

Mr. White



Primary aldo and high salt for Tom Lohmeier. After Mr. Dixon who got 2000 pMol/Min (normal is 330) from an infusion pump. Here we turn on a tumor in the zona glomerulosa to 2000 and also slide table salt up to 300 mMol/Day.

Mr. White has severe hypokalemia. If we advance the solution for 1 week, he shows V-fib on day 3.

Load Mr. White (MR_WHITE.ICS) using the **File / Load Initial Conditions** main menu selection.

Is Mr. White OK? In his thumbnail sketch on the Charts panel, he says the he feels OK.

Check his blood pressure, heart rate, temperature and respiration using the Monitor panel.

Normal values were taken from Norm Subject.

Variable	Mr. White	N. Subject	Units
Blood Pressure		120 / 80	mmHg
Heart Rate		72	Beats / Min



Temperature		98.6	degree F
Respiration Rate		12	Breaths / Min

Do No Harm

We might first observe Mr. White for awhile. Use the **Go** main menu selection to advance the solution for 1 week.

Blood Chemistry

Maybe Mr. White needs more aggressive treatment. Click the **Restart** main menu selection to restart Mr. White.

Its time for some blood chemistry. Go to the Blood And Urine Samples panel. Get venous blood gases. Click Take Sample Now in the Venous Blood Gases box. Is there evidence of an acid/base disturbance?

Variable	Mr. White	N. Subject	Units
pCO2		45	mmHg
pH		7.39	pH Units
[H+]		41	pMol/L



[HCO ₃ ⁻]		26	mEq/L
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Check blood electrolytes. Click Take Sample Now in the Venous Blood Sample box. Are the blood electrolytes normal?

Variable	Mr. White	N. Subject	Units
[Na ⁺]		144	mEq/L
[K ⁺]		4.4	mEq/L
[Cl ⁻]		108	mEq/L
[BUN]		12	mG/dL
[Protein]		7.0	G/dL
Osmolality		292	mOsm/L
Hematocrit		45	%

Invasive Studies

Use the **View / Basic Physiology** and **Nephron Details** main menu selections to install the basic physiology and nephron toolbar buttons.

The blood samples taken above suggest that something is abnormal in Mr. White's electrolyte balance. We will now get numbers for Na⁺ and K⁺ excretion.



Go to the Urine panel and note the rate of Na⁺ and K⁺ excretion.

Na⁺ _____ mEq/Min x 1440 = _____ mEq/Day

K⁺ _____ mEq/Min x 1440 = _____ mEq/Day

If Mr. White is in balance, these excretion values will be nearly the same as Mr. White's dietary intake values. But, Mr. White may not be in balance. We better check it out.

Go to the Diet panel and note daily electrolyte intake.

Variable	Mr. White	N. Subject	Units
Na ⁺ Intake		180	mEq/Day
Na ⁺ Output		180	mEq/Day
K ⁺ Intake		70	mEq/Day
K ⁺ Output		70	mEq/Day

Mr. White appears to be a big salt user. We will look at his extracellular Na⁺ mass. Go to Na⁺ and note the extracellular Na⁺ mass.

Variable	Mr. White	N. Subject	Units
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ECFV Na+ Mass		2150	mEq
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Expanded extracellular Na+ may be contributing to Mr. White's hypertension. A low salt diet may be beneficial. We'll return to this idea later.

But for now, the electrolyte balance data suggests a bigger problem. It appears that Mr. White is excreting considerably more K+ than he is taking in. If this has persisted for awhile, Mr. White could be severely K+ depleted.

Go to K+ and note the extracellular and intracellular K+ mass and concentration.

Variable	Mr. White	N. Subject	Units
ECFV K+ Mass		66	mEq
ECFV [K+]		4.4	mEq/L
Cell K+ Mass		3960	mEq
Cell [K+]		141	mEq/L

Note that hypokalemia increases the risk of cardiac dysrhythmias.

Hormones In The Blood

We're getting close to an explanation. Go to Blood Chemistry and examine the



hormones in the blood.

Variable	Mr. White	N. Subject	Units
[AII]		20	pG/mL
Renin (PRA)		2.0	GU/mL
[Aldo]		330	pMol/L
[ADH]		2.0	pG/mL
[ANP]		20	pMol/L

Examine the values above, remembering that Mr. White is on a high-salt diet, and explain any unusual values. What is your diagnosis at this point?

Note the forces influencing hormone secretion.

Mr. White's Kidneys

Three nephron segments will be examined: the distal tubule, the glomerulus and the proximal tubule.

Go to Distal Tubule and note the status of sodium reabsorption.



Variable	Mr. White	N. Subject	Units
Na ⁺ Inflow		1.8	mEq/Min
Na ⁺ Reabsorption		1.4	mEq/Min
Na ⁺ Outflow		0.4	mEq/Min
Fractional Na ⁺ Reabsorption		78	%

Note also the status of potassium secretion. Effects on secretion can be estimated from the bar graph.

Variable	Mr. White	N. Subject	Units
K ⁺ Secretion		0.05	mEq/Min
[Aldo] Effect		1.0	X Normal
[K ⁺] Effect		1.0	X Normal
Na ⁺ Load Effect		1.0	X Normal

Go to Glomerulus and note the glomerular filtration rate.

Variable	Mr. White	N. Subject	Units



GFR		125	mL/Min

What factors are causing the change in glomerular filtration rate? What factors are opposing the change?

Go to Proximal Tubule and note the status of sodium reabsorption.

Variable	Mr. White	N. Subject	Units
Na ⁺ Inflow		17.3	mEq/Min
Na ⁺ Reabsorption		10.1	mEq/Min
Na ⁺ Outflow		7.2	mEq/Min
Fractional Reabsorption		58	%

Note the forces influencing potassium excretion. What effect will this reabsorption pattern have on downstream sodium movement?

Treatment

Initial treatment should focus on correcting the abnormal potassium values and on lowering blood pressure.



We'll work on the potassium first, administering a potassium supplement. Begin by recording initial values (Day 1). Note the time and date display in the upper, right-hand corner of most panels. Next, go to Diet and slide potassium up to 130 and extra chloride up to 80. Go to the Monitor panel to track blood pressure. Advance the solution 1 week and record values at the end of the week (Day 8).

Check on blood pressure and plasma [K+].

Variable	Day 1	Day 8	Units
Blood Pressure			mmHg
Plasma [K+]			mEq/L

So far, so good.

Next, we'll block the formation of angiotensin formation. Go to Blockers and slide converting enzyme inhibition up to 100%. Again, go to the Monitor panel to track blood pressure. Advance the solution 1 week and record values at the end of the week (Day 15)

Check on blood pressure and plasma [K+].

Variable	Day 8	Day 15	Units
Blood Pressure			mmHg



Plasma [K ⁺]			mEq/L
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Norm Subject's response to 100% converting enzyme over one week is shown below.

Variable	Day 1	Day 8	Units
Blood Pressure	120/81	109/71	mmHg
Plasma [K ⁺]	4.4	4.6	mEq/L

Describe and explain the differences between Mr. White's response and Norm Subject's response to converting enzyme inhibition.

Finally, let's reduce the amount of NaCl in Mr. White's diet. But first, we should remove the effects of converting enzyme inhibition. Record current (Day 15) data below. Then go to Blockers and slide converting enzyme inhibition back down to 0%. Again, go to the Monitor panel to track blood pressure. Advance the solution 1 week and record values at the end of the week (Day 22).

Variable	Day 15	Day 22	Units
Blood Pressure			mmHg
Plasma [K ⁺]			mEq/L

Mr. White is now ready for a reduction in salt intake. Record current (Day 22) data below. Then go to Diet and slide table salt (mMol/Day) down to 100. Again, go to the Charts panel to track blood pressure. Advance the solution 1 week and record values at the end of

the week (Day 29).

Variable	Day 22	Day 29	Units
Blood Pressure			mmHg
Plasma [K ⁺]			mEq/L

How can a change in sodium intake alter K⁺ balance?

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Fractional Reabsorption		78	%

Note also the change in the forces influencing potassium excretion. Effects on secretion can be estimated from the bar graph.



Variable	Mr. White	N. Subject	Units
K+ Secretion		0.05	mEq/Min
[Aldo] Effect		1.0	X Normal
[K+] Effect		1.0	X Normal
Na+ Load Effect		1.0	X Normal

Wrap up by revisiting all important variables and then making a general assessment of Mr. White's condition. K+ is worth a look. What is your final diagnosis?

Mr. White - Notes



Mr. White's thumbnail sketch notes only that he says that he feels pretty good. Of course, he is mistaken.

Mr. White is suffering from the 1 – 2 punch of an aldosterone secreting tumor plus elevated dietary table salt intake. This combination will create a fatal hypokalemia (via ventricular fibrillation) if left untreated.

Creating Mr. White

The tumor is turned on and intake of table salt is increased. The new parameter values are:

“Zona Glomerulosa, Tumor Secretion” = 2000.0

“Diet Goal, Table Salt (mMol/Day)” = 300.0

The units for tumor aldosterone secretion are pMol/Min. It appears that the tumor is not displayed in any panel, so it is a hidden variable.

Then the solution was advanced for 10 days (10080 minutes).

Mr. White is ready.



Recap

Uncontrolled secretion of aldosterone by adrenal tissue produces inappropriately high potassium excretion that decreases both intracellular and extracellular potassium stores. Severe hypokalemia can cause serious (and potentially fatal) dysrhythmias.

Excessive aldosterone secretion also leads to sodium retention and hypertension.

We would expect renin, angiotensin and aldosterone concentrations to be decreased with a high salt diet. Low renin with high aldosterone concentration on a high salt diet is abnormal; a defect in aldosterone synthesis or secretion is highly likely.

The primary site of aldosterone's action for both potassium secretion and sodium reabsorption is the kidney's distal tubule.

With regard to Mr. White's distal sodium reabsorption, aldosterone has caused a large increase in fractional reabsorption. The body's response has been to retain sodium, increase blood pressure, increase glomerular filtration rate and to increase sodium flow into the distal tubule. Sodium balance has been reestablished; the price is hypertension.

With regard to Mr. White's distal potassium secretion, aldosterone has caused a large increase in secretion that has been made worse by increased distal tubule sodium flow. The body's response has been to lose potassium that in turn decreases the plasma potassium concentration. This hypokalemia works at the distal tubule to offset (partially) the effect of increased aldosterone and increased sodium flow; the price is the likelihood of a fatal dysrhythmia.

High salt intake makes both the hypokalemia and hypertension worse.



Postscript

Mr. White has an aldosterone secreting tumor.

Use the **View / Organ Details** main menu selection to install the organ details toolbar buttons. Then go to Zona Glomerulosa to confirm the tumor secretion rate.

You can simulate surgical excision of the tumor by decreasing tumor secretion to zero.

But before doing surgery, note what Williams Textbook of Endocrinology, 9th Edition has to say: "All patients should receive medical treatment prior to surgery to control blood pressure and replete potassium stores."

We have replaced Mr. White's potassium loss and treated his hypertension, so he appears to be ready for surgery. Slide tumor secretion down to 0. Advance the solution for 1 week. Note additional changes in blood pressure and plasma [K+].

Variable	At Surgery	1 Week Post-OP	Units
Blood Pressure			mmHg
Plasma [K+]			mEq/L

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Mr. White Wrap-up



Summary

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