

Biochemistry/Physiology Discussion 2

(Small Group)

OBJECTIVES

- Describe pathways for synthesis of adrenocorticoid hormones. Explain the consequences of deficient activity of the key enzymes in adrenocorticoid synthesis. Explain the consequences of excessive adrenocortical androgen production pre- and post-puberty.
- Explain the effects of deficient glucocorticoid activity on hypothalamo-pituitary axis.
- Explain the effects of ACTH on adrenal cortex and understand the reasons for and the consequences of excessive ACTH production.
- Describe the effects of deficient glucocorticoid receptor on HPA axis.
- Describe the effects of glucocorticoids on glucose homeostasis and energy metabolism.
- Describe the effects of glucocorticoids on cardiovascular system.
- Describe pathways for adrenomedullary hormone synthesis and metabolism.
- Describe the effect of sympathetic system on insulin release.
- Describe the effects of excess catecholamine activity on cardiovascular system.

KEY WORDS

11-beta-hydroxylase	beta-melanocyte stimulating hormone
17-alpha-hydroxylase	congenital adrenal hyperplasia (CAH)
21-beta-hydroxylase	proopiomelanocortin
alpha-melanocyte stimulating hormone	vanillylmandelic acid (VMA)

INTRODUCTION

The purpose of this small group is to expand on and reinforce the concepts presented in the Required Reading titled, "Medical Endocrinology" and the lecture titled "Introduction to the HPA Axis."

- For additional background information, you can consult Boron and Boulpaep, Medical Physiology, 1st edition (Chapters 46 and 49) as well as other textbooks (e.g. Harrison), or reliable web sites (e.g., eMedicine.com).

Before coming to class you should:

- Read the syllabus sections for those lectures.
- Read through the problems described below, gather the information you think you'll need to complete the problems and begin to formulate answers to the questions. You may be assigned by your group leader to a smaller group of students, with whom you will present the answers and how you arrived at them. Details will be posted by your small group leader on iROCKET.

PROBLEM 1

A couple from another country who is visiting relatives in SF has brought a female baby to the emergency room. The baby is 8-months-old and has been lethargic ever since their arrival three days ago. This morning the baby started vomiting and her parents brought her to the ER. The physician examines the child and finds her to be severely dehydrated. Her physical development appears below her chronological age (she is in the 3rd percentile for both height and weight). Inspection of her genitalia reveals clitoromegaly (enlarged clitoris) and partial labial fusion, both signs of masculinization. The physician orders immediate fluid replacement and her blood is drawn.

Here are some of the laboratory results:

Glucose = 55.0 mg/dl	(normal fasting 70-110 mg/dl)
Na ⁺ = 125 mmol/L	(normal 135-145 mmol/L)
K ⁺ = 6.3 mmol/L	(normal 3.5-5.0 mmol/L)
Bicarbonate = 18 mmol/L	(normal 22-26 mmol/L)

- 1) After seeing her labs, the physician suspects an adrenocortical problem. What do you think led him to this conclusion?
- 2) Bicarbonate levels are low. What do you think is the reason?
- 3) Blood glucose is also low. How could an adrenocortical problem result in low blood glucose?
- 4) What do you suspect is the underlying cause of this child's problems? (Try to be precise and explain your reasoning!)

PROBLEM 2

A 31-year-old man visits your preceptor's office. He and his wife are having their fertility assessed and he needs a referral for urology. As the patient has never visited the office your preceptor decides to do a full physical exam and asks you to perform it. The patient is 5'5" and 145 lb and in apparently good physical condition. Except for cystic acne, his history and physical exam are unremarkable. You repeatedly find his BP to be high (155/105). He volunteers that he has had high BP measurements previously, but he has no other problems except some fatigue (which he attributes to his work) so he never felt he should follow up. As you probe further, he tells you that other people in his family have high BP, and one of his older sisters has no children after 15 years of marriage. As the patient waits for you in the exam room you and your preceptor discuss the case. Your preceptor suggests that you should follow up the high BP with appropriate labs but he also suggests you check with the patient about the onset of his puberty. Following the patient's disclosure of a precocious puberty your preceptor asks you:

- 1) What other labs would you order? Why? What results do you expect?

PROBLEM 3

A 60-year-old man visits you (an endocrinologist) at your clinic. He has been treated for type 2 diabetes for 10 years by his primary care physician. However, his condition seems to be worsening so his wife implored him to see a specialist. He tells you that his blood glucose was initially well-controlled with tolbutamide - a sulfonylurea compound, which stimulates insulin release. However, he says he had episodes of weakness, dizziness, and confusion after taking the drug. After some time the tolbutamide became less effective, and he had to start using insulin. Over 10 years he has lost 55 pounds but the weight loss accelerated over the last several months. He is 5'6", 135 lb. His BP is 150/100 and HR 90. His blood glucose (random) is 165 mg/dl. You ask him about his BP and he said that it used to be low but it was "kind of creeping up" perhaps because of all of the stress he is exposed to at work. In fact, he said that he can sometimes get so anxious that he can feel his heart "trying to jump out of his chest" and his blood pressure gets so high that his "head hurts as if it is about to split". Fortunately, "those things" don't last very long although they are more and more frequent. He owns a small business and tells you that it is getting "harder and harder to stay afloat" and wonders if this stress is the reason for his diabetes. (Repeated BP is 155/105.)

- 1) You ask the patient to collect 24 h. urine for analysis and results show elevated vanillylmandelic acid (VMA) and norepinephrine. MRI shows a round nodule on his right adrenal gland. What do you think is the most likely diagnosis?
- 2) The patient is complaining of blackouts when standing up from sitting or laying positions. What do you think is causing these episodes of orthostatic hypotension?
- 3) Can this diagnosis explain his diabetes?
- 4) The patient complained that he would have episodes of weakness and blackouts after using tolbutamide. These were most likely tolbutamide-evoked hypoglycemias. Can you explain why he would have such a strong reaction to the drug?
- 5) How would you treat this condition?