1984

Bostonia: v. 58, no. 5-6

Boston University.


Boston University
HORMONES
The Invisible Messengers
A Guide to the Body’s Communication System
books, et al.
Hormones In-Depth

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Knowing when to seek endocrinologic help and how to find it have become major problems for the consumer. Part of the problem is the complexity of the field. Another reason is that hormones have commercially come into vogue.
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Community responsibilities rank only behind educational ones in the priorities assigned to an American institution of higher learning. Boston University, because of its quality, community concern and intellectual resources, has traditionally accepted more than a fair share of public interest activities.

With the issuance of this in-depth publication, "Hormones: The Invisible Messengers—A Guide to the Body's Communication System," Bostonia Magazine is continuing its series of lay-oriented discussions designed to service its many audiences: students, faculty, parents, staff, alumni, neighbors, government officials, opinion leaders and the general public. Bostonia’s first report in this series was reprinted by Bantam Books under the title: Boston University Medical Center’s Heart Risk Book. The second and third issues on Stress and Nutrition have been reprinted in several languages.

I hope you enjoy and greatly benefit from this publication and the others that will follow.

John R. Silber
President
Boston University

Dear Reader,

THE SOPHISTICATED PROCESSES and language surrounding medical advances in body chemistry are intimidating and often forbidding. Part of the problem in any discussion of hormones is the complexity of the body’s chemical system. Hormones and other chemical substances that set body changes in motion are invisible to the eye. For years medical researchers have known that hormones play a central role in life's processes, but the actual system was a mystery. Within the last two decades, however, advances in technology have enabled scientists to have a clearer notion of how the body’s communication system actually works. But because the technology is very new and the accompanying terminology is complicated, the field of endocrinology has remained a shrouded one for most of us.

The human body works best when the balance within the organs' tissues and cells is closely monitored and regulated. Second by second, hour by hour and day by day, the endocrine system, consisting of glands and their chemical products, hormones, modulate cell activities. Minuscule in size, hormones are secreted by various glands and travel through the blood, delivering messages that stimulate changes. In this way, hormones regulate the rhythms of life. Waking and sleeping, sexual arousal and satisfaction, growth and maturation, are all directed by the brain's chemical messengers.

Throughout this In-Depth issue of Bostonia Magazine, we have presented the most recent research on hormones, sex and reproduction. Although each article is presented as a separate chapter, I urge you to read this issue in context. Dr. Judith Vaitukaitis, an outstanding endocrinologist and specialist in reproduction, and co-author Robert N. Ross present a step-by-step guide to understanding the body's hormones.

We tend to take puberty, sexuality, fertility and reproduction for granted until there is a problem. When problems occur, they are often rooted in the body's endocrine system. It is my hope that this issue will alert you to the many advances in this field that could have an impact on your life. During the past few months, news of steroids and growth hormones used to increase athletic ability in Olympic stars has been widely circulated. Reports of Siamese twins who required a sex change operation and other medical feats no longer astound. Unfortunately, there is rarely space to present these advances in context. The ethical and moral questions they raise are many and the obvious answers are few.

Consequently, opportunists have exploited and others have misinterpreted many of the recent findings in hormone research. It is my hope that this issue of Bostonia Magazine will serve as a guide to use in weighing new information and as a springboard to assist you in finding answers to individual questions that you may have.

Laura Freid
Editor-in-Chief
A Special Invitation from the President of Boston University

"I am sure that you share our pride and delight in the progress that has been made at Boston University in the last decade. We now have a foundation of excellence that makes it increasingly easy to recruit outstanding faculty, students and staff. As our momentum builds, we must now supply the improvements in facilities needed by the great artists, scholars and scientists we have attracted."

"To the extent that you contribute to our efforts, I am confident that we can have a University better than our wildest dreams of ten years ago."

John R. Silber
President, Boston University

For the first time in its history, Boston University is proud to announce the enhancement of its leadership gift clubs. Alumni, parents and friends of this institution are invited to join in this company of select and distinguished benefactors. Qualifications of membership are:

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Announcements

Boston University Faculty Union Ruled Improper

A federal judge has ruled that Boston University faculty members are considered managers and supervisors and as such cannot be represented by a union.

In a decision issued in Washington, D.C., on June 29, Administrative Law Judge George S. McNerny said that the Boston University Chapter of the American Association of University Professors (BUCAAUP) was not a bona fide labor organization because faculty members are not employees under the meaning of the National Labor Relations Act. The ruling followed 157 days of hearings held between December 1980 and March 1983.

"I am pleased that the position taken by Boston University has been vindicated," commented University President John R. Silber. "Trade unionism is an essential feature of American life, but it has no place among the faculty of a great university. In consequence, this is an important decision not only for Boston University but for higher education in general."

Silber said that the University trustees have instructed the administration not to negotiate a new contract with the BUCAAUP, which has nearly 900 members and represents all full-time faculty members on the University’s Charles River campus, except the Law School. The union’s board has voted to appeal the court decision. The current collective bargaining agreement, however, will remain in effect until it expires on October 10.

In a letter to the faculty, the administration pledged to make no major changes in procedures governing hiring, promotions or tenure after the contract’s expiration. The letter also promised faculty members a six percent merit pay increase.

The June 29 ruling was based on a landmark 1980 Supreme Court decision that held that faculty at Yeshiva University in New York could not unionize because they were managers who participated in setting and implementing university policies. The majority of related cases since decided by the National Labor Relations Board has been in accord with the Yeshiva decision.

Metcalf Nominations

Nominations for the Metcalf Cup and Prize and the Metcalf Awards for Excellence in Teaching are now being accepted from deans, department chairmen, faculty, students and alumni. The awards, which are endowed by Dr. Arthur G. B. Metcalf, President of the Electronics Corporation of America and chairman of the University’s Board of Trustees, are presented annually during Commencement exercises.

All nominations, which should be accompanied by a one-page statement of support, will be considered by a committee of faculty members and students that will make recommendations to the Board of Trustees. Nominations should refer to the specific teaching qualities of the professor. The deadline is November 1, 1984.

Please send nominations to: Sonia Parker, assistant to the Provost, 145 Bay State Road, Boston, Massachusetts 02215.

College of Liberal Arts

Chaos Conference

A stream of smoke rises from a cigarette, suddenly twists chaotically, then continues smoothly upward. Although no physicist could precisely predict when that chaotic jumble of smoke would occur or its exact shape and duration, many scientists believe that the prediction could be made if all variables—air currents, combustion rate of the cigarette, impurities in the tobacco, etc.—were known.
Not necessarily so, however. The behavior of many common, seemingly simple phenomena, because of the complexity and number of variables involved, defies logical prediction. The scientific solutions to many real-world problems, such as the change in population of a group of animals or the movement of planets, can be literally meaningless and chaotic.

For centuries, scientists have been aware of, but at the mercy of, the problem of chaos. Recently, however, mathematicians such as Robert L. Devaney, chairman of the Department of Mathematics, have put computers to the task of approximating meaningful solutions to these seemingly unsolvable problems. The solutions are typically represented in graphic displays as colorful, swirling designs whose patterns can be generally interpreted. Although still in the research phase, many scientists from fields outside of mathematics are interested in how computers can be used to solve chaotic problems, and the solutions will have a variety of practical applications.

Devaney is organizing “Chaos: Applications of Nonlinear Dynamics in the Sciences,” which will be held October 24 and 25 in the George Sherman Union and present the latest developments in the field. The conference is expected to attract scientists from a variety of disciplines, including mathematics, physics, biology and meteorology. Speakers will include William Thurston, 1982 winner of the Fields Medal in Mathematics, and Cornell Professor Mitchell Feigenbaum. For more information, write to the Chaos Conference, Department of Mathematics, Boston University, 111 Cummington Street, Boston, Massachusetts 02215, or call (617) 353-2560.

Huntington Theatre Company

New Season Offerings

Hoping to duplicate their success of last season, the Huntington Theatre's 1984–85 line-up includes a Boston premiere, three all-time classic plays and even a long-lost Cole Porter musical. Under the leadership of Producing Director Peter Altman, the Huntington's third year will begin September 29 and run through June 16, 1985, at the Boston University Theatre.

The season will open with Cole Porter's You Never Know, an unusual romantic farce featuring a dozen favorite Porter songs, including “At Long Last Love” and “What Shall I Do?” You Never Know previews September 29 and runs through October 21.

Twelfth Night, Shakespeare's masterpiece of love and infatuation, opens December 5 and plays through December 23. It will be followed by Uncle Vanya, Chekhov's rich and tender portrait of life in turn-of-the-century Russia. The drama, which has not been presented by a professional company in Boston in more than a decade, will run January 12 through February 3.

One of the most successful American plays in recent years, Terra Nova, will be a first for Boston and the Huntington Theatre. Ted Talley's saga of a Norwegian expedition's race in 1912 to become the first men to reach the South Pole has
been widely acclaimed as a contemporary classic about valor and adventure. After a preview performance on March 9, Terra Nova will run March 13 through March 31. Rounding out the season will be playwright Sean O'Casey's classic drama about the struggle for Irish independence, The Plough and the Stars, which will be previewed on May 25 and run May 29 through June 16.

Subscriptions for the 1984-85 season are now available and will be sold through the run of You Never Know. For a free brochure or to charge subscriptions by phone, call the Subscription Hotline at (617) 266-3996 or write to the Huntington Theatre at 264 Huntington Avenue, Boston, Massachusetts 02115.

**Metropolitan College**

**Celebrity Seminar Series**

Throughout the fall, Metropolitan College at Boston University is sponsoring a series of celebrity seminars exploring life and culture in Boston.

On Tuesdays from September 25 to October 30, for example, the seminar "The Hub of Power" will examine Boston government and feature local politicians as speakers. "Not Necessarily the Evening News" will run Wednesdays from October 10—November 14 and address issues surrounding the broadcast industry. And "How to Create Your Own Mystery," taught by suspense writer P.D. James, will be offered the weekends of October 19—20 and November 30—December 1.

Other programs in the series include a month of lectures on Boston architecture; a program on the Boston classical music scene; and an inside look at the local sports world. Tuition for the individual programs runs from $150 to $250. For seminar details and information on scheduling and registration fees, contact Michaeline Fall at (617) 353-4746 or write to Metropolitan College at 755 Commonwealth Avenue, Boston, Massachusetts 02215.

**Photographic Resource Center**

**Regional Photographic Education Conference**

I n cooperation with Boston University School of Public Communication, the Photographic Resource Center will host the 1984 annual conference for the Society for Photographic Education, Northeast Region, October 19—21.

A national service organization, the Society for Photographic Education was founded in 1963 to "promote high standards in photography and in photographic education," as well as to "foster a greater public understanding of the medium of photography." The 1984 Northeast Region conference will feature lectures and panel discussions within four different tracks: Photojournalism, Imagemakers, Education and High Technology. Presentations will be made by regional photographers and instructors. And two major lectures, open to the public, will take place in Morse Auditorium, 602 Commonwealth Avenue, at 8 p.m., Friday, October 19, featuring Magnum Inc. photojournalist Eugene Richard, and Saturday, October 20, featuring Cornell Capa, director of the International Center for Photography in New York.

Early registration fees for the SPE conference are $30.00 for SPE, PRC and Boston University members; $40.00 for students and $40.00 for the general public. Late registration fees, after October 5, are slightly higher. For a complete brochure, call the Photographic Resource Center at (617) 783-9333.

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**Boston University Graduate Affinity Centers Update**

**Cooks Center**

Submissions to the new International Cookbook are now being accepted. Send us your favorite ethnic recipe with name, address, school/year, country of origin and any pertinent anecdote or observation. We are also accepting title suggestions. Please note that the first cookbook, Cooking By Degrees, is still available at an alumni discount price of $12.95 plus $2 handling charge.

**Poetry Center**

The annual Poetry Reading Evening is scheduled for Tuesday, October 16, 7 p.m., at the Castle. Wine and cheese will be served. Winners of the 7th Competition will be the featured guests, and Professor George Starbuck, a long-time member of the poetry jury, will chair the meeting. R.S.V.P. to Bert Hirshberg at (617) 353-8988 or 353-3081. Submissions for the 8th Competition are now being accepted.

**Writing Center**

Writers, this is your last chance to enter the Third Writing Competition. The deadline is October 15. No more than 1500 words for published work and 2500 for unpublished. Only one entry from each contestant will be accepted. For published entries, please send only those within the last two years. Note your name and school and the category. All winning material that is published will be protected by Boston's copyright.

Address all correspondence to the Graduate Affinity Centers, 10 Lenox Street, Brookline, Massachusetts 02146; (617) 353-8988/3081.
School of Medicine
Humphrey Center
Director Named

Dean John Sandson of the Boston University Medical Center recently announced the appointment of Herbert H. Wotiz, Ph.D., as the director of the Hubert H. Humphrey Cancer Research Center. Wotiz succeeds Paul H. Black, M.D., who resigned to devote more time to research and his responsibilities as chairman of the Department of Microbiology.

Wotiz, who joined the BUSM faculty in 1950, is also a professor of Biochemistry. In 1982, he was appointed the Center's deputy director, and he became research coordinator at the Center in 1983.

"Dr. Herbert Wotiz is one of the outstanding scientists in the field of cancer research. I am certain he will provide the leadership to keep the Center at the forefront of research in this important field," said Dean Sandson.

School of Nursing
Executive Nurse Leadership Program

A new executive nurse leadership program, designed to enhance the administrative capabilities of nurses serving in upper management at teaching hospitals, was launched this semester at Boston University's School of Nursing.

The School is one of only three in the country chosen to present the short-term, intensive educational program. The Commonwealth Fund, a private foundation, awarded the University $200,000 for the project last spring. And the first 10 participants, selected from hospitals around the country, began the three-and-a-half month program on August 27.

Courses focus on topics such as the role of the nurse executive, the changing health care environment, corporate behavior and management policy, and financial and organizational management. The curriculum is led by professors in nursing, public health and medicine.

The participants receive a certificate of completion and continuing education credits. For more information on the Course, write to the School of Nursing, 635 Commonwealth Avenue, Boston, Massachusetts 02215.

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Photograph: Andrew Dean Powell
At the Helm
Terrier Football Coach Takes on New Role as Athletic Director

It is no secret that when it comes to winners, everybody wants a piece of the action. Just ask Terrier head football coach Rick Taylor, whose winning ways in football recently helped earn him a promotion to athletic director at Boston University. The Terrier teams will undoubtedly look to Taylor for the same inspiration and guidance that enabled him to take on a football team in 1977 whose previous six-year record was 21-39-1 and turn it around in the next seven years to 46-36-4.

Taylor was promoted last June to replace former athletic director John Simpson, who has become National Director of Development for Alumni and Athletics. The winningest coach in Terrier history, Taylor will continue to coach the football team at least through the 1984 season. And if this turns out to be Taylor's last year at the helm, it promises to be an exciting one.

The Terriers are coming off a season in which they finished 9-4, captured their second consecutive Yankee Conference title, earned their second straight invitation to the NCAA I-AA playoffs and advanced farther than any previous Terrier team in that tournament. And in honor of his team's impressive accomplishments, Taylor was named the 1983 Yankee Conference Coach of the Year.

Of course, the Terriers' success in 1983 presents a formidable challenge for this year's team and its head coach. Perhaps the most encouraging prospect is that senior tailback Paul Lewis, considered the finest running back ever to play at Boston University, will return as the top rusher in Division I-AA. The quarterback position is a little less secure since Jim English, last year's talented quarterback and co-MVP, has graduated. Taylor has high hopes; however, for sophomore Pat Mancini who, "Right now, is a better quarterback than (former Terrier and now Miami Dolphin) Jim Jensen was at this point in his career." He is also expecting good things from his returning lettermen.

Recently, Bostonia staff writer Jon Queijo spoke to Taylor about his dual role as Boston University athletic director and Terrier head football coach.

Bostonia: Is the 1984 Terrier football team as good as last year's squad?

Taylor: "Potential" is an overused word, but I think we have the potential to be as good. Overall, we're not dominating in any one place, with the possible exception of our tailback position (All-American Paul Lewis). But we have a lot of players coming back with experience and, from a coaching standpoint, you can't underestimate that. These kids know that if they work, they're good enough to compete against any team.

Bostonia: Where does the team need the most improvement?

Taylor: We're young. In the offensive line, however, we need to develop some depth in the event of injury. Right now we're still working on that, pushing some kids to play up to their ability. Defensively, if we stay healthy in a couple of positions, we've got not only good starters, but good depth.

Bostonia: Do you expect another great year from Paul Lewis?

Taylor: The norm for Paul Lewis is tremendous for anybody else. He's really spoiled us because he's had two phenomenal years. If he can repeat what he did last year, and that's asking a great deal, that would be super.

Bostonia: What makes Lewis so effective?

Taylor: He's fast, durable, exceptionally strong and very quick—the prototype of what you'd like in a tailback. People look at him in a uniform, he's 5'8", and think he's small, but he's anything but small. He bench presses 400 pounds. There's no question he could play anywhere in the country and be good.

Bostonia: How do you feel about Pat Mancini's quarterbacking abilities?

Taylor: I have a lot of confidence in him. I think the coaches, the team and the fans will have to realize he's still a freshman from the standpoint of eligibility and experience. Will he do everything perfectly? No. Will he run the team well and be a good quarterback? Yes. He's got a real good grasp of the game and he can throw the ball. He's big and he can scramble.

Bostonia: After seven years as head football coach, what has been your greatest satisfaction?

Taylor: I think it's the kids that make up the program now. Last year was probably the best year I've had, and this year's...
program has taken off right from it. We got to the point where we had the type of players we needed. They represented us well, and they were winners—and not only on the field. It was very, very emotional in the locker room last year when we lost the second playoff game, but we'll look back on the things we all shared and that none of us will forget. The same type of attitude exists this season, the same type of kids. Bostonia: As athletic director, how much involvement will you have with the 22 Terrier teams?

Taylor: When I first took over, I met with the coaches and told them individually what I expected. People will have to realize, of course, that I'm very involved with the football team, but I hope to see parts of every team's practices and help make sure the season is progressing the way the coaches want it to. I see it as my job to make the coaches look good. I want to be in the background, but if I can do anything to make them look good, and if it's financially feasible, we'll do it.

Bostonia: Do you have any immediate plans for improving the athletic program?

Taylor: We operate pretty efficiently right now. But if I have a peeve, it's that we have very little alumni and student involvement. I'd like to kick off a new era of pride. We're all part of a pretty damn good university, so let's manifest it by attending some athletic events and cheering just for the very sake of Boston University.

Bostonia: Boston University teams will be wearing a new logo this year. What brought about the idea?

Taylor: Over the summer, we decided one of our new goals was to establish a corporate identity for the entire athletic department. We felt we needed one consistent identification for our teams, and eventually all the sports will have it on their stationery and their uniforms. The first public showing was on the football helmets.

Bostonia: Is this your last year as head football coach?

Taylor: I don't know. I think a lot of people have assumed that. But (Boston University President) Dr. Silber and I have discussed it, and we will sit down at the end of the season and make a decision.

Bostonia: As an experienced football coach, do you have a personal philosophy you would like to convey to the other Terrier coaches?

Taylor: Only that if it's worth doing, it's worth doing well. In football, we tell the kids that if you're doing a drill and you cut it short by six inches, that habit could conceivably continue until someday you miss a tackle by six inches. It just takes a little more effort to go the final six inches and do it right. We've always done that on the football field, and if we can run the Athletic Department that way, we'll be in pretty good shape. If you pay attention to detail, you'll find the major things come automatically.

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**CALENDAR OF ALUMNI EVENTS**

**MADISON, WISCONSIN** October 12, Boston University vs. University of Wisconsin Hockey Game; University of Wisconsin; contact Jonathan Hibbard, (617) 353-2386

**WASHINGTON, D.C./MARYLAND/N. VIRGINIA** October 12–14, Boston University/Williamsburg Football Weekend; Patrick Henry Inn, Williamsburg, Virginia, and College of William and Mary; contact Charles Gordon. (301) 565-3960 or Alumni Office at (617) 353-2386

**CAPE COD, MASSACHUSETTS** October 13, Reception and Luncheon with Dr. John R. Silber; Sheraton Regal, Hyannis; contact Patty Flint, (617) 353-2386

**MADISON, WISCONSIN** October 13, Boston University vs. University of Wisconsin Hockey Game and Pre-Game Buffet; University of Wisconsin; contact Jonathan Hibbard, (617) 353-2386

**Worcester County Women's Club** October 13, Annual Membership Tea; speaker: Mrs. Elizabeth Shannon on "Ireland through Embassy Windows"; Home of Elpida Miliias; contact Barnette Shuman, (617) 353-2248

**Senior Alumni** October 17, Autumn Day in Newport, R.I.; Bus trip to mansions and wharf area; contact Patty Flint, (617) 353-2386

**CHICAGO, ILLINOIS** October 18, Boston University Alumni Day in Chicago; Host: Mayor Harold Washington; City Hall; contact Rob Taylor, (312) 747-3512

**Northern New Jersey** October 20, Western Night; BBQ and Square Dancing; contact Jenniann Barile, (201) 420-0616

**WASHINGTON, D.C.** October 25, NBC Tour and Reception; speaker: Les Kretman, SPC '63; NBC Studios, Washington, D.C.; contact Charles Gordon, (301) 565-3960

**WASHINGTON, D.C.** November 1, Reception for Dean Geoffrey Barnister, College of Liberal Arts; Washington Marriott Hotel, Washington, D.C.; contact Charles Gordon, (301) 565-3960

**Young Alumni** November 2, Reunion Celebration for 1969, 1974 and 1979 Graduates; "Upstairs at Jason's"; contact Barnette Shuman, (617) 353-2248

**New Graduates' Club** November 3, Homecoming 1984; Alumni Awards, Parade and Football game; Boston University campus; contact Patty Flint, (617) 353-2386

**Young Alumni** November 3, Reunion Celebration for 1969, 1974 and 1979 Graduates; Alumni Awards, Parade, Football Game and Victor's Party; contact Barnette Shuman, (617) 353-2248

**ATLANTA, GEORGIA** November 8, "Paths to Excellence" Film and Reception; Guest Speaker: Daniel J. Finn, University Trustee; Marriott Hotel at the Perimeter Center; contact Charles Gordon, (301) 565-3960

**Women Graduates' Club** November 14, "Creating You—The Dimensions of Feminism"—Seminar, Fashion Show and Reception; George Sherman Union; contact Patty Flint, (617) 353-2386

**Southwestern Connecticut** November 17, Alumni Night at the Palace; contact Pat Tyre, (203) 325-0152

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**October—November 1984**

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INTRODUCTION

SEX AND HORMONES. EVEN THE MOST CASUAL MENTION of these topics is sure to raise the eyebrows of some people and the hackles of others. At one time or another, hormones have been a medical, moral, scientific and even a political issue.

Some experts quoted in the popular press and on television would have us believe that the monthly circulation of some women’s hormones affects their mood swings powerfully. In extreme cases, we are told, women may be maddened by the changes in their physiology to the point of committing emotional mayhem and even murder. Other popularly quoted experts blame some men’s uncontrollable and violent sexual behaviors on abnormal hormones. Hormone disturbances are held accountable for infertility, unhealthy reactions to stress, heart disease, high blood pressure and many other unhealthy and unpleasant condi-

HORMONES

Sex and Reproduction

DR. JUDITH VAITUKAITIS AND
ROBERT N. ROSS, PH.D.
EDITED BY LAURA FREID
As a result, vast industries are dedicated to marketing hormone drugs to relieve discomforts and diseases.

"Raging hormones"—the notion that uncontrollable behaviors can be triggered by an inevitable flow of chemicals in the body—is still a common misconception.

HORMONE DISTURBANCES ARE held accountable for infertility, unhealthy reactions to stress, heart disease, high blood pressure and many other unpleasant conditions.

The misconception is fed by inadequate knowledge, poor research and the desire on the part of both professionals and lay people to find simple answers to complicated questions.

Reality is far more complex than most scientific explanations. Hormones are important in sickness and health. Hormones make up one of the two systems we need to regulate the chemical plant we call our bodies. The other is the nervous system.

When hormones are invoked to explain behavior, especially sexual behavior, theory often outstrips reality. For when popularizers of modern endocrinology describe the human being as a "clockwork organism," whose chemicals switch behaviors and feelings on and off, they forget that we also have a brain. In fact, some of the most exciting work now being done in endocrinology is devoted to explaining the brain's role in the otherwise mindless play of the body's chemicals.

The research is still new. Much remains to be learned. Theories surrounding sex and hormones raise more questions than they answer. What are hormones? How do they control sex and reproduction? How do hormones make a boy grow to be a man and a girl become a woman? Are emotions the cause or the effect of shifting hormones in the body? How do the nervous system and the endocrine system interact?

This issue of Bostonia Magazine presents an overview of what we know about the role of hormones in sex and reproduction. We are living in a time of increased sexual awareness, and our society is deeply concerned about health. By knowing how our hormonal and reproductive systems work, we will be able to recognize problems that may occur and be better able to maintain healthy lifestyles.

Hormones give shape and reason to all of life's processes. Fertility, pregnancy, birth, growth, puberty and renewal of the fertility cycle; generation after generation, all depend on the chemical messages carried by hormones. The man troubled by impotence, the woman distressed by extreme menstrual discomfort, the parents of a child whose growth is slower than normal, the teen-age girl who is not maturing sexually as fast as her friends—all may be baffled and upset. Hormone problems can take so many forms that it is not always easy to see a one-to-one relationship between the symptoms we experience and the underlying disorders.

"RAGING HORMONES"—THE notion that uncontrollable behaviors can be triggered by an inevitable flow of chemicals in the body—is still a common misconception.

Until recently, even physicians barely understood the underlying causes of problems in growth, maturation and fertility. The general public, too, often failed to recognize endocrine problems that, if treated early, could be successfully resolved.

Patients who suffer with problems of the endocrine system are often confused by the disease, shuttled from one authority or source of information to another, and frustrated by the complexities of the disease and of the medical care required.

The person seeking help is legitimately confused. What problems are treated by an endocrinologist? Who can give the best help? How can we evaluate the treatments we get?

Sex and reproduction are among the most intimate aspects of our lives. Ancient cultures relied on myths of fertility to explain the mystery of how life goes on. Today we have the clarity of science and the precision of technology. Both the myth and the science are important; for the science is an attempt to describe how life begets life and the myth describes why.

HORMONES GIVE SHAPE TO all of life's processes. Fertility, pregnancy, birth, growth, puberty and renewal of the fertility cycle; generation after generation, all depend on the chemical messages carried by hormones.

The information presented in this issue deals with the science of endocrinology. But it is impossible to separate endocrinology from the sociological issues that border it. Consequently, throughout the text, sidebar stories address contemporary concerns and controversies. It is the science of endocrinology, however, that will provide the answers.

*Note: Common technical terms are defined in a Glossary at the end of this issue.
The body’s internal environment is maintained by a web of signals and responses, all depending on the

MIND-BODY CONNECTION:

HOW THE MIND TALKS TO THE BODY

The brain controls thinking, feeling, remembering and all the other processes that comprise your mental life. Your brain also controls your physical actions. When nerves carry the message “lift finger” to your hand, you lift your finger. The mental and physical activities of the brain are familiar. Less familiar is the fact that your brain is also a gland; and perhaps even more surprising, your brain might be called a sex gland. For as a gland, it plays a major role in controlling sex and reproduction.

We need a nervous system to adapt our behavior to fast-changing conditions inside and outside the body. For example, an itch or a pain, a sudden sound or a noxious smell, all call for a quick response. Messages from our sense organs inside and outside the body eventually reach the central communication centers of the brain. Messages are processed in the brain and answers are sent back out to the body along another set of outgoing nerves or by chemicals, including hormones, secreted by specialized portions of the brain and the pituitary gland.
WHERE

THE MIND AND

BODY MEET

PHILOSOPHERS have debated for centuries about the apparent split between the mind and body. Explaining how thoughts and feelings can move bodies to action seemed an insoluble problem. After millennia of philosophical inquiry, scientific research has now given us a glimpse of one place where mind and body meet. The place is a bulge on the underside of the brain, the hypothalamus. Clusters of nerve cells within that bulge translate mental information to chemical forms that the body can understand.

Direct communication between the mind and the body is impossible. However, the gap between thinking cells of the nervous system and action cells may be only the 0.00004 millimeter space known as a synapse. But space is space no matter how small. The two cells do not touch each other.

One of the most important systems by which mind and body communicate is through the endocrine system. Endocrine tissues are transmitters, very much like radio transmitters, that send chemical signals out to the rest of the body. Receivers for the hormones' chemical messages are located throughout the body.

Receptors on target tissues throughout the body serve the function of radios in our analogy. These receptors, like radio receivers tuned to a particular station, respond to only one signal, although many different ones are present at the same time. The signal prompts the receiver to do something. Whereas the electronic circuits of the radio convert the inaudible radio signal to sounds, chemical receptors throughout the body respond to freely circulating hormones in the blood and prompt the cells to perform their genetically programmed function.

Cells of the adrenal glands, for instance, respond to hormone signals meant only for them and release their own hormones. Smooth muscle cells lining the walls of the arteries respond to their own hormone signals by contracting and raising blood pressure. Eggs within developing follicles in the ovary respond to their signals by maturing so that they can be ovulated and fertilized.

The message delivered by a hormone is a simple one. “Here I am. Turn on.” The striking feature of the system, however, is how precisely it is designed to guarantee that the message gets to the right place. Many steps are required to translate events in the brain into bodily action.

Nerve fibers go back and forth between the hypothalamus and the limbic region of the brain, a central portion of the brain responsible for maintaining attention and emotional arousal.

The hypothalamus is a primitive part of the brain above which rise parts of the brain controlling such higher functions as sensation, language, planning and thought. Below the hypothalamus parts of the brain and spinal cord controlling the reflexes and such automatic bodily functions as breathing, heart rate and body temperature on which life depends.

Our sensory organs and nerves feed the hypothalamic information about light, heat, sound, odors, pain and other information about the external world. Much of this information goes directly to the hypothalamus without registering on our consciousness.

As a result, the hypothalamus directs responses, of which we are hardly aware, to conditions in the world. These unconscious responses may be so important to health that a new field called biobehavioral medicine is developing. Through biofeedback, patients may become aware of how they might control reactions mediated by the hypothalamus. Once people are aware of the reactions they normally ignore, according to the proponents of biobehavioral medicine, they will be able to control them. Such control may help relieve a variety of conditions once known by the slightly pejorative term, psychosomatic diseases.

Suspended from the floor of the hypothalamus is a delicate short stalk ending in a small enlarged portion, the pituitary gland. After the information is analyzed, a chemical message is then passed down specialized nerves from the hypothalamus toward the pituitary. The nerve fibers pass down the short stalk by which the pituitary hangs from the hypothalamus; but they do not connect directly to the pituitary. The chemical messengers are transferred into the blood and carried to cells within the anterior pituitary where they are synthesized.

It should be noted that the pituitary is really divided into two: the posterior and the anterior pituitary. The posterior pituitary is a direct extension of the hypothalamus, whereas the anterior pituitary is separate, reflecting a difference in embryonic origin of both parts. Chemical messages are transported in the blood from the hypothalamus to the anterior pituitary. There, the hormones are completely synthesized before being transported via nerve fibers for storage in the posterior pituitary. This is known as the pituitary portal system. As far as the hormonal control of the body is concerned, the gap between the hypothalamic fibers and the pituitary receptors is the mind-body split so painstakingly debated by the philosophers.

THE BRAIN

IS IN CONTROL

THE ENDOCRINE system needs the nervous system for many of its functions. Without it, the strictly chemical reactions of the endocrine system would be mechanical and mindless. In fact, the levels of hormones circulated by the endocrine system are often controlled by a negative feedback system like that of a household thermostat.

When the household temperature gets lower than the pre-set temperature at which the thermostat will switch on the heating plant, the heat is turned on. When the household temperature gets higher than this pre-set temperature, the heat is turned off. In this way, the thermostat maintains a constant temperature.

But the thermostat is a mechanical device that cannot think for itself. If you want to conserve fuel, for example, you need to set the thermostat at a lower temperature. If your aunt from Florida is spending New Year's Eve with you in Minneapolis, you might want to set the

Changes in sex drive in men and women are not directly and exclusively attributable to changes in hormone levels.
The brain is a gland. More surprising, it might be called a sex gland.

corpus callosum

midbrain

cerebellum

medulla

pons

There are three major anatomical parts of the brain—the forebrain, midbrain, and hindbrain. Within the forebrain are the cerebral hemispheres, thalamus, hypothalamus and limbic system. The top inch of the brain stem is the midbrain. And the cerebellum, the pons and the medulla make up the hindbrain.

The cerebral cortex is a thin, outermost layer of brain tissue responsible for sensory and motor processes.

The thalamus integrates information coming into the brain and is responsible, in part, for attention and arousal.

The hypothalamus is the crucial link between the nervous system and the endocrine system. Within the hypothalamus is the limbic system, which controls memory and emotion.

The pituitary is suspended from the hypothalamus and controls the function of other endocrine glands and tissues.

thermostat at a higher temperature. In just this way, the endocrine system needs the nervous system to override it.

amounts of the chemical substances produced by the brain. Now, with the help of these tools, scientists can identify some of the chemical transmitters that regulate digestion, the conversion of fuel to useful energy, water balance, blood sugar levels and several other vital processes that ordinarily go on unnoticed.

Growth, maturation, puberty and periods of a woman's fertility may all seem to occur by a logic of their own. But they are controlled by hormones. Brain hormones also regulate the rhythms of life: wakefulness and sleep, activity and quiet, sexual arousal and satisfaction. Except in relatively rare instances, most people go through these changes according to programs written in their genes. Scientists learn a great deal from studying how normal patterns can be disrupted. But there is still much to learn about what signals the beginning of these processes, what controls their normal course and what brings them to a close.

When these subtle but powerful regulators get disorganized, the consequences may be merely annoying or they may be seriously life-threatening. Long distance flights across time zones, for instance, often produce the uncomfortable symptoms of sleep disturbance, fatigue and psychological and physical malaise known as "jet lag." No one knows what causes jet lag. Explanations have invoked such factors as changes in the light-dark cycle when the body is abruptly cast into longer days or nights, changing magnetic fields, or disruption of the many familiar patterns on which the body depends for its orientation. But although the causes of jet lag remain a mystery, the mechanism by which the body is upset is becoming.
The hypothalamus

Nerves connect the hypothalamus to other centers of the brain and body. The medial forebrain nerve bundle connects the hypothalamus to the higher sensory and motor areas of the cerebral cortex. The dorsal longitudinal bundle sends messages concerning digestion back to the body. The mamillo thalamic tract is involved in emotion. The fornix connects the hypothalamus with memory centers in the limbic system.

The neurosecretory tracts channel hypothalamic hormones to the posterior pituitary gland.

The pituitary gland

The pituitary hangs suspended from the hypothalamus connected by nerves and blood vessels and controls the function of other endocrine glands and tissues.

The human pituitary gland has two lobes. Other animals have three, but in human beings, one lobe has been reduced to almost nothing through evolution. The anterior lobe manufactures and releases hormones. The posterior lobe simply passes along hormones it receives ready-made from the hypothalamus.

Pituitary lobes and hormones

<table>
<thead>
<tr>
<th>Anterior Lobe</th>
<th>Posterior Lobe</th>
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<tr>
<td>Thyroid stimulating hormone (TSH)</td>
<td>Oxytocin</td>
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<tr>
<td>Follicle stimulating hormone (FSH)</td>
<td>Antidiuretic hormone</td>
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<td>Luteinizing hormone (LH)</td>
<td>(vasopressin)</td>
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<td>Growth hormone (GH)</td>
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<td>Prolactin (PRL)</td>
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<td>Pre-opiomelanocortin (POMC)</td>
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<td>Adrenocorticotropic hormone (ACTH)</td>
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<td>beta-Lipotropin</td>
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<td>gamma-Melanocyte stimulating hormone (gamma-MSH)</td>
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<tr>
<td>Corticotropin-like intermediate peptide (CLIP)</td>
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<td>Endorphins</td>
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clear. Jet lag results when the fine synchronization of the endocrine system is somehow knocked awry. Weeks later, systems of the body may still be struggling to reorganize themselves.

**LIFE PROCESSES DEPEND ON HORMONES**

YOUR UNIQUE MIX of environment, heredity, experience and hormones helps control such major life processes as birth, growth, puberty, fertility and pregnancy. For example, sex, nutrition, weight, general health and even altitude, can all affect the time when puberty begins and how long the process takes. Regardless of the environmental factors, however, the prime mover of puberty is the basic hormonal pattern laid down by the genes. The processes of puberty may begin for one person at age 12 and at 14 for another. The changes may proceed at different rates. The transition from childhood to adolescence generally takes three to five years.

Fertility likewise depends on the proper functioning of the endocrine glands and their hormones. Ovulation by women, production of sperm by men and many of the physiological and psychological processes required to bring together sperm and egg require the greatest coordination of men's and women's hormones. Pregnancy, birth, production of milk and the many processes responsible for maintaining the fetus and infant likewise rely on proper hormone balances.

Hormones are such an important part of reproduction that regulating the levels of certain hormones in a man's or woman's body can control fertility. The Pill is a familiar and common form of contraception for women. Similar strategies for controlling male fertility are not so well developed at this point but are possible and will be available in time.

More controversial is the use of hormones to regulate aberrant sexual behavior. In several states, the hormone progesterone has been prescribed as a form of chemotherapy to reduce sexual arousal in men convicted of violent sexual assaults. Whether this treatment will prove effective in the short or the long-term remains to be seen.

According to some people, women may be moved to irrational and uncontrollable violence by disturbances in their hormone balance. K. Dalton and others in Great Britain have gained a measure of notoriety by using the Premenstrual Syndrome (PMS) as a legal defense in murder trials. The defense has maintained that the women defendants were impelled by their hormones to commit acts of violence that they would not otherwise have committed.

Because of the many methodological problems with research into PMS, the existence of such an abnormal medical syndrome is still in question. PMS may, in fact, be a normal part of the menstrual cycle. It is well-documented in the medical literature that at least 60 percent of normal women experience distressing symptoms associated with menstruation: emotional tension, anxiety, depression, irritability, hostility, bloating, swelling, tenderness of the breasts, headache, backache, avoidance of other people, changes in work habits, increased tendency to pick fights (especially with spouse or children), crying spells; changes in appetite, sexual feelings and motor control. It is the extreme reaction to those symptoms that is categorized as PMS.

**HORMONES ARE USED AS DRUGS**

Hormones are also used as drugs to treat a variety of diseases and disorders. Steroids are prescribed to treat such inflammatory diseases as arthritis and asthma. Hormone supplements are prescribed to replace missing hormones when the endocrine glands do not produce enough. Thyroid supplements are familiar. And more recently, synthetic growth hormone has been developed. Parents who think their children are too short may soon be able to take them to an endocrinologist for treatment with growth hormone, as parents now take their children to the orthodontist to have their teeth straightened.

Steroids are taken illicitly by some athletes to increase their muscle mass. The effects of this treatment are questionable. Although these hormones do help build up an athlete's muscle mass, there is no evidence to show that taking steroids increases the athlete's performance. Growth hormone may also be taken illicitly by athletes to help build muscles. Steroids are stored in fat tissue and can be detected for months by means of sensitive measuring instruments now available. Growth hormone, unlike steroids, is rapidly metabolized by the body so that it cannot be detected after a very short time. The problem with growth hormone, however, is that it is very expensive and, like steroids, seems to have little effect on athletic performance.

**DO HORMONES CONTROL SEXUAL ACTIVITY?**

**Finally, there is** the supposed effect of hormones on sexual behavior. Contrary to popular belief, changes in sexual desire and sex drive in men and women are not directly and exclusively attributable to changes in hormone levels. Androgens—so-called male sex hormones—are found in both men and women and are known to partly regulate sex drive. This cannot be the entire story, however, because post-menopausal women lose their sexual desire somewhat but do not have much of a change in their androgen levels. Nobody knows the mechanism by which sexual desire is controlled.

In animals, changes in the male hormone testosterone may be associated with changes in sex drive. But men who produce no testosterone at all because of disease or surgery may nonetheless be sexually active.

And perhaps more than in any other side of life, mind and body come together in sexual behavior so that there is no good reason to expect that sexual desire will be directly related to the rise and fall of chemicals in the blood. Experience, peer pressures, environment, age and whatever it is we mean by love, all play essential roles in controlling sexual desire. And for these things, so far, there are no good laboratory tests.
Life's patterns are shaped by glands that secrete minuscule amounts of hormones: the chemical messengers.

The word "hormone" was invented in 1905 by E.H. Starling to mean a substance that moves processes of the body. To what extent hormones control those processes is still in question. They are remarkable chemical messengers, however. Hormones organize responses to ever-changing environments inside and outside the body.

Day after day, month after month and through the many changes that constitute a lifetime, the endocrine system secretes and distributes its chemical messages. Starting long before birth and continuing through periods of growth, maturation and finally death, the endocrine glands of the body release into the bloodstream minute amounts of hormones, chemicals that control or modify many of life's chemical reactions.

What tasks do hormones perform? They
- Help the body maintain a uniform internal environment despite great changes in the external world;
- Turn on and off the countless processes by which the body maintains itself and grows;
- Set the seasonal, daily and even hourly rhythms of growth and adaptation in plants, animals and human beings alike.
Most important for the survival of the species, hormones direct the processes of sex and reproduction.

Sex hormones:

- Carry out orders programmed in the genes of selected cells to direct growth of the fetus toward being male and female;
- Direct changes in the tissues of boys and girls that make them fertile men and women;
- Prompt and organize the sometimes baffling behaviors and physiological processes by which sexually mature men and women are attracted to each other to reproduce.

The endocrine glands in an adult man or woman are so small and weigh so little that you would need to collect all the endocrine tissue from three or four people to get a pound. Despite their small size and miniscule output of hormones, the endocrine glands initiate, control and give shape to some of the most basic processes of life itself. During the course of a lifetime the total output of this tiny mass of endocrine tissue is likewise very small. Nonetheless, those infinitesimal doses of hormone in the blood are powerful enough to control the course of your growth and development.

Before puberty, for example, boys and girls have roughly the same amount of the male sex hormone testosterone, about 20 to 30 nanograms of testosterone per 100 milliliters of plasma (a nanogram is one-billionth of a gram). Many of the differences between men and women can be explained in part by the fact that in males testosterone plasma levels increase more than twentyfold during puberty. Similarly, boys and girls have about the same amount of the female sex hormone 17-beta-estradiol circulating within their blood, less than 20 picograms per milliliter (a picogram is one-trillionth of a gram). By the time a girl reaches age 10, however, her estradiol levels have more than doubled. Yet, despite the large relative difference between males and females, the actual measurable difference in hormone levels is a mere 100-billionths of a gram per 100 milliliters.

Although there is no conclusive evidence that hormones directly influence the powerful emotions that accompany sexual attraction, chemical changes in the body indirectly affect emotions. Drugs, alcohol and behaviors known to alter the chemistry of the body all can affect moods and thinking. Much more research is needed, however, before we can confidently describe the impact of hormones on mental processes.

Advances in endocrinology within the past few decades have opened up vast and still mysterious areas of study. Progress in the science of hormones and their effects on the body has also raised profound medical, social and ethical questions. If so much of the human frame and behavior is shaped by internal chemical control, how much can be shaped by external chemical control? What does it mean that we can now administer hormone-like drugs and other treatments to regulate growth, fertility and perhaps even behavior?

The information in the chart above shows the many different systems affected by disorders of a single endocrine gland.
their growth. Boys who mature later in their lives have a longer time before they obtain high levels of sex steroids to turn off bone growth.

The communication system can also break down if there are too few receptors on target cells. Some people may produce plenty of growth hormones and still fail to grow if, for a variety of reasons, their target tissues lack receptors to recognize the presence of growth hormone.

Some failures of the communication system can be treated; others cannot. If the problem is too little hormone, often replacing the missing hormone is enough to correct the condition. If the problem is due to missing receptors, little can be done. Without receptors to recognize the presence of the hormone, raising the hormone levels with drugs will have little effect.

**How the cell receives the message**

CHEMICAL MESSAGES FROM THE brain and endocrine system are sent out in extremely small quantities and without specific addresses. Many different kinds of chemical messages may pass down the stalk from the hypothalamus to the pituitary. Yet the pituitary distinguishes one message from another and responds specifically by synthesizing and possibly releasing the appropriate hormones. When the hypothalamus tells the pituitary to synthesize and release thyroid stimulating hormone, it does not normally misunderstand the message and release LH, although the pituitary is continually prepared to manufacture and release these and many other hormones.

When the pituitary gland sends out the biologically potent hormone adrenocorticotropic (ACTH), for instance, it does not send the ACTH exclusively to target cells in the adrenal cortex. The hormone is simply released into the bloodstream. The same blood supply that eventually carries the ACTH to the adrenal cortex also carries it to the thyroid, liver, lungs, heart and all the rest of the body. Yet the adrenal cortex responds to ACTH as if the hormone were addressed specifically to that tissue; most of the rest of the body ignores it.

How just the right messages could be selected from all the others completely baffled scientists before they unraveled some of the mysteries of chemical receptors.

**Human antidiuretic hormone (ADH) and Oxytocin**

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<tr>
<th>Antidiuretic hormone</th>
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<td><strong>Antidiuretic hormone</strong></td>
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<td><strong>cys-tyr-PHE-glu-asp-cys-pro-ARG-gly</strong></td>
<td><strong>cys-tyr-ILE-glu-asp-cys-pro-LEU-gly</strong></td>
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<td>S</td>
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<tr>
<td><strong>Functions:</strong></td>
<td><strong>Functions:</strong></td>
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<tr>
<td>Accelerate water reabsorption by kidneys</td>
<td>Contract uterine smooth muscle</td>
</tr>
<tr>
<td>Constrict blood vessels when given in large doses</td>
<td>Eject milk from breast</td>
</tr>
<tr>
<td>Stimulate muscles of ureter, urinary bladder, intestine, gall bladder</td>
<td>Stimulate muscles of ureter, urinary bladder, intestine, gall bladder</td>
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**Key:**

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<th>Abbreviation</th>
<th>Amino Acid</th>
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<td>cys</td>
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<td>asp</td>
<td>aspartic acid</td>
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<td>sulfur</td>
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**Abbreviation:**

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**Note that not all physiological functions are listed.**

Molecular biologists have now identified some receptors and have described their chemical structures. In general, they have found that hormone receptors have structures that will bind hormones with a particular molecular configuration. If the hormone molecule can present to the receptor a binding site, the two bind and the act of binding sets off a signal for the cell membrane and then the cell itself to respond in their characteristic ways.

Receptors of the endocrine system are sensitive to small differences in circulating hormones. As an indication of how sensitive the hormonal system is to even slight differences in molecular structure: the two hormones produced by the hypothalamus—ADH and oxytocin—are almost identical and yet have very different effects. ADH controls water balance in the body; oxytocin controls the contraction of smooth, autonomic muscle. And yet the two molecules differ in only two amino acids. (See accompanying chart.)

Receptors are constantly being made within the cell and then incorporated within the cell’s plasma membrane as well as taken back into the cell by mechanisms that pinch off sections of the cell surface and bring them back into the cell.

Hormones actually modulate the concentration of specific receptors in target cells. The rate of receptor turnover can be affected by concentrations of hormones present. In general, the lower the concentration of circulating hormones under normal conditions, the greater the concentration or density of receptors within the cell’s membrane. Conversely, when high concentration of hormones circulate normally, receptor concentration is significantly lower.

Molecular biologists have discovered several processes by which binding hormone and receptor sets off the cascade of events that eventually stir the cell into action. These biochemical processes are too complex and diverse to describe here.
Proteins and steroids

HORMONES CAN BE DIVIDED INTO two groups, protein hormones and steroid hormones. The difference is in their chemical structures; and the chemical structures define many of their properties. Many hormones, vitamins, body substances and steroids have in common the steroid skeleton of joined rings. Protein hormones, on the other hand, are built of many amino acids linked together in chains called polypeptides. These chemical differences are important because they determine how the hormones turn on their target cells.

Protein hormones are large molecules. They are too big to pass through the cell membrane into the cell. Instead, they are brought into the cell as small sections of the cell membrane pinch inward and carry the large protein molecules inside. Steroid hormones, on the other hand, are small. They can pass through the cell membrane. Steroid hormones can also dissolve in the fatty substance that makes up much of the cell's plasma membrane.

Common features

DESPITE THEIR MANY DIFFERENT roles in the economy of the body, hormones have several features in common.

People whose pituitary glands produce too little growth hormone, remain small because their bodies wait in vain for the proper chemical signals to trigger growth.

The Depo-Provera Controversy

For women, it may be the closest thing yet to an ideal contraceptive. For men whose hormonal imbalances drive them to commit sex offenses, it may provide an alternative to prison. For the U.S. Food and Drug Administration, however—currently debating for the third time if benefits outweigh risks—it is like a recurring nightmare.

The controversial drug in question is Depo-Provera, a man-made chemical that is related to the female sex hormone progesterone. When injected in women, Depo-Provera suppresses hormones responsible for releasing the egg cell. Used by some 11 million women in more than 80 countries outside the United States, Depo-Provera offers several advantages over other contraceptives. It is as reliable as The Pill, convenient, long-lasting (one injection can prevent conception for at least three months) and free of serious side effects.

When injected in men, Depo-Provera may suppress sexual desire by lowering testosterone, the principal male sex hormone. The drug does not make men impotent. Rather, in some men a large dose of Depo-Provera reduces testosterone to abnormally low levels and may temporarily diminish overwhelming sex drives. Researchers at Johns Hopkins University, in cooperation with the courts, have treated more than 70 male sex offenders with weekly injections of the drug as an alternative to jail, and participants claim that the program has dramatically helped control their deviant sexual behavior.

There is considerable controversy concerning potential benefits and possible health risks of Depo-Provera. The FDA has already twice denied licensing of the drug. The first denial was in 1974, after Depo-Provera was linked to an increase in birth defects. And it was turned down again in 1978, when laboratory tests suggested a link to breast cancer and cancer of the uterine lining. Despite these apparent health risks, the Upjohn Company, which manufactures the drug, asked the FDA in January 1983 to again consider licensing. The FDA agreed, partly because Upjohn scientists provided evidence that the previous tests were invalid.

An FDA approval would grant the use of Depo-Provera as a contraceptive. Because the drug is already approved for treating cancer of the kidney and of the uterus, and because approved drugs can be used by doctors for purposes other than what they were approved for, Depo-Provera can be used to treat male sex offenders.

The use of Depo-Provera to treat male sex offenders has its own controversy, however. Critics claim that because issues of health safety have yet to be resolved, men receiving treatment are, in effect, being used for human experimentation. In addition, although participants are warned of possible health risks, some opponents claim that being given the choice of going to prison or facing a possible health risk is a "mockery" of informed consent.

As is true for many drugs, the case for licensing Depo-Provera will come down to whether benefits outweigh risks. Some opponents claim the drug has not been adequately tested and that this alone is sufficient reason not to approve it. Proponents, on the other hand, including independent, international agencies such as the World Health Organization and International Planned Parenthood, point out that Depo-Provera has been used overseas by millions of women with no apparent increase in cancer risks.

According to Edward Nida, an FDA spokesman, the public board of inquiry that was convened in January 1983 to study the issue will soon release its recommendations to the Commissioner, who will have the final word—at least this time around.

JON QUEIRO
Steroids: The Key to Athletic Success?

Fifteen athletes from 10 Western countries were disqualified from the Pan American Games in 1983. The reason: anabolic steroids and other stimulants were detected in their systems. The result: the biggest drug crackdown in sports history.

The international incident dramatized the growing use and abuse of steroids by athletes at all levels of competition. In their never ending quest to be that much stronger, athletes, particularly weight lifters and football players, have routinely used steroids since the 1950s. But in recent years, supported by a large black market, steroid use has become a widespread problem.

On what the world class level, for example, American athletes use steroids, hoping to gain the same "edge" as athletes from communist bloc and other countries where steroids are cheap and even said to be routinely fed to youngsters in sports camps. In addition, more and more high school and college athletes are turning to the drugs with hopes of improving performances to ensure college scholarships or pro careers.

Steroids used by athletes are synthetic variations of the male hormone testosterone and serve to help the body build muscle tissue and store nitrogen. The drugs have been available by prescription under trade names such as Durabolin and Anavar for years and are occasionally prescribed for geriatric and post-operative patients to aid tissue and muscle repair. Many athletes, however, can easily obtain steroids from black market sources that now openly advertise at many gyms and health clubs.

But some scientists report that steroids have little or no effect on strength. They warn that the hazards may far outweigh the supposed benefits, particularly for younger athletes, because the drugs can stunt the growth of those who are still developing. Among women, the use of steroids can lead to increased muscle development and facial hair, as well as a deeper voice. By raising the level of testosterone in the male bloodstream, the drugs signal the pituitary gland to stop production of the hormone by the testicles. A lower sperm count and testicular atrophy could result. Increased testosterone can also contribute to enlargement of the prostate gland. And since steroids are metabolized by the liver, prolonged use has been linked to the development of liver tumors, or hepatomas.

To combat the problem, medical and sports authorities are urging the expanded use of urine testing of amateur and professional athletes of all levels, as well as better drug education.

**CHERYL COLLINS**

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**Men who matured sexually early are likely to be shorter than men who matured later. Boys who mature sexually early, "Young Hercules," produce high levels of male steroids.**

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**Hormones act on specific body tissues.** Hormones circulate in the blood. They come into contact with all the potentially responsive tissues. And yet there is a remarkably efficient and effective addressing system so that the appropriate hormone triggers the appropriate response. This is because the tissues have highly specific receptors, like antennae, waiting for just the right chemical signal.

**Hormones trigger a cascade of events in responding cells.** Once contact is made between the hormone molecule and the receptor molecules, a sequence of processes is begun in which each step amplifies the products of the step before. In this way, the tiny glands and their infinitesimal products can control great changes in the body and how it works.
The hormonal constitution is as hereditary as eye color, body structure or any other physical trait carried by Genes: Our individual programing system

Nature occasionally produces tragic experiments in which disease or heredity disturbs the body’s hormone balance. Unfortunate as these occurrences are, they nonetheless teach scientists a great deal about how the endocrine system works in health and disease.

New knowledge about the endocrine system comes slowly and often by chance; for it is difficult and often unethical to perform genetic research on human beings. People cannot be bred like laboratory animals. Affected individuals and their families are scattered around the world. The genetic conditions are rare. And few physicians are interested in research so that many instances simply go unrecorded.

Animal research on hormones is no substitute for human research. Animals’ hormones, especially animal sex hormones and fertility cycles, are somewhat unlike those of human beings. Monkeys, it is true, most closely resemble human beings; but research with monkeys is expensive and difficult. And monkeys are still not the same as people.

Medical investigators therefore, must simply wait for those unlikely experiments of nature and be ready to learn from them whenever and wherever they occur. Despite the many problems, this research is beginning to show the connections between genes and hormones, sex and fertility.
Many factors influence the endocrine system

ONE FUNCTION OF GENES IS TO shuffle the biological deck repeatedly so that individuals of a species differ from each other. The genes responsible for controlling hormones are no exception to this rule. People differ as to how much of a particular hormone they produce, in the sensitivity and number of their receptors for a hormone on target tissues, and in the ability of target tissues to respond to their hormones' chemical signals.

Many genetic factors are involved in a programming system with so many variables. But the complexity of the endocrine system notwithstanding, each element must be the expression of programs written in the genes.

The genes are often overruled by forces that are not genetic. Genes simply give a program for how the body will function. Many cultural, social, environmental, nutritional and many other factors have cooperated to change the basic pattern. That women menstruate and go through menopause, for example, is determined by the genes that make a woman. Both menarche and menopause are the expression of hormones, in turn controlled by processes set up by the genes. Today 95 percent of young women in Europe and the United States have their first menarche in the same for the past several centuries, the average age of menarche has been coming down about three years a century for the less developed countries, showing again the importance of social, environmental and nutritional factors on maturation. Menopause, in contrast, has been delayed by about three years a century and it is safe to assume that this, too, is because of environmental and nutritional factors.

Nonetheless, despite wide variations in human hormones, it is clear that genes must be at least partly responsible for the patterns of hormone actions, the types of hormones produced and the body's sensitivity to them. This is certain because:

- Certain hormonal problems run in families;
- Animals of different species have similar but not identical hormones;
- And, perhaps the most telling piece of evidence, males differ from females. The difference between males and females is genetically determined. Somehow in the genes are the instructions that make males and females produce different hormones or the same hormones in different amounts.

Genes determine hormones and hormones determine sex

GENES INHERITED FROM THE mother and the father establish a person's sex. By the time a human fertilized egg has divided three times, it is either male or female. Its sex is genetically determined at the moment of fertilization and the genetic pattern already makes a difference when the embryo is only eight cells large. There are no outward signs of sex yet, of course. These will not appear until the fetus has grown for another two months. But particularly from the moment of conception, the chemical potential is programmed into the embryo's cells for the person to be of one sex or the other.

Before the eight-cell stage of the embryo, the X chromosome runs the show. In the earliest cell divisions, cells of the growing embryo seem to pay no attention to whether the other chromosome is an X (that is, the embryo is female) or a Y (that is, the embryo is male).

If the embryo is genetically male, the Y chromosome begins to dominate the scene after the eight-cell stage and eventually directs the chemical processes that stimulate the growth of testes and male germ cells. The baby is a boy.

If the embryo does not have a Y chromosome, testes do not develop, and the fetus grows ovaries. The baby is a girl.

The genetics of sex

Every cell of a human being (except for the sperm and egg) has 23 pairs of chromosomes. Twenty-two pairs determine traits of the body. One pair determines the person's sex. Sex chromosomes, like all the other chromosomes, have come from the parents: one of a pair from the mother and one of a pair from the father. Sex chromosomes are either X or Y, so called because of their shape when examined under the microscope.

The first step that brings together the combination of genes for male or female determines most of the steps that follow. In the normal course of events, a female has two X chromosomes (XX) and a male has one X and one Y chromosome (XY). These combinations are dealt in the moment that a sperm (carrying either a single X or Y chromosome) fertilizes an egg (carrying one of the mother's X chromosomes). The genes carried on these chromosomes carry the family history. In the moment of fertilization, they project that history one more generation into the future.

Sex chromosomes

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<tr>
<th>Father's Sex Chromosomes</th>
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Male Sex Hormones

THE EMBRYO'S TESTES PRODUCE male hormones, notably testosterone, and a variety of other powerful substances that may be said loosely to "feminize" and "masculinize" the growing male fetus. This is a gross oversimplification. But animal research and some work with human beings does seem to show that if nothing changes the original pattern, you get a girl. To get a boy, the fetus needs to change some of
Animal research and some work with human beings does seem to show that if nothing is done to change the original genetic pattern, you get a girl. To get a boy, the fetus needs to change.

the starting materials. And the agents of change are hormones.

French biologist Alfred Jost studied this process, mostly in rabbits, more than 30 years ago and found that the process of sexual differentiation is sequential, ordered and simple.

When Jost removed the testes from a genetically male (XY) rabbit fetus, he produced a female. She was sterile, of course, because she lacked ovaries; but she was in most other ways a female.

When Jost implanted a testis in the neck of a genetically female (XX) rabbit fetus, he produced a male. He was sterile, too, because he lacked the male germ cells to produce sperm. But otherwise he was a male. Jost concluded that the difference between males and females is in the action of sex hormones in the fetus—hormones for which the genes carry the programs.

Once the genes have given their chemical instructions for the fetus to develop along the male model, the fetus takes over, helping to determine how it will look by producing more sex hormones.

In the early embryo, the developing testis secretes testosterone and a protein substance called Mullerian regression factor (MRF). MRF is responsible, in a sense, for "defeminizing" the male embryo. In the female embryo, a set of tubes called Mullerian ducts normally develops into the structures of the female reproductive system—Fallopian tubes, uterus and upper part of the vagina. In the male, almost nothing remains of the primitive Mullerian ducts because the protein messenger MRF instructs the embryo to absorb them.

A second hormone, human chorionic gonadotropin (hCG), starts the processes by which male sexual structures develop. Produced by the placenta, hCG stimulates cells of the testis (Leydig cells) to synthesize testosterone, which gives the signal for another set of tubes called Wolffian ducts to develop in the male. Wolffian ducts eventually become seminiferous tubules and the vas deferens. Testosterone secreted by the Leydig cells also diffuses into areas of the embryo that will become the male external genitalia—penis, scrotum, prostate and urethra.

Once testosterone is produced, male development proceeds quickly because the little bit of testosterone produced stimulates the production of more. Blood vessels invade the tissues that will become the testes, the Mullerian ducts that have been characteristically female structures degenerate and male Wolffian ducts develop. All this happens within the first trimester. In contrast, ovaries do not develop until the second trimester.

This situation is not so simple, however. True, in the normal course of events, the presence of a Y chromosome in mammals is necessary to force development toward maleness. But it takes more than the presence of the Y chromosome and the enzymes it codes to make a male. There must also be a sufficient number of receptors on the appropriate tissues to receive the chemical signal from the Y chromosome. The tissue receptors must be sensitive enough to respond to the signal, and the small response of recognition on the part of the receptors must be capable of triggering a greater response by the cell.

There are cases of people with the normal XY genetic endowment who nevertheless appear female. Their Y chromosome produces the proper enzymes but their bodies lack the receptors to stimulate the growth and development of male tissues.

This is not the end of the story of X and Y. The female has two X chromosomes. For many years, research scientists wondered if both X chromosomes contributed to the development of the ovary and female characteristics. Research has now come up with the surprising finding that one of the X chromosomes is actually inactivated in the female. Only one X chromosome is responsible for directing the course of female fetal development. Even more surprising, the X chromosome is inactivated in males, too. In fact, having an activated X chromosome in males interferes with the normal processes by which germ cells divide and mature to be sperm cells. Men with the genetic anomaly, XXY, develop testes but because they do not inactivate their X chromosome, they do not usually produce sperm. Sometime later in development, a female takes advantage of having both X chromosomes in producing eggs.

The significance of these complex patterns of turning on and off genes and their enzyme products and the secrets of the silent X chromosome remain mysteries of evolutionary history.

The genetics of sterility

Hormones are not the entire story. In one kind of male infertility, testes are normal but they produce no sperm. The explanation is to be found in the chromosomes. Part of the Y chromosome near the center codes for enzymes that produce structures of the testis; another part of the Y chromosome, further out on one of the arms of the Y-shaped structure, codes for the messengers that produce the sperm. It is possible, therefore, to have a normal testis, producing all the right hormones, without having any sperm at all.

 Gonads and the primitive cells that eventually mature to germ cells arise from two different sources in the embryo. The germ cells that will become sperm cells or eggs actually arise in the yolk sac, not strictly speaking part of the embryo itself. They then migrate to a part of the developing embryo known as the genital ridges. These migratory cells differentiate and mature to become eggs or sperm, depending on which hormones act on them. The tissue of the ovaries or testes, however, comes from a different part of the growing embryo. The result is that it is possible for gonads to develop normally in response to the hormones triggered by the presence of a Y chromosome and still have no sperm or eggs.
Sometimes the message gets garbled

FOUR STEPS ARE REQUIRED FOR normal development of a male:
- Leydig cells must produce normal concentrations of testosterone;
- Synthesis of Mullerian regression factor (MRF) must be normal;
- Testosterone must be converted to the more biologically potent androgen, dihydrotestosterone; and
- Sex hormones must actually induce their effects within cells.

Sometimes, however, the message gets garbled. The appropriate androgens or Mullerian regression factor cannot exert their effects within the cells. If androgens are not effective, either because they are not being synthesized in high enough concentration or because something is wrong with the androgen receptors, an individual who is a genetic male—that is, whose genotype is XY—matures like a woman at puberty. The condition is known as testicular feminization.

If Mullerian regression factor (MRF) does not instruct the embryo to absorb the Mullerian ducts, genetic males may grow to have some of the sexual structures of females. Men may look normal but may actually have incompletely developed Fallopian tubes and uterus.

Do hormones shape behavior?

THE BODY PARTS THAT DISTINGUISH males from females are clearly shaped by genes and hormones. How much of human behavior—and especially behaviors directly and indirectly related to mating—is initiated and shaped by hormones? The answer is that no one knows if there is a connection between hormone levels and human behavior.

Males have more circulating testosterone than females do. Males may differ from females in activity level, preference for physical contact in sports and demonstrations of anger, assertiveness and aggressiveness. There are many problems with this research. Separating the effects of genetics from the effects of culture is almost impossible. Even if the differences in male and female behavior are real, whether the differences in behavior are related to differences in hormone levels simply cannot be determined.

For a long time it was an attractive hypothesis that men with the genetic endowment of XYY, that is, an extra Y chromosome capable of triggering the production of abnormally high levels of testosterone—might account for the abnormally high levels of violent and assaultive behavior in some men. XYY men may be impulsive, but endocrin-
ologic studies have not shown a close relationship between the XXY genetic endowment and higher levels of testosterone in all XXY men.

Some medical and correctional authorities, for example, would like to show that the assaultive behaviors of violent criminals are due, in part, to their higher levels of testosterone or the abnormal sensitivity of tissues in their brain to circulating testosterone. If this were the case, dealing with the complex social, economic, psychological and other factors involved in criminal behavior would be reduced to the simple expedient of treating the criminal’s hormone levels. But at this point, no one knows if hormones and behavior are so related.

Drugs have been used to lower the testosterone levels of violent sexual offenders in hopes of reducing their sexual urges and impulsive acts. It has turned out, however, that physicians must prescribe so much of the drug that the person’s testosterone levels are reduced 50 to 70 percent below normal, not simply to normal levels. Drugs do not seem to reduce non-sexual violent behaviors; and when they do, it is more because they lower excitability in general and not because they have a specific effect.

There is no clear connection between levels of testosterone in normal men and their levels of resentment, hostility, assaultive behavior or irritability. On the other hand, there is some evidence to show that violent and assaultive prisoners have higher than normal levels of circulating testosterone, especially prisoners with long histories of violent behaviors. Separating cause from effect is a problem; for it is not clear whether the environmental and social conditions provoking the violence raises the testosterone levels or whether the already raised testosterone levels predisposes the person to act violently.

**Hormones and behavior**

**TESTOSTERONE HAS MANY EFFECTS**

On tissues of the body other than developing sexual tissues, including the brain. It would be surprising if hormones affected the brain and not behavior. The central nervous system plays such an important role in controlling mating behaviors, the selection of mates, the timing of mating, hormonal changes in pregnancy, rearing the young and so forth, it would be surprising indeed if the brain and hormones were not intimately related.

Anecdotal evidence and crude experiments have shown that this is the case. Recently, careful experiments to show precisely what parts of the brain have receptors for sex hormones have proved the case. Many male behaviors are controlled by centers in the brain prompted by androgens circulating in the blood.

As with so many of these experiments, the work has been done with animals, not people, and so it is difficult to generally apply the results to human beings. That genes affect hormones, hormones affect the brain, the brain affects behavior is a reasonable hypothesis, however. But human beings, perhaps unlike the rest of the animal kingdom, have powerful social and psychological determinants of behavior, as well as the chemical determinants. Hormones make a difference but they cannot account for the entire difference between men and women or between violent and less violent individuals.

The significance of these complex patterns of turning on and off genes and their enzyme products and the secrets of the silent X chromosome remain a mystery of evolutionary history.

**Testosterone also affects the brain.**

In animals, such “male” behaviors as courtship, aggressiveness, defense of territory and so on, are directly related to testosterone levels in the blood. In the brain, receptors recognize the presence of testosterone and trigger the appropriate reproductive and nonreproductive behaviors. In lower animals, testosterone is related to:

- Regulation of gonadotropin and prolactin;
- Courtship and other reproductive behaviors;
- Activity levels;
- Aggressiveness;
- Play;
- Taste preferences;
- Scent marking;
- Feeding and body weight;
- Learning;
- Circadian rhythms;
- Brain function.

In human beings, the role of hormones in determining behavior is not quite so clear. There is considerable evidence, however, that hormones do play a major role in shaping behavior.

There have been studies of the relationship between hormones and rearing in the development of sexual definition and gender identity. Most information has come from studies of children born without clear biological sexual definition.
Unclear sexual definition

Testicular feminization and congenital adrenal hyperplasia

For a variety of reasons, the genetic definition of sexual identity may not agree with the outward signs of sexual definition. When this happens, parents raise their children as the opposite of the child's biological definition. Biologic boys are raised as girls in a condition known as testicular feminization, for example; and biologic girls are raised as boys in the condition known as congenital adrenal hyperplasia. In the first, males are born with normal testes and produce normal testosterone but the tissues of the rest of the body lack receptors (or somehow fail to get the message) for testosterone and fail to develop in the normal male pattern. The boy takes on feminine characteristics. In the second, a biologic female has an abnormal adrenal gland that produces testosterone rather than cortisone. As a result, the girl's tissues throughout the body respond to testosterone and she develops male characteristics.

Sexual definition and gender orientation

If left untreated, testicular feminization and congenital adrenal hyperplasia create serious problems when biological and gender identities conflict. It is an odd fact of human psychology, however, that gender identity is stronger than biological sex identity. Even when secondary sexual characteristics of the opposite sex begin at puberty, the child raised as a girl continues to think of herself as a girl; the child raised as a boy continues to think of himself as a boy.

When these conditions are treated early, gender identity and sexual identity are in harmony. (Hormones and sexual identity were in conflict only during the time of gestation.) The unfortunate condition nonetheless gives researchers the opportunity to study the relative contributions of hormones and rearing to sexual identity. Much research has now been devoted to the question of whether abnormally high or low androgens, progestogens or estrogens in fetal development have a continuing effect on the person's behavior. The hypothesis is that, even when the hormonal abnormalities are corrected after birth, prenatal exposure to high levels of androgens will produce "male" behavior and high levels of estrogens or low levels of androgens will produce "female behaviors."

Researchers have studied several behaviors:

- Activity levels, outdoor play and athletic skills;
- Physical and verbal fighting;
- Play as rehearsal of the parent role;
- Preference in clothes, grooming, jewelry.

The research shows that prenatal hormone levels do not affect gender identity. Even in children with abnormalities leading to opposing biologic and gender sex identities, the gender identity given by the child's rearing dominates. However, the research also shows that behaviors are determined by prenatal androgen levels.

Biologic females exposed to high levels of androgen before birth have been shown to prefer intense outdoor play,
associate with boys for the most part, think of themselves and be labeled by others as tomboys. They do not play with dolls or rehearse parental roles. They are more likely to engage in body contact sports.

Boys can also have abnormalities that expose them to excessive levels of androgens before birth. Naturally these boys are physically and genetically male; there is no ambiguity as in the case of females exposed to androgens. But these boys differ from normally developing boys in being more active, more interested in physical contact sports and perhaps have higher levels of aggressiveness.

In contrast, boys with testicular feminization, whose androgen levels during prenatal development are normal but incapable of stimulating male development in tissues of the body, are stereotypically feminine. The problem with such research, however, is that these biologic males are reared as females because they lack characteristic male appearance. There is no way to separate the effects of rearing from those of hormones.

Most researchers are quick to point out that sexual orientation is the result of complex and little understood psychological, social, environmental factors, as well as genetic and hormonal ones. Few people would argue that hormones alone strictly define sexual orientation. That they play a role, however, is clear.

Biologic females exposed to high levels of androgen before birth have been shown to prefer intense outdoor play, associate with boys for the most part, think of themselves and be labeled by others as tomboys.

The Nature vs. Nurture Debate

It is well-known that hormones play an essential role in the development of physical differences in males and females. But to what extent an individual's sexual identity is influenced by hormones versus his or her social environment has long been debated by scientists.

As in other areas of hormone research, studies are complicated by the difficulty of investigating the subtleties of physiology without harming human subjects. To understand healthy functioning, said Dr. Judith Vaitukaitis, professor of Medicine and Physiology at Boston University Medical Center, researchers often must work backward to find out what went wrong, and then infer what is "normal." In fact, it was in this way—the retrospective study of abnormalities of nature—that medical researchers recently provided insight into the "nature versus nurture" issue of gender identity.

In 1979, researchers from the Cornell University Medical College and the National University Pedro Henríquez Urena reported in the New England Journal of Medicine a study of a group of boys from the Dominican Republic who were born with "female-appearing" external genitalia and who were subsequently raised as girls. The condition was caused by deficiency of an enzyme that in normal boys activates testosterone before birth to stimulate growth of male genitals.

The Dominican Republic boys, lacking male genitals, were raised as girls during childhood. The onset of puberty, however, resulted in normal increases in testosterone, which, in turn, stimulated the long-delayed development of a penis and scrotum. The boys consequently underwent an identity transition over the course of several years, passing through stages of "no longer feeling like girls, to feeling like men, to the conscious awareness that they were indeed men."

The researchers wrote that of 18 subjects "unambiguously" raised as girls, 16 changed to a "male-gender role," despite social pressure that included parental amazement and confusion. Because the boys made the transition with relatively little difficulty—in spite of a cultural environment that emphasizes a "definite socialization of children according to sex"—the researchers concluded that "environmental or sociocultural factors are not solely responsible for the formation of a male-gender identity. Androgens make a strong and definite contribution."

JON QUELIO

Can you recognize the problem?

A woman and her husband have been trying to conceive a child for almost two years. She has had her period regularly every 28 to 32 days and is apparently in good health. Her gynecologist tested her to be certain that she had no infection and that her tubes were not blocked. Her husband was also examined and the tests showed that his sperm was entirely normal. At this point, she is told by her physician that there is nothing wrong with her, she should just relax, and nature will take its course. Is the physician right?

A. Yes
B. No
C. Can't be certain

Answer: The answer is C, the physician cannot be certain, and the wife should be tested further if she and her husband want to have children. Approximately 15 to 20 percent of couples trying to conceive cannot although there is no immediately obvious reason for the difficulty. Nevertheless, in such cases a woman may be abnormal endocrinologically. She may have regular menstrual bleeding and appear normal but still have anovulatory cycles in which no mature egg is produced. More sophisticated testing is required before both husband and wife can be given a clean bill of health. Ironically, it is just these apparently normal cases that are the most difficult to diagnose and treat. The more marked the menstrual disturbance, the easier it is to correct, provided there are potentially fertilizable eggs in the follicles within her ovary.

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works in secret and mysterious ways. In most cases, we are not aware of it when it is working well or when it is not working well. The symptoms usually appear in parts of the body far removed from the endocrine problem itself. But if we know the physical and biochemical changes to look for, we can often recognize when the system is in trouble.

Sometimes the effects of endocrine disorders are clear and obvious. If you are seven feet tall, you may not know that your pituitary has been making and releasing too much growth hormone. In fact, in a now classic study it turned out that some of the tallest professional basketball players showed signs of having had pituitary tumors in their childhood. The tumor eventually disappeared by itself. But before it did, it released unusually high levels of growth hormone. Many people walk around with such benign disturbances of their endocrine systems.

In other cases, people ignore potentially serious problems because they are not aware that the symptoms and the hormones might be related. Endocrinologists can determine exactly what part of the system is awry and often can measure the magnitude of the problem. For the endocrinologist to evaluate the problem, however, first requires that we recognize the symptoms as possible endocrine trouble. This is not as difficult as it sounds.

It is important to pay attention to minor signs and symptoms of
trouble. The onset of some conditions is slow but steady. Treating them when they are in their early stages often minimizes or reverses the damage. The problem, all too often, however, is that many of the most insidious changes happen so slowly that people think they are merely signs of growing old.

**PATTERNS OF HORMONAL PROBLEMS**

Physicians are still learning about the nature of endocrine disorders. They once believed that endocrine disease was simply the result of too much or too little hormone circulating in the blood. With modern advances in endocrinology, it is now clear that there are many different patterns of endocrine disease, each with its own treatment. Some problems clear up by themselves; some have no treatment yet. The difficulty for both physicians and patients is knowing one from the other.

Sometimes the problem is in the endocrine glands themselves. The endocrine glands may be producing and secreting too much of their hormone, usually as a result of benign tumors. Endocrine glands may also secrete too much of their hormone if they are overstimulated by the anterior pituitary hormone controlling them. Likewise, a target endocrine gland may fail to produce enough of its hormone, despite adequate stimulation, because of some disease or other functional failure; or the pituitary may not be sending the target gland enough hormone for the target gland to perform its proper function. Finally, tumors of non-endocrine tissue may produce hormones indistinguishable from those synthesized by endocrine glands.

It is now believed that all cells can produce all the hormones. Poorly understood processes in the nucleus of the cell turn off some of the genes and turn on others so that cells produce one hormone or another. In tumors, however, the cell is so disrupted that whatever turns these genes on and off functions improperly and non-endocrine cells nonetheless synthesize and secrete endocrine hormones.

The hormones secreted by the endocrine glands need receptors at the target organs to switch on the target organ. Some endocrine diseases may be due to failures of the receptors and not due to failures of the glands. Certain kinds of diabetes, parathyroid disease and testicular feminization are caused by the lack of receptors or failure of receptors. As a result, the tissues of the body fail to get the proper messages and they fail to develop normally.

Glands may sometimes produce altered forms of hormones so that the receptors cannot recognize the message. Endocrine tissues may be producing normal hormones but in such low concentrations that the chance of a hormone molecule binding to a receptor molecule is low and the hormone can, therefore, not trigger the cell's normal response. In other cases, the endocrine cells may synthesize incomplete hormone molecules; and part of a molecule usually does not have the biologic effect of the whole molecule.

Finally, in other conditions, nonendocrine tissues (for instance, the lung, thymus or pancreas) may produce hormones. In certain kinds of cancer of the lung, thymus or pancreas, these nonendocrine tissues can produce endocrine hormones. In general, however, the endocrine system is a set of glands highly receptive to instructions from the primary endocrine gland and capable of producing and releasing into the circulating hormones, chemical substances that change the function of
specialized tissues throughout the body. The body's receptors are programmed to recognize a specific chemical signal; they do not care where the signal comes from.

Some disorders of the nervous system as well as inborn defects of metabolism and the immune response can be traced to failures of membranes to recognize and respond to vital messages coming to them. Annoying conditions that do not respond to vital messages coming to them may leave another person's relatively unmoved. For this reason, it is difficult to generalize about signs and symptoms of endocrine problems. When disruptions in menstrual cycles, fertility, potency, growth and all the other functions regulated by the endocrine system are noticeable, they are worthy of expert medical attention.

**Can you recognize the problem?**

**A 31-year-old woman's period is 10 days late and she begins to feel symptoms that her friends have told her are the first signs of pregnancy — enlarged and tender breasts, queasy stomach and mild lethargy. Is she pregnant?**

A. Yes
B. No
C. Can't tell

**Answer:** Can't tell. Simply missing a period is not sufficient to be sure that she is pregnant. She may have had an anovulatory cycle, that is, a menstrual cycle in which no mature egg was released and the developing follicle did not produce enough estrogen to significantly change the lining of her uterus. As a result, there was not enough tissue to slough off at the time of her menses and she had no period or a very light one.

**A 29-year-old man has become impotent. He has been working long hours at a job that is physically and emotionally demanding. To relax, he has been drinking at least a six-pack of beer a day and smokes as many as five marijuana “joints” a day. Although he is worried about his impotence, he assumes that it is related to the intense work stress and that, when he can just “cool out” with his beer and marijuana, he will be his old self once again. Is he right?**

A. Yes
B. No
C. Can't be sure

**Answer:** The answer is probably No. The stress certainly contributes to his impotence. But it is also true that both marijuana and alcohol disturb the function of his Leydig cells so that his testes are producing less than normal amounts of testosterone. At the same time, alcohol and marijuana upset the function of his hypothalamus and pituitary so that they are producing and secreting too little gonadotropin to stimulate his gonads. The impotence is usually reversed by cutting down the alcohol and drugs and, of course, by developing better skills for coping with the stress.

A 40-year-old man has had a severe bout of the flu, with a fever of 103 for four days. While he was being examined by his family physician, he mentioned that he and his wife have been trying to conceive a baby for several months without success. The physician sends him for a semen analysis. On the basis of the laboratory reports that the man's semen is abnormal, the physician tells him that he is infertile. Is this necessarily the case?

A. Yes
B. No

**Answer:** No. The laboratory performing the semen analysis did not know about the man's flu and his high fever. High fever can severely disrupt a man's sperm production. The condition usually clears by itself, however, and does not need treatment. By the end of the normal 70-day cycle of spermatogenesis, he is likely to have motile sperm in adequate numbers.

Your 18-year-old daughter has failed to start menstruating. Should you wait to see what happens or take her to see a physician?

A. Wait
B. Seek medical attention

**Answer:** Seek medical attention. Menarche may be delayed for many reasons. More than 95 percent of young women in the United States will have begun normal cycling by the age of 16. If your daughter is delayed much beyond age 16, she may be perfectly normal; but getting a medical opinion is a good idea. A careful history, physical examination, endocrinologic profile of the hormones controlling menstruation (FSH, estradiol and prolactin) may be required to evaluate her medical condition.
We usually think of the endocrine glands—pituitary, adrenal, thyroid, parathyroid, pancreas, pineal, and the ovaries and testes—as the only sources of internal secretions. This is not entirely true; for several other tissues of the body produce hormones. The placenta, for example, produces hormones also produced by the ovaries, corpus luteum and the anterior pituitary. The intestine produces a hormone called cholecystokinin, which contracts the gall bladder. The stomach produces two hormones, enterogastrone and gastrin, and many others which affect gastric motility and increase the secretion of digestive fluids. Entire textbooks are written on each of the endocrine glands. All we can do here is give a very brief overview of the glands and some of their important hormones.

**ADRENALS**

An adrenal gland perches like a cap on top of each kidney. In human beings, the inner medulla and outer cortex of the adrenals produce quite different substances. The medulla, in fact, is more like a large knot of nervous tissue (a ganglion) than an endocrine gland. When stimulated by the sympathetic division of the autonomic nervous system, the adrenal medulla secretes two powerful substances—primarily epinephrine (adrenalin) but also norepinephrine (nonadrenalin). Epinephrine constricts the blood vessels, stimulates the heart to beat faster, increases the conversion of glycogen and fats to energy and opens the major airways of the lungs. In short, epinephrine prepares the body for sudden and vigorous work. Norepinephrine also constricts blood vessels but does not affect the heart and airways as markedly.

The adrenal cortex, on the other hand, produces three kinds of steroid hormones. Glucocorticoids (cortisol) affect glucose metabolism and reduce inflammation. They also affect adrenergic receptors. Mineralocorticoids (aldosterone) control the balance of minerals and water in the body. The adrenal cortex also produces sex steroids, male hormones (androgens) and some female hormones (estrogens).

In general, the hormones of the adrenal cortex:
- Control the salt/water balance;
- Release glucose from the liver;
- Increase glucose synthesis for energy;
- Increase the utilization of glucose for energy;
- Increase the secretion of digestive juices in the stomach: hydrochloric acid, pepsinogen, trypsinogen;
- Reduce the inflammation reaction;
- Reduce the effects of shock; and
- Secrete sex hormones adrostenedione, estradiol and testosterone, 17-alpha-hydroxyprogesterone and dehydroepiandrosterone.

**Endocrine glands**

The major human endocrine glands are depicted in the accompanying illustration. The figure represents an androgynous human and contains both male and female reproductive organs.
THYROID
The thyroid is endowed with a prodigious blood supply: about five quarts of blood pass through this gland every hour. Although the thyroid is one of the largest glands in the body, weighing about seven-tenths of an ounce, it is still quite small; and the good blood supply is therefore all the more dramatic and testifies to the importance of the gland.

Thyroxine (T₄) is one of the active iodine-containing hormones of the thyroid gland. Another hormone, triiodothyronine (T₃) is also present and is 10 times as potent as thyroxine. T₄ accelerates cellular reactions throughout the body, except for tissues of the brain, thyroid itself, spleen, testes and uterus. It stimulates enzyme systems to increase glucose oxidation, synthesis of proteins from amino acids and respiration. In this way, thyroxine raises the metabolic rate and the rate at which most cells of the body consume oxygen. T₃ increases the number of adrenergic receptors in blood vessels and thus plays an important role in maintaining blood pressure.

Because thyroxine requires four iodine atoms for each molecule, thyroid tissue must work hard to trap most iodides from the 30 gallons of blood that pass through the thyroid every day. The thyroid is so efficient in this filtering of iodide that the concentration of iodine inside the thyroid may be 25 times the concentration in the blood passing through. The thyroid is also so diligent in its work that if the blood does not contain even this small amount of necessary iodine, cells of the thyroid multiply and grow to take advantage of what iodine is present. As the thyroid grows to disproportionate size, it swells the neck, forming a goiter. In areas where iodine is not naturally available in the water or food, goiters may be so common that not to have one is considered a deformity. Now, however, with iodized salt and other forms of iodine in food, it is possible to prevent goiter from iodine deficiency.

PARATHYROIDS
Ever since they were discovered in 1850 by a British anatomist dissecting an Indian rhinoceros, the parathyroids have remained somewhat mysterious. These tiny glands (6x4x2mm) are located behind the two lobes of the thyroid, usually two on each side in humans. Cases are known, however, of as many as eight parathyroids: and they may be located anywhere in the neck and chest.

The parathyroids secrete parathyroid hormone to control the calcium balance and the phosphate balance of the body. They increase the excretion of phosphate in urine, increase the reabsorption of calcium from bone and indirectly increase the absorption of calcium from the gut into the blood.

Vitamin D is an important part of this process. The parathyroids and vitamin D work together to control the absorption of calcium from the gut.

PANCREAS
The pancreas has been called the salivary gland of the abdomen. We can ignore its digestive function—supplying the intestine with pancreatic juices to help digest proteins and fats. The endocrine functions of the pancreas, however, are to control blood glucose levels by means of the endocrine hormones, insulin and glucagon. The pancreas also produces pancreatic polypeptide and somatostatin, but at such small concentrations that their physiologic functions are not fully understood.

PINEAL
Very little is known about the function of the pineal gland in the human. This tiny pine cone-shaped structure in the brain was widely thought to be the seat of the soul. Descartes argued that because the pineal is the only unpaired structure in the brain, it must be the organ of the soul. The idea was believed well into the 19th century. In other animals, the pineal is a kind of unpaired eye, a light receptor responsible for controlling seasonal behaviors like mating or migrating. In humans, it is known that the pineal secretes melatonin; but the function is not understood. In lower animals, secretions of the pineal exert antigonal effects.

GONADS
The gonads—ovaries in the female and testes in the male—produce the egg and sperm as well as many endocrine hormones. Steroid hormones synthesized and secreted by Leydig cells in the testis are necessary for the proper development of sperm. Likewise, steroid hormones synthesized by cells in the ovary are necessary for the proper maturation of the Graafian follicle containing a fertilizable ovum. These statements give the misleading impression, however, that male and female hormones are mutually exclusive. Actually, both “male” and “female” sex steroids are found in both sexes. The difference between the sexes is quantitative, not qualitative.

Endocrine glands and their major hormones (indicated by arrows).

- Hypothalamus → “brain hormones”
- Anterior pituitary → TSH, FSH, LH, ACTH, GH, PRL, B-LPH
- Intermediate pituitary → melanocyte stimulating hormone, ACTH
- Posterior pituitary → oxytocin and ADH (from hypothalamus)
- Thyroid → thyroxine, triiodothyronine, calcitonin
- Adrenal cortex → glucocorticoids, mineralocorticoids, sex steroids
- Adrenal medulla → epinephrine, norepinephrine
- Pancreas → insulin, glucagon, pancreatic polypeptide
- Parathyroid → parathormone
- Pineal → melatonin
- Testis → testosterone
- Ovary → estradiol, progesterone, ova
- Placenta → hCG, steroids (DHEA, progesterone, LH-like hormone, chorionic gonadotropin)

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One important function of the endocrine system, after all, is to adjust the body to stressors inside and outside the body. Along with the autonomic nervous system, which automatically regulates the body’s rapid adjustments to a changing environment, the endocrine glands and their products prepare the body for long-lasting maintenance efforts.

When the body is stressed by physical or psychological demands, the adrenal glands release hormones to the body and chemical signals to the nerves that dramatically change activities of the heart and blood vessels, mobilize metabolic processes for converting stored fat to energy for fight or flight and prepare the immune systems. These powerful hormones also affect the pituitary.

Men under stress, whether the stress is on-the-job, in their personal lives or from hard physical training, frequently have abnormal sperm. Low sperm count leads to decreased motility of the sperm. And absence of sperm motility is by far the most important abnormality if the man is interested in fathering children.

Women under similar stress may also have problems with fertility. They may have irregular periods or periods without producing a mature egg. Or women may also entirely miss menstrual periods.

Physical and psychological stress can lead to fertility problems. In both cases, behaviors, disease and the cumulative effects of coping poorly with the strains of daily life reduce or change the secretion of sex hormones needed to stimulate the testes and ovaries.

For women, alterations in the regular menstrual pattern can serve as an early warning system that something is awry. The underlying cause of a missed period is not always endocrinologic, but any disturbance of the

"At the Bedside" by Henry Tonks (1862–1937);
regular pattern is worth some attention. It is usually more difficult for men to recognize that stress or disease are adversely affecting fertility, however. Men do not have the same obvious pattern of changes as women. Changes in a man's fertility may go ignored unless the man is interested in having a family.

Androgens are responsible for sex drive or libido in both men and women. In contrast to what happens in women, healthy men maintain relatively constant testosterone levels into their seventh, eighth and ninth decades. When illness decreases levels of LH, testosterone secretion and libido decrease in men. Men may become aware of the fact that they are shaving less frequently and that they do not have the sex drive they had before.

Men who are older than 40 or 50, who develop abnormalities resulting in decreased testosterone secretion, frequently attribute change in libido and infrequency of sexual activities to "getting older." This is a problem. Men develop pituitary tumors that frequently go undiagnosed for much longer than those in women simply because the changes are so insidious that most men are unaware or simply attribute their changes to age. The changes in LH and FSH secretions are usually so slow that the accompanying decrease in testosterone secretion goes unnoticed. Decreased spermatogenesis as a result of inadequate gonadotropin stimulation goes unnoticed, too, unless the man has been trying to have children.

In responding to stress, a portion of the pituitary gland sends tiny amounts of a chemical called adrenocorticotropic hormone (ACTH) into the bloodstream. Cells of the adrenal gland respond by releasing hormones (called glucocorticoids) and other cells in the adrenals and nerves, responding to other chemical messages from the brain, release epinephrine and norepinephrine.

The autonomic nervous system is remarkably sensitive; and the chemical messengers (catecholamines) it produces, principally in the adrenal medulla, are potent substances that quicken the heartbeat, constrict the blood vessels and mobilize the body's energy stores for action. Norepinephrine (reflecting activity of the sympathetic nerves) and epinephrine (reflecting activity of the adrenal medulla) change in stressful conditions as shown in the accompanying chart. The result is a coordinated response to the stressor.

And one-half hours a day. The goal of the research project was to exercise healthy, normally menstruating women until their periods were upset. (See Bostonia, Volume 57, Number 3, July/August 1983)

The women recruited for the study were healthy and normally active but had not been involved in any rigorous exercise program. They were menstruating and ovulating normally. During the research project, investigators measured the women's production of stress hormones, weight and diet and hormones regulating the menstrual cycle: luteinizing hormone, follicle stimulating hormone, estradiol and progesterone.

Of the 25 women participating in the study, only two subjects showed no change in menstrual patterns and hormone levels. One of the women had been abnormal before entering the study. The other woman, it was discovered later, had not run the course. She started with the others but then found a comfortable place to sit for three-quarters of an hour before trotting back to the starting point. Of the rest of the group, 22 percent of the women had shortened luteal phases and luteal insufficiency and 46 percent of the women did not ovulate.

After the eight-week research program, the women returned to their normal levels of activity. Six months later, when the investigators reexamined them, all the women who had participated in the study regained their normal menstrual and ovulatory cycles.

Before we can understand the effects of stress on fertility, we must know something about how sperm and egg are produced normally.

**Maturation and puberty**

PUBERTY IS A BEWILDERING TIME. The word estrogen, one of the principal hormones of female sexual maturation, reflects this bewilderment; for it comes from the Latin meaning both poetic inspiration and irresistible impulse. The changes are expected and predictable; but reactions to the changes of approaching

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**FERTILITY**

**ONE IMPORTANT FUNCTION OF THE endocrine system, after all, is to adjust the body to stressors inside and outside the body.**

**Stress-induced changes in epinephrine and norepinephrine**

<table>
<thead>
<tr>
<th>Activity</th>
<th>Epinephrine</th>
<th>Norepinephrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change posture</td>
<td>Small rise</td>
<td>Up 200-300%</td>
</tr>
<tr>
<td>Public speaking</td>
<td>Up 200%</td>
<td>Up 50%</td>
</tr>
<tr>
<td>Mental arithmetic</td>
<td>Up 50%</td>
<td>Up 200%</td>
</tr>
<tr>
<td>Physical stress, cold, heat, exercise and surgery also raise epinephrine and norepinephrine levels.</td>
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<td></td>
</tr>
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In addition to the catecholamines, a set of stress hormones, also, help the body adapt to the many demands placed on it. Often, however, the body's rapid adaptation to immediate stressors has adverse long-term effects on other functions. The reproductive system, for example, can be disturbed by a wide variety of physical and psychological stressors.
"The Fall of Man (Adam and Eve)" by Albrecht Dürer (1471–1528)
maturity are usually so personal and idiosyncratic that no adult would hazard a guess as to how the adolescent will behave. The adolescent, likewise, is often so confused by internal and external changes that everything seems to be out of control. Not since infancy has the body grown so fast. Never before have such strong sexual urges asserted themselves. At the root of these changes are profound changes in concentrations of the hormones that govern sexual maturation and behavior; and behind those changes in the endocrine system is the ever-present timing mechanism built into the hypothalamus in the midbrain.

During puberty, the girl’s external sexual characteristics grow and mature. Her internal sexual organs—notably the uterus and ovaries—also grow larger, at the same time, and take on their adult function. At the time of menarche, for example, a girl’s ovaries have begun to grow. By the time she is 20, her ovaries will have more than doubled in weight and size. Her uterus, too, has begun to grow when she is about 10 and doubles in size by the time she is 18.

Likewise, boys’ external and internal sexual organs, muscle mass, voice and behaviors change toward the adult patterns.

Shifting hormones during puberty have widespread effects in addition to observable effects on the sexual organs. In females, the rapid increase in production of estrogenic hormones:
- Increases and maintains normal adult size of the vagina, uterus and tubes;
- Helps to control secretion by pituitary of gonadotropic hormones;
- Influences growth and development of secondary sexual characteristics;
- Controls deposition of fat in adult patterns;
- Maintains nasal and oral mucous membranes;
- Influences normal uterine contractions;
- Controls growth of breast ducts along with progesterone; and
- Causes emotional changes.

Changes in the hormone output of the ovaries do not chiefly affect sexual behavior, however. Women who have had their ovaries removed continue to have normal urges, because most of the androgen responsible for libido is secreted by the adrenals. The principal hormonal regulation of sex drive is from the pituitary and adrenals, not from the ovaries. Women who have had their pituitary and adrenal glands removed have almost universally reported that their sex drive was dramatically reduced.

In the maturing boy, the increased production of luteinizing hormone (LH) by the pituitary stimulates the testes to secrete testosterone. FSH controls the initial processes in the production of sperm by the seminiferous tubules. For sperm to mature, however, also requires LH. In the absence of LH, spermatogenesis is halted before the spermatozoa fully mature.

LH is principally responsible for stimulating and regulated by hormones coming from the pituitary acting on cells in the gonads (gonadotropic hormones). Luteinizing hormone (LH) and follicle stimulating hormone (FSH) are the principal gonadotropic hormones in males. For ongoing spermatogenesis, the testes need both—LH and FSH.

Cells, containing specific FSH receptors called sertoli cells, line the base of the seminiferous tubules and help nurture those cells that will eventually develop into mature sperm. Why FSH is needed for normal spermatogenesis is unknown. Testosterone cannot get into the testis from outside. Even if testosterone is given to a normal man in relatively high concentrations, very little crosses into the testis because of an anatomic barrier, referred to as the blood-testis barrier. Leydig cell function within the testis is essential for normal spermatogenesis because the Leydig cells are responsible for maintaining adequately high levels of testosterone within the testis. A protein referred to as inhibin also has been isolated from fluid within the seminiferous tubule. Several animal studies strongly suggest that inhibin regulates FSH secretion. Whether inhibin is important in the human under normal physiologic conditions is not certain.

IT TAKES ALMOST TWO AND ONE-HALF months for a normal mature sperm to develop from precursor cells within the seminiferous tubules.

Spermatogenesis

The illustration depicts a cross sectional view of a testis which is an oval gland about two inches long.

Sperm is produced in the testis. Within the more than 200 lobes of the mature testis, hundreds of delicate tubes (seminiferous tubules) produce about 200 million sperm every 24 hours. Between the tubules are groups of cells that secrete male hormones (androgens).

How sperm cells are produced (spermatogenesis) is still not completely understood; although it is clear that sperm production is

Within the past two years, investigators have discovered new proteins that may play important roles in spermatogenesis. Some of these new proteins are found only in the testis; others are found in other parts of the body but seem to have special functions in the testis unlike those elsewhere. Like hormones, they trigger and regulate the production of sperm. But unlike hormones, they operate strictly at the local level. These proteins are called transferrin, ceruloplasmin and seminiferous growth factor.

The sperm itself is loaded with several exotic metals—selenium, copper, cobalt, iron, calcium, sulphur—at unusually high levels and we do not know why. Each metal may have its own transfer mechanisms like those for the transfer of iron. Transferrin and ceruloplasmin apparently play central roles in getting these exotic metals into sperm cells.

A third protein, being researched by Tony Bellvé at Harvard Medical School, may be a seminiferous growth factor. This protein may be produced by Sertoli cells. Seminiferous growth factor is apparently synthesized very early in fetal development and may be the reason, according to Bellvé development shifts from a female ovary to a male testis. This may be the very earliest signal. All indications are that this protein is already there, programed in the Sertoli cell, at time zero. Testosterone then appears about three days later.
FERTILITY

Lating the Leydig cells of the testis to produce testosterone, which stimulates the growth and maturation of secondary male sexual characteristics. In addition, testosterone is also responsible for:

- Dryness and itching of the skin;
- Retention of chloride and water;
- Peripheral blood circulation;
- Size and function of the kidneys;
- Irritability and other functions of the central nervous system; and
- Mental functioning.

Recent research suggests that boys and girls have different attitudes about puberty. Early maturation in boys is associated with high self-esteem. girls, on the other hand, have a more ambivalent attitude about early maturation. The stereotypical lean and lithe look of pre-pubertal girls has become such a strong social standard that young girls are apparently reluctant to give it up. Other research also shows that young girls have ambivalent feelings about the onset of menstruation. Unlike boys, boys take unalloyed pride and satisfaction in their course toward adulthood. The greater strength and other outward signs of potency have both biological and social value.

Abnormal spermatogenesis

The seminiferous tubule is very sensitive to any kind of injury, including infection—much more so than the Leydig cells. Consequently, processes of spermatogenesis may be disturbed or stopped entirely by a variety of conditions that do not directly affect testosterone production. These abnormal conditions often disappear on their own when the stressful conditions are removed. But since it takes almost two and one-half months for a normal mature sperm to develop from precursor cells within the seminiferous tubules, usually several months are required before normal spermatogenesis is restored.

Recreational drugs—marijuana and alcohol—may also result in abnormal spermatogenesis. They have a direct effect on the testis, and, in extreme cases, may severely impair the function of Leydig cells. Usually, however, abnormalities due to excessive use of drugs are reversible after discontinuing use of the drugs.

A high fever of 103 or 104 may cause abnormalities of spermatogenesis that can last for several months. And men undergoing chemotherapy or surgery may be permanently prevented from making sperm. In this case, sperm may be collected and stored in special sperm banks for future use. This is an important consideration, especially if the man is young and has a primary tumor of the testis. He has a high likelihood of being cured but also a high risk of being left sterile.

When abnormal spermatogenesis is a result of decreased or absent gonadotropin stimulation, giving appropriate hormones to replace the missing ones will usually restore normal sperm production and sexual function. Unfortunately, replacement hormonal therapy is expensive and few endocrinologists or urologists are trained in this form of treatment. But many couples are willing to assume the expense because the prospects for adopting children are so poor.

Infertility

In the absence of contraception, approximately half the couples having frequent intercourse will achieve a pregnancy within six months. Ninety percent are successful within 18 months. The decline in fertility with age, however, suggests that couples over 30 should seek professional attention if they have not achieved a pregnancy after six months.

The menstrual cycle

Women menstruate spontaneously during the years they are capable of becoming pregnant. The menstrual cycle is the result of the integrated effects of many hormones secreted by the pituitary, the ovaries and specialized portions of the brain known as hypothalamic nuclei. The outward sign of the beginning of the menstrual cycle is menstrual bleeding, or periods, which usually occur every 26 to 32 days.

The pituitary secretes two hormones—luteinizing hormone (LH) and follicle stimulating hormone (FSH)—collectively referred to as gonadotropins. These hormones stimulate specialized areas within the ovaries called follicles. The follicles are composed of a central egg surrounded by one or more layers of supporting cells. These cells secrete steroid hormones as well as other substances, some of which are yet to be defined, or characterized. If one were to obtain a blood sample from a woman with normal menstrual cycles and measure the concentrations of LH and FSH, one would observe a strikingly higher concentration of LH approximately halfway through the menstrual cycle. That high concentration of LH occurs approximately 12 to 36 hours before ovulation and also helps to divide the menstrual cycle into the follicular and luteal phases.

The early phase of the menstrual cycle is named the follicular phase because during that time in the cycle many follicles are being stimulated, predominantly by FSH, to become Graafian follicles, which will contain a mature egg. One of those follicles is usually selected midway through the first half of the menstrual cycle. In the early part of the luteal phase, or second half of the menstrual cycle, the follicle gives up its mature egg. At the time of ovulation, the mature egg and many cells near the egg are extruded from the Graafian follicle. The remainder of the Graafian follicle changes its function and becomes a tiny endocrine organ known as the corpus luteum. The corpus luteum secretes several different steroids that help prepare the lining of the uterus for implantation, should the egg be fertilized during that cycle.

If fertilization, or conception, does occur, the corpus luteum will continue to synthesize and secrete steroids for maintaining pregnancy for the first four to six weeks. The function of the corpus luteum is supported by another glycoprotein hormone secreted by cells destined to become the placenta. That hormone is human chorionic gonadotropin (hCG), which has a biologic function indistinguishable from that of its pituitary counterpart, luteinizing hormone (LH). Although hCG is present throughout pregnancy and tenfold higher in the first third of pregnancy, a function of hCG during other parts of pregnancy is unknown.

One portion of the hCG molecule has been used to develop a specific pregnancy test (usually called the beta-subunit assay). Before the assay was developed, a woman had to wait several weeks after she missed her period to be sure she was pregnant. With the beta-subunit assay, her pregnancy can be diagnosed several days before she misses her next period.
“Dancing Couple: Green Version” by Oskar Kokoschka (1886–1980);
Courtesy, Museum of Fine Arts, Boston/Bequest of Mrs. Sarah Reed Blodgett Platt.
months.

Infertility and sterility are two different conditions. Infertility is defined as the inability of a couple to conceive but with the potential for doing so if certain abnormalities are corrected. For most couples, the problem is failure to conceive. For a smaller number of couples, infertility is due to repeated pregnancy losses, or miscarriages. Sterility, in contrast, is the unrectractable inability of a man or woman to conceive.

Fertility is affected by many factors: the woman's age, the man's age and the timing of sexual intercourse are primary concerns. Fertility is greatest in women at approximately age 24, declining gradually until age 30 and then declining rapidly. Fertility is greatest in men at about the same age, but declines more slowly with age than for women.

To be fertile, sperm and egg must have ample opportunity to meet. The man must be able to produce motile sperm in sufficient number. Sperm must be motile and freely ejaculated. The woman must produce a normal and fertilizable egg (ovum) which enters the Fallopian tube shortly after being released by the ovary. Finally, sperm must be deposited in the vagina, be able to penetrate the cervical secretions, to ascend through the uterus to the Fallopian tube, where it fertilizes the egg. A great variety of mechanical and chemical features must cooperate to enhance the likelihood that sperm and egg will meet. Similarly, a great number of factors can individually or in concert interfere with this normal process.

In addition to individual physical and physiological impairments, many occupational and environmental conditions adversely affect fertility. Larry Ewing of Johns Hopkins School of Public Health (Baltimore, Maryland) has found that male rats exposed to high doses of lead in their drinking water showed a sharp drop in their ability to produce testosterone. Current tests for toxic effects of lower doses of lead on the reproductive tracts of men working in jobs that expose them to high levels of lead may not be sensitive enough.

When both the man and woman receive complete medical evaluations, 30 to 40 percent point to the woman alone; and 20 to 30 percent to a combination of factors involving both man and woman. Approximately 20 percent of the fertility problems have no detectable cause.

Improved knowledge of the male and female reproductive systems has increased the success rate in diagnosing and treating infertility problems.

Disorders of the menstrual cycle

MANY FACTORS CAN DISTURB A woman's normal menstrual cycle. In addition to pregnancy, illness, drugs to treat high blood pressure or anxiety, and high prolactin levels can also disrupt the cycle. Perhaps the most surprising is exercise.

Recently it has become fashionable for men and women to jog long distances, to do intensive aerobic workouts and to play strenuous sports. Any activities that result in intense physical conditioning can lead to irregular or absent menses. Some women, in fact, will jog up to 30 or 40 miles per week just to avoid the intense cramping of dysmenorrhea they usually experience with their periods.

When women with exercise-induced amenorrhea discontinue the physical activity, they get their period again unless other factors have arisen. If, for example, they have lost a great deal of weight because of their exercise program, if their nutrition is poor or if they are using too much marijuana or alcohol, women can upset the ability of their ovaries, pituitary and hypothalamus to produce the hormones that control ovulation and menstruation.

Women who stop having periods for a prolonged time, for whatever reasons, may develop thinned bones (osteopenia). The condition usually is due to decreased content of bones (osteoporosis), resulting from decreased calcium in the diet. It has been thought that jogging protected women from this problem because the constant stimulation to bone would strengthen it. Recent research contradicts the belief, showing that women who

The Menstrual Cycle

The flow of hormones during the 28-day menstrual cycle is illustrated in the accompanying chart.
Where is the male birth-control pill? Researchers are still working to provide answers to the question long posed by feminists and population experts. But a male birth-control pill has yet to materialize.

Why? Some feminists charge that birth-control is still widely perceived as the woman's problem and that insufficient federal and private funds are being allocated for male contraceptive research. The drug companies that produce the female pill maintain that a male counterpart would not sell, and only one company has ever launched an inquiring research project. The biological problem is that the male reproductive system makes it difficult to chemically block or inhibit sperm, in part because millions are contained in ejaculation. In addition, chemical birth-control methods may damage sperm but do not destroy it completely, which could result in a damaged embryo.

Still, a breakthrough may be in sight. Clinical trials have been initiated on several possible male contraceptives, although all are far from general use. The only promising drug now in pill form is gossypol, a yellow pigment derived from cottonseed. The compound, which suppresses enzymes in the sperm and testes, was discovered when scientists linked high incidences of sterility among Chinese peasants with widespread consumption of cottonseed oil. Tests on 10,000 Chinese men revealed that small daily dosages of the drug produced a 99 percent efficiency rate. Side effects, however, ranged from weakness and nausea to reduced libido and potassium levels. The Chinese tests also indicated that gossypol might not be completely reversible. About 20 percent of the men who took the drug for more than a year failed to regain fertility. A number of U.S. laboratories are now conducting preliminary testing of the compound on rats and other animals before conducting experiments on volunteers.

Another possibility is LHRR, a hormone produced by the brain that signals pituitary gland hormones regulating the production and release of testosterone. Although the drug can presently only be administered by injection, research shows that administration of LHRR, or a chemical copy, temporarily and safely blocks sperm production. But side effects include reduction of sexual drive and secondary sex characteristics such as body and facial hair.

Last year a male contraceptive in the form of a hormone salve was introduced by Larry Ewing, a reproductive biologist at Johns Hopkins University. The substance is designed to be rubbed on the stomach and carries testosterone and estradiol, an estrogen found in small quantities in men, to the bloodstream. Testosterone and estradiol normally become concentrated in the blood when the testes have produced enough sperm, after which the hypophysal arms stops sperm production. The hormonal components of the salve “trick” the brain into the same response, without inhibiting sex drive or secondary sex characteristics. After a decade of animal experiments, Ewing has applied to the federal Food and Drug Administration for permission to test the salve on humans.

CHERYL COLLINS

The Search for a Male Contraceptive

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CHERYL COLLINS

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Reproductive disorder

POLYCYSTIC OVARY SYNDROME (PCO) occurs in an estimated 3.5 to 7 percent of women during their reproductive years. Its clinical manifestations vary considerably. When it was first identified, PCO was characterized by its most dramatic manifestations. Women had hair growth like a man's, were obese, amenorrheic and had enlarged ovaries with multiple fluid-filled sacs (cysts). Physicians now know that PCO can be much more subtle. Most women with PCO are not overweight, do not have flagrant excessive hair growth and do not have enlarged ovaries.

In some cases, the clinical manifestations of PCO can be so mild that the woman seeks no medical help. Many women with PCO may have regular menstrual cycles, but most of the menstrual cycles are abnormal in that a mature, potentially fertilizable ovum is not developed. Until she attempts to conceive and has difficulty doing so, a woman may not realize she has PCO.

Many women with PCO complain of intense premenstrual symptoms of bloating, fatigue, emotional lability and headache. Some women may be hirsute and overweight but can improve with weight reduction, reducing the percent of body fat. Usually, the excess fat is not the primary cause of the disorder. But in some obese women, the excess fat can be responsible for converting precursors to androgens, resulting in excess hair and menstrual disorders. In approximately 30 percent of women with the syndrome, low-dose glucocorticoids given at night significantly suppress the amount of androgens produced. If the woman wants to be fertile, she can take the antiestrogen clomiphene (Clomid or Serophene) to induce stimulation of the ovary indirectly.

MANY WOMEN COMPLAIN OF DECREASED
libido around the time of menopause. Estrogens play no role in libido.

exercise excessively and develop amenorrhea also may develop osteoporosis.
Menopause

WOMEN REACH MENOPAUSE in well-developed countries sometimes in their mid-50s. For reasons not entirely clear, the age of menopause has been slowly getting later in life. Permanent cessation of menses as a result of no functional follicles remaining in the ovary is a signal for the completion of the reproductive years of a woman’s life. At the time of birth, the ovaries are endowed with several million eggs within follicles. The follicles undergo progressive atresia or involution throughout the lifespan, even before the onset of the first spontaneous period, or menarche. Only a very small fraction of those eggs are ever fully matured to become fertilizable. During each menstrual cycle, many follicles are initially stimulated but usually only one is chosen to develop to a mature Graafian follicle capable of setting free a mature egg that can be fertilized. Even when women stop having menses for whatever of a variety of reasons, the process of atresia continues. Very little is known about it, however.

The mechanism of hot flushes is also poorly understood. It has something to do with changing estrogen levels. The symptoms can be corrected by giving replacement estrogens but may also be corrected by giving progestins or a drug that affects the sympathetic nervous system.

Women also lose bone mass during menopause. Several factors are responsible for the bone changes—decreased calcium in the diet, as well as decreased estrogen production. Estrogen protects a woman’s bones from losing calcium. But estrogen alone may not be adequate to protect women from osteoporosis.

Many women complain of decreased libido around the time of menopause. Estrogens play no role in libido. It is androgen, which is predominantly secreted by the adrenal gland in women, that is responsible for sex drive and not estrogen.

Premenstrual syndrome

MOST WOMEN EXPERIENCE SOME discomfort during their menstrual cycles. Some women are uncomfortable before their period (premenstrual distress) and others are uncomfortable during or after their periods (dysmenorrhea). Despite the great public attention paid to the Premenstrual Syndrome (PMS), dysmenorrhea is by far the more common problem. In fact, dysmenorrhea is the most common gynecologic complaint. An estimated 52 percent of all postpubescent females are affected by dysmenorrhea; about 10 percent of this group is so severely affected that they are incapacitated. In the United States, dysmenorrhea costs young women 140 million lost days from work and school per year.

PMS and dysmenorrhea are two different conditions with quite different underlying mechanisms. For one thing, the two conditions are differentiated on the basis of when they occur. PMS occurs during the luteal phase of the menstrual cycle, when the corpus luteum is functioning and if conception doesn’t occur, its function ceases before the onset of the next cycle. Thus PMS is the result of changes occurring in the second half of the menstrual cycle. Dysmenorrhea occurs in the early follicular phase, when follicles are being stimulated and sex steroid levels are low. It is becoming increasingly clear that dysmenorrhea is the result of the effects of prostaglandins on the muscles of the uterus, causing them to contract in spasms.

Some discomfort is normal and unavoidable. But women differ in their physi-

THE STANDARD DEFINITION OF PMS IS A cyclic occurrence of symptoms that is sufficiently severe to interfere with some aspects of life and which appears with a consistent and predictable relationship to the menstrual cycle.

PMS

The graph represents the relationship between age and premenstrual tension (Hargrove and Abraham, 1982).
BECAUSE MOST WOMEN IN THE UNITED
States and Great Britain are bothered by some
premenstrual cramps, backaches, headaches, irrit-
ability, mood swings, tensions or depression, a
major industry has developed around providing
drugs, psychotherapies and other aids.

Symptoms of
dysmenorrhea

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percent in women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower backache</td>
<td>60</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>89</td>
</tr>
<tr>
<td>Diarrhea or loose stool</td>
<td>60</td>
</tr>
<tr>
<td>Headache</td>
<td>45</td>
</tr>
<tr>
<td>Tiredness</td>
<td>85</td>
</tr>
<tr>
<td>Nervousness</td>
<td>67</td>
</tr>
<tr>
<td>Dizziness</td>
<td>60</td>
</tr>
</tbody>
</table>

Source: O. Ylikorkala and M.Y. Dawood,
New Concepts in Dysmenorrhea. American
Journal of Obstetrics and Gynecology, 1 April

For approximately 10 percent of women
who experience severe psychological and
physical discomfort for the several days
before menstruation, the problems of Pre-
menstrual Syndrome (PMS) may be a
regular and recurring nightmare. And for
some proportion of that group, the pre-
menstrual phases of the cycle may be
associated with acute psychiatric illness,
medical and surgical problems, industrial
and other accidents, violence directed at
self and others and profound depression.
PMS is a real condition. It might even be
a normal part of the menstrual cycle for
some women. But the discomforts of
menstruation follow a continuum. Some
women are discomforted more than oth-
ers. The abnormal part of PMS is the
physical and psychological reaction to the
discomfort. Some women have extreme
discomfort and extreme reactions to their
discomfort. This is PMS.

Only a decade ago, dysmenorrhea was
so poorly understood that many phy-
sicians sent women complaining of
menstrual distress to a psychiatrist for
treatment of their “neurosis.” Today, with
the role of prostaglandins recognized,
women are treated for their physiologic
disorder. PMS is now where dysmenor-
rhea was a decade ago.

Researchers know little about the
causes and treatment of PMS. There is
some considerable controversy, in fact,
moderate symptoms of the sensation of
weight gain, swelling, tender breasts and
bloating; eight percent reported “severe”
symptoms.

These symptoms are reported in many
studies; but the findings of other studies
are often confused by the simple fact that
the reported severity of symptoms changes
with age. Hargrove and Abraham, for
instance, found that younger and older
women were less likely to report signifi-
cant premenstrual tension than women in
the age group 30 to 40 (see accompanying
chart).

Several questionnaires have been used
to measure the degree of premenstrual
distress [see Moos Menstrual Distress
Questionnaire, 1968; Steiner adaptation
of Moos, 1980; Abraham, 1980; Hal-
brecht, Endicott et al., 1982]. The ques-
tionnaire constructed by Halbrecht, Endi-
cott and colleagues is considered the best
because, unlike the other questionnaires
in use, the Halbrecht-Endicott question-
naire does more than simply list symp-
toms and ask for a yes/no response. This
questionnaire focuses on the degree of
change from customary levels of feeling,
acting and so forth. The presence or
absence of symptoms characteristic of
PMS is important; but simply having the
symptoms is not a clear sign of the condi-
tion itself. As Judith M. Abplanalp has
written, it is necessary to study:

• The number and combination of particu-
lar symptoms;
• The severity of the symptoms;
• The timing of the symptoms with the
menstrual cycle;
• The age of the woman; and
• The validity of the information about the
symptoms.

Hormone
imbalances

THERE ARE MANY POSSI-
BLE explanations of PMS. The most com-
mon theories explain the symptoms of
PMS by imbalances in the hormones that
control menstruation. Estrogen is one
candidate to examine because, in the
normal menstrual cycle, estrogen levels peak
during ovulation (midway through the
cycle) and during the luteal phase (about
day 21). The other major hormone in
menstruation—progesterone—is secreted
near the middle of the cycle and reaches
its highest concentration about days 21 to
24. The hormonal situation is compi-
lcated. Estrogen is secreted throughout a
woman’s cycle but at different levels; and
for the latter part of the cycle, estrogen and progesterone are both secreted. At the end of the cycle, if pregnancy does not occur, both estrogen and progesterone levels fall abruptly.

It has been recognized for many years that both estrogen and progesterone affect brain function and behavior. Experiments have shown that estrogen can lower seizure thresholds and thus make the central nervous system more susceptible to overwhelming stimulation. Megadoses of progesterone, on the other hand, raise seizure thresholds. Large doses of progesterone, in fact, can produce sedation and even general anesthesia. Researchers have found that women during the premenstrual phase, as progesterone levels are rising abruptly, report that they cannot concentrate as clearly. In experimental settings, women show changes in their time perception and visual perception.

Other hormones may also play a role in PMS: for the endocrine system is connected in such ways that changes in one hormone will almost necessarily effect changes in others. Likely candidates in PMS are aldosterone and prolactin. Aldosterone and angiotensin, for example, control water balance in the body and may well be part of the explanation of the bloating and swelling associated with premenstrual distress in many women. There is a well-known relationship between changes in progesterone and levels of aldosterone.

The hypotheses relating progesterone, estrogen, prolactin and aldosterone to the several symptoms of PMS and premenstrual tension are logical. The only problem is that studies have not unequivocally borne them out. Of 10 studies of the relationship of progesterone to PMS, five showed lowered progesterone in the mid-to late-luteal phase, one showed generally low progesterone throughout the cycle, one showed elevated progesterone in the mid-luteal phase, and three showed no abnormal progesterone levels at all. Of the nine estrogen studies, four showed elevated estrogen during the late luteal phase, one showed a clear relationship between estrogen levels and irritability, and four showed no abnormalities in estrogen levels. No studies of prolactin have shown significant differences between normally menstruating women and women suffering symptoms of PMS. Aldosterone studies likewise have shown no specific differences in women suffering PMS.

There is some evidence that the critical factor is not the absolute amount of estrogen or progesterone circulating in the blood but rather the ratio of the progesterone to estrogen levels. Estrogen may have a stimulating (adrenergic) effect on the central nervous system (perhaps by inhibiting brain monoamine oxidase), progesterone may counteract this stimulating effect, or prostaglandins may stimulate muscle contractions of the uterus and provoke changes in the central nervous system.

The answer is not yet clear. Nonetheless, studies of PMS may help explain the profound relationship between chemical balances in the body and thinking and behavior.

The relationship among hormones, the brain and behavior is still a mysterious one. There is some evidence that changes in gonadal steroid hormones may cause changes in endogenous opioid peptide activity [R.L. Reid, Lancet, 1 October 1983, 786]. The drug naloxone, an antagonist for opioid receptors in the brain, apparently raises levels of luteinizing hormone normally suppressed by opioids during the luteal phase and late follicular phase, but not in the early part of the menstrual cycle. In monkeys, at any rate, levels of beta-endorphins in the pituitary portal circulation peak during the luteal phase and are undetectable at the onset of menstrual bleeding.

Another hypothesis is that changes in brain levels of serotonin and GABA are affected by feedback from the estrogen system. This disturbance in serotonin, an important neurotransmitter in the central nervous system, may account for the anger, aggression and suicidal thinking that may accompany PMS.

### Treatment of PMS

**THERE ARE FEW GOOD studies of response to different treatments of PMS. The only two double blind, placebo-controlled, cross-over studies with progesterone treatment show negative results. Results with synthetic progesterone are unclear. Treatments with bromocriptine, lithium carbonate, pyridoxine (vitamin B6) and diuretic agents have all shown promise but no conclusive evidence. Treatment with mefanamic acid, which inhibits the synthesis of prostaglandins, is another possibility but not yet proved.**

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**PMS as a Legal Defense**

Millions of women experience varying degrees of aches, pains and mood swings prior to menstruation. Extreme cases of premenstrual syndrome, or PMS, have received a great deal of attention from the medical community. But doctors and patients aren't the only ones interested in the latest PMS developments. Recently, lawyers have used the condition as a possible defense against violent crimes, and won.

PMS first went on trial in 1981 when English barmian Sandie Smith was convicted of stabbing a co-worker but received probation after convincing the judge that she suffered from PMS. That same year, again in Great Britain, Christine English was permitted to plead guilty to manslaughter instead of murder, on the grounds of “diminished responsibility” resulting from PMS, which caused her to run over her lover.

The following year, the escalating controversy surrounding PMS and the law moved to the United States. In Brooklyn, lawyer Stephanie Benson argued that child-beating charges against her client, Shirley Santos, should be dropped because Santos suffered from PMS. In defending Santos, Benson maintained that the mother blacked out during a severe PMS attack and was unaware of her actions. The PMS claim was later dropped and Santos instead pleaded guilty to harassment, in return for criminal charges being dropped. But the new legal dimension focused even more public attention on the syndrome's symptoms and treatment.

The legal cases helped publicize the legitimacy of the medical aspects of premenstrual stress, which to some degree affects an estimated 60 percent of all women. Most commonly, the monthly hormonal imbalance during the menstrual cycle may trigger mild to severe headaches, backaches, bloating, tension and depression. Physicians maintain that severe cases occur much less frequently, and of the women who may experience deep depression or rage, few can be drawn to violence.

Despite the importance of recognizing PMS as a health issue, feminists point out that using PMS as a defense for crime only serves to strengthen the false notion that women are driven by their biological processes and are irresponsible for their actions. Additional doubts have been expressed within the legal community since successfully using PMS as a complete defense for crime not only requires proving that the syndrome is a recognized illness and that the accused actually suffers from it, but that a definite link between the disease and the action can be shown. Many believe that until more is known about PMS, legal cases may be premature.

CHERYL COLLINS
Although endocrinology is a highly specialized science, everyone should know about

HORMONES

A Consumer’s Guide

THE VAST POWERS

OF MODERN ENDOCRINOLOGY, DEVELOPED FOR THE MOST part within the past decade, introduce the possibility of new and powerful hormonal control over mind and body. These new powers pose social, medical and ethical dilemmas. Birth control is, perhaps, the most obvious; but it is only one of many.

The endocrine system is involved in virtually every function of the mind and body. Major life events are orchestrated by the endocrine system—birth, growth, puberty, fertility cycles, pregnancy and, to some extent, sexual arousal and many other reproductive processes. In addition, disturbances in your hormone balance can upset how you think, feel and act. How we feel, our sleeping, eating, mobilize stored fat for energy and more, are also partly controlled by hormones.

How much of our behavior and feelings is determined by hormones is still an open and hotly debated question. Medical disorders of the hormone system are often accompanied by psychological disorders. But not always. We also have a brain that, although closely connected to the endocrine system, is separate from it. And that brain is a powerful organ capable of regulating how other organs of the body work, including the endocrine system. For, as we have seen, the brain secretes hormones of its own that directly and indirectly regulate secretions of the endocrine glands.

Scientists have devised many uses of hormones and chemicals to change or correct how the hormone system works. Physicians have recently learned a great deal about how the exogenous (from outside...
the body) hormones and hormone-like substances can be used to treat diseases. Infertility, hypertension, growth disorders, asthma and other inflammatory diseases and many more, are now routinely treated with hormones.

Knowing when to seek endocrinologic help and how to find it have become major problems for the consumer. In part, the problem is caused by the sheer complexity of the field. Endocrinologic problems are not immediately obvious, not to the lay person and not even to the physician. It takes special training and, perhaps, a special kind of imagination to understand the mechanisms of endocrinologic problems and how to treat them. The general surgeon who must set a broken bone knows that he must work on that bone, align it properly and set it so that it will heal normally. The physician treating a strep throat knows that he must give the patient the right antibiotic to control the growth of streptococci in the throat. As in the case of the broken bone, the physician can see the simple relationship between the problem and the cure.

The endocrinologist, on the other hand, must often work two and three times removed from the source. The problem may appear as disturbances in the menstrual cycle, but the problem can be in the pituitary. The problem may appear as male infertility, but the problem may be due to emotional or physical stress, heat, radiation, drugs, infection, obstruction of the vas deferens, mumps or a variety of ejaculatory problems due to disturbances in the nervous system or endocrine system.

How much of our behavior and feelings is determined by hormones is still an open and hotly debated question.

Where to go for help is therefore a major problem. For years, women have gone to their gynecologists for reproductive and menstrual problems. Often, however, the gynecologist, who is trained for the most part as a surgeon, minimizes the endocrinologic aspects of the disorder. Women complaining of dysmenorrhea, for example, were usually treated with a dilation and curettage (D and C) in which the lining of the uterus is scraped. Often this procedure is called for and is effective. Oftentimes, however, it is not, but it is the conventional, non-endocrinologic treatment. Likewise, men have sought the attention of urologists for a variety of male reproductive disorders. Urologists, like gynecologists, are also trained as surgeons, and not as endocrinologists.

If the problem is an organic defect, surgery helps. If the problem is functional, only treatment that remedies the dysfunction will help.

Reproductive endocrinology is a new field of internal medicine. There are few training programs and few specialists. Finding appropriate care is difficult. The difficulty is that medical specialties are usually defined by parts of the body. And who does a woman consult whose pituitary tumor is disrupting her normal menstrual cycle? a gynecologist? a neurosurgeon? In many medical centers, she is treated by a team, including a reproductive endocrinologist.

New types of birth control

RESEARCH IN ENDOCRINOLOGY is also coming up with several new approaches to birth control, new treatments of old, baffling disorders and deeper understanding of how the system works.

Modifications of gonadotropin-releasing hormone (GnRH) are currently under investigation as potential agents for contraception in men and women. Different modifications of the ten-amino acid molecule (polypeptide) have been made so that GnRH either works like the native GnRH, that is, it acts as an agonist, or on the other hand, other modifications have been made so it works as an antagonist, in that it will bind to GnRH receptors on the pituitary cells and block the action of GnRH formed within the hypothalamus and delivered to the pituitary. Unfortunately, although GnRH agonists significantly decrease spermatogenesis, they do not totally inhibit spermatogenesis. In addition, they decrease testosterone secretion significantly.

It appears, therefore, that the currently available agonists will not be effective contraceptives for men. The decreased testosterone production by Leydig cells as a result of decreased endogenous LH secretion can be overcome by administering long-reacting forms of testosterone to men. But since spermatogenesis is not totally stopped, current GnRH agonists are not sufficiently effective as contraceptives.

In women, on the other hand, GnRH agonists can affect the cyclic release of gonadotropin and formation of the mature Graafian follicle with a mature, fertilizable egg. Cessation of menses or anovulatory cycles may be induced with the GnRH, but it is unclear whether untoward side effects observed on a long-term basis (over several years) will create a problem among women receiving the GnRH agonist. Studies with the GnRH antagonists are not sufficiently far along to evaluate their potential for use as contraceptives.

Other forms of contraceptive agents are currently undergoing evaluation. Chinese investigators had observed that an extract of cotton oil, gossypol, resulted in significantly decreased gonadal function. Unfortunately, in preliminary studies carried out in the United States, untoward side effects have been observed in the liver and other organs of the body. Studies are currently focused on attempting to identify the active agent with gossypol in hopes that it is free of side effects and will nonetheless be an effective contraceptive.

Another form of contraceptive therapy currently being investigated, especially in lesser developed countries, is long-acting forms of progesterone-like hormones (progestins). An implant of the progestin is placed under the skin with a specially designed needle and the progestrone is continuously released. Those implants can be designed to deliver progestins for at least a year. There are many organizations undertaking systematic studies of both gossypol derivatives and progestins. These are being directed primarily by the World Health Organization and the Population Council at Rockefeller University in New York.

Finally, another potential form of con-
traception in women has been under investigation for many years, primarily in lesser developed countries. A vaccine which results in the generation of an antibody to the specific subunit of hCG, the hormone created in large amounts by the developing placenta, or conjugated to tetanus toxoid or some other carrier protein has been termed a "pregnancy vaccine." Unfortunately, one has little control over the generation of the kinds of antibodies produced or the binding strength with which those antibodies will take up hCG. Animals immunized with a similar approach usually will abort within the first several weeks of pregnancy. Similar observations have been made in women immunized with the "pregnancy vaccine." However, the role of the vaccine in population control is still unclear even though studies of the vaccine's potential have been going on for more than a decade.

TREATING INFERTILITY

Hormone problems come into fashion from time to time as the popular press takes special notice of them. Menstrual disturbances are now topical. In the past, thyroid or adrenal hormones held the public's interest.

Can you recognize the problem?

A young woman college student is a track and field star at her university. During high school and her first year of college, she trained for the long-distance runs. In her second year of college, she was picked as a candidate for the Olympic team and she began intensive physical training, running an average of 60 miles a week. Some weeks she trained even harder. Until beginning the intensive training program, her periods had been regular; but when she started the more rigorous training program, her periods became irregular and then stopped entirely. Should she assume that her amenorrhea is caused by her strenuous exercise program and ignore the symptoms until after the Olympic games?

A. Yes
B. No

Answer: No. The overwhelming probability is that this young woman is experiencing exercise-induced menstrual dysfunction, induced by her rigorous physical conditioning. When she stops training so hard, she will almost certainly resume her normal cycling. However, her menstrual change may or may not be due to the exercise. She may have lost so much weight or changed the composition of her body as a result of her training that she will not resume normal cycling until she regains the weight or former composition. In this case, she should pay close attention to her diet, being sure that she gets enough calories in her diet to gain the lost weight. It is also important to make sure that she does not have an endocrine abnormality at the same time her physical conditioning is disturbing her hypothalamic control of her menstrual pattern. The symptoms of abnormal prolactin secretion and hypothalamic disturbance may be the same, but the treatment is quite different.
process of in vitro fertilization is about $5000. Because these fees are not covered by most health insurance plans, the couple must pay most of the large fee. The success rate with this technique varies from center to center and, at best, is 25 to 30 percent. But most centers probably have a success rate around 15 to 20 percent. By inducing multiple ovulations, the success rate has been increased. This technique is really nothing new since it had been done for many years in animal husbandry. However, its application in people is new.

Radio, television, newspapers and magazines announcing the latest medical marvels to the lay audience frequently describe new techniques being developed in the United States and throughout the world. Unfortunately, the information is not always presented in the appropriate perspective and creates false hope for many patients. On the other hand, the lay press frequently focuses a patient’s attention on problems that might otherwise go unnoticed.

**Other uses of GnRH**

In some cases, young boys and young girls begin the processes of puberty too early and have a clinical syndrome referred to as precocious puberty. When that process is initiated by centers within the hypothalamus, GnRH agonist therapy appears to be relatively effective in significantly decreasing gonadotropin released by the pituitary and subsequent stimulation of the ovary or testis. This form of therapy appears to be effective for at least a few years in affected children; but whether its therapeutic effect can be maintained over a long period of time and whether there will be any long-term side effects is unknown.

The treatment is still so new that patients simply have not been followed for enough time for investigators to learn the long-term effects of GnRH therapy. The use of GnRH analogs is important in this syndrome because young girls and boys undergoing (precocious) puberty develop secondary sexual characteristics typical of adults. Since sex steroid concentrations increase, the growing portions of the end points of the bone have a shorter growing time and result in significantly shorter stature among affected young girls.

Long-acting GnRH agonists are currently undergoing evaluation in men with metastatic prostatic cancer. Using the GnRH analogs makes unnecessary the present conventional treatment of removing the gonads in men, which are the major source of androgens in men which, in turn, usually stimulate the growth of cancer cells that are dependent on sex steroids. The advantage of this form of therapy is that it is not associated with the usual side effects of traditional chemotherapy, which affects the bone marrow and other organ systems in the body. That form of therapy is also accompanied by nausea, malaise and other debilitating effects.

**CONCLUSION**

Media announcements of the latest medical techniques concerning hormones often present the material in the wrong light and create false hope for many patients.

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**Consumer beware**

The rapidity with which new approaches to diagnosis and understanding disease processes takes place frequently does not reach the nonspecialized physicians as rapidly as one would wish. Moreover, when some physicians poorly understand the manifestations of some endocrinologic abnormalities, the patient’s complaints more readily suggest psychological disturbances than physiological ones. Often these physicians refer their patients with baffling symptoms to psychologists and psychiatrists when, in fact, they should be sending them to endocrinologists. Patients who have abnormal calcium metabolism or excess cortisol production are frequently also depressed or have otherwise abnormal behaviors. The symptoms are totally reversed when the underlying endocrinologic abnormality is corrected.

Hormone problems come into fashion from time to time as the popular press takes special notice of them. Menstrual disturbances are now topical. In the past, thyroid or adrenal hormones held the public’s interest.

If you feel healthy, strong, relatively undaunted by life’s stressors and if when you want one, you are able to conceive a child, your endocrine system is probably serving you well.
Hormones: The Invisible Messengers is one of Bostonia Magazine's In-Depth issues designed to serve as a family resource and guide to leading a healthy and productive life. The In-Depth series was initiated six years ago with the publication of What's Your Risk: A Layman's Guide to Cardiovascular Disease. That issue, based on research directed by Dr. Aram V. Chobanian, director of the Boston University Cardiovascular Institute, and a team of doctors working on the Framingham Heart Study, was subsequently published by Bantam Books as The Heart Risk Book.

Bostonia's second In-Depth issue, Stress: What Can Be Done? featured research from the Division of Psychiatry at Boston University's Medical Center. In that issue, Dr. Sanford Cohen, chairman of the Division of Psychiatry, and Lyle Miller, chairman of the Department of Biobehavioral Science, identified stressors and methods that may help reduce the physical and psychological burdens created when stress is not managed properly. Since its publication, the stress issue, co-authored by science writer Robert N. Ross, has been referenced in daily newspapers, weekly news magazines and the national media.

Most recently, Bostonia published Nutrition: In An Age of Affluence, written by Ross and Dr. Joseph Vitale, professor of Pathology and Community Medicine and associate dean for International Health Programs at Boston University School of Medicine. The Nutrition issue, like those preceding it, presented research that outlined dietary requirements for good health and identified ways to maintain a lifestyle that promotes well-being.

In-Depth issues on Nutrition and Stress have been purchased by individuals across the country, many of whom are teachers or administrators of facilities concerned with health.

Hormones: A Guide to the Body's Communication System, is Bostonia's most ambitious project to date. Much of the material presented in the preceding pages has never been published for a non-medical audience. This material can be used as a foundation on which to understand the latest scientific breakthroughs concerning hormones and reproduction that are being publicized almost daily. An expert in a brand-new medical specialty, Dr. Judith Vaitukaitis, is truly a natural resource. Her depth of knowledge and research acumen is well-known in the medical arena. The science of endocrinology, the study of the body's internal secretions, is advancing as quickly as the technology that supports it. Future In-Depth issues will focus on other areas of medicine as well as research in the social sciences that is central to our understanding of ourselves and to the world we live in.
About the writers

JUDITH L. VAITUKAITIS, M.D., is professor of Medicine and Physiology at Boston University School of Medicine. She is also the program director for the General Clinical Research Center at BUMC and the head of the section of Endocrinology and Metabolism at Boston City Hospital. A graduate of Tufts University and BUMC, Vaitukaitis served as a senior investigator, medical officer and attending physician for the National Institute of Child Health and Human Development, NIH, before joining the Boston University faculty in 1974. She has authored numerous research articles and abstracts and published the book Clinical Reproductive Neuroendocrinology in 1982. She sits on the editorial boards of several publications including Endocrine Research and is a member of numerous professional organizations.

ROBERT N. ROSS, PH.D., is a medical and science writer living in Cambridge, Massachusetts. He attended medical school and holds a doctorate in literature, has done medical research and writes about science and medicine for both professional and general audiences. Ross has written books on penicillin, allergy and immunology, language and psychiatry and prison medicine. Ross is a graduate of Williams College, Cornell University and a post-doctoral fellow of the Boston University School of Medicine training program for research in psychiatry. He has taught at the University of Pennsylvania and University of California at Irvine and has served as director of the Boston University Graduate Program in Science Communication.

Glossary

ACTH/adrenocorticotropin hormone:

(ad = to + ren = kidney + cortico = outer covering or bark + tropic = having effect on) Pituitary hormone controlling production and release of stress hormones by the adrenal cortex.

ADH/antidiuretic hormone:

(anti = against + diuretic = excretion of water from body in urine) Pituitary hormone that controls water balance by regulating excretion of water in urine.

agonist:

(agon = contest) A drug that can combine with receptors on cells and exert a biological effect.

amennorhea:

(a = negative + men = month + rhoea = flow) Absence or abnormal stoppage of menses.

androgen:

(andro = man + geman = to produce) Any agent, usually a hormone, that stimulates activity of male sex organs or encourages development of male sexual characteristics.

antagonist:

(anti = against + agon = contest) A drug that works against the action of another drug.

atresia:

(a = without + tresis = hole) Destruction of ovarian follicle without perforation and release of an egg.

autonomic nervous system:

(auto = self + nomos = law + nervous system) Part of the nervous system that normally functions outside deliberate, conscious control and which directs such functions as breathing, digestion, heart rate and release of certain hormones. The autonomic nervous system is divided into two branches. The SYMPATHETIC nervous system prepares the body for vigorous action to adapt to stressful situations. The PARASYMPATHETIC nervous system controls life-sustaining organs of the body.

chromosome:

(chromo = color + soma = body) A threadlike body in the nucleus of animal cells containing DNA, that transmits genetic information.
climacteric:
(klimakter = rung of a ladder, critical point in a person's life) The cluster of endocrine, bodily and psychological changes that accompany the end of a woman's and perhaps a man's reproductive period.

catecholamines:
(catech = East Indian shrub from which an astringent substance is isolated = amine = an organic chemical compound containing nitrogen) A class of chemicals, notably EPINEPHRINE and NOREPINEPHRINE produced by the body and found elsewhere, capable of stimulating the sympathetic branch of the autonomic nervous system.

cortex:
(cortex = bark) The outer covering of a gland or the brain.

decrionic:
(endo = inner + crine = to separate) Pertaining to organs and structures that secrete internally, directly into the blood stream and without ducts.

derphiin:
(endo = within + orphin = morphine-like) A class of morphine-like substances first isolated from the brain but now found in many parts of the body, responsible for complex roles in pleasure and pain.

enkephalin:
(en = within + kephalo = head) Chemical substance in the brain involved in the sense of pain.

enzyme:
(en = in + zyme = leaven) A protein capable of facilitating chemical reactions in the body without itself being changed in the process.

epinephrine:
(epi = upon + nephros = kidney) Catecholamine produced by the adrenal medulla to increase the heart rate, relax smooth muscle of the airways and contract smooth muscle of the blood vessels.

estrone:
(oistros = any vehement desire + gennan = to produce) Any agent, usually a hormone, that stimulates activity of the female sex organs or encourages development of female sexual characteristics.

FSH/follicle stimulating hormone:
(Pituitary hormone that helps regulate maturation of the Graafian follicle in the female and in the male helps stimulate the production of sperm.

gene:
(gennan = to produce) The biologic unit of heredity, self-reproducing and located at a definite position on the chromosome.

GH: growth hormone:
(Hormone secreted by the pituitary that promotes body growth, mobilizes fat and inhibits utilization of glucose.

gland:
(glans = acorn) A secreting organ.

gonad:
(gone = seed) An organ that produces sex cells: ovary in female and testis in male.

Graafian follicle:
(Reijnier de Graaf (1641–1673), Dutch microscopist + follicle = small sac) Small structure in ovary within which egg matures.

hormone:
(hormaein = to set in motion) A chemical substance formed in one organ or part of the body and carried in the blood to another organ or part and capable of altering the functional activity or structure of the target organ.

hypothalamus:
(hypo = below + thalamus = bridal chamber) Portion forming the floor of the brain responsible for controlling endocrine activity, autonomic functions and regulation of such bodily functions as water balance, body temperature, sleep, food intake and the development of secondary sexual characteristics.

Leydig cell:
(Franz von Leydig (1821–1908), German anatomist) Also called interstitial cells of the testis, believed to secrete the male sex hormone testosterone.

LH/luteinizing hormone:
(luteus = saffron-yellow) Hormone that stimulates the final ripening of the follicles in the female and stimulates interstitial cells in male to produce testosterone.

menarche:
(men = month + arche = begin) The time of the first menstrual period.

menopause:
(men = month + pausis = cessation) The time when menstruation normally ceases in the human female, generally between ages 48 and 50.

medulla:
(medulla = marrow) The soft, marrow-like innermost portion of an anatomic structure.

norepinephrine:
(nor = elimination of one methylene group from a molecule + epinephrine) Chemical substance closely resembling epinephrine with many of the excitatory effects of epinephrine but without its inhibitory effects.

oogenesis:
(oon = egg + genesis = origin) Process of formation and development of the egg.

pituitary:
(pituita = phlegm) The master gland of the endocrine system, suspended from the hypothalamus and closely connected to it by nervous and circulatory pathways.

PRL/prolactin:
(pro = before + lac = milk) Hormone that stimulates the secretion of milk.

prostaglandin:
(pro = before + stata = stand + glandin = production of a gland) A class of physiologically active substances present in many tissues, capable of relaxing the walls of blood vessels, stimulating intestinal smooth muscle, stimulating contractions of the uterus and acting against hormones that influence metabolism of fats.

receptor:
(recipio = to receive) A specific site on the membrane of a cell where biologically active molecules bind to activate the cell.

steroid:
(stereos = solid + oid = like) A large class of chemical compounds, including several hormones, with a variety of biological effects.

target tissue (organ):
The tissue or organ that is affected by a particular hormone.

testosterone:
(testis = male gonad + ster = steroid + one = hormone) The hormone produced by the interstitial cells of the testis that stimulates development of male secondary sexual characteristics and maintains their function in maturity.
Discover

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- Designed at Boston University and created at the Couroc Art Colony in Monterey Bay, our burnished satin black trays feature a hand inlaid Boston University Seal. These trays are available with or without brass accents (please specify).

<table>
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<th>ITEM NUMBER</th>
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<td>10&quot; round</td>
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<tr>
<td>#9834</td>
<td>18&quot; rectangle</td>
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### Buttons

**Boston University Blazer Buttons**
- Boston University's seal is hand-crafted in cloisonné enamel and 24-karat gold-plate. Each set consists of three large and four small buttons.

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<td>- $40.00</td>
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### Magazines

**Bostonia Magazine**
- With your voluntary subscription, this tax-deductible donation will entitle you to be considered a contributing reader of Bostonia Magazine.

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### Scarses

**Boston University Scarf**
- Hand-screened 100% silk, 27" square.

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<td>#9838</td>
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### Ties

**University Shield Tie**
- Polyester/silk blend

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**Bostonia T-shirt**
- Non-shrink polyester/cotton blend, available in navy with white lettering or tan with navy lettering. S, M, L, XL (Please specify).

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<td>#9840</td>
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Make checks payable to Boston University. Send orders to: Bostonia Marketplace, 10 Lenox Street, Brookline, Mass. 02146.

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1984

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9:00 a.m. Breakfast
9:45 a.m. Concert by University String Orchestra
10:00 a.m. Award Presentations

Beatrice Sherman Ballroom
George Sherman Union,
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Christopher A. Barreca, Esq.
DG’S/52/LAW/53: Labor and Employment Law Counsel. General Electric Company; Member, Boston University Board of Trustees; Past President, General Alumni Association; Member, National Alumni Council

Pong Sarasin
SMG/51: Managing Director, Thai Pure Drinks Company, Ltd; Director, Siam Commercial Bank, Monda Cars (Thailand); President, Alumni Association of Thailand

Dr. Albert S. Kahn
(Mrs. A. S. Kahn accepting)
SED/59/62: Faculty member, Boston University School of Education (1962-76); Treasurer and Director, Purity Supreme; Member, National Alumni Council; Massachusetts Bar Association

Distinguished Public Service to the Profession

Patricia D. Donahoe, M.D.
SAR/58: Chief of Pediatric Surgery, Massachusetts General Hospital; Principal Investigator, Pediatric Surgical Research; Member, Executive Committee on Research, MGH; Member, National Alumni Council

Gerald Gitner
CLA/66: Executive Vice President for Finance, Chief Financial Officer, Director, Pan Am World Airways; Founder, People Express Airlines; Member, National Alumni Council

Elma Lewis
SED/44: Founder, Elma Lewis School of Fine Arts; Founder, National Center of Afro-American Artists; Multiple Honorary Degree Recipient; Member, National Alumni Council

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64 • September/October 1984 • Bostonia
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