stages. Modification of Sloan's diet (and a modest increase in calories) allowed her to resume exercising, lose weight, and feel better.*

## IODINE AND THE THYROID

Iodine, element 53 on the periodic table, is a dark gray to purple-black solid that is used in a wide variety of products, including photographic chemicals, preservatives, food colorings, antiseptics, and medications. Iodine is an important part of a functioning thyroid and critical for hormonal balance. In the body, this element is primarily used to make thyroid hormones. As much as 75 percent of the body's iodine is stored in the thyroid gland. If iodine is lacking in the diet, a goiter—swelling of the thyroid—will result. Eventually, thyroid hormone production will slow to a crawl. Too much iodine can be as harmful as too little; high iodine intake causes thyroid dysfunction. If the body is exposed to toxic amounts of iodine, the result can be headaches, vomiting, mouth sores, a metallic taste in the mouth, swollen salivary glands, or a rash.

The recommended daily allowance (RDA) for iodine is 150 micrograms a day. However, in the United States, the usual consumption ranges between 300 and 700 micrograms a day—a testament to our love of salt and salty products, for most of the salt used in the United States is iodized. (One teaspoon of iodized salt contains more than 300 µg of iodine). Iodine has nothing to do with sodium; it's just added to the salt. Non-iodized salt (known as *free running*) and kosher salt do not contain iodine. Iodine also comes from seafood and sea vegetables, and is found in preservatives and in *red dye #3* (red dye #40 does not contain iodine). Many red, orange, or brown processed foods, pills, and capsules contain red dye #3. Iodine is in many medications, including amiodarone, levothyroxine, liothyronine, cough syrups (expectorants), betadine, and iv contrast dye. On food labels, the words *iodate*, *iodide*, and *sodium iodide* refer to iodine.

Iodine is found in a variety of *thyroid support formulas* in the form of *kelp*, *bugleweed*, or *bladderwrack*. These so-called support formulas often try to foist iodine supplements on people as a way of staying healthy. Kelp is particularly popular. “Look at the Japanese,” you might hear, a reference to that nation's traditional reliance on seafood and the relatively low incidence of obesity and certain illnesses there. But thyroid support supplements can put *thousands* of milligrams of iodine into a healthy system—way too much for your thyroid to process. (Incidentally, the Japanese also have a very high rate of autoimmune



thyroid disease.) So if there's one thing Americans generally *don't* need, it's iodine supplements—despite the chorus of claims to the contrary. Sources of dietary iodine include seaweed sushi wraps, seafood, dairy products, commercial baked goods and snack foods, egg yolks, chocolate, molasses, soy products, rhubarb, potato skins, and fruits and vegetables grown in iodine-rich soil (usually near the coast). Iodine is also found in most multivitamin and mineral supplements.

### ***Tina's Story***

*Tina thought she had thyroid problems. Her doctor did the routine TSH test, and it was normal. Tina started taking kelp tablets on the recommendation of her local health food store. Shortly after starting the kelp, her symptoms became much worse. In a month she gained 15 pounds. Although she had a normal thyroid test prior to starting the kelp, a repeat test showed a high TSH and low thyroid hormone levels. Tina quit taking the kelp. She started feeling better and her thyroid tests returned to normal after a few weeks.*

If the thyroid gland is overwhelmed with iodine, it shuts down, inhibiting production of thyroid hormone. Sometimes a different consequence of thyroid overload, iodine-induced *hyperthyroidism*, has been known to occur. If you have a smoldering, low-level thyroid disease and then consume a large amount of iodine (such as by taking kelp tablets), the consequences can be devastating. The effect is like spraying a fire with gasoline: huge amounts of thyroid hormone are suddenly produced, resulting in severe hyperthyroidism. Either way, it is not a good idea to flood your system with iodine.

## **FEATURES OF HYPOTHYROIDISM**

The initial symptoms of hypothyroidism are usually mild and not concentrated in a specific part of the body. Symptoms may be disregarded or attributed to other causes, such as old age, fibromyalgia, menopause, depression, or life stress. As thyroid levels decline, symptoms become more obvious. Symptoms of hypothyroidism are related to the severity and duration of the disease, the rapidity with which it

occurs, and the individual characteristics of the person who has it. One common feature of hypothyroidism, however, is weight gain.

It is estimated that 2 percent of the population have severe hypothyroidism. But 7 to 15 percent of the population—maybe more—suffer from low-grade hypothyroidism, known as *mild thyroid failure*. Stress or a diet low in iodine, selenium, or zinc or high in iodine or copper can aggravate hypothyroidism. Hypothyroidism commonly comes on during times of stress or times of change, such as menopause. How do you know if you have hypothyroidism? There are literally dozens of signs and symptoms. In general, these symptoms occur because of your body's effort to compensate for a lack of thyroid hormone—too little fuel to run the body's metabolism. The list of features of hypothyroidism is so long because thyroid hormone affects every aspect of the body.

### ***Linda's Story***

*Linda, a 32-year-old mother of two, came to see me after having been diagnosed with chronic fatigue syndrome. Her doctor had done extensive blood testing, including a test of Linda's thyroid hormone level, and assured her that everything was normal. She wanted a second opinion.*

*A former college athlete, Linda had not been active in years. She admitted she had had less energy since she stopped exercising, but suddenly all her energy was gone. At first, Linda blamed her fatigue on her job, her kids, and her age. But deep down she knew something was wrong. Linda had gained a remarkable 45 pounds in one year. She stated, "No matter what I do, I can't lose weight. I have cut way back on what I am eating, but it is not doing any good. I am tired all the time. I never feel like exercising any more."*

*She went on to relate a frightening story. "I was out running errands last week and suddenly I just broke down crying. I did not know why I was crying; I just couldn't help myself. I sat in the car and cried all afternoon. Then, as I was pulling myself together, I realized that I had forgotten to pick up my oldest son from basketball practice. By the time I got to the school, the coach had already driven him home."*

*I reviewed Linda's blood tests. Although her thyroid hormone level was normal, her TSH test was slightly elevated, a sign of early thyroid dysfunction. I explained to her that TSH, or thyroid-stimulating hormone, is produced by the pituitary gland, which is located in the brain. When the brain senses thyroid dysfunction, it increases its production of TSH. The increased levels of TSH try to stimulate the thyroid gland to make more hormone. The diseased gland eventually gives up and hormone levels drop. In the early stages of thyroid disease, it is very common to have normal thyroid hormone levels despite significant symptoms. I performed a **thyroid antibody** test, the result of which was incredibly high. This meant that Linda's immune system was attacking her thyroid gland. It was only a matter of time before her thyroid gland would fail completely.*

*Linda was treated with a thyroid hormone medication known as levothyroxine. Her mood and memory improved and she regained her energy. After four months on the medication, Linda had shed 25 pounds. She had reached a plateau, however, and wanted to lose the remaining 20 pounds. I recommended dietary changes and added a specific vitamin and mineral supplement to Linda's weight loss program. Linda now had enough energy to start exercising again.*

*At her last visit she remarked, "I haven't felt this good in years. I don't know what to do with all this energy. I actually played basketball with my son the other day. I've only got 5 pounds to go, and I know I can do it."*

*Linda had a classic example of **mild thyroid failure**, one of the most common hormonal problems in women. The underproduction of thyroid hormone slowed her metabolism to a virtual crawl. Since her thyroid hormone test turned out normal, the diagnosis was initially missed. Thyroid hormone pills returned Linda's metabolism to near normal. As is typical for many thyroid patients, the medication alone was not enough. Lifestyle, dietary, and nutritional modifications were also required for Linda to achieve normal thyroid function and to optimize her metabolism.*

### **Weight Gain**

Low thyroid hormone plunges the body into a vicious cycle. Chief among this cycle's indicators is weight gain. The lack of thyroid hormone prompts the body to slow its metabolism, so the body uses calories more slowly. As your metabolism slows and your cells need less energy, the body stores extra calories as fat. Most people with hypothyroidism say they are gaining weight even though they are eating less. As weight is gained, other hormone problems such as insulin resistance kick in, which increases weight gain. There may also be weight gain because of the fluid retention caused by hypothyroidism.

Women who have trouble losing weight after giving birth may have a form of hypothyroidism. Transient hypothyroidism lasting about one year is common after pregnancy and is known as *postpartum hypothyroidism*. The condition may be misdiagnosed as *postpartum depression* and never properly treated. Most of the time, the hypothyroidism improves by itself and is forgotten. But the afflicted woman, by this time, has been miserable for about a year and has likely gained tremendous amounts of weight. This condition occurs in up to 5 percent of American women.

### **Loss of Appetite**

Even though weight gain is an inevitable part of hypothyroidism, most people with this condition report loss of appetite. This is because thyroid hormone regulates appetite centers in the brain. Low thyroid also causes the gastrointestinal tract to slow down.

### **Fatigue, Exhaustion, or Drowsiness**

Fatigue is one of the most common symptoms in people with hypothyroidism. Reduced metabolism leads to low energy levels. People with low thyroid levels are tired all the time. They simply have no energy. Many report sleeping 12 to 14 hours each night.

### **Premature Aging**

Cosmetically, hypothyroidism causes people to look older. One need not look any farther than the case of Boris Yeltsin, the former president of Russia. In 1991, when he took over the country, Yeltsin was the very picture of vigor. Who can forget the youthful 60-year-old rallying people in the streets of Moscow after an aborted takeover by Soviet hard-liners?

But within five years Yeltsin appeared old, tired, and out of touch. He slurred his speech; his face was puffy and bloated. In 1996, prior to a heart bypass operation, he was diagnosed with hypothyroidism. The diagnosis was almost certainly overdue, since the disease had probably started much earlier—perhaps brought on by the stress of his job and exacerbated by Yeltsin's alcoholism. Interestingly, once Yeltsin's thyroid was treated, his heart problems got worse. This is not uncommon. Thyroid hormone accelerates metabolism throughout the body, including the heart. The accelerated metabolism increased the oxygen demand of his heart, and because of his coronary artery disease, not enough blood could get to the heart muscle.

### **Menopausal Symptoms**

As many as 20 percent of menopausal women have an underactive thyroid gland. Symptoms of weight gain, mood swings, depression, hair loss, and dry skin attributed to menopause could actually be due to undiagnosed thyroid disease.

### **Goiter**

A deficiency of thyroid hormone can cause the thyroid gland to enlarge. An enlarged thyroid gland is known as a goiter. A goiter is not necessarily an indicator of hypothyroidism; it only means the thyroid is enlarged. However, a goiter with any one of the other symptoms on this list is highly suggestive of thyroid problems. Goiters can cause a feeling of fullness in the neck. Some people with goiters report a choking sensation, hoarseness, or difficulty swallowing.

### **Joint and Muscle Aches or Muscle Cramps**

Hypothyroidism causes your joints and muscles to feel stiff, painful, and sore—symptoms that can be misdiagnosed as arthritis.

### **Feeling Cold or Being Cold**

Many people with hypothyroidism say they feel cold when others think the temperature is normal. Body temperature is a function of metabolism, so as metabolism slows, less body heat is generated. Hypothyroidism also causes blood vessels in the skin to constrict, making it cool to the touch. Basal body temperature measurements that are low have been touted as an early indicator of thyroid dysfunction. Most thyroid experts do not recommend that you take your temperature, however, because it is not a reliable test of low thyroid activity.

### **Decreased Sweating**

Lowered metabolism means less body heat, which leads to decreased sweating.

### **Constipation**

Hypothyroidism causes a general slowing of bowel function. Hard, painful bowel movements and bloating are signs of hypothyroidism, but like many others on this list, these signs are often dismissed as being caused by something else.

### **Loss of Memory and Inability to Concentrate**

Given the relationship between hypothyroidism, slowed metabolism, and fatigue, memory is often sacrificed in favor of other brain functions. The body becomes obsessed with its drives, most notably sleeping and eating. Concentrating and remembering take a back seat. Hypothyroidism is

associated with forgetfulness; inability to concentrate; and diminished intellectual function, speech capability, energy, libido, and motivation. Mild hypothyroidism causes forgetfulness and difficulty concentrating. More severe hypothyroidism causes problems that can be mistaken for Alzheimer's disease, especially in older people.

### **Depression**

Ten to 15 percent of people with depression have hypothyroidism. Hypothyroidism causes a generalized slowing of bodily function, including that of the brain. Hypothyroidism also injures brain cells that produce serotonin, a chemical linked to depression. Reduced serotonin levels lead to negative moods, the inability to experience pleasure, pessimism, and feelings of inadequacy and doom.

Depression is one of the most common misdiagnoses of hypothyroidism. Nowadays, it's easy to blame depression for so many things. We all have moments when we're feeling down, and for a sizable minority of Americans, full-blown depression is a real threat and illness. But even though it's just as important to look at the physiological roots of depression as it is the psychological roots, many physicians don't investigate that avenue. And one of the indicators of depression can be hypothyroidism.

### **Skin Problems**

With low thyroid hormone, skin becomes dry and itchy and develops cracks. In more severe cases of hypothyroidism, the skin takes on a yellow tinge due to build-up of carotene. Skin may also be cool to the touch due to constriction of blood vessels. Hypothyroidism can also cause the skin to bruise easily.

### **Hair, Eyebrow, and Fingernail Problems**

A lowered metabolic rate brought on by thyroid hormone underproduction can slow the growth of hair and cause it to become coarse and

brittle. Hypothyroidism also causes hair to fall out, sometimes in clumps. People with hypothyroidism frequently lose the hair in the outer third of the eyebrows. Fingernails can also become brittle with hypothyroidism.

### **Fluid Retention**

Hypothyroidism causes fluid retention, resulting in puffiness in the face or around the eyes; thickened lips; and swelling of the hands, feet, or legs (known as *edema*). Swelling of the tissues in the belly can lead to a sensation of bloating.

### **Heart Failure**

Fluid retention can cause problems in the heart muscle and in tissues around the heart. Fluid buildup weakens the heart, causing it to swell, and interferes with its ability to pump blood throughout the body. This condition is called *myxedema of the heart*, which can lead to insufficient circulation of blood to the organs and tissues. When the heart can't pump enough blood, it's known as *congestive heart failure* (CHF).

### **High Cholesterol**

Due to a general slowdown of bodily functions, hypothyroidism causes cholesterol to rise. The lower the thyroid levels, the higher the cholesterol. Anyone with high cholesterol should be tested for thyroid problems.

### **High Blood Pressure**

Abnormal thyroid levels, either high or low, can cause high blood pressure. Anyone who has been diagnosed with high blood pressure should have his or her thyroid checked.



### **Slow Heart Rate**

Hypothyroidism has a profound effect on the heart. A slow heart rate is a result of the total body slowdown.

### **Cardiovascular Disease**

Studies have linked hypothyroidism to atherosclerosis and premature cardiovascular disease. An underactive thyroid lets the body's cholesterol levels climb, particularly so-called bad cholesterol (LDL, or low-density lipoprotein cholesterol). In combination with high blood pressure, this puts a person at increased risk for a heart attack or a stroke.

Recent studies have also linked elevations of homocysteine levels with hypothyroidism. Homocysteine is an amino acid found in the blood and is linked to heart disease. Hypothyroidism makes the levels of homocysteine increase, just as it does cholesterol levels. Treatment of hypothyroidism tends to lower cholesterol and homocysteine levels, and thus is good for the heart. In patients with normal thyroid levels, elevated homocysteine may be the result of dietary deficiency of folate or vitamin B<sub>6</sub>, so increasing fruit and vegetable intake also helps reduce homocysteine levels.

Thyroid hormone has direct effects on the heart. Underproduction of thyroid hormone prompts the heart to beat less forcefully and more slowly, and may cause fluid to build up around it. Thyroid hormone speeds up the heart and strengthens its pumping action. For these reasons, doctors must be very careful when giving thyroid hormone replacement to people at risk for heart problems. A sudden increase in metabolism can strain the heart and cause a heart attack.

### **Menstrual Problems and Infertility**

Hypothyroidism can wreak havoc with the female reproductive system. Periods may be longer and heavier, and may become prolonged—with more time between them—or irregular. Increased blood flow, or *menorrhagia*, is common; the thyroid controls muscle contraction in the uterus. Without the proper contraction of the muscle, the uterus cannot

clamp off the bleeding blood vessels. Hypothyroidism can also prompt *anovulation*, a condition where the ovary does not release an egg at all.

Some women actually have reduced menstrual flow, or lose their periods altogether. Loss of menstrual cycle with symptoms of low thyroid could mean *central hypothyroidism*, where pituitary gland problems result in low thyroid hormone production.

### **Gruff or Hoarse Voice**

Many people with hypothyroidism report that their voice becomes hoarse, husky, and gravelly or simply sounds deeper. This is caused by thickening and swelling of the vocal cords.

### **Anemia**

Anemia means a low level of red blood cells. The most common symptom of anemia is fatigue. Hypothyroidism commonly causes a low-grade anemia that is often dismissed by physicians.

Anemia in association with hypothyroidism may also be due to an autoimmune disorder called pernicious anemia. Pernicious anemia is caused by problems with absorption of vitamin B<sub>12</sub>. Symptoms of vitamin B<sub>12</sub> deficiency include weakness, nervous system problems, and gastrointestinal problems, in addition to anemia. It is treated with regular injections of vitamin B<sub>12</sub>.

### **Slow Reflexes**

This sign can be a key to diagnosing hypothyroidism, and endocrinologists examine reflexes very carefully when determining if a patient may have thyroid disease. In hypothyroidism, the *relaxation phase* of the reflex is slowed. For example, in the standard knee-jerk reflex, a doctor hits a knee with a reflex hammer and the knee kicks out. In a patient with hypothyroidism, the return of the knee to the resting position is delayed. The delay may not be apparent to the untrained eye,

but an experienced endocrinologist knows that this is the most sensitive way of determining subtle thyroid deficiencies at the bedside. Through its effects on the nervous system, hypothyroidism can also cause problems like muscle cramps, numbness or tingling in the hands and feet, and even carpal tunnel syndrome.

### **Snoring or Sleep Apnea**

Sleep apnea occurs when excess tissue in the neck cuts off breathing during the night, leading to snoring, poor sleep, daytime sleepiness, high blood pressure, and—if left untreated—eventual heart and lung failure. Sleep apnea is not uncommon among overweight people, and the slowing of metabolism caused by hypothyroidism can contribute to this condition.

### **Allergies or Hives**

Many people with thyroid problems notice worsening of their allergies. Treating the thyroid makes the allergy symptoms better. Some people with normal thyroid hormone levels, but with evidence of immune system attack on the thyroid (known as *euthyroid Hashimoto's disease*), have shown dramatic improvement in their allergies when treated with low doses of thyroid hormone. Hypothyroidism has also been known to cause an increased sensitivity to medications in some people.

### **Breast Milk Production**

This is a rare event, but it does happen. As the brain vigorously tries to produce more TSH, more of another hormone, prolactin, can also be produced. Prolactin stimulates breast milk production and can cause menstrual abnormalities. In some cases, this situation is misdiagnosed as a brain tumor, and patients have been known to undergo unnecessary removal of the pituitary gland, when all that was needed was a thyroid hormone replacement.

## CAUSES OF HYPOTHYROIDISM

Thyroid gland failure, also known as *primary hypothyroidism*, is the most common cause of hypothyroidism. Most cases of primary hypothyroidism are caused by immune system destruction of the thyroid gland—Hashimoto's thyroiditis. Occasionally, however, if the pituitary gland or hypothalamus develops a problem, signals to the thyroid gland are disrupted, leading to *central hypothyroidism*.

The early stage of hypothyroidism is known as *mild thyroid failure* or *subclinical hypothyroidism*. During this phase, the symptoms may be mild or nonexistent but are sometimes more severe. Most endocrinologists advocate starting low-dose thyroid hormone replacement therapy during this phase because it has been shown to lower cholesterol and reduce the risk of cardiovascular disease. More severe hypothyroidism and eventual total thyroid failure almost always occur with time, requiring larger doses of thyroid hormone replacement. Long-standing untreated hypothyroidism is called *myxedema*. This term refers to the swelling of organs and tissues throughout the body. Eventually, serious difficulties will arise in all major, life-sustaining systems, leading to coma, known as *myxedema coma*.

### Hashimoto's Thyroiditis

Hashimoto's thyroiditis is also known as autoimmune hypothyroidism, Hashimoto's disease, Hashimoto's hypothyroidism, autoimmune thyroiditis, or chronic lymphocytic thyroiditis. It's the number one cause of hypothyroidism and is estimated to affect approximately 15 million people in the United States. Hashimoto's thyroiditis may begin with a short period of hyperthyroidism lasting anywhere from a few weeks to several months. This condition, known as *Hashitoxicosis*, is caused by the release of preformed hormones in the thyroid gland as it is being destroyed by the immune system. Hashimoto's thyroiditis is hereditary, and it is seven times more likely to affect women than men. People with Hashimoto's thyroiditis are at risk for other immune system problems, such as type 1 diabetes, pernicious anemia, Addison's disease, or premature ovarian failure.

### **Atrophic Thyroiditis**

Atrophic thyroiditis is similar to Hashimoto's thyroiditis, except a goiter is not present.

### **Subacute Thyroiditis**

This condition, also called painful thyroiditis or de Quervain's thyroiditis, can be brought on by the immune system, toxins, or a viral illness. Inflammation causes the thyroid to become swollen and tender. The pain sometimes spreads to the throat, ears, or jaw. Subacute thyroiditis may start with a 2–4-month period of hyperthyroidism.

### **Postpartum Thyroiditis**

Up to 10 percent of new mothers develop an inflammation of the thyroid gland 3 to 12 months after giving birth. Most of the time, the condition is temporary, but in about 30 percent of cases the condition is permanent and requires lifelong thyroid hormone replacement. Postpartum thyroiditis is a common cause of problems with weight loss after pregnancy.

### **Reidel's Thyroiditis**

Reidel's thyroiditis is a very rare cause of hypothyroidism. For unknown reasons, normal thyroid tissue is invaded by rigid, fibrous tissue that destroys thyroid function.

### **Congenital Hypothyroidism**

Some people are born with a defect in one of the enzymes necessary for thyroid hormone production. In the United States, all newborn infants are tested for this condition. Thyroid hormone is necessary for normal growth and development.

### **Central Hypothyroidism**

When hypothyroidism begins in the brain instead of in the thyroid gland, it is called central hypothyroidism. It develops when either the hypothalamus or the pituitary gland is damaged or destroyed—for example, by tumors, infections, or injury. Central hypothyroidism is almost always accompanied by deficiencies in other pituitary gland hormones and rarely occurs alone.

### **Idiopathic Hypothyroidism**

This is the designation doctors use when they don't know the cause of the hypothyroidism. Most of the time, idiopathic hypothyroidism is caused by immune system destruction of the thyroid gland, but for some reason blood tests for antibodies are normal.

### **Treatment for Hyperthyroidism, Goiter, or Thyroid Cancer**

Surgical removal of all or most of the thyroid is known as a total thyroidectomy. This is an obvious cause of hypothyroidism, known as surgical hypothyroidism. Hypothyroidism is also a frequent outcome of radioactive iodine treatment for hyperthyroidism or thyroid cancer, in which case it is known as postablative hypothyroidism.

### **Drugs**

The medication lithium is known to cause hypothyroidism. Drugs used for epilepsy, including phenytoin and carbamazepine, reduce thyroid levels. Medications that contain iodine, such as amiodarone, expectorant cough medications, and antiseptics like betadine, have properties that affect the thyroid, although their effects are almost always reversible when they are stopped. Some drugs used in cancer chemotherapy or to fight infections (interleukins, sulfamethoxazole and other sulfa drugs, interferon alpha, and ribavirin) can cause hypothyroidism. Drugs used to treat an overactive thyroid, propylthiouracil (PTU) and methimazole, have unpredictable dosing and may result in hypothyroidism.

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## Toxins

Toxins and pollutants can cause thyroid problems. Known as *environmental endocrine disruptors*, these substances can slow thyroid function and disrupt hormonal balance. The chemical *carbon tetrachloride* is known to cause thyroid dysfunction and has been found in samples of drinking water. Pesticides have a chronic mineral-depleting effect and can lead to thyroid problems. *Polychlorinated biphenyl* (PCB) exposure has been associated with impaired intellectual functioning, memory problems, and learning problems that are thought to be due in part to thyroid dysfunction. The weed killer Roundup, which contains the chemical *glyphosate*, has been blamed for thyroid problems. Smoking may contribute to thyroid disease because of several toxins, including *cadmium*, found in tobacco leaves. Cadmium has been linked to thyroid dysfunction. Dried fruits (which are often dried on galvanized chicken wire) can contain high amounts of cadmium as well. *Nitrates* have also been linked to thyroid problems.

Antibacterial products, from dishwashing liquids to bar soap and toothpaste, have become very popular in the last few years, promising cleaner skin and less risk of infection. But many of these products contain a chemical called *triclosan*, which is thought to interfere with thyroid hormone metabolism. My recommendation is to avoid antibacterial products. The “regular” versions of the products do an excellent job of killing microbes, and without potential risk to your thyroid.

## Excess Iodine

If the thyroid gland is overwhelmed with iodine, it shuts down, inhibiting production of thyroid hormone.

## Radiation Exposure

Radiation treatments for cancers or acne in the head and neck area increase the risk for hypothyroidism as well as thyroid nodules and thyroid cancer. People who live (or used to live) in locations where

nuclear bombs were tested or there was leakage of nuclear waste are at risk for thyroid problems. I have seen many patients who lived in or visited the area near Chernobyl who now have thyroid problems.

### **Dietary Causes**

Uncooked vegetables from the *Brassica* family, known as *goitrogens*, can cause hypothyroidism. These vegetables include broccoli, cauliflower, brussels sprouts, cabbage, mustard, kale, radishes, and turnips. These vegetables do not cause problems if cooked or if consumed raw in small quantities. Soy products, pine nuts, and peanuts may also slow thyroid function, but usually only when consumed in excessive amounts. Excessive dietary iodine from kelp or iodine supplements commonly results in hypothyroidism.

#### ***Rebecca's Story***

*Rebecca, a sales rep for a software company, came to visit her doctor. In her mid-20s, this vivacious, attractive young woman was complaining of irritability, fatigue, and weight gain—symptoms that could have been written off as related to stress, for she had a very stressful position, or to her pregnancy, which was in the first trimester. Her doctor measured her total T4. The figure came out within the normal range. The doctor sent her on her way with mild reprimands to slow down, watch her diet, and exercise more.*

*Eventually, Rebecca came to see me. Upon testing her total and free T4 levels, I determined that her free T4 was low, but her total T4 falsely appeared normal because she had increased levels of thyroid-binding globulin (TBG) protein in her blood. In her case, the excess TBG was a result of her being pregnant. Subsequent testing showed a low free T4 and a high TSH. Rebecca was treated with thyroid hormone and had a normal pregnancy. Unfortunately, however, her child is showing developmental delay and lower-than-average intelligence, problems not uncommon for children of women with untreated thyroid deficiency.*



## HYPOTHYROIDISM IN PREGNANCY

Hypothyroidism in pregnancy is a serious issue. It is estimated that 2.5 percent of pregnant women have some form of hypothyroidism. However, the symptoms of hypothyroidism may overlap with those of pregnancy, and the diagnosis may be missed. Hypothyroidism is associated with an increased risk of pregnancy complications. Moreover, as in the case of Rebecca, a recent study in the *New England Journal of Medicine* showed that women with mild thyroid deficiency during their pregnancy had children with subsequent developmental and intelligence defects. All pregnant women should have their thyroid tested. If you are pregnant and have hypothyroidism, you should have your levels tested every 6 to 8 weeks. Most women need several medication adjustments (usually increases in dose) during their pregnancy.

## HYPERTHYROIDISM

Hyperthyroidism is the opposite of hypothyroidism: instead of the body producing too little thyroid hormone, it's producing too much. The symptoms are usually the reverse of those of hypothyroidism. Instead of the metabolism slowing, it speeds up. So hyperthyroidism usually produces weight loss, not weight gain.

But there's a twist. One of hyperthyroidism's major effects is increasing appetite. If appetite increases faster than metabolism, guess what happens. Weight gain.

The primary symptom of hyperthyroidism is uncontrollable appetite. Patients complain of not being able to eat enough, of always being hungry, of waking up ravenous and going to sleep the same way—even if they've eaten far more than is recommended during the day.

You might recognize other symptoms as reverse images of hypothyroid symptoms. They include feeling hot, hyperactivity, increased sweating, irritability, nervousness, tremor, heart palpitations, insomnia, brittle nails, diarrhea, and increased frequency of bowel movements. Interestingly, fatigue is a symptom of both hypo- and hyperthyroidism.

One extreme form of hyperthyroidism is called *thyroid storm*. Patients can have vomiting, fever, liver problems, mental confusion, and—sometimes—seizures. This form requires hospitalization.

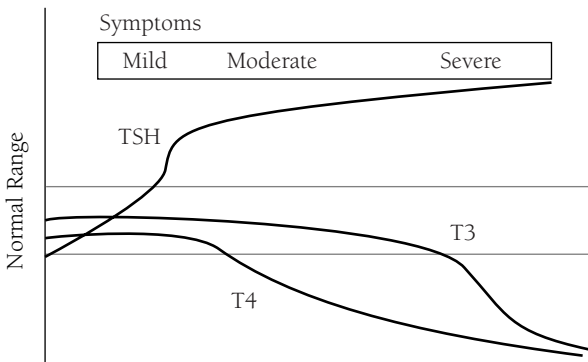
Like hypothyroidism, hyperthyroidism is frequently caused by an overactive immune system attacking the thyroid gland. The most common cause of hyperthyroidism is Graves' disease. Graves' disease is an attack on the thyroid gland by the immune system, usually kicked off by stress. The most famous case in recent years occurred in 1991, when President George Bush came down with the ailment in the aftermath of the Persian Gulf War—the war likely having put the president under extreme stress for several months. The disease caused heart fibrillations, forcing the president into the hospital. Eventually, after observation and tests, the president's Graves' disease was treated with medication. Treatments for hyperthyroidism include radioactive iodine, antithyroid drugs such as methimazole or PTU, and—in some cases—surgical removal of the thyroid.

### **TESTING FOR THYROID DISEASE**

Testing for thyroid imbalance is a tricky business. Most doctors rely on a simple blood test, the TSH test, to determine if a patient is suffering from hypo- or hyperthyroidism; however, the range for such a determination can be so narrow that some doctors may dismiss a patient as normal even if a thyroid imbalance exists. At the other extreme are physicians and healers who, without taking a blood test, note that a patient has one or more of the indications of thyroid imbalance and treat these symptoms with prescriptions of thyroid hormone (a medication available in both natural and synthetic varieties). Patients with these symptoms, however, may not be suffering from hypo- or hyperthyroidism at all, or certainly not to a degree to warrant this level of treatment. Thus, neither group is well served by their medical care.

#### **The TSH Test**

Thyroid experts recognize the TSH test as the test of choice when thyroid disease is suspected. The primary reason is that TSH begins to rise *before* thyroid hormones drop below the normal range. Thus, it's a better indicator of early thyroid dysfunction.

**Figure 7.3****PROGRESSION OF HORMONE DECLINE IN HYPOTHYROIDISM**

In the evolution of hypothyroidism, subtle deficiencies in thyroid hormone levels are sensed by the brain and pituitary gland. The TSH rise is generally detectable before thyroid hormone levels fall below the normal range. During this phase, symptoms are generally mild. As T4 and T3 levels fall, symptoms worsen.

TSH is the hormone that comes from the pituitary gland and communicates with the thyroid gland, stimulating it to make and release thyroid hormones. Early in hypothyroidism, TSH goes up in the effort to coax the thyroid to do its job. If hypothyroidism is present, the thyroid won't be able to do that job properly. Meanwhile, TSH levels keep going up as the thyroid is continually prodded back toward normal production of thyroid hormones; the thyroid level thus continues to decline. After a while, the thyroid hormone levels drop below normal—but by that time, hypothyroidism has already taken effect and is likely getting worse.

The TSH test is a good (but not perfect) test for thyroid disease. TSH values above the normal range indicate hypothyroidism, and the higher the number, the more severe the hypothyroidism. Low TSH values are usually caused by an overactive thyroid (hyperthyroidism).

Early hypothyroidism, when TSH is high but thyroid hormone levels are normal, is known as “subclinical hypothyroidism” or “mild thyroid failure.” Many physicians are reluctant to treat this condition. Mild thyroid failure is increasingly being recognized as a real disease and is being treated.

If TSH is mildly elevated, the usual diagnosis is mild thyroid failure. There are exceptions, however, though they are rare.

- *Pituitary tumor.* If the pituitary gland has a tumor, it may overproduce TSH on its own. Patients with this problem usually have symptoms of an overactive thyroid (hyperthyroidism), but those symptoms may overlap with those of an underactive thyroid.
- *Medication.* Anti-nausea medication (e.g., Phenergan or Reglan) and psychiatric medications (e.g., Haldol or Prolixin) can throw TSH readings out of whack.
- *Timing.* TSH should always be tested during the day. TSH levels often surge at night, and testing at this time can give an indication of high TSH levels when they're actually normal.
- *Immune problems.* TSH antibodies can give false readings, making a normal test result appear high.

### **TRH Stimulation Test**

This test measures the ability of the pituitary gland to respond to an injection of TRH (thyrotropin-releasing hormone). TSH is measured, TRH is injected, and TSH is measured again 30 minutes later. If the TSH is not increased, a pituitary gland problem is suspected. If the TSH rises to a level of greater than expected, it can indicate hypothyroidism. TRH is no longer available in the United States, but some endocrinologists will import it from Europe.

### **Total Thyroxine (TT4)**

This test measures the level of all thyroxine (T<sub>4</sub>) in the blood. More than 99 percent of thyroid hormone is bound to the blood protein TBG. This bound hormone is inactive. Problems with TBG can invalidate this test. Estrogen-containing medications such as those used in hormone replacement therapy (HRT) or birth control pills increase TBG levels, making the TT<sub>4</sub> test of limited usefulness in women who take these medications.

### **Free Thyroxine (FT4)**

This test measures only the 1 percent of thyroid hormone that is unbound. This “free hormone” is the active hormone; bound hormone has no biological activity. By testing for free thyroxine, the possibility of being misled by a protein problem is eliminated. In general, *free* hormone levels are more accurate than *total* hormone levels.

### **Total Triiodothyronine (TT3)**

Like the total thyroxine test, this test measures both bound and unbound T3 levels. TBG problems can lead to problems with this test.

### **Free Triiodothyronine (FT3)**

This test measures only the unbound portion of T3 and is not subject to protein problems. This is an important test for people who have problems converting T4 to T3.

### **Reverse T3 (RT3)**

This test measures the level of an inactive hormone produced when T4 is improperly processed. Thyroid experts rarely order this test, but inexperienced “natural” doctors frequently do. It is very expensive and is usually not helpful in determining if there are problems with the conversion of T4 to T3.

### **Thyroid-Binding Globulin (TBG)**

This test measures actual levels of binding proteins in the blood. TBG problems cause false readings for total but not free hormone levels. One cause of elevated TBG, incidentally, is a high estrogen level. This can be caused by pregnancy, birth control pills, estrogen replacement therapy, environmental estrogens (see the discussion of estrogen and menopause in Chapter 6), and high consumption of soy products.

### **Antithyroid Antibodies (ATA)**

Antithyroid antibodies indicate whether or not you have an autoimmune thyroid disorder (the most common cause of hypothyroidism). There are two tests available: *antithyroglobulin antibodies* and *antimicrosomal antibodies* (also known as *antithyroid peroxidase*—TPO antibodies). Thyroid antibodies indicate the level of attack the immune system is waging on the thyroid gland. High levels in any of these tests indicate a more intense attack and, if your TSH is already high, signify a greater chance of progression to severe disease.

Many people with symptoms of hypothyroidism but a normal TSH test will have a positive antibody test result. Thyroid antibodies may be a clue to thyroid disease; however, they do not guarantee it.

### **Testing for Autoimmune Disorders**

Thyroid problems are frequently caused by immune system problems. Having one autoimmune disorder puts you at risk for others. If you have been diagnosed with autoimmune thyroid disease (Hashimoto's or Graves'), you should be evaluated for other autoimmune problems. The types of tests will depend on your symptoms but may include blood sugar, cortisol, calcium, parathyroid hormone, cortisol testing, vitamin B<sub>12</sub>, rheumatoid factor, antinuclear antibody (ANA), platelets, and blood counts.

### **Saliva Tests**

Salivary measurements of thyroid hormones are not reliable. Salivary testing is not accurate enough, and the normal range has not been clearly defined. Salivary hormone measurements hold promise, though, and in the future may be more reliable.

### **Basal Body Temperature**

Basal body temperature measurements are not reliable for detecting thyroid problems.

## **Thyroid Ultrasound**

A thyroid ultrasound gives information about the size and shape of the thyroid, as well as the presence of nodules or cysts. If a thyroid ultrasound shows a suspicious nodule or cyst, your doctor may order a fine-needle aspiration (FNA) or biopsy.

## **NORMAL TESTS, LOW THYROID FUNCTION**

Do you have symptoms of hypothyroidism but have been told that your thyroid test is normal? There are several conditions that result in low thyroid function despite normal thyroid tests—including both TSH and T<sub>4</sub> tests. Each of these conditions can cause hypothyroidism symptoms, most notably low metabolism and weight gain.

### **Presubclinical Hypothyroidism**

As noted in Figure 7.3, showing the natural history of thyroid disease, the first indicator of a dysfunctional thyroid is not reduced T<sub>4</sub> levels, but heightened TSH levels. If your TSH is normally at the low end of the normal range—as is the case for the majority of us—then a doubling, tripling, or even quadrupling of the level (e.g., from 1 mIU/L to 4 mIU/L) may be highly significant and indicative of low thyroid function.

Please note that normal range for all these tests depends on the laboratory. However, the normal range for TSH is generally 0.5 mIU/L to 5.5 mIU/L. In other words, 5 mIU/L is considered normal—but for most people normal is around 1.0 mIU/L. This means that your TSH can increase 500 percent and still be considered normal! If you have symptoms of hypothyroidism and a TSH test result at the upper range of normal, you may have presubclinical hypothyroidism. I recommend testing thyroid antibodies in this situation. If antibodies are positive or if you have a goiter, then you may be a good candidate for low-dose thyroid hormone replacement.

The only way to know if you really have presubclinical hypothyroidism is to wait until you develop full-blown hypothyroidism. A study

was done to determine if treatment with thyroid hormone could improve the symptoms of hypothyroidism in people with normal thyroid function tests. The results, published in the *British Medical Journal*, showed that thyroid hormone was no more effective than placebo in relieving symptoms.

### **Sick Euthyroid Syndrome**

When the body is under stress—and stress can be caused by major life cycle events, such as a death in the family, or seemingly innocuous physical changes, such as those brought on by a fad diet—one possible consequence is the production of reverse T<sub>3</sub>, created when the wrong iodine molecule is removed from the T<sub>4</sub> hormone. Reverse T<sub>3</sub>, you'll remember, is completely inert. Stress also causes the brain to shut down production of TRH and TSH, so that the body cannot compensate for low thyroid hormone levels.

The name given to this cycle is sick euthyroid syndrome. The “eu” prefix to “thyroid” is derived from the Greek for “good” or “well,” so *sick euthyroid syndrome* implies that the thyroid is well but the rest of the body is sick. It is thought that in response to low thyroid levels, the body is put at a lower level of metabolism to protect it from whatever illness or stress it is experiencing. It's all a natural biological adaptation to stress.

Dieting may not seem like a stressful situation on the surface, certainly not compared with being wounded in battle or undergoing the breakup of a long-term relationship. But the upshot is the same: all the body knows is that something has changed. One day it had plenty of food; the next day it's starving. It reacts by slowing metabolism and, as the regulator of metabolism, the thyroid and its hormones act as leaders in this slowdown.

Interestingly, sick euthyroid syndrome often happens in conjunction with mild thyroid failure. I see this all the time among my patients. The person has mild thyroid failure but the TSH test, pushed and pulled in opposite directions, ends up normal. The result: normal thyroid hormone levels and normal TSH with symptoms of hypothyroidism. It is a situation frequently missed by doctors. Patients are severely symptomatic but are told nothing is wrong.



Regardless of how the problem starts, doctors often overlook it. The standard requirement for hypothyroidism is high production of TSH. In the case of sick euthyroid syndrome with its related conversion problems, the opposite happens: TSH production is low or nonexistent. The pituitary gland may not sense a T3 deficiency because T4 levels are normal, and the pituitary gland senses T4. The normal T4 levels fool the pituitary gland into thinking that everything is just fine, when in reality the body is deficient in T3, the active hormone. Even some endocrinologists who are quite familiar with sick euthyroid syndrome and conversion problems are convinced that it occurs only in very sick patients—such as those on life support.

Let me emphasize: *you don't have to be sick to have these conditions*. Stress from any source, including mental strain, a minor illness, or fad dieting, can produce these problems, though to a lesser degree compared with the conditions suffered by critically ill patients.

### **Central Hypothyroidism**

In rare cases—about 1 in 20,000 people—hypothyroidism is caused not by failure of the thyroid gland but by failure of the pituitary gland or hypothalamus. The most common cause of this condition is a pituitary gland tumor. Other causes of central hypothyroidism include head trauma, brain tumors, problems with blood flow to the pituitary gland, tuberculosis, syphilis and other infections, and diseases such as hemochromatosis and sarcoidosis. Sometimes a tumor in the pituitary gland causes an abnormal and nonfunctional form of TSH to be produced. Through all this, the TSH level may be normal while free T4 is in the low normal range or obviously low. Though central hypothyroidism is rare, the diagnosis should not be overlooked—particularly since it may involve a brain tumor. Early in the disease, all testing may be normal. The first indication may be something as simple as weight gain.

### **Thyroid Hormone Resistance**

Complete thyroid hormone resistance is an extremely rare condition: there have only been about 600 cases reported to date. In thyroid

hormone resistance, the thyroid gland is perfectly normal. The problem lies in every cell of the body—each of which contains the thyroid hormone receptor and binding sites for the hormone receptor complex to bind to DNA and turn genes on and off. It is described as “reduced tissue responsiveness” to thyroid hormone. The problem is caused by a defect in the gene that makes a component of the thyroid hormone receptor, so that proper binding cannot occur.

Individuals with thyroid hormone resistance typically have mild symptoms of hypothyroidism and an enlarged thyroid gland. In reality, the TSH test is normal but T4 and T3 levels may be elevated. The reason: there is enough thyroid hormone available, but it is not working properly. Thyroid hormone resistance typically runs in families. It is rarely diagnosed, and cases of *partial thyroid hormone resistance* may escape diagnosis altogether. One tip-off to thyroid hormone resistance may be a failure to lose weight or to otherwise improve when treated for low thyroid, despite increasing dosages of medication.

### ***Rhonda's Story***

*Rhonda, a bank teller, started experiencing mood swings. One week she was down in the dumps and could hardly get out of bed; the next week she was agitated and sleepless. Rhonda was told she had bipolar disorder and started taking the medication, lithium. This is when her problems really began. The mood swings became more and more violent until she found herself contemplating suicide. Ultimately, we discovered that she did not have bipolar disorder at all. She had thyroiditis. Her thyroid gland had become inflamed and would periodically release bursts of thyroid hormone into her system. These periods were followed by episodes of low thyroid hormone. The swings in thyroid hormone were causing her moods to go on a roller coaster ride. The lithium Rhonda took made her thyroid problems worse. Eventually, her thyroid shut down altogether (which is not uncommon), and she was put on a stable prescription of thyroid hormones. The mood swings vanished.*

## **Thyroiditis**

Thyroiditis is a temporary inflammation of the thyroid gland caused by antibodies or infection. Symptoms, and abnormal blood tests, can come and go. Sometimes the flow of antibodies and the autoimmune attack on the thyroid are unpredictable. Antibody levels can wax and wane, resulting in alternating periods of hyper- and hypothyroidism. This antibody flux is related to life stressors, so relieving the stress tends to make the problem better. Thyroiditis can be caused by a virus. Some patients report the occurrence of a flu-like illness a few weeks prior to the onset of symptoms

The catch: the thyroid tests are abnormal only if you measure them at the right time. At other times the testing is normal, but the hormones are only transiently in the normal range, on their way to becoming higher or lower. Thyroiditis can make your neck swollen or tender, but this symptom doesn't always occur. Because of the effect hypo- or hyperthyroidism has on mental health, patients with thyroiditis are commonly misdiagnosed as having bipolar disorder—popularly known as manic depression.

## **Not Your Thyroid**

Most of the time, if thyroid tests are normal, especially the TSH level, thyroid function is adequate. If thyroid testing is repeatedly normal and there is no evidence of central hypothyroidism, then I usually assume that the thyroid is probably not the cause of a person's symptoms. It's important to rule out thyroid disease as the cause of symptoms, but if I determine that thyroid function is normal, then I recommend looking for other causes. Many of the hormonal disorders in this book have symptoms that overlap with those of hypothyroidism.

## **WILSON'S SYNDROME**

In the early 1990s a Florida physician, Dr. E. Denis Wilson, theorized that many of the symptoms of hypothyroidism were caused by low levels of thyroid hormone, despite normal thyroid tests. He reported that

his patients showed dramatic improvement when treated with thyroid hormone, most notably T3. He called this condition “Wilson’s syndrome.” Dr. Wilson popularized his theory with an expensive advertising campaign. Wilson subsequently was the subject of complaints to the Florida medical licensing board and was forced to pay a \$10,000 fine and to stop practicing medicine for 6 months.

Despite this, Wilson’s syndrome and T3 therapy has gained tremendous popularity among physicians that practice alternative medicine and anti-aging medicine. Thyroid experts as well as the American Thyroid Association confirm that there is no scientific evidence for Wilson’s syndrome and do not recognize its existence.

### **TREATMENT OPTIONS FOR HYPOTHYROIDISM**

If there’s a positive aspect to hypothyroidism, it’s that it is easily treatable. The main goal of therapy is to restore thyroid hormone levels to normal. This means that you must have periodic blood tests to make sure all your levels remain in the proper range.

The reference range for TSH varies among labs, but is usually about 0.5–5.5  $\mu\text{U/mL}$ . This is not the same as the *therapeutic target* for thyroid hormone replacement therapy, which is a TSH level near 1  $\mu\text{U/mL}$ . This is because most people feel best when the TSH is at the lower end of the reference range. Because such precise thyroid hormone levels are necessary for optimal hormonal balance, TSH is said to have a *narrow therapeutic index*. This means that it’s very important to take the medication as directed. Most people who need thyroid hormone replacement therapy have permanent hypothyroidism and need to take it for the rest of their lives.

### **Levothyroxine (Levothroid, Levoxyl, Synthroid)**

Thyroid experts agree that levothyroxine is the best form of thyroid hormone replacement. One small pill a day is all that is needed to completely cure hypothyroidism. Levothyroxine is synthetic T4 that is chemically identical to the natural form produced by the body. Levothyroxine is converted by the body to the active form, T3, and provides the base of the thyroid cycle.

Most thyroid experts agree that brand-name levothyroxine—Synthroid, Levothroid, or Levoxyl—offers an advantage over generics. The quality control for the branded versions is much better than for generics. Differences in the inert ingredients or fillers that make up the tablet lead to differences in absorption of the medication, which can affect blood levels. Since the cost between brand-name and generic formulations is only a few dollars each month, I recommend you avoid the generic version of thyroid hormone.

Several medications, medical conditions, and minerals interfere with levothyroxine efficacy and absorption. Among them are Zoloft, Questran, iron supplements or vitamins with iron, calcium supplements, Maalox, Mylanta or other aluminum-containing antacids, soybeans and soy products, bowel problems (in which the pill is not absorbed completely), forgetfulness (the pill must be taken every day), and high temperatures (the pills are damaged by heat, so they should not be kept in a car or near a stove). Estrogen-containing medications can affect levels as well. Food can affect the absorption of thyroxine through the intestines. For best results, thyroxine should be taken on an empty stomach. One of the features of levothyroxine is that it is a very long-acting medication. This means that once you start taking it, it takes 5 to 6 weeks to achieve stable blood levels. But it takes even longer to achieve stable tissue levels and thus bring resolution of symptoms. Every time your dose is changed, it will take another 5 to 6 weeks for levels to stabilize. If you forget to take a pill one day, you can take a double the dose the next day and maintain hormonal balance.

The average dose of levothyroxine needed is about 0.75 µg per pound of body weight, so a 150-pound person usually needs to take the 112 µg tablet. This calculation is just an estimate. The dose must also be adjusted according to the person's symptoms and TSH level.

### **Liothyronine (Cytomel)**

Some people with hypothyroidism do not feel well on standard levothyroxine therapy. This is because levothyroxine provides the body only with T<sub>4</sub>, and its effectiveness depends on the body's ability to convert T<sub>4</sub> to T<sub>3</sub>. Some people have problems with this conversion process. Because of this, some doctors add liothyronine, a synthetic

form of triiodothyronine (T3), to standard levothyroxine therapy. This treatment has helped some patients but is still controversial among endocrinologists.

In 1999 a study appeared in the *New England Journal of Medicine* titled “Effects of Thyroxine as Compared with Thyroxine plus Triiodothyronine in Patients with Hypothyroidism.” The protocol of this study was to reduce the dose of levothyroxine by 50 µg per day and replace it with a single daily dose of 12.5 µg of triiodothyronine. Patients reported improvement as a result of adding T3. Since the publication of this paper, several similar studies have failed to reproduce this effect. Despite this, many patients say they prefer to take a low dose of T3 in addition to their levothyroxine therapy.

The body is supposed to produce T3 from T4, but for patients with conversion problems from illness, nutritional deficiencies, or stress, this process can be inhibited. Some patients on T4-only regimens cannot produce adequate amounts of the necessary T3, resulting in symptoms such as weight gain and fatigue—signs that active thyroid hormone is low, even though blood tests may show that T4 and TSH levels are normal.

There are limitations to this therapy, of course. The exact dose of T3 is controversial. The thyroid gland makes about 20 percent T3 and 80 percent T4; however, most physicians feel that this does not translate to thyroid hormone medication dosing. I recommend that the dose of T3 not exceed 10 percent of the total thyroid hormone dosage. Most patients do well by taking just half of the 5 µg Cytomel tablet. I usually recommend taking a dose first thing in the morning and a second dose in the early afternoon. Cytomel can be taken three times a day, but it can cause insomnia if taken too close to bedtime. Unlike levothyroxine, if you forget a dose, you cannot double up on Cytomel.

Compounding pharmacies can make their own versions of time-released T3; however, the quality control will vary from pharmacy to pharmacy. One of the main problems with Cytomel is that it can cause thyroid levels to go too high. If you take Cytomel, your physician will need to check your blood tests more frequently. If thyroid levels are too high (TSH too low), your doctor can reduce the dose of levothyroxine or Cytomel to bring them back into the normal range.

### **Sustained-Release T3**

Sustained-release T3, custom-made by compounding pharmacists, has shown promise as the “perfect” method of taking T3. This is because the T3 that is in Cytomel, Thyrolar, and Armour Thyroid is very short-acting. The majority of the T3 from these products is out of your system after a few hours. Sustained-release T3 comes in special capsules that provide a slow release of the hormone into your system over 12 to 24 hours. The problem with sustained-release T3 is the same as that with all products made by compounding pharmacists: quality control varies widely. In March 2001 officials from the Georgia Drugs and Narcotics Agency became concerned when several patients who had their T3 prescriptions filled at a Georgia compounding pharmacy were hospitalized for a condition known as thyrotoxicosis (life-threatening high thyroid levels). It was thought that the pills might have contained 100 times the prescribed dose of T3.

Several pharmaceutical companies have expressed interest in developing a standardized version of long-acting T3. Until this option is available, I recommend that you be extremely cautious using custom compounded T3.

### **Liotrix (Thyrolar)**

Liotrix is a synthetic mixture of liothyronine (T3) and levothyroxine (T4) that comes in a single tablet. Available in different strengths, the ratio of T3 to T4 in this fixed-combination tablet is 1:4 (1 µg of T3 for every 4 µg of T4). This is approximately the same ratio of T3 to T4 that is produced by the thyroid gland. Despite this, many doctors feel that the percentage of T3 is too high. Another problem with Thyrolar is that it requires refrigeration.

### **Desiccated Thyroid (Armour Thyroid)**

Some patients prefer the natural thyroid hormone, known as Armour Thyroid—the hormone made of dried cow or pig thyroid—which already contains both T4 and T3. Unfortunately, these pills’ quality and

potency vary widely from tablet to tablet, and T3 levels vary along with the pills. Because of the health risks associated with high levels of T3, it is easier—and safer—to use synthetic but bioidentical thyroid hormones. I have seen a few patients who feel great and have perfect thyroid levels on Armour Thyroid.

### **Custom T3-T4 Combination Products**

Compounding pharmacies can make just about any dose combination of T3 (usually in sustained-release form) and T4. These products offer no advantage over standard prescription formulations and are not recommended because of concerns about quality control.

### **Thyroid Hormone Abuse**

Some people adhere to the philosophy “If a little is good for me, then more must be better.” Maybe that’s the case with some things, but with thyroid hormone it is a prescription for disaster. Unfortunately, since thyroid hormone is usually recommended for people suffering from weight gain caused by hypothyroidism (and that’s key—it’s not simply weight gain), some patients will increase the dosage on their own, thinking that taking more hormone will speed their metabolism and help them lose weight even faster. Let me emphasize: *this is extremely dangerous.*

First of all, the “benefits” (if you want to call them that) are short-term at best. Yes, metabolism may pick up. Yes, this may help you shed a few more pounds. But the body is as ill equipped to handle what becomes a “forced hyperthyroidism” as it is to handle hypothyroidism. Increased dosages will send blood pressure sky high, cause the heart to fibrillate and function poorly, weaken muscle tissues, and initiate thinning of the bones (osteoporosis).

Thyroid hormone is a serious matter. Endocrinologists painstakingly work to find exactly the right dosage for their patients, tweaking the daily regimen by as little as 12 µg—that’s 12 millionths of a gram, or 0.000012 g—and having patients come in regularly for blood tests to make sure that the dosage is still correct. Like any other drug, it is not to be abused. The results can be calamitous.



### **Estrogen and Thyroid Hormone**

If you take thyroid hormone and either start or stop taking any type of estrogen medication, your thyroid hormone levels will be affected. This includes starting or stopping HRT or birth control pills. If you become pregnant, you will have much higher estrogen levels, which can also influence your thyroid hormone levels. Estrogen increases TBG levels, soaking up free thyroid hormone. The result is that you need more to get the job done. If there is a change in your estrogen status, you should have your thyroid levels monitored carefully.

### **DIET AND LIFESTYLE FOR A HEALTHY THYROID**

The Hormonal Health Diet is ideal for people with thyroid problems. This diet not only helps you lose weight; it also promotes optimal thyroid balance, psychological well-being, and physical health.

#### **Lots of Fruits and Vegetables**

Fruits and vegetables act as antioxidants. Among the best-known antioxidants are beta-carotene, vitamin A, and vitamin C. Antioxidants promote the binding of what are called “free radicals”—oxygen-rich substances in the body that damage cells and hinder the immune system. Immune system attack is the main cause of hypothyroidism. Antioxidants clear toxins from the body and are even thought to help ward against cancer.

#### **Foods High in Selenium and Zinc**

Selenium and zinc function as antioxidants. Moreover, selenium has a dual role: besides its antioxidantizing properties, it helps convert T4 to T3. Lack of selenium and zinc can reduce levels of active T3 by preventing its conversion from T4. Although selenium and zinc supplements are available from most health food stores, I recommend that you increase your consumption of these vital minerals by eating the proper foods.

Foods high in selenium include whole grains, tuna, halibut, mushrooms, oatmeal, wheat germ, and sunflower seeds.

Because selenium is also needed for the survival of bacteria, persons infected with a bacterial illness often find themselves with a selenium deficiency—and get a double whammy because the bacteria, growing fat and happy off all the selenium they're diverting, also produce substances detrimental to the production of thyroid hormone.

Too much selenium can be as damaging as too little. Among the side effects of too much selenium are abdominal pain, nerve damage, and diarrhea. It is estimated that 50 µg a day is enough to keep your thyroid healthy and provide an adequate amount of antioxidant activity.

Diets low in zinc have been found to promote damage to the thyroid gland. Down syndrome children usually have low zinc levels, and many are hypothyroid as well. Obese people have the same problem. A diet featuring the proper level of this trace mineral can help assuage the problems caused by thyroid dysfunction. Foods high in zinc include beef, herring, maple syrup, turkey, wheat bran, and sunflower seeds.

### **Don't Eat Too Many Raw Goitrogens**

Goitrogens contain naturally occurring substances known as *isothiocyanates* that interfere with the function of the thyroid gland. They're found in cruciferous vegetables from the *Brassica* family, like cabbage, broccoli, brussels sprouts, turnips, rutabaga, mustard, kohlrabi, radishes, cauliflower, cassava, millet, and kale. These vegetables are considered a problem only when consumed raw. Peaches, peanuts, pine nuts, spinach, and strawberries also may inhibit thyroid function if consumed in large amounts. There's no evidence that these foods cause health problems for most people, though. In fact, these foods have many health benefits. The key is not to eliminate these foods, but to eat them in amounts that are not excessive, especially if they are raw.

### **Don't Eat Too Much Soy**

Soy products have many health benefits. Soy is a healthy source of protein. Soy also contains natural estrogen-like compounds (see Chapter 6). When it comes to the thyroid, however, too much soy can cause

problems. Studies have shown that over-consumption of soy products blocks the absorption and action of thyroid hormone and may even induce autoimmune thyroid disease. The estrogen-like effect of soy also increases binding proteins in the blood, lowering free thyroid hormone levels. Soy-derived menopause products that contain isoflavones can also cause thyroid problems. It's OK to have some soy; just don't overdo it, and make sure that you take any thyroid medication at least 2 hours before or after any soy consumption.

### **Physical Activity**

Regular physical activity is a critical element in maintaining hormonal balance and a healthy metabolism. Hypothyroidism makes people tired, less energetic, and less motivated to exercise. Try to exercise during a time in the day when your energy levels are at their peak.

### **Stress Reduction**

Stress can cause improper processing of thyroid hormone, triggering the condition of sick euthyroid syndrome. Stress reduction can improve thyroid hormone processing, increase metabolism, and help you lose weight.

### **Beware of “Thyroid Support Formulas”**

These products, which usually come as dietary supplements, promise to “supply the nutritional needs of the thyroid” and contain iodine (in the form of kelp, bugleweed, or bladderwrack), vitamins, minerals, and L-tyrosine. Tyrosine is the backbone of the thyroid hormone molecule. It's all well and good, but I'm not sure it has much of an effect; you get vitamins and minerals from a balanced diet (or, if need be, supplements), and you get tyrosine from protein.

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## CORTISOL, THE STRESS HORMONE

AS YOU'VE READ THIS BOOK, YOU'VE SEEN THE WAY THE BODY, ITS GLANDS, AND ITS ORGANS FUNCTION BASED ON FEEDBACK. Produce too much or too little of a particular hormone, and metabolism goes haywire; the metabolism problems, in turn, change the amounts of other hormones going through the body; and those hormone levels, continuing the chain of events, throw off other body functions. The body is a versatile mechanism, and it can handle a multitude of variations in diet, exercise, stress, and weight—for a time. But it remains a machine that must be kept within certain limits—it must be continually well tuned—or problems result, problems that tend to cause other problems.

Cortisol has a wide variety of roles in the body and is produced in excess during times of stress. This can lead to health problems, including slower metabolism and weight gain. The body can create a vicious circle. Too much cortisol will make you gain weight; being overweight makes your adrenal gland produce more cortisol. The problems with cortisol excess are very similar to those of insulin resistance discussed in Chapter 3. Cortisol controls body fat in terms of both the amount and distribution. Cortisol also influences your muscles—their bulk and strength.

A condition known as *Cushing's syndrome* results in extremely high cortisol levels and is caused by a tumor of the pituitary gland or the adrenal gland. People with Cushing's syndrome can have a variety of presentations, from very subtle to incredibly severe. Cortisol

deficiency, known as *Addison's disease*, occurs when the adrenal glands cannot make enough cortisol. People with deficiencies of cortisol tend to lose weight and feel tired all the time. If cortisol levels continue to drop, the body shuts down (goes into "shock"), especially when exposed to stress. People with Addison's disease must take cortisol-like medications in order to live. As with all hormones, balance is key.

### STRESS AND THE ADRENAL GLAND

The main function of the adrenal gland is to make stress hormones; it works overtime when the body believes it is under stress. Stress comes in many forms: a fad diet causes one kind of stress, while a tight deadline at work causes another kind. Constant worrying or physical exertion is also a source of stress. Excess weight or other health problems also put stress on the body. Any one of these stressors can cause the adrenal gland to kick into overdrive.

The most immediate manifestation of overdrive is the *fight-or-flight response*. The first hormone the adrenal gland produces under stress is *adrenaline* (also known as *epinephrine*), which makes your heart beat faster and revs up your body. Adrenaline is produced in the center portion of the adrenal gland, known as the *adrenal medulla*. Adrenaline is a *counterinsulin hormone*, so insulin and blood sugar go up when there's lots of adrenaline around. Under normal conditions, adrenaline levels are spiked: they shoot up, the body responds, and then things go back to normal. For a short time, you may want something to calm your nerves (food, alcohol, whatever), but when the spike wears off, body systems return to normal. So adrenaline, overall, has little effect on your weight.

But the body also produces cortisol when it's under stress. Cortisol is produced in the outer portion of the adrenal gland, known as the *adrenal cortex*. Cortisol tends to stick around, and causes symptoms that lead to weight gain. Yes, chronic stress causes weight gain by increasing cortisol levels. It's all part of a vicious circle. Early on, you may not notice the effects of excess cortisol— putting on a few extra pounds, catching a cold more easily, lowered sex drive, less energy, poor memory. You may blame the stress itself, or just "getting older," but the real problem may be your cortisol.

Now, we all have sources of stress in our lives. For the most part, the body can handle cortisol surges caused by stress. But if there's too much stress, the body can't keep up with the detrimental effects of cortisol surges. Today, almost anyone is susceptible to chronic stress. Poor sleep or a fad diet can make matters even worse, causing cortisol levels to climb. As the *Journal of the American Medical Association* noted in 1999, "Chronic stress . . . that evokes prolonged distress can influence cardiovascular, immune and endocrine function, and these alterations are sufficient to enhance a variety of health threats."

People under chronic stress have shorter lives. Much of the stress that we experience today is *psychological stress*. But any type of stress (fad diets, environmental toxins, excessive exercise/overtraining, chronic illness, even the stress of obesity itself) can raise cortisol levels. Stress can cause a heart attack; that's a commonly known fact. But we tend to overlook the hormonal bases for this: High stress leads to high cortisol. High cortisol leads to insulin resistance. Insulin resistance leads to coronary artery disease. The heart attack is the final straw.

How does cortisol excess slow metabolism? High cortisol causes muscle breakdown and accumulation of fat. This altered body composition slows metabolism, which increases weight, leading to even higher cortisol levels. Cortisol is a *counterinsulin hormone* and causes the accumulation of "metabolically evil" fat in the abdominal region, which increases insulin resistance and increases your risk for metabolic syndrome and cardiovascular disease. Insulin resistance and cortisol together magnify each other's effects. High cortisol levels, over a period of time, may even lead to diabetes.

Cortisol excess lowers the levels of two types of hormones that build muscle: androgens (see Chapter 4) and growth hormone (see Chapter 9). Cortisol excess also inhibits thyroid function, further slowing metabolism (see Chapter 6). Cortisol is a hunger hormone, increasing your appetite and causing carbohydrate cravings.

Cortisol excess causes the breakdown of vital tissues such as muscle, bone, tendons, ligaments, and skin. This tissue destruction causes fatigue, weakness, thinning of the bones, and easy bruising. Studies have linked elevated cortisol to high blood pressure, elevated cholesterol and triglycerides, gastroesophageal reflux disease, peptic ulcer disease, irritable bowel syndrome, chronic fatigue syndrome, fibromyalgia, and Alzheimer's disease. High cortisol is tied to mood

disorders such as depression, anxiety, and mood swings. Cortisol lowers the immune system and can make you more susceptible to infections, colds, and the flu.

The twenty-first-century American lifestyle makes stress avoidance very difficult. Modern-day stressors are hard to escape. Some stress is normal, and our bodies can deal with it, as long as it eventually goes away. It's that stress that never goes away that causes cortisol levels to climb. The good news is that you can lower your cortisol levels, and you don't have to quit your job and move to a tropical island to do so (although this would certainly do it too!). The Hormonal Health Diet along with the lifestyle suggestions in this chapter will put you on the road to lower cortisol levels and hormonal balance.

### **CORTISOL IS NECESSARY FOR LIFE**

Cortisol is not all bad. Your body needs some cortisol to function properly. In fact, cortisol helps the body cope with the stress of daily life. Short bouts of stress do not cause a problem with cortisol. It's the long-term, chronic stress that makes cortisol levels stay high. Cortisol is produced by the adrenal glands (small, triangular glands that sit on top of the kidney), which are regulated by the pituitary gland and the hypothalamus. This link is known as the *hypothalamic-pituitary-adrenal* (HPA) *axis*. The HPA axis monitors the body's level of stress and directs the adrenal gland to pump out hormones accordingly. Normally, the body produces cortisol according to a *circadian rhythm*, or regular 24-hour cycle. Cortisol peaks around 8:00 A.M. (to get us going in the morning) and gradually falls throughout the day, hitting its lowest level around 3:00 A.M. Even during times of extreme stress, cortisol tends to maintain this circadian rhythm. But cortisol-containing medications or tumors of the adrenal gland or pituitary gland can disrupt this rhythm.

Let me offer a brief word on cortisol deficiency, also known as Addison's disease or adrenal insufficiency. Addison's disease is most frequently caused by autoimmune destruction of the adrenal gland. John F. Kennedy was a famous sufferer of Addison's disease. Usually, Addison's disease is slow and smoldering: people feel tired and sick, lose weight, and may have belly pain. A simple blood test for cortisol is usually not reliable enough to prompt a diagnosis of adrenal



insufficiency. The standard test for Addison's disease is called a *Cortrosyn stimulation test*. Here, a blood sample for cortisol is taken. Then an injection of the medication Cortrosyn is given. Cortrosyn is synthetic ACTH, the pituitary gland hormone that stimulates the adrenal glands. Thirty to 60 minutes after the injection, a second cortisol blood test is administered (sometimes doctors will take three or more blood samples over time). Normally, the Cortrosyn injection will cause the cortisol level to rise. If it does not go high enough, the diagnosis of Addison's disease is made. Other tests, such as *ACTH level* and *adrenal gland antibodies*, can be helpful in determining the cause of Addison's disease, but are not necessary to make the diagnosis.

Sometimes, an infection of the adrenal gland can cause a more sudden and pronounced loss of cortisol. This is a bad situation.

### ***Marcia's Story***

*Marcia, an 18-year-old high school senior, went to Mexico for spring break. While there, she got sick but decided to wait until she got home to go to the doctor. On the plane ride back, she fell seriously ill and broke out in a rash. Her blood pressure was dangerously low; her stomach hurt. Upon landing, she was immediately taken to a hospital, but it was too late. She died two days later.*

*Marcia had contracted an infection known as meningococcemia, an ailment that attacks the adrenal glands, destroys them, and causes loss of glucocorticoids and rapid death. Although it is a rare condition, I have seen several other cases of meningococcemia in my career as an endocrinologist. Every one has had the same sad outcome.*

It's unusual to encounter such a severe situation, known as *acute adrenal insufficiency*, but it illustrates the fact that cortisol is necessary for life. When adrenal insufficiency is caused by autoimmune destruction of the adrenal glands, it is frequently associated with other autoimmune diseases. Adrenal insufficiency is the key feature of *Schmidt's syndrome* (also known as *polyendocrine autoimmune disease, type II*), which includes Hashimoto's thyroiditis and type 1 diabetes. Patients with adrenal insufficiency should be monitored for the other autoimmune conditions (see Chapter 7 for a detailed list).

Adrenal insufficiency is sometimes referred to as *adrenal fatigue*, *adrenal burnout*, or *adrenal exhaustion*. Proponents of this “syndrome” claim that this condition is different from Addison’s disease, because low adrenal function results in chronic fatigue and weight gain. They promote a variety of unproven herbal remedies and even corticosteroid medications to treat the condition.

### ***Hanna’s Story***

*Hanna had chronic fatigue. She was tired all the time and was gaining weight. She went to her family physician, who told her that she needed to improve her nutrition and increase her physical activity, which was practically nonexistent. She didn’t believe him. The physician had done some blood tests, but she was convinced that something was wrong. She started searching the Internet and found a “natural” physician in her area. She went to see him; he told her that she had adrenal exhaustion and started her on prednisone, a steroid medication. She took the medication for 6 months and then realized that all her problems had slowly gotten worse; she had gained more weight and was more tired than ever before. By the time she came to see me, her body was dependent on the prednisone. It took her another 6 months to wean her off of it, but by the end of that time she was feeling much better. I had finally convinced her to start exercising and to go on the Hormonal Health Diet. She started losing weight before she was completely off the prednisone, but once she was off, the weight loss increased. Eventually, she was back to a normal weight and no longer felt tired. It turned out the original doctor was right, but it took over a year prove it.*

Whatever you want to call it—adrenal fatigue, adrenal exhaustion, adrenal burnout—it is not a real hormonal condition. This “syndrome” is a made-up condition that has no scientific basis. Endocrinologists have very strict definitions of cortisol deficiency. Taking cortisol medications is serious business. If you have been told that you need to take cortisol medications to treat adrenal fatigue, I recommend that you get a second opinion from a board-certified endocrinologist.

## ADRENAL GLAND HORMONES

The adrenal glands are triangle-shaped glands located on top of the kidney, and—like the kidney and many other organs—there are two of them. Also like the kidney, you only need one of them to survive. Five major hormones are produced by the adrenal gland—three types of steroid hormones (testosterone, DHEA, and aldosterone) and two types of non-steroid hormones, epinephrine (adrenaline) and norepinephrine (noradrenaline).

The adrenal gland is really two organs rolled into one. The outer portion of the adrenal gland, known as the *adrenal cortex*, is responsible for making steroid hormones. The adrenal cortex has three layers: the *zona glomerulosa*, which produces aldosterone; the *zona fasciculata*, which produces cortisol; and the *zona reticularis*, which produces aldosterone and DHEA.

Aldosterone is what's known as a *mineralocorticoid*, a type of steroid hormone that controls the body's minerals. Aldosterone can act a bit like cortisol, but its main function is to control the body's salt and water balance. It also plays a major role in controlling blood pressure; aldosterone-producing tumors (a condition known as *Conn's syndrome*) cause very high blood pressure and low potassium levels. In addition, some cancers of the adrenal gland can produce too much glucocorticoid and too much mineralocorticoid. Aldosterone excess causes insulin resistance, in part by lowering potassium levels. Potassium is a critical factor for proper insulin action (see Chapter 3).

The middle part of the adrenal gland is called the *adrenal medulla*. It's like a separate gland. The adrenal medulla produces epinephrine and norepinephrine, which are considered stress hormones. As with aldosterone, excessive production of adrenaline can cause high blood pressure, and that excessive production can be brought on by a tumor known as a *pheochromocytoma*.

The term “steroid” is a generic term for any hormone with the classic four-ring structure derived from cholesterol. Steroids include androgens, estrogens, progesterone, and many other hormones. Corticosteroids are not to be confused with *anabolic steroids* or *androgenic steroids*, discussed in Chapter 4. Anabolic steroids build muscle tissue and promote fat loss. Corticosteroids, in many ways, have the opposite actions of anabolic steroids. Corticosteroids promote fat

accumulation and muscle loss. Cortisol belongs to a specific class of steroid hormones known as *glucocorticoids* or *corticosteroids*. These hormones raise blood sugar levels, in part, by breaking down muscle tissue (*glucose*—hence the name *glucocorticoid*). This class of steroid hormones plays a major role in the control of glucose and other nutrients. Glucocorticoid hormones include cortisol, cortisone, and many medications.

When your hormones are balanced, anabolic steroids and corticosteroids work in harmony to maintain the optimal balance of muscle and fat. Corticosteroids are beneficial for life, and when balanced with the other hormones in our bodies, they contribute positively to our well-being. But, as always, too much or too little causes trouble. In the case of glucocorticoids, only too much makes you fat. People with cortisol deficiency universally lose weight.

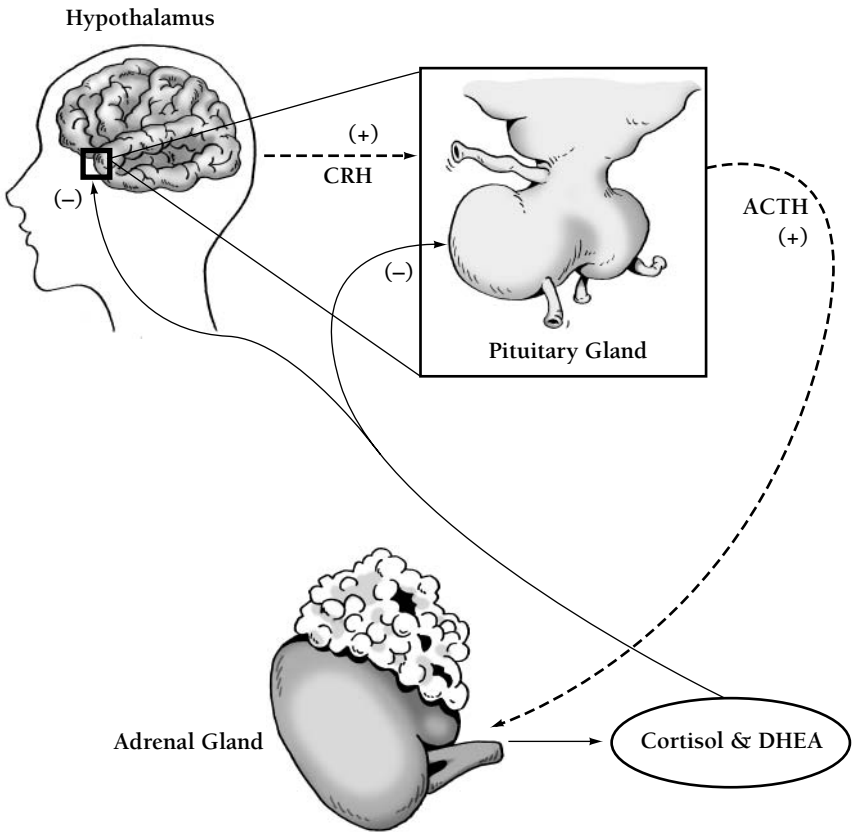
## THE BRAIN AND THE ADRENAL GLANDS

How does cortisol work? It interacts directly with your genes, the same as other steroid hormones. Glucocorticoids bind to the glucocorticoid receptor inside the cell, and this entire complex binds to DNA, turning genes on and off. Think about what was described in Chapter 1, the lock-and-key design for hormone-receptor interactions.

The brain and the pituitary gland control the adrenal gland, just as they do the thyroid, testicles, and ovaries.

The brain sends signals through a region known as the hypothalamus, the most important part of the brain for regulating hunger, weight, and metabolism. The hypothalamus produces a hormone called *corticotrophin-releasing hormone*, or CRH for short. CRH stimulates the pituitary gland to release its hormone, *adrenocorticotrophic hormone* (ACTH), which, in turn, tells the adrenal gland to make glucocorticoids. Normally, when cortisol levels go up, a signal is sent to the brain to ease up on CRH or ACTH production. This careful balance ensures that you have the right amount of glucocorticoids.

But what is the right amount? It depends. Glucocorticoid levels fluctuate throughout the day. They surge early in the morning and gradually fall throughout the day, hitting a low sometime around 4 P.M. This is why timing is critical in the administration of a blood test.



**Figure 8.1**  
**GLUCOCORTICOID ENDOCRINOLOGY:**  
**HORMONE FEEDBACK LOOPS**

Higher centers in the brain send signals to the hypothalamus, which produces pulses of corticotrophin-releasing hormone (CRH). CRH stimulates the pituitary gland to make adrenocorticotrophic hormone (ACTH). ACTH stimulates the adrenal gland to produce cortisol and DHEA. Cortisol and DHEA “feed back” to the hypothalamus and pituitary gland, slowing ACTH production. Positive “feedback” is denoted by (+) and negative “feedback” is denoted by (-).

There is a strong link between glucocorticoids and mood. Most people who are depressed have very high cortisol levels, though the reason isn't exactly known; it is thought that the brain may be very stressed by depression. Whatever the reason, people who are depressed frequently have many of the signs of cortisol excess. Cortisol excess can cause depression, severe mood swings, or even euphoria, as well as anxiety and insomnia. In some cases involving tumors or excessively high doses of medication, cortisol excess has even been known to cause psychosis with wild hallucinations. Glucocorticoids influence the release of brain chemicals (aka *neurotransmitters*) such as *serotonin* and *norepinephrine*, and cortisol excess disrupts the delicate balance between the pituitary gland and the adrenal gland. Almost any psychiatric illness, even a mild one, may result in cortisol excess; the reverse can occur as well. The body's fine balance works both ways.

### GLUCOCORTICOID MEDICATIONS

There are a number of medications containing glucocorticoids. They come in all forms: pills, creams, eye drops, nasal sprays, gels, enemas, inhalers, and injections, with names like prednisone, prednisolone, dexamethasone, triamcinolone, cortisone, and hydrocortisone. You've probably heard of the most common ones—prednisone and cortisone—and the terms people use when they're taking them: “on cortisone” or “on steroids.” These medications are necessary to treat many medical conditions caused by an overactive immune system, such as inflammatory bowel disease, lupus, sarcoidosis, arthritis, kidney disease, and liver disease. These medications, because of their immunosuppressive ability, are also used frequently in organ transplant patients. Even some types of cancer may be treated in part with glucocorticoids. Although very effective in treating these conditions, glucocorticoid medications have horrible side effects. They flood the body with extra corticosteroids and induce what doctors call a “disease state,” in which conditions like Cushing's syndrome can suddenly take root. (The induced version is called *iatrogenic Cushing's syndrome*.)

Because these medications are so frequently prescribed, patients and even physicians forget about the serious side effects. Let me remind you, the side effects of these medications can be as serious as

having Cushing's syndrome. If you take any of these medications—especially the pills—on a daily basis, you should be closely monitored by your physician. You should work with your physician to get on the lowest possible dose of steroids and develop a plan to try to taper the steroids even further. In my career, I have had very few patients who could not eventually stop taking steroid medications. Many doctors think it is too dangerous to stop the steroids, but I believe it is more dangerous to continue taking them.

*A note to patients:* If you have been taking steroids for more than 30 days, your body is dependent on them; some would say addicted. If you stop taking them abruptly, you might face serious medical consequences. Your adrenal gland has turned off its steroid production. Your steroid dose must be slowly tapered. Most endocrinologists will tell you that you need to take about as many days to taper off the steroids as you have been taking them. For example, if you have been taking corticosteroids for a year, you should slowly decrease your dose over the course of one year before completely discontinuing the medication. I do not recommend that you do this by yourself; this requires careful monitoring by an endocrinologist.

## EFFECTS OF EXCESS GLUCOCORTICOIDS

In excessive amounts, from medications or adrenal gland overactivity, glucocorticoids have many negative effects:

- Acne
- Anxiety
- Binge eating
- Bone loss (osteoporosis and osteopenia)
- Bruising
- Carbohydrate cravings
- Decreased muscle mass
- Decreased sex drive
- Decreased well-being
- Depression
- Facial hair (for women)
- Facial redness

- Facial rounding
- Fatigue
- Fractures
- Frequent infections
- Frequent colds/flu
- Gastroesophageal reflux disease (GERD)
- High cholesterol
- High triglycerides
- Increased appetite
- Increased blood pressure
- Increased blood sugar
- Increased body fat, especially in the belly
- Insomnia
- Kidney stones
- Menstrual cycle problems
- Mood swings
- Muscle wasting
- Overeating
- Poor concentration
- Poor memory
- Poor sleep
- Poor wound healing
- Slow metabolism
- Stretch marks
- Stomach ulcers
- Thin arms and legs
- Thin skin
- Upset stomach
- Weakness
- Weight gain

Some of these symptoms deserve particular attention.

### **Weight Gain**

Glucocorticoids increase the amount of fat in your body and in a particular distribution. Glucocorticoids cause fat buildup in the belly, chest, and face—the apple shape—the worst type of “metabolically evil” fat. This fat buildup can cause many of the symptoms of insulin resistance and the metabolic syndrome.



### **Increased Appetite**

People who take a steroid medication will tell you they can never get enough to eat. Glucocorticoids stimulate hunger centers in the brain.

### **Tissue Breakdown**

Cortisol causes muscle breakdown, leading to muscle weakness, slowed metabolism, and insulin resistance. Cortisol is known as a *catabolic hormone* because it breaks down muscle tissue. Androgens are called anabolic hormones; they build muscle up. Catabolic, of course, is the opposite. Muscle wasting means less muscle, so your metabolism slows. You feel weak and tired. You don't want to exercise, even though it would be good for you (and would probably help take off some of that stress naturally). Glucocorticoids also lead to breakdown of other tissues, such as bone and skin. Bone loss leads to osteoporosis, and skin breakdown leads to easy bruising, stretch marks, or thin skin with a ruddy appearance.

### **Immune Suppression**

Glucocorticoids keep the immune system in check. They have potent anti-inflammatory properties but also interact with white blood cells to suppress your immune system. This is why people under a lot of stress tend to get sick: the immune system has been weakened by stress via glucocorticoids. And yet doctors prescribe glucocorticoids such as cortisone or prednisone to treat medical disorders caused by immune overactivity. Glucocorticoids are also used to treat severe allergies. It's a difficult balance.

### **Upset Stomach, Ulcers, Esophageal Reflux (GERD), Increased Stomach Acid Production**

Have you ever been really upset and ended up with an upset stomach? Here's why: excess glucocorticoids crank up stomach acid production, leading to upset stomach and possible stomach ulcers. And that's why stress causes stomach ulcers.

## **Bloating and Fluid Retention**

Earlier we briefly discussed aldosterone and its fluid retention properties. Glucocorticoids have some overlap with the actions of mineralocorticoids. They will stimulate the glucocorticoid receptor very well, but they also stimulate the mineralocorticoid receptor to some extent. The result is salt, water retention, and bloating. Excess mineralocorticoid activity can also make your blood potassium drop—leading to insulin resistance (see Chapter 3).

## **CUSHING’S SYNDROME**

Cushing’s syndrome is named after a famous Boston neurosurgeon, Harvey Cushing, who first described the condition. He discovered that the most common cause of the syndrome was a small tumor in the pituitary gland. Cushing’s syndrome (CS) caused by a pituitary tumor is called *Cushing’s disease*. Other cortisol excess conditions are part of the “syndrome”; only the pituitary cause is the “disease.” The condition is fairly rare: about 1 in 1,000 people have Cushing’s. But not everyone has been diagnosed. Women are four times as likely to develop Cushing’s as men, and some overweight people have Cushing’s but don’t know it.

Cortisol-like medications can also cause symptoms as severe as a tumor (known as *iatrogenic Cushing’s syndrome*). Although the severity of this condition can be highly variable at presentation, most people have much more severe manifestations than those with cortisol excess from chronic stress. In CS, symptoms tend to get worse over time. People with CS can have any of the symptoms listed above; however, some symptoms are of greater concern than others.

Weight gain can be variable. Some people gain huge amounts of weight in a short period of time. Regardless of the pace of weight gain, *body fat distribution* can be an indicator of cortisol excess. Along with fat that accumulates in the abdominal region, fat may also build up in the hollow space over the collarbones (known as *supraclavicular fat pads*), the back of the neck between the shoulder blades (known as the *dosocervical fat pad*, or *buffalo hump*), and in the face (known as moon face). Doctors refer to this appearance as *cushingoid*. Although

all people who look cushingoid do not have CS, this appearance should alert your doctor to measure cortisol levels.

Muscle weakness and wasting can be severe. While the midsection grows, the arms and legs become very thin. The muscles may become quite weak, to the point where it is difficult rising from a chair. The thigh and shoulder muscles are particularly affected; this is known as *proximal muscle weakness*, because the muscles close to the torso are affected more than distal muscles like the calf and forearm. Stretch marks (known as *striae*) are common in many people with cortisol excess, but the striae of CS may take on a peculiar appearance. The striae may develop quite rapidly and may develop on the belly, armpits, forearms, groin, or other parts of the body. The striae of CS are usually wide (more than a half-inch) and may be red or purple in color. Pink or flesh-colored striae are less suggestive of CS. Skin problems are common with cortisol excess. If you are young, thinning of the skin can be a warning sign of CS. (For older folks, thinning of the skin is a normal part of the aging process.) The skin of the face can become thin, resulting in a red or ruddy appearance (known as *plethora*). Other skin problems, such as easy bruising, poor wound healing, and acne, can also occur but are not as specific for CS.

High blood pressure that is difficult to control can be a warning sign of CS. High blood pressure is a common condition and can be linked to a variety of hormone problems, including insulin resistance, thyroid problems, growth hormone excess, and others. High blood pressure caused by CS may go up and down (known as *labile hypertension*) or may be difficult to control on multiple medications (more than three different types of blood pressure medications).

Psychological problems are extremely common in CS. Depression and anxiety are common in all types of cortisol excess; however, in the setting of other features of CS, problems with mood may be a warning sign. Patients with CS have reported all degrees of psychological problems, from poor sex drive, poor memory, poor sleep, anxiety, and inability to concentrate to severe depression and even psychosis.

Infections can occur in patients with CS because of the immune system-lowering effects of cortisol. Common infections include colds, sinus infections, yeast infections, and bladder infections. Patients with CS may also come down with exotic infections typically seen in AIDS patients.

Menstrual cycle problems are common and are usually not due to CS. It is very unusual, however, to have CS and not have menstrual cycle problems. Therefore, women with a normal menstrual cycle almost never have CS. Sometimes adrenal gland overactivity leads to excessive production of male hormones. Female facial hair growth can be severe (known as *virilization*) and may be associated with balding (in a pattern similar to a man's), deepening of the voice, and growth of the clitoris into what may resemble a small penis (known as *clitoromegaly*). While male hormones cause problems other than CS, these extreme effects are always cause for concern. (For more information on male hormone problems in women, see Chapter 5.)

### *Warning Signs for Cushing's Syndrome*

- Cushingoid body habitus
- Rapid or excessive weight gain
- Muscle weakness
- Stretch marks that are red, purple, or wider than a half-inch
- Thinning of the skin
- High blood pressure
- Elevated blood sugar
- Depression or anxiety
- Frequent infections
- Severe cystic acne
- Menstrual cycle problems
- Male-pattern balding (in women)
- Facial hair growth (in women)

### ***Tamika's Story***

*Tamika was a 40-year-old woman. She'd had two children, was a stay-at-home mother, and wasn't much into exercise. So when she started gaining weight, she mostly disregarded it—even though her face became round and moonlike, her belly got big with purple stretch marks, and her arms and legs became skinny. She felt lousy and tired all the time. Just signs of becoming old and fat, she thought.*

*Eventually, she stopped having menses and went to visit her doctor. His initial recommendation: diet and exercise. These had little effect, and she went back. Blood tests determined she*

*had diabetes and high blood pressure, and further investigation indicated a microscopic tumor in her pituitary gland. The tumor was removed (to give you an idea of how small it was, it was removed through her nose). With the tumor removed, the woman's diet and exercise started having the proper effect, and her body returned to normal.*

Tamika was lucky; not all people are. Another patient of mine, Anita, discussed in Chapter 5, began having similar symptoms. However, along with the weight gain and fatigue, she also grew hair on her face. It turned out she had a very large cancer of the adrenal gland. Despite extensive surgery and chemotherapy, she died two years later, the length of her life a remarkable feat in itself; she had only been expected to survive 6 months.

Please note that although the symptoms were similar, these women had different conditions. Adrenal gland cancer is a cause of CS, but most of the time CS isn't cancer at all, but a benign, hormone-producing tumor that can be removed surgically.

If these cases sound like insulin resistance, that's because—in one way—they are. Glucocorticoids such as cortisol are known as *counter-insulin hormones*. They work against the actions of insulin, thus creating the need for higher insulin levels and producing the components of metabolic syndrome.

Cushing's syndrome is called a "syndrome" because it describes many conditions that all result in cortisol excess. The main causes of CS are:

- Pituitary gland tumor (also known as *Cushing's disease*)
- Adrenal gland tumor
- Various other cancers that produce ACTH (known as *ectopic ACTH-producing tumors*); these tumors are most common in the lung
- Steroid medications (iatrogenic CS)

### ***Seth's Story***

*Seth was a 48-year-old man who had to take daily steroids because of his severe asthma. The steroids made him gain weight and gave him a number of the symptoms listed in this chapter. He followed the Hormonal Health Diet, lessened the*

*stress in his life, and started exercising, all of which contributed to his losing weight and feeling better and healthier. Unfortunately, the steroids had taken their toll. One day Seth developed severe back pain. He had suffered a compression fracture of the vertebra, a telltale sign of osteoporosis.*

Incidentally, many pets are given steroids to help with allergies. They can get all of the same problems as humans.

### **TESTING FOR CUSHING'S SYNDROME**

Testing for CS can be tricky and should be done only through a qualified physician. Most general-practice physicians are able to run screening tests for CS, but all abnormal screening tests should be referred to an endocrinologist. There are several different types of tests, and experts still argue about which test is best. Testing is not perfect, and often a series of tests is required to confirm the diagnosis of CS. Although there are many causes of Cushing's syndrome, the initial testing is the same for all forms. The first set of testing is to determine if you have an overproduction of cortisol. If so, your endocrinologist will do additional tests to determine which type of Cushing's you may have.

#### **24-Hour Urine Free Cortisol (UFC)**

This remains the current standard screening test for CS. Yes, you have to collect all of your urine in a container over a 24-hour period. This is a good test for assuring yourself that you do not have CS; however, a positive UFC does not guarantee CS. The higher the level, the more likely it is CS; levels more than four times the upper limit of normal (ULN) almost always signify CS. Obesity, depression, pregnancy, excessive exercise, and excessive alcohol use have been shown to cause mild elevation of the UFC; however, these conditions never cause it to go over four times the ULN. An elevated UFC that is less than four times the ULN is considered to be in a "gray zone" and requires further testing to sort things out. Midnight serum or salivary cortisol levels are a great way of determining if the UFC represents true CS or pseudo-Cushing's syndrome.

The term “pseudo–Cushing’s syndrome” has been given to the condition that is characterized by many of the symptoms and physical features of CS and excess cortisol but without the presence of a tumor. Urine cortisol levels are usually in the “gray zone.” Chronic stress as well as obesity, depression, excessive exercise, diabetes, pregnancy, and excessive alcohol use can all elevate cortisol levels and cause pseudo-CS. Contrary to the treatment for CS (surgical removal of the tumor), the approach for pseudo-CS is to treat the underlying illness and remove the stress.

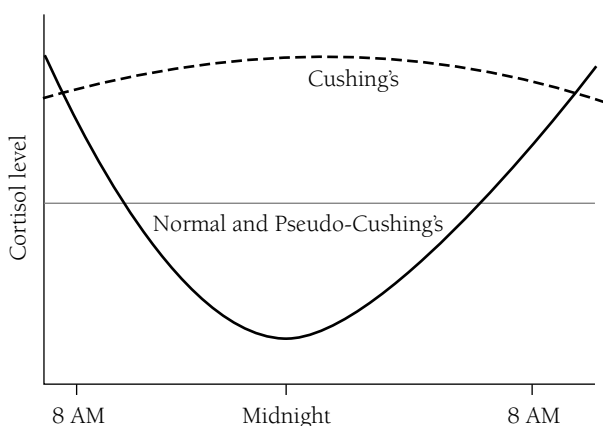
### **Serum Cortisol Level**

This is one of the best tests for CS, but timing is everything. The key to interpreting cortisol levels is the fact that people with CS lose their diurnal rhythm (see Figure 8.2); the cortisol levels are high all day and all night long. Therefore, a high cortisol level at midnight, when the level should be at its lowest, is a very reliable indicator of CS. Although measuring the midnight serum cortisol level is a very accurate test, it can be very inconvenient. Serum cortisol levels from other times of the day are not very useful when it comes to diagnosing CS.

### **Salivary Cortisol Level**

Most saliva tests are considered unreliable; however, salivary cortisol testing is an exception. The salivary cortisol test is a very accurate and reliable way to measure cortisol at specific times of the day through the saliva. The test is valid only for diagnosing cortisol excess; it is not reliable for diagnosing cortisol deficiency.

A sample of saliva is collected in a small cotton cylinder and sent to a laboratory for analysis. The key to this test is that you should not eat, drink, or exercise for at least 2 hours prior to taking the sample. I usually get two salivary cortisol levels, at midnight and 8 A.M. Normal ranges have been established for specific times of the day. I like to see both levels in the normal range, as well as a nice diurnal rise in the 8 A.M. specimen.



**Figure 8.2**  
**DIURNAL CORTISOL FLUXES**

In normal people, and in those with pseudo-Cushing's syndrome, cortisol levels vary throughout the day. The peak is usually around 8 A.M., the nadir around midnight. Patients with Cushing's syndrome lose diurnal rhythms, and cortisol levels stay constant and high throughout the day.

### Suppression Testing

A test known as the *overnight dexamethasone suppression test* is a fairly good way of ruling out CS. Like the UFC, this test can be falsely positive, especially if you have the conditions that lead to pseudo-CS. You must take a 1 mg tablet of dexamethasone (Decadron) at midnight the night before your test. At 8 A.M. the next day, blood is collected and cortisol is measured. Under normal circumstances, dexamethasone, a synthetic glucocorticoid, will suppress the adrenal glands' natural cortisol production. If the "suppressed" cortisol level is above 5  $\mu\text{g/dL}$  (some experts have lowered the cutoff to 3.5  $\mu\text{g/dL}$ ), CS is suspected.

### Confirmatory Testing

Most of the time, additional testing is necessary to "rule in" CS. Testing protocols vary among endocrinologists and can be cumbersome and



lengthy. Confirmatory tests include more sophisticated versions of the dexamethasone suppression test, the *dexamethasone-suppressed CRH stimulation test*, other stimulation and suppression tests, MRI and CT scans, and even direct measurement of blood hormone levels from the pituitary gland (known as *inferior petrosal sinus sampling*, or IPSS).

### CAUTIONS ABOUT TESTING FOR CUSHING'S SYNDROME

- Testing for CS is one of the most controversial subjects in the field of endocrinology. Experts continue to have heated arguments about testing protocols.
- Testing is still crude. Tests that are easy to perform usually give unreliable results. The more reliable tests usually require a patient to take medication (sometimes for days) or receive injections of very expensive medications prior to blood testing. These “stimulation” and “suppression” tests require an up-to-date endocrinologist, because protocols frequently change.
- Many people are inappropriately tested for Cushing's with a simple blood cortisol test. Because cortisol levels in the blood fluctuate, a simple blood test alone is rarely helpful. Unless the doctor draws blood at a specific time, the serum cortisol reading is useless.
- Many people with symptoms suggestive of Cushing's are not tested by their doctor. If you think you have CS, ask your doctor to test you.
- An elevated test result does not mean you definitely have Cushing's. Confirmatory tests are almost always needed. Do not become overly concerned that you may have adrenal gland cancer or some other horrific problem. Your levels are most likely elevated because of excess stress or excess weight.
- On the other hand, a normal test does not always mean you are OK. Sometimes cortisol is produced episodically, and can be missed on initial testing. If you have symptoms that are very suggestive of Cushing's but have a normal test, ask your doctor to repeat the test. I have had patients who tested negative the first two tries but on the third were positive, and subsequently were found to have tumors.
- A rare variant of Cushing's, known as *food-induced Cushing's syndrome*, has been known to occur. Since Cushing's itself is rare, this

variant is really, really rare. In food-induced Cushing's, the body's hormone-receptor system gets "cross-wired," and one of the hormones produced by the body when it detects food in the stomach, known as *gastric inhibitory polypeptide* (GIP), stimulates the adrenal gland to produce corticosteroids. This condition can be detected only if you are tested right after you eat.

### **I HAVE A POSITIVE TEST FOR CUSHING'S; WHAT DO I DO NOW?**

Most people with positive tests actually do not have Cushing's. Just being overweight can cause you to produce excess cortisol in levels high enough to make your test result abnormal. Stress—mental and emotional—and heavy drinking can also do this. If you have a positive test, your endocrinologist must do further testing to determine if you have true Cushing's or pseudo-Cushing's syndrome.

#### **What If Confirmatory Tests Are Positive?**

If further tests are also positive, you probably have Cushing's. Now your endocrinologist needs to find out where the excess cortisol is coming from. At this point your doctor will do more blood tests as well as imaging studies such as CT or MRI scans to determine the type and location of your cortisol-producing tumor. If your tumor is found (usually in the pituitary gland or adrenal gland, but sometimes in the lung), it should be removed surgically.

#### **What If Confirmatory Tests Are Negative?**

In this case, you probably still have cortisol excess, but the cause is not a tumor. The cause is stress! It's either the stress your fat is putting on your body, or some other physical or emotional stress in your life. (That includes the stress of drinking a lot of alcohol.) And don't forget: if you have the serious symptoms of CS (see above), ask your doctor to retest you.

## **PSEUDO—CUSHING’S SYNDROME**

The term “pseudo-Cushing’s” has been given to the condition that has all the appearances of Cushing’s but without the physical presence of a tumor. Many people with this disorder are overweight and have many of the features of Cushing’s described above, most notably the central obesity, moon-shaped face, diabetes, and high blood pressure. Here the body feedback loops come into play once again: cortisol makes you fat—there is no doubt about that—and being fat makes you have too much cortisol. The vicious cycle goes around and comes around.

Fat is what throws everything off. Too much fat disrupts hormonal regulation and leads, finally, to cortisol excess. The thing is, fat is an endocrine organ itself. It is a gland, and it makes hormones just like any other gland. The major hormone made by fat cells is leptin (see Chapter 10), but fat cells produce many other substances as well. One in particular, called *inflammatory cytokines*, revs up the immune system, prompting the adrenal gland to pump out more corticosteroids to calm it down. The process wreaks havoc on your fat cells. The result: more cortisol, more fat, and more inflammatory cytokines. It’s another vicious cycle.

## **LOWER YOUR CORTISOL**

Cortisol excess makes people ravenous. If you follow the suggestions listed below, your cortisol levels will be reduced. Your insulin will stop surging, and you will be able to use your calories to give you increased energy instead of having those calories turn into fat.

## **The Hormonal Health Diet**

The Hormonal Health Diet is the ideal diet for lowering cortisol levels. Although it is designed to achieve total hormonal balance, cortisol levels are a major factor in its design. The diet allows for stress eating by permitting a variety of foods. The balance of carbohydrates, protein, and fat, as well as the use of small, frequent meals, are ideal for lowering cortisol levels, controlling cravings, and reducing hunger.

### **Eat Small, Frequent Meals**

This prevents insulin surges and controls hunger and cravings.

### **Cut Down on Salt**

Because of the side effects mentioned earlier—bloating and high blood pressure—a low-salt diet will help you lower your cortisol. Salt makes you retain water. Salt also deprives bones of calcium. Avoid added salt as much as possible and have your blood pressure checked regularly.

### **Cut Down on Alcohol**

Heavy alcohol consumption makes the adrenal gland overreact and may induce pseudo-Cushing's syndrome. Drinking in moderation (one or two drinks per day) is OK; just don't overdo it.

### **Drink Caffeine in Moderation**

Drinking more than two or three cups of coffee per day can raise cortisol levels. Caffeine also raises metabolism, decreases the risk of diabetes, and improves lung function and exercise performance. Does coffee make you gain weight? Probably not. Coffee does not need to be eliminated, but you should limit consumption to two or three cups each day.

### **Cut Down on Stress**

This may be the hardest change of all. Many people use food as a way of coping with stress. Food is enjoyable; food is comfortable. In a stressful situation, whether the stress is emotional or physical, it's natural to want food. It may not make the stress go away, but it seems to ease the mind, if only for a few minutes, and so much of stress is in the mind.

Unfortunately, you can't eat without consuming calories and nutrients, however empty. Here comes that vicious circle again: you get stressed, you eat, you gain weight, you feel more stressed, you eat again. You have to break the cycle. Find new stress reduction techniques. Work out a few times a week. Take a walk. Practice relaxation. Think of using food for its nutritional value, not for its ability to make you feel good. When you relieve stress by means other than eating, you take a double step closer to balancing your hormones. Not only do your cortisol levels drop, but your insulin doesn't spike—one of the major triggers of those cycles.

Here are a few simple ways of reducing stress:

- *Physical activity.* Exercise is critical to maintaining optimal cortisol levels and hormonal balance. Physical activity helps your body better handle stress by improving the cardiovascular and musculoskeletal systems. Exercise improves insulin resistance. If your body is healthier, it will be better able to withstand the physical drain of stress. But note: the best type of exercise for lowering cortisol is slow and steady. Extreme exercise, such as marathon running, can actually raise your cortisol. No time to exercise or too tired to exercise? These are the two most common excuses for not exercising. The vast majority of people who are “too tired to exercise” report having increased energy and less fatigue after exercising. If even very light exercise exhausts you, this could be a sign of CS or another serious medical condition such as heart disease, lung disease, kidney failure, liver failure, a muscular disorder, or a neurological disorder. You should incorporate physical activity into your daily routine by making it a priority. Many people enjoy waking up an hour earlier and getting some physical activity in before they begin their day. This is an effective strategy I have used myself. After a while, you will not feel as good if you miss a morning of exercise. Exercise does not have to be done all at once. Short bouts of a variety of activities (e.g., shopping, gardening, walking, cleaning the house, marching in place) can be done for a few minutes at a time and have a cumulative effect. If you have true CS or are taking steroid medications, you should exercise with caution. Your muscles have become weakened from the excess steroids and are susceptible to a condition known as *rhabdomyolysis* (literally, death of the muscle).

- *Control your hunger.* Many people deal with stress by overeating. Sometimes this can get out of control. If you have to eat a lot of food, then the Hormonal Health Diet is the perfect diet for you.
- *Comfort foods.* Most people use food as “anti-stress medicine.” Stress eating is a common reaction to nervous tension and contributes to weight gain. People tend to gravitate toward “comfort foods” during times of stress. What is comfort food? It’s food that makes you feel good. Comfort foods do help relieve stress. The problem is that they also make you gain weight. For many people, comfort foods are home-cooked foods like spaghetti and meatballs, macaroni and cheese, or fried chicken and mashed potatoes. For others, comfort food is fast food or junk food. Comfort foods are usually high in fat, carbohydrates, and calories, but they don’t have to be.
- *Practice positive self-talk and improve your self-esteem.* Tell yourself that you can do it. You talk to yourself every day. Think about what you are saying. Are you hard on yourself? Do you give up easily? You determine how you talk to yourself. Tell yourself that you are in control. As you see results, it will be easier and easier to give yourself psychological rewards. Don’t worry about failure. Remind yourself that it not an easy road, but you can do it.
- *Meditation, Yoga, Tai Chi, and Chi Gong.* All are excellent ways to lower stress. They combine strength, stretching, breathing, and meditation and can be done by almost anyone. Yoga is a growing fitness craze and has expanded to specialty practices such as power yoga, disco yoga, Bikram (hot) yoga, and even Ruff yoga (with your dog), invented by Suzi Teitelman. Meditation relaxes your mind. Yoga combines meditative techniques with stretching, one of the most overlooked parts of exercise. Important to all of these methods—in fact, to all forms of exercise and stress reduction, period—is that you drink lots of water.
- *Massage.* Massage works the muscles, loosening the knots and freeing the toxins that have collected during the stressful times.
- *Make time for yourself.* Too busy all the time? Many people are stressed because they have too much to do. Organizing and simplifying your life can be an incredible way to lower stress levels, especially for type A personalities. I recommend the book *Organizing the Good Life: A Path to Joyful Simplicity—Home to*

*Work and Back*, by Celia Rocks, as well as the classic *The 7 Habits of Highly Effective People*, by Stephen Covey.

- *Spend time with friends and family.* Your friends and family are your greatest support. Let them know what is going on with your life. If you are trying to lose a meaningful amount of weight, involve them in the process. You will receive support up front and will also benefit from ongoing congratulations and encouragement every time they see that you have lost more weight.
- *Herbal products.* Several herbal products have been touted as stress relievers. Be careful with herbals: for many, their claims remain unproven. Some herbal preparations can react with prescription medications, producing toxic effects.
- *Medications.* SSRI medications such as Prozac, Zoloft, Paxil, and Celexa, originally used only for depression, are now widely prescribed for anxiety. For some, these medications may be helpful. Older medications available for stress and anxiety include a class of drugs known as benzodiazepines such as Xanax, Ativan, and Valium. These drugs tend to be addictive. Unless you have a true anxiety disorder, diagnosed by a psychiatrist, I do not recommend these medications. It has become all too easy for us to pop a pill instead of facing the issues in our life.

### Cortisol-Lowering Products

In the past few years several herbal products claiming to lower cortisol levels have hit the Internet and infomercial airways. These products, with names like CortiSlim™, CortiStress™, CortiSlender™, CortiSyn™, CortiBurn™, Corti-Sol™, Corticel™, CortiDrene™, LipoCort™, TheraStress™, and Relacore™, are called “cortisol blockers.” The manufacturers claim that these products help control cortisol, reduce belly fat, and help you lose weight. They contain such ingredients as *bitter orange peel, magnolia bark, green tea extract, beta-sitosterol, chromium polynicotinate, citrus aurantium, passion flower, ginseng, jujuba fruit, and vanadyl sulfate.*

In 2004 the Federal Trade Commission charged marketers of CortiSlim and CortiStress with claiming falsely that their products can cause weight loss and reduce the risk of, or prevent, serious health

conditions. The manufacturers paid about \$4.5 million in a settlement. Several class-action lawsuits are also under way. One suit seeks a refund for all customers who purchased CortiSlim because of the product's deceptive advertising campaign. Despite this legal action, these products remain on the market. These products have unproven benefits and unknown health risks. I recommend avoiding them entirely.



# GROWTH HORMONE

GROWTH HORMONE (GH) WAS ONCE THE PROVINCE OF PEDIATRICIANS AND PEDIATRIC ENDOCRINOLOGISTS. For children who were small for their age, these professionals would prescribe GH to make them taller. It works like a charm.

Today we are seeing GH in a new light. GH is increasingly being recognized as an important hormone for *all* ages. *Growth hormone deficiency* (GHD) is now recognized as an adult disease. And treatment with GH has a number of benefits. It reduces the amount of fat in the body and increases muscle mass, it improves heart function and exercise performance, it improves mood and the sense of “well-being,” it strengthens bones, and it helps wounds heal faster. This chapter will examine the ways that GHD can make you lose muscle and gain fat, and how the addition of GH can reverse that trend.

But a caution is in order: GH is not a cure-all. Excesses of GH can cause a number of problems, most notably insulin resistance, diabetes, high blood pressure, carpal tunnel syndrome, male breast enlargement, and even cancer.

However, you don’t need GH—in a pharmaceutical form—to improve your health. Your body makes GH naturally, and if you follow the Hormonal Health Diet, exercise, and cut your fat intake, your GH levels will naturally improve and will help with the work of losing weight.

Growth hormone is so named because it makes children grow. But it’s much more than that. It’s an *anabolic* hormone—a muscle

builder—but not a steroid. GH and testosterone have similar effects on body composition, decreasing fat and increasing muscle mass. GH has a structure different from the four-ring chemical structure of a steroid. It's known as a peptide hormone, and unlike steroids—which are made from cholesterol—GH is made from amino acids, the building blocks of proteins. Peptide hormones cannot be taken by mouth, because they'll be digested like food. Rather, like insulin, peptide hormones must be injected.

During childhood, GH—combined with genetics—determines one's height. Children who do not produce GH are very short. Until the 1980s, GH extracted from human pituitary gland extracts was given to short children to make them grow. Unfortunately, a rare and fatal brain disease known as *Creutzfeldt-Jakob disease* (similar to mad cow disease) was linked to natural GH. In 1981 a synthetic form of GH was approved, and this is the kind that's used today.

Although GH can influence many different types of cells in your body, the main target of GH is the liver. GH tells the liver (and other organs) to produce a second hormone known as *insulin-like growth factor-1* or *IGF-1*, a hormone so called because its chemical structure is similar to insulin. (IGF-1 is also known as *somatomedin C*.) IGF-1 is extremely important; in fact, most of what we consider to be the action of GH is actually the action of IGF-1.

## **GROWTH HORMONE, BODY WEIGHT, AND BODY COMPOSITION**

Growth hormone deficiency can make you gain weight. And studies show that GH replacement helps you *lose fat and gain muscle*; but to lose weight, you must optimize the effectiveness of GH with proper nutrition, sleep, and physical activity. GH, whether produced naturally or taken as an injection, has potent muscle building and fat burning effects. GH improves your mood and gives you more energy, so you feel like exercising.

If you suffer from growth hormone deficiency, your body will have several indications of obesity and related problems. GHD is associated with central obesity—fat around the belly. This is the “metabolically evil” type of fat that is associated with insulin resistance, type 2 diabetes, high cholesterol, and cardiovascular disease. There is also a condition called *obesity-related hyposomatotropism*. This is another

example of the vicious circles created when the body is out of hormonal balance. Obesity inhibits GH secretion. Obesity-related hypsomatotropism is a form of GHD and almost always gets better with weight loss. So being overweight lowers your GH levels, and having lower GH levels makes it easier for you to gain weight. Central obesity also contributes to weight gain, because it lowers your GH levels. In other words, obesity itself can cause severe GHD.

And the problem gets worse as you get older. Just as fat lowers your GH levels, so does aging. Talk about vicious cycles.

Scientists suspect that the obesity-GH link may be due to another hormone, leptin (see Chapter 10). Others believe the problem lies deeper in the brain. And still others blame insulin or free fatty acids for lowering GH in obese people.

Enhancing GH can help you lose that extra fat around the middle—and keep it off. Moreover, removing that extra fat around the middle will also improve insulin resistance. How does GH do it? GH helps you lose fat by making the fat burnable as fuel. The by-product of this change is more energy. Fat cells have GH and IGF-1 receptors, and the stimulation of these receptors causes fat cells to break down fat. GH also counters the effects of insulin. It's an interesting contradiction. Insulin promotes fat accumulation, but GH promotes fat breakdown.

But here's where GH can be dangerous. Because it counters the effects of insulin, taking GH can cause diabetes in some people. However, since it helps improve insulin resistance as well, the opposite effect may occur. The upshot is that some people who take GH may get diabetes while others will not. Many people see an initial elevation of blood sugars, but as they build muscle and lower fat, the insulin resistance abates and blood sugars actually become lower than before the GH therapy. This is all the more reason to make sure that if you take GH, you are closely monitored by a physician experienced in its use. Hormonal balance is critical. GH is an important component of hormonal balance, but more is not necessarily better.

## **THE BRAIN AND GROWTH HORMONE**

Like other hormones produced by the pituitary gland, GH is strongly influenced by feedback (see Chapter 1). When the body reports the need for more GH, the pituitary springs into action. Similarly, when the

pituitary detects a rise or fall in the level of GH, it takes steps to adjust its production. Once again, the brain influences the hormone and the hormone influences the brain.

Special cells in the pituitary gland called *somatotrophs* make GH. Signals come from the brain by way of the hypothalamus, and it is a hormone made by the hypothalamus, called *growth hormone-releasing hormone* (GHRH), that stimulates the pituitary gland to make GH.

A second hypothalamic hormone, *somatostatin*, inhibits pituitary gland production of GH. Interestingly, medications that mimic somatostatin cause dramatic weight loss in some people (see Chapter 10). Obviously, GH acts not by itself, but in concert with many other hormones.

How does the system work? The pituitary gland secretes GH in a pulsatile manner. Like other hormones, it's secreted according to the *diurnal rhythms* of the body. GH secretion is greatest while you sleep.

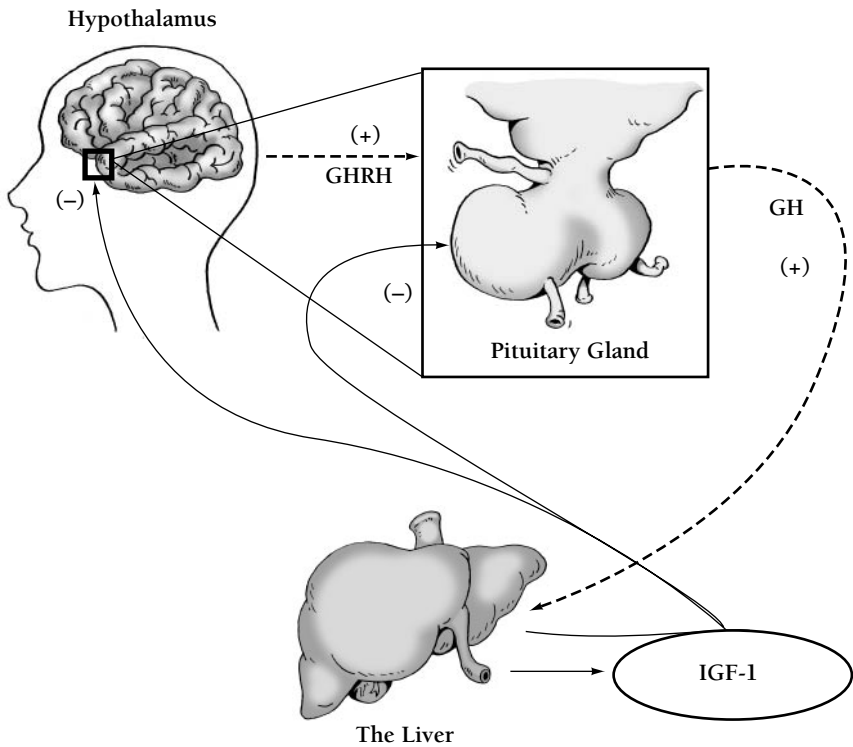
GH has effects throughout the body, but the liver is the major target. Both GH and IGF-1 feed back to the hypothalamus, signaling proper (or improper) levels—a delicate regulatory system. Food also influences the pituitary gland and its production of GH.

But GH isn't just a hormone for the body. As we have discussed, GH (or lack of it) can have potent effects on the mind. GH deficiency (GHD) is associated with a decreased sense of well-being, poor energy, and emotional lability. GH replacement, on the other hand, can have beneficial effects: the memory may improve, as can your mood, sense of well-being, and energy level.

And it can help you sleep better. This quality has the circular effect of helping your GH levels surge, since GH is produced while you sleep. Healthy sleep leads to a rise in GH levels; poor sleep can lead to a decline. A continued pattern one way or the other can steadily boost or deplete GH levels, and the circle keeps on going around.

## **AGING AND GROWTH HORMONE**

The problem of declining GH gets worse as you get older. As you might expect, GH levels peak during puberty and slowly fall throughout the rest of your life. By age 30 to 40, levels are half of what they were. This natural decline in GH levels is known as *somatopause*.



**Figure 9.1**  
**GROWTH HORMONE ENDOCRINOLOGY:**  
**HORMONE FEEDBACK LOOPS**

Higher centers in the brain send signals to the hypothalamus, which produces pulses of growth hormone–releasing hormone (GHRH). GHRH pulses stimulate the pituitary gland to make growth hormone (GH). GH stimulates the liver to produce insulin-like growth factor-1 (IGF-1). IGF-1 “feeds back” to the hypothalamus and pituitary gland, slowing GH production. Positive “feedback” is denoted by (+) and negative “feedback” is denoted by (–).



**Figure 9.2**  
**GH DECLINE WITH AGE**

Growth hormone levels peak during puberty and then decline throughout the rest of life. By age 30 to 40, levels are half of their pubertal peak.

In the past, this drop was considered normal. But as a result of research, as with other hormones, doctors are realizing that this may not be so. As a recent article in the *New England Journal of Medicine* observed, “There is evidence that GH deficiency in adults is deleterious, increasing the risk of death from cardiovascular disease.”

Many anti-aging physicians now advocate GH supplementation in older individuals. The goal is to restore the GH level to that of a 30- to 40-year-old. However, most endocrinologists do not advocate the use of GH as an anti-aging medication.

**GROWTH HORMONE RESISTANCE**

As we’ve seen so many times, stress can disrupt hormonal balance in such a manner as to promote weight gain. Stress can be physical, emotional, or a result of diseases such as hypothyroidism, diabetes, liver disease, kidney disease, AIDS, or severe burns. The excess fat in our bodies can also cause physical (and hormonal) stress. Where GH is concerned, stress causes a multitude of problems. Stress can lead to sleep problems. Since GH is made when you sleep, sleeping less means less GH production. Even without sleep problems, however,

stress can have a direct effect on your brain and pituitary gland, causing reduced GH production. Stress also causes damage to GH receptors and GH resistance. Damaged GH receptors mean that the GH does not function properly. This is similar to insulin resistance, discussed in Chapter 3. The difference with GH resistance is that unlike insulin, the body cannot compensate with heightened GH levels. The pituitary gland is already too pooped out to keep up with the demand.

The most severe form of GH resistance is known as *Laron's syndrome*. This genetic condition is caused by a severe mutation of the GH receptors. GH levels are very high, but IGF-1 levels are low (the GH receptor in the liver doesn't work, and IGF-1 cannot be made). The result is an individual of very short stature, one who cannot be helped by treatment with GH. Fortunately, we now know enough to treat such children with IGF-1, bypassing the GH receptor entirely. *Mecasermin* (Increlex) is an IGF-1 medication approved to treat growth failure in children with severe primary IGF-1 deficiency or GH gene deletion.

AIDS is a condition associated with high-level GH resistance. Because of this, doctors are now treating AIDS patients with megadoses of GH in an attempt to overcome this resistance. GH therapy improves muscle mass and muscle strength, but studies have not yet shown that it can prolong life. There is very limited information on the long-term safety of and proper dosing for GH in AIDS patients.

## GROWTH HORMONE AND INSULIN

So far we have concentrated on the positive effects of GH. As noted before, this would seem to be *the* wonder drug, the hormone to have if you want to lose weight.

But as we've seen before, hormonal balance is critical. If GH levels are not perfect, insulin is adversely affected. Abnormal GH levels, whether high or low, can cause insulin resistance. GH is a counter-insulin hormone and, when high, can cause the body to boost insulin production in order to compensate. Low GH causes low muscle mass and high fat mass, another setup for insulin resistance. Then there's outright GH deficiency, which also causes insulin resistance. So either way, too high or too low, abnormal GH levels cause insulin resistance.

Insulin and GH have a push-pull relationship. When you eat, and insulin is released from your pancreas a few hours later, there's a surge

of GH to help suppress the insulin surge. If you have a decent-size meal and then don't eat for 4 to 6 hours, you can temporarily raise your GH levels. Then hit the weight room for an intense workout. A strenuous workout at this time makes GH levels surge even higher, stimulating muscle growth.

But this runs counter to the way the best diets work, which is based on the concept of grazing—eating several small meals over the course of a day. That's one reason high GH levels can cause diabetes. And diabetes, of course, drops you into a cycle where—if you're not careful—you may eat in such a way as to make insulin levels peak and then plunge, as opposed to carefully moderating them throughout the day.

### **GROWTH HORMONE DEFICIENCY (GHD)**

The symptoms of adult GHD (also known as *acquired growth hormone deficiency*) are very vague and often ignored. The symptoms may cause GHD to be mistaken for other hormonal imbalances. Among the indicators are:

- Cholesterol problems
- Decline in kidney function
- Depression
- Difficulties with sex life—loss of libido
- Difficulty relating to others
- Emotional irritability
- Heart disease
- Increase in body fat
- Insomnia
- Lack of a sense of well-being
- Lack of energy/fatigue
- Loss of muscle mass
- Poor general health
- Poor memory
- Premature aging
- Reduced capacity for exercise
- Social isolation—loss of zest for life
- Thinning of the bones (osteoporosis or osteopenia)
- Weight gain
- Wrinkling skin, thin skin, or dry skin



## **GHD AND YOUR HEART**

Studies have shown that patients with severe GHD (from pituitary gland problems) have twice the risk of dying from heart disease. A GH imbalance of any type can cause heart problems. GH increases the thickness of the heart's walls and affects its function. If there's a deficiency, it can cause a condition known as *dilated cardiomyopathy*—the heart gets big, floppy, and weak. The condition leads to heart failure.

GHD is associated with premature atherosclerosis and with decreased HDL (good) cholesterol and increased LDL (bad) cholesterol. Of course, it's well known that high cholesterol is a cause of coronary artery disease and heart attacks. Restoring normal GH levels can improve the cholesterol profile and the health of the heart.

Again, balance is important. GH excess can cause heart problems as easily as GHD can: the heart gets very big and thick and has trouble pumping (part of the phenomenon called acromegaly—see below). Heart disease is the number 1 cause of death in patients with growth hormone excess.

## **CAUSES OF GHD**

There are many causes of GHD. The two main categories of GHD are congenital and acquired. “Congenital” means that you were born with it. “Acquired” means that a tumor, disease, or trauma has injured the pituitary gland, resulting in a deficiency of growth hormone. As with all hormonal conditions, severe, moderate, and mild forms exist. Usually, the most severe cases of adult-onset GHD—90 percent, in fact—are caused by a tumor in the pituitary gland. Pituitary tumor patients can be deficient in many hormones, but GHD is the most common hormonal deficiency. Despite this, many pituitary patients are not offered the opportunity for GH replacement. Although pituitary gland problems cause the most severe form of GHD in adults, even stress can decrease GH levels. (You'll recall that cortisol rises and testosterone and thyroid hormone fall in response to stress.)

### **Congenital Growth Hormone Deficiency**

The classic form of GHD is congenital or childhood GHD. Children born with GHD do not grow, and pediatric endocrinologists administer GH

to restore normal growth. If untreated, these children will remain short. They are considered “midgets,” a term no longer used in polite conversation; the term “little people” is more politically correct. Most, however, take on a pudgy appearance—keep in mind the GH effect on fat and muscle—so that many resemble cherubs. In the past, patients stopped taking GH when they achieved a normal height. Now most endocrinologists advocate lifelong treatment with GH, although the dosages decrease after adult height is achieved.

### ***Danielle’s Story***

*Danielle suffered from a pituitary gland tumor. She underwent surgery and everything appeared to be going well. All of her hormones were replaced properly—except the GH. Danielle didn’t feel “right.” She told her doctor that she felt weak and enervated and was gaining weight. The doctor didn’t think much of it; after all, the tumor was gone and Danielle was obviously healthy, if not lively. But then Danielle fell and broke her wrist. Upon examination, she was found to have osteoporosis. At that point, tests indicated that her GH levels were extremely low. She was put on GH injections. Not only did her bone heal, but she was able to resume a normal life.*

## **Pituitary Gland Tumors**

Pituitary gland tumors sound terrible, but most of them are benign (noncancerous) growths, not malignant. The main reason they cause problems is that they get bigger. Sometimes pituitary gland tumors compress the normal gland, and this compression can cause a hormone deficiency. Sometimes the tumor itself makes too much of a particular hormone; for example, too much GH causes acromegaly (see below), while too much ACTH causes Cushing’s disease (see Chapter 8). Growth hormone deficiency is the most common hormonal abnormality caused by pituitary tumors.

Sometimes GH levels are OK until the tumor is removed. (Surgery through the nose—*transsphenoidal*—is the treatment of choice for most pituitary tumors, in case you were wondering.) GH levels tend to fall after the pituitary gland has been operated on.

Some pituitary tumor patients have multiple hormone deficiencies, including growth hormone, thyroid (TSH), sex hormones (LH and FSH), and cortisol (ACTH). This is known as *panhypopituitarism*. Less frequently, the back of the pituitary is damaged. This part of the gland (known as the posterior pituitary gland) produces a hormone known as *vasopressin* (aka *antidiuretic hormone*). This hormone prevents you from urinating too much. Without it, you may urinate up to 5 gallons (yes, *5 gallons*) each day. This is called *diabetes insipidus*, as opposed to the more common type of diabetes, which is called diabetes mellitus.

### **Brain Tumors**

Brain tumors, including *craniopharyngiomas*, *meningiomas*, and others, can cause pituitary gland dysfunction and growth hormone deficiency.

### **Empty Sella Syndrome**

Empty sella syndrome is caused by a small anatomical defect above the pituitary gland that increases pressure in a portion of the skull known as the sella turcica. This causes the pituitary gland to flatten out along the walls of the sella turcica. Empty sella syndrome is more common in overweight people and those with high blood pressure. Empty sella syndrome sometimes results in growth hormone deficiency or other pituitary hormone deficiencies.

### **Head Injuries**

Head injuries, even remote ones, are a commonly overlooked cause of GHD. Severe head injuries can cause dysfunction of any or all of the pituitary gland hormones and are associated with a condition known as *postconcussion syndrome*. Growth hormone is one of the hormones most susceptible to head injury. Even minor head injuries that occurred several years prior have been known to cause growth hormone deficiency. If you have symptoms of growth hormone deficiency and a history of head trauma, you should discuss this with your physician.

### **Radiation**

Anyone with a history of radiation to the head or neck is at risk for growth hormone deficiency.

### **Obesity**

When someone has growth hormone deficiency due to obesity alone, it's called *obesity-related hyposomatotropism*. Obesity can lower growth hormone levels for many reasons. Being overweight worsens the age-related decline of growth hormone. Other hormone signals, such as leptin and cortisol (see Chapters 8 and 10), can lower growth hormone levels to a significant extent—and these two hormones' levels increase as you gain weight. Fat cells produce hormones (called *inflammatory cytokines* or *adipokines*) that lower growth hormone by slowing signals from the hypothalamus and pituitary gland. So it's a vicious cycle: being overweight (or having a high percentage of body fat) disrupts growth hormone balance and overall hormonal balance, making you lose muscle and gain fat.

Growth hormone replacement therapy for obesity-related hyposomatotropism is a very controversial topic. Most insurance companies do not pay for growth hormone therapy if obesity-related hyposomatotropism is the cause.

### **Hereditary Hemochromatosis (HH)**

This is a genetic disease in which the body absorbs too much iron, which is deposited in organs, causing tissue damage. HH frequently causes endocrine dysfunction because of iron deposits in the glands, especially the pancreas and the pituitary gland. Growth hormone deficiency is a common feature of HH. Low testosterone, type 1 diabetes, high blood counts, and liver problems are also common. For more information on HH, see Chapter 4.

### **Sarcoidosis**

Sarcoidosis is a disorder of unknown cause that is characterized by the formation of substances known as *granulomas*. Granulomas can occur

anywhere in the body but are most common in the lungs. When sarcoidosis affects the brain, it is known as *neurosarcoidosis*. Neurosarcoidosis can cause growth hormone deficiency when it damages the hypothalamus and pituitary gland. Typically, neurosarcoidosis causes multiple deficiencies of pituitary gland hormones, but growth hormone may be the first to go. For more information on sarcoidosis, see Chapter 4.

### **Aging**

Another cause of GHD is simple aging. As we age, we lose lean body mass and gain fat. GH declines are partially responsible for this. Advocates of GH as an anti-aging hormone claim that restoring GH levels to those of a 30- to 40-year-old will reverse the muscle loss-fat gain cycle. Most endocrinologists do not recommend GH as anti-aging medicine.

### **Stress**

Depression, severe mental stress, emotional deprivation, and other forms of stress can lower GH levels. Stress, because of its effects on a variety of hormones, is one of the many causes of weight gain (see Chapter 1). Stress disrupts your body's hormonal balance, slowing your metabolism and halting progress.

## **TESTING FOR GHD**

Testing for GHD is usually more complicated than a simple blood test. Most of the time, a growth hormone stimulation test is necessary to make the diagnosis of growth hormone deficiency. Patients with multiple pituitary gland hormone deficiencies, a condition known as *panhypopituitarism*, are virtually guaranteed of having GHD and do not need to be tested.

### **Growth Hormone Levels**

A simple growth hormone measurement is not a reliable test for diagnosing growth hormone deficiency. GH is secreted from the pituitary

gland in pulses, so hormone levels fluctuate greatly. Even a level of zero could be normal.

### **Insulin-Like Growth Factor-1 (IGF-1) Levels**

A low IGF-1 level is very suggestive of GHD. But here the problem is interpretation: who is to say what level is “low”? A normal IGF-1 level, in fact, is seen in many patients with severe GHD. For this reason, if you have symptoms of GHD and an IGF-1 level in the lower half of the normal range, you may still have growth hormone deficiency. Most endocrinologists feel that you should compare IGF-1 levels against age-adjusted normal values. Either way, IGF-1 levels should be monitored at least once every 6 months for those people who take GH.

### **Binding Proteins**

There has been a lot of interest in measuring one of the binding proteins, *insulin-like growth factor binding protein-3* (IGFBP-3), as a way of diagnosing GHD. At this time, however, this test is mostly used in research settings.

### **Stimulation Tests**

The *growth hormone stimulation test* is the best and most accurate way of testing for GHD. The classic stimulation test is known as the *insulin tolerance test*. This is a good test, but dangerous. Here a patient is given a large dose of insulin. The blood sugar drops to dangerous levels, which somehow provokes the release of GH. (GH is a *counter-insulin hormone*.) Now, GH *secretagogues* (medications that stimulate GH secretion from the pituitary gland) such as GHRH, arginine, clonidine, glucagon, hexarelin, and levodopa can be administered to patients to stimulate GH secretion. Usually, a baseline sample of blood is obtained, and then the secretagogue is administered. Repeat samples of blood are drawn every 30 minutes or so for the next couple of hours. All of the stimulated GH levels must be less than 5 mg/L to produce a diagnosis of GHD. In children, however, a GH level less than 10 mg/L is considered abnormal.

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## **Pituitary Gland Testing**

Growth hormone deficiency can be a clue to other pituitary gland hormone deficiencies or excesses. Anyone diagnosed with growth hormone deficiency should have a full pituitary gland evaluation, including thyroid hormone, cortisol, testosterone, prolactin, estrogen, LH, FSH, and ACTH levels.

## **Lipid Profile**

GHD can cause elevated LDL (bad) cholesterol and lowered HDL (good) cholesterol. Cholesterol measurements are an important part of testing for growth hormone deficiency. Your doctor will monitor your lipid profile periodically if you are on growth hormone replacement therapy.

## **Blood Sugar**

Growth hormone deficiency is associated with insulin resistance, so it's important to measure blood sugar as part of the initial evaluation. Blood sugar should also be monitored regularly if you are taking growth hormone replacement.

## **Bone Density Testing**

Growth hormone deficiency is an important causal factor in thinning of the bones (osteopenia or osteoporosis); everyone with growth hormone deficiency should have bone density testing or a *bone mineral density* (BMD) test performed. *Dual-energy X-ray absorptiometry* (DEXA) is the most accurate and advanced test available for measuring bone density. The test is quick and painless and gives very important information about the density of bones.

## **MRI Scan**

An MRI scan will give information about the structure of the pituitary gland as well as the presence of any tumors. Open MRI scanners are

not very accurate for diagnosing pituitary gland problems. For the most accurate result, I recommend a closed MRI scan.

### **Cancer Screening**

Growth hormone replacement has not been definitively shown to cause cancer. Active tumor growth, however, is a contraindication to the use of growth hormone. All patients who are considering starting growth hormone replacement should undergo a basic cancer screen with their primary care physician. This should include screening for breast cancer, cervical cancer, prostate cancer, and colon cancer. I also recommend a total body skin exam for suspicious moles that could be early skin cancer.

### **GROWTH HORMONE REPLACEMENT THERAPY**

In 1996 GH therapy was approved for treatment of adult GHD. Despite this, treatment is still debated among endocrinologists. Most, however, agree that GHD should probably be treated. Studies as long as 10 years have been published demonstrating that long-term treatment with GH is both safe and effective.

GH is given as a daily injection, although some patients take it less often. GH comes either as a powder that must be mixed with water or in a premixed form. Injection devices can be easier to use than standard injection. Aside from convenience factors, all brands of GH are essentially equal.

The goals of GH therapy are to lose fat, gain muscle (restore normal body composition), improve muscle and heart function, normalize cholesterol, increase energy, and improve quality of life. You should use GH only under the supervision of a qualified endocrinologist.

How much is the right amount? Studies have reported a highly variable response to dosing of GH. In the past, dosing was based on body weight. Today, most doctors start with a low dose and slowly increase the dose according to side effects and patient response to therapy. This is known as *individualized dose titration*. There are many reasons individuals respond so differently to similar doses of GH. Stress and illness cause GH resistance, and higher doses may be necessary to overcome



this resistance. Some people will respond to very low doses of GH, whereas others require much higher doses. I usually have patients start on a dose of 0.2 mg at bedtime for a couple of months, and then increase to 0.4 mg. (Some measure GH in IU, or international units; 1 mg = 3 IU.) The dose can be further increased every few months. Most patients with adult GHD rarely need more than 1.6 mg of GH per day. Bodybuilders and patients with AIDS may take doses of GH as high as 6 mg per day. These mega-doses are along the same lines as taking high doses of anabolic steroids.

Women who take estrogen medications such as hormone replacement therapy or birth control pills need higher doses of growth hormone. This is because estrogen cranks up the enzymes in the liver that break down growth hormone. Estrogen patches do not have the same effect as pills and are preferred for women who are on growth hormone replacement therapy.

Dosing also depends on side effects. I generally start my patients with a very low dose, monitor IGF-1 levels, and slowly increase the dose over several months until the IGF-1 is on the high end of “normal for age.” If side effects occur, I back off on the dose for a few weeks and then try to increase it again.

To closely correspond to your diurnal rhythms, I recommend you take your injection at bedtime. It may take as long as 6 months to even begin to notice an effect.

The lack of consensus extends even to the optimal way of monitoring GH therapy. Most doctors follow IGF-1 levels as a marker of therapy. Traditional endocrinologists provide treatment to raise IGF-1 levels to the “normal for age” level. Different ages have different normal values; the older you are, the lower your “normal” value. Other physicians recommend treating to attain a level considered normal for a 30–40-year-old, regardless of actual patient age.

### **SIDE EFFECTS OF GH REPLACEMENT THERAPY**

Side effects occur more frequently in older patients and heavier patients. Side effects are related to the dose. If you lower your dose of GH, the side effects usually subside. The most common side effects of GH therapy are muscle and joint aches and pains (myalgias and arthralgias) and fluid retention. High blood pressure, bloating, and edema can

be due to the water and salt retention caused by GH. Other side effects include headache, blurred vision, and carpal tunnel syndrome.

Blood sugar problems and even diabetes can also occur as side effects of growth hormone replacement. GH has an effect that varies with blood sugar and insulin resistance. Abnormal GH, whether high or low, can cause insulin resistance and possible diabetes. You must have your blood sugar checked periodically if you are on growth hormone therapy.

Almost 10 percent of men and women have reported breast enlargement from GH. There is also concern about cancer risk from growth hormone replacement. Any substance that causes cells to grow has the potential of causing cancer. Increased IGF-1 levels have been linked to prostate cancer in men, and GH has been shown to cause cancer in laboratory animals. Patients with GH excess (see the discussion of acromegaly, below) do have an increased risk of certain forms of cancer (including breast, prostate, and colon cancer). However, thus far, GH therapy in replacement doses has not been definitively linked to cancer. Some even argue that GH may *prevent* certain forms of cancer. The bottom line: the issue remains unresolved.

GH therapy does have other “side effects.” Foremost among them is the cost. Full replacement doses can cost up to \$20,000 per year. Children with true GHD and AIDS patients need the highest doses. In many cases, this treatment is covered by insurance, and insurance companies will pay for treatment of adult GHD if proper stimulation testing has been done. Most of the manufacturers of GH have programs that will help you get your insurance company to pay for GH. Because of the high cost, many insurance companies will raise your insurance premiums (sometimes double or triple) after you start taking GH.

## **OPTIMIZE YOUR BODY’S NATURAL GH**

There are several ways of tapping into your body’s natural supply of this mostly beneficial hormone.

### **The Hormonal Health Diet**

The more body fat you have, the lower your GH level. And as you lose fat, your GH levels will surge, helping you lose more fat. Fad diets,

however, lower GH levels. The Hormonal Health Diet is the ideal diet for enhancing GH levels, with one exception: the nibbling concept for keeping insulin levels low. Unfortunately, this also can keep GH levels low. To really boost your GH levels, you should eat three meals a day with 4–6 hours of fasting between meals. I do not recommend this, however, if you are also trying to fight insulin resistance. If insulin resistance and GHD are both issues, I recommend you use the “frequent, small meals” approach as recommended in Chapter 11. If you want to maximize GH levels, and insulin resistance is not an issue, the “fast-fast cycle” may give you an additional advantage.

### **Water**

You must drink enough water. I cannot emphasize this enough. Drink at least eight 8 oz. glasses a day. Water is a major component of muscle. Without enough water, you become dehydrated and your muscles suffer.

### **Protein**

Protein is critical to making the “weight loss–GH gain” cycle work. Protein is used to build muscle. If you raise your GH levels but are not eating enough protein, you won’t see much benefit; you have to provide your body with all the necessary tools. Eat the right amount of protein. Extra protein is easily converted to fat and stored in fat cells. Hormones are increasingly being used in animals as a means of boosting muscle mass—and profits. We really don’t know if the GH given to animals has an effect on humans who consume the animals. GH is a peptide hormone and, if not destroyed by cooking, is likely destroyed by digestion. Animal GH does not work in humans. Unlike other animal hormones (for example, see the discussion of Premarin in Chapter 6 or Armour Thyroid in Chapter 7), GH is very species specific. So the GH in the meat you eat has no effect on your body.

### **Physical Activity**

Physical activity is very important in lowering weight and raising GH levels. The best workouts for GH are strenuous ones. Intensive exercise

can make GH levels surge. Once you start exercising, GH will help you keep exercising, making your muscles stronger. The more you exercise, the stronger you get. This has long been a truism, but few realize GH's role in this process.

## **Sleep**

GH is released when you sleep. If you don't sleep well, you won't produce enough GH.

## **Growth Hormone Stimulators**

These medications and herbal products stimulate the pituitary gland to make GH. GH secretagogues fall into two categories: those used in a research setting and for stimulating, and those sold as nutritional supplements. *Growth hormone-releasing hormone* (GHRH) has been approved only as a research tool and is used in GH stimulation testing. In experimental settings, it has restored normal GH levels. In the future, GHRH may be used as an alternative to GH; but for GHRH to work, the pituitary gland must be normal. Growth hormone-releasing proteins (GHRPs) MK-677 and hexarelin are also GH-releasing agents used in experimental settings.

Several amino acids, taken in high enough doses, will stimulate the pituitary gland to make GH. They're touted as a "natural" way of enhancing GH levels. When I test patients for GHD, I give them an intravenous infusion of arginine. Over-the-counter growth hormone products usually contain one or several amino acids that increase growth hormone production. I don't recommend the use of these supplements.

## **Prescription Medications**

I do not recommend that you take these medications to raise your GH levels. However, if you are taking these medications for other reasons, you should know that they may be raising your GH levels as a side effect.

- *Levodopa (Sinemet)*. This medication, used to treat Parkinson's disease, resembles the brain chemical dopamine. It's often used to test for GHD, and it's a very potent releaser of GH.
- *Ergoloid mesylates (Hydergine)*. In the past, Hydergine was widely used in an attempt to improve memory in older people. It's rarely used today. You may have heard it referred to as a "smart drug," but for some it's not all that smart: it can cause headaches and insomnia.
- *Clonidine (Catapres)*. Clonidine is a widely used blood pressure medication, available in both pill and patch forms. It's another potent stimulator of GH, and—like GHB—can make you sleepy. Clonidine is also used to treat the symptoms of menopause (see Chapter 6). There's a reason some of these GH releasers make you sleepy: GH is released when you sleep. These medications are simply assisting what comes naturally, though in much more potent form than your normal body processes.
- *Phenytoin (Dilantin)*. Phenytoin, a commonly used medication, is used to prevent seizures. GH stimulation is merely incidental.

## ACROMEGALY AND GIGANTISM

For most of this chapter, we've talked about how GH makes bones and cartilage grow. But there is a dark side to this growth. Sometimes the pituitary gland develops a tumor that produces excessive amounts of GH. This condition is known as acromegaly.

What effects does this have? You've probably seen someone with acromegaly in the *Guinness Book of World Records* or on a professional wrestling show. If a child develops a GH-producing pituitary tumor before puberty, he will become a "giant," a condition given the rather obvious name *gigantism*. Today, most of these children are diagnosed and treated.

People with gigantism don't usually grow up to be basketball players or Herculean strongmen. Gigantism provides them with a whole new set of problems, particularly skeletal and muscular conditions. The human body isn't usually meant to be 8 feet tall. For those who develop a problem with GH excess after puberty, once growth has ceased, it's even worse.

Then there's acromegaly, the condition caused by GH excess in adults. People with acromegaly end up with very large hands and feet—the name itself means “big extremity”—and a variety of other problems, listed below. Interestingly, acromegaly can mimic insulin resistance. Why? When produced in high levels, GH directly works against insulin, creating insulin resistance.

### ***Sandra's Story***

*It started slowly. One day, Sandra—a 50-year-old homemaker in Miami, Florida—put on her shoes and noticed that they didn't fit right. It was as if her feet had grown a half-size or so almost overnight. As time went on, she realized that her feet had indeed grown—and so had her hands. Her health started deteriorating. Her blood pressure shot up and she developed diabetes.*

*One day she went to the dentist for a checkup. The dentist took X-rays and posted them on a light board for Sandra to look at. “The spaces between your teeth,” he said, using the handle of a dental mirror as a pointer, “are growing larger.”*

*It all started coming together. Sandra told him about her feet and her hands. The dentist referred her to an endocrinologist, who diagnosed acromegaly. He booked Sandra into surgery to remove the pituitary tumor that had caused all the trouble. Within months after the surgery, Sandra was feeling better. Her hands and feet and the spaces between her teeth, however, remained enlarged.*

## **FEATURES OF ACROMEGALY**

- **Weight gain.** Both GHD and GH excess are associated with weight gain.
- **Diabetes.** GH is a counter-insulin hormone and, at high levels, causes insulin resistance that can lead to diabetes.
- **Change in appearance.** Besides growth of the hands and feet, acromegaly causes the brow to thicken, the nose to broaden, the jaw to protrude, the teeth to space out, the tongue to grow, and the forehead to develop a large, deep furrowing. The professional wrestler Andre the Giant, who had acromegaly, had a number of these features.

- *High blood pressure*
- *High cholesterol*
- *Acanthosis nigricans*. This is a skin condition that causes a dark, velvet-like skin rash on the neck, armpits, face, and knuckles (see Chapter 3).
- *Heart disease*. In acromegaly, the heart gets big and thick. High cholesterol levels lead to an increased risk of heart attack; in fact, the leading killer among people with acromegaly is heart attacks.
- *Growth of hands and feet*
- *Carpal tunnel syndrome*. This pain of the wrist joint is particularly common.
- *Arthritis*
- *Risk of cancer*. Several types of cancer, most notably colon cancer, occur more often in people with acromegaly.
- *Skin tags*. These tiny growths of excess skin are often seen in patients with acromegaly. Interestingly, the greater the number of skin tags, the greater the risk of colon cancer. Skin tags are also seen in association with insulin resistance (see Chapter 3).

### ACROMEGALY TREATMENT OPTIONS

What can you do if you have acromegaly? Fortunately, it's not irreversible. Surgery, radiation, and medications are all options, and all have been known to control—or even resolve—the problem. Most endocrinologists recommend surgery as first-line therapy, but new and more effective medications are available for those who are not cured by surgery. There are three classes of medications available to treat acromegaly. *Somatostatin analogues* (*octreotide*, *lanreotide*) slow the production of growth hormone from the pituitary gland. *Dopamine agonists* like *Cabergoline* also slow growth hormone production. The newest and probably most effective medication for acromegaly is a *growth hormone receptor antagonist* (*pegvisomant*). This drug works by blocking the receptor for growth hormone.

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# HUNGER HORMONES AND THE FUTURE OF WEIGHT LOSS

THE MOST COMMON HORMONAL DISORDER IS NOT HYPOTHYROIDISM, NOT DIABETES, NOT MENOPAUSE. The most common hormonal disorder is obesity.

If you've read the book this far, this should come as no surprise to you. Everything I've talked about comes back to obesity. A lack or overabundance of certain hormones causes changes in metabolism. Those changes either prompt the body to start putting on weight immediately or trigger a boomerang effect that will cause it to put on weight soon enough. Either way, the end result is a weight problem—and that weight problem can lead to a whole host of other problems.

You'd think the endocrinology community would be aware of this. In fact, the opposite is true. For years, the endocrinology community has ignored obesity. For the most part, in fact, endocrinologists haven't seen the forest for the trees. They treat the individual hormonal problems contributing to obesity, or caused by obesity, but they don't treat the obesity itself.

It's only recently that new discoveries have opened endocrinologists' eyes. Most neuroscientists agree that hunger originates in a portion of the brain called the hypothalamus. As I've noted elsewhere in this book, the hypothalamus is the part of the brain that controls the pituitary gland—the master gland—and thus many of our hormones. But studying how the hypothalamus affects hunger—the “science of hunger”—is only beginning. It's a fairly wide open field. In fact, even

infection with a virus has been linked to obesity. A virus known as *adenovirus Ad36*, from a family of viruses that cause the common cold, has been implicated in the development of obesity.

Certain things are known about hunger and the hypothalamus. One is the idea of *satiety*, the concept that you eat until you're satisfied. In the hypothalamus there is a sector called the *ventromedial hypothalamus*, nicknamed the *satiety center*. The *lateral hypothalamus* is the *feeding center*. Together, these two portions of the hypothalamus balance hunger and satiety.

There are literally dozens of hormones that influence appetite, satiety, and metabolism. The list includes:

- Acyl stimulation protein
- Adiponectin
- Agouti-related peptide (AgRP)
- Amylin
- Bombesin
- Cholecystokinin (CCK)
- Ciliary neurotrophic factor (CNTF)
- Cocaine- and amphetamine-regulated transcript (CART)
- Corticotropin-releasing hormone (CRH)
- Cortisol
- Dopamine
- Dynorphin
- Endocannabinoids
- $\beta$ -Endorphin
- Enkephalins
- Enterostatin
- Estrogen
- GABA
- Galanin
- Gastric inhibitory peptide (aka glucose-dependent insulinotropic peptide) (GIP)
- Ghrelin
- Glucagon
- Glucagon-like peptide-1 (GLP-1)
- Glutamate
- Insulin
- Interleukin-6 (IL-6)
- Leptin

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Melanin-concentrating hormone (MCH)  
Melanocyte-stimulating hormone ( $\alpha$ -MSH)  
Neuromedin S  
Neuropeptide Y (NPY)  
Neurotensin  
Norepinephrine  
Obestatin  
Omentin  
Orexin  
Oxyntomodulin  
Pancreatic polypeptide (PP)  
Peptide YY (PYY)  
Pituitary adenylate cyclase-activating polypeptide (PACAP)  
Progesterone  
Pro-opiomelanocortin (POMC)  
Relaxin  
Resistin  
Secretin  
Serotonin  
Somatostatin  
TGF- $\beta$   
Thyroid hormones  
TNF- $\alpha$   
Urocortin  
Visfatin

This chapter will discuss the most recent breakthroughs in this area. However, as you will see, there is a great deal more to discover. This area of endocrinology is really in its infancy. For more detailed information on hunger hormones, please read my book *The Leptin Boost Diet* (Ulysses Press, 2006).

### **WHAT ARE HUNGER HORMONES?**

To an extent, most hormones can influence your appetite. Insulin, thyroid hormone, estrogen, progesterone, and cortisol—all have potent effects on appetite. We have discussed these hormones in great detail

because there is so much known about them. But there are hundreds of other hormones that also affect appetite, and, unlike those listed above, they're not necessarily made in the traditional way, by glands.

In fact, one of the biggest hormone producers in the body is . . . the fat cell. Yes, the same little piece of the puzzle that collects and reproduces and causes so much of our misery also makes hormones. Until recently, the fat cell was seen as an innocent bystander in the obesity saga, but now we know better. The fat cell turns out to be one of the biggest hormone producers in the body. It is the culprit, not the victim.

Hunger hormones are produced by other parts of the body central to digestion and food storage. The intestines produce potent hunger hormones, influenced by the foods you eat. These hormones, known as *gut peptides*, have effects on hunger and satiety. Our knowledge of these hormones is limited but is growing every day.

*Leptin* was one of the first hormones discovered to be produced by fat cells. It is known as a *satiety factor* because of its potent effects on appetite. Satiety has both hormonal (physiological) and psychological overtones. During times of satiety, hunger is at a minimum. Yet some people never feel satisfied. They never reach satiety. For some, this may be a hormonal disorder.

Other hormones have also been linked to quelling appetite. These hormones, known as cytokines, cause extreme loss of appetite and wasting from diseases such as cancer and AIDS. Cytokines have powerful abilities to fight cancer and infections, but for some reason they can also eliminate hunger. Needless to say, these dread diseases are not recommended ways of losing weight.

If the satiety center of the hypothalamus is damaged, it can lead to an uncontrollable appetite. Physicians have spent decades of research focused on satiety centers and "satiety factors"—hypothetical hormones that make the brain feel full—in attempts to help control appetite without killing it off altogether.

Another part of the hypothalamus, one related to the satiety center, is the *hunger center*—the lateral hypothalamus. This part of the hypothalamus produces the sensation of hunger. If this region is damaged, there is no hunger. Scientists theorize that the condition *anorexia nervosa* may be linked to damage to this brain region.

Ultimately, hormones trigger hunger, uniting your brain, your glands, and your appetite.

## THE EVOLUTION OF HUNGER

Our hormone mechanisms are the products of extensive evolution. They have developed to cope with times of famine, to make the most of the nutrients we consume, and to prompt us to respond to food in our vicinity. However, today, with abundant sources of high-calorie food all around, our antiquated hormone/hunger mechanism works against us. For example, if you are overweight, your body does not need food. In fact, depending on how overweight you are, you could go without eating for weeks to months without harming your body. Your body fights against this, though, causing you to be hungry hours after you last ate.

What about when you were hungry for that dessert? Your body just consumed a healthy meal, and all of a sudden you're hungry for dessert! Why? Well, that's just millions of years of evolution working against you.

Our senses, our organs, our very being demands that we search for—and eat—food. Consider:

- *Taste and smell.* Imagine walking down the street and smelling freshly baked bread. Suddenly, you are hungry. Smelling or anticipating the taste of delicious food can activate the hunger centers of the brain. And if you eat a little good food (an appetizer, for example), you get hungrier! Similarly, if it smells and tastes bad, you lose your appetite.
- *Appearance of food.* Just looking at good food makes you hungry.
- *Variety.* Variety makes us hungry. This may be why you get hungry for dessert even though your stomach is bursting. This also explains the success of many fad diets. These diets frequently have very limited food choices. The monotony of the diet somehow reduces appetite. This is also why meal replacement products such as bars and shakes can be so successful.
- *Stomach distension.* Distension of the stomach sends powerful hormonal signals to the brain, inducing satiety. Foods high in fiber, which distend the stomach without adding a lot of calories, can greatly improve satiety. Refer to Chapter 2 for more information on fiber.
- *The fat cell is a smart cell.* It knows and regulates your body weight.

- *The “set point.”* Many scientists believe in the concept of a set point. Think of it as a natural resting point for your body weight. Each of us has a somewhat predetermined body weight. If you become heavier than your set point, your appetite is turned off and you lose weight. If your weight drops below the set point, you get hungry and gain weight. I believe that the set point does exist to an extent; however, if you follow our eating suggestions and exercise regularly, you can lower your set point so that your body will feel comfortable at a lower weight.

Your body tends toward stability. If your weight drifts above your set point, your appetite tends to go down and you shed a few pounds. If you lose weight, the opposite occurs: your metabolism slows and hunger increases as your body craves to get back to the set weight.

The concept of a set point is not new, and it is not unique to humans. Animals tend to have their own set points. But you can change a set point with a delicious diet. Take the family dog, for example. If he gets dog food only, he'll be lean and trim. But add those table scraps, and Rover starts to plump up—particularly if he's not getting much exercise.

What is new is research on brain control of the set point by means of the newly discovered hunger hormones. After all, the brain affects behavior, physical activity, cravings, hunger . . . and produces potent hormones.

The set point concept also takes us back to the concept of satiety. Satiety hormones (also known as satiety factors) are the key regulators of body weight. They send a “stop eating” signal to the brain.

The upshot of all this is simple: don't be a victim of your set point. You can change your set point. As you achieve a new healthy weight, and balance your hormones, you can achieve a new set point.

- *Genetics.* For the vast majority of us, both genes and environment control body weight. In some cases, however, severe obesity can be caused by a variety of genetic mutations.

How do genetics and environment combine? The Pima Indians, discussed in Chapter 3, are a good example. As man has developed, food has become easier to come by—cheaper, in larger quantities, more

calorie-rich, and fatter. Combine this with the invention of the car and now the computer, and the levels of exercise and physical expenditure have sunk to an all-time low.

So the genes that allowed your great great grandfather to stay lean are working against you. If you were to adopt the diet and activity level of someone who lived 200 or 300 years ago, you would likely lose weight. Genes and environment thrive on one another.

Much of evolution has favored fat storage. Now evolution is working against us.

### THE THREE FUNCTIONS OF FAT CELLS

Fat was once thought of as an “inert” storage depot for excess calories. But fat is much more than blubber. Fat is a dynamic hormone-producing machine that regulates appetite, body temperature, and metabolism. In Chapter 3 I talked about how excess fat leads to insulin resistance and, therefore, obesity. When your body is in storage mode, fat cells increase, storing your excess calories for the future—making you fat. When your body is in the fat-burning mode, fat is burned as fuel instead of being stored. Fat is important for regulating body temperature and metabolism. The production of body heat is called *thermogenesis*. It’s a major indicator of metabolism. Believe it or not, fat is the largest endocrine organ in the body. Fat cells produce many different hormones that regulate appetite and metabolism

Through complex brain-hormone interactions, the body controls its own temperature. (A fever is an extreme example of this.) A higher body temperature—increased thermogenesis—is the result of increased metabolism. It’s like running an engine: the harder it runs, the hotter it gets. The hormones that raise metabolism, in fact, do so mainly by increasing thermogenesis. Low body temperature means lowered metabolism; we’ve seen that this is an indicator of low thyroid function.

There are two types of fat, brown fat and white fat. Most thermogenesis occurs in brown fat tissue (also known as *brown adipose tissue*, or BAT). BAT produces a specialized blood protein known as *thermogenin* that allows for the production of body heat.

BAT is controlled by nerves and stress hormones. The stress hormones *epinephrine* and *norepinephrine*, released from nerve cells and

the adrenal gland, activate BAT, increasing thermogenesis. The special receptor for these hormones is found only in BAT. It is called a  $\beta$ -3 *receptor*. (Other tissues in the body have  $\beta$ -1 and/or  $\beta$ -2 receptors.)

Stimulation of the  $\beta$ -3 receptor increases metabolism. It does this by increasing thermogenesis (heat production) and lipolysis (fat breakdown). And the hormones epinephrine and norepinephrine work by stimulating  $\beta$ -receptors.

Just as healthy BAT can be part of the cycle for losing weight, dysfunctional BAT can get in the way. And, ironically—or perhaps not so ironically, considering the constant feedback loops of the body—obesity can cause BAT dysfunction. If you are very overweight, your brown fat tissue cannot produce heat properly, so your metabolism is lowered and it becomes even harder to lose weight—ad infinitum.

Since the only place  $\beta$ -3 receptors are found is in BAT, this makes it the ideal target for a metabolic enhancement drug. Theoretically, there should be very few side effects, because only the  $\beta$ -3 receptor is being affected. This would likely be the magic drug we've all waited for. And, indeed, several major pharmaceutical companies are investigating  $\beta$ -3 receptor stimulator medications as a way of enhancing metabolism and helping with weight loss. Unfortunately, it is not as great as it seems. It turns out that the original  $\beta$ -3 research was done on mice. And, as we must continue to remind ourselves, mice are different from humans. Humans do have  $\beta$ -3 receptors, but we lose most of them within the first six months of life. After that, there aren't many  $\beta$ -3 receptors at all. Studies of  $\beta$ -3 medications on humans have been, as expected, disappointing. Newer compounds still under investigation hold promise, but no one knows if these medications will really work.

In another area being hotly investigated by drug companies, thermogenins are made by brown fat tissue and are responsible for body heat production. Thermogenins are regulated by blood proteins, known as *uncoupling proteins*. The more uncoupling proteins there are in your system, the higher your metabolism. There are three types of uncoupling proteins: the prosaically named UCP-1, UCP-2, and UCP-3. UCP-2 and UCP-3 are the most promising for weight loss, but so far research has been limited to mice. Scientists have been working on ways to increase uncoupling proteins as a way of increasing metabolism and causing weight loss. There are also medications mimicking UCPs under development that could be injected and would speed metabolism.



*White adipose tissue* (WAT) is quite different from BAT. WAT produces hormones. However, we know relatively little about the hormones made from fat cells. New fat cell hormones are being discovered all the time.

### Three Functions of Fat Cells

- Storage depot for excess calories
- Body heat production
- Hormone production

## LEPTIN

Leptin is simply one of the most significant discoveries in the study of obesity. A mutant strain of mice known as *ob/ob* (a designation for a double mutation of a gene that results in obesity) was found to have a syndrome of obesity and related complications very similar to *metabolic syndrome* in humans. The *ob/ob* mouse was hungry all the time and had high insulin levels, increased body fat, high cortisol levels, low thyroid levels, and high blood sugar. In addition, these mice had low body temperature, indicating low metabolism.

Scientists believed that the *ob/ob* mouse lacked a *satiety factor*—a hormone, still undiscovered, that they called “leptin.” To prove this theory, in the 1970s a scientist named Doug Coleman performed some odd experiments (which would make animal rights activists cringe) that are now considered classics of the genre. These studies, known as *parabiosis experiments*, sought to prove the existence of leptin.

Parabiosis is not the kind of experiment that is performed on humans. Two creatures, in this case mice, are surgically joined right down to their circulation, like artificial Siamese twins. Hormones made in one mouse, therefore, can be transferred to the other mouse.

When a fat *ob/ob* mouse was united with a lean mouse, a startling thing happened. The mutant obese mouse lost weight! The theory that these obese mice lacked a blood-born factor that shuts off appetite signals in the brain was strengthened.

But it would take many years for the actual gene (known as the *ob* gene) and its hormone product, leptin, to be discovered. That finally happened in 1995. The obesity gene was cloned, and leptin (initially known as the *ob* protein) made prime time. Researchers demonstrated that they could make the *ob/ob* mouse lose weight by injecting it with the missing hormone. This critical study provided direct evidence that leptin regulates body weight and body fat.

Since that time, the fat cell has been viewed as an endocrine organ and obesity has been viewed as a hormonal disorder. So what is leptin? Leptin is a traditional hormone in every sense of the word. It's produced by white fat cells and is secreted into the bloodstream, where it travels throughout the body and binds with a receptor, in the traditional lock-and-key fashion, to turn on and off genes.

Leptin is the hormone that signals to the brain that the stomach is full. It's the hormone that acts on the brain to regulate appetite and energy expenditure. Because of this, scientists have referred to leptin as an *adipostatic hormone*.

Leptin is similar to many other hormones:

- Like all hormones, leptin has a receptor—actually, several different types of receptors.
- As with most hormones, mutations of the leptin receptor cause leptin resistance and result in obesity.
- To help leptin work properly, the body needs zinc, the same mineral that helps insulin work properly.
- Interestingly, leptin also controls body temperature.

The main target of leptin is the hypothalamus, the place that regulates food intake and body weight, where it finds lots of leptin receptors. Scientists have linked the hypothalamus to body weight for many years, but the discovery that leptin, a hormone produced by fat cells, acts directly on the hypothalamus was a huge breakthrough. It quieted skeptics who had claimed that obesity is simply a matter of a lack of willpower. Among endocrinologists, there's no longer any argument: obesity is a hormonal disorder.

There has been a tremendous amount of research on leptin in the past several years, and the more that's discovered, the more complicated leptin becomes. It seems that leptin is involved in all aspects of life.

As an endocrinologist, I find it amazing that this hormone, of such tremendous importance, was only recently discovered. Given the speed at which news travels in the modern scientific world, countless scientists are now jumping on the leptin bandwagon doing their own research—and more power to them. Since the discovery of leptin, many more fat cell hormones have been discovered.

Although it is very rare, in some humans *leptin deficiency*—just like that in the *ob/ob* mouse—has been identified. These were among the first people to receive injections of leptin. Studies have shown that injections of *genetically engineered leptin* (made similar to the way that insulin, GH, and other hormones are manufactured) can make very obese individuals with leptin deficiency lose weight. In fact, they can lose lots of weight. These individuals are still being treated with leptin, and they are still losing weight.

But though the results are quite dramatic, leptin deficiency appears to be very rare, and most obese individuals should not expect such dramatic results.

However, although leptin deficiency is rare, *leptin resistance* is quite common. Leptin resistance is like insulin resistance: the more weight you gain, the more resistance you develop. At this time, though, testing for leptin levels is not widely available. Most testing is done at research centers, not doctor's offices, and the process has yet to become commonplace.

After the initial excitement of making fat mice thin, researchers, hoping for similar results, turned their attention to obese humans. But contrary to mice, the vast majority of obese humans have high leptin levels. This is known as *hyperleptinemia* (*hyper* = high, + *emia* = in the blood). And the fatter humans are, the higher their leptin levels.

The view on what to do, then, is mixed. Some researchers believe that injecting obese humans with leptin would do more harm than good. Other scientists have taken the opposing view, deciding to treat overweight humans who have leptin resistance with very high doses of leptin in an attempt to overcome the resistance. This concept may seem innovative, but it's not so new. For example, the best way to treat type 2 diabetes is to improve insulin resistance—with diet, exercise, and medications. But if that can't get blood sugar under control, what do doctors do? They prescribe insulin. They adopt the attitude, "If you can't beat them, join them." Even though insulin levels are already

high, insulin injections are used to get the insulin levels even higher in order to overcome the resistance.

So when it comes to leptin, why not try the same strategy? Maybe obesity in humans, some researchers think, is caused by leptin resistance.

Again we can look to parallels in the mouse world. Another strain of obese mice, known as *db/db*, shows resistance to leptin. This is due to a problem with the receptor for leptin. The *db/db* mouse is identical to the *ob/ob* mouse, but instead of low leptin levels, the *db/db* mouse has very high leptin levels—just like obese humans. And this is because the *db/db* mouse has a dysfunctional, mutated leptin receptor.

Humans cause their own leptin resistance by becoming overweight. The obesity actually causes the receptor to become dysfunctional, something known as an acquired defect. But when it comes to losing weight, at least, this is a good thing. The leptin resistance in humans is reversible, whereas in the *db/db* mouse—which is born with it—it is not.

So obesity causes leptin resistance. The fatter you are, the higher your leptin levels; and the higher your levels, the greater your resistance. It all makes sense: the more fat cells you have, the more leptin they can make. It's all another vicious cycle. However, when you lose weight, leptin levels plunge.

So far, studies on leptin have been disappointing for most people. But you will continue to hear about leptin. New types of leptin, medications that mimic leptin, and medications that enhance the action of leptin are all under development.

## OTHER FAT CELL HORMONES

Leptin is just one of a multitude of hormones made by fat cells. White adipose tissue (WAT) is glandular tissue, secreting hormones just like any other gland.

### Tumor Necrosis Factor-Alpha

Fat cells produce substances known as *cytokines* or *adipokines*. Tumor necrosis factor-alpha (TNF- $\alpha$ ) is one of the best known of these. The main action of TNF is to cause *inflammation*. By increasing inflammation, TNF- $\alpha$  increases insulin resistance and raises cortisol levels. TNF- $\alpha$  is also made by white blood cells and is used to fight infections.

### Ways to Enhance Your Leptin

- Follow the Hormonal Health Diet. It is the ideal diet for enhancing leptin function.
- Lose weight. Break the vicious cycle. Weight loss markedly improves the ability of leptin to enter the brain and function properly.
- Improve insulin resistance. Insulin resistance and leptin resistance go together. Follow the insulin reduction strategies in Chapter 3 and your leptin action will be improved.
- Lower cortisol levels. High cortisol inhibits leptin's effect. Reduce the stress in your life as discussed in Chapter 8.
- Enhance your growth hormone levels. Recall that leptin resistance can lower your GH levels. As GH levels rise, leptin action is improved. As leptin action improves, GH rises. (See Chapter 9.)
- Get plenty of zinc. Leptin is regulated by the mineral zinc, and zinc helps leptin work properly. Foods high in zinc include oysters, beef, wheat germ, lima beans, and dairy products.
- Don't smoke. Smoking lowers leptin levels, giving you yet another reason to quit.

**Note:** BEWARE OF FRAUDULENT LEPTIN PRODUCTS. There are some nutritional supplements on the market that are promoted to help leptin balance. These products contain vitamins, minerals, and other products. Some of these products contain ingredients that are untested and potentially dangerous. None of these products have been proven to actually improve your leptin. My recommendation is to stay away from these products altogether.

Obese humans have very high levels of TNF- $\alpha$ . TNF- $\alpha$  in high levels is toxic to the body and may be associated with complications of obesity, such as pseudo-Cushing's syndrome, diabetes, and male hypogonadism. TNF- $\alpha$  has also been linked to heart disease and strokes.

### Interleukin-6

Interleukin-6 (IL-6) is another cytokine hormone made by fat cells. It is well known for causing inflammation and insulin resistance. The heavier you are, the higher your IL-6 levels. Weight loss dramatically lowers IL-6 levels.

### **Resistin**

This is a cytokine hormone made by fat cells. Resistin does just what it says: it resists insulin and links excess fat to insulin resistance. The more fat you have, the more resistin you make. Researchers are working on medications that can neutralize resistin (known as *resistin antagonists*) as a possible treatment for obesity, diabetes, and insulin resistance.

### **Adiponectin**

Adiponectin is a beneficial fat cell hormone. Low levels of adiponectin are associated with insulin resistance, metabolic syndrome, and obesity. Adiponectin has anti-inflammatory properties and has the ability to lower blood sugar and reverse cardiovascular disease. *Thiazolidinedione* (TZD) medications like *pioglitazone* and *rosiglitazone* (see Chapter 3) have the ability to improve insulin resistance as well as increase adiponectin levels. Research is ongoing to develop adiponectin itself as a medication to treat obesity, insulin resistance, diabetes, and cardiovascular disease.

## **BRAIN HORMONES**

Just like other glands, the brain produces many hormones that are important in the regulation of appetite, satiety, and metabolism.

### **Orexins**

The name “orexin” comes from the Greek word *orexis* (meaning “appetite”—*anorexia* means “lack of appetite”). Because this class of hormones stimulates appetite, they were originally called hypocretins. The two main orexin hormones are orexin A and orexin B. Orexins also work in the gut, stimulating the bowels, and have the effect of keeping you awake. Have you ever awoken hungry with a rumbling stomach?

### **Neuropeptide Y (NPY)**

NPY is the most potent stimulator of appetite known to man. NPY is a brain hormone that is directly influenced by the fat cell hormone leptin. Leptin works in the hypothalamus to keep NPY levels low. Neuropeptide Y has complex actions on the hypothalamus and other areas of the brain, promoting the accumulation of body fat and slowing metabolism.

When you go on a diet, neuropeptide Y levels skyrocket, working against you. NPY increases production of the hypothalamic hormone *corticotropin-releasing hormone* (CRH), which stimulates the pituitary gland to make ACTH, which then stimulates the adrenal gland to make too much cortisol. At least five pharmaceutical companies are working on potential weight loss medications that work by blocking NPY (*NPY inhibitors*).

### **Agouti-Related Protein (AgRP)**

This protein hormone, produced by the hypothalamus, stimulates appetite and increases insulin resistance and leptin resistance. It's been linked to diabetes and fertility problems. Agouti is co-secreted with NPY when low leptin levels are detected. AgRP blocks the actions of  $\alpha$ -MSH and the MCR-4 receptor (see below), enhancing appetite and causing weight gain. AgRP and  $\alpha$ -MSH have opposite effects on appetite, both acting via the MCR-4 receptor.

Agouti stimulates production of red and yellow pigments and inhibits the production of black and brown pigments. The upshot is that it tends to lighten skin and hair. The Agouti mouse, from which the protein takes its name, has a genetic mutation causing it to have very high AgRP levels throughout the body, not just in its skin. The mouse is very fat and has light-colored fur. Levels of AgRP are increased in obese humans as well.

The study of this hormone is just getting started. But pharmaceutical companies are using the new knowledge of AgRP to investigate potential weight loss medications.

### **Melanin-Concentrating Hormone (MCH)**

MCH—yet another hormone made by the brain, this time in the lateral hypothalamus—is a hormone that is critical to the regulation of appetite and metabolism. It is a peptide hormone and is a potent stimulator of appetite. Mice with a mutated MCH gene have been studied, and they're very lean; they just don't eat much. But mice with high MCH levels are very hungry, and very fat. Like most brain hormones, MCH is regulated by leptin. When leptin is low (or there is leptin resistance), MCH goes up.

Research is at hand on MCH and its corresponding receptor. The MCH receptor is located in parts of the brain that control functions such as taste, smell, appetite, and feeding urges. Together, these brain regions coordinate to regulate food intake and body weight. Medications that block the MCH receptor are potentially an excellent approach to the development of new weight loss medications. If you can block the actions of MCH, appetite goes down.

### **Endocannabinoids**

Tetrahydrocannabinol, the active component of marijuana, was identified in the 1960s. This compound is known to cause increased appetite in marijuana smokers, an effect known as the “munchies.” It is now known that the brain produces its own set of marijuana-like compounds known as endocannabinoids. The first endocannabinoid was named *anandamide*, from the Sanskrit word *ananda*, for “bliss.” Receptors for endocannabinoids are found all over the brain and all over the body. The medication *dronabinol* (Marinol) is synthetic tetrahydrocannabinol and is used to increase appetite in patients who suffer from cancer or the effects of AIDS wasting. *Rimonabant* (Acomplia), called anti-marijuana because it acts by blocking the actions of endocannabinoids, allows people to lose their cravings and helps prevent overeating. Rimonabant also helps reduce cravings for cigarettes and thus can also help you quit smoking. Both smokers and overweight people have overstimulated endocannabinoid systems.

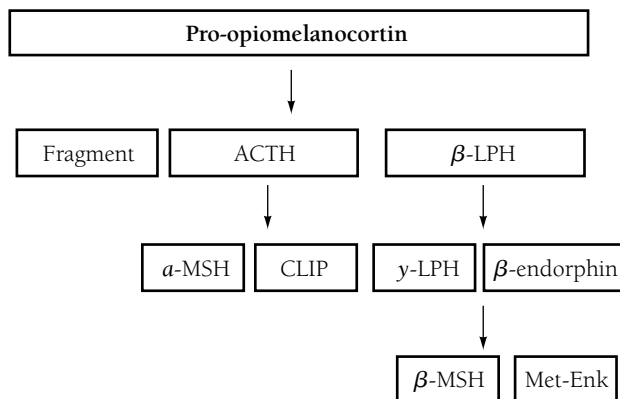


## Galanin

Galanin is a brain hormone that stimulates appetite and has been associated with elevated blood sugar levels. Galanin also increases growth hormone levels. Galanin has other effects, such as increasing memory and blocking the effects of a pain hormone known as *substance P*. Several medications are being studied that have the potential to block the receptor for galanin. Such medications may be helpful in treating multiple problems like obesity, diabetes, Alzheimer's disease, and chronic pain syndromes.

## Pro-opiomelanocortin (POMC)

POMC, also known as *melanocortin*, is a special hormone made by the pituitary gland. It is known as a *probormone* because, by itself, it doesn't do much.



**Figure 10.1.**

### PRO-OPIOMELANOCORTIN AND ITS ACTIVE FRAGMENTS

Pro-opiomelanocortin (POMC) is a large “precursor” hormone produced by the pituitary gland. This inactive hormone is broken apart by special enzymes into several active hormones, including adrenocorticotrophic hormone (ACTH), alpha- and beta-melanocyte-stimulating hormone (MSH), and endorphins.

**Red Hair?**

People with red hair and excess weight may have problems with the POMC system.

Leptin stimulates the pituitary gland to pump out POMC. Special enzymes break apart POMC into a variety of hormones, each having its own special activity.

Mice with a mutated POMC gene are very fat. Mice with POMC mutations also have a dirty-blond coat. That's because one of the POMC hormones gives pigment to skin and hair, and without it—that is, with the mutated version—you get a “dirty blond” or “red hair” appearance. These mice also have adrenal gland problems. ACTH, the pituitary hormone that stimulates the adrenal gland, also comes from the breakup of POMC.

Treatment of these mice with  $\alpha$ -MSH—discussed next—helps them lose weight. In addition, the blond hairs went away.

Humans with POMC mutations have also been identified. Just like the mice, these individuals are obese and have light skin and red hair. If you are very overweight and have light skin and red hair, you may have a POMC mutation.

**Alpha-Melanocyte-Stimulating Hormone ( $\alpha$ -MSH)**

$\alpha$ -MSH is a POMC-derived hormone that is responsible for suppressing appetite.  $\alpha$ -MSH is key to understanding obesity. It makes you feel full and tells fat cells to quit storing fat.  $\alpha$ -MSH has its own special receptor known as the *melanocortin-4 receptor* (MCR-4). Scientists have found that the interaction of  $\alpha$ -MSH with its receptor is vital in maintaining a normal body weight. Though the study of  $\alpha$ -MSH and MCR-4 is still in its infancy, chemical compounds are in development that act like  $\alpha$ -MSH and stimulate MCR-4, compounds known as *MCR-4 agonists*. These compounds suppress appetite and are being studied by pharmaceutical companies as potential weight loss medications.

## **β-Endorphin**

β-Endorphin is a POMC-derived hormone that stimulates appetite. β-Endorphin is known as an *endogenous opioid* because it has actions similar to those of opium and morphine.

## **Serotonin**

You're probably quite familiar with this substance, since its discovery has led to a greater understanding of depression and to an entire class of what are known as *SSRI reuptake inhibitors*—antidepressant drugs such as Prozac, Paxil, Celexa, Lexapro, Remeron, and Zoloft. Not officially a hormone, serotonin is a brain chemical known as a neurotransmitter that helps regulate hunger and appetite. It's made from the amino acid tryptophan, and because of serotonin's importance in regulating hunger and appetite, tryptophan is known as an essential amino acid.

Reactive hypoglycemia and carbohydrate cravings are linked to serotonin. This fits in with commonsense notions of depression and fatigue, since many people “treat” their problem by eating, and usually by eating sweets. You feel bad, you have low energy, so you grab some sweets to make it go away—which a sugar rush initially does. But then the spike subsides, even plunges, and it's back on the roller coaster.

Some people do not produce enough serotonin. This can be caused by stress, high-carbohydrate diets, and weight gain around the middle. Serotonin problems can interfere with mood (causing depression or anxiety), sleep (reducing GH production), weight, and even the menstrual cycle. Low serotonin levels have been linked to depression, anxiety, and PMS. SSRIs are now used to treat all of these conditions.

But SSRIs also have an interesting side effect: they can influence your weight, causing either weight *loss* or weight *gain*. In my clinical practice, I have seen that Prozac and Zoloft commonly cause weight loss (in the first 6 months only), but Paxil and Remeron usually cause weight gain. But I have also seen the opposite occur with each of them! And these drugs aren't too different from prescription diet pills such as Phen-Fen. And, of course, some people even gained weight on these medications. The point is that serotonin has a powerful influence on your weight, but it is not the *only* factor.

The antidepressant medications *venlafaxine* (Effexor) and *duloxetine* (Cymbalta) and the weight loss medication *sibutramine* (Meridia) work by increasing levels of serotonin, norepinephrine, and dopamine. This combination approach seems to both decrease hunger and increase satiety. Patients who take sibutramine tend to lose about 25 pounds in 6 months. If the medication is discontinued, however, the weight is regained. The antidepressant medication *bupropion* (Wellbutrin) affects both the norepinephrine and dopamine systems and also causes weight loss. So it seems that serotonin, norepinephrine, and dopamine are interrelated when it comes to weight.

Designer serotonin medications are under development. These medications work by stimulating special serotonin receptors known as 5HT1B and 5HT2A/2C receptors. Research shows that the 2C receptor is the one that is most important when it comes to hunger and appetite. Early reports claim that the medication works better than available medications and with fewer side effects.

*Saint-John's-wort* is an herbal supplement that affects the serotonin system in a way similar to SSRIs. It has been promoted as an herbal treatment for both depression and obesity. Studies on Saint-John's-wort have not been consistent. It appears that Saint-John's-wort is not very effective for weight loss and can have potentially dangerous side effects.

### **Gamma-Aminobutyric Acid (GABA)**

GABA is a potent brain chemical that is affected by several prescription medications. *Benzodiazepine* medications such as Xanax, Valium, and Librium relieve anxiety and make you sleepy by stimulating the receptor for GABA. This class of medications has also reported to promote weight gain. A medication indicated for the treatment of epilepsy, *topiramate* (Topamax), has a slightly different effect on the GABA receptor. Unlike benzodiazepines, topiramate causes weight loss. It seems to be particularly beneficial in reducing binge eating and nighttime eating. Although not yet approved for the treatment of weight loss, I have seen many patients benefit tremendously from this medication.

### **Corticotropin-Releasing Hormone (CRH) and Urocortin**

CRH is a brain hormone involved in the production of the hunger hormone, cortisol (see Chapter 8). High levels of CRH decrease appetite, however. Another hormone that may be developed as a diet drug in the future is urocortin. Urocortin is a brain hormone that is similar to CRH and is released when the body is stressed. In animals, it's been shown to reduce appetite and cause weight loss.

### **Cocaine- and Amphetamine-Regulated Transcript (CART)**

CART is a brain hormone involved in appetite, reward, and reinforcement. Not much is known about CART, but it's thought to hold promise as a potential target area for medications.

### **Melatonin**

Melatonin is made by a poorly understood gland in the brain known as the *pineal gland*. (Interesting bit of trivia: because we don't understand what, exactly, the pineal gland does, in years past it was thought to be the seat of the soul.) Though many doctors think melatonin can help with weight loss, I'm not among them. Recent evidence suggests that melatonin may even cause weight *gain*.

## **PANCREATIC HORMONES**

The main hormone made by the pancreas is insulin. But it's not the only one. The pancreas is really two organs rolled into one. The exocrine pancreas makes digestive enzymes that are secreted into the gut. The endocrine pancreas is found in specialized islands of cells known as the islets of Langerhans and produces hormones that are secreted into the blood. Different cells in the islets produce different hormones.

Three important pancreatic hormones are glucagon, somatostatin, and amylin. Each, like insulin, is closely related to the food you eat, and each affects your appetite.

## Glucagon

Glucagon is a digestive hormone, released when food—particularly protein—leaves the stomach and enters the small intestine. It helps perform a wide variety of tasks: it slows the exit of food from the stomach, making you feel full; it raises blood sugar; and it tells the liver to pump out glucose.

Glucagon is also known as a *counter-insulin hormone*. People with diabetes who are prone to hypoglycemia carry a syringe of glucagon. If they have severely low blood sugar, a shot of the glucagon will make the blood sugar shoot right up.

Rare cases exist of tumors of glucagon-producing cells, known as *glucagonomas*. In these cases, the extremely high glucagon levels created by the tumors cause diabetes. The condition is accompanied by an itchy, red, sandpaper-like rash. And yes, though this is very, very rare, I bring it up because it's not rare if you're the one who has it. If you have diabetes and an itchy red rash, visit your endocrinologist and ask to have your glucagon levels tested. He may look at you funny at first, but be persistent.

## Somatostatin

In Chapter 9, somatostatin was discussed as a hormone that lowers growth hormone levels. Higher GH levels aid in weight loss, so somatostatin is not necessarily conducive to weight loss. Somatostatin is primarily produced by the hypothalamus, but it's also created in the islets of Langerhans in the pancreas, just like insulin and glucagon. Again, it's a hormone that blocks other hormones—in this case, the secretion of its sister pancreatic hormones, insulin and glucagon. It shuts down  $\beta$ -cells, the pancreatic cells responsible for insulin secretion.

But in certain situations, somatostatin may help with weight loss, despite its counterproductive effects on GH. One of these situations is *hypothalamic obesity*, a condition in which a brain injury or certain brain tumors cause obesity by damaging satiety centers in the ventromedial hypothalamus. Hypothalamic obesity is perhaps the most difficult form of obesity to treat. Insulin levels are very high, but not because of insulin resistance—rather, by something known as PIH syndrome (*primary insulin hypersecretion syndrome*). Scientists hypothesize that damage to

the hypothalamus may increase nerve signals to the pancreas, boosting insulin levels and causing extreme hunger. The high insulin levels also cause nutrients to be stored as fat instead of being burned as energy.

Somatostatin injections in these patients dramatically lower insulin levels. Once the insulin levels go down, weight is lost and leptin levels also go down. Carbohydrate cravings are dramatically reduced.

There's also a long-acting form of somatostatin, known as *octreotide*, which causes dramatic weight loss in some obese patients with hypothalamic obesity.

This treatment does not work for everyone, and even those with hypothalamic obesity don't all respond. For some reason, whites tend to have a higher response rate than other racial groups. But the interesting thing is that for those in whom this treatment does work, it really works well. People lose a great deal of weight, and without going on a special diet or exercising. Long-term studies are ongoing.

## Amylin

Amylin is co-secreted with insulin from the  $\beta$ -cells of the pancreas. Like insulin, amylin is secreted in response to food. Amylin reduces appetite and slows the release of food from the stomach. This reduces the rate of entry of food into the intestines, increasing feelings of fullness.

The synthetic form of the hormone is available in a medication known as *pramlintide* (Symlin). It is an injectable medication that is used to treat diabetes, but it also helps with weight loss. For more information, see Chapter 3.

## GUT HORMONES

The stomach and intestines, known as the *gut*, comprise one of the largest endocrine organs in the body. The first gut hormone to be discovered, *secretin* was described by Ernest Starling and William Bayliss in 1902. Since that time, many more gut hormones have been identified. Gut hormones are responsible for proper gut health and motility and have actions in the brain that regulate appetite and satiety. There is a *gut-brain connection* that regulates food intake through control of appetite, satiety, and gut motility.

## Ghrelin

Ghrelin is a protein hormone produced by special cells in the stomach. Ghrelin increases appetite. Ghrelin (*gh* stands for “growth hormone”; *relin* means “releasing”) was initially given its name because it is involved in GH release. But it’s now known that ghrelin’s major role is in regulating hunger, appetite, and satiety. Surgical weight loss procedures like *gastric bypass surgery* work in part by reducing ghrelin levels by up to 85 percent. Ghrelin-blocking medications hold promise for the future.

## Cholecystokinin (CCK)

CCK is a peptide hormone produced by the small intestine. It’s sometimes known as the “feel-full protein.” It slows stomach emptying and decreases appetite. CCK works in several parts of the body, notably in a circular muscle at the bottom of the stomach known as a *sphincter*. CCK tightens the sphincter, and with the sphincter tight, food stays in the stomach. Nerves from the stomach transmit the feeling “I’ve had enough to eat” to the brain. CCK also acts directly on the appetite centers of the brain, regulating appetite and making another satiety hormone. CCK also slows the movement of food out of the stomach and into the intestines, making you feel full longer.

## Glucagon-Like Peptide-1 (GLP-1)

A cousin of glucagon, glucagon-like peptide-1 has been gaining lots of attention in the medical community since the FDA approval of the GLP-1 medication *exenatide* (Byetta). GLP-1, produced by the gut, controls insulin secretion and feeding behavior. Like CCK, GLP-1 slows emptying of the stomach and reduces hunger.

Incidentally, another hormone, known as *gastric inhibitory polypeptide* (GIP) is secreted along with GLP-1. GIP is also thought to play a role in hunger and satiety, but less is known about this gut hormone. Recall that in the rare condition of food-induced Cushing’s syndrome, the GIP and cortisol systems get cross-wired so that GIP stimulates the ACTH receptors in the adrenal gland, resulting in high cor-



tisol levels after every meal (see Chapter 8). High glucagon levels block the secretion of GLP-1.

Many studies on GLP-1 have been performed in animals, but humans have not yet been tested. Early studies are promising, though. GLP-1 also increases insulin secretion, and for this reason GLP-1 is effective as a treatment for diabetes. Since GLP-1 is a peptide, it cannot be taken in pill form; the stomach will simply digest it. It must be injected. For more information, see Chapter 3.

### **Enterostatin**

Enterostatin is a hormone made by the stomach and small intestine that decreases appetite. Initial studies are promising for this hormone's use as a weight loss agent.

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# LOSING WEIGHT Now

SINCE THE FIRST EDITION OF *HORMONAL BALANCE* CAME OUT IN 2002, MANY FAD DIETS HAVE COME AND GONE. Meanwhile, the Hormonal Health Diet has stood strong as an easy yet effective way to take weight off and keep it off permanently. We have seen the fat-free craze, low-carb, no-carb, and the others. The Hormonal Health Diet is not a fad diet. It is an approach to permanently changing your way of eating that will help you achieve hormonal balance.

The truth is that you can lose weight on almost any diet. The real challenge is taking the weight off and keeping it off for the long haul. I don't consider a diet successful if you take off weight and then gain it all back. In order to lose weight permanently, your hormones have to be balanced. The Hormonal Health Diet will help you to balance your hormones and lose weight at the same time.

Throughout this book, you've read about hormones and how they influence your weight. The human body is a machine that was designed to move. If we walked as much as we should, and if we did the occasional labor to firm up the muscles in our arms and our stomachs, we wouldn't be in the bind we are today. Yes, we are a fast-paced society, and a fast-paced society has little time for walking, lifting, and preparing well-balanced meals. Instead we go full blast in our heads all day long, pop in a microwaveable dinner when we get home, and then veg out in front of the TV set. I used to do it too; it's hard not to.

But it's worth a try to move toward a healthier lifestyle. Often the most rewarding things in life are not the easiest. They take a little effort. But they're well worth it once they're done—when you've established the habits that will take you to the next level.

On the following pages are eating suggestions and menus for a better, healthier life.

### ***Annabelle's Story***

*Annabelle was a 42-year-old woman who had been struggling with her weight for many years. She gained 50 pounds with the birth of her first child and never took it all off. She gained more weight with each successive pregnancy. She had tried just about every diet and considered herself an “expert” in nutrition. She knew how to eat healthy. She knew about good and bad carbs, eating breakfast, eating frequently, protein, and vitamin supplements. Still, she could not lose weight. She would either be too hungry or just too tempted by delicious food. She loved going out to restaurants, and couldn't always force herself to make the best choices on the menu. Annabelle was convinced that the only way she could lose weight was with medications. Before starting medications, however, she decided to try the Hormonal Health Diet. She had never found a diet that had so many choices of foods. She realized that she didn't have to be hungry. As time went on, she realized that the quantity of food was more than she had ever eaten before, and she was amazed that she felt so full all the time. She realized there was a difference between “not feeling hungry” and “feeling full.” When she felt full, there were no temptations. She didn't feel like eating the wrong choices. She didn't need to take an appetite suppressant because she felt full all the time. And she was losing weight. It felt strange, feeling full and losing weight.*

## **MAKE YOURSELF FEEL FULL**

The key to success on the Hormonal Health Diet is feeling full. Why? You should never feel hungry on a diet. If you are hungry, you are probably miserable, and who wants to feel that way? But not feeling

hungry is not enough. Most people who aren't hungry can still eat. Stress eating, for example, is not done out of hunger. If you are not hungry but are offered a delicious treat, you are likely to take a bite. Feeling full is a different story. Think about a time when you ate so much that you were uncomfortably full. Your belly was stretched and ached. This was a time when you were very unlikely to eat anything else, because you felt full. The Hormonal Health Diet is designed to enable you to feel full most of the time. The diet has a minimum amount of food that you must consume every day. In addition, vegetables, fruits, and egg whites are unlimited. You should eat as much as it takes to feel full all the time.

### **MAKE IT A HABIT**

Changing your lifestyle for the better requires commitment to that change until it has become a habit, a way of life, and no longer a burden. Just like the habit of getting up in the morning and the systematic way that we prepare for work, the practice of following an improved dietary and exercise regimen will become automatic. The key to success is that the change becomes a habit!

### **GOAL SETTING**

For every action you take there must be a plan for guidance and a goal to define your achievement. You must determine how much weight loss is appropriate and how you will achieve it. Obviously, that will require changes in eating and exercise habits.

You should start with separate lists of short-term goals and long-term goals. Short-term goals are geared for success in the short run. The last thing you want is to be overwhelmed by goals that seem too lofty to be attained. Short-term success breeds long-term success. When you get off to a fast start and lose a significant amount of weight in the first month, you are more likely to be successful in the long run. The Hormonal Health Diet will help you get off to a very quick start. The immediate success you will see in the short term will give you motivation to stick with it for the long run.

Objectives that are vital to your success are:

- *Put your goals in writing.* Writing down your goals will help you keep them in mind. Keep your list on the refrigerator or on the bathroom mirror. Continually review and update your goals.
- *Set a date for the completion of your goal.* Setting a date will help you to stay focused and motivated.
- *Keep a food diary.* This will help you note the frequency of eating, the foods you eat, and the quantities. Analysis of this record keeping will allow you to make more specific changes. Use your food diary to help you with grocery shopping and meal planning. I've provided a sample food diary at the end of this book that you can copy and use as part of your daily routine.
- *Identify precise exercise goals.* Be specific about the kind of exercise you will engage in. Determine your short-term goal for duration of exercise and a long-term goal that will be necessary for you to achieve your weight loss target.
- *Change your behavior.* This will be one of your biggest challenges. To be successful you must, in some way, change your habits. You became overweight by engaging in specific behaviors, which will have to be changed. Perhaps you worked late into the evening, didn't have time to exercise, and ate fast food on the way home. You may now need to consider exercising in the morning before work, for example. To overcome a fast food attraction, you may have to prepare meals and snacks at home to take to the office.

## SETTING GOALS FOR YOUR WEIGHT

How much weight should you lose? This is a difficult decision. Many of us will have difficulty achieving a "normal" body weight. However, this does not mean that some weight loss will not be beneficial. In fact, many scientific studies have shown that loss of as little as 5–10 percent of your initial body weight will help regulate hormones and improve medical problems caused by obesity, such as diabetes, high blood pressure, and arthritis. For others, this seemingly small amount of weight loss will not be enough. We strive to maintain a "normal" weight. But what is normal?

### STANDARDIZING HEIGHT AND WEIGHT: BODY MASS INDEX (BMI)

The BMI, or Body Mass Index, is the standard for adjusting weight to height, assigning a numerical value to this ratio. BMI is a widely used standard to determine if you fall in the healthy (or “normal”) range or if you are overweight or obese. BMI is defined as body weight in kilograms divided by the square of height in meters ( $\text{kg}/\text{m}^2$ ). This is a complicated metric formula that is easily converted to pounds and inches. You can calculate your own BMI by using the following formula:

$$\text{BMI} = \frac{(\text{weight in pounds}) \times 703}{(\text{height in inches}) \times (\text{height in inches})}$$

For example, if you weigh 180 pounds and are 5'6",

$$\text{BMI} = (180 \times 703) / (66 \times 66) = \mathbf{29}$$

A normal or healthy BMI range is between 18.5 and 25  $\text{kg}/\text{m}^2$ . BMI values greater than 25  $\text{kg}/\text{m}^2$  are good indicators of the degree of excess fat and associated health risks. Overweight is defined as a BMI of 25 to 29.9, and obesity is defined as a BMI of 30 or above.

BMI is now the standard used by scientists and doctors to study weight and health risk. The higher your BMI, the higher your risk of medical problems and death.

BMI	Weight Category
$\leq 18.4$	Underweight
18.5–24.9	Normal
25–29.9	Overweight
30–34.9	Class I obesity
35–39.9	Class II obesity
$\geq 40$ –59.9	Class III obesity
$\geq 60$	Super-obesity

## BEYOND THE BMI

The Body Mass Index is a ratio of weight and height. Factors such as body frame, waistline, and body composition are not part of the BMI—but are important variables to consider in measuring health risk.

Waist circumference is a measure of the fat in the belly, which is more dangerous than other types of fat (see Chapter 3). The waist circumference is an excellent measure for determining if you have *central obesity*. Men with a waist circumference more than 40 inches and women with a waist circumference more than 35 inches have central obesity.

Body fat analysis helps you to determine how much of your weight is lean tissue (muscle, blood, and bone) and how much is fat. There are many methods of measuring body composition or your percentage of body fat, including underwater weighing, CT scanning, ultrasound, bioimpedance analysis (BIA), body calipers, and DEXA. Each of these methods has advantages and disadvantages. In general, tests that are easy to perform, such as bioimpedance analysis and body calipers, are less accurate (but easier and cheaper) than tests such as underwater weighing, CT scanning, and DEXA. Despite this, I believe that bioimpedance analysis or body calipers are excellent ways of keeping track of your body fat.

Body fat analysis can be useful when you hit a plateau. Since lean tissue is denser than bone, it is possible to lose body fat and maintain your weight. Although your weight is the same, you are leaner and your clothes will be looser.

## SET GOALS FOR PHYSICAL ACTIVITY

Many people are overwhelmed by the thought of starting an exercise program. The truth is that you don't have to do formal "exercise" to lose weight. Any type of physical activity, most notably walking, is an effective way to help you achieve hormonal balance.

### Planned Physical Activity

If you aren't currently exercising and are over the age of 35, or are at risk for cardiovascular disease, then you should see your doctor before starting an exercise program. Set a realistic short-term goal that is achievable—for example, "I will walk four times per week for 15



minutes.” Then gradually increase the amount each week.

Regular exercise is the key to maintaining lost weight. **Weight loss without exercise is temporary.**

### **Increase Daily Activities**

Formal exercise is not the only way you can burn calories. Any type of activity, from shopping to gardening, can burn calories. One of the reasons obesity has reached epidemic proportions is that modern technology has practically eliminated the need to move your body. The car, telephone, elevator, electric garage door opener, and television with remote control are all contributors to this phenomenon. You can get rid of some of these “conveniences” and burn extra calories.

The following are recommendations to increase physical activity in your life:

- Walk up stairs instead of taking the elevator or the escalator.
- Shop until you drop.
- Walk on the treadmill while watching TV.
- Walk in place while talking on the phone.
- Throw away the remote control.
- Park your car a little farther away from your destination and walk the extra distance.
- Take a short walk around the block.
- Play actively with the kids.
- Mow the lawn.
- Pull the weeds.
- Clean out the garage.
- Clean the house.

### **HAVE REALISTIC EXPECTATIONS**

Your weight loss results will depend on whether you are a novice or a veteran at attempting to lose weight. If this is your first attempt at weight loss, you may be more optimistic and a lot more confident in your ability to succeed than someone who has attempted every diet ever designed. A positive attitude is critical, as is confidence in your ability to follow the diet plan and make the appropriate choices of foods as well as portion sizes.

### **Rate of Weight Loss**

Your rate of weight loss will vary considerably, as it is dependent upon multiple factors:

1. How closely are you following the diet? Are you getting in all your minimums? Are you actively eating until you feel full? Are you drinking enough water?
2. Are you getting regular physical activity?
3. How do you view this effort to lose weight—as a diet or a lifestyle change?
4. What is your starting weight?
5. Are you on medications that may affect your weight?
6. Do you have medical problems that may affect the rate of weight loss?
7. Are you committed to making changes and breaking habits?

Additionally, the greater the weight loss needed to place you in the healthy weight range, the greater the initial weight loss necessary. However, as you near your goal, the required loss amount will taper. Those needing to lose 10 pounds can expect a target loss of 2 to 3 pounds per week. For the goal of a loss of 50 pounds or greater, the initial weight loss may be as much as 5 to 10 pounds the first couple of weeks. A good rule of thumb is that there are 3500 calories in a pound of fat. If you are at a stable weight and reduce your calories by 500–1000 per day, you will lose 1 to 2 pounds per week.

<b>1 pound of fat = 3500 calories</b>
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### **PREPLANNING**

Preplanning is a critical element of success on the Hormonal Health Diet. Preplanning will keep you on your diet and keep you successful. You must have enough of the right foods around at all times. This means having lots of fresh fruits and vegetables throughout the week.

I recommend shopping once a week from a list. With proper storage and preparation methods, you will have no problem keeping fruits

and vegetables around. Plan on bringing your lunch every day. Prepare snacks in advance.

Don't let lack of preparation make you fail. By having the proper foods available, you've already won half the battle. Eating all these delicious foods is the easy part.

### **KEEP A FOOD DIARY**

The food diary is one of the most helpful ways of accounting to yourself. Keep a small notebook with you at all times. Record everything that you eat. Awareness is paramount to changing habits. The food diary will make you very aware of what you eat. It will help you exercise control over eating and is an honest tally of your daily intake. I've provided a sample food diary at the end of this book for you to use as a tool to keep yourself accountable.

A few tips on keeping a food diary:

- Record every item eaten.
- Record the amount of each item eaten.
- Record the times you eat during the day.
- Record where you eat and what you are doing.
- Do not wait to record your intake at the end of the day. It will be inaccurate.
- Record immediately after eating.

### **EATING IN RESTAURANTS**

It is easier to be in control of your eating habits when you are the person shopping for the food and preparing it. However, whether it is business or pleasure that takes you away, you are now faced with the task of maintaining your new habits in unfamiliar surroundings. Eating out can be a great challenge, but it can be simplified if you have a plan.

1. Try to select from a menu versus an all-you-can-eat buffet.
2. Order a green salad with fat-free dressing before your meal.
3. Order two extra sides of steamed vegetables and a side of fresh fruit.

4. Avoid high-fat appetizers.
5. Drink water throughout your meal.
6. Order sauces and dressings on the side.
7. When possible, choose dishes that are steamed, poached, boiled, broiled, or grilled.
8. Choose red sauces instead of creamed sauces for pasta dishes.
9. Avoid filling up on bread before the meal; ask that the breadbasket be removed.
10. Choose fresh fruit for dessert, or at least share a dessert.
11. Avoid alcoholic beverages.

### **PREPARING TO SHOP**

The trip to the grocery store can be the initial link in the chain of events that determines how successful your eating habits will be on subsequent days. If the choices made here are in keeping with the diet plan, then the meals prepared and eaten will be too. Following are guidelines to help you adhere to your goals.

- Shop only from a list.
- Do not be tempted by unhealthy items that are shelved conspicuously throughout the grocery store.
- Do not shop when hungry. Shopping on an empty stomach will only lead to compulsive buying and will likely lead to the purchase of prepackaged foods that can be consumed fast. Such foods are often laden with fat and salt and are unwise food choices.
- Prepare meals. Prepare as many meals as possible. The time it takes to prepare a meal can often prevent the impulsive, uncontrolled eating that occurs with fast foods.
- Shop as little as possible. The more frequent the trips, the more numerous the temptations. I recommend that you shop once a week. With the suggestions listed in this section, you will have fresh fruits and vegetables available for the entire week.
- Don't shop for the family favorites. These are likely to be your favorites too.
- Don't be tempted by the store's free food samples as you shop.

## **PLANNING FOR UNPLANNED EVENTS**

Although you may feel that your exercise is now becoming routine, you're adapting well to changed eating habits, and the pounds are gradually being lost, there will always be the unplanned occasion. If your goals have not addressed these events, you will not be adequately prepared for the foods that may be available or the choices you will have to make, should the menu include foods that you ordinarily consider off-limits.

When such events arise, attempt to determine ahead of time the food that is available and make a note of what you will eat. Then when you arrive at the event you will be less likely to eat impulsively.

## **MAKE THIS YOUR LAST DIET**

The hardest part of losing weight is keeping it off. This must be seen as your new way of life, not as a defined period in your life with a starting and stopping point. The fact that you have met your weight loss goal indicates motivation and success in forming new habits. This is the critical phase, the phase in which you must adhere stringently to your initial goals—this is now your way of life. It is not a quick fix for a special occasion. You've made the commitment to eat healthy and be more active. Now you need to continue to maintain these habits.

Be sure to revisit your goals frequently to avoid accepting old habits again:

- Eat nutritionally balanced meals.
- Follow the plan. Reassure yourself that your diet plan is an integral component of your weight loss.
- Make a commitment to keep a food diary. Use the food diary at the end of this book as an example.
- Your success is always at risk of being threatened by old habits and situations. Before you succumb to your former ways, be prepared to return to the beginning when you first set out on this journey.
- Continue regular physical activity.
- Remain positive. A positive attitude will help you through the tough times, always reassuring you that you are making the right choices and changes in your life.

- Be flexible. You will always be changing and adjusting to accommodate your new lifestyle.
- Remain patient.

## THE HORMONAL HEALTH DIET

In the pages that follow are eating suggestions and meal plans to help you achieve hormonal balance. This diet is designed for anyone—whether you want to lose weight, achieve hormonal balance, or both. The only variable is portion size. If you want to lose weight, portions will be smaller than if you want to maintain your weight. If you have a particular hormonal disorder such as diabetes, insulin resistance, PCOS, menopause, or thyroid disease, this diet is also good for you. The chapters on these disorders have additional eating suggestions.

This diet, like many others, uses “exchanges” as a method of tracking particular food groups. “Exchange” is a term used to describe precise portion sizes of food items in the same category to provide equivalent amounts of calories and nutrients (i.e., protein, carbohydrates, and fat). For example, one protein exchange will provide 7 grams of protein, one starch exchange will yield 15 grams of carbohydrate, and one fat exchange will yield 5 grams of fat. Exchanges are a method of “portion control.” They remind us how much of a particular food category we can have in a day.

The Hormonal Health Diet uses the exchange system in a unique way. There are no strict numbers given for exchanges. Instead, we provide *minimums* and *maximums* for each exchange. In order to be successful, you must consume at least the minimum of each exchange group and you must not consume more than the maximum.

Three exchange categories have no maximums: vegetables, fruits, and egg whites. These foods may be consumed in unlimited quantities on this diet.

You should eat until you feel full. Don’t ever let yourself get hungry; you can eat and eat without breaking the diet. The key to success is to feel full so that you can stay within the parameters of the diet. Starches (including processed fruits and juices), proteins (other than egg whites), and fats are limited. You must not consume more than the set number of exchanges.

Many of you may think this sounds like a crazy fad diet. I assure you it's not. This diet has stood the test of time and has helped many people achieve *permanent weight loss*. With time you will become accustomed to this way of eating and will feel unhealthy if you return to your old eating style.

For those of you who are not accustomed to eating vegetables and fruits, it will be a challenge to get in your minimums. I encourage you to try your best to get in all your vegetable, fruit, and protein exchanges. These foods will fill you up and make you less hungry for the "bad" foods. In addition, they will provide the fuel your body needs to maintain a healthy metabolism.

Unlimited Foods	Limited Foods
Vegetables	Starches
Fruits	Milk
Egg whites	Protein (other than egg whites)
	Fats

The Hormonal Health Diet provides for three meals and three snacks a day. It is important that you have all of these meals. Small, frequent feedings keep hormones in balance and prevent excessive hunger (see Chapter 3). You should try to eat some protein at breakfast and your mid-morning snack. This provides energy and quenches hunger later in the day. Lunch and the mid-afternoon snack should be light. Dinner is protein, starch, and lots of vegetables. A snack in the evening is important to fuel your metabolism throughout the night.

Although it is important to get all six meals in each day, I cannot overemphasize how important it is to eat breakfast. You've heard it before: breakfast is the most important meal of the day. This is true. Having breakfast will help you to keep insulin levels (and hunger) low, increasing your chances of success (see the plight of the sumo in Chapter 3).

This table lists the *minimum* and *maximum* exchanges for one full day (divided into three meals and three snacks) for both the Weight

Loss Diet and the Weight Maintenance Diet. A range is given for both minimums and maximums. It is important that you follow both the minimums and maximums. Be sure to have at least five servings of vegetables, five servings of fruit, and six servings of protein every day. The maximum allowance of vegetables, fruits, and egg whites is unlimited. Remember, don't let yourself get hungry; eat until you feel full.

**Table 11.1**  
**Exchanges (Minimum–Maximum)**

<b>Food Group</b>	<b>Weight Loss Diet</b>	<b>Weight Maintenance Diet</b>
Vegetables	5–unlimited	5–unlimited
Fruit*	5–unlimited	5–unlimited
Milk	0–3	0–4
Starch	0–4	0–6
Protein**	6–8	6–10
Fat	0–2	0–14

\* Maximum for bananas, grapes, and watermelon limited to 5 exchanges per day.  
\*\*Maximums do not include egg whites.

**THE HORMONAL HEALTH DIET:**  
**BREAKDOWN BY EXCHANGES**

Here is the technical stuff. Remember, exact numbers aren't always important. These numbers are to be used as a guide to getting in the proper number of exchanges. You can use this as a guide to plan your daily meals. The key is sticking to your minimums and maximums and getting in three meals and three snacks. In the pages that follow are easy-to-follow meal plans and eating suggestions to help you keep on the diet.



**Table 11.2**

<b>Meal</b>	<b>Vegetables</b>	<b>Fruit</b>	<b>Milk</b>	<b>Starch</b>	<b>Protein</b>	<b>Fat</b>
Breakfast	0	1	1	1	1	0
Mid-AM	0	1	0	1	1	0
Lunch	2	1	0	1	2	1
Mid-PM	1	0	0	0	0	0
Supper	2	1	0	1	4	1
Evening	0	1	1	0	0	0

### **Carbohydrate Exchanges**

Carbohydrates include vegetables, fruits, milk, and starches. As discussed in Chapter 2, not all carbohydrates are created equal. Fruits and vegetables are the best carbohydrates to eat. Carbohydrates that are rapidly digested cause insulin surges and disrupt hormonal balance.

#### *Vegetables (Minimum 5, Maximum Unlimited)*

One vegetable exchange yields 0–5 grams of carbohydrate, 0–2 grams of protein, zero fat, and 0–25 calories.

An exchange is one cup of fresh vegetables or one-half cup of cooked vegetables. Therefore, three vegetable exchanges have the same calorie content as one starch exchange. It is very difficult to overeat vegetables. This explains why they are unlimited on the Hormonal Health Diet. Besides, all that fiber contributes to early satiety before you can possibly overeat on vegetables!

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**Artichoke**
**Asparagus**
**Beans**
**Beets**
**Broccoli**
**Brussels sprouts**
**Cabbage**
**Cauliflower**
**Celery**
**Cucumbers**
**Eggplant**
**Greens**
**Leeks**
**Lettuce**
**Mushrooms**
**Okra**
**Onions**
**Pea pods**
**Peppers**
**Pumpkin**
**Radishes**
**Spinach**
**Sprouts**
**Squash**
**Tomatoes**
**Turnips**
**Zucchini**

*Vegetable Purchasing, Storage, and Preparation Tips*

**Artichoke:** An artichoke is a flower and should be treated as such. Inspect it carefully before purchasing. Artichoke flowers will get brown at the edges as they age. Give the artichoke a gentle squeeze. A fresh artichoke will have tightly packed leaves and will feel firm, but an older artichoke's leaves spread apart and it feels spongy. Artichoke flowers should be placed in water just like other flowers. Use a small glass for each artichoke. Cut  $\frac{1}{8}$  inch off the bottom of the artichoke to expose fresh stem and place it in the glass of water. To extend storage time, cover the artichoke top with a small plastic bag and use a rubber band to form a seal between the bag and the glass. Artichokes can be steamed whole (40–45 minutes) or in quarters (30–35 minutes) and served with lemon. Remember to remove the “choke” (the purple, fuzzy middle) before eating. To eat it, scrape the top of each leaf with your teeth. Save the center “heart” for the end—it's the best part!

**Asparagus:** Asparagus has a relatively short shelf life, and stores may keep them out after they have started to spoil. Look at the “flower” tip of the asparagus. Can you see the individual parts of the flower? Or has the tip started to decay? Asparagus should be stored in water like artichokes. Place a bunch of asparagus in a large plastic cup filled one-third with water. Cover the asparagus bunch with a plastic bag and use a rubber band to seal over the cup. Even with proper storage, asparagus tends to spoil quickly. It should be eaten before other vegetables. To eat, gently snap off the lower part of the asparagus stem at its natural breaking point. Do not cut the ends of the asparagus. Asparagus can be eaten raw, blanched, poached, steamed, or stir-fried. Be careful not to overcook. Asparagus should retain a crunch after cooking. Asparagus may also be steamed and then marinated in balsamic vinegar, lemon juice, and spices and served cold.

**Beans and pea pods:** Fresh beans are available in many varieties, including green beans (also known as snap beans or string beans), haricots, verts, and wax beans. Chinese pea pods and sugar snap peas have similar nutritional value as green beans, but lima beans, peas, and other beans are considered starches (see below). Pre-wash beans and pea pods and keep dry in a ziplock bag. Eat raw as a snack or in salads, or steam, blanch, poach, or stir-fry.

**Broccoli and cauliflower:** These vegetables are delicious and inexpensive and can be kept fresh for a fairly long period of time. Broccoli and cauliflower are flowers and can be stored in a manner similar to that used for artichokes and asparagus, though this takes up a great deal of space. These vegetables also can be pre-processed and kept ready to eat. After washing, divide the florets into tennis ball-size pieces. Dry well. Store in a ziplock bag or vegetable bag. Place a paper towel in the bag to absorb any extra moisture. Replace the paper towel every 1–2 days. Broccoli and cauliflower can be kept fresh for 7–10 days in this manner. Pre-processed broccoli and cauliflower florets are also available at most grocery stores, but are considerably more expensive. Soak florets in cold water for 10 minutes before cooking. Broccoli and cauliflower may be eaten raw, steamed, poached, or stir-fried.

*Broccoli:* Chose heads that are all green and have no yellow. Broccoli leaves should not be discarded; they have the highest nutritional content of the entire vegetable. Leaves should be prepared in a manner similar to other greens (see below). Broccoli stems are also a delicious and distinctive part of the vegetable. During pre-processing, separate stems from florets. Peel with a potato peeler and eat raw as a crunchy snack or cook like greens.

*Cauliflower:* This flower comes in white, green, and purple varieties. All three taste about the same. Cauliflower gets a brownish discoloration as it gets older. The discoloration can be easily removed with a sharp knife; the rest of the cauliflower is still good to eat.

**Cabbage:** Cabbage comes in many varieties, including green and red head cabbage, Savoy cabbage, bok-choi, Chinese cabbage, kale, and Swiss chard. Brussels sprouts are a miniature variety of cabbage. Most cabbage, especially head cabbage, can be stored in the vegetable drawer of your refrigerator for 1–2 weeks. Quarter cabbage heads and steam, or shred and steam or stir-fry. One pound of raw cabbage cooks down to about 2 cups. Be careful—eating too much raw cabbage can cause thyroid dysfunction (see Chapter 7).

**Carrots:** Some diet experts have maligned carrots, claiming that they are high in sugar. I am not one of them. Carrots are low in calories but high in taste and high on the crunch scale. Many of us need this type of crunch (and carbohydrate) for our snacks. Carrots are available in

the large and the pre-peeled “baby” varieties. Peel carrots using a potato peeler or use them unpeeled, cut into slices. Carrots will store well in the vegetable drawer of your refrigerator for 7–10 days.

**Celery and cucumbers:** Celery and cucumbers have few to no calories, but they taste great and are an outstanding snack or salad ingredient. I recommend trying to eat at least one bunch of celery and three cucumbers each week. Substitute sliced celery and cucumbers for potato chips. Celery can be chopped and added to soups or other vegetable dishes. The darker the celery stalk, the higher the vitamin content. Fresh cucumbers should feel firm and rigid. Grocery stores frequently leave old cucumbers on the shelves. Inspect carefully before buying. Cucumbers should be well washed with soap and water to remove the vegetable oil or wax that is applied by grocery stores. Even better, grow your own cucumbers. Cucumbers are one of the easiest vegetables to grow from seed. To extend the storage life of cucumbers, wrap them in a paper towel and place in a ziplock bag. Cucumbers can be sliced and marinated with sliced onion, red wine vinegar, 1–2 tablespoons of table sugar, and spices for a delicious cucumber salad.

**Eggplant:** If you do not regularly eat eggplant, you should start. There are many varieties of eggplant. Each has its own distinctive texture and taste. Eggplant will stay fresh in your vegetable drawer for at least one week. The vegetable contains a huge amount of water. When cooking, it is usually necessary to drain excess water from time to time. Eggplant slices can be salted and drained of excess moisture on a rack. It discolors shortly after being cut, but adding lemon juice can eliminate this. Eggplant cooks best in stainless steel, pottery, or glass containers and can be sautéed, stir-fried, stuffed, baked, or grilled. Eggplant is also an excellent addition to spaghetti sauce.

**Greens:** There are countless types of greens, including many wild varieties. Common store varieties of greens include spinach, collard greens, turnip greens, mustard greens, and beet greens. Wash greens carefully to remove the grit. Spinach can be eaten raw or lightly steamed. Other greens usually need to be steamed or simmered for 25–40 minutes until tender. Substitute smoked turkey for ham hocks and serve with vinegar.

**Leeks and onions:** Leeks and onions are an excellent addition to salads and recipes. Slice leeks in half, marinate in vinegar and spices, and grill. Onions will usually keep in dry storage for 2–3 weeks or in your refrigerator for even longer. Because of their high sugar content, onions must not be cooked with high heat. Lower heat helps prevent discoloration. Raw onion slices are a great addition to a sandwich.

**Lettuce:** It is a challenge to keep fresh lettuce in your refrigerator for a whole week, but it can be done. Wash the lettuce head using the spray attachment on your sink, carefully keeping the head intact. Dry the head as best you can and wrap in a towel and place in a ziplock bag or plastic container. Replace the towel every 2–3 days. Romaine and iceberg lettuce will store for 7–10 days using this technique. Other varieties of lettuce stay fresh for shorter periods of time. In general, the smaller the lettuce leaf, the shorter the shelf life. I recommend using small leaf lettuces early in the week and romaine or iceberg later in the week, thus ensuring a variety of fresh lettuce for the whole week.

**Mushrooms:** Never use a mushroom that shows any sign of decay. Mushroom decay is full of toxins. The key to keeping mushrooms fresh is keeping them dry and well ventilated. Mushrooms should not be washed until just prior to use. But wash gently; most of the flavor is in the skins. Mushrooms are great raw, steamed, or stir-fried and require a very short cooking time.

**Okra:** This southern favorite is often used in stews, where its gooey quality helps thicken the dish. This consistency is often referred to as “gumbo.” The smaller the okra pod, the more tender. Okra is great stewed or sautéed with tomatoes, peppers, and onions.

**Peppers:** There are many varieties of peppers, including sweet, bell, banana, pimento, and hot. Peppers will stay fresh for 7–8 days in the vegetable drawer of your refrigerator. Raw peppers are a great snack or salad item. Peppers are also great steamed, stewed, sautéed, stir-fried, or stuffed. Hot peppers are a wonderful addition to many recipes.

**Radishes and turnips:** These are great raw as a snack. A turnip can be eaten like an apple.

**Sprouts:** Many types of sprouts are available, including bean, alfalfa, radish, sunflower, and broccoli. Most sprouts, except bean sprouts, are purchased while still growing. They will usually last for 5–7 days in your refrigerator. Sprouts are a great addition to salads and sandwiches. Bean sprouts are excellent stir-fried.

**Squash:** The many varieties of squash make it perhaps the most versatile of all the vegetables. Summer squashes, such as yellow and zucchini, are thin-skinned and enjoyable raw or cooked. Avoid buying summer squash that appears tough or with a stem that is very dry. Summer squash will store in the vegetable drawer of the refrigerator for about a week. To extend shelf life, wrap summer squash in a paper towel and place in a ziplock bag. Winter squash, also known as hard squash, includes acorn, butternut, pumpkin, and spaghetti squash. Hard squashes will keep for several weeks in your refrigerator. Hard squashes can be steamed, stuffed, or baked and require 15–45 minutes of cooking. Steamed pumpkin with fresh grated nutmeg is a delicious fall treat. Fill acorn squash with cranberries and bake for 45–50 minutes for a beautiful addition to your Thanksgiving table.

**Tomatoes:** In many parts of the country, it is very difficult to get good tomatoes. Tomatoes are easy and fun to grow during the summer and taste much better when grown at home. Tomatoes should not be kept in the refrigerator, but rather on your counter. Most tomatoes require ripening on your kitchen counter for 2–3 days. Buy tomatoes in varying stages of ripeness and eat them as they ripen. Cherry or grape tomatoes usually last for a week when kept on your counter. Green tomatoes are delicious sautéed or stir-fried with onions. Ripe tomatoes are great raw, stewed, sautéed, or baked. Cut tomatoes into cubes and marinate with sliced onions, red wine, or balsamic vinegar and spices.

### *Fruit (Minimum 5, Maximum Unlimited)*

One fruit exchange yields 15 grams of carbohydrate, zero protein and fat, and about 60 calories.

Despite their higher carbohydrate content compared with vegetables, fruits are unlimited in this plan. Because of their high water and fiber content, one becomes full easily without overconsumption of calories. It is also for these reasons that fruit juices and processed fruits

are *not* unlimited; they can be found in the starch category. Though not truly a starchy food, processed fruits are easily consumed in a quantity that rapidly provides large amounts of calories without the corresponding fullness. Processed fruits and juices are high in calories and have a very high glycemic index, as discussed in Chapter 2.

Keep plenty of fresh fruit around. Most fruits will last in the fruit and vegetable drawer of your refrigerator for a week or so. Mangoes, melons, and pears may be left on the kitchen counter until they ripen (become softer and develop a sweet smell) and then moved to the refrigerator.

Table 11.3

Fruit	Quantity	Fruit	Quantity
Apple	1 small	Limes	2
Apricots	4 whole	Mango	½
Banana*	1 small	Nectarine	1
Blackberries	¾ cup	Orange	1 small
Blueberries	¾ cup	Peach	1 medium
Cantaloupe	¼ of 6" melon (1 cup, cubed)	Pear	1 small
Cherries	12	Pineapple, fresh**	½ cup chopped
Grapefruit	½	Plums	2
Grapes*	17	Raspberries	1 cup
Honeydew melon	⅛ of 7" melon (1 cup, cubed)	Strawberries	1 ¼ cup
Kiwi	1	Tangerine	2
Lemons	2	Watermelon*	4" × ½" or 1 ¼ cups cubed

\* Quantities for bananas, grapes, and watermelon are limited to a maximum of 5 exchanges per day.

\*\*See Starch Exchanges for canned pineapple.

The Hormonal Health Diet allows for unlimited fruits, with three exceptions: bananas, grapes, and watermelon. These three fruits, although very healthy, have a higher glycemic index and can be overeaten. Bananas, grapes, and watermelon are not off-limits. Just remember, these fruits should be eaten in moderation. Try to have no more than five servings total of these three fruits each day.

You must have a minimum of five fruit exchanges every day. Table 11.3 lists portion sizes that equal one fruit exchange.

*Milk (Minimum 0, Maximum 3–4)*

One milk exchange provides 12 grams of carbohydrate, 8 grams of protein, and variable fat. (Maximum 3 exchanges for weight loss, 4 exchanges for weight maintenance.)

The choice of milk and yogurt will determine the amount of fat. However, this diet plan strongly urges skim and low-fat or nonfat products. An allergy to milk or lactose intolerance can eliminate this group from the diet. For those of you who fall into this category, there are other options. Soy milk is a great alternative to cow’s milk, and there is such a large variety of soy products on the market. The protein content and carbohydrate content vary greatly, so it is wise to label shop for the product with the most protein and least carbohydrate and fat content. Eden Soy Original and Extra Original provide 13 grams of carbohydrate, 10 grams of protein, and 5 and 3 grams of fat, respectively. Be aware that some varieties provide as much as 27 grams of carbohydrate, equivalent to almost two carbohydrate exchanges.

By eliminating or restricting milk in the diet, you risk inadequate calcium intake. Most soy milks are fortified with calcium; however, this may not be enough.

Table 11.4

Product	Quantity
Skim milk	1 cup
Skim milk (powdered)	½ cup
Yogurt (low-fat or fat-free)	1 cup
Plain/light sweetened	1 cup
Soy milk (low-fat)	1 cup



*Starch (Minimum 0, Maximum 4–6)*

One starch exchange provides 15 grams of carbohydrate, 3 grams of protein, zero fat (unless prepared with fat), and 80 calories. (Maximum 4 exchanges for weight loss, 6 exchanges for weight maintenance.)

Starch is frequently considered the culprit in failed weight loss attempts. It is not that starch is bad for you, but of all the macronutrients—starch, protein, and fat—it is the most overeaten. Additionally, starchy foods in meals and snacks all too often are accompanied by fat or sugary condiments, such as butter and jellies.

When choosing foods from this group, strive to choose high-fiber, unprocessed varieties. This will add bulk to your diet and consequently provide early satiety. The best starches have a low “glycemic index.” For more information on good starches and the glycemic index, see Chapter 2. See Table 11.5 for examples of foods with starch.

*Processed Fruit Exchanges*

One processed fruit exchange provides 15 to 19 grams of carbohydrate, zero grams of protein and fat, and 60 to 85 calories.

These foods include dried fruits and juices without added sugar. They are a concentrated source of carbohydrates and are limited on this diet owing to the fact that they are easily consumed in large quantities before you get full. For example, one-half glass of orange juice is more quickly consumed compared with a whole fresh orange. Yet both provide the same amounts of calories and carbohydrates. Although the nutritional value of processed fruit is slightly less compared with their fresh source, these fruits remain rich in potassium, many vitamins, and health-protective phytochemicals. See Table 11.6 for examples of processed fruits.

**Protein (Minimum 6, Maximum 8–10)**

One protein exchange provides 7 grams of protein, zero carbohydrates, and variable fat depending on the cut of meat or the choice of meat substitute chosen. (Maximum 8 exchanges for weight loss, 10 exchanges for weight maintenance.)

Table 11.5

Starch	Quantity	Starch	Quantity
Bread: white, wheat, French, rye, pumpernickel	1 slice	Matzo	1" × 5" square
Bagel	1/3	Fat-free muffin	1 small
Biscuit or roll (low-fat)	1 small	Melba toast	4
Bread crumbs	1/4 cup	Pasta	1/2 cup
Breadsticks	1		
Bun: hamburger or frankfurter	1/2	English muffin	1/2
Cooked cereal	1/2 cup	Rice cakes	2
Puffed cereal	1 1/2 cup	Tortilla, small	1
Bran cereal	1/2 cup	Pasta	1/2 cup
Unsweetened, ready-to-eat cereal	3/4 cup	Peas	1/2 cup
Corn	1/2 cup or 1 small ear	Pita bread	1 small
Graham crackers	3 × 2 1/2" squares	Popcorn (air-popped)	3 cups
Oyster crackers	1/2 cup	White potato	1 small or 1/2 cup mashed
Saltine crackers	6	Sweet potato	1/2 cup
Soda crackers	6	Pretzels	1/2 cup
Macaroni noodles (cooked)	1/2 cup	Rice cakes	2
English muffin	1/2	Tortilla small	1

Table 11.6

Juice	Quantity	Dried Fruit	Quantity
Apple	½ cup	Apricots	8 halves
Grape	½ cup	Apples	4 rings
Grapefruit	½ cup	Dates	3 small
Lemon	½ cup	Figs	3 small
Orange	½ cup	Mango slices	4 strips
Prune	½ cup	Peaches	2 halves
		Pears	3 halves
<b>Other</b>		Prunes	4 medium
Applesauce	½ cup	Raisins	2 Tbsp
Fruit cocktail (unsweetened)	¾ cup		
Pineapple crushed (in own juice)	½ cup		
Pineapple rings	2		
Jam or jelly, low-sugar	2 tsp		
Syrup, sugar-free	2 Tbsp		

This diet plan recommends very lean and lean meats and meat substitutes. A very lean exchange will provide 0 to 1 gram of fat and 35 calories, and a lean exchange will provide 3 grams of fat and 55 calories. Grill, bake, or broil meats in such a manner as to remove all possible fat.

Egg whites are unlimited. Yes, on this diet plan you may have as many egg whites as you want. Egg whites are pure protein, without any fat or carbohydrates. In any weight loss program, adequate protein intake eliminates hunger and prevents muscle loss. I recommend an egg white omelet as a delicious way to get in your protein. But egg whites can also be used in recipes in many creative ways. See Table 11.7 for examples of meats and meat substitutes.

**Table 11.7**

<b>Meat/Meat Substitute</b>	<b>Quantity</b> (1 oz of the following unless otherwise indicated)
Beef	Lean, trimmed of fat Choose round or loin cuts Flank steak, roast (rib, chuck, rump), steak (T-bone, porterhouse, strip, filet), lean ground.
Pork	Fresh ham, Canadian bacon, tenderloin, center loin chop
Poultry	White meat, no skin
Fish	Cod, flounder, grouper, haddock, halibut, trout, tuna, salmon, snapper Canned tuna or salmon in water (? cup)
Shellfish	Clams, crab, lobster, scallops, shrimp, imitation shellfish
Game	Buffalo, ostrich, venison
Cheese (non-fat or low-fat)	Less than 3 grams per slice
Cottage cheese (low-fat or fat-free)	$\frac{1}{4}$ cup
Egg whites*	Unlimited (2 are equivalent to 1 very lean protein exchange)
Egg substitute* (fat-free)	Unlimited ( $\frac{1}{2}$ cup is equivalent to 1 very lean protein exchange)
Whole egg	(1 protein and 1 fat)
Lunch meat (fat-free)	1 oz
Soy	
Tofu	3 oz
Soy burger	(counts as 2 protein and $\frac{1}{2}$ starch)
Cooked beans	$\frac{1}{2}$ cup (1 protein and 1 starch)

\* Egg whites and egg substitutes are unlimited owing to their zero fat content. They contain only protein, which is important during caloric restriction and weight loss phases.

**Fat (Minimum 0, Maximum 2–4)**

One fat exchange provides 5 grams of fat, and zero protein and carbohydrates. (Maximum 2 exchanges for weight loss, 4 exchanges for weight maintenance.)

All fats have the same number of calories. (See Chapter 2 for more information on types of fat.) It is important to realize that even a “good” fat is still fat, providing the same amount of calories as a “bad” or saturated fat. Although unsaturated fats are recommended, they are limited as part of a healthy diet. Fat exchanges are listed in Table 11.8.

**Free Food Exchanges—Unlimited**

The foods in this section may be consumed in unlimited quantities on this diet.

- Bouillon
- Club soda or mineral water
- Coffee
- Diet shakes (low-calorie)
- Diet soft drinks
- Egg whites
- Flavoring extracts
- Fruit
- Garlic
- Gelatin dessert, sugar-free
- Herbs, fresh or dried
- Mustard
- Pepper rings, hot
- Pickles
- Pudding, fat-free, sugar-free
- Salsa
- Soy sauce
- Spices
- Sugar substitutes
- Tea
- Vegetables
- Vinegar
- Worcestershire sauce

**Table 11.8**  
**FAT EXCHANGES**

<b>Monounsaturated Fat</b>	<b>Quantity</b>
Oil (canola, olive, peanut)	⅓ tsp
Olives: ripe (black)	8 large
green, stuffed	10 large
Nuts	
almonds, cashews	6
mixed	6
pecans	4 halves
Peanut butter	2 tsp
Sesame seeds	1 Tbsp

<b>Polyunsaturated Fat</b>	<b>Quantity</b>
Margarine: stick, tub, or squeeze	1 tsp
Lower fat (30 to 50% veg oil)	1 Tbsp
Mayonnaise (reduced-fat)	2 Tbsp
Nuts, walnuts, English	4 halves
Oil (corn, safflower, soybean)	1 tsp
Salad dressing (reduced-fat)	2 Tbsp
Miracle Whip salad dressing (reduced fat)	1 Tbsp
Seeds: pumpkin, sunflower	1 Tbsp

<b>Saturated Fat</b>	<b>Quantity</b>
Bacon	1 slice
Butter	1 Tbsp
Cheese (regular)	½ ounce
Cream cheese	1 Tbsp
Margarine, fat-free	4 Tbsp
Margarine, reduced-fat	1 tsp
Mayonnaise, fat-free	1 Tbsp
Mayonnaise, reduced-fat	1 tsp
Mayonnaise, regular	1 tsp
Miracle Whip salad dressing (reduced fat)	1 Tbsp
Nuts, walnuts	4 halves
Oil (corn, safflower, soybean)	1 tsp
Salad dressing (reduced-fat)	2 Tbsp
Seeds: pumpkin, sunflower	1 Tbsp
Sour cream, fat-free	1 Tbsp

## BACK TO BASICS

The *Basic Meal Plan* is a simple version of the Hormonal Health Diet. It is designed to be:

- Easy to plan for (preplanning is key in any diet—see below)
- Easy to prepare
- Easy to follow

The Basic Meal Plan is designed to help you achieve hormonal balance by emphasizing the eating guidelines presented in this book. The diet uses a 3-day rotation schedule. You should follow the days in order, starting again at day 1 after you finish day 3. I suggest you follow this diet for 10–14 days before moving on to a diet with more variety, such as the 7-day meal plan.

Make a special effort to adhere to this diet as best you can. The quantities of fruits, vegetables, and egg whites on this diet are the *minimum* you should consume; you may always have more. If you are excessively hungry, eat only the “free foods” that you are allowed to have in unlimited quantities. These include free food exchanges, fresh fruits, vegetables, and egg whites. (Quantities for bananas, grapes, and watermelon are limited to a maximum of 5 exchanges per day.)

Many people, including myself, are able to follow this meal plan on a daily basis without getting bored of the simple meals. You do not have to follow such a simple eating style, however. After you become familiar with the basics of the diet, you can learn to be more creative with your meals, eliminating the monotony of this simplified approach.

Part of the fun of this eating style is that the choices are endless. The key is learning new ways to combine proteins, starches, fruits, and vegetables into delicious recipes that allow you to stay on the diet and not get bored. In the pages that follow, the Basic Meal Plan is presented as a 7-day version of the Hormonal Health Diet. The 7-day Meal Plan is designed to be a transition from the Basic Meal Plan. As you get used to this style of eating, you should be able to design your own diet, maintaining the appropriate amount of protein, starches, and fats. And don't forget about fruits and vegetables—minimums always apply.

The key to long-term success is variety. Never let yourself get bored with the diet. The ingredients that you have to work with can be

combined into an unlimited number of recipes. There are many outstanding cookbooks and websites devoted to healthy cooking. My website, [www.intelligenthealthcenter.com](http://www.intelligenthealthcenter.com), has hundreds of recipes that work great with this diet. Experiment with at least two new recipes every week. Just keep cooking!

### **GET READY FOR SUCCESS!**

The most basic element required for you to be successful in following this diet is something I've already talked about: preplanning. After all, you'll have a lot of difficulty following the diet if you don't have the proper ingredients in your kitchen.

Think about it. You get home from work. It's late; you haven't exercised, and you're tired and hungry. You look in the refrigerator and there is nothing to cook, so you order take-out Chinese, or a pizza, and pig out. There goes the day. Your diet may not be shot, but you've just taken a step backward.

On the other hand, if you have healthy food available, you will be much more likely to eat healthy. Make grocery shopping part of your weekly diet routine. Plan on shopping on the same day every week, and plan on buying enough groceries to get you through the entire week. This may take some practice at first, but it can be done. The key is to buy enough vegetables and fruits, but not so much that you can't eat them all in a week's time. Use the shopping list in this book (page 413) as a guide for your shopping.



## THE BASIC MEAL PLAN

	Day 1	Day 2	Day 3
<b>Breakfast</b>	Egg white omelet* 1 cup fat free yogurt ½ cup juice (apple, orange, grapefruit) 1 fruit exchange	2 lean protein exchanges 1 slice of bread 1 cup skim milk 1 fruit exchange	1 cup cottage cheese, fat-free 1 fruit exchange
<b>Mid-AM snack</b>	½ cup pretzels 1 fruit exchange	½ sandwich made with 2 oz fat-free lunch meat 1 fruit exchange	5 saltine crackers 1 fruit exchange
<b>Lunch</b>	½ sandwich made with 2 oz fat-free lunch meat 1 cup celery sticks 1 fruit exchange	Vegetable soup* (2 servings) 2 Tbsp Parmesan cheese	4 hard-boiled egg whites 1 cup spinach 1 tomato 1 cucumber Basic vinaigrette dressing* 1 fruit exchange
<b>Mid-PM snack</b>	1 cup carrot sticks	¾ cup unsweetened breakfast cereal ½ cup milk 1 fruit exchange	1 cup sliced bell pepper
<b>Supper</b>	Green salad Basic vinaigrette dressing* 4–6 oz grilled lean meat or fish 2 cups cooked vegetables ½ cup brown rice 1 fruit exchange	Green salad Basic vinaigrette dressing* 4–6 oz grilled lean meat or fish 2 cups cooked vegetables 1 ear of corn 1 fruit exchange	Green salad Basic vinaigrette dressing* 4–6 oz grilled lean meat or fish 2 cups cooked vegetables 1 small potato 1 fruit exchange
<b>Evening snack</b>	1 cup fat-free yogurt 1 fruit exchange	1 cup fat-free yogurt 1 fruit exchange	1 cup fat-free yogurt 1 fruit exchange

**Sandwich Tips:** Use lots of vegetables, sliced tomato, onion, lettuce, sprouts, and so on, to make the sandwich large and filling. Fat-free lunch meats include turkey, chicken, and ham. You may also substitute 2 oz grilled chicken, fish, or lean beef or canned tuna or salmon (in water). Use mustard and/or a very small amount of fat-free mayonnaise.

All fruits and vegetable exchanges are minimums. Additional fruits, vegetables, and egg whites can always be added if you are hungry.

\* Recipe included

## Seven-Day Meal Plan

The portions of vegetables and fruits in this meal plan are the minimum amount you should eat. If you are not feeling full, you may include more free food exchanges, vegetables, fruits, or egg whites. Remember, these items are unlimited. After you become accustomed to this style, you can start creating your own meals. Just use the exchange table above as your guide. Be creative! Make healthy cooking and eating your passion.

### DAY 1

#### Breakfast

Egg white omelet\* with asparagus, tomatoes, spinach, and fat-free feta cheese

1 whole grapefruit

1 cup skim milk

#### Mid-Morning Snack

½ cup fat-free yogurt

¼ cup breakfast cereal

Fresh berries

#### Lunch

Vegetable soup\* with 4 oz cooked chicken breast added

Fruit smoothie\*

#### Mid-Afternoon Snack

Baby carrots

#### Supper

Large salad with low-calorie dressing

Beef tenderloin with cherry sauce\*

½ baked sweet potato with cinnamon

Sautéed mushrooms\*

#### Evening Snack

Fresh berries

½ cup fat-free yogurt

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\*Recipe included

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**DAY 2****Breakfast**

1½ cups breakfast cereal with protein (Kashi™, Quaker Weight Control Instant Oatmeal™, etc.; should contain at least 7 grams protein per cup)  
1 cup skim milk  
1 small banana  
1 hard-boiled egg

**Mid-Morning Snack**

One-half sandwich:

1 slice whole grain bread  
2 oz fat-free turkey or chicken  
Lettuce and tomato

**Lunch**

Large green salad:

3 oz boiled, peeled shrimp or chopped, cooked chicken breast  
3 hard-boiled eggs (whites only; discard yolks), chopped  
Chopped raw or lightly steamed vegetables (more is better)  
Cherry tomatoes (more is better)

Basic vinaigrette dressing\*

1 large apple

**Mid-Afternoon Snack**

Fruit smoothie\*

**Supper**

Large salad with low-calorie dressing  
6 oz grilled or broiled fish or chicken  
Yellow pepper sauce\*  
½ cup basmati rice  
Garlic green beans\*  
Broccoli supreme\*

**Evening Snack**

Fruit salad\*

**DAY 3****Breakfast**

Egg white omelet\* with mushrooms, onions, peppers, and mozzarella cheese

1 whole grapefruit

1 cup skim milk

**Mid-Morning Snack**

One-half sandwich:

1 slice whole grain bread

½ cup tuna (packed in water)

Lettuce and tomato

1 Tbsp fat-free mayonnaise

**Lunch**

Black bean and orzo salad\*

1 large peach or 2 plums

**Mid-Afternoon Snack**

Cut-up green and red peppers

**Supper**

Large salad with low-calorie dressing

Chicken noodle bake\*

Roasted asparagus with carrots and onions\*

**Evening Snack**

Fruit smoothie\*

**DAY 4****Breakfast**

1 cup breakfast cereal with protein  
Blueberries  
1 cup skim milk  
1 hard-boiled egg

**Mid-Morning Snack**

½ cup chopped pineapple  
½ cup fat-free cottage cheese

**Lunch**

Shrimp and vegetable salad\*

**Mid-Afternoon Snack**

Fruit smoothie\*

**Supper**

Large salad with low-calorie dressing  
Chicken and vegetable pasta sauce\*  
½ cup whole wheat or low-carb pasta

**Evening Snack**

Unsweetened canned fruit (peaches, pears, mandarin oranges)  
1 cup fat-free yogurt

**DAY 5****Breakfast**

- 1 slice whole grain toast
- 1 tsp low-sugar jam
- 4 egg whites, scrambled
- 2 oz soy breakfast links or low-fat turkey sausage
- 1 whole grapefruit

**Mid-Morning Snack**

Pita pocket:

- 1 small pita bread pocket
- ½ cup vegetables, precooked or raw
- 1–2 oz fat-free feta cheese

Fruit salad\*

**Lunch**

- Vegetable soup\* with 4 oz cooked chicken breast added
- Fruit smoothie\*

**Mid-Afternoon Snack**

Orange cucumbers\*

**Supper**

- Large salad with low-calorie dressing
- Bouillabaisse\*
- Steamed fresh vegetables

**Evening Snack**

- ¼ cup breakfast cereal
- ½ cup skim milk
- Fresh berries

**DAY 6****Breakfast**

Fruit smoothie\*

1 hard-boiled egg

**Mid-Morning Snack**

½ cup fat-free cottage cheese

Unsweetened, canned fruit

**Lunch**

1 low-calorie frozen entrée

1 package frozen vegetables

**Mid-Afternoon Snack**

Cut-up radishes, celery, and carrots

**Supper**

Large salad with low-calorie dressing

Brandy chicken breasts with scallions\*

Braised spinach and red potatoes\*

**Evening Snack**

1 medium peach

1 cup fat-free yogurt

**DAY 7****Breakfast**

1 cup breakfast cereal with protein  
1 cup skim milk  
½ cup unsweetened applesauce  
4 scrambled egg whites

**Mid-Morning Snack**

1 oz low-fat cheese  
6 whole grain, low-fat crackers  
Kiwi fruit

**Lunch**

½ cup whole wheat or low-carb pasta  
4 oz grilled chicken  
Steamed vegetables  
1 tsp olive oil  
2 small tangerines

**Mid-Afternoon Snack**

Cut-up celery and carrots

**Supper**

Large salad with low-calorie dressing  
Charbroiled tuna with oregano mango sauce\*  
Red cabbage and apples\*

**Evening Snack**

½ mango with chili powder and lime juice



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# RECIPES FOR THE HORMONAL HEALTH DIET

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## EGG WHITE OMELET

### Makes 1 Serving

3	Egg whites
1	Egg yolk (optional)
1 slice	Fat-free cheese (optional)
1 cup	Vegetables*
	Fat-free cooking spray
¼ teaspoon	Salt (optional)
¼ teaspoon	Pepper

\*Onion, mushroom, broccoli, peppers, asparagus, spinach, and/or squash

This recipe works best when an **8–10" nonstick omelet pan** is used.

1. Chop about 1 cup raw vegetables.
2. Cook vegetables in pan with fat-free cooking spray for 3–4 minutes until soft.
3. Remove vegetables from pan, place in small dish.
4. Clean vegetable residue from pan and place back on medium-high heat.
5. Combine egg whites, egg yolk, salt, and pepper in a small bowl and whisk thoroughly.
6. After pan is hot (about 30–45 seconds), spray nonfat cooking spray, then add egg white mixture.
7. Place most (but not all) of the cooked vegetables over half of the egg white mixture as it is cooking.
8. Place 1–2 slices of fat-free cheese over the vegetables (optional).
9. Cover for 2–3 minutes. When egg mixture is completely solidified, gently fold the omelet together, keeping the half with vegetables on the bottom.
10. Gently slide the omelet onto a plate.
11. Garnish with remaining vegetables.

### **Nutritional Analysis**

*Per serving:* 273 calories, 5.1 g fat (17.3 percent of calories from fat), 49.7 g protein, 5.7 g carbohydrates. *Exchanges:* 4 proteins, 1 fat.

## VEGETABLE SOUP

### 10 Servings

1 cup	Chopped onions or leeks
2 cloves	Garlic, crushed
10–12 oz can	Diced or crushed tomatoes
2 cups	Yellow squash or zucchini, cut into small pieces
1 cup	Chopped celery
1 cup	Chopped carrots
8–10 oz can	Beans (pinto, navy, black, kidney)
1 box	Frozen cut corn
8 cups	Low-fat chicken broth or vegetable broth
1	Bay leaf
1 teaspoon	Pepper
Optional	Salt

1. Heat a large pot and coat with cooking spray, and add onions or leeks and garlic. Cook for 4–5 minutes.
2. Add tomatoes, squash, carrots, celery, and corn; cook for 10 minutes, stirring occasionally.
3. Add beans, bay leaf, pepper, and broth.
4. Bring to a boil and simmer for 1½ hours.
5. Add salt if necessary.

### **Nutritional Analysis**

*Per serving:* 223 calories, 3.6 g fat (13.9 percent of calories from fat), 10.5 g protein, 39.8 g carbohydrates. *Exchanges:* 1 starch, ½ protein, 2½ vegetable, ½ fat.

**FRUIT SMOOTHIE**

1 package (or 1 scoop)	Weight loss shake mix or protein powder, or ½ cup fat-free yogurt
1 cup	Frozen fruit (strawberries, blueberries, peaches, etc.)
½	Banana (optional)
1 package	Sugar substitute (optional)
2–6	Ice cubes
6–8 oz	Cold water

1. Put water in blender and turn on low.
2. Pour in shake mix and continue blending on low.
3. Add ice cubes and frozen fruit slowly as it blends.
4. When all ingredients are added, secure the lid and blend on low for 60 seconds and then on high for 30 seconds.

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**BASIC VINAIGRETTE DRESSING****Makes 8 Servings**

1½ cups	Vinegar (balsamic, red wine, rice)
¼ cup	Olive oil
1 clove	Garlic, crushed
3 tablespoons	Sugar
½ teaspoon	Pepper
¼ teaspoon	Salt (optional)
2 tablespoons	Spices, freshly chopped*

\*Chives, basil, oregano, cilantro, and/or tarragon

1. Combine all ingredients in a small jar or salad dressing container.
2. Shake well.
3. Serve over salad.

May be stored, without refrigeration, for 7–10 days.

***Nutritional Analysis***

*Per serving:* 50 calories, 3.4 g fat (59.7 percent of calories from fat), 0.1 g protein, 5.1 g carbohydrates. *Exchanges:* ½ fat.

**BEEF TENDERLOIN WITH CHERRY SAUCE****Makes 10 Servings**

	Vegetable cooking spray
½ cup	Minced shallot
½ cup	Minced celery
½ cup	Minced carrot
1 cup	Cabernet Sauvignon or other dry red wine
2 cups	Beef broth
2 cloves	Garlic, minced
¼ teaspoon	Ground pepper
2 tablespoons	Low-sugar cherry preserves
1 cup	Dried cherries
2 pounds	Beef tenderloin, well trimmed
1½ teaspoons	Fresh thyme
1½ teaspoons	Coarsely ground pepper
1 teaspoon	Orange peel
½ teaspoon	Salt
½ teaspoon	Ground coriander
½ teaspoon	Fresh oregano
¼ teaspoon	Ground cinnamon
1 teaspoon	Vegetable oil
1 tablespoon	Cornstarch
1 tablespoon	Water

1. Coat a large saucepan with cooking spray; place over medium-high heat until hot.
2. Add shallot, celery, and carrot; sauté 6 minutes or until tender.
3. Add wine; bring to a boil.
4. Reduce heat, and simmer, uncovered, 5 minutes.
5. Add beef broth and garlic; bring to a boil. Reduce heat, and simmer, uncovered, 5 minutes.
6. Strain wine mixture into a bowl; discard the vegetables. Return wine mixture to pan.
7. Add ¼ teaspoon pepper, cherry preserves, and dried cherries; stir well. Cook over medium heat until cherry preserves melt.
8. Remove from heat; let stand, partially covered, 1 hour.

9. Trim fat from tenderloin.
10. Combine thyme and next 8 ingredients.
11. Brush vegetable oil over tenderloin; rub with thyme mixture.
12. Place tenderloin on a rack coated with cooking spray; place rack in a shallow roasting pan.
13. Insert meat thermometer into thickest portion of tenderloin.
14. Bake at 350 degrees for 40 minutes or until meat thermometer registers 140 degrees (rare) to 160 degrees (medium).
15. Place tenderloin on a large serving platter; cover loosely with aluminum foil, and let stand 10 minutes.
16. Combine cornstarch and water; stir well. Add to cherry mixture. Bring to a boil, and cook 1 minute, stirring constantly.
17. Cut tenderloin into ½-inch-thick slices; serve with cherry sauce.

### ***Nutritional Analysis***

*Per serving:* 320 calories, 21.5 g fat (63.1 percent of calories from fat), 18.9 g protein, 9.4 g carbohydrate, 64 mg cholesterol, 433 mg sodium. *Exchanges:* 2½ lean meat, 3 fat.

**SAUTÉED MUSHROOMS****Makes 4 Servings**

1 tablespoon	Olive oil
2	Scallions, sliced
1 pound	Sliced mushrooms
	Salt, to taste
	Freshly ground pepper, to taste

1. In a large skillet over medium heat, melt butter; add sugar, mushrooms, and scallions.
2. Sauté, stirring frequently until tender, about 3 to 4 minutes.
3. Season to taste with salt and pepper.

***Nutritional Analysis***

*Per serving:* 52 calories, 2.1 g fat (27.4 percent of calories from fat), 3.4 g protein, 9.4 g carbohydrates. *Exchanges:* 1½ vegetable, ½ fat.



## YELLOW PEPPER SAUCE

### Makes 6 Servings

3 medium	Yellow bell peppers
1 tablespoon	Olive oil
1 medium	Yellow onion, diced
1 tablespoon	White balsamic vinegar
2 tablespoons	Dry white wine
1 tablespoon	Fresh oregano, minced
1 cup	Chicken stock or canned chicken broth
1 clove	Garlic, minced
1 teaspoon	Salt
½ teaspoon	White pepper

1. Roast bell peppers over a gas flame, under the broiler, or on the grill, until skins blacken and blister.
2. Cool, peel, seed, and chop bell peppers coarse; set aside.
3. Heat oil in a medium skillet.
4. Add onions and bell peppers; sauté until onions soften, about 3 minutes.
5. Add vinegar; simmer until vinegar evaporates, about 1 minute.
6. Add wine; simmer until liquid reduces to 1 tablespoon, about 2 minutes.
7. Add stock; simmer until liquid reduces to ½ cup, about 10 minutes.
8. Cool slightly, then transfer to a food processor; add oregano, 1 teaspoon salt, and ½ teaspoon pepper; purée until smooth.
9. Set sauce aside. (Can be cooled, covered, and refrigerated up to 3 days.)

### To Serve

Warm over low heat. Spoon a portion of sauce onto each warm dinner plate. Arrange a portion of meat in each pool of sauce and serve immediately.

### Nutritional Analysis

*Per serving:* 60 calories, 2.5 g fat (49 percent of calories from fat), 0.8 g protein, 5.0 g carbohydrates. *Exchanges:* ½ vegetable, ½ fat.

**GARLIC GREEN BEANS****Makes 8 Servings**

2 pounds	Whole green beans
1 teaspoon	Lemon pepper
4 cloves	Garlic, chopped
¼ teaspoon	Salt
4	Scallions or green onions
1 tablespoon	Olive oil

1. Trim ends on the green beans.
2. Steam or microwave until lightly cooked (5–7 minutes).
3. In a large pan or wok, sauté chopped garlic and green onions with olive oil for 3–5 minutes.
4. Add salt and lemon pepper.
5. Add green beans to pan and mix well, cooking over high heat for 1–2 minutes.

***Nutritional Analysis***

*Per serving:* 23 calories, 0.1 g fat (2.7 percent of calories from fat), 1.1 g protein, 6.1 g carbohydrates. *Exchanges:* 1 vegetable.

## BROCCOLI SUPREME

### Makes 6 Servings

1 pound	Broccoli, cooked
	Vegetable cooking spray
1½ cups	Carrot, thinly sliced
½ cup	Onion, chopped
1 cup	Croutons, seasoned
¼ cup	Fat-free milk
¼ teaspoon	Pepper
8 oz	No-salt-added cream-style corn (1 can)
1	Egg, lightly beaten
3 tablespoons	Grated Parmesan cheese

1. Place broccoli on paper towels; drain.
2. Coat a nonstick skillet with cooking spray; place over medium-high heat until hot.
3. Add carrot and onion; sauté 5 minutes.
4. Remove from heat; stir in broccoli, croutons, milk, pepper, corn, and egg.
5. Spoon into a 1½-quart casserole coated with cooking spray; sprinkle with cheese.
6. Bake, uncovered, at 350 degrees for 35 minutes.

### Nutritional Analysis

*Per serving:* 127.7 calories, 28 g fat (17.9 percent of calories from fat), 6.9 g protein, 21.8 g carbohydrates, 38 mg cholesterol, 256 mg sodium. *Exchanges:* ½ starch, ½ lean meat, 2 vegetable

**FRUIT SALAD**

*Makes a delicious fruit salad that lasts for several days in the refrigerator.*

4	Large oranges
2	White grapefruit
2	Pink grapefruit
½	Pineapple, diced
3	Apples, cored
½ pound	Grapes

1. Use a sharp knife to slice the skin off the oranges and grapefruit.
2. Cut all fruit into bite-size pieces. Leave grapes whole.
3. Mix together in a bowl. The citrus juice will prevent the apples from turning brown.

## BLACK BEAN AND ORZO SALAD

### Makes 6 Servings

3½ cups	Cooked orzo (rice-shaped pasta)
1 cup	Chopped red bell pepper
½ cup	Chopped purple onion
½ cup	Chopped fresh parsley
¼ cup	Chopped fresh basil
15 ounces	Black beans, drained
¼ cup	Red wine vinegar
3 tablespoons	Water
2 tablespoons	Balsamic vinegar
1 tablespoon	Olive oil
1½ teaspoons	Sugar
¾ teaspoon	Salt
2 cloves	Garlic, minced

1. Combine bell pepper, onion, parsley, and basil in a large bowl; toss well and set aside.
2. Combine red wine vinegar, beans, balsamic vinegar, water, olive oil, sugar, salt, and garlic in a bowl; stir well.
3. Pour over orzo mixture, and toss well. Cover and chill.

### Nutritional Analysis

*Per serving* (excluding unknown items): 396.4 calories, 3.99 g fat (8.7 percent of calories from fat), 19.9 g protein, 72.3 g carbohydrates, 0 mg cholesterol, 277 mg sodium. *Exchanges*: 4½ starch, 1 lean meat, ½ vegetable, ½ fat.

## CHICKEN NOODLE BAKE

### Makes 8 Servings

8 oz	Fat-free cottage cheese
4 oz	Fat-free cream cheese
4 oz	Fat-free sour cream
4 oz	Fat-free mayonnaise
½ cup	Scallions, thinly sliced
½ cup	Red bell pepper, chopped
¼ cup	Fresh parsley, minced
2 tablespoons	Margarine
⅓ cup	All-purpose flour
½ cup	Skim milk
10½ ounces	Low-salt chicken broth
½ teaspoon	Poultry seasoning
¼ teaspoon	Salt
¼ teaspoon	Pepper
Dash	Garlic powder
6	Lasagna noodles, cooked
	Vegetable cooking spray
3 cups	Boneless, skinless chicken breasts, cooked and diced
½ cup	Dry bread crumbs
2 tablespoons	Chopped fresh parsley
¼ teaspoon	Paprika

1. Combine cottage cheese, cream cheese, sour cream, and mayonnaise in a medium bowl; beat with mixer at high speed until well blended.
2. Stir in scallion, bell pepper, and ¼ cup parsley; set aside.
3. Melt the margarine in a medium saucepan over medium heat.
4. Add flour, and cook 1 minute, stirring constantly with a wire whisk. Gradually add milk and broth, stirring constantly.
5. Bring to a boil over medium heat, and cook 3 minutes or until thickened, stirring constantly.
6. Stir in poultry seasoning, salt, pepper, and garlic powder. Remove from heat; set sauce aside.

7. Arrange noodles in bottom of a 13 × 9-inch baking dish coated with cooking spray; top with half of cottage cheese mixture, half of chicken, and half of sauce.
8. Repeat layers, ending with sauce.
9. Combine bread crumbs, 2 tablespoons parsley, and paprika; sprinkle over casserole.
10. Bake, uncovered, at 375 degrees for 30 minutes.

***Nutritional Analysis***

*Per serving:* 396 calories, 6 g fat (10 percent of calories from fat), 40 g protein, 65 g carbohydrates, 62 mg cholesterol, 61 mg sodium.

*Exchanges:* 4 starches, 4 lean meats, 1 fat.

**ROASTED ASPARAGUS WITH CARROTS AND ONIONS****Makes 4 Servings**

½ pound	Asparagus
1 medium	White onion, sliced
½ pound	Thinly sliced carrots
4 cloves	Garlic, sliced
½ tablespoon	Olive oil
¼ cup	Balsamic vinegar
	Salt
	Pepper

1. Preheat oven to 350 degrees.
2. Wash and dry asparagus. Cut off ends. Evenly distribute asparagus and carrots in oblong roasting dish.
3. Top asparagus with sliced onion and sliced garlic cloves.
4. Season with salt and pepper. Drizzle olive oil over the vegetables.
5. Bake in 350-degree oven for 30 minutes. Remove from oven when done. Sprinkle with balsamic vinegar.

***Nutritional Analysis***

*Per serving:* 110 calories, 1.2 g fat (8.6 percent of calories from fat), 3.5 g protein, 26.0 g carbohydrates. *Exchanges:* 4 vegetables.



## SHRIMP AND VEGETABLE SALAD

### Makes 4 Servings

½ pound	Green beans
2 cups	Tomato, chopped
1 cup	Red onion, thinly sliced and separated into rings
1 pound	Shrimp, jumbo, cooked, peeled
1 cup	Puffed ripe olives
11 oz	No-salt-added whole-kernel corn (1 can), drained
1½ cups	Picante sauce
2 tablespoons	Rice vinegar, seasoned
2 tablespoons	Olive oil
1½ teaspoons	Fresh oregano, minced
Sprig	Fresh oregano, optional

1. Trim ends from beans and remove strings.
2. Steam beans, covered, 20 minutes or until crisp-tender.
3. Combine beans, tomato, onion, shrimp, olives, and corn in a large bowl, and toss well.
4. Combine picante sauce, vinegar, oil, and tarragon in a small bowl; stir well. Pour over shrimp mixture, tossing to coat. Garnish with tarragon sprigs, if desired.

### Nutritional Analysis

*Per serving:* 368.4 calories, 13.4 g fat (31.3 percent of calories from fat), 29.0 g protein, 37.2 g carbohydrates, 173 mg cholesterol, 1183 mg sodium. *Exchanges:* 1 starch, 2½ lean meat, 3½ vegetable, 2 fat.

**CHICKEN AND VEGETABLE PASTA SAUCE****Makes 8 Servings**

1 pound	Precooked, chopped chicken breast
1 tablespoon	Olive oil
1 medium	Onion, diced
1 cup	Mushrooms, sliced
¼ cup	Green bell pepper, diced
1 cup	Carrots, diced
½ cup	Celery, diced
¼ cup	Red wine
¾ cup	Tomato paste
3 cups	Tomatoes, chopped (fresh or canned)
3 cloves	Garlic, minced
2 tablespoon	Fresh basil (1 tablespoon dried)
1 tablespoon	Fresh oregano (½ tablespoon dried)
1 tablespoon	Fresh thyme (½ tablespoon dried)
1 teaspoon	Brown sugar
	Black pepper, to taste
	Salt, to taste

1. Melt butter in oil and swirl together.
2. Sauté onion until clear; add carrots, celery, and mushrooms.
3. Sauté for about 5 more minutes, stirring frequently. Add green bell pepper and the rest of the ingredients. Simmer for 30 minutes.
4. If sauce is too thick, add water. Cook 15 minutes more, and add salt and pepper to taste.

***Nutritional Analysis***

*Per serving:* 210 calories, 7 g fat (36.3 percent of calories from fat), 30 g protein, 13.6 g carbohydrates.

## ORANGE CUCUMBERS

### Makes 4 Servings

2	Cucumbers
2 teaspoons	Fat-free sour cream
¼ cup	Orange marmalade, light
2 tablespoons	Lemon juice
	Sea salt

1. Slice cucumbers crosswise about ¼ inch thick. Sprinkle with lemon juice. Lightly salt.
2. Top each slice with sour cream and low-fat orange marmalade.
3. *Optional:* Place on a bed of greens to serve as a salad.

### ***Nutritional Analysis***

*Per serving:* 44 calories, 0.4 g fat (7 percent of calories from fat), 2.1 g protein, 9.8 g carbohydrates. *Exchanges:* 2 vegetables.

### BOUILLABAISSE (SEAFOOD STEW)

*This hearty stew is made with an assortment of fish and shellfish, onions, tomatoes, olive oil, garlic, saffron, and herbs. Turmeric may be substituted for saffron.*

#### Makes 6 Servings

1½ pounds	Red potatoes (4 medium)
1½ cups	Thinly sliced leeks
½ cup	Dry white wine
¼ cup	Chopped fresh parsley
1½ tablespoons	Tomato paste
1 tablespoon	Olive oil
½ teaspoon	Fresh thyme
¼ teaspoon	Sea salt
¼ teaspoon	Saffron threads
¼ teaspoon	Pepper
⅛ teaspoon	Fennel seeds
16 oz	Clam juice (2 bottles)
2 cloves	Garlic, minced
2 slices	Lemon
14½ ounces	No-salt-added whole tomatoes (1 can), drained
1	Bay leaf
¾ pound	Medium peeled shrimp
¾ pound	Cod or other lean white fish fillets, 1-inch pieces

1. Pierce potatoes with a fork. Arrange potatoes in a circle on a paper towel in the bottom of microwave oven. Microwave at HIGH 10 minutes, rearranging potatoes after 5 minutes. Wrap potatoes in a towel, and let stand 5 minutes. Peel and cube potatoes; set aside.
2. Combine leek, wine, parsley, tomato paste, olive oil, thyme, salt, saffron, pepper, fennel, clam juice, garlic, lemon, tomatoes, and bay leaf in a 3-quart casserole; stir well. Cover with casserole lid, and microwave at HIGH 10 minutes, stirring after 5 minutes.

3. Stir in potato, shrimp, and fish. Cover and microwave at HIGH 3 minutes or until fish flakes easily when tested with a fork. Discard bay leaf.

***Nutritional Analysis***

*Per serving:* 270.3 calories, 4.1 g fat (13.8 percent of calories from fat), 25.3 g protein, 32.7 g carbohydrates, 111 mg cholesterol, 546 mg sodium. *Exchanges:* 1½ starch, 2½ lean meat; 1 vegetable, ½ fat.

**BRANDY CHICKEN BREASTS WITH SCALLIONS**

*Sautéed chicken breasts served in a brandy, broth, lemon, onion, and Dijon sauce.*

**Makes 4 Servings**

4 large	Boneless chicken breasts
½ teaspoon	Salt
½ teaspoon	Black pepper
1 tablespoon	Oil
1 tablespoon	Fat-free butter substitute
3 tablespoons	Chopped fresh chives or 3 tablespoons chopped green onions
1½ tablespoons	Fresh lemon juice
2 tablespoons	Brandy or cognac
3 tablespoons	Chopped parsley
2 teaspoons	Dijon mustard
¼ cup	Chicken stock

1. Pound the chicken breasts gently with a mallet between wax paper sheets. Sprinkle with salt and pepper.
2. Heat half of the measure of butter substitute and half the measure of oil in a large skillet. Cook chicken breasts 4 minutes, turning once, over high heat. Do not cook longer because they will get overcooked and dry. Transfer to a warm serving platter.
3. Add everything except the broth and the remaining butter substitute and oil. Cook 15 seconds, stirring constantly. Stir in the broth, and continue stirring until mixture is smooth. Now stir in the remaining butter substitute and oil.
4. Pour all of this over the chicken and serve immediately.

**Nutritional Analysis**

*Per serving:* 236.6 calories, 5 g fat (24.2 percent of calories from fat), 38.7 g protein, 96 mg cholesterol, 542 mg sodium. *Exchanges:* 5½ lean meat, ½ fat.

## BRAISED SPINACH AND RED POTATOES

### Makes 6 Servings

1½ pounds	Spinach, coarsely chopped
1 pound	Red potatoes, ¼-inch diced
8 oz	Water
½ teaspoon	Salt
1 teaspoon	Vegetable oil
¼ teaspoon	Crushed red pepper
3 cloves	Garlic, thinly sliced

1. Combine spinach, potatoes, water, and salt in a skillet; bring to a boil.
2. Cover, reduce heat to medium, and cook 5 minutes.
3. Uncover; cook over high heat until water evaporates. Spoon spinach-potato mixture into a bowl; set aside and keep warm.
4. Heat oil in skillet over medium-low heat. Add pepper and garlic; sauté 3 minutes. Spoon over vegetables; toss.
5. Substitute collard greens for spinach, if desired.

### **Nutritional Analysis**

*Per serving:* 79.0 calories, 1.2 g fat (12.7 percent of calories from fat), 4.5 g protein, 14.7 g carbohydrates, 0 mg cholesterol, 272 mg sodium.  
*Exchanges:* ½ starch, 1 vegetable.

**RED CABBAGE AND APPLES****Makes 4 Servings**

½ tablespoon	Butter
2 cups	Chopped red cabbage
⅓ cup	Red wine
2	Unpeeled yellow apples

1. Melt butter over low heat in a sauté pan or skillet; slice apples into pan and add cabbage, stirring.
2. Cook 5 minutes over medium heat. Stir in wine. Cover pan and cook 6–7 minutes.

(*Note:* Cooking cabbage eliminates any potential of causing thyroid dysfunction; see Chapter 7.)

***Nutritional Analysis***

*Per serving:* 68 calories, 1.8 g fat (22.8 percent of calories from fat), 0.7 g protein, 12.8 g carbohydrates. *Exchanges:* ½ vegetable, ½ fruit, ½ fat.



## CHARBROILED TUNA WITH OREGANO MANGO SAUCE

### Makes 4 Servings

1½ pounds	Tuna steaks
2 cloves	Garlic, minced
1	Lime, juiced
1 cup	Fat-free milk
¼ cup	Sherry
1 tablespoon	Fresh oregano, minced
1	Mango, peeled

1. Preheat broiler.
2. Season tuna with a little salt and fresh crushed garlic. Sprinkle with lime juice. Broil for about 2 minutes on each side.
3. Blend mango into a purée.
4. In a saucepan, reduce milk to about half. Add mango, sherry, lemon juice, and oregano. Boil for 2 minutes. Store in plastic container.
5. Pour mango sauce over tuna. Broil 3 minutes. Serve immediately.

### **Nutritional Analysis**

*Per serving:* 320 calories, 10 g fat (29.3 percent of calories from fat), 42.7 g protein, 11.5 g carbohydrates. *Exchanges:* 5½ protein, ½ fruit, ½ fat.

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# FOOD DIARY

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Date:

Notes/Comments:

Day:

- Monday
- Tuesday
- Wednesday
- Thursday
- Friday
- Saturday
- Sunday

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**Meal: Breakfast**

**Breakfast Time:**

Food & Beverage:	Serving Size/ Exchanges:	Calories:	Total Breakfast Caloric Intake:	Goal Breakfast Caloric Intake:
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**Meal: Mid-Morning Snack**

**MM Snack Time:**

Food & Beverage:	Serving Size/ Exchanges:	Calories:	Total MM Snack Caloric Intake:	Goal MM Snack Caloric Intake:
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**Meal: Lunch**

**Lunch Time:**

Food & Beverage:	Serving Size/ Exchanges:	Calories:	Total Lunch Caloric Intake:	Goal Lunch Caloric Intake:
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### MA Snack Time:

Goal MA  
Snack  
Caloric  
Intake:

### Dinner Time:

Goal Dinner  
Caloric  
Intake:

### Evening Snack Time:

Goal  
Evening  
Snack  
Caloric  
Intake:

TOTAL GOAL CALORIC INTAKE:

\_\_\_\_ Yes  
\_\_\_\_ No

If not, make note below of obstacles and challenges to help with future goal setting, meal planning, and grocery shopping.

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# SHOPPING LIST

## VEGETABLES

*Minimum of 35 1-cup servings*

- ☐ Artichokes
- ☐ Asparagus
- ☐ Beans
- ☐ Beets
- ☐ Broccoli
- ☐ Brussels sprouts
- ☐ Cabbage
- ☐ Cauliflower
- ☐ Celery
- ☐ Cucumbers
- ☐ Eggplant
- ☐ Greens
- ☐ Leeks
- ☐ Lettuce
- ☐ Mushrooms
- ☐ Okra
- ☐ Onions
- ☐ Pea pods
- ☐ Peppers
- ☐ Pumpkin

- ☐ Radishes
- ☐ Spinach
- ☐ Sprouts
- ☐ Squash
- ☐ Tomatoes
- ☐ Turnips
- ☐ Zucchini

## FRUITS

*Minimum of 35 servings*

- ☐ Apples
- ☐ Apricots
- ☐ Bananas
- ☐ Blackberries
- ☐ Blueberries
- ☐ Cantaloupe
- ☐ Cherries
- ☐ Grapefruit
- ☐ Grapes
- ☐ Honeydew melon

\_\_\_ Kiwi

### **FRUITS (CONTINUED)**

\_\_\_ Lemons

\_\_\_ Limes

\_\_\_ Mangos

\_\_\_ Nectarines

\_\_\_ Oranges

\_\_\_ Peaches

\_\_\_ Pears

\_\_\_ Pineapple

\_\_\_ Plums

\_\_\_ Raspberries

\_\_\_ Strawberries

\_\_\_ Tangerines

\_\_\_ Watermelon

### **DAIRY**

\_\_\_ Cheese, fat-free

\_\_\_ Cheese, Parmesan

\_\_\_ Cottage cheese, fat-free

\_\_\_ Egg substitute

\_\_\_ Eggs

\_\_\_ Skim milk

\_\_\_ Soy milk, low-fat

\_\_\_ Yogurt, fat-free

### **STARCHES**

\_\_\_ Breakfast cereal

\_\_\_ Pasta

\_\_\_ Potatoes

\_\_\_ Pretzels

\_\_\_ Rice, brown

\_\_\_ Saltine crackers

\_\_\_ Whole-wheat bread

### **JUICE**

\_\_\_ Apple

\_\_\_ Grapefruit

\_\_\_ Orange

### **PROTEIN**

\_\_\_ Beef

\_\_\_ Chicken

\_\_\_ Fish

\_\_\_ Pork

\_\_\_ Soy burger

\_\_\_ Soy links

### **LUNCH MEAT**

\_\_\_ Chicken

\_\_\_ Ham

\_\_\_ Turkey breast

\_\_\_ Turkey, smoked

### **CANNED FISH**

\_\_\_ Salmon, in water

\_\_\_ Tuna, in water

### **OTHER**

\_\_\_ Diet shakes

\_\_\_ Mustard

\_\_\_ Olive oil

\_\_\_ Pickles

\_\_\_ Spices

\_\_\_ Vinegar

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# HORMONE DISORDERS: A GUIDE TO SYMPTOMS

THIS CHART IS DESIGNED to help you determine if your symptoms are associated with a particular hormone problem. A single symptom can be nonspecific and may be associated with a variety of possible problems.

DM	=	Type 2 diabetes (Chapter 3)
IR	=	Insulin resistance (Chapter 3)
RH	=	Reactive hypoglycemia (Chapter 2)
IN	=	Insulinoma (Chapter 2)
MH	=	Male hypogonadism (Chapter 4)
PCOS	=	Polycystic ovary syndrome (Chapter 5)
VIR	=	Virilism (Chapter 5)
MP	=	Menopausal or perimenopausal (Chapter 6)
HT	=	Hypothyroidism (Chapter 7)
CS	=	Cushing's syndrome (Chapter 8)
PC	=	Pseudo-Cushing's (Chapter 8)
GHD	=	Growth hormone deficiency (Chapter 9)
ACR	=	Acromegaly (Chapter 9)

	DM	IR	RH	IN	MH	FLAS	PCOS	VIR	MP	HT	CS	PC	GHD
Acanthosis nigricans	X	X					X	X			X	X	
Aches and pains									X	X			X
Acne	X	X					X	X			X	X	
Aggressiveness								X			X		
Allergies/Hives										X			
Anemia					X	X				X			X
Anxiety			X	X	X	X	X		X	X	X	X	X
Bloating							X		X	X	X	X	
Blurred vision	X			X									
Body odor, excessive								X					
Bruising											X		
Buffalo hump											X	X	
Carbohydrate cravings	X	X	X				X				X	X	
Carpal tunnel syndrome	X									X			
Cheeks red											X		
Cheeks round	X	X									X	X	
Circulation problems	X	X							X				
Concentration problems			X	X					X		X		X
Confusion				X									
Constipation										X			
Decreased endurance					X	X			X	X	X		X
Depression					X	X	X	X	X	X	X	X	X
Deterioration in work performance				X	X	X			X	X	X	X	X
Difficulty concentrating				X	X	X			X	X	X	X	X
Difficulty relating to others					X	X			X	X	X	X	X



	DM	IR	RH	IN	MH	PCOS	VIR	MP	HT	CS	PC	GHD	ACR
Colon cancer	X	X				X		X					X
Concentration problems			X	X				X		X		X	X
Confusion				X									
Constipation									X				
Decreased endurance					X			X	X	X		X	
Decreased quality of life	X	X	X	X	X	X	X	X	X	X	X	X	X
Decreased sense of being	X	X	X	X	X	X	X	X	X	X	X	X	X
Depression					X	X	X	X	X	X	X	X	X
Deterioration in work performance				X	X			X	X	X	X	X	X
Diabetes	X	X	X			X		X		X			X
Difficulty concentrating				X	X			X	X	X	X	X	X
Difficulty relating to others					X			X	X	X	X	X	
Dry skin					X			X	X			X	
Edema									X	X	X		X
Eyebrows thinner									X				
Face round (moon face)	X	X								X	X		
Facial puffiness									X	X	X		
Family history of diabetes	X	X				X					X		
Family history of heart disease		X				X							
Family history of high blood pressure		X				X							
Family history of thyroid problems									X				
Fat over the collarbones										X	X		
Fatigue	X	X	X	X	X	X	X	X	X	X	X	X	X
Feeling cold									X			X	
Fingernails brittle									X				



	DM	IR	RH	IN	MH	PCOS	VIR	MP	HT	CS	PC	GHD	ACR
Increased body fat	X	X		X	X	X		X	X	X	X	X	
Increased fat in the belly	X	X			X	X		X		X	X	X	
Infections, frequent	X									X			
Infertility	X	X		X	X	X	X	X	X	X			X
Insomnia								X		X			X
Irritability				X				X	X			X	
Joint aches								X	X			X	X
Kidney disease	X	X				X	X			X			X
Kidney stones										X			
Libido, decreased					X		X	X		X		X	X
Liver disease						X	X			X	X	X	X
Loss of consciousness				X									
Loss of zest for life					X			X	X	X	X	X	
Low HDL (good) cholesterol	X	X				X	X	X		X	X	X	X
Low potassium	X						X			X			
Memory loss				X				X	X	X		X	X
Mood swings					X	X	X	X	X	X	X		
Muscle wasting					X					X		X	
Muscle weakness					X				X	X		X	
Nausea			X										
Numbness or tingling	X			X					X				
Osteoporosis or osteopenia					X			X		X		X	
Overeating	X	X								X			X
Peripheral vascular disease	X	X						X					X
Personality changes				X			X	X		X			X

	DM	IR	RH	IN	MH	PCOS	VIR	MP	HT	CS	PC	GHD	ACR
Poor general health	X	X			X	X	X	X	X	X	X	X	X
Poor wound healing	X						X			X			
Premature aging					X				X			X	
Protein in urine	X	X				X							X
Sedentary lifestyle	X	X				X					X		
Seizure				X									
Sense of well-being, decreased					X			X				X	
Skin tags	X	X				X				X	X		X
Skin, darker	X	X				X				X	X		
Skin, pale					X				X			X	
Skin, red								X		X			
Skin, thin								X		X		X	
Skin, yellow									X				
Sleep apnea									X	X	X		X
Sleeping too much					X			X	X			X	
Slow reflexes									X				
Sluggishness in the afternoons	X	X	X					X		X	X	X	
Sluggishness in the morning								X		X			
Smoke cigarettes		X						X					
Snoring									X	X	X		X
Social isolation					X	X						X	
Stomach ulcers										X			
Stretch marks, pink or white										X	X		
Stretch marks, red or purple										X			
Stretch marks, wider than ½ inch										X			

	DM	IR	RH	IN	MH	PCOS	VIR	MP	HT	CS	PC	GHD	ACR
Strokes	X	X						X					X
Stuffy nose									X				
Sweating, decreased									X				
Sweating, increased								X		X	X		
Thin arms and legs										X	X		
Thirst, excessive	X									X			
Unrestful sleep								X					
Urinary incontinence								X					
Urination, frequent	X									X			
Vision problems	X									X			X
Vision blurred	X			X									
Voice, deeper							X		X				
Weight gain	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight loss					X		X					X	
<b>Female only</b>													
Balding							X			X			
Birth to child over 10 pounds	X	X											
Breast cancer	X	X				X							X
Breast shrinkage							X			X			
Enlargement of the clitoris							X			X			
Extensive muscle growth							X			X			
Hirsutism	X	X				X	X	X		X	X		
Infections, urinary	X							X		X			
Infections, yeast	X									X			



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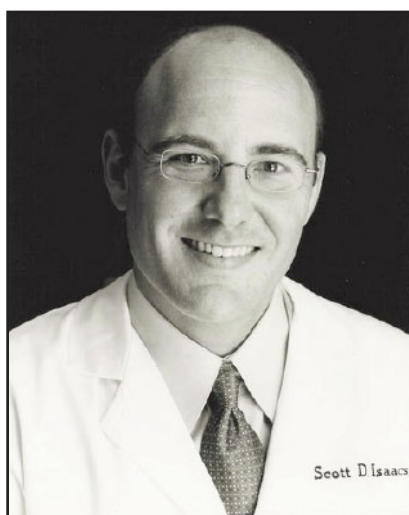
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# INDEX

- Acanthosis nigraicans, 81, 158, 164, 319
- Acarbose, 103
- Accupril, 106-107
- ACE inhibitors, 106-107
- Aceon, 106-107
- Acne, 157, 164, 279
- Acomplia, 109, 336
- Acromegaly, 156, 166, 306, 317-319
- Activella, 196, 216
- Actoplus Met, 103
- Actos, 102-103, 178
- Addison's disease, 229, 244, 270, 272-273
- Adenovirus Ad36, 322
- Adipex, 108
- Adipokines, 332
- Adiponectin, 8, 334
- Adipose tissue, 328, 329, 332
- Adrenal
- fatigue/exhaustion/burnout, 273-274
  - gland, 15, 17, 155, 270, 272
  - and the brain, 276-278
  - cancer, 156, 157, 162
  - hormones, 275-276
  - insufficiency, acute, 273-274
- Agenerase, 113
- Aging, 8, 10, 66, 309
- premature, 126, 237
- Agouti-related protein (AgRP), 335
- Albumin, 143
- Alcohol, 95, 135, 292
- Aldactone, 107, 122, 180-181
- Aldosterone, 116, 275
- Allesse, 196
- Alli, 53, 108
- Allergies, 243
- Allostasis, 16
- Alopecia, 157
- areata, 229
- Alora, 214
- Alpha-melanocyte-stimulating hormone, 338
- Altace, 106-107
- Altoprev, 104
- Amaryl, 112
- Amiloride, 107
- Amino acids, 49-50
- Amiodarone, 227
- Amlodipine, 113
- Amprenavir, 113
- Amylin, 341, 343

- Anabolic steroid abuse, 149-150, 151
- Anandamide, 336
- Anastrozole, 120, 148
- Androderm, 147
- Androgel, 146, 183
- Androgen, 8, 12, 19, 115-153
- challenges of measuring, 138-139
  - conversion, 120-121
  - disorders in women, 155-183
  - excess, 155-181
    - testing for, 170-176, 209
    - treating, 177-181
  - insensitivity syndrome, 121
  - supplements, 150-151
  - syndrome, female low, 182-181
- Androstenedione, 115, 116, 120, 150-151, 155, 172
- Anemia, 127, 230, 242, 244
- Anger, 125, 203, 207
- Angiotensin receptor blockers (ARBs), 107
- Anorexia nervosa, 203
- Antara, 105
- Anti-aging medicine, 10
- Antidepressants, 109-110, 113, 339
- Antihistamines, 114
- Antipsychotic medications, 114
- Antiseizure/antimigraine medications, 110, 113
- Anxiety, 63, 159, 207, 223, 278, 279
- Appetite, 11. *See also* Hunger hormones.
  - increased, 62, 281
  - loss of, 236
- Apri, 198
- Aptivus, 113
- Arimidex, 120, 148
- Aromatase inhibitors, 148
- Aromasin, 120, 148
- Arteritis, 230
- Arthritis, 2, 126, 134, 230, 319
- Artichoke, 362
- Asparagus, 362
- Aspirin, 110
- Atacand, 107
- Atazanavir, 113
- Atenolol, 107, 112
- Atherosclerosis, 73, 74, 241, 305
- Ativan, 295
- Atorvastatin, 104
- Attention deficit disorder, 75
- Auto immune syndromes, 133
- Avandamet, 103
- Avandia, 102-103, 178
- Avapro, 107
- Aviane, 196
- Avodart, 120, 181
- Aygestin, 112, 196
- $\beta$ -endorphin, 339
- Balding, male pattern, 120, 156
- Basic Meal Plan, 375-377
- Beans and pea pods, 362
- Beef tenderloin with cherry sauce, 390-391
- Benazepril, 106-107
- Benicar, 107
- Benzodiazepine, 340
- Beta
  - blocker, 107, 112
  - cells, 25, 29
- Bile acid sequestrants, 106
- Binge eating, 279
- Bioidentical hormone, 213
- Biotin, 99
- Birth control pills, 112, 177, 178-179, 194, 200, 313
- Black bean and orzo salad, 397
- Bloating, 188-192, 282
- Blood
  - pressure
    - high, 2, 61, 62, 66, 72, 73, 78, 123, 127, 156, 159, 240, 297, 319
    - medications, 106-107
    - sugar/glucose, 27, 78, 84

- 
- Body  
  dysmorphic disorder (BDD), 149-150  
  mass index (BMI), 351, 352  
  odor, 158  
Bone density test, 210  
Bouillabaisse, 404-405  
Brain  
  hormones, 224-241  
  problems, 137  
  tumors, 307  
Braised spinach and red potatoes, 407  
Brandy chicken breast with scallions, 406  
Breakfast, 47-48, 50  
Breast  
  enlargement, male, 297  
  milk production, 243  
Breath testing, 86  
Brevicon, 196  
Broccoli  
  and cauliflower, 303  
  supreme, 395  
Brown-Sequard, Charles Edouard, 21  
Bruising, 279  
Bumetamide, 112  
Bumex, 112  
Bupropion, 109-110, 113  
Byetta, 103-104  
  
Cabbage, 363  
Caffeine, 292  
Calan, 113  
Calcium, 218-219  
  channel blockers, 113  
Calories, measuring, 35-36  
Cancer, 2, 29, 77  
  breast, 120  
  liver, 134  
  ovarian, 156, 157, 160-161  
  signs of, 160, 169  
  uterine, 215  
  
Candesartan, 107  
Candida infections (yeast), 69-70  
Capoten 106-107  
Captopril, 106-107  
Carbamazepine, 110, 113  
Carbohydrates  
  complex, 29, 32-35  
  consuming, 37, 46  
  cravings, 26, 27, 57-58, 279, 339  
  exchanges, 361-369  
    and glycemic index/load, 35-37, 38-45  
    and weight gain, 29-31  
Cardiazem, 113  
Cardiovascular disease, 29, 50, 51, 61, 62, 66, 73-74, 76, 77, 90, 105, 156, 160, 164, 207, 212, 241, 298, 304, 305, 334  
  testing for, 92  
Carotid artery disease, 74  
Carpal tunnel syndrome, 297, 319  
Carrots, 363-364  
Carvedilol, 107  
Catapres, 217, 317  
Celery and cucumbers, 364  
Celexa, 58, 295, 339  
Celiac disease, 230  
Cenestin, 215  
Cerebral vascular disease, 74  
Charbroiled tuna with oregano  
  mango sauce, 409  
Chemotherapy, 136  
Chewing, 34  
Chicken  
  noodle bake, 398-399  
  and vegetable pasta sauce, 402  
Chitosan, 53  
Chlorothiazide, 112  
Chocolate, 221-222  
Cholecystokinin (CCK), 344  
Cholesterol, 89, 104, 115  
  abnormal, 159

- high, 240
- testing for, 175
- Cholestyramine, 106
- Chromium, 96-97
- Chron's disease, 230
- Cialis, 124
- Cinnamon, 100
- Cirrhosis, 75, 134, 135
- Climara, 196, 214
- Clitoris, enlarged, 156, 160, 284
- Clomid, 149, 181
- Clomiphene citrate, 149, 181
- Clonidine, 217, 317
- Clotting, increased blood, 74
- Cocaine and amphetamine-regulated transcript (CART), 341
- Cold, feeling, 238
- Colesevelam, 106
- Colestid, 106
- Colestipol, 106
- CombiPatch 196, 216
- Conn's syndrome, 275
- Constipation, 238
- Copper, 98
- Coreg, 107
- Coronary artery disease, 74
- Corticosteroids, 111, 275-276
- Corticotrophin-releasing hormone (CRH), 341
- Cortisol, 8, 12, 63, 67, 96, 116, 269-296, 323
  - excess, 135, 167
  - lowering, 291-296
- Cortisone, 278
- Cortrosyn stimulation test, 273
- Cozaar, 107
- C-reactive protein (CRP), 90
- Crestor, 104
- Crinone, 180, 198
- Crixivan, 113
- Cushingoid, 282, 283
- Cushing's syndrome, 8, 155, 203, 269, 278, 279, 282-286, 306
  - food-induced, 289-290
  - pseudo-, 286-287, 291
  - testing for, 286-290
- Cyclessa, 198
- Cymbalta, 109-110, 113
- Cytokines, 332
- Cytomel, 261-262
- Darunavir, 113
- Deep vein thrombosis, 74
- Dehydroepiandrosterone (DHEA), 115, 151, 155, 172, 275
- Del Castillo syndrome, 137
- Demadex, 112
- Depo-Provera, 112, 195, 197
- Depression, 8, 63, 117, 123, 125, 159, 195, 203, 207, 223, 233, 239, 278, 279, 339
  - postpartum, 236
- Desogen, 198
- Desogestrel, 195, 196
- Dexamethasone, 111, 278
- Diabeta, 112
- Diabetes, 2, 25, 29, 53, 61, 64-65, 67, 69, 70-71, 73, 76, 77, 84, 123, 130, 131, 134, 156, 159, 164, 229, 230, 244, 297, 298, 299, 302, 304, 318, 334
  - gestational, 66, 76
  - insipidus, 307
  - medications to treat, 101-104
- Diatest, 86
- Dieting, 67
  - weight loss, 1, 2, 5, 18-19
- Digestion, 34-35, 51
- Dihydrotestosterone (DHT), 120
- Dilantin, 317
- Dilated cardiomyopathy, 305
- Diltiazem, 113
- Diocan, 107

- Disaccharides, 28
- Diseases of civilization, 3
- Diuretics, 112  
    potassium-sparing, 107
- Diuril, 112
- Dronabinol, 336
- Drospirenone, 195
- Drugs, illegal, 135
- Duloxetine, 109-110, 113, 340
- Dutasteride, 120, 181
- Dyrenium, 107
- Dyslipidemia, 72-73
- Eating, guidelines for healthy, 58-59
- Effexor, 109-110, 113, 340
- Eggplant, 364
- Egg white omelet, 386
- Empty sella syndrome, 307
- Enalapril, 106-107
- Endocannabinoids, 336
- Endocrine system, 11-13, 15
- Endometrial biopsy, 176
- Enterostatin, 345
- Enzymes, 34
- Epilepsy, 340
- Epinephrine, 63, 275, 327, 328
- Eplerenone, 107
- Eprosartan, 107
- Erectile dysfunction, 123, 124
- Ergoloid mesylates, 317
- Estrace, 213
- Estraderm, 214
- Estradiol, 120, 187, 199, 208, 213-214, 216  
    patches, 214
- Estriol, 187, 208
- Estrogen, 8, 12, 116, 120, 143, 174, 185, 186-187, 204, 205, 323  
    and body fat, 199-200  
    conjugated equine (CEE), 214-215  
    conjugated synthetic, 215  
    designer, 217  
    in foods, 220-221  
    progesterone combination therapy, 215  
    replacement therapy, 211  
    testing levels of, 208-209
- Estrone, 120, 187, 199, 208
- Estropipate, 215
- Estrostep Fe, 196
- Euglycemic clamp, 81
- Eulexin, 181
- Evista, 217
- Exchanges, 360-374
- Exemestane, 120, 148
- Exenatide, 103-104
- Exercise, 63, 152, 191, 219. *See also*  
    Physical activity.
- Ezetimibe, 106
- 5-alpha reductase, 120
- Facial  
    hair, excess, 279, 284  
    redness, 279
- Fat, 3, 4-5, 6, 26  
    abdominal, 62, 78, 89  
    body, 48  
    cell, 324, 325, 327-329  
    exchange, 373, 374  
    -free products, 31, 33  
    from food, 50-53  
    hormones, 329-334  
    saturated, 51-52  
    trans, 51-52  
    unsaturated, 51-52
- Fatigue, 62, 75, 77, 123, 125, 203, 207, 236
- Fatty acids, essential, 52-53
- Femara, 120, 148
- FemHRT, 196, 216
- Fenofibrate, 105
- Fertility monitors, 173
- Fiber, 48-49, 100-101
- Fibrates, 105

- Fibroid tumors, 204
- Fibromyalgia, 233
- Finasteride, 120, 181
- Fish, 93, 94
- Fluid retention, 136, 188-192, 240, 282
- Flutamide, 181
- Fluvastatin, 104
- Folic acid, 98-99
- Follicle-stimulating hormone (FSH), 118, 208
- Food, 10-11
  - diary, 355, 411-412
  - shopping for, 356
- Fortamet, 101-102, 178
- Fortovase, 113
- Fosamprenavir, 113
- Free food exchanges, 373
- Fructose, 27-28, 29
- Fruit, 27, 31, 366-368, 371
  - processed, 369
  - salad, 396
  - smoothie, 388
- Full, feeling, 348-349
- Furosemide, 112
  
- Gabapentin, 110, 113
- Galactorrhea, 137, 203
- Galactose, 28, 29
- Galanin, 337
- Gall bladder conditions, 2
- Gallstones, 77
- Gamma-aminobutyric acid (GABA), 340
- Garlic, 100
  - green beans, 394
- Gastric bypass surgery, 56
- Gemfibrozil, 105
- Genetics, 326-327
- Genitalia, ambiguous, 168
- Ghrelin, 344
- Gigantism, 317
  
- Glucagon, 25, 341, 342
  - like peptide-1 (GLP-1), 344-345
- Glucocorticoid, 111, 276-278
  - excess, effects of, 279-282
  - medications, 278-279
- Glucophage, XR, 101-102, 178
- Glucophage, 101-102, 178
- Glucose, 27, 29
  - testing, 10, 118, 174
  - fasting plasma, 82
  - and insulin calculations, 85-86
  - random plasma, 82
  - self-monitored blood, 83
- Glucotrol, 112
- Glycemic index/load, 26, 35-37, 38-45, 49, 93
- Glyset, 103
- GnRH pumps, 148
- Goals, 349-350, 352
- Goiter, 237
- Goitrogens, 266
- Gonadotropin, 142, 172
  - releasing hormone (GnRH), 118
- Goodpasture's syndrome, 230
- Gout, 76
- Graham, Sylvester, 32-33
- Granuloma, 308-309
- Grave's disease, 229, 250
- Greens, 364
- Growth hormone (GH), 8, 19, 153, 297-319
  - replacement therapy, 111, 312
  - suppression test, 91, 173
- Gut
  - hormones, 343-345
  - peptides, 324
- Gynecomastia, 126, 137
  
- Hair
  - excess, 156-157, 164
  - getting rid of, 181-182
  - loss, 99, 127, 157, 164

- Hashimoto's Disease, 229, 244  
HCTZ, 112  
Head injury, 130-131, 137, 307  
Heart  
    attack, 25, 29, 305  
    disease, 2  
    failure, 74, 240, 305  
Hematocrit, 210  
Hemochromatosis, 67  
    hereditary (HH), 134-135, 137, 308  
Hemoglobin, 210  
    A1c, 84  
Hepatitis, 134, 230  
Herbal products, 295  
Herbs, 96-101  
Hirsutism, idiopathic/ benign familial,  
    168, 169-170, 181-182  
HIV/AIDS, 132, 302, 303  
    medications, 113  
Hives, 243  
HMG CoA reductase inhibitors. *See*  
    Statins.  
Homocysteine, 90  
Hormonal Health Diet, 26, 28, 31, 57,  
    58, 93, 99, 101, 153, 177, 219, 291,  
    297, 314-315, 347, 358-384  
    recipes, 385-409  
Hormone  
    disorders, 19-21  
    symptoms of, 415-422  
    and metabolism, 1-23  
    replacement therapy, 183, 205-206,  
        210-217, 313  
    women's, 185-222  
        testing for problems with, 207-  
        210  
Hot flashes, 127, 167, 205, 207, 208,  
    211  
Hunger, 325-327  
    center, 324  
    hormones, 8, 321-345  
Hyderygine, 317  
Hydrochlorothiazide, 112  
Hydrocortisone, 111, 278  
Hydrodivril, 112  
Hyperaldosteronism, 72, 86-87  
Hyperandrogenism, 155-181  
    features of, 156-160  
    testing for, 170-176  
    treating, 177-181  
Hyperglycemia, 68  
    symptoms of, 71  
Hyperplasia, congenital adrenal (CAH),  
    167-168  
Hypertension, 25, 72  
Hyperthyroidism, 167, 233, 249  
Hypoglycemia, 26, 35, 47, 50, 54-57,  
    339  
Hypogonadism, 76, 111, 117, 120,  
    122-153, 230  
    causes of, 128-137  
    testing for, 138, 139-145  
Hypokalemia, 67  
Hypoparathyroidism, 230  
Hypothalamic amenorrhea, 203  
Hypothalamus, 118, 227  
Hypothyroidism, 8, 167, 202, 223,  
    255-260, 302  
    causes of, 244-248  
    central, 244, 246, 257  
    congenital, 245  
    during pregnancy, 248, 249  
    features of, 233-243  
    idiopathic, 246  
    postpartum, 236  
    presubclinical, 255  
    primary, 244  
    subclinical, 244  
    treatment for, 260-265  
Hysterectomy, 205  
Ibesartan, 107  
Idiopathic pulmonary fibrosis, 230

- 
- Immune
    - suppression, 281
    - system testing, 91
  - Impaired
    - fasting glucose, 70, 159
    - glucose tolerance, 70, 159
  - Indapamide, 112
  - Inderal, 107, 112, 226
  - Indinavir, 113
  - Industrial Revolution, 4
  - Infertility, 158, 241-242
    - female, 163-164
    - male, 128
  - Inflammation, 66, 332, 333
  - Inflammatory cytokines, 63
  - Insomnia, 75, 125, 278
  - Inspira, 107
  - Insulin, 4, 7-8, 11, 12, 323, 341, 342
    - and food, 25-59
    - and growth hormone, 303-304
    - like growth factor-1 (IGF-1), 91, 173, 298
    - resistance, 8, 61-114, 131, 134, 155, 156, 159, 162, 163, 164, 167, 211, 275, 297, 298, 318, 333, 334
      - and glucose calculations, 85-86
    - levels test, 85
    - medications that worsen, 111-114
    - medications to treat, 101-111
    - and progesterone, 194-199
    - physical features of, 78-81
    - testing for, 81-92, 175
    - treating, 92-101, 178-181
    - type B, 229, 269
  - syndrome, 78
    - vitamins, minerals and herbs for, 96-101
  - Insulinoma, 55, 56
  - Interleukin-6, 63, 333
  - Invirase, 113
  - Iodine and thyroid, 232-233, 247
  - Irritable bowel syndrome, 18
  - Joint/muscle pain, 238
  - Kallmann's syndrome, 122, 137
  - Kariva, 198
  - Kidney disease, 29, 67, 77, 302
  - Klinefelters syndrome, 122, 137
  - Lactase deficiency, 28
  - Lactose, 28
  - Laron's syndrome, 303
  - Lasix, 112
  - Leeks and onions, 365
  - Left ventricular hypertrophy (LVH), 74
  - Lenolenic acid, 52
  - Leptin, 8, 324, 329-332, 333
    - resistance, 331-332
  - Lescol, 104
  - Lessina, 196
  - Letrozole, 120, 148
  - Lettuce, 365
  - Levitra, 124
  - Levlen, 196
  - Lev-lite, 196
  - Levodopa, 317
  - Levonorgestrel, 195, 196
  - Levora, 196
  - Levothyroid, 206-261
  - Levothyroxine, 260-261
  - Levoxyl, 260-261
  - Lexapro, 58, 339
  - Lexiva, 113
  - Libido, 124
  - Librium, 340
  - Linoleic acid, 52
  - Liothyronine, 261-262
  - Liotrix, 263



- 
- Lipid  
  medications, 104-106  
  profile, 87-89
- Lipitor, 104
- Lipoprotein  
  high-density (HDL), 72-73, 87-89  
  low-density (LDL), 72-73, 87-89
- Lisinopril, 106-107
- Lithium, 246
- Liver  
  disease, 29, 67, 75, 136, 302  
  function tests, 210
- Loestrin, 196
- Lofibra, 105
- Lo Ovral, 197
- Lopid, 105
- Losartan, 107
- Lotensin, 106-107
- Lovastatin, 104
- Low-Ogestrel, 197
- Lozol, 112
- Lunelle, 197
- Lupus, 230
- Luteinizing hormone (LH), 118
- Male  
  breast enlargement, 297  
  hypogonadism, 8. *See also*  
    Hypogonadism.
- Marinol, 336
- Masculinization, 157
- Massage, 294
- Mavik, 106-107
- Meal tolerance test, 83
- Meat, 372
- Medications, 68, 101-114, 295, 316, 317  
  antidepressants, 109-110, 113  
  antihistamines, 114  
  antipsychotics, 114  
  antiseizure/antimigraine, 110, 113  
  aspirin, 110  
  beta blockers, 112  
  blood pressure, 106-107  
  calcium channel blockers, 113  
  corticosteroids, 111  
  diabetes, 101-104  
  diuretics, 112  
  HIV/AIDS, 113  
  lipid, 104-106  
  sulfonylureas, 112  
  synthetic progestins, 112  
  weight loss, 108-109
- Meditation, 294
- Medroxyprogesterone, 112, 195, 196
- Megace, 112
- Megestrol, 112
- Melanin-concentrating hormone  
  (MCH), 336
- Melatonin, 341
- Memory, 125  
  loss, 238-239
- Menopause, 8, 66, 163, 217, 218, 233,  
  237  
  male, 128  
  premature, 167, 204  
  supplements for, 219  
  weight gain during, 204-207
- Mental illness, 63
- Menstrual cycle, 3, 188  
  problems, 158, 241-242, 284
- Meridia, 108, 340
- Metabolic syndrome, 8, 25, 62, 77-79,  
  329, 334
- Metabolism, 25, 327, 328  
  and hormones, 1-23  
  lowered, 223, 224, 255, 269
- Metformin, 101-102, 178  
  -TZD combination tablets, 103
- Methylprednisolone, 111
- Metoprolol, 107, 112
- Mevacor, 104
- Micardis, 107
- Microgestin, 196
- Micronor, 112, 196

- Microzide, 112
- Midamor, 107
- Milk, 368
- Miglitol, 103
- Migraine headaches, 207, 211
- Mineralocorticoid, 275
- Minerals, 96-101
- Mircette, 198
- Mirena, 180, 196
- Mood, 3
  - swings, 278
- Monosaccharides, 27-28, 29
- Mumps, 132
- Muscle breakdown, 281, 283
- Muscle
  - pain, 238
  - weakness, 124
    - tips for boosting, 151-153
- Mushrooms, 365
  - sautéed, 392
- Myasthenia gravis, 230
  
- Nausea, 211
- Nelfinavir, 113
- Nesidioblastosis, 56
- Neuroglycopenia, 56
- Neurontin, 110, 113
- Neuropeptide (NPY), 335
- Neurosarcoidosis, 135, 137, 309
- Niacin, 99-100, 105
- Niaspan, 105
- Nifedipine, 113
- Nopal cactus, 53
- Nordette, 196
- Norepinephrine, 275, 327, 328
- Norethindrone, 112, 195, 196
- Norgestimate, 195, 198
- Norgestrel, 195, 196
- Norplant, 112, 196
- Nor-QD, 112, 196
- Norvasc, 113
- Norvir, 113
  
- Nutraceuticals, 22-23
  
- Obesity, 2-3, 8, 18, 48, 50, 61, 64-65,  
74, 120, 121, 132, 163, 321-345
  - android/central, 80, 298-299, 318
  - related hyposomatotropism, 298,  
308
  - genetics, 4-5
  - gynecoid/peripheral, 80
- Ogen, 215
- Okra, 365
- Olanzapine, 114
- Olean, 53
- Olestra, 53
- Olmesartan, 107
- Omacor, 98, 106
- Omega-3 fatty acids, 52-53, 93, 94,  
98, 106
- Orange cucumbers, 403
- Orexins, 334
- Orlistat, 53, 108
- Ortho-Cept, 198
- Ortho-Cyclen, 198
- Ortho-Est, 215
- Ortho Tri-Cyclen, 198
- Osteoporosis/Osteopenia, 126, 129,  
207, 279, 311
- Ovarian
  - cancer, 156, 157, 160-161, 165
  - failure, premature, 167, 204-207,  
230, 244
  - hyperthecosis, 165
- Ovary, 155
  - polycystic, 164
- Overweight, 2
- Ovrette, 112
- Ovulation, 188
- Oxandrin, 148
- Oxandrolone, 148
  
- Pain
  - chronic, 123, 136
  - joint/muscle, 238

- 
- Pancreas, 25
- Pancreatic
- amylase, 34
  - hormones, 341-343
- Panhypopituitarism, 309
- Parabiosis experiments, 329
- Paxil, 58, 295, 339
- Peppers, 365
- Perimenopause, 204-207
- Perindopril, 106-107
- Peripheral
- arterial disease, 74
  - vascular disease, 25
- Phentermine, 108
- Phenytoin, 317
- Pheochromocytoma, 275
- Phlebotomy, 134, 135
- Physical activity, 92, 95, 177, 267, 293, 315-316, 352-353
- PIH syndrome, 342
- Pima Indians, 64
- Pioglitazone, 178
- Pituitary gland, 12, 13, 14, 17 118, 227
- problems, 137
  - tumors, 156, 202-203, 306-307
- Plan B, 196
- Plasminogenactivator inhibitor-1 (PAI-1), 90
- Polycystic ovary syndrome (PCOS), 8, 61, 76, 81, 155, 162-166, 167, 168
- Polyendocrine autoimmune disease, 229, 273
- Polyglandular autoimmune syndrome, 229
- Polyphagia, 26
- Polysaccharides, 29
- Polysomnography, 91
- Portia, 196
- Postpartum thyroiditis, 202
- Potassium,
- food high in, 94
  - low, 67, 72, 86
- Pramlintide, 104
- Pravastatin, 104
- Precose, 103
- Prediabetes, 71, 159
- Prednisolone, 278
- Prednisone, 111, 278
- Preeclampsia, 76
- Prefest, 195, 198
- Pregnancy, 66
- complications, 76
- Pregnenolone, 116
- Premenstrual syndrome, 188, 192-194
- Premphase, 197
- Prempro, 197
- Preplanning, 376
- Prevachol, 104
- Preven, 196
- Prezista, 113
- Primary biliary sclerosis, 230
- Procardia, 113
- Prochieve, 180, 198
- Progestasert, 180, 198
- Progesterone, 116, 174, 180, 185, 186, 188, 190, 191, 192, 323
- containing intrauterine devices, 180
  - creams, 199
  - in foods, 220-221
  - gel, 180
  - and insulin resistance, 194-199
  - micronized, 180
  - natural, 198, 199
- Progestin, 169, 180, 194-199
- pulsed HRT, 216
  - synthetic, 112
- Prolactin, 143, 185, 195, 203, 309
- Prolactinoma, 166, 203
- Prometrium, 180, 197, 198
- Pro-opiomelanocortin (POMC), 337-338
- Propranolol, 107, 112, 226

- Prostate,
  - cancer, 150
  - enlarged, 120
- Protein, 26, 48, 49-50, 315, 369-372
  - supplements, 153
  - uncoupling, 328
- Provera, 112, 197
- Prozac, 58, 295, 339
- Psychosis, 278
- Puberty, 66-67
  - premature, 159
- Pulmonary embolism, 74
- Quality of life, 125
- Quetiapine, 114
- Questran, 106
- Quinapril, 106-107
- Radiation, 136, 308
  - exposure, 247-248
- Radishes and turnips, 365
- Raloxifene, 217
- Ramapril, 106-107
- Raynaud's syndrome, 230
- Red cabbage and apples, 408
- Reflexes, slow, 242-243
- Remeron, 339
- Renal vascular disease, 74
- Renin, 86-87
- Resistin, 8, 334
- Restaurants, 355-356
- Restless leg syndrome, 75
- Retrogradation, 32
- Reyataz, 113
- Rimonabant, 109, 336
- Riomet, 101-102, 178
- Risperdal, 114
- Risperidone, 114
- Ritonavir, 113
- Roasted asparagus with carrots and onions, 400
- Rosiglitazone, 178
- Rosuvastatin, 104
- 17-hydroxyprogesterone (17-OH-P), 173
- Saint John's wort, 340
- Salt, decreasing intake of, 292
- Saquinavir, 113
- Sarcoidosis, 135, 308-309
- Satiety, 322, 324, 325, 326, 329, 348-349
- Schmidt's syndrome, 229
- Scleroderma, 230
- Seasonale, 196
- Secretin, 343
- Selenium, 98
- Self-confidence, 177
- Seroquel, 114
- Serotonin, 57-58, 339-340
- Set point, 326
- Seven-Day Meal Plan, 378-384
- Sex
  - drive, 117
  - decreased, 123, 124, 208, 279
  - hormone binding globulin, 91, 172
- Shopping list, 413-414
- Shrimp and vegetable salad, 401
- Sibutramine, 108, 340
- Sick euthyroid syndrome, 256-27
- Simvastatin, 104
- Sinemet, 317
- Skin
  - problems, 76, 239
  - tags, 80, 319
- Sleep 153, 316
  - apnea, 74-75, 91, 156, 160, 176, 243
  - study, 91, 176
- Smoking, 68, 336
- Snoring, 243
- Somatopause, 300
- Somatostatin, 25, 341, 342-343
- Soy, 266-267
- Spironolactone, 107, 122, 180-181

- Sprouts, 366
- Squash, 366
- SSRI reuptake inhibitors, 339
- Starch, 29, 32-35, 369, 370. *See also* Carbohydrates.
- Statins, 104
- Stein-Levanthal syndrome, 155, 162-164
- Steroid, 115-117, 186, 275, 278-279  
  anabolic, 116-117, 275, 276  
  androgenic, 275  
  corticosteroids, 111, 275-276  
  glucocorticoids, 276  
  side effects of, 278
- Stomach, upset and reflux, 281
- Stress, 8, 14-18, 63, 96, 309  
  and adrenal gland, 269-296  
  relief, 152, 292-295  
  and thyroid, 230-231, 256, 267
- Striant, 147
- Stroke, 25, 29, 73
- Sucrose, 28
- Sugar, 30. *See also* Carbohydrates.
- Sulfonylureas, 112
- Sustained-release T3, 263
- Sweating, 238
- Sweeteners, 30
- Symlin, 104
- Symptoms, 415-422
- Syndrome X, 78
- Synthroid, 260-261
- Tegretol, 110, 113
- Telnisartan, 107
- Tenormin, 107, 112
- Testosterone, 12, 19, 21, 86, 115, 116, 117-120, 155, 188, 275  
  age-related decline, 128-129  
  gel, 132, 146, 183  
  injections, 145-146  
  low, 122-123  
  measuring, 171  
  patches, 147  
  replacement therapy, 111, 117, 126, 129, 131, 145-149  
  side effects of, 149-150  
  resistance, 121-122
- Testicles  
  infection of, 132  
  shrinking of, 128  
  trauma/injury to, 129
- Testim, 146-147, 183
- Testoderm, 147
- Tests  
  androgen excess, 170-176  
  Cushings' syndrome, 286-290  
  growth hormone deficiency, 309-312  
  hypogonadism, 139-145  
  insulin resistance, 81-92, 175  
  thyroid disease, 250-255
- Tetrahydrocannabinol, 336
- Teveten, 107
- Thermogins, 327, 328
- Thiazolidinediones, 102-103
- Thrombocytopenic purpura, 230
- Thyroid, 8, 12, 19, 133, 209, 323  
  desiccated (Armour Thyroid) 263-264  
  disease, 224-225  
  testing for, 175, 250-255  
  failure, mild, 235, 244  
  healthy, diet and lifestyle for, 265-267  
  hormone, 223-267  
    abuse, 264  
    autoimmune, 229-230  
    and estrogen, 265  
    and iodine, 232-233, 247  
  resistance, 257-258  
    and stress, 230-231  
  storm, 249  
  support formulas, 267
- Thyroidectomy, 246

- 
- Thyroiditis, 259
    - atrophic, 245
    - Hashimoto's, 229, 244
    - postpartum, 245
    - Reidel's, 245
    - subacute, 245
  - Thyrolar, 263
  - Tipranavir, 113
  - Tomatoes, 366
  - Topamax, 110, 113, 340
  - Topiramate, 110, 113, 340
  - Toprol, 107, 112
  - Toremide, 112
  - Trandolapril, 106-107
  - Triamterine, 107
  - Triamcinolone, 278
  - Tricor, 105
  - Triglide, 105
  - Triglycerides, 72-73, 87-89
  - Tumor necrosis factor, 63
    - alpha, 332-333
  - Ulcers, 281
  - Ultrasound, 91
    - pelvic, 176
  - Urinary
    - luteinizing hormone (LH), 173
    - microalbumin, 86
  - Urocortin, 341
  - Urologic problems, 129-130
  - Vaginal dryness, 207, 214
  - Valium, 295, 340
  - Valsartan, 107
  - Vanadium, 97
  - Vaniqa, 182
  - Vasculitis, 230
  - Vasectomy, 130
  - Vasotec, 106-107
  - Vegetables, 31
    - soup, 387
  - Venlafaxine, 109-110, 113, 340
  - Verapamil, 113
  - Viagra, 124, 131
  - Vinaigrette dressing 389
  - Viracept, 113
  - Virilism, 156, 161
  - Vitamins
    - A, 98
    - biotin, 99
    - Bs, 98, 99-100
    - C, 98
    - D, 116, 218, 1520153
    - E, 98
    - folic acid, 98-99
    - minerals and herbs, 96-101
    - niacin, 99-100
  - Vitiligo, 230
  - Vivelle, 213
  - Voice, deepening of 160, 242
  - Water, 315
  - Wegener's granulomatosis, 230
  - Weight
    - gain, 29-31, 48, 54, 55, 62, 123, 124, 156, 167, 203, 207, 223, 234, 236, 255, 269, 280, 282, 284, 298, 304, 318, 341
    - during perimenopause and menopause, 204-207
    - and PMS, 192-194
    - loss, 92, 249, 347-384. *See also* Dieting.
    - after pregnancy, 202
    - and hunger hormones, 321-345
    - medications, 108-109
    - products, 22-23
    - training, 152
  - WelChol, 106
  - Wellbutrin, 109-110, 113
  - Willpower, 2, 3
  - Wilson's syndrome, 259-260
  - Xanax, 295, 340

- 
- |                          |                      |
|--------------------------|----------------------|
| Xenical, 53, 108         | Zetia, 106           |
| Xenoestrogens, 186       | Zinc, 98             |
|                          | Zocor, 104           |
| Yeast infections, 69-70  | Zoloft, 58, 295, 339 |
| Yellow pepper sauce, 393 | Zonegran, 110, 113   |
|                          | Zonisamide, 110, 113 |
| Zestril, 106-107         | Zyprexa, 114         |