THE SCIENCE OF FEELING GOOD & FEELING BAD WITH ALCOHOL
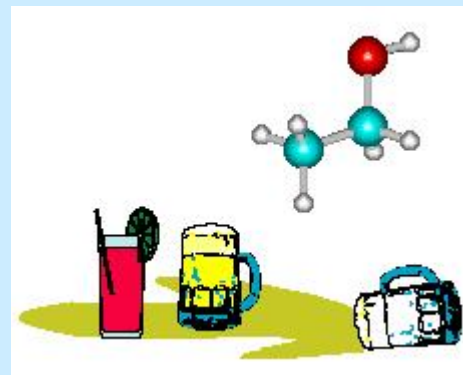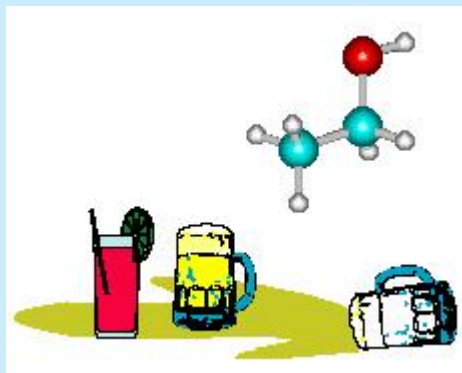
Professor David W. Craig

Department of Chemistry

Hobart and William Smith Colleges

7:30 – 8:30 pm
Tuesday, October 17, 2006
Geneva Room

Alcohol Awareness Week
Lecture Series

Behavioral and Sensation Manifestations of Alcohol Ingestion

- With 1 to 2 drinks (.01-.05 g/dL BAC) -- euphoria and perceived reduction in anxiety

- With .06-.10 g/dL BAC -- judgement and motor coordination impaired, sometimes increased aggression

- With .20-.25 g/dL BAC) -- sedation

- With 0.30 g/dL BAC -- memory impairment and loss of consciousness

- With 0.40 to .50 g/dL BAC -- depressed respiration , coma, death

*BACs for inexperienced adult user

What Factors Determine a Person's Blood Alcohol Concentration (BAC in g/dL)?

- Number of Drinks Consumed
- Body Size and Build
- Sex
- Time
- Past Drinking Experiences
- Is Stomach Empty or Full?

SOURCE: Estes and Heinemann, *Alcoholism: Development, Consequences and Interventions*, C. V. Mosby Co. (1986)

Ethyl Alcohol $CH_3\text{-}CH_2\text{-}OH$

Dose – Number of drinks consumed
- 12 oz Beer 3.6-4.0% alcohol contains 13-17g alcohol
- 4 oz Wine 12-14% alcohol contains 14-17g alcohol
- 1-1.5 oz 86 proof Whiskey contains 13-19g alcohol

Body size, build, and sex determines the volume accessible to ethanol

Chemical Solubility
- Completely soluble in water
- Somewhat soluble in fat
- 30x more soluble in water that in fat

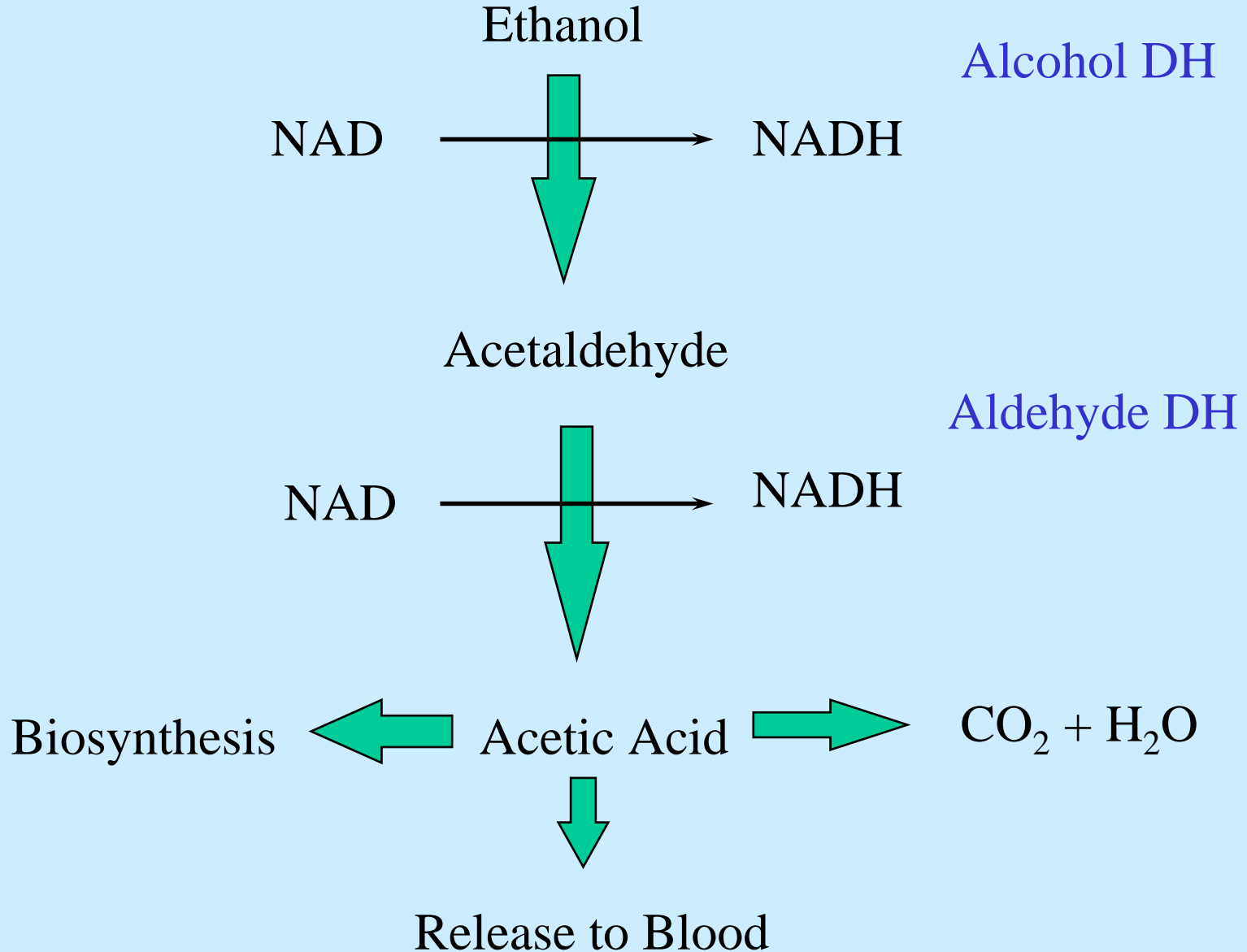- Proportion water in the body: Men .58, Women .49

Time – How rapidly can ethanol be absorbed?

- Rate of absorption is dependent on:
  - concentration gradient between gut and blood
  - surface area of contact
  - degree of vascularization
- Effect of Food on Absorption
  - food dilutes alcohol in the digestive system
  - fatty foods are slow to digest and slow to move from the stomach to the small intestine

Time – How rapidly can ethanol removed?

- Ethanol clearance is zero order … the rate of clearance is independent of the ethanol concentration

- Average ethanol clearance rates
  - For moderate drinkers - .017 g/dL/hr
  - Drinkers consuming >60 drinks/month - .020 g/dL/hr
  - 80% of adult population > .012 g/dL/hr

Major Pathway for Alcohol Metabolism

Ethanol

Alcohol DH

NAD → NADH

Acetaldehyde

Aldehyde DH

NAD → NADH

Biosynthesis ← Acetic Acid → $CO_2 + H_2O$

Release to Blood

Estimation of BAC

Calculation of BAC for inexperied drinkers -- The American Happy Hour Experience

		male		
	Weight lb	187		
	Frac H2O	0.58		
Drinks	**Time (hr)**	**BAC (g EtOH/dL Blood)**		
1	0.25	0.020		
2	0.5	0.040		
3	0.75	0.060		

In experiment, subjects drink 1.5oz shots of 80proof scotch on 15min intervals, measuring BAC 15min after each dose of alcohol.

Ref: National Highway traffic Safety Administration
http://www.nhtsa.dot.gov/people/injury/alcohol/bacreport.html

Effect of Rate of Ingestion of 10 Drinks on BAC (following a light meal)

SOURCE: Estes and Heinemann, *Alcoholism: Development, Consequences and Interventions*, C. V. Mosby Co. (1986) p 95

Alcohol Affects Neuro-transmitter Function in the Brain

- Increases **Dopamine** concentration

- Increases **Serotonin** release

- Stimulates **Opiate Neuropeptide** Release

- Potentiates **GABA** receptor function

- Inhibits **Glutamate** receptor function

Affect on Dopamine, Serotonin, and Endogenous Opiates (.01-.05 BAC)

- **Dopamine** simulates pleasure centers and functions in positive reinforcement
  - alcohol increases Dopamine concentrations in nucleus acumbens and other reward centers
- **Serotonin** functions in mood, sleep, and positive reinforcement
  - alcoholics and thrill seekers have low serotonin levels and alcohol consumption (and thrill activities) brings theses levels up to normal. Serotonergic drugs lead to reduced alcohol consumption by alcoholics.
- **Endorphins** and **Enkephalins** are natural neural peptides that bind to opiate receptors and produce euphoric effects.
  - Endorphins and Enkephalins are released by the brain when exposed to alcohol
  - Euphoria seems to stimulate further drinking

SOURCE: *Eighth Special Report to the US Congress on Alcohol and Health*, US Dept. of HHS (1993), p 86-94

Affect on GABA function (~>.06 BAC)

- GABA is major inhibitory neurotransmitter controlling "arousal state" as well as sensory and motor activity

- Alcohol Potentiates GABA receptor function

- Major Site of Affects include:
  - medial septal nucleus -- controls "arousal state"
  - Purkinje neurons in cerebellar cortex -- controls sensory and motor activity

Affect on Glutamate Function (~>.2 BAC)

- Glutamate is major excitatory neurotransmitter
- Inhibits glutamate receptor function
- Impaired Glutamate Receptor Function Causes:
  - cognitive impairment and amnesia
  - inability to learn new information

Alcohol and Sex

- Physiological responses
  - Erections slower to rise and quicker to fall
  - Reduction in vaginal lubrication
- Psychological Perceptions
  - 45% of men and 68% of women say alcohol enhances sexual enjoyment
- Rutgers study (2-3 standard drinks)
  - Subjects who thought they drank alcohol were most highly aroused (those that did not actually get alcohol were slightly less aroused)
  - Subjects who expected tonic but actually got alcohol were less aroused than those that expected alcohol but did not.

SOURCE: Braun, Stephen, Buzz: The Science and Lore of Alcohol and Caffeine, Penguin Books, 1996.

Effect of Chronic Use

- Tolerance
  - <u>Functional Tolerance</u> -- changes in number and type GABA and Glutamate receptors
  - <u>Acute Tolerance</u> -- occurs within a drinking session
  - <u>Metabolic Tolerance</u>
- Withdrawal
  - increased Anxiety within hours -- GABA
  - seizures -- Glutamate
- Dependence
  - changes in Dopamine and Serotonin function appear to be long lasting

What Causes a Hangover?

- Pounding Headache
  - Caused by reduced blood pressure in cranial vessels
- General Lethargy
  - Caused by buildup of lactic acid and acidosis by release of acetic acid
- Hypersensitivity to Light and Sound
  - Alcohol withdrawal leads to increased excitability, depressed mood, and sensitivity to stimuli
- Queasy Stomach
  - Empty stomach, overly acidic
  - Also due to withdrawal
- What about taking a drink to relieve hangover symptoms?

Differences Between Men and Women

- Women are smaller than men

- Women have lower total body water content (49%) than men (58%) of comparable size

- Gastric ADH lower in women
  - virtually nonexistent in alcoholic women

- Fluctuations in gonadal hormone levels during the menstrual cycle may affect the rate of alcohol metabolism
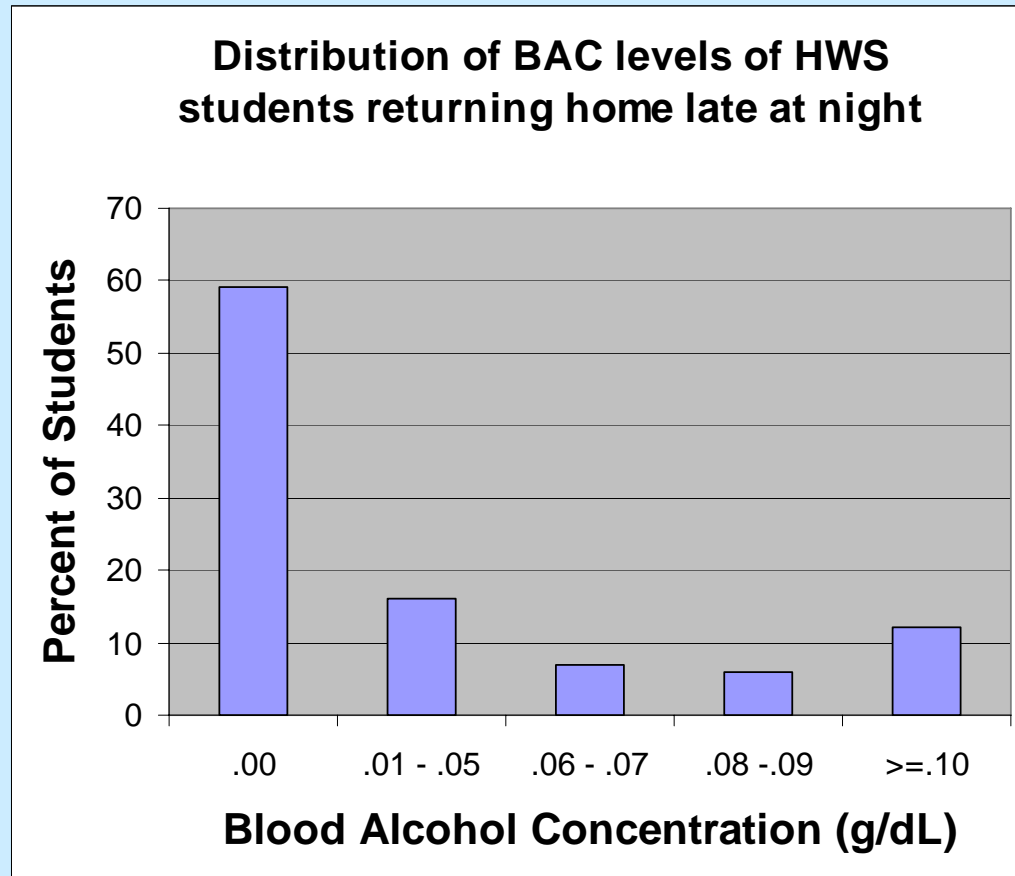
Estimation of BAC

Calculation of BAC for inexperied drinkers -- The American Happy Hour Experience

		male	female
	Weight lb	187	120
	Frac H2O	0.58	0.49
Drinks	**Time (hr)**	**BAC**	**BAC**
1	0.25	0.020	0.039
2	0.5	0.040	0.078
3	0.75	0.060	0.118

In experiment, subjects drink 1.5oz shots of 80proof scotch on 15min intervals, measuring BAC 15min after each dose of alcohol.
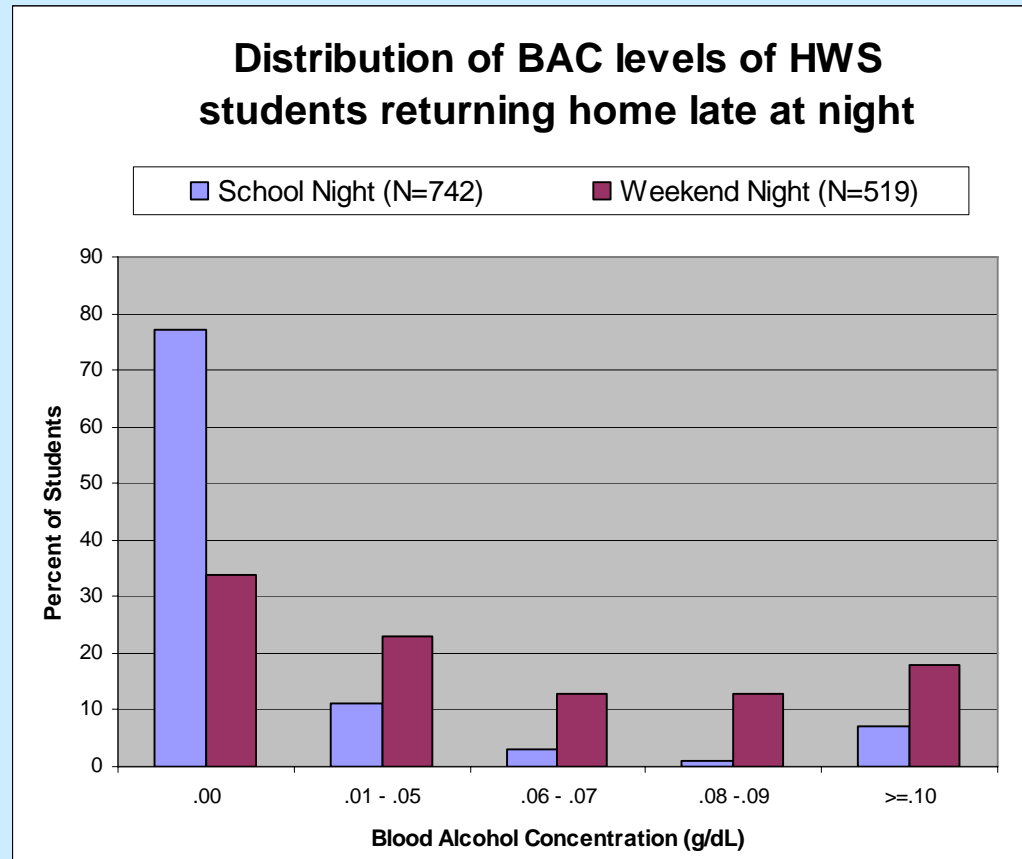
Ref: National Highway traffic Safety Administration
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BAC distribution of HWS students returning home late at night

Distribution of BAC levels of HWS students returning home late at night
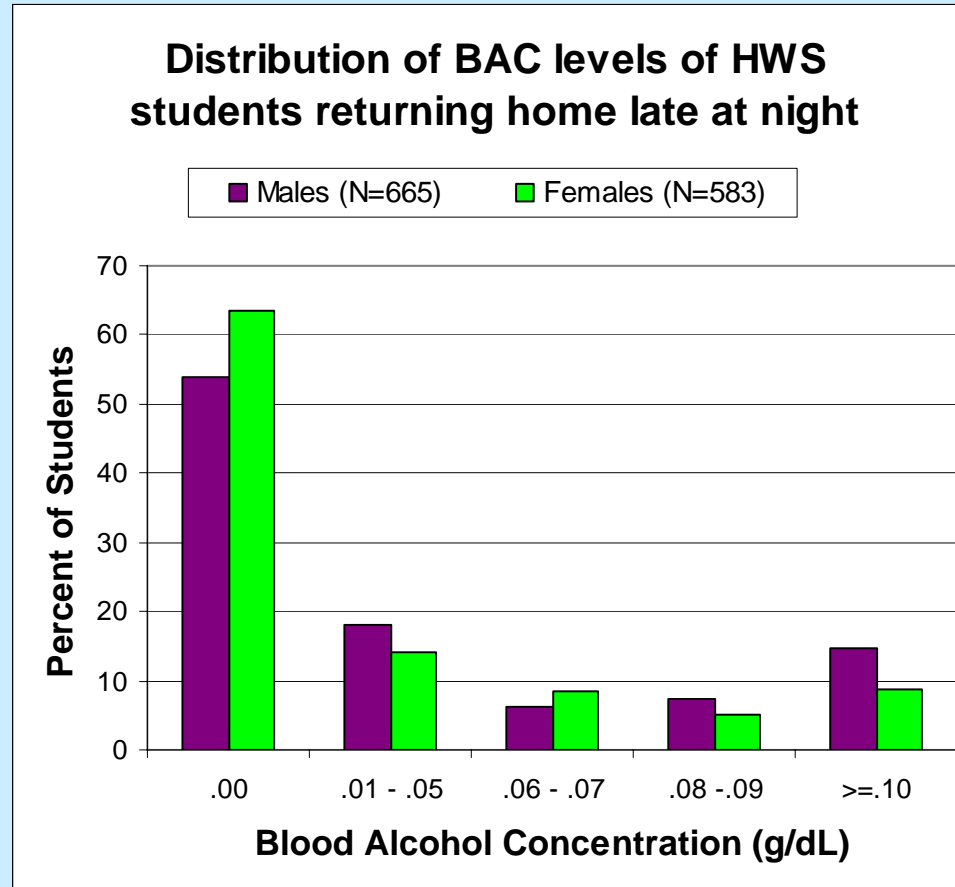
Data collected from 1,263 randomly selected students returning to residence halls late at night between 11pm and 3am during Spring `03, Fall `03, Spring `04, Fall `04, and Spring '05 terms. BAC measurements were collected every night of the week (59% of sample from school nights, 41% from weekend nights). Men are 53% of the sample and women are 47% of the sample.

BAC distribution of HWS students returning home late at night

Distribution of BAC levels of HWS students returning home late at night

☐ School Night (N=742) ■ Weekend Night (N=519)

Percent of Students (y-axis: 0 to 90)

Blood Alcohol Concentration (g/dL): .00, .01 - .05, .06 - .07, .08 - .09, >=.10

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BAC distribution of HWS students returning home late at night

Distribution of BAC levels of HWS students returning home late at night

■ Males (N=665)   ■ Females (N=583)

Percent of Students

70
60
50
40
30
20
10
0

.00   .01 - .05   .06 - .07   .08 -.09   >=.10

Blood Alcohol Concentration (g/dL)

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