American Journal of Pharmaceutical Education **2007; 71 (5) Article 96.**

TEACHERS' TOPICS

The Central Endocrine Glands: Intertwining Physiology and Pharmacy

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Submitted January 31, 2007; accepted April 8, 2007; published October 15, 2007.

The initial courses in didactic pharmacy curriculum are designed to provide core scientific knowledge and develop learning skills that are the basis for highly competent application and practice of pharmacy. Commonly, students interpret this scientific base as ancillary to the practice of pharmacy. Physiology courses present a natural opportunity for the instructor to introduce basic pharmaceutical principles that form the foundation of pharmacological application early in the professional curriculum. *Human Physiology I* is the first of a 2-course physiology sequence that pharmacy students take upon matriculating into Midwestern University College of Pharmacy-Glendale. The endocrine physiology section of this course is designed to emphasize the regulatory and compensatory nature of this system in maintaining homeostasis, but also includes aspects of basic pharmaceutical principles. In this way the dependency of physiology and pharmacy upon one another is accentuated. The lecture format and content described in this manuscript focus on the central endocrine glands and illustrates their vital role in normal body function, compensatory responses to disease states, and their components as pharmacotherapy targets. The integration of these pharmaceutical principles at the introductory level supports an environment that can alleviate any perceived disparity between science foundation and practical application in the profession of pharmacy.

Keywords: endocrine, physiology, hypothalamus, pituitary gland, hormone, endocrine pharmacology

INTRODUCTION

At Midwestern University (MWU) College of Pharmacy-Glendale (CPG), matriculating pharmacy students begin a 2-course, 2-quarter series covering human physiology. The first course, *Human Physiology I*, is taken upon entry into the doctor or pharmacy (PharmD) program and begins with a discussion of general physiologic principles such as homeostasis, cellular structure, body fluids and electrolytes, membrane potentials, and excitability, with the remaining topics structured in an organ system-based manner (including the central and autonomic nervous systems, muscle types and function, the senses, and endocrine physiology). This topic order is designed to assist the student in the development of a deeper understanding of the regulatory systems that control the proper function of organ systems discussed in *Human Physiology II*, which include the cardiovascular, respiratory, renal, and gastrointestinal systems. These 2 courses are designed to provide pharmacy students with the core knowledge necessary to promote an understanding of normal body function, as well as the ability to analyze and interpret compensatory responses initiated in the presence of disease, with the overall goal of facilitating a whole-body approach to the maintenance of homeostasis.

The Department of Physiology in the Division of Basic Sciences coordinates both human physiology courses. Three faculty members from the Department of Pharmaceutical Sciences of CPG deliver approximately 67% of the content in *Human Physiology I*. This involvement is key to the introduction of basic and clinical pharmaceutical principles at the onset of the PharmD curriculum at CPG and the presence of pharmacy faculty members assists in the interweaving of this basic biomedical science into pharmacy.

Physiology, like many of the initial courses to which students are initially exposed, is centered on foundational knowledge in the basic biomedical sciences. It is not uncommon to receive feedback and frustration from students that these courses do not "feel" like pharmacy school to them. This is not an optimal situation and represents an opportunity for instructors to better integrate the application of biomedical principles to the profession of pharmacy, and it should be accomplished while the scientific foundation is being laid. Discussion with the students of the intimate relationship between physiology and pharmacology, and pharmacology and pharmaceutical care, is a

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logical stage to begin. One of the challenges that face instructors in the physiology sequence is the lecture-based nature of the courses. Furthermore, *Human Physiology I* contains 130 pharmacy students and approximately 15 students pursuing a bachelor of science degree in biomedical science and meets for 1 hour 4 times a week. With the large class size and limited time allotted, this is not the most favorable situation for conducting active-learning techniques; however, the instructors in the courses have been creative in their approaches and use a variety of methods to keep the class engaged, facilitate discussion, encourage question and answer sessions, and stimulate thought regarding applicability to future practice. Workshops covering cell excitability, central nervous system control of function, and endocrine-based disease state patient cases are utilized to further emphasize this application.

The core of the CPG curriculum consists of the *Integrated Sequence*, an 11-module group of courses organized in a disease-state fashion that emphasizes the pathophysiology, pharmacology, and therapeutics of major disease states. The medicinal chemistry of the therapeutically useful agents is also comprehensively discussed. These modules begin in the quarter following the completion of the *Human Physiology I, II* sequence; thus, students have been provided with the foundational knowledge base to begin more advanced discussion with emphasis on pharmaceutical care. There is continuity throughout the CPG curriculum with respect to topic expertise and instruction. As an example, the endocrine physiology lectures which are provided in *Human Physiology I* are later expanded on during a presentation of the pathophysiology and pharmacology of endocrine disorders discussed in a more advanced manner in the fourth module of the *Integrated Sequence*. This continuity is favorable as it allows consistency in content and quality, as well as a natural progression from simple principles to more complex pharmacological application. It also provides for a more comfortable environment from the students' perspective in that they know what the expectations of the faculty member are and are familiar with their style of lecture.

The physiology sequence utilizes as a primary textbook, *Human Physiology, From Cells to Systems*.[1] Other appropriate resources including other textbooks of pharmacology, pathophysiology, and pharmacotherapy, as well as the scientific and clinical literature are employed to emphasize the complimentary nature of these various aspects of pharmacy.[2-6] The following content is from 1 of 7 lectures provided on endocrine physiology and is specific to the central endocrine glands. Other lectures in this series include the general principles of endocrinology, the hormonal control of growth, the thyroid gland, the adrenal glands, the endocrine control of fuel metabolism, and the parathyroid glands and calcium homeostasis.

After attending these lectures, completing the required reading, and studying these handouts, students should be able to:

- Describe the anatomy of the hypothalamus and pituitary gland.
- State the major hormones produced and secreted by the hypothalamus, pituitary gland, and pineal gland.
- List the controlling factors that induce or inhibit the secretion of the hormones produced by the hypothalamus, pituitary gland, and pineal gland.
- Discuss the major functions of posterior pituitary hormones vasopressin and oxytocin.
- Discuss the major effects on the anterior pituitary of the hypophysiotropic hormones thyrotropin-releasing hormone, corticotropin-releasing hormone, gonadotropin-releasing hormone, growth hormone-releasing hormone, growth hormone-inhibiting hormone, prolactin-releasing hormone, and prolactin-inhibiting hormone.
- State the major target organs for the anterior pituitary hormones and the primary effects of thyrotropin, adrenocorticotropin, the gonadotropins, growth hormone, and prolactin on their target organs.
- Describe the proposed functions of melatonin and identify the two major self-prescribed uses.
- Discuss the etiology, clinical manifestations, and pharmacological treatment of diabetes insipidus.

INSTRUCTIONAL DESIGN

The author uses a Microsoft PowerPoint-based slide presentation and handout as a backbone for the material presented. All slides are also uploaded to the BlackBoard Learning System and are available to the students on their computers at any time. The format of the lecture consists of an introduction to the learning objectives; a discussion of the relevant anatomy of the hypothalamus and pituitary gland; identification of the hormones produced by these glands and what controls their secretion; examination of their major functions; and examples of the use of hormonal analogs in diagnostics and therapeutics.

The Hypothalamus

Through the integration of signals from the brain, body, and the environment, the hypothalamus coordinates the physiologic responses of organs that assist in the maintenance of homeostasis. The hypothalamus plays key roles in the preservation of a constant internal environment,

adaptation to stressful situations, the promotion of growth and development, and reproductive activity that are necessary for proper body function and propagation of the species.[1(p654)] Located between the thalamus and the midbrain, the hypothalamus is part of a neuroendocrine system constantly receiving input from the brain. It also forms an anatomical and functional relationship with the pituitary gland, or hypophysis, which centrally controls the activities of many other peripheral endocrine glands.[1(pp662-4)]

The pituitary gland is divided into 2 distinct anatomical and functional regions: the posterior pituitary lobe and the anterior pituitary lobe. The posterior pituitary, or neurohypophysis, is actually an extension of the hypothalamus, deriving embryologically as an evagination of the hypothalamus, and consists of nervous tissue.[7] Cell bodies of magnocellular neurons that reside in the paraventricular and supraoptic nuclei of the hypothalamus extend axons through the rear region of the pituitary stalk, or infundibulum, and these axons ultimately terminate on capillaries located in the posterior lobe. Each of these neurons makes 1 of 2 primary peptide hormones, either vasopressin or oxytocin.[1(pp662-3)] Like other peptides, these 2 nonapeptide hormones are synthesized in the endoplasmic reticulum as pre-prohormones and are packaged into secretory granules in the Golgi apparatus. These granules are moved by axonal transport down the pituitary stalk, altered by the process of post-translational modification, and stored in the axon terminals. Upon appropriate stimulation, which is triggered by neuronal depolarization and calcium influx, they are released by exocytosis.

Vasopressin

Vasopressin, or anti-diuretic hormone (ADH), has 2 major functions, each identified by its 2 names. It elicits contraction of arteriolar smooth muscle, resulting in vasoconstriction, which can assist in the maintenance of blood pressure (the pressor effect), and more important physiologically, it enhances water reabsorption by the kidneys, thus decreasing urine volume (the anti-diuretic effect). There are 2 main regulatory factors that stimulate vasopressin release, (1) increased plasma osmolarity and (2) hypovolemia or hypotension. An increase in plasma osmolarity as small as a few percentage points can be sensed by osmoreceptors located in the hypothalamus. These osmoreceptors sense the increase in plasma osmolarity as cell shrinkage and signal for an increase in vasopressin release even before thirst occurs. The regulation caused by decreases in volume or blood pressure is much less sensitive and involves the sympathetic nervous system. Baroreceptors predominantly located in the carotid sinus and aortic arch can sense a decrease in pressure of approximately 10%-15%. The carotid sinus baroreceptors are innervated by the sinus nerve of Hering, a branch of the glossopharyngeal nerve (cranial nerve IX) and the aortic arch baroreceptors are innervated by the vagus nerve (cranial nerve X). These nerves transfer afferent signals to the nucleus of the tractus solitarius in the medulla where they are relayed to magnocellular neurons of the hypothalamus whose axons terminate in the posterior pituitary and increase vasopressin release.[8]

The pharmacodynamics of each of the major functions of vasopressin is distinct as well. There are 3 vasopressin receptor types. The V_1 receptor is responsible for the pressor effect on arterioles and is also found in gastrointestinal tract smooth muscle. The V_2 receptor mediates the antidiuretic effect and is located in the basolateral membrane of the principle cells of the collecting tubule of the nephron. A third receptor, V_3, is present in anterior pituitary corticotrophs where it mediates a minor control in the increased secretion of adrenocorticotropin (ACTH).[8]

When vasopressin stimulates the V_2 receptor, the $G\alpha_s$ subunit of the associated G protein is activated and induces the production of cAMP by adenylate cyclase.[9] This cAMP then activates protein kinase A, which results in the production and translocation of specific water channels called aquaporins. Aquaporin-2 (AQP2) molecules are a particular type of water channel that are localized and stored in the cytoplasm of the principle cell. Upon stimulation of the V_2 receptor and the resultant signal transduction, new AQP2 channels are produced, but much more rapidly, the pool of AQP2 channels stored in the cytoplasm translocate to the apical membrane of the principle cell and act as a conduit for water to enter the cell from the collecting tubule lumen.[8] This water that is reabsorbed exits the principle cell through 2 other types of aquaporins, AQP3 and AQP4, which are located in the basolateral membrane, and enters the interstitial space for movement into the plasma compartment.[9]

Spotlight on Disease – Diabetes Insipidus

The spotlight on disease sections of the endocrine physiology lectures introduce a pathophysiologic disorder to the students to reinforce the physiologic roles of the hormones just covered. There are 10 ''Spotlight on Disease'' sections across the endocrine physiology lectures. A preliminary conversation is initiated in which the definition of the disease state, etiology, clinical manifestations, and possible pharmacological treatments are discussed. This is a particularly useful method of instruction that students have expressed has assisted the learning process. Once a physiologic concept has been discussed, the immediate ''flipping'' of the topic to pathophysiologic disease state permits the student to see the detrimental

effects of hormonal excess or deficiency and facilitates the linking of hormone-effect-clinical manifestation. This furthers the development of a logical thought process in students that allows for prediction of clinical manifestations if the major functions of the hormone are known. This also allows the students to be exposed to pharmacological application during the first quarter of their first-professional year, and as is the case with many disorders related to a hormone deficiency, reinforcement of the point that supplementation with the actual hormone or an analog is often the best pharmacotherapy strategy.

Diabetes insipidus (DI) is a disorder characterized by polyuria from the inability to concentrate urine and conserve water as a result of decreased vasopressin action.[10] The term "diabetes" refers to a siphon, or "running through" and directly describes the frequent urination that accompanies this disorder and diabetes mellitus. The term "insipidus" refers to the tasteless aspect of the urine of patients with this disorder. This is in contrast to the term "mellitus" which refers to the sweet nature of the urine of a patient with diabetes mellitus due to the excessive presence of glucose.[1(p708)]

There are 2 major types of DI: (1) central DI, which is due to decreased synthesis or secretion of vasopressin, and (2) nephrogenic DI, which is due to the loss of the kidney's ability to respond to normal circulating levels of vasopressin by retaining water.[10(pp550-2)] Central DI is more common and is due to trauma in the locations of the hypothalamus or posterior pituitary gland as a result of stroke, tumor, neurosurgery, or other injury. Nephrogenic DI can be associated with hereditary disorders resulting in abnormal V_2 receptors or nonfunctional AQP2 water channels, as well as a result from kidney disease (such as polycystic kidney disease), hypercalcemia, or as an effect of certain drugs like lithium and demeclocyline). Both lithium, a small ion, and demeclocycline, a bacteriostatic tetracycline, are antagonists of the V_2 receptor and thus induce a DI state.[8(pp160-2)] This is due to a direct action by the drug and resolves after discontinuance of the drug. Regardless of cause, the clinical manifestations of DI include dilute urine, even with hypernatremia, dehydration, weakness, and if not matched with fluid input, progressive obtundation, with the possibility of seizures and coma.[10(pp550-2)]

The pharmacological treatment of DI is established by the cause, thus etiologic determination is necessary. To determine if the patient has DI, as opposed to simply excessive fluid intake, the patient is subjected to a dehydration or water deprivation test. In a controlled environment, the patient's urine output and composition, as well as body weight are measured in the absence of fluid intake. A patient with DI will become hyperosmolar and will not concentrate urine.[8(pp160-2)] To determine the etiology, plasma vasopressin levels are measured and a desmopressin stimulation test is conducted. Desmopressin is a synthetic vasopressin analog. If the patient has low or undetectable vasopressin levels and responds to the desmopressin by concentrating urine and reducing urine output, central DI is determined and further imaging examinations of the hypothalamus, pituitary, and brain may be necessary. If the patient has a high plasma vasopressin level and does not respond to the desmopressin challenge, nephrogenic DI is determined.[8(160-2)] Central DI patients respond well to desmopressin pharmacotherapy, the goal of which is to replace the defective hormone. Nephrogenic DI patients do not respond to desmopressin and are treated with a thiazide diuretic, typically hydrochlorothiazide, and sodium restriction.[9(pp783-6)] This apparent paradox is effective due to natriuresis, which reduces the extracellular fluid volume, decreases glomerular filtration rate, and lowers the amount of fluid that reaches the collecting duct thus diminishing urine volume.[8(p164),9(pp783-6)]

Oxytocin

Oxytocin is a peptide hormone that differs in amino acid sequence from vasopressin by 2 amino acids. Oxytocin binds to and activates oxytocin receptors and functions to mediate uterine contraction and facilitate milk ejection.[1(p663)] It is released from the area of the posterior pituitary in response to increased estrogen levels, upon sensory stimuli received from the stretch of the cervix and vagina at the end of pregnancy, and suckling of the breast which induces contraction of myoepithelial cells during nursing of an infant.[8(pp169-70)] Oxytocin is unique in that its secretion is controlled in a positive feedback fashion during both labor and the nursing of an infant.[8(pp169-70)] This means the more oxytocin that is released, the greater the progression of labor and milk ejection which results in even greater amounts of oxytocin secretion until these processes are complete. Recall that most hormones are regulated in a negative feedback manner where stimulation of a particular hormone's secretion is attenuated when its levels are high.

Like most peptides, oxytocin is destroyed in the gastrointestinal tract when given orally. Therefore injection or nasal spray of synthetic oxytocin preparations is utilized to induce labor and facilitate the progression of labor to parturition. Other uses include assisting lactation in cases of insufficient milk ejection and controlling postpartum uterine hemorrhage and involution.

Hypophysiotropic Hormones

The hypothalamus has a different anatomical relationship with the anterior lobe of the pituitary gland, or

adenohypophysis, reflecting that they are distinct glands. The anterior pituitary is of ectodermal origin and is derived from Rathke's pouch.[7] The anterior pituitary has a rich blood supply and is connected with the hypothalamus by a hypothalamic-hypophyseal portal blood system. This portal system consists of a capillary bed that communicates with the hypothalamus and receives systemic arterial flow, a vessel system that extends downward through the pituitary stalk into the anterior lobe of the pituitary, and a second capillary bed that results in systemic venous outflow. The hypothalamus secretes at least 7 different hypophysiotropic hormones into the hypothalamic-hypophyseal portal system that travel to the anterior pituitary and induce or inhibit further hormonal release. The term hypophysiotropic refers to a growth or nourishing effect on the hypophysis or pituitary gland. The hypophysiotropic hormones include thyrotropin-releasing hormone (TRH), corticotropin-releasing hormone (CRH), gonadotropin-releasing hormone (GnRH), growth hormone-releasing hormone (GHRH), growth hormone-inhibiting hormone (GHIH; somatostatin), prolactin-releasing hormone (PRH), and dopamine (prolactin-inhibiting hormone, PIH).[1(pp662-4)]

By releasing hypophysiotropic hormones, the hypothalamus is at the top of the hormonal hierarchy. That is, the hypothalamus releases a particular hormone that stimulates the anterior pituitary to secrete a second hormone that is released into the systemic circulation. This second hormone then stimulates its peripheral target endocrine gland to secrete a third hormone that ultimately mediates the physiologic effect by binding to receptors in its target organ. This hormonal hierarchy is a basic tenet in the control of the endocrine system and is distinct from the posterior pituitary hormones. This particular organization is especially conducive to the physiologic principle of negative feedback. This process ensures that once a hormonal system is activated, its secretion does not continue unabated.[1(p668)] In negative feedback, hormones secreted from the anterior pituitary can inhibit the release of their specific hypophysiotropic hormone. This idea is extended in the fact that many target endocrine gland hormones can inhibit the secretion of their particular hypophysiotropic hormone as well as the tropic hormone that was released by the anterior pituitary to directly stimulate the target gland hormone's release.[1(p666)] Thus the two major factors that control anterior pituitary hormonal release are hypophysiotropic hormones and negative feedback systems.

The Anterior Pituitary

The anterior pituitary contains several discrete cell types that are derived from specific cellular lineages and are defined based on their hormonal products.[7(pp104-6)] Somatotrophs, which are located laterally in the gland, account for approximately 50% of all anterior pituitary cells and synthesize and secrete growth hormone (GH). Lactotrophs are more diffuse in location and synthesize and secrete prolactin. These particular cells are stimulated to proliferate during pregnancy by the associated increase in estrogen levels. Thyrotrophs secrete thyrotropin (thyroid-stimulating hormone, TSH) and are the least common of all anterior pituitary cell types. Corticotrophs secrete adrenocorticotropin (ACTH) and represent 15%-20% of all anterior pituitary cells. Gonadotrophs are also diffusely located and secrete the gonadotropins follicle-stimulating hormone (FSH) and luteinizing hormone (LH).[7(pp104-6)] Other cell types present in the anterior pituitary are null cells, which may represent primitive, undifferentiated cells, support cells which may release paracrine factors that maintain proper anterior pituitary function, and mammosomatotrophs that contain both GH and prolactin. These particular cells are associated with pituitary tumors and may contribute to acromegaly, a disorder of excessive GH secretion in an adult patient.[7(pp104-6)] While each hypothalamic-anterior pituitary-target gland axis will be discussed in detail over the next several lectures, it is appropriate that we introduce each axis at this time.

The Hypothalamic-Anterior Pituitary-Target Endocrine Gland Axes

The hypothalamic-anterior pituitary-thyroid gland axis begins with the hypothalamic release of the tripeptide TRH into the hypothalamic-hypophyseal portal system. This TRH stimulates thyrotrophs of the anterior pituitary to synthesize and secrete the glycoprotein TSH into the capillary bed that contains venous outflow to the systemic circulation. The TSH ultimately stimulates the thyroid gland by binding to and activating specific TSH receptors which increase cAMP production.[7(pp106-10)] This signal transduction results in increased iodide uptake by the thyroid gland, enhanced thyroid hormone synthesis, release of the thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3), and maintenance of gland size and vascularity. Thyroid hormones have several target glands with a major function in controlling metabolic rate.[1(p665)]

The hypothalamic-anterior pituitary-adrenal gland axis is initiated with the hypothalamic release of the 41 amino acid peptide CRH into the hypothalamic-hypophyseal portal system. This CRH stimulates ACTH production by the anterior pituitary. The ACTH released enters the systemic circulation and stimulates receptors found in the adrenal cortex that also utilize increased cAMP as a second messenger.[7(106-10)] The ACTH acts primarily

to promote the production and secretion of the glucocorticoid cortisol. It also functions as a minor regulator for the synthesis of the mineralocorticoid aldosterone, and the androgen dehydroepiandrosterone (DHEA). Each of these adrenal hormones are steroids that bind to nuclear type receptors that function as transcription factors, thus their effects are mediated more slowly than ion channels and G protein-coupled receptors. Cortisol has major functions in the proper blood levels of metabolic substrates and adaptation to stressful situations. Aldosterone functions primarily in the maintenance of plasma sodium levels and blood volume. The DHEA produced by the adrenal cortex has androgenic properties and its use as a supplement is controversial both to enhance athletic performance and attenuate the aging process. In males, its actions are overshadowed by testosterone, but in postmenopausal females, it is the major precursor to estrogen production.[1(p665)]

The secretion of the 198 amino acid peptide prolactin by lactotrophs of the anterior pituitary is stimulated by PRH and is inhibited by dopamine. Many other factors can stimulate prolactin release, including TRH, vasoactive intestinal peptide, and the neurotransmitter serotonin. Prolactin secretion increases during pregnancy where it functions to assist in breast tissue development and it stimulates lactation in the postpartum period.[1(p665),7(pp106-10)]

The production and release of the 191 amino acid peptide GH by somatotrophs of the anterior pituitary is stimulated by GHRH binding to specific receptors that utilize increased cAMP as a second messenger.[7(106-10)] The stimulatory effect of GHRH on GH can be inhibited by somatostatin decreasing cAMP levels upon receptor binding.[7(106-10)] Synthetic analogs of somatostatin including octreotide, which is actually more potent than natural somatostatin, are useful therapeutically in treating disorders of GH excess.[11] The GH secreted by the anterior pituitary has several target organs and both metabolic and growth-promoting effects. Growth hormone binds to a receptor of the JAK/STAT cytokine receptor superfamily that utilizes phosphorylation as its signaling pathway. Metabolically, GH promotes cellular amino acid uptake and protein synthesis, increases lipolysis, and increases plasma glucose. In terms of growth, GH stimulates primarily the liver, but also bone, cartilage, muscle, and the kidneys to produce somatomedins such as insulin-like growth factor-1 (IGF-1).[1(p665),12] The IGF-1 produced has an opposite effect on blood glucose levels due to its ability to bind to the insulin receptor and stimulate glucose uptake and directly promotes longitudinal growth until the epiphyseal plates close and has anabolic effects on muscle.[12]

The hypothalamic-anterior pituitary-gonadal axis begins with the hypothalamic release of GnRH which stimulates the synthesis and secretion of the glycoproteins FSH and LH by the anterior pituitary gonadotrophs. Target organs for the gonadotropins include the ovaries in females and the testes in males. FSH and LH bind to specific receptors in these tissues where they regulate gonadal function through the promotion of sex steroid synthesis and gametogenesis. In males, FSH stimulates sperm development and in females it supports the development of the ovarian follicle.[1(p665),7(pp106-10)] In males, LH stimulates Leydig cell production of testosterone, while in females it stimulates the production of estrogen and progesterone by the corpus luteum. The secretion of LH by the anterior pituitary dramatically surges at the approximate midpoint of the female menstrual cycle. This LH surge is responsible for follicle rupture inducing ovulation and also begins the process of luteinization of the follicle.[1(p759)]

The hypothalamic-anterior pituitary-target endocrine gland axes just discussed elegantly illustrate the precise and complex control of hormonal secretion. The process of negative feedback allows for this meticulous control and assists to maintain proper hormonal levels under normal conditions and in response to stimuli.

Diurnal Rhythms and the Pineal Gland

The suprachiasmatic nucleus of the hypothalamus is considered the pacemaker for diurnal or circadian rhythms. These rhythms refer to an approximately 24-hour cycle of repetitive hormonal secretion in response to the self-induced firing of the neurons located in this nucleus. These neurons work in conjunction with the pineal gland, a midline brain structure near the third ventricle, which secretes melatonin and assists in the synchronization of diurnal rhythms with a 24-hour day/night cycle. It is this synchronization that promotes the normal, repetitive hormonal secretion that is linked to waking and sleeping.[1(pp676-8)]

Melatonin, a derivative of tryptophan, is considered the hormone of darkness. Its secretion increases up to 10-fold during nighttime and decreases during the day. Many different roles have been ascribed to melatonin, with the best characterized being the inducement of natural sleep and its ability to act as an antioxidant. The enhancement of sleep is the reason for its promotion as a substance that can alleviate jet lag. Studies in animals have also alluded to a modulatory effect on reproduction. Melatonin can inhibit GnRH-induced LH release which may be important in seasonal breeding cycles and suggests a possible role in birth control. Claims have also been made that melatonin can slow the aging process and can enhance immunity.[1(pp676-8)]

Melatonin has been available as a health food supplement and the two main self-prescribed uses are to prevent jet lag and as a sleep aid.[1(pp676-8)] Recently, a melatonin receptor agonist available by prescription, ramelteon, (Rozerem), has been recommended for the treatment of insomnia.[13]

At this point in the lecture, the *CNN Today* video short "Melatonin Claims" is shown. This 2½-minute video analyzing the proposed physiologic roles of melatonin described above was produced in 1997 and is associated with the text *Human Physiology, From Cells to Systems*, edited by L. Sherwood.[1] This video, while somewhat dated, presents various expert opinions on a subject that most pharmacy students are somewhat familiar with and is relevant in the current pharmacy setting. It facilitates good discussion related to many topics in pharmacy including self-prescribing of supplements in general and melatonin specifically, animal studies and human data interpretation, the development of an effective medication based on the pharmacology of melatonin, and counseling points when confronted by a patient asking for professional advice. This video clip and the 3 others shown during the endocrine physiology lectures facilitate the discussion of the pharmacy topics listed above during the first quarter of the professional curriculum where typically little discussion on these topics occurs. The change in media and exposure to other expert discussion focuses the students on extension of the physiologic principles currently being studied and the practical application of aspects of pharmacy that they likely have little knowledge about presently, but will become key to their future practice. This discussion is a good way to reengage the class from the lecture-based question and answer format and allows the class session to end with a free flow of ideas and opinions. The students appreciate their active role in this discussion as it enhances their learning and they value the incorporation of more practical pharmacy-related topics in what they often perceive as solely a basic science course.

ASSESSMENT

The students' comprehension and understanding of the material presented above as well as from the other endocrine physiology lectures are assessed utilizing a multiple-choice examination. Emphasizing the cooperative relationship between the Department of Pharmaceutical Sciences and the Department of Physiology, all faculty members who lecture in *Human Physiology I*, as well as the Chairs of each Department, are given drafts of test questions approximately 1 week prior to the examination date. After individual review, all faculty members meet together to discuss each question in terms of content accuracy, clarity, difficulty level, and appropriateness. This constructive criticism has been invaluable and has assisted the development of a test item bank that contains questions of a high caliber. This is reflected in student evaluations remarking fair expectations and fair assessment. Over the past 3 years, pharmacy students have performed with a class average of approximately 83%-86% on this examination. *Human Physiology I* is consistently ranked as a favorite course by first-year pharmacy students.

SUMMARY

The initial courses in the pharmacy curriculum are designed to provide core knowledge and assist in the building of a strong foundation for future learning for the student. It is not uncommon for students to interpret this base knowledge as peripheral to pharmacy and not to see the practical application of it. *Human Physiology I* is the first of a 2-course sequence that pharmacy students take upon matriculating into Midwestern University College of Pharmacy-Glendale. This course offers ample opportunity for the instructor to bridge this perceived gap, emphasize the complimentary nature of physiology and pharmacy, and intertwine principles in such a way as to impart the fact that they are dependent upon one another. Through the use of an active, enthusiastic lecture style that encourages questions, a nonjudgmental and supportive classroom environment, samples of basic disease state pharmacotherapy and its pharmacological basis, and visual aids that stimulate discussion, as well as pharmacy-related endocrine physiology content, a strong effort is made to accomplish this.

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