

Bonus: Drug Paper Handout

This assignment is strictly optional. It is the only extra credit assignment available for the class. If you want to do the assignment these are the instructions you need to follow. This paper is due on Monday, April 19, 2010.

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Human Physiology
Spring 2010

You need to answer the following questions in your paper. The answers should flow like an essay. Do not put a question number by each of your answers. A few of the questions ask for a list. The lists can be in paragraph format (example: hypertension, nephritis, and lipidosi) or as a list (example: hypertension

nephritis
lipidosi)

You need to show your work for all calculations. Calculations may be handwritten or typed. Calculations need to show each step and be in a logical order.

1. Give the brand name and the generic name of your drug.
2. Why is the drug prescribed? What are its indications?
3. List five (5) side effects (if there are fewer than five side effects, list them all). Choose three (3) of these side effects and explain why they occur and what causes them. You need a minimum of one (1) dedicated paragraph per side effect. Depending on the side effect, two or more paragraphs may be needed to explain the side effect on the entire body. A one sentence explanation will not be sufficient to explain side effects.
4. List three (3) reasons when and why this drug should not be prescribed (if there are fewer than three reasons, list them all). The reasons when and/or why a drug should not be used is called a contraindication. Choose one of these reasons and explain why the drug is contraindicated in this patient. You need a minimum of one (1) dedicated paragraph for the contraindication. Depending on the contraindication, two or more paragraphs may be needed to explain the side effect on the entire body. A one sentence explanation will not be sufficient to explain side effects.
5. What is the adult dosage (amount of drug and its frequency) per dose and per day. If there is more than one dosage listed, pick just one.
6. Calculate the amount of medication a 165 pound person would need.
7. Does the medication come as a tablet, capsule, gel cap, powder, or some other form?
8. How is the drug administered?
9. What strength, in mg, is the drug formulated in? List all sizes/strengths of the drug.
10. Based on the calculated dose above (see question 6), how much medication will the patient need per dose and per day? (Keep in mind that tablets can often be cut into pieces, but capsules can't.)

This assignment is to be typed using Times New Roman font, 12 font size. The final report will be double spaced. It is to be in essay format. If references other than the text are used, they must be

properly cited in the paper and a Bibliography included at the end of the paper. For instructions on how I want a Bibliography, if one is needed, see end of this handout. Do **NOT** turn in copies of any of the references you make.

A cover page is required. See below for instructions.

Your grade will be based on content, grammar, and the structure of the paper.

Content.

You need to adequately cover the main topics covered in class over each side effect or contraindication. For example, if your drug causes tachycardia (rapid heart rate) explain the mechanism causing the tachycardia. If your drug is contraindicated for a person with glaucoma, explain why glaucoma patients should not receive this drug. You may want to include signs and symptoms seen with the side effect or the signs and symptoms that may arise if a person with a condition that the drug is contraindicated for occurs. If one of the side effects is death then explain why the drug caused death.

Grammar.

I will grade grammar. Watch sentence structure, punctuation, quotations, spelling, clarity of ideas, etc. **Remember essays will have more than 1 paragraph and each paragraph needs to be indented.** Avoid unclear or confusing sentences. In instances where the drug has no side effects or contraindications you should pick three (3) different body systems and explain why there is no side effect in this body system. You need at least one paragraph (for each body system) stating why the drug isn't affecting each body system you choose.

If you quote, either directly or indirectly, from one of your references, give proper credit to the original author.

Structure.

Your paper must include a **title page**. You will follow these guidelines for the paper:

- You are to use Times New Roman font
- Use 12 pitch font size
- Margins will be the standard 1-inch top and bottom, and 1.25 inches for the right and left margins.
- All work will be double-spaced.
- Papers will be printed only on one side of a piece of white paper.

See below for directions for the Title Page. Do not turn in copies of this handout or copies of any articles you use for this essay.

You need to properly cite your references (including your textbook) in your paper and include a Bibliography. See below for Directions for the Bibliography.

This is to be your original work.

The title of your paper will be centered 12 lines down from the top of the page. The title should be in 16-pitch font size, Times New Roman font. It may be more than 1 line long.

Below it put your name (12 pitch font size).

Followed by Drug Paper (12 pitch font size).

Date the Assignment is Due (12 pitch font size).

Bibliography. (The word Bibliography must be in 16-pitch font size, Times New Roman font.)
You must cite all references you use, including your textbook, in the following format:

Books.

Book citations include author(s), title of chapter; “In:”, the editors of the text (followed by eds.), title of the book, the publisher of the book, the year book was published, and the page number(s) of the reference. The name of the text is written in *italics*.

For example:

Osborne CA, Polzin DJ, Feeney DA, et al The urinary system: pathophysiology, diagnosis, treatment. In: Gourley IM, Vasseur PB, eds. *General small animal surgery*. Philadelphia: Lippincott Williams & Wilkins, 1985;479-658.

Journal Articles:

Journal citations include author, title of article, (abbreviated) name of journal, year article was published in journal, volume of the journal the article appeared in, and the pages the reference was taken from. The name of the journal is written in *italics*.

For example:

Hansen JS. Urachal remnant in the cat: occurrence and relationship to the feline urological syndrome. *Vet Med* 1977;72:1735-1746.

Web sites:

Web site citations include authors, date of material, title of article/page, organization, web site URL, and the date the information was retrieved (according to the handout you received from the librarians in our trip to the library during lab).

For example (also taken from the library handout):

Siegel, J. (1996, May 31). Aging into the 21st century. Administration on Aging: Statistical information on older persons. Retrieved April 10, 2003, from <http://www.aoa.gov/aoa/stats/statpage.html>

Don't forget to indent the second, third, etc. line of the bibliography after the first line.

Number each entry in your bibliography. Do not separate the types of references (books, journal articles, web sites, etc). I'll be able to tell one type of reference from another.

For this bibliography list your references in the order in which you use them in your paper.

Do not include references in your bibliography that you do not use in your essay.

Do not forget to properly annotate which reference or references you are citing as you use the reference(s). In scientific writing it is customary to only write the reference number in the body of the paper when you cite the reference. The first reference will be “1.” and should be listed in the paper as (1) and be the first reference in your Bibliography.

Acid-base and hormonal abnormalities in dogs with naturally occurring diabetes mellitus

Lawren L. Durocher, dvm, ms, dacvim; Kenneth W. Hinchcliff, bvsc, phd, dacvim; Stephen P. DiBartola, dvm, dacvim; Susan E. Johnson, dvm, ms, dacvim

Objective—To examine acid-base and hormonal abnormalities in dogs with diabetes mellitus.

Design—Cross-sectional study.

Animals—48 dogs with diabetes mellitus and 17 healthy dogs.

Procedures—Blood was collected and serum ketone, glucose, lactate, electrolytes, insulin, glucagon, cortisol, epinephrine, norepinephrine, nonesterified fatty acid, and triglyceride concentrations were measured. Indicators of acid-base status were calculated and compared between groups.

Results—Serum ketone and glucose concentrations were significantly higher in diabetic than in healthy dogs, but there was no difference in venous blood pH or base excess between groups. Anion gap and strong ion difference were significantly higher and strong ion gap and serum bicarbonate concentration were significantly lower in the diabetic dogs. There were significant linear relationships between measures of acid-base status and serum ketone concentration, but not between measures of acid-base status and serum lactate concentration. Serum insulin concentration did not differ significantly between groups, but diabetic dogs had a wider range of values. All diabetic dogs with a serum ketone concentration > 1,000 $\mu\text{mol/L}$ had a serum insulin concentration < 5 $\mu\text{U/mL}$. There were strong relationships between serum ketone concentration and serum glucagon-insulin ratio, serum cortisol concentration, and plasma norepinephrine concentration. Serum β -hydroxybutyrate concentration, expressed as a percentage of serum ketone concentration, decreased as serum ketone concentration increased.

Conclusions and Clinical Relevance—Results suggested that ketosis in diabetic dogs was related to the glucagon-insulin ratio with only low concentrations of insulin required to prevent ketosis. Acidosis in ketotic dogs was attributable largely to high serum ketone concentrations. (*J Am Vet Med Assoc* 2008;232:1310–1320)

Abbreviation

NEFA Nonesterified fatty acid

In dogs with metabolically unstable diabetes mellitus, production of ketone bodies exceeds utilization of them for energy, resulting in an increase in serum ketone concentration. Most diabetic dogs have serum ketone concentrations that are higher than those in healthy dogs. Although mild ketonemia might not be clinically apparent, the accumulation of ketones in serum is associated with metabolic acidosis that, in its most extreme form, manifests as diabetic ketoacidosis. Organic anions believed to contribute to acidosis in ketotic dogs include ketone and lactate, although the relative contributions of ketone and lactate to acid-base status have not been examined in dogs with spontaneous diabetes mellitus. **Ketoacidosis is proposed to result from a relative lack of insulin and an increase in counter-regulatory hormones, such as glucagon, cortisol, epinephrine, and norepinephrine.**¹ These changes have been documented in humans with diabetic ketoacidosis, but hormonal abnormalities in dogs with naturally occurring diabetes mellitus and any degree of ketonemia have not been elucidated.²

Hormones other than insulin that play an important role in glucose regulation include glucagon, cortisol, epinephrine, and norepinephrine. Glucagon increases glycogenolysis and gluconeogenesis in the liver, but has little or no effect on peripheral tissues such as muscle or fat.^{3,4} Cortisol increases blood glucose concentrations by stimulating synthesis of gluconeogenic enzymes and facilitating mobilization of gluconeogenic precursors.⁵ It also promotes ketogenesis by increasing lipolysis, which releases ketogenic substrates from fat.⁵ Epinephrine and norepinephrine activate glycogen phosphorylase and glucose-6-phosphatase in the liver and increase gluconeogenesis and peripheral lipolysis, resulting in increases in serum glycerol, NEFA, and ketone concentrations.^{6–8} Although these hormones have been shown to be associated with ketonemia in humans and dogs with experimentally induced diabetes mellitus, their role in dogs with naturally occurring diabetes mellitus is unknown.

Nonesterified fatty acid is used for production of ketones in the liver.^{2,9} Thus, serum NEFA concentration is an important

indicator of metabolic status in dogs with diabetes mellitus, but the relationship between increases in serum NEFA concentration and severity of ketonemia in dogs with naturally occurring diabetes mellitus is unclear.

The purposes of the study reported here were to document acid-base abnormalities in dogs with naturally occurring diabetes mellitus, to determine the relative contributions of serum lactate and ketone concentrations to acidosis in dogs with hyperketonemia, and to compare serum ketone and hormone concentrations in diabetic dogs with concentrations in dogs without diabetes mellitus to identify the potential role of these hormones in the development of ketonemia. We hypothesized that diabetic dogs would have lower concentrations of insulin and higher concentrations of glucagon, cortisol, epinephrine, and norepinephrine than would healthy dogs and that in diabetic dogs, the degree of ketonemia would correlate with serum insulin, glucagon, cortisol, epinephrine, norepinephrine, glucose, and NEFA concentrations.

References

1. Unger RH, Dobbs RE. Insulin, glucagon, and somatostatin secretion in the regulation of metabolism. *Annu Rev Physiol* 1978;40: 307–343.

2. Kerl ME. Diabetic ketoacidosis: pathophysiology and clinical and laboratory presentation. *Compend Contin Educ Pract Vet* 2001; 23:220–229.
3. Jiang G, Zhang BB. Glucagon and regulation of glucose metabolism. *Am J Physiol Endocrinol Metab* 2003;284:E671–E678.
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5. Johnston DG, Pernet A, McCulloch A, et al. Some hormonal influences on glucose and ketone body metabolism in normal human subjects. In: *Metabolic acidosis*. London: Pitman Books Ltd (CIBA Foundation Symposium 87), 1982;168–191.
6. Shimazu T, Amakawa A. Regulation of glycogen metabolism in liver by the autonomic nervous system. 3. Differential effects of sympathetic-nerve stimulation and of catecholamines on liver phosphorylase. *Biochim Biophys Acta* 1968;165:349–356.
7. Chu CA, Sindelar DK, Neal DW. Comparison of the direct and indirect effects of epinephrine on hepatic glucose production. *J Clin Invest* 1997;99:1044–1056.
8. Connolly CC, Steiner KE, Stevenson RW, et al. Regulation of lipolysis and ketogenesis by norepinephrine in conscious dogs. *Am J Physiol Endocrinol Metab* 1991;261:E466–E472.
9. Basso LV, Havel RJ. Hepatic metabolism of free fatty acids in normal and diabetic dogs. *J Clin Invest* 1970;49:537–547.
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13. Ford SL, Nelson RW, Feldman EC, et al. Insulin resistance in three dogs with hypothyroidism and diabetes mellitus. *J Am Vet Med Assoc* 1993;202:1478–1480.
14. Constable PD, Stampfli HR. Experimental determination of net protein charge and Atot and Ka of nonvolatile buffers in canine plasma. *J Vet Intern Med* 2005;19:507–514.

Note how references are made in this scientific article. The sentence that ends at the top of column two, on page 1310, reads as follows:

“Ketoacidosis is proposed to result from a relative lack of insulin and an increase in counter-regulatory hormones, such as glucagon, cortisol, epinephrine, and norepinephrine.¹”

In this instance the “¹” indicates that this is the first reference in the References, or Bibliography, section.

The sentence, in the paragraphs above, that reads:

“Nonesterified fatty acid is used for the production of ketones in the liver.^{2,9}”

In this instance the “^{2,9}” indicates the 2nd and 9th references were used for this quote.

The article I used for this example came from the following reference:

Durocher LL, Hinchcliff KW, DiBartola SP, Johnson SE. Acid-base and hormonal abnormalities in dogs with naturally occurring diabetes mellitus. *JAVMA* 2008;232:1310-1320.