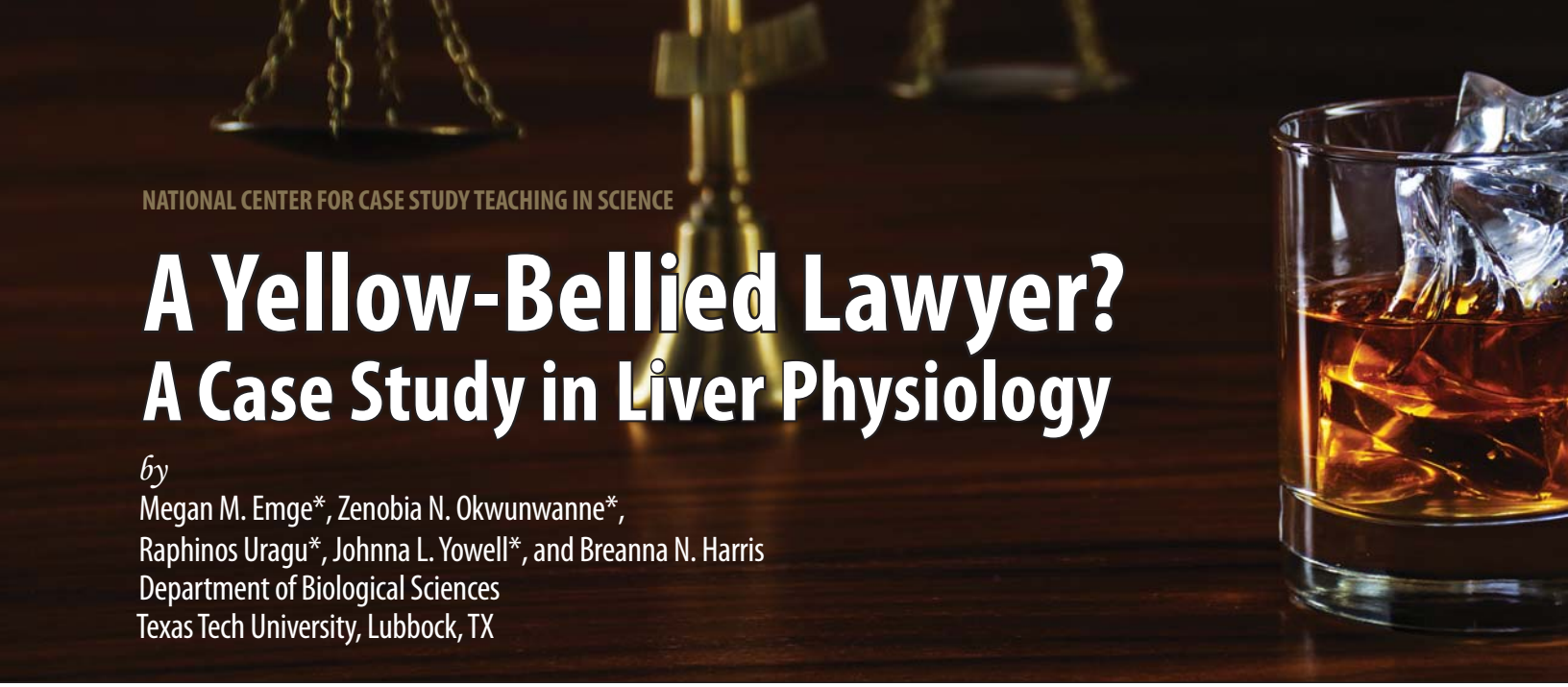

NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

A Yellow-Bellied Lawyer?
A Case Study in Liver Physiology

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Part I – Admittance

Michael was a 35-year-old Caucasian male who had graduated from Harvard Law School with honors. His career path had led him to New York where he had become a prosecutor handling high-profile murder cases. After a stressful day of court, he usually headed to the pub near his office to unwind. One particular evening he invited his colleague Robert to join him. As soon as they reached the pub, Michael ordered a double scotch on the rocks. Soon after Michael finished his drink, he ran into a former colleague who ordered each of them two rounds of shots. They all sat down and ended up chatting the night away. By the end of the evening, in a total of four hours, Michael had consumed nine standard drinks. As he was getting ready to leave he noticed that he was having abdominal pains.

Robert became worried about Michael and decided it was best to give Michael's sister, Alice, a call to come get him. As soon as Alice arrived, she hurried in and rushed Michael out of the bar. She then noticed that Michael was slightly yellow, confused, and was clutching right side. Once they got outside Michael vomited. Alice was reminded of their father and grew concerned; she decided to take Michael to the nearest hospital.

Upon arrival, Alice checked Michael into the emergency room and the nurse handed her paperwork to fill out. She proceeded to list Michael's symptoms and his weight, which was 180 pounds. The nurse asked if Michael had been drinking and Alice said yes. They then sat down and patiently waited for the doctor.

Questions

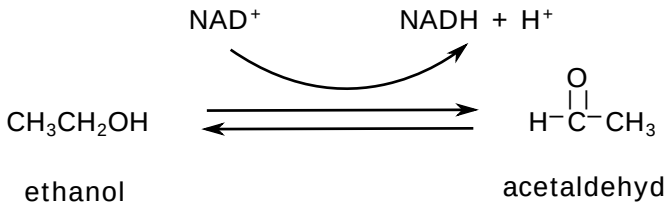
1. What symptoms is Michael experiencing?

2. According to the National Institute on Alcohol Abuse and Alcoholism (NIAAA), how much beer, wine, or liquor constitutes a standard drink? <http://pubs.niaaa.nih.gov/publications/practitioner/pocketguide/pocket_guide2.htm>

*These four undergraduate students contributed equally to the creation of this case study and are listed in alphabetical order.

After ingestion, alcohol is absorbed by the stomach and small intestine, enters the blood stream, and is then metabolized by the liver. After absorption from the digestive tract, alcohol passes to the liver via the hepatic portal system where a small percentage is metabolized before the alcohol makes its way to the main systemic circulation. Once in the systemic circulation, the alcohol is metabolized when the blood passes through the liver.

Alcohol metabolism occurs via several enzymes, with the main ones being alcohol dehydrogenase (ADH), the cytochrome P450 enzyme family, and aldehyde dehydrogenase (ADH2). ADH converts ethanol (alcohol) to acetaldehyde in the reaction shown below.



Acetaldehyde is a toxic product that is broken down to acetate (acetic acid) by ADH2. In the non-alcoholic person, the cytochrome P450 pathway plays a minor role in alcohol metabolism. At most concentrations, the breakdown of alcohol by the liver follows zero-order kinetics, meaning the liver metabolizes alcohol at a constant rate, regardless of how much alcohol was consumed. Because the body metabolizes alcohol at a constant rate, this means that any excess amount remains in the blood, which is then reflected in blood alcohol concentration. In a non-alcoholic individual, the body clears the percentage of alcohol in the blood by about 0.015 (15 mg/dL) per hour. In alcoholics, the metabolism of alcohol tends to be faster.

Blood alcohol concentration, or BAC, is a measure of the percentage of alcohol in whole blood. In the United States, a BAC of 0.08 percent or above is considered legally intoxicated; this number translates to roughly 80 mg of alcohol in 1 deciliter of whole blood (80 mg/dL). A standard drink contains roughly 14 g of alcohol, and the average man and woman have 5 and 4L (50 and 40 dL) of whole blood, respectively. Several factors can influence BAC (e.g., sex, age, body mass, genetics, hydration and food, drinking frequency), but BAC can be estimated using the Widmark Formula:

$$\text{BAC} = [\text{alcohol consumed in grams} / (\text{body weight in grams} * r)] \times 100.$$

Here, r is a constant related to the distribution of water in the body and differs by sex; 0.55 is used for females and 0.68 for males. As mentioned earlier, the length of time over which the alcohol is cosumed also needs to be taken into account.

BAC can also be calculated using several different websites and handy cell phone apps. For instance, the Cleveland Clinic has an on-line calculator which can be found here: <http://my.clevelandclinic.org/health/tools-quizzes/Blood_Alcohol_Calculator>.

Questions

3. Based on the information given above, calculate Michael's BAC level.

4. List the physiological roles of the liver. Describe the hepatocytes, liver lobules, and the Kupffer cells.

5. Describe the process of hemoglobin degradation/bilirubin metabolism.

Part II – Examination

Dr. Sues grew concerned after examing Michael and ordered blood work. The doctor also ordered a magnetic resonance elastography (MRE) session; MRE is an imaging technique that would allow Dr. Sues to determine if Michael's liver had stiffened or hardened. While the nurse drew blood from Michael, Alice and the doctor stepped out of the room. Alice mentioned to the doctor that their family had a history of alcoholism and that she was concerned about her brother. Lately, Michael hadn't been himself; he had been sleeping a lot, missing work, and overall seemed very absent and distant towards her. She was concerned that this was due to his excessive drinking. Dr. Sues thanked Alice for sharing her concerns and shared his suspicion that Michael had some form of alcohol-induced liver damage.

Dr. Sues explained that alcohol-induced liver damage is classified in three stages: alcoholic fatty liver, alcoholic hepatitis, and alcoholic cirrhosis. Alcoholic fatty liver is the least severe of the diagnoses and is an extra buildup of fat in the liver, which is usually symptom-free and reversible with abstinence. Alcoholic hepatitis is defined by fatty build-up, inflammation, and scarring; this can be mild or severe and usually presents with symptoms. Alcoholic cirrhosis is the most severe and is characterized by hard scarring and disruption of normal liver structure; this can be very serious and lead to death. Dr. Sues was mindful of the fact that alcoholism and alcohol-related accidents pose a great burden financially, physically, and emotionally (see NIAAA Alcohol Alert – Measuring the Burden of Alcohol and/or the CDC Alcohol Fact Sheet).

Dr. Sues suggested they run some tests to determine if Michael had fatty liver disease, alcohol hepatitis, or alcohol cirrhosis. Depending on the outcome of the blood tests, the next step would be to determine the risk factor for severity of alcoholic hepatitis and prognosis using Maddrey's discriminant function (DF) formula:
Risk factor = 4.6 × (prothrombin time prolongation in seconds – control prothrombin time) + serum bilirubin level (mg/dL).
A score above 32 is indicative of severe alcoholic hepatitis.

Additionally, Dr. Sues wanted to look at Michael's aspartate transaminase (AST) and alanine transaminase (ALT) levels, as well as their ratio (AST/ALT). Both of these enzymes are found in the liver (and other tissues), and when levels are elevated they indicate death of liver cells and/or liver damage. Fatty liver causes mild increases in AST and ALT levels. For diagnosis of acute alcoholic hepatitis, the AST/ALT ratio is usually over 2.0 with AST being in the 100–300 IU/L range (a ratio of 3.0 is strongly indicative of alcoholic hepatitis).

Questions

1. Aside from alcohol, what are some causes of liver failure/damage/cirrhosis?

2. What are the symptoms of liver cirrhosis?

3. According to the NIAAA website (http://pubs.niaaa.nih.gov/publications/aa42.htm), what does excessive, long-term alcohol abuse do to the liver, physiologically?

The results of Michael's blood work and MRE are shown below; use them to answer the following questions.

Test	*Michael's levels*	*Normal ranges*
Blood pressure (mmHg)	118/78	<120/80
Body Mass Index (BMI)	23.7	18.5–24.9
Heart Rate (BPM)	80	60–100
Glucose (mg/dL)	86	70–100
Alanine transaminase (ALT) (IU/L)	82	10–40
Aspartate transaminase (AST) (IU/L)	245	10–34
Alkaline phosphatase (ALP) (IU/L)	170	44–147
Gamma-glutamyl transpeptidase (GGT) (IU/L)	164	0–51
Total bilirubin (mg/dL)	4	0.3–1.9
Viral hepatitis Test	Negative	Negative
Prothrombin Time (sec.)	20	11–13.5
Albumin (g/dL)	2	3.4–5.4
Globulin (g/dL)	0.5	2.0–3.5

Liver MRE interpretation: Scores range from a Fibrosis (F) stage of 0 to 4. F0 = no fibrosis; F2 = portal fibrosis; F3 = septa, but no cirrhosis; F4 = cirrhosis).

Liver MRE Score	F4	F0

Questions

4. Are there any abnormalities in Michael's blood work? If so, which ones and are they high or low?

5. What is Michael's Maddrey's DF score? (Use the high end of the normal range for prothrombin time in your calculation.)

6. Based on the information above and the supplemental information provided to you, what is your diagnosis for Michael?

Part III –Diagnosis

Dr. Sues checked on Michael and realized that his jaundice had advanced. The doctor explained to him the extent of his condition and informed Michael that cirrhosis is a serious condition and that he must work on decreasing his alcohol consumption and begin treatment. Dr. Sues explained that if Michael did not abstain from drinking alcohol, death was a real possibility.

Questions

1. What is jaundice?

2. How can liver damage result in jaundice (hyperbilirubinemia)?