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Articles

The Human Ovarian Cycle:
Why Are Undergraduate Texts Still Getting It Wrong?
By Robert S. Rawding, Ph.D. ................................................................. 3

The Role of Endoscopic Retrograde Cholangiopancreatography in Pancreaticobiliary Disease
By Sarah Cooper .................................................................................. 11

Human Interest and Activities for Students:
Biology in Beirut
By David Evans, Ph.D. ........................................................................... 14

Project Update for Conference Workshop
POGIL Project Update for Las Vegas Conference Workshop
By Murray Jensen ................................................................................ 17

EDU-Snippets
Snippets
By Roberta Meehan ............................................................................. 18

COVER ART: Scott Rawlins graduated from Earlham College with a degree in biology, and holds graduate degrees in museum education and medical & biological illustration from the George Washington University and the University of Michigan respectively. For many years Scott was a museum curator, working in this capacity at the Children’s Museum of Indianapolis, the Calvert Marine Museum and the Public Museum of Grand Rapids, MI. Since 1994 Scott has been a member of the art faculty at Arcadia University where he holds the position of Professor and teaches scientific illustration and design. He regularly exhibits his artwork nationally and has served on the boards of the American Society of Botanical Artists and the Guild of Natural Science Illustrators. He will assume the role of president of the Guild in July. His illustrations have appeared in the Society of Vertebrate Zoology, the Bulletin of the Museum of Comparative Zoology, Invertebrate Biology and Acta Zoologica, among others. Scott is presently acting as a research assistant in the paleontology department at the Academy of Natural Sciences in Philadelphia.
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References
It is the responsibility of the author to make sure that the information on each reference is complete, accurate and properly formatted. References should be included in the body of the manuscript where appropriate using the following format: Author’s last name and date of publication, (Martini, 2011). A list of ‘Literature Cited’ should appear at the end of the paper alphabetically by author’s last name. The following format should be used:

For an article

For a book

For the internet
Author’s last name (if known), Date of Publication or last revision (if known) in parenthesis, Title of document, Title of complete work (if applicable), italicized or underlined, URL, in angle brackets, Date of access, in parenthesis

Examples of internet citations

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The review process is single blinded which means that the reviewers know the identity of the authors of the manuscript but the authors do not have access to information regarding the identity of the reviewers.

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The Human Ovarian Cycle: Why Are Undergraduate Texts Still Getting It Wrong?

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ABSTRACT: In most undergraduate and some graduate texts there are two misconstrued inferences. The first is the misconception that an ovulatory follicle in human females undergoes about a 14-day rapid ripening period during the follicular phase of the ovarian cycle. A second misconception surrounds the impetus actually triggering the follicle’s expulsion from the ovary. More than 30 undergraduate and graduate texts in anatomy & physiology, physiology, endocrinology, and reproductive biology typical of undergraduate texts related to reproductive function were surveyed. I compared their treatment of pre-ovulatory follicular concepts and the proximate cause for peri-ovulatory signaling. This paper reports on 17 texts. Some suggestions for amending text-versus-research inconsistencies are offered, as well as several excellent resources for further review.

INTRODUCTION
In the spring of 2012, I was engaging students in a lesson on human reproductive physiology for a freshman course called Animal Form and Function. This course is the second in a three-course sequence for biology majors and other students who are enrolled in pre-professional programs such as physician assistant, physical therapy, pre-pharmacy, and pre-med. Our department had adopted a new biology text for this course. Much to my chagrin, the new text didn’t quite “get it right” with respect to ovulatory follicle maturation time in human ovarian cycles or the immediate triggers for ovulation itself. This finding indicates that misconceptions about female reproductive biology are not found solely in anatomy and physiology (A&P) texts.

There are numerous published reports that provide clear evidence that more than 350 days are required to progress from a primordial follicle, present in the prenatal ovary, to an ovulated oocyte stage. At a bare minimum, 85+ days are required to progress from an antral follicular stage to ovulation. Model makers and illustrators further obscure this reality by showing far too few follicles and arranging them peripherally in the cortex in something approximating a chronological sequence. Students have a tendency to visualize this scenario as movement of the follicles themselves as they mature. Many components within the anatomical model are improperly scaled to size; primordial and primary follicles are often shown too large and the corpora lutea / corpora albicans are shown too small. The model keys are likewise inappropriate describing events in a “typical” 28-day ovarian cycle.

Further complicating the issue is that contrary to what is postulated by most textbook writers, the stimulus that actually triggers the expulsion of the oocyte from the ovary is not luteinizing hormone (LH) per se, but a coordinated set of paracrine responses, including prostaglandins and plasminogen, induced by a synergistic coupling of signals from follicle stimulating hormone (FSH) and LH. Progesterone also plays a major role in preparing the ovulatory follicle for oocyte ejection.

For students to learn that more than seven million primordial follicles are present at three months of prenatal life, that they diminish to 400,000 at puberty, and virtually disappear at menopause begs the question, “Where do they all go?” I noticed that general biology texts and most A&P texts have a nebulous description of this issue and I was bothered by their assertion that the pre-ovulatory luteinizing hormone surge, often attributed directly to ovulatory follicle expulsion, was the sole cause of ovulation. It is not. FSH in high enough concentrations can also trigger ovulation. Ovulation follows about 16 to 20 hours after the LH surge. The intervening processes are very complicated, but not completely unknown. For example, there are more than 88 genes that are transcribed after the LH surge, evidence that a great deal of cellular activity is taking place (Goodman 2009, Espy and Richards 2001, Straus and Williams 2009).

I decided to examine these two concepts further in copies of on-hand texts: (A) How do these books present the pre-ovulatory development of ovarian primary follicles and the atresia (follicular apoptosis) of most ovarian follicles? (B) Do textbook authors adequately describe the proximate cause(s) of ovulation?
ovulation? I state firmly at the outset that this is not a pejorative criticism of texts and authors, who, I recognize, work diligently to bring us quality-teaching tools. I only wish to create a conduit for improving instructional content so our students may be more enlightened.

HISTORICAL PERSPECTIVES
ABOUT OVULATORY FOLLICLE DEVELOPMENT

In 1986, Alain Gougeon published a seminal paper (no pun intended) on his observations of follicle development in ovaries he obtained via ovarectomies from gynecological surgeries. He used 31 sets of samples for study obtained from patients aged 19 to 49 years (mean ± SD = 38.9 ± 7.5 years). In his 1996 follow-up publication, which has been cited more than 770 times in other published works according to Google Scholar, Gougeon provides an excellent summary and updated findings in the 10 years that had elapsed since his first paper (Gougeon 1986, Gougeon 1996).

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Without minimal FSH, follicles do not develop beyond the early antral stage and atresia occurs. Some of the selected follicles are “rescued” from atresia by FSH, which likely induces a huge increase in LH receptors among the granulosa thecal cells. These latter cells can be stimulated by LH to develop further and produce aromatases for 17-β-estradiol (E₂) synthesis. E₂’s negative feedback on the pituitary-hypothalamic axis reduces FSH concentrations considerably. The duration of time required for the growth of a follicle from the primordial stage to the large pre-antral stage takes therefore in excess of 150 days (Gougeon 1986). Thus, a follicle which ovulates in any given menstrual cycle will actually have begun to grow at least five menstrual cycles earlier (Gougeon 1986, Zeleznik 2004).

The “take home message” is that an ovulatory follicle began its initiation about one year (355 days) earlier - not in just the 14 days prior to ovulation, which would be an incredible feat, even for the human oöcyte. Realistically, a selected preovulatory follicle can fully mature in the two week time span, but most of the texts I researched aren't specific enough in explaining this observation. Conservatively, the minimal development time from antral stage to ovulation is at least 85 days but may be 150 days or more (Gougeon 1996, Zeleznik 2004).

ABOUT OVULATION

Text authors generally delineate correctly the interaction between hypothalamic gonadotropin releasing hormone, GnRH, gonadotrope cells’ resultant (Continued on next page)
production of FSH and LH, and the roles played by estradiol, E2, and progesterone in the hormonal mechanisms that promote ovulation. They “get right” the slow release of LH prior to its mid-cycle massive surge, the positive feedback role of E2 on the pituitary gonadotrope cells, rising progesterone levels after ovulation and the formation of the corpus luteum after the corpus hemorrhagicus is repaired. Where there is much disparity lies in the descriptions that complete the picture of ovulatory events.

**Figure 2** illustrates some of the details surrounding ovulation that are either omitted from texts or generally misconstrued. The numbers in black circles correspond to those in the figure. FSH, at very low levels, stimulates the production of plasminogen activator (PA) by the granulosa cells. PA catalyzes the conversion of plasminogen from the granulosa cells to plasmin that targets the cells of the follicular wall, weakening their intercellular adhesion. FSH also induces the huge expansion of the cumulus oophorus (by mucification) which also includes up-regulation of LH receptors on the granulosa cells’ surfaces. Thus the only targets of FSH in the ovary are the granulosa cells. FSH’s role in ovulation is key for up-regulating LH receptors in the granulosa cells prior to the LH surge. The mucification step appears to be also particularly important for the pickup and entry of the ovulated secondary oöcyte into the uterine tube, then its transport down the tube. Clearly a concomitant surge of FSH along with low levels of LH exerts a permissive effect on granulosa cells to augment their LH receptors. Luteinizing hormone (LH) induces the resumption of meiosis (by the mid-cycle surge) as well as luteinization of the granulosa and theca lutein cells (right image) already initiating the formation of the corpus luteum. LH also induces the follicle corona cells to make and release progesterone that induces prostaglandins (PG’s) E and F production. These PG’s trigger the presumptive stigma cells of the ovarian wall to make and release a number of proteases that break down the ovarian matrix and the follicular tunica albuginea; this ultimately allows for follicular expansion by the liquor folliculi and exit of the ovulated oöcyte through the ovarian cuboidal epithelium at the stigma. The proximal cause for ovulation is the effector ADAMTS-1, a disintegrin and metalloproteinase with thrombospondin repeats - motif 1, whose concentration increases more than 10x, inducing the cumulus oophorus complex to expand and break loose from the granulosa cells of the follicle wall. This metalloproteinase completes the tissue catalysis (Goodman 2009).

The actual trigger to induce ejection of the oöcyte from the ovary at ovulation appears to be not the “overplayed” LH surge alone, which certainly contributes a strong signal, but a well-coordinated synergistic coupling of a dual FSH-LH induction of prostaglandins, progesterone, and a protein, plasmin. Espey and Richards provide an excellent ‘play-by-play’ description of the factors (factors as signaling compounds) and processes promoting ovulation (Espey and Richards 2006).

Another myth is that the ovulatory follicle bursts are due to the expansion pressure from accumulating liquor folliculi within the antrum, sometimes described analogous to the popping or breaking of a blister. The intrafollicular pressure does not increase because the follicle becomes more expandible as proteolytic enzymes break down the connective tissues of the cortical matrix, all set in motion principally by LH. ADAMTS-1 then finalizes the secondary oöcyte’s escape from the follicle at the stigma by completing cortical tissue breakdown (Goodman 2009).

**DISCUSSION**

**THE REALITY IN TEXTBOOKS**

Few textbook authors have developed ovulation mechanism concepts completely. Only a handful of authors are correct in their description of the proximate cause of ovulation. The following excerpt is typical of perpetuating three misconceptions:

“At the beginning of each menstrual cycle, 10 to 25 of these preantral and early antral follicles begin to develop into larger antral follicles. About one week into the cycle, a further selection process occurs: only one of the larger antral follicles, the dominant follicle, continues to develop, and the other follicles (in both ovaries) that had begun to enlarge undergo a degenerative process called

(Continued on next page)
atresia (an example of programmed cell death, or apoptosis). The eggs in the degenerating follicles also die.” (Widmaier 2004).

Sounds logical, right?

Misconception #1: the pre-antral follicles and early antral follicles cannot complete their development to an ovulatory follicle in 13 days. Gougeon demonstrated that this would require no less than 75 days for pre-antral and about 60 days for early antral follicles (Figure 2). Misconception #2: The actual selection of “the” ovulatory follicle occurs also much earlier than only days before ovulation; likely several ovarian cycles prior to ovulation. In addition, there can be multiple selected follicles. Misconception #3: atresia is an ongoing process that influences follicular development for all Class 1 through Class 7 follicles, to varying degrees. All of these classes are present in a post-menarcheal through pre-menopausal human ovary (Gougeon 1986, Zeleznik 2004).

Graduate texts are not immune to similar errors. From a Board Review Series text by Linda Costanzo, “1. Follicular phase (days 0-14) ■ A primordial follicle develops to the graafian stage, with atresia of neighboring follicles” (pg. 254). As above Misconception #1 applies; a primordial follicle cannot develop within a 14-day window, and Misconception #3: atresia is not restricted just to neighboring follicles (Costanzo 2011).

I think that it is important to correctly describe these events and observations. How much time and energy do we expend teaching students cranial nerve mnemonics, bone markings for all elements of the skeleton, or blood flow through the kidney, to ensure that they “get it right”? 

### COMPARISON TABLE FOR TEXT TREATMENT OF THESE TWO CONCEPTS

I have referenced 17 texts (Table 1) for this analysis. I recognize that student skill levels targeted by these texts vary widely, accounting for many of the differences in textual content. I have also included the graduate-level text by Costanzo for comparison.

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<thead>
<tr>
<th>Author(s), Year &amp; Title</th>
<th>Follicle Development &amp; Comments</th>
<th>Ovulation Events &amp; Comments</th>
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<tbody>
<tr>
<td>Brooker et. al. (2011) Biology (2nd ed.)</td>
<td>“During the first week of the ovarian cycle in humans, several primary oocytes begin to mature, each within a follicle. At the beginning of the second week, all but one of the growing follicles and its primary oocyte degenerate, and the single remaining follicle continues to develop and enlarge.” (Misinformation. Follicles are pre-antral or antral age, not primary.)</td>
<td>“The LH released from the pituitary as a result of positive feedback by estradiol induces rupture of the follicle and ovulation.” (No other intervening processes are mentioned).</td>
</tr>
<tr>
<td>Costanzo (2011) Physiology [Board Review Series]</td>
<td>“Menstrual Cycle 1. Follicular phase (days 0-14) ■ A primordial follicle develops to the graafian stage, with atresia of neighboring follicles” (Misinformation. Primordial follicles cannot develop that rapidly; to evolve into an ovulatory follicle that quickly is a misconception.)</td>
<td>“LH and FSH receptors are up-regulated in the theca and granulosa cells.” (Yes and no; yes, LH receptors are up-regulated by FSH, but, no, FSH does not act on the theca cells.)</td>
</tr>
<tr>
<td>Fox (2011) Human Physiology (12th ed.)</td>
<td>“…new follicles start to develop toward the end of one cycle in preparation for the next.” (Yet one text figure shows primordial follicles in same cycle as ovulatory)</td>
<td>“Ovulation occurs as a result of the estrogen-induced LH surge.” (Erroneous to a degree; FSH is obligatory for ovulation as well; ensuing LH-surge events are not delineated well.)</td>
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<tr>
<td>Jenkins &amp; Tortora (2013) Anatomy &amp; Physiology: From Science to Life (3rd ed.)</td>
<td>“Each month...FSH and LH...further stimulate the development of several primordial follicles...developing into primary follicles...may not reach maturity until several menstrual cycles later.” (Indeterminate development length, but primordial follicles rightly not depicted in same ovulatory cycle as primary follicles, primary follicles not depicted as pre-antral, thus, erroneous time for procession to ovulatory in same cycle)</td>
<td>“The resulting surge of LH causes rupture of the mature follicle and expulsion of a secondary oocyte.” (No mention of any other intervening chemical events prior to ovulation.)</td>
</tr>
<tr>
<td>Mader and Windelspecht (2010) Human Biology (12th ed.)</td>
<td>“As the follicle matures during the ovarian cycle, it changes from a primary to a secondary to a vesicular (Graafian) follicle.” (Clearly in error; pre-antral follicle is shown as part of the current ovarian cycle and doesn’t mature through the remaining stages in less than two weeks.)</td>
<td>“The LH surge triggers ovulation at about day 14 of a 28-day cycle.” (Nothing else is described beyond the LH surge).</td>
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</table>
No text in those surveyed mentions the presumptive stigma (Erickson 2001), the anatomical ‘escape point’ for the ovulated oocyte and corona radiata cell complex (cumulus oophoros). See Figure 1. I suggest abandoning eponym-based terminology, despite clinicians’ use of the eponyms. More than a few authors still use the term “graafian” follicle to describe a tertiary, pre-ovulatory follicle, as well as “fallopian” tube. Most texts show primordial or primary follicles in the same composite illustration as an ovulatory follicle - clearly needing redrawing or deletion of primordial, primary, and non-antral follicles from composite figures. Some authors don’t distinguish between primary and secondary oocytes versus primordial, primary, secondary, pre-antral, and antral follicles. I included parenthetical remarks when necessary.

STRATEGIES FOR STUDENTS TO DISCOVER BY OBSERVATION

The simplest strategy to overcome the model / illustration shortcoming discussed in the introduction, is to provide microscope slides of transverse sections of a human (or other mammalian) ovary on microscopes with low-, medium-, and high-power objectives (10x, 40x, and 100x) and a 10x eyepiece. Ideally, the microscopes would have a micrometer for dimensioning follicular sizes. During a laboratory, use several microscopes to examine ovaries with appropriately-labeled histology text images (micrographs) beside each ‘scope: (A) low microscope magnification (about 100x) to give students an overview of the tremendous numbers of follicles present at many different stages of development, (B) a medium-magnification view (about 400x) near the junctional zone of the ovary’s cortex and stroma to highlight vascularization, (C) a high-magnification view (1000x, oil immersion) of a corpus luteum or corpus albicans, and (D) a high-magnification view of primordial and primary or secondary follicular development. It would also be helpful to include a secondary and tertiary follicle at 1,000X to illustrate the large numbers of theca and granulosa cells, to reinforce Gougeon’s illustration (Figure 2). An inexpensive alternative is to use digital images during the pre-lab discussion illustrating ovarian follicular development and general ovarian morphology of diverse follicle stages and walk students through the images. We have captured microscope images by digitizing and projecting them with PowerPoint. Resolutions of 300 pixels per inch (technically, samples per inch) are aptly suitable.

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<td>Marieb and Hoehn (2013) Human Anatomy &amp; Physiology (9th ed.)</td>
<td>“When a primordial follicle … is activated (this occurs almost a year before its possible ovulation)”</td>
<td>“[LH] increases local vascular permeability and triggers an inflammatory response that promotes release of metalloproteinase enzymes that weaken the ovary wall.”</td>
</tr>
<tr>
<td>Martini (2006) Fundamentals of Anatomy &amp; Physiology (7th ed.)</td>
<td>“The ovarian cycle can be divided into a follicular phase…and a luteal phase…The ovarian cycle begins as activated primordial follicles develop into primary follicles.”</td>
<td>“…massive release of LH from the pituitary gland. This sudden surge in LH concentration triggers…(2) the rupture of the follicular wall, and (3) ovulation…ovulation occurs 34-38 hours after the LH surge begins”</td>
</tr>
<tr>
<td>McKinley et. al. (2013) Anatomy &amp; Physiology: An Integrative Approach</td>
<td>“At the beginning of the follicular phase, FSH and LH stimulate up to about 20 primordial follicles, to mature into primary follicles…Late in the follicular phase, typically only one secondary follicle in an ovary matures into a vesicular follicle.”</td>
<td>“The positive feedback loop [by estrogen onto pituitary gonatotropes] results in an LH surge from the anterior pituitary which induces ovulation.”</td>
</tr>
<tr>
<td>Reece, et al. (2012) Campbell Biology: Concepts &amp; Connections</td>
<td>“FSH stimulates the growth of an ovarian follicle, in effect starting the ovarian cycle.”</td>
<td>“It [LH] also signals enzymes to rupture the follicle, allowing ovulation to occur”</td>
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The complement to student identification is to use an image such as Figure 2 and have students compare image to slide follicles and sizes, through estimating numbers of theca cells observed around follicles. Digital micrographs displaying several of these kinds of ovarian images are also helpful. Students immediately understand the shortcomings of ovary models, even after spending five to ten minutes with the microscope slides. The slides have the additional “plus” of being less expensive than even one model of the ovary. Prepared slides of the ovary cost about US$8 each; an ovary model will cost about US$225. An excellent histology text is also warranted, especially if digital images are available with the book. Many publishers’ texts and lab manuals have images that are suited to the task, with the only limitation being a lack of diversity of follicle views, rather than the one or two images often included to satisfy the minimalist view of “well, here’s an ovary.” Students are amazed when they observe ovarian follicle densities and the diversity in follicular stage development in a prepared slide. They get a truer representation of the real ovary and follicle cohorts and comment about how ‘simple the model is now.’

I found two exquisite resources that are good reading, aside from Gougeon and Erickson. Goodman has an excellent running commentary in Chapter 13 on ovulatory endocrinology that is an ‘easy read’ over a cup or two of coffee or tea. Espey and Richards from Knobil and Neill’s Physiology of Reproduction, 3rd ed., is strongly recommended as a fascinating take on the multifaceted details of ovarian function, a good “go to” book (Goodman 2009, Erickson 2001, Gougeon 1986, Gougeon 1996, Espey and Richards 2006).

### SUMMARY

What emerges are two considerations that I suggest for teaching female reproductive anatomy and physiology: (1) the LH surge about 16-20 hours prior to ovulation sets in motion a complex series of interactions between LH, FSH, progesterone, prostaglandins, and numerous proteins (either transcription factors or proteolytic enzymes). The surge is a culmination of nearly one year’s follicular development, with explosive development of a selected follicle’s multicellular activity which, in two weeks, changes the follicle’s size from about 7 mm to 18

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<tr>
<td>Rizzo (2010) Delmar’s Fundamentals of Anatomy and Physiology (3rd ed)</td>
<td>“The ovarian follicles, known as primary follicles, begin their development. During the early phase of each menstrual cycle, 20 to 25 primary follicles begin to produce very low levels of estrogen. A clear membrane, the zona pellucida, also develops around the eggs. Later on in the phase at day 4 to 5, about 20 of the primary follicles develop into secondary follicles. These secrete a follicular fluid that forces the ovum to the edge of the secondary follicle.” (Misinformation about follicle development; primary follicles are too developmentally immature to pass to the ovulatory stage in two weeks.)</td>
<td>“Ovulation is the rupturing of the graafian follicle.” (LH is not mentioned until after ovulation is discussed; figure in Chapter 19 still shows primary follicles in current ovulatory cycle).</td>
</tr>
<tr>
<td>Saladin (2009) Anatomy and Physiology (5th ed.)</td>
<td>“Preparation for the follicular phase begins almost two months earlier.” (Too short an interval)</td>
<td>“The follicular wall and adjacent ovarian tissue are weakened by inflammation and a proteolytic enzyme. With mounting internal pressure and a weakening wall, the mature follicle approaches rupture.” (Prostaglandins mediate but aren’t, in this case, promoting an inflammatory response per se; they emerge from LH’s influence on granulosa cells’ production of them)</td>
</tr>
<tr>
<td>Sherwood (2013) Human Physiology: From Cells to Systems, (8th ed.)</td>
<td>“The early stages of follicular development that occur without gonadotropin influence take about two months and are not part of the follicular phase of the ovarian cycle... Only follicles that have developed sufficiently to respond to FSH stimulation (preantral) are recruited when FHS levels rise” (Mechanism of follicle development is not clear: two months, again, is too short an interval).</td>
<td>“[LH] triggers production of local prostaglandins, which induce ovulation by promoting vascular changes that cause rapid follicular swelling while inducing enzymatic digestion of the follicular wall.” (There is no specifying the source of the enzymes nor their targeted tissues The prostaglandin production is triggered by progesterone, not LH.)</td>
</tr>
<tr>
<td>Shier et al. (2010) Hole’s Essentials of Human Anatomy &amp; Physiology (12th ed.)</td>
<td>“With each reproductive cycle, some of the primordial follicles mature...” (Misinformation on follicle development; little discrimination between names of follicles, other than “primary” and “secondary”; text figure 22.24 indicates a pre-antral follicle as a ‘maturing follicle’.)</td>
<td>“Release of LH from the anterior pituitary gland triggers ovulation, which rapidly swells the mature follicle and weakens its wall. Eventually the wall ruptures, and the follicular fluid, accompanied by the secondary oocyte, oozes outward from the surface of the ovary” (Minimal information; LH itself does not induce the &quot;rapidly swelling[ing]&quot; follicle. Corona radiata accompanying the secondary oocyte is ‘one or two layers’ only.)</td>
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mm, a nearly 3X enlargement. (2) The final events leading to expulsion of the secondary oocyte from the ovulatory follicle are mediated by one signal, ADAMTS-1 which triggers the final rupture of the ovarian epithelium and movement of the oocyte with its cumulus oophorus into the uterine tube, ending the dissolution of the cortical matrix initiated by progesterone.

Simple exercises that employ sectioned human ovaries under various magnifications will "put to rest" the ovary models' oversimplified anatomy. I urge faculty to add such lab components to enlighten students about ovarian complexity and also suggest that text authors - and their publishers - revisit and emend their chapters on details of reproductive physiology to make them more attuned to recent advances in the field.

ABOUT THE AUTHOR

Dr. Robert Rawding is an assistant professor of Biology and teaches Animal Form and Function, multiple courses and labs in Human Anatomy & Physiology, and Endocrinology for Biology majors who are pursuing pre-med / pre-dental, and physician assistant programs. Dr. Rawding's dissertation research established the cycling of melatonin secretion in amphibians, with Necturus maculosus as his research model. His current research focuses on how the thermal biology of goldfish, Carassius auratus, is influenced by multiple combinations of temperature and photoperiod regimes.

ACKNOWLEDGMENTS

I thank Dr. Mary C. Vagula for manuscript suggestions, and Dr. Elisa Konieczko and Dr. Rev. Joseph Gregorek for thoughtful critiques of the manuscript. All are Biology department colleagues at Gannon University.

DISCLAIMER

The author has no vested interests in any of the texts cited in this paper.

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<table>
<thead>
<tr>
<th>Author(s), Year &amp; Title</th>
<th>Follicle Development &amp; Comments</th>
<th>Ovulation Events &amp; Comments</th>
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<tbody>
<tr>
<td>Silverthorn (2010) Human Physiology: An Integrated Approach (5th ed.)</td>
<td>&quot;This [follicular] phase is the most variable and lasts from 10 days to 3 weeks.&quot; (Follicles constantly progressing; primary follicles still erroneously included in ovarian cycle composite image)</td>
<td>&quot;The breakdown products of collagen create an inflammatory reaction, attracting leukocytes that secrete prostaglandins into the follicle.&quot; (No supporting literature for the leukocyte-prostaglandin mechanism; rather granulosa cells are induced by LH's induction of progesterone (possibly) to stimulate production of COX-II leading to prostaglandin output)</td>
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<td>Tate (2012) Seeley's Principles of Anatomy &amp; Physiology (2nd ed)</td>
<td>&quot;The FSH surge initiates the development of follicles that develop and may ovulate during later ovarian cycles... The follicles that start to develop in response to FSH may not ovulate during the same cycle in which they begin to mature, but they may ovulate one or two cycles later. (Incorrect timing for follicular development; which follicles are also not specified; ovulatory cycle composite image shows primordial and primary follicles develop within same cycle as ovulation but which type attaining ovulation is not specified)</td>
<td>&quot;The LH surge causes the primary oocyte to complete the first meiotic division and become a secondary oocyte, stimulates ovulation, and causes the ovulated follicle to become the corpus luteum... &quot;Shortly after ovulation... remaining granulosa and thecal cells of the ovulated follicle are converted to corpus luteum cells and begin to secrete progesterone and some estrogen.&quot; (No subsequent elapsed time to ovulation is indicated, nor any other details noted beyond this description; progesterone synthesis is occurring prior to ovulation and the LH surge.)</td>
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<td>Tortora and Derrickson (2012) Principles of Anatomy and Physiology 13th ed.</td>
<td>&quot;Some of the secondary follicles in the ovaries begin to secrete estrogens and inhibit. By about day 6, a single secondary follicle in one of the two ovaries has outgrown all the others to become the dominant follicle... Estrogens and inhibin secreted by the dominant follicle decrease the secretion of FSH, which causes other, less well-developed follicles to stop growing and undergo atresia.&quot; (There may be multiple selected follicles; atresia occurs at all stages of follicular development.)</td>
<td>LH causes rupture of the mature (graafian) follicle and expulsion of a secondary oocyte about 9 hours after the peak of the LH surge. The ovulated oocyte and its corona radiata cells are usually swept into the uterine tube. (No details of the events between the LH surge and the expulsion of the oocyte; many more reactions are occurring between the two processes.)</td>
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<tr>
<td>Widmaier et. al. (2004) Vander's Human Physiology: The Mechanisms of Body Function (9th ed.)</td>
<td>&quot;... there are also always present a relatively constant number of preantral and early antral follicles. At the beginning of each menstrual cycle, 10 to 25 of these preantral and early antral follicles begin to develop into larger antral follicles&quot; (But the authors state the follicles are available only from the immediately prior cycle, clearly too brief an interval)</td>
<td>&quot;The midcycle surge of LH is the event that induces ovulation... Enzymes and prostaglandins, synthesized by the granulosa cells, break down the follicular-ovarian membranes. These weakened membranes rupture, allowing the oocyte and its surrounding granulosa cells to be carried out onto the surface of the ovary.&quot; (Prostaglandins can’t act as proteolytic enzymes, but rather as paracrine inducing agents; follicular-ovarian membranes are also not membranes, but connective tissue matrices and simple cuboidal epithelia; LH triggers ovulation, but does not proximally induce it)</td>
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REFERENCES

The Role of Endoscopic Retrograde Cholangiopancreatography in Pancreaticobiliary Disease

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Abstract: Endoscopic retrograde cholangiopancreatography (ERCP) is a useful procedure for the evaluation and management of diseases of the gall bladder and pancreas. It can be successfully used for draining fluids from the biliary system and for extraction of gallstones. Additional applications for this technology include pancreatic sphincterotomy, dilation of stenosed areas that affect the pancreaticobiliary system, pancreatic duct stenting, and treatment of leaks in associated ducts. The future looks bright for less invasive procedures such as ERCP and it is expected that applications for these procedures will proliferate along with the non-invasive imaging techniques that make them possible.

Endoscopic Retrograde Cholangiopancreatography (ERCP) is an endoscopic procedure used to diagnose and treat diseases of the pancreas, liver, gall bladder and the bile duct system. It is termed retrograde because the direction of viewing and treatment is opposite that of the flow of bile. Since its introduction in 1968, ERCP has evolved from being primarily a diagnostic tool to its current state of therapeutic importance in the treatment of acute pancreatitis, gallstone disease, Sphincter of Oddi dysfunction and microlithiasis. Sphincter of Oddi dysfunction is characterized by the inability to regulate the release of pancreatic juice and bile into the duodenum due to an abnormality in the contractility of circular muscle fibers. Microlithiasis, sometimes known as biliary sludge, is a viscous substance containing mucin, calcium bilirubinate, and cholesterol, which can block the pancreatic duct with tiny gall stones that are too small to be picked up on image scanning equipment such as ultrasound. Historically, patients with gall bladder disease or symptoms of pancreatitis have needed surgery to fully diagnose and treat their condition. Effective use of ERCP since the early 1970’s has made it possible for doctors to have high quality x-rays of the common bile duct and the pancreatic duct and, with the use of contrast dyes, to view related biliary structures without surgical intervention. Using ERCP, bile ducts can be freed of gallstones and bile can be drained from previously blocked bile ducts. Under certain circumstances, doctors using this procedure can even stretch areas where related tissues, such as the pyloric sphincter and the distal common bile duct, exhibit problematic narrowing (Canlas 2007, Chatzinoff 2012).

Pancreaticobiliary disorders can be complex and difficult to treat and they are seen frequently in clinical practice. Since 1992 it has been generally acknowledged that acute pancreatitis is a reversible condition that is characterized by an acute inflammatory process with visible involvement of the surrounding tissues. The incidence of acute pancreatitis in the US is estimated to be 17 cases per 100,000 people. The disease accounts for approximately 333,000 hospital admissions each year and an estimated 911,000 doctors’ office visits. The most common causes of acute pancreatitis in the adult population are gallstone disease and the excessive use of alcohol. However, as many as 20% to 30% of the time, the cause cannot (Continued on next page)
be determined and the condition is simply listed as idiopathic acute pancreatitis (Canalas 2007).

The pathogenesis of acute pancreatitis follows a predictable course, which involves the inappropriate conversion of trypsinogen to trypsin, in quantities large enough to make it impossible for the pancreas to eliminate the excess trypsin. Pancreatic tissue is injured by the trypsin overload and the result is a very intense inflammatory response. As a result of the inflammation, there are injuries to pancreatic circulation, cytokines are released, and oxidative stress occurs. Abnormally high levels of pancreatic enzymes damage the vascular epithelium, the interstitial areas and acinar cells. As a result of this damage, pancreatic tissue suffers ischemia, which increases the permeability of pancreatic blood vessels and leads to edema of the pancreatic tissues, which is termed interstitial pancreatitis. The edema may be carried over into the digestive system secondary to hypovolemia (decrease in blood volume) and arteriovenous shunting. This can facilitate the movement of bacteria from the digestive system into systemic circulation and the result may be severe pancreatitis, which leads to life threatening complications including acute respiratory distress syndrome, kidney failure, circulatory shock, and multiple organ failure. Approximately 20% of patients with acute pancreatitis will enter the severe pancreatitis pathway, which carries a 10% to 30% mortality rate. Improvements in intensive care capabilities in the 1990’s brought mortality rates down from previously higher levels but the mortality numbers have remained constant since that time (Canalas 2007).

In the ERCP procedure, a specialist who is usually a gastroenterologist inserts an endoscope through the mouth of the patient, into the stomach, through the pyloric sphincter and into the duodenum where the entrance to the Ampulla of Vater, the common opening of the common bile duct and the pancreatic duct, can be seen. A small catheter is threaded into the common passageway distal to the Ampulla of Vater where it releases contrast dye into the duct system. Fluoroscopic visualization, made possible by the presence of contrast dye, enables the clinician to see the common bile duct, the left hepatic duct, intrahepatic ducts and the pancreatic ducts. Once the source of the problem has been identified, the doctor may decide to take appropriate actions such as removal of gallstones that are blocking the common bile duct or performing a sphincterotomy in which a small incision is made into the Sphincter of Oddi, the muscular valve that normally controls the opening of the Ampulla of Vater. A sphincterotomy allows small gallstones and bile to drain more freely into the duodenum. Sometimes a papillotomy is done with an electrified wire to enlarge or remove the opening of the duodenal papilla, a small raised area in the duodenum through which bile drains from the Ampulla of Vater into the small intestine. This procedure may further open up the gallbladder drainage system. The pyloric sphincter and the common bile duct may be stretched with balloon dilators and debris can be removed using balloon pull-throughs or tiny basket-like devices designed for this purpose (Chatzinooff 2012).

Biliary pancreatitis that is secondary to gallstones (choledocholithiasis) is one of the most common causes for emergency ERCP with sphincterotomy, accounting for 40% of cases. Biliary pancreatitis is believed to be caused when pancreatic acinar cells are injured due to increasing pressure in the pancreatic duct brought about by obstructive gallstones blocking the Ampulla of Vater (Canalas 2007). Excessive use to alcohol is implicated in about 35% of cases of acute pancreatitis. Alcohol causes the accumulation of digestive enzymes in interstitial fluids, which increases the permeability of the smaller pancreatic ductlets. Increased permeability of the ductlets allows digestive enzymes to reach pancreatic parenchyma cells, causing tissue damage. Alcohol also increases the protein content of pancreatic secretions that results in numerous tiny protein plugs that can block small pancreatic ducts. Less common causes of acute peritonitis include prolonged exposure to organophosphate pesticides, scorpion stings and snake bites. Toxins found in these substances are believed to cause hyperstimulation of the pancreas that results in the production of abnormally high amounts of pancreatic enzymes (Chatzuboff 2012).

The complication rate from the ERCP procedure is reported to be between 5% and 7%. Pancreatitis that results from the procedure itself is a possible complication as are perforations of surrounding tissues, hemorrhage and cardiopulmonary difficulties. Perforations are believed to be related to the skill and technological dexterity of the clinician. The bowel can be perforated by the endoscope, resulting in intraperitoneal perforation. Retroperitoneal leakage can result from unwanted extension of the sphincterotomy incision and manipulation of guide-wires and other necessary equipment can cause damage to various related tissues. Fortunately, perforation is rare, occurring less that 1% of the time. Bowel wall perforations are commonly repaired surgically while other equipment related perforations can often be treated endoscopically (Canalas 2007, Kahaleh 2012). In addition to perforations, the risks of ERCP seem to be determined as much by the characteristics of patients who undergo the procedure as by the technique of the clinician. Younger age is considered a risk factor for ERCP because younger patients may have a smaller common bile duct, which may make cannulation more difficult. Patients with previous post-ERCP pancreatitis are at greater risk of complications as are those who have difficult common bile cannulations due to stenosis. Complications have also been known to result from adverse reactions to the contrast dye. Sphincter of Oddi dysfunction is seen almost exclusively in females so being female is also
a risk factor for the ERCP procedure. The risk factor for females is further complicated by the fact that, for reasons that are not well understood, most of the severe or fatal cases of post-ERCP pancreatitis are seen in women (Kahaleh 2012).

In the future, more complex ERCP procedures, such as the placement of pancreatic duct stents, are expected to become more commonplace and these procedures will likely give rise to other more technically difficult procedures that will have a fairly long learning curve for clinicians. The emphasis will be on appropriate training and maximizing the expertise of the doctors who do ERCP procedures. The literature suggests that full competency in advanced ERCP requires that an endoscopist complete at least 180 ERCP procedures (Kim 2012). As the role of ERCP increases in academic medical centers, new accessories for the diagnostic and therapeutic use of ERCP are expected to proliferate. The tools will be expensive and it will require advanced training to use them effectively. Because of the added expense and training, the new tools will likely be used on patients with complex disease conditions. Basic cholangioscopy allows the endoscopic visualization of the bile ducts and it greatly improves the accuracy of therapeutic procedures and diagnosis. Now, and to a greater extent in the future, endoscopic visualization can be enhanced by the addition of the SpyGlass visualization system and direct peroral cholangioscopy, both of which use ultra-thin endoscopes in addition to standard endoscopic equipment. Probe-based confocal laser endomicroscopy allows histological diagnosis using a fluoroscope. Intraductal ultrasonography, using very thin ultrasound probes that are passed through the endoscopic channel, allows the clinician to visualize the common bile duct and the pancreatic duct without using contrast dye. Intraductal ultrasonography can also be used to diagnose very tiny gallstones and both intraductal and extraductal lesions (Kim 2012).

The future looks bright for less invasive procedures such as ERCP, although laproscopic cholecystectomy still remains the gold standard for the relief of gallstone symptoms (Chatzinoff 2012). The risks associated with ERCP remain significant and will have to be addressed if the procedure is ever going to emerge as the treatment of choice for gallstone disease and related pancreatitis. The availability of newer, non-invasive imaging techniques, like ultrasonography (EUS) and magnetic resonance cholangiopancreatography (MRCP), has made it possible to restrict ERCP to therapeutic uses so it is rarely used today without therapeutic intent. ERCP can be used to manage gallstone disease, microlithiasis and related pancreatic and Sphincter of Oddi dysfunctions and it is also useful in identifying anatomical abnormalities, such as stenosis of the pyloric sphincter or common bile duct, that can contribute to acute pancreatitis (Cherian 2007). It will be interesting to see what the future of ERCP technology will be like. The hope is that the future will be a bright one for the patients whose treatment may be significantly advanced and fine-tuned by this dynamic procedure.

Literature Cited


Illustration Credit

Illustration used with permission.

The illustration of the Sphincter of Oddi and related structures is original art used with the permission of Scott Rawlins of the Arcadia University Art Department, January 2013.
Abstract: Teaching biology at the American University of Beirut in the 1980’s had unusual challenges and rewards. Among the challenges in teaching during the Lebanese Civil War was dealing with a heavily traumatized group of students. The rewards came when those students emerged as uniquely driven scholars. My students and I were able to persevere under the most adverse conditions. We ultimately prevailed over those conditions to have our work published in international peer-reviewed research journals. Every bit of work that was done with vertebrates was performed ethically and all of the vertebrates were released at the end of each project. This article describes our investigations of three types of naturally-occurring poisons common in Middle Eastern plants and animals: cardiac glycosides, cyanogens, and histamine.

I. Introduction

I turned on the BBC World News first thing one morning in the early 1980’s and heard the usual opening music, the time in Greenwich, and the name of the presenter who said: “This is London.” The news that day, as was often true during the 19-year long Lebanese Civil War, was grim. Since my wife, Henriette, and I were living on the campus of American University of Beirut, which is situated on a peninsula jutting out into the Mediterranean, the BBC was generally our only source of reliable information about the outside world. It also served as our primary source of information about what was going on in the city of Beirut itself.

That day there was news of a colossal armed struggle in a distant neighborhood of the city. Statistics of those killed and wounded were sad as always, the reason for the fight obscure and basically pointless. Neighborhood battles typically involved small caliber weapons and usually included a few rocket-propelled grenade and mortar launchings. Some apartments would undoubtedly be gutted and an untold number of people would be injured; a few people would be killed. We could imagine people huddled in bomb shelters with dozens of others. Bomb shelters typically lacked electricity, sewage, running water, and emergency services. In a bomb shelter it would not be unusual to hear a few people screaming from physical and emotional injury. Can you imagine a whole night of that?

I had a special interest in that neighborhood since a number of my students lived there. Nevertheless, I ate my breakfast and made my way over to my office to oversee my graduate students and prepare for my class.

I was about to go to my first lecture of the morning when Mohammed (not his real name), one of my biology undergraduate students, came to my office door. I was astonished because Mohammed lived in the neighborhood where the armed struggle had just taken place. What was he doing in school on this day of all days? How did he manage to find his way through the remains of the battle?

I said: "Mohammed, I hear you had a bad night in your area."

He replied: “It was awful Professor Evans.”

The unadorned grief with which he delivered that sentence was all I needed to understand a little of what he must have gone through but he still came to the university for his education!

What do you think your students would say if you asked them if they believe their education is worth as much as Mohammed thought his was worth?

Fortunately for all of us, not all days were that bad and most were amazing. Scientifically, it was the most productive time of my postdoctoral career. My students, collaborators, and I published more than twenty refereed articles and a book in less than six years. Our articles were about all sorts of things: dolphins, gulls, snails, prawns, insects, thermoregulation, the sense of taste in birds, game theory, cardiac glycosides, cyanogens, and histamine. We were amongst the first in the world to publish work on some of these things. We performed all of our research with vertebrates ethically and in accordance with international standards. Every vertebrate was released at the end of each test replication of each experiment.

(Continued on next page)
II. The toxins and sample questions for your students

Many of our investigations in Beirut centered on toxins including the cardiac glycosides, cyanogens, and histamine.

A. Cardiac glycosides

The cardiac glycoside (also called cardenolides or cardiotonic steroids) most people are familiar with is digoxin, which is an ancient drug that was probably first used in England. It was originally derived from the foxglove plant and it is used to this day to treat atrial fibrillation. Generally, digoxin and its derivatives are steroids connected to a 7-carbon sugar (Uglow 2002). We were also interested in a Lebanese cardenolide source, the oleander plant. Oleanders have several different related compounds but the primary chemical is called oleandrin (Anon 2009). Oleandrin is intensely bitter and quite toxic. As is true of other cardiac glycosides, it increases the sodium ion/calcium ion exchange, thereby increasing intracellular calcium.

Cardiotonic steroids appear to parallel those that occur naturally as hormones in mammals. Oleandrin also prevents tumor proliferation, so perhaps oleandrin will one day have a non-cardiological role in medicine (Schoner and Scheiner 2007).

Suggested question for students:

How might cardiac glycosides affect the contractions of heart muscle cells?

Possible answer: Increasing the intracellular calcium ion concentration will increase the force of contractions.

Historical note: According to an elderly cardiologist I spoke with, Lebanon did not have access to normal pharmaceutical supplies during World War II and no digoxin was available to cardiologists to prescribe for their patients. Cardiologists attempted to substitute oleander’s cardenolides for atrial fibrillation patients but the substitution was not always successful because there was difficulty in obtaining an oleander product of reliable purity and concentration.

Our research centered on the use of these cardenolides by oleander-consuming herbivores, such as the rock hyrax and a variety of insects, in their own immune defense against predators. Interestingly (to us!), we discovered that oleander poisons only enhanced, but were not essential to, the oleander-consuming herbivore’s internally-developed defenses (Evans, et al 1986).

B. Cyanogens

Cyanogens are bitter poisons that contain a cyanide group (or CN-) which can be liberated from the molecule. Probably the most famous of these is amygdaline, also known as laetrile, which is found in stone fruits. It is especially abundant in apricot pits. Cyanogens offer protection to the embryo in the seed because the cyanide is released in the herbivore’s stomach and the herbivore will likely die before it has a chance to digest all the way to the embryo. The plant can safely store cyanogens since plants do not digest cyanogens (Zagrobelny, et al. 2004). What you may be surprised to know is that everyone seems to be able to tolerate a small amount of cyanogen in their food; cherries, for instance, just do not taste right unless they contain a little bit of amygdaline in the fleshy part of the fruit. Just don’t mess with the pits!

Suggested questions for students:

1. If cyanide inhibits the enzyme cytochrome c oxidase, how would it kill a person in high doses (i.e., acute poisoning)?

   Suggested answer: Cytochrome oxidation is vital in oxidative phosphorylation (or the electron transport chain) so that ATP can be produced in the mitochondria.

2. What part of the cell is most frequently associated with cytochrome c?

   Suggested answer: The mitochondria are the most impacted organelles in most cells.

3. What are the clinical issues that would most likely lead to death?

   Suggested answer: Cyanide binds with hemoglobin also so the symptoms of asphyxiation would be noted for that reason alone. Additionally, little ATP can be synthesized, a fact that inevitably leads to reduced muscle contractions (but other issues will be affected too). Since muscle contractions for all practical purposes cease, cardiac muscle will be impacted profoundly. Another possible response is respiratory failure since ventilation requires muscle activity. Basically, it amounts to hypoxia with oxygen (Zagrobelny, 2004).

What is not generally known is that there are a few animals (we worked with a locally common burnet moth) that have cyanogens sequestered in their own bodies (Zagrobelny, et al. 2004). We wanted to know if the cyanogens actually helped to defend those creatures. We were astonished to discover that our hand-raised birds were relatively tolerant to cyanogens when they were presented in flour-and-water shaped into “worms” (Muhtasib and Evans 1987). We knew that whole moths were repugnant to birds so we wondered why the birds would accept the “worms” and not the moths. Our research eventually expanded to examine this issue in greater detail.

(Continued on next page)
C. Histamine

Histamine helps to orchestrate numerous activities in the inflammatory response and there are several different membrane receptors for histamine in the body (Jutel, et al 2005). However, most people are familiar with the molecule in a much more negative way: it is the underlying cause of allergy symptoms. Certain common foods and drinks have some low level of histamine in them although sensitive people cannot drink some varieties of wine because of histamine and related compounds. Fortunately for the vintners, we aren’t all in that category!

Some stinging insects have histamine as part of their venom ensemble and this seems to be part of the reason why the sting of bees and wasps can be so dangerous. The pain due to the sting itself is trivial but the histamine introduced with the sting can be very problematic. In our research we found that burnet moths have a lot of histamine in them. We thought our birds would reject histamine-laced “worms” but they ate that food until we increased the histamine levels well beyond what would normally be present in nature. However, if we offered combinations of cyanogens and histamine, the birds showed clear aversion and would not eat this material after the first nibble. This was the first time anyone had been able to show synergy in the avian bitter taste sense (Muhtasib and Evans 1987).

Suggested question for students:
What specifically are the most dangerous issues raised in excessive histamine secretion (i.e. in a case of extreme hypersensitivity) in humans?

Suggested answer: Histamine can cause broncoconstriction, excessive mucus secretion, and circulatory shock. The smooth muscles in respiratory passages typically constrict so the airways can be severely obstructed. Histamine causes venous smooth muscles to relax, allowing for vasodilation, leading to venous pooling (Jutel 2005). A thoughtful student might be interested in the fact that histamine causes different effects in different sets of smooth muscles so you might direct them to Jutel for further reading.

III. The end came one day

I was very fortunate to have wonderful postdoctoral and graduate students during my stay in Beirut. During the time I spent there I taught some of the brightest undergraduates I have ever had the pleasure of teaching and I was very fortunate to have unlimited research opportunities. My wife and I lived in a lovely home with a magnificent garden and most of the Lebanese I knew treated me as their brother. It made me happy to think that I might have that life for the rest of my career, but it was not to be.

In later years, when people learn of all that my family endured in those Beirut years, they often ask why we stayed for as long as we did. That is a great question. The US government offered twice to extract us during the time we were in Beirut. We knew that Americans had been kidnapped from a nearby university and a large number of people had been carted off to undisclosed locations. We learned that some of them had been murdered and at least one had been tortured to death. I knew of one entire Lebanese family that vanished, never to be seen again. Incidences like these were not often mentioned on the BBC World News. So why did we stay? Ask Mohammed. He persevered through horrible adversity for his education. He and thousands like him needed someone to teach them; someone had to step up to the job and I thought it could be me. We stayed for as long as we could until the day came when I was told that I was next on the list to be kidnapped since there were no other Americans to be singled out for this fate.

Mohammed knew how dangerous the situation had become and he had protected me, and several others, for quite a few years. I knew that if I were kidnapped, it would cause unnecessary suffering for my students and I didn’t want any of them to be hurt on my account. As a result of all of these things, at an agreed upon time, some very heavily armed Lebanese people quickly and discreetly smuggled my wife and me out of the city. When was this done? How was it done? Who risked their lives to save us? To this day, I cannot tell anyone about what happened but I remain forever grateful to these brave people.

I.V. Cited references


Process Oriented Guided Inquiry Learning (POGIL) is a teaching method that promotes active learning through curriculum materials that are designed to promote discussion and inquiry within small cooperative groups of students. POGIL has been used in chemistry for over ten years, but is new to anatomy and physiology. With financial support from the National Science Foundation (DUE-1044221), a group of 9 A & P instructors from the Midwest have been developing POGIL materials for entry-level A & P courses. The two-year project will come to an end this May at the HAPS conference in Las Vegas where the materials will be made available to HAPS members.

POGIL related events in Las Vegas will start on Sunday, May 26th, when Dr. Rick Moog, Executive Director of the POGIL Program, will give a keynote address. Dr. Moog is a chemistry professor at Franklin & Marshall College and has provided the vision and energy behind the POGIL program since its inception in 1994. On Tuesday and Wednesday of the Las Vegas conference, three POGIL workshops will be offered by the 9 members of the A & P curriculum development team. The first will be a general introduction to the POGIL project and the POGIL teaching method. The second and third workshops will feature the POGIL materials that have been developed through the project.

Currently the development team is working on about 20 activities. Over the next few months, 10-15 of the best will be revised and polished. The final set will hopefully cover several different topics in A & P, but in no way will it be a comprehensive curriculum package. Over the next few years, we hope to continue the project and add more items to the collection.

It is important to note that the curriculum items presented in Las Vegas will not be officially “POGIL” materials; to achieve POGIL endorsement they must go through a review process within the POGIL program. This review process will not be complete until after the May 2013 HAPS conference in Las Vegas. (Even after our NSF project has been completed, HAPS members will be able to develop and submit materials to the POGIL Program for endorsement.) After approval from the POGIL Program, all the materials will be archived as .pdf files on the HAPS Web Site where they will be available to all HAPS members free of charge.

All POGIL activities are intended to provide instructors with a viable alternative to lecture. They are simple tools for instructors to use to promote cooperative group learning and inquiry in the classroom. This is not easy to achieve because of the considerable work involved on the part of the instructor. Teaching with inquiry and group learning takes considerable practice, but the POGIL materials developed in the POGIL program and the workshops at the Las Vegas conference represent a good start. To take the next step we highly recommend attending a 2-3 day POGIL workshop where instructors receive more focused instruction on how to use POGIL materials in the classroom.

The development process used in our project has involved several different classrooms and instructors. It is clear that what works well in one classroom is not successful in another. The academic level of the students and the expectations of the instructor are critical elements. Our materials target entry-level anatomy and physiology. More advanced students will find the materials too easy, and others will find them too difficult.

The original NSF proposal made clear that the intent of the A & P POGIL materials would be help instructors move from being a “sage on the stage” to a “guide on the side.” If you are an instructor who wishes to start promoting more active learning in your classroom, and maybe get away from Power Point for a few days, we highly encourage you to attend the POGIL sessions at HAPS in Las Vegas.

You may find related information on the following links:

POGIL Project Web Site:
http://pogil.org/

Overview of the HAPS POGIL Project
http://msjensen.cehd.umn.edu/POGIL/Brief_Intro.html
EDU-Snippets: Bones, Art Work, Excitation, and Neurotransmission

EDU-Snippets – A column that survives because you - the members - send in your Snippets

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EDU-Snippets is a column designed to let you, the members of HAPS, share your “ways to make sure your students get it.” Since EDU-Snippets began, our members have been continuously amazed at how many teaching and demonstration ideas pop up and how easily these ideas are transferred from one instructor to another through Snippets. This edition is no exception. Below you will see some great ideas – stimulating, tantalizing, and well within everyone’s budget!

I. Osteo-Snippet

Janice Fritz (St. Clair County Community College, jfritz@sc4.edu) sent in three Snippets. Each one deserves its own header. Janice has been concerned – as I am certain we all have been – about students keeping the different “osteo-” words straight. So, here is what Janice does.

When I have had trouble getting my students to understand that osteogenic cells, osteoblasts, and osteocytes are different stages of the same lineage, I try comparing them to human life stages. An osteogenic cell is a teenager sitting around the house, not accomplishing very much. With the proper motivation in the form of growth factors, the teenage osteogenic cell matures into a hard-working adult osteoblast. The osteoblast works hard contributing to society by producing bone matrix. Once it has done its work and is surrounded bone matrix, the osteoblast is able to retire in its lacuna as an osteocyte. The osteocyte may not go to work every day, but it is still important for keeping an eye on the neighborhood and motivating teenagers by responding to bone stress and activating osteoblasts.

II. Artistic Histo-Snippets

Janice Fritz (St. Clair County Community College, jfritz@sc4.edu) continued her ventures into Snippet-land with this interesting idea. This idea might have numerous applications in our various lab and lecture settings.

I tried this quick activity with a group of adults to illustrate the importance of observation and how drawing improves observation. I wanted to have my students try something before I asked them to sketch tissues during our histology unit.

I made 40 cards with pictures of similar smiles on one side and an identifying number on the other. Each student got two cards, which I passed out picture side down. They recorded the number of the first card and then looked at it for two minutes trying to draw it. I collected all the cards, mixed them up, and laid them out picture side up. With few exceptions, students easily located the card they drew, but had trouble finding the one they only looked at. In this 5-minute activity, they were convinced that taking the time to make a drawing makes a great deal of difference.

III. Coupling Snippet

Janice Fritz (St. Clair County Community College, jfritz@sc4.edu) came up with one more Snippet that our students should find most informative.

This activity takes some time and a little space, but I really enjoy the student response to seeing excitation/contraction coupling in action.

After the blank looks I get as I explain the steps involved in getting from the release of acetylcholine to a muscle contraction, I make my students act it out themselves. I use tape to mark the plasma membrane, T-tubules, and sarcoplasmic reticulum on the floor of my classroom. Then I gather the students in the back and randomly hand out cards assigning them to their roles: neuron, acetylcholine, acetylcholine receptor, voltage-gated ion channels, ryanodine receptors, Na+, K+, Ca2+, etc. I adjust as needed for the number of students. (There is always room for more Na+ and K+ in large groups and I get to be the neuron if the class is small.

As the students identify which molecule or ion they represent, I...
have the group direct them to their correct location in a resting muscle. Then we walk through the process from the neuron releasing acetylcholine to the calcium binding to the troponin. The students must each explain what they are doing as they move to their new location in the excited muscle fiber. The first time is a little rough and the second is better, but when they switch roles and run it through the third time, I definitely see the light of understanding in their eyes!

IV. Electrical and Neurotransmitted Snippet

Robert Rawding (Gannon University, rawding001@gannon.edu) asks a very critical question, a question we should all pay close attention to.

Why Are “Neurotransmission” and “Electricity” Mentioned in the Same Breath?

Unless we had a fairly astute teacher, we all learned that transmission of impulses along the axon of a neuron was electrical, right? Wrong, wrong, wrong, wrong.

We can do better than our teachers. I assembled a short table of contrasting elements for each process, electrical versus neuron conduction. The table elements with hashtags are common to both processes.

There are likely other comparisons; these are not meant to be exhaustive but to illustrate the point: be careful when comparing neurotransmission to electricity.

<table>
<thead>
<tr>
<th>Electrical Conduction</th>
<th>Neuron Conduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Field properties based on the flow of electrons through a conductor</td>
<td>Flow of ions “across” a neuron membrane (ions move through channels)</td>
</tr>
<tr>
<td>All negatively charged, -</td>
<td>Some ions positively charged, some negatively charged</td>
</tr>
<tr>
<td>Conducting ‘particles’, small (e-)</td>
<td>Conducting ‘particles’, large (ions)</td>
</tr>
<tr>
<td>Conducting particles, one-way flow</td>
<td>Conducting particles, can flow in both directions</td>
</tr>
<tr>
<td>Conduction velocity is near the speed of light, specifically 3.0 x 10^8 meters sec^-1</td>
<td>Conduction velocity variable, but maximal at slightly greater than 1.0 x 10^6 meters sec^-1 (more than six orders of magnitude slower)</td>
</tr>
<tr>
<td>Not typically saltatory (although we can get an electrically-based charge to jump or arc across gaps (e.g. in a spark plug))</td>
<td>Can be saltatory or continuous</td>
</tr>
<tr>
<td>Energy-driven (electricity “is” energy)</td>
<td>Requires energy (Na+K+-ATPase pumps)</td>
</tr>
<tr>
<td>Conduction faster in a cold conductor</td>
<td>Cold “conductor” reduces conduction speed</td>
</tr>
<tr>
<td>Complete circuits required for current to flow (open [broken] circuits don’t work)</td>
<td>Can end without a complete circuit (e.g. motor neuron transmission across a motor endplate to electrochemically-controlled sarcoplasmic reticulum calcium channels)</td>
</tr>
<tr>
<td>Current (flow) can be alternating or direct</td>
<td>Current (flow), i.e. ion movement, is alternating (in/out/in or out/in/out)</td>
</tr>
<tr>
<td># Can be monitored by a volt meter</td>
<td># Can be monitored by a volt meter</td>
</tr>
<tr>
<td>Conductor is passive</td>
<td>Conductor is active</td>
</tr>
<tr>
<td>Conductor requires no maintenance operations</td>
<td>Conductor maintained by membrane components</td>
</tr>
<tr>
<td># Can short-circuit</td>
<td># Can short-circuit</td>
</tr>
<tr>
<td>Conduction itself warms the conductor</td>
<td>Little or no apparent warming during conduction</td>
</tr>
<tr>
<td>No dichotomous distribution of ions/charges</td>
<td>Dichotomous distribution of ions/charges</td>
</tr>
<tr>
<td># Can be conducted by electrolyte solutions</td>
<td># Is conducted through electrolyte solutions</td>
</tr>
<tr>
<td># Insulation important but not entirely necessary</td>
<td># Insulation important but not entirely necessary (non-myelinated axons are present in certain locations)</td>
</tr>
<tr>
<td>Flow establishes electromagnetic fields</td>
<td>Flow does not establish electromagnetic fields, but changing charge distributions</td>
</tr>
</tbody>
</table>

**In my classes, I use the term electrochemical to illustrate that the voltage can be measured in resting and active neurons (we are really measuring the net charges on the ions that are dominant at any instant inside the neuromplasm). In a ‘resting’ neuron, proteins at pH 7.4 have negative charges and are trapped by the neuron membrane, so the voltmeter reflects the dominant negativity inside. As Na+ and K+ channels open, they move with their charges to opposite sides of the membrane, swinging the voltmeter to a positive direction due initially to massive influx of Na+ ions and their charges.** The chemical part of electrochemical reflects the chemicals that are involved in changing the potential. Electrons are not chemicals; ions are.

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V. And We Hope You Will….  

Keep those cards and letters coming! Thank you all for your EDU-Snippet contributions. The influx of Snippets has been great! Please keep it up because more are always needed! Your ideas are tremendous! If you have thoughts or ideas, or any interesting ways to help our students understand anatomy and physiology, EDU-Snippets would love to hear from you! Once again, EDU-Snippets encourages new submitters to submit – and regulars to keep on submitting!

For the next issue of the HAPS-Educator, send your EDU-Snippet experiences and ideas to biology@ctos.com as soon as possible. You will also find a reminder on the HAPS-L list. Plan ahead. You can even submit your ideas now and maybe next issue you too will see your EDU-Snippet in print!
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