The Edges of Life – 7pm at Centennial Hall

Wednesday, February 20
Life’s Human Edge: Changing Perspectives on the End of Life
Michael G.E. Amassian, Professor, Philosophy

Nothing looms with more certainty than the final edge of one’s own life. But in fact, the edge between life and death is anything but clear. This lecture will address the attempts that have been made to define the line between life and death and will explore the biological, legal, ethical, and spiritual debates that have raged around that line.

Wednesday, March 5
Life’s Technological Edge: The Singularity Is Near: When Humans Transcend Biology
Ray Kurzweil, via Teleporter, Teleporter
Founder, Chairman, and Chief Executive Officer, Kurzweil Technologies

Inevitability is on the edge of a new transformation, when what it means to be human will be both enriched and challenged. Inventor and futurist Ray Kurzweil will introduce this radically optimistic singularity, an era when we bring our genetic potential to create a postbiological intelligence, millions of times more powerful than today. In this new world, humans will transcend biology, extend aging, and invent our own lives.

This lecture co-sponsored by: UA College of Engineering and UA College of Science

These do not count as physiology lectures.

Endocrine System

1. Hormone action often amplified by second messenger cascade
2. Hormones often released in very low concentrations made them difficult to study!

Glycogenolysis Example:
- Epi (muscle) (glycogen -> glucose)
- Glucagon (liver)

Goal is to increase blood [glucose]
Chap 14. Endocrine System - Glands and Hormones

Secretions with consequences
All cells secrete, but
Specialized secretory cells grouped into glands
Secrete same specialized substance (e.g., hormone)

Nervous System neurotransmitter acts near and fast
Other secretions, such as hormones, may act more distantly and over a longer time period

Categories of cellular secretions:
- Autocrine - affect the secreting cell directly
- Paracrine - affect neighboring cells (e.g., histamine and inflammation)
- Endocrine - release into bloodstream
- Exocrine - release onto epithelial surface (e.g., sweat onto skin, bile into digestive system)
- Pheromone - exocrine secretion to signal other individuals
- Neuroendocrine - secretion from axon terminal into blood stream

Neuroendocrine Cells and Neurohormones control much of the endocrine system

Three Hormone Classes
1. Amines - small (e.g., epinephrine, norepi, thyroid, melatonin)
2. Steroid Hormones from cholesterol (e.g., testosterone, estrogen)
3. Peptide Hormones - common, large, complex (e.g., insulin, ADH, GH)
Amines – small (e.g., epi, norepi, thyroid)

Modified Amino Acids
1. catecholamines (epi, norepi, dopamine; tyrosine)
2. thyroid (lipid soluble; tyrosine)
3. melatonin (tryptophan)

Glandular Secretion
Response to stimulus
Hormone
Neurotransmitter
Action Potential etc. (e.g., osmolarity and ADH)

Storage before Secretion
Large molecules easily stored because can’t leave readily
Small molecules often stored bound to accessory proteins
Some molecules actively/continuously taken into vesicles
Steroid hormones (lipid soluble) tend to leak out soon
Hydrophobic steroid and thyroid hormones move in blood, bound to carrier proteins

TABLE 14.1 Summary of major blood-borne hormones in mammals (Part 1)

<table>
<thead>
<tr>
<th>Endocrine tissue</th>
<th>Hormone</th>
<th>Class of molecules</th>
<th>Main functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal cortex</td>
<td>Aldosterone</td>
<td>Steroid</td>
<td>Stimulates Na reabsorption and K secretion in kidney</td>
</tr>
<tr>
<td></td>
<td>Androgens</td>
<td>Steroid</td>
<td>Acts on bone to cause growth and helps increase in size in men by action on brain</td>
</tr>
<tr>
<td></td>
<td>Glucocorticoids</td>
<td>Steroid</td>
<td>Part of stress response affects metabolism of many tissues to increase blood glucose and free fatty acids</td>
</tr>
<tr>
<td>Adrenal medulla</td>
<td>Epinephrine and norepinephrine</td>
<td>Catecholamines</td>
<td>Part of stress response balances carbohydrate function and metabolism of many tissues</td>
</tr>
</tbody>
</table>

Hormone ACTION!
Where are the receptors?

1. Lipid Soluble
   - Steroid and Thyroid Hormones (~long-lived)
   - Through Membrane
   - Bind cytoplasmic receptors, then to Nucleus
   - Directly affect transcription (therefore long-term)

2. Lipid Insoluble
   - Bind cell-surface receptors
   - Often one or more 2nd messengers
   - Amplification
   - Rapid, short-duration responses

Possible 2nd messengers:
1. cAMP, cGMP (cyclic nucleotide monophosphates)
2. IP3, DAG (diacylglycerol; inositol phospholipids)
3. Ca^{2+} ions

Glandular Secretion

Secretory Vesicles

Exocytosis - common release mechanism

Regulation via Calcium - free cytosolic calcium concentration is correlated with exocytosis (including of NT, hormones, etc.)

Ca^{2+} ions
- Intracellular stores (ER)
- Influx from extracellular fluid

1. binds and activates Troponin C in skeletal muscle
2. binds and activates Calmodulin also

Randall et al. 2002

<table>
<thead>
<tr>
<th>Signal</th>
<th>Tissue</th>
<th>Cellular response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulatory</td>
<td>Epidermal (hair follicles)</td>
<td>Hair growth</td>
</tr>
<tr>
<td></td>
<td>Epithelial (endocrine)</td>
<td>Skeletal muscle: Increased muscle tone</td>
</tr>
<tr>
<td></td>
<td>Endothelium (vascular)</td>
<td>Increased vascular permeability</td>
</tr>
<tr>
<td></td>
<td>Endothelium (vascular)</td>
<td>Smooth muscle: Vasoconstriction</td>
</tr>
<tr>
<td></td>
<td>Glandular (endocrine)</td>
<td>Increased epithelial cell activity</td>
</tr>
<tr>
<td></td>
<td>Glandular (endocrine)</td>
<td>Increased glandular secretion</td>
</tr>
<tr>
<td></td>
<td>Glandular (endocrine)</td>
<td>Increased ductal activity</td>
</tr>
<tr>
<td>Inhibitory</td>
<td>Adipocytes (fat cells)</td>
<td>Decreased lipolysis</td>
</tr>
<tr>
<td></td>
<td>Adipocytes (fat cells)</td>
<td>Decreased thermogenesis</td>
</tr>
<tr>
<td></td>
<td>Adipocytes (fat cells)</td>
<td>Decreased insulin sensitivity</td>
</tr>
<tr>
<td></td>
<td>Adipocytes (fat cells)</td>
<td>Decreased glucose metabolism</td>
</tr>
</tbody>
</table>

Randall et al. 2002
Multiple Cleavage Events to Make Active Hormone

Major Endocrine Players

Hypothalamus
- (~7 neurohormones)
- mostly peptides

Pituitary (9 hormones)
1. Anterior (~nonneuronal)
2. Posterior (~neuronal control)

Posterior Pituitary

Oxytocin - uterine contractions, milk ejection
Antidiuretic Hormone (ADH) - water retention in kidney

Both are peptide hormones
Both are similar and highly conserved...

Tropic Hormones

Endocrine gland

Tropic hormones = act on other endocrine tissues
(e.g., adrenal cortex, thyroid, gonads)

Negative Feedback

Anterior Pituitary
Tropic Hormones of Anterior Pituitary

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Structure</th>
<th>Target tissue</th>
<th>Primary action in mammals</th>
<th>Regulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH</td>
<td>Peptide</td>
<td>Adrenal cortex</td>
<td>Increases synthesis and secretion of stress hormones</td>
<td>Cortisol-releasing hormone (CRH) stimulates release of CRH</td>
</tr>
<tr>
<td>Follicle-stimulating hormone (FSH)</td>
<td>Glycoprotein</td>
<td>Ovarian follicles (female); secondary sex organs (male)</td>
<td>In females, stimulates maturation of ovarian follicles; in males, increases spermatogenesis</td>
<td>GtH-stimulates release of FSH and induces secretion of estradiol</td>
</tr>
<tr>
<td>LH</td>
<td>Glycoprotein</td>
<td>Ovarian interstitial cells (female); testicular interstitial cells (male)</td>
<td>In females, induces fluid retention in ovarian follicles; in males, suppresses spermatozoa formation, and gynecomastia occurs</td>
<td>GtH-stimulates release of LH and increases secretion of estradiol</td>
</tr>
<tr>
<td>TSH</td>
<td>Glycoprotein</td>
<td>Thyroid gland</td>
<td>Increases synthesis and secretion of thyroid hormones</td>
<td>TSH inhibits secretion of thyroid hormones and increases release of TSH</td>
</tr>
</tbody>
</table>

Note: Key to abbreviations: FSH - Follicle-stimulating hormone, LH - Luteinizing hormone, TSH - Thyroid-stimulating hormone.

In response to cold, fright, pain etc...

**Hypothalamus**
- corticotropin-releasing hormone (CRH)
- Anterior Pituitary
  - Adrenocorticotropic (ACTH)
  - Blood Stream

Adrenal Cortex
  - (cortico)sterone; stress hormones

**Mammalian Stress Response**

Glucocorticoids (from adrenal cortex)
- Includes 'Stress Hormones'
  - Cortisol, cortisone, corticosterone
  - Released in response to ACTH (Adrenocorticotropic) from Anterior Pituitary

Steroid hormones (lipid soluble) derived from cholesterol (mobilize a.a.s and glucose, suppress immune system etc.)

Blood loss:
- ↑ vasopressin → ↑ water reabsorption at kidney
- ↑ aldosterone → ↑ Na reabsorption at kidney
  - ↑ fluid retention
  - ↑ blood volume
  - ↑ blood pressure

Negative Feedback Loop
**Water and Electrolyte Balance**

**Hormones**

Randall et al. 2002

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Tissue of origin</th>
<th>Structure</th>
<th>Target tissue</th>
<th>Primary action</th>
<th>Regulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidiuretic hormone (ADH, vasopressin)</td>
<td>Posterior pituitary</td>
<td>Neuropeptide</td>
<td>Kidneys</td>
<td>Increases water reabsorption in the collecting ducts</td>
<td>Known stimuli are circulating osmolality or decreased blood volume; stimulates water reabsorption</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>Isthmus</td>
<td>Peptide</td>
<td>Bones, kidneys</td>
<td>Decrease Ca++ in blood</td>
<td>Known stimuli are high Ca++ or pH</td>
</tr>
</tbody>
</table>

Calcitonin decreases Ca++ in blood; PTH increases Ca++ in blood

**Catecholamines**

Randall et al. 2002

Catecholamines (e.g. epinephrine)

- **Fight/flight**
  - Catecholamines from the adrenal medulla
- **Response**
  - Bronchodilation, vasodilation to major muscles, vasoconstriction to stomach and skin, increased heart rate, mobilization of resources

**Thyroid Hormone**

(aka Thyroxine)

- **T₃ and T₄ (# of iodines)**
- **Being cold can stimulate**

**Insulin and Glucagon**

Classic NEGATIVE FEEDBACK

- Increase in blood glucose
- Decrease in blood glucose
- Release of glucose from liver
- Decrease in circulating glucagon
Insulin and Glucagon Regulate blood glucose:
- Insulin in response to high glucose levels
- Glucagon in response to low glucose levels

Both from pancreatic gland:
- Insulin from beta cells
- Glucagon from alpha cells

Type 1 Diabetes:
- when beta cells decrease insulin production
Type 2 Diabetes:
- when insulin receptor signal pathway defective

Insulin from beta cells
Glucagon from alpha cells

Growth Hormone
Metabolic and developmental effects

From Anterior Pituitary

Often has opposite effect of insulin

Stimulates gluconeogenesis
Reserves glucose for NS
Promotes use of fatty acids as fuel

Gigantism / Acromegaly

Gigantism
Acromegaly

Dwarfism

Vertebrate Reproduction

Asexual Parthenogenetic Whiptail Lizards

Reproductive Hormones
Steroid Hormones from Adrenal cortex and Gonads

Hypothalamus
- GnRH
Anterior Pituitary
- FSH, LH
Gonads, Adrenal Cortex

See Fig 14.1, Hill et al. 2004

Steroid Hormones from Adrenal cortex and Gonads

9-19 Rastel et al. 2002
Male Sex Hormones

**Testosterone and other androgens**

Released from Leydig Cells in response to LH, FSH

FSH binding to Sertoli cells stimulates spermatogenesis

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Female Sex Hormones

**Estrogens**

Ova created and stored before birth (mammals and birds)

Repro cycle in 2 phases:
- Follicular and Luteal
- FSH stimulates beginning of follicular phase -> development of ovarian follicles

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Steroid Abuse

**Homeostasis & Negative Feedback**

What happens if you take too much exogenous testosterone?

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**Follicular Phase**

1. FSH
   - Causing follicular maturation
2. LH
   - LH and FSH help generate Estrogen (3)
   - This Estrogen causes hypothal and ant. pit. to release spike of LH and FSH leading to ovulation (4)
   - (endometrium 5)
   - release of ovum (6)

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**Luteal Phase**

7. FSH, LH
   - Estrogen
8. LH changes ruptured follicle into corpus luteum
9. corpus luteum secretes estrogen and progesterone which inhibit FSH, LH release from anterior pituitary by slowing GnRH
10. progesterone leads to richer endometrium
11. without fert., cycle begins again
12. with fert., Chorionic gonadotropin maintains CL, maintaining high levels of estrogen and progesterone; maintaining endometrium; follicular development inhibited
13. Placenta takes over hormone production
Dear Cecil:

I just hit 40 and still have an unanswered question from my teens that has always bothered me. Aerosmith in “Sweet Emotion” sings about being accused of impregnating a girl. At the end of the verse they sing, “can’t catch me ’cause the rabbit done died,” referring to a pregnancy test. Arguments start over just what this test entails. Most say the bunny will die, but can’t agree as to why. Some say the rabbit will always die because they kill it before they take its blood (which seems pretty dumb). Some say they inject it with some fluid taken from the woman and it dies a horrible, convulsive death. And some say they have to dissect the rabbit after it has been injected. This was before those home test kits, but wasn’t there a better way? --Joe Shredl, Colonial Heights, Virginia