I. **Announcements** Thanks for checking the roster & signing in each day. Staff: Kelsey, Hannah, Katie & Pat

https://blogs.uoregon.edu/bi358/winter-2018/

Discussions today 10am, 12n, 2 pm 130 HUE, registration Q?

II. **Outline Handout** Office hr, text (G&H), discussion-lecture notebook (DLN), optional text, attendance & participation, feedback, quizzes, presentation & paper, expectations, Q?

III. **Dr. Eugene Evonuk, Dr. Arthur Guyton & Dr. John Hall**

IV. **Discussion Preview** Cigarettes & addiction, e-cigarettes?

V. **Introduction to Human & Medical Physiology**

Anatomy vs. Physiology, Structure vs. Function

VI. **Body Levels of Organization** LS

VII. **Homeostasis + 4 Key Q?** G&H + DLN

A. Brief History G&H p 3
B. What? → Maintenance of ECF G&H p 4
C. Where? → ECF = Plasma + interstitium G&H pp 4-5, fig 1-2
D. Why? → Required for cell survival LS + G&H p 8, 9
E. ECF Balances + e.g.? H₂O, T°C Dr. Evonuk DLN p A-1, A-2
F. How? → Simplified homeostatic model (Norris & Evonuk) - feedback e.g. pp 8-9, + feedback G&H fig 1-4, p 9
G&H
New $120.00 Used $90.00 Rental $75.00

DLN
Discussion-Lecture Notebook (DLN)
Eugene, OR 97403
Winter 2018

Biology 358:
Investigations in Medical Physiology

http://uoduckstore.com/
...I ♡ U of O!

Students who succeed are usually those who:

(1) **Attend** class regularly
(2) **Ask** questions
(3) **Come** to office hours & problem-solving sessions
(4) **Study** outside class both alone & in study groups
(5) **Seek** to understand **methods & overarching principles/concepts** rather than specific answers
(6) **Teach** or tutor others &
(7) **Discuss** concepts informally with fellow students.

Dedication to Dr. Eugene Evonuk, 1921-1984
Director, Laboratory of Applied Physiology
University of Oregon, 1967-1984
http://blogs.uoregon.edu/evonuk/
“Never be so narrow as to lose sight of the big picture!”
Walking Medical Dictionary, Demanding Mentor with Unending Dedication & Love for His Students & Family
Infectious Curiosity & Love for Life & the Outdoor World!
Gene, we can always get another plane!
In Memoriam

Arthur C. Guyton, MD
(1919–2003)

The sudden loss of Dr. Arthur C. Guyton in an automobile accident on April 3, 2003 and the loss of his devoted and remarkable wife, Ruth Weigle Guyton, one week later as a result of injuries from the accident stunned and saddened all who were privileged to know them. Arthur Guyton was a giant in the fields of physiology and medicine, a leader among leaders, a master teacher, and an inspiring role model for people throughout the world.

Arthur Clifton Guyton was born in Oxford, Mississippi, to Dr. William (Billy) S. Guyton, an eye, ear, nose, and throat specialist and dean of the University of Mississippi Medical School, and Kate Smallwood Guyton, a math and physics teacher who had been a missionary in China before their marriage. During his formative years, he enjoyed watching his father work at the Guyton Clinic, playing chess and swapping stories with William Faulkner, and building sailboats (one of which he later sold to Faulkner) and countless mechanical and electrical devices, which he continued to do throughout his life. Arthur Guyton’s brilliance shone early. He graduated top in inventions he received a Presidential Citation. He returned to Oxford where he devoted himself to teaching and research at the University of Mississippi School of Medicine and was named chair of the Department of Physiology in 1948. In 1951 he was named one of the 10 outstanding men in the nation. When the University of Mississippi moved its medical school to Jackson in 1955, he rapidly developed one of the world’s premier cardiovascular research programs. His remarkable life as a scientist, author, and devoted father is detailed in a biography published on the occasion of his “retirement” in 1989.1

A Great Scientist

Arthur Guyton’s research contributions, which include more than 600 papers and 40 books, are legendary and place him among the greatest figures in the history of cardiovascular research. His research covered virtually all areas of cardiovascular regulation and led to many seminal concepts that are now an integral part of our understanding cardiovascular physiology and disorders such as hypertension, heart failure, and edema. It is difficult to discuss cardiovascular

http://hyper.ahajournals.org/cgi/content/full/41/6/1175
Dr. Guyton Teaching & in the Lab

https://www.umc.edu/About_Us/History/Dr_Arthur_Guyton.aspx
John E. Hall, PhD
Arthur C. Guyton Professor & Chair
Department of Physiology & Biophysics
University of Mississippi Medical Center
Jackson, Mississippi

https://www.umc.edu/Education/Schools/Medicine/Basic_Science/Physiology_and_Biophysics/John_E_Hall,_PhD.aspx
Not only the Lungs, Heart & Brain, but 100s of Other Tissues & Organs are Adversely Affected!

So sorry I was forced to deliver!
Cigarettes ≡ Patient-Assisted Drug-Delivery System
Inhaling Bypasses the Systemic Circulation
& Is Powerfully Reinforcing!
SMOKING ≡ ASTHMA?

Petri-dish Effect

Ugh!!
Cough!
Cough!!
Tracing the Route of Cigarette Smoke Puff to Brain Time 5 to 8 seconds!!

Mouth → Pharynx → Larynx → Trachea → Bronchi → Bronchioles → Alveoli

Blood → Pulmonary Veins → Left Atrium → Left Ventricle → Aorta → Heart → Brain

Systemic Circulation → Respiratory Membrane
Cigarette + Smoke: > 7000 Chemicals; ~600 Tobacco Company Additives
Atherogenic, Carcinogenic (C), Tumor Initiating, Tumor Promoting (TP),
Toxic (T), Cornucoppia of Unknowns, Synergistic, Reactive...?

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Type</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-aminobiphenyl</td>
<td>C</td>
<td>140 ng per cigarette...</td>
</tr>
<tr>
<td>benz(a)anthracene</td>
<td>C</td>
<td>40-200 ng</td>
</tr>
<tr>
<td>benzene</td>
<td>C</td>
<td>400 μg</td>
</tr>
<tr>
<td>benz(o)pyrene</td>
<td>C</td>
<td>40-70 ng</td>
</tr>
<tr>
<td>carbon monoxide</td>
<td>T</td>
<td>26.8-61 mg</td>
</tr>
<tr>
<td>formaldehyde</td>
<td>C</td>
<td>1500 μg</td>
</tr>
<tr>
<td>hydrazine</td>
<td>C</td>
<td>90 ng</td>
</tr>
<tr>
<td>hydrogen cyanide</td>
<td>T</td>
<td>14-110 μg</td>
</tr>
<tr>
<td>2-napthylamine</td>
<td>C</td>
<td>70 ng</td>
</tr>
<tr>
<td>nitrogen oxides</td>
<td>T</td>
<td>500-2000 μg</td>
</tr>
<tr>
<td>N-nitrosodimethylamine</td>
<td>C</td>
<td>200-1040 ng</td>
</tr>
<tr>
<td>N-nitrosodiethanolamine</td>
<td>C</td>
<td>43 ng</td>
</tr>
<tr>
<td>N-nitrospyrrolide</td>
<td>C</td>
<td>30-390 ng</td>
</tr>
<tr>
<td>phenol</td>
<td>TP</td>
<td>70-250 μg</td>
</tr>
<tr>
<td>polonium 210</td>
<td>C</td>
<td>0.5-1.6 pCi</td>
</tr>
<tr>
<td>quinoline</td>
<td>C</td>
<td>15-20 μg</td>
</tr>
<tr>
<td>O-toluidine</td>
<td>C</td>
<td>3 μg</td>
</tr>
</tbody>
</table>

**Sources:** US Surgeon General's Office, American Cancer Society, American Heart Association.
Absorbs $\text{H}_2\text{O}$
Preserves tobacco
Antifreeze & de-icing
Polyester compounds
Artificial smoke in Theater & e-cigarettes
American Cancer Society
What in tobacco smoke is harmful?

US Food & Drug Administration
Constituents in tobacco?
http://pmep.cce.cornell.edu/profiles/

http://livealittlelonger.wordpress.com/tobacco/whats-inside-that-cigarette/
http://www.smokefree.gov/
**Parasympathetic**

Ach = Acetylcholine

- = Nicotinic Receptor

- = Muscarinic Receptor

**Sympathetic**

NE = Norepinephrine

= α Receptor ($\alpha_1$, $\alpha_2$)

= β Receptor ($\beta_1$, $\beta_2$)
The tobacco industry has acknowledged that nearly 600 chemicals are added to cigarettes. It is not clear, however, how much of the various additives are used or which combinations appear together. Some of the chemicals among cigarette additives most questioned by tobacco opponents include:

■ **Megastigmatrienone**: A flavoring that tobacco companies contend is found naturally in grapefruit juice.

■ **Dehydromenthofurolactone**: A flavoring that tobacco companies say is found in peppermint.

■ **Ethyl furoate**: Found naturally in coffee, kiwi and peanuts.

■ **Maltitol**: A sweetener used in chewing gum and diabetic candy.

■ **Sclareolide**: A synthetic form of a naturally occurring tobacco element.

■ **Ammonia**: A processing aid.

■ **Methoprene**: An insecticide that toxicologists say is biodegradable.

■ **Other additives**: Yeast, wine, caffeine, beeswax, beta carotene, chocolate, coconut oil.
Ammonia converts nicotine, the additive agent in tobacco, into a more volatile form, Pankow said. “Ammonia is the thing that helps tobacco companies hook the smoker by providing a means of delivering the nicotine.”

Last October, a former tobacco industry employee revealed that secret industry documents indicated that ammonia was added to tobacco to double the impact of nicotine. Research now indicates that ammonia can boost nicotine availability up to 100x! The Oregon Graduate Institute (now a part of OHSU) was the 1st to research!

http://pubs.acs.org/doi/abs/10.1021/es970402f
http://www.nasw.org/users/sperkins/nicotine.html
Arsenic 33
- Shotgun pellets
- Metal for mirrors
- Glass, lasers
- Light emitting diodes = LED
- 74.9216

Polonium 84
- Nuclear batteries
- Neutron source
- Antistatic agents
- Film cleaner
- 209
Tobacco-free Campus

For better health, smoking and use of tobacco products are prohibited everywhere on our property.

September 1, 2012

For a healthier community and cleaner environment, the University of Oregon will be smoke and tobacco-free.

Ready to Quit Tobacco?
Visit tobaccofree.uoregon.edu for free and low-cost resources.

UO BI 358 Alum!  U.S. Surgeon General
Josh Buehler  Regina Benjamin

For a healthier community and cleaner environment, the University of Oregon is smoke and tobacco-free.
Health risks of e-cigarettes emerge

Vaping pollutes lungs with toxic chemicals and may even make antibiotic-resistant bacteria harder to kill

By JANET RALOFF  4:31PM, JUNE 3, 2014
Discussion/Questions?
ANATOMY vs PHYSIOLOGY
STRUCTURE vs FUNCTION
WHAT? vs HOW?
WHERE? vs WHY?
Structure begets function!
Structure gives rise to function!
Structure & function are inseparable!
Body Levels of Organization

1. Molecular
2. Cellular
3. Tissue
4. Organ
5. System
6. Organism

LS 2012 fig 1-1 p 2
Maintenance of a relative constancy in the Internal environment = ECF = fluid outside of cells

milieu interieur?

100 trillion cells working intimately

Claude Bernard

Walter B. Cannon
ICF = Intracellular

ECF = Extracellular

Plasma (within CV System)

Interstitium (eg, between muscle cells)
FIGURE 1–2 Components of the Extracellular Fluid (Internal Environment)
~ 10 billion capillaries → Cells only a few cell d away from soup kitchen & waste dump!
Where is extracellular fluid (ECF)?

As long as between/outside cells, ECF everywhere!

Plasma and Interstitium mix/mingle @ Capillary.
FIGURE 1-3 Interdependent Relationship of Cells, Body Systems, and Homeostasis  

The depicted interdependent relationship serves as the foundation for modern-day physiology: Body systems maintain homeostasis, homeostasis is essential for survival of cells, and cells make up body systems.
Dr. Evonuk’s 6 Balances

Metabolic

$\text{H}_2\text{O}$

$\text{ToC}$

$\text{O}_2$/CO$_2$

Ion$^{+/-}$

pH
<table>
<thead>
<tr>
<th></th>
<th>Normal Value</th>
<th>Normal Range</th>
<th>Approximate Short-Term Nonlethal Limit</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen (venous)</td>
<td>40</td>
<td>35-45</td>
<td>10-1000</td>
<td>mmHg</td>
</tr>
<tr>
<td>Carbon dioxide (venous)</td>
<td>45</td>
<td>35-45</td>
<td>5-80</td>
<td>mmHg</td>
</tr>
<tr>
<td>Sodium ion</td>
<td>142</td>
<td>138-146</td>
<td>115-175</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Potassium ion</td>
<td>4.2</td>
<td>3.8-5.0</td>
<td>1.5-9.0</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Calcium ion</td>
<td>1.2</td>
<td>1.0-1.4</td>
<td>0.5-2.0</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Chloride ion</td>
<td>106</td>
<td>103-112</td>
<td>70-130</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Bicarbonate ion</td>
<td>24</td>
<td>24-32</td>
<td>8-45</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Glucose</td>
<td>90</td>
<td>75-95</td>
<td>20-1500</td>
<td>mg/dl</td>
</tr>
<tr>
<td>Body temperature</td>
<td>98.4 (37.0)</td>
<td>98-98.8 (37.0)</td>
<td>65-110 (18.3-43.3)</td>
<td>°F (°C)</td>
</tr>
<tr>
<td>Acid-base</td>
<td>7.4</td>
<td>7.3-7.5</td>
<td>6.9-8.0</td>
<td>pH</td>
</tr>
</tbody>
</table>

Table 1-1 G&H 2016
70% $\text{H}_2\text{O}$ = 49L

INPUT
Dietary Drink 1200 mL
Dietary Eat 400 mL
Oxidation 400 mL
Total = 2000 mL

OUTPUT
Urine 1000 mL
Sweat + Insensible 900 mL
Feces 100 mL
Total = 2000 mL

ECF = 14L
- Interstitium = 11L
- Plasma = 3L

H$_2$O BALANCE!

70% $\text{H}_2\text{O}$

eg 70 kg

Dietary Drink

Dietary Eat

Oxidation

Total

Urine

Sweat + Insensible

Feces

Total

ECF

Interstitium

Plasma

H$_2$O
Controller = Hypothalamus with Set Point

True Diurnal Variation

- Protein Denaturation
- Mild Hypothermia
- Profound Hypothermia

Set Point: 98.6°F

Time of Day:
- 0600
- 1400

Temperature Ranges:
- < 30°C (Lethal)
- 33°C
- 35°C
- 37°C
- 42°C (Lethal)
- 110°F
Invariably, Negative Feedback
**NB:** Though most often negative feedback, there are exceptions:

Selected +FB *e.g.*:

- LH Surge $\rightarrow$ Ovulation
- Oxytocin $\rightarrow$ Uterine Contraction
- Blood Clotting Cascade
- cAMP Cascade
- Na$^+$ influx during AP

Nonpathological! Temporarily amplifies, but ultimately turned off by - FB!
Figure 1-4 G&H 2016

Pumping effectiveness of heart (Liters pumped per minute)

- Bled 1 liter
- Bled 2 liters

Return to normal

Death

+ FB pathological!
- FB eg
How Effective is a System at Maintaining Relative Constancy? Feedback Gain?

\[ \text{Gain} = \frac{\text{Correction}}{\text{Error}} \]

e.g., Transfuse large volume of blood into person with non-functioning Baroreceptor system

BP: 100 mm Hg → 175 mm Hg

...into person with functioning system

BP: 100 mm Hg → 125 mm Hg