



Mr. Wilson



Load Mr. Wilson (Mr Wilson.ICS) using the **File | Load Initial Conditions** main menu selection.

Is Mr. Wilson OK? Actually, the thumbnail sketch on the  Charts panel suggests that he is not OK. It indicates that he is having a seizure and this is verified by the neurological signs workup.

To get a rough idea of Mr. Wilson's condition, advance the solution in 5 minute intervals for a total 10 minutes, collecting data at the start and at the end of each interval. Check Mr. Wilson's blood pressure, heart rate, temperature and respiration using the Monitor  panel.

Variable	12:00	12:05	12:10
Systolic Blood Pressure (mmHg)			
Diastolic Blood Pressure (mmHg)			
Heart Rate (/Min)			
Temperature (deg F)			
Respiration Rate			



(/Min)				
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Which values are outside of the normal range? What does this data set, in total, suggest.

Click main menu selection Restart to restart the solution.

Attend to Mr. Wilson. Be prepared to discuss the following points.

- What is the matter with Mr. Wilson?
- What interventions are possible? Which do you recommend? Can you describe a beneficial course of action?
- What physiological and pathophysiological mechanisms are causing Mr. Wilson's condition?
- Specifically, what are the neurological, endocrine, and metabolic components of Mr. Wilson's condition?



Mr. Wilson – Notes



Mr. Wilson was seen in the Emergency Room as his thumbnail sketch indicates. An injection thought to be an analgesic turned out instead to be a rather large dose of insulin.

Mr. Wilson's blood glucose dropped rapidly, he had a seizure with very a significant activation of the sympathetic nervous system. He will soon fall into a hypoglycemic coma.

Creating Mr. Wilson

Mr. Wilson was created by injecting 40 units of regular insulin. In addition, dietary goals were set to zero, although this probably is not necessary.

The following parameter changes were made:

“Diet Goal, Carbo's (kCal/Day)” = 0.0

“Diet Goal, Fat (kCal/Day)” = 0.0

“Diet Goal, Protein (kCal/Day)” = 0.0

“Insulin Inject, Amount Injected” = 40.0

Then a function named “INS_INJECT” was fired and the solution was advanced 40 minutes. Blood glucose fell steadily during this period while blood insulin was increasing.



Interventions

The severe hypertension with tachycardia (not bradycardia) suggest a primary CNS lesion such as a stroke. But the low blood glucose level is fully diagnostic.

The value for blood glucose concentration can be obtained at the Blood Chemistry panel. The toolbar button group named Basic Physiology must be visible – use the View main menu selection to make it visible.

The proper intervention for insulin overdose is glucose infusion. A glucose infusion pump is available at the Infusion Pumps panel.

The question then is how much glucose is needed. Dump it in and do a follow up blood sample. I used 1000 mG/Min with a good outcome.

Some useful panels are

Glucose

Insulin

Glucagon

References

I'm looking for some suitable references now.



Mr. Wilson – Instructors Notes



Mr. Wilson has Type I diabetes mellitus (IDDM).

Unfortunately Mr. Wilson has been given too much insulin and has fallen into a diabetic coma.

Need to revive him. Glucose drip.

It's severe. If you advance the solution for 1 week without intervention, Mr. Johnson develops a fatal case of pulmonary edema.

The clinical buttons toolbar group has several useful interventions.

- Dietary salt.

- Diuretics

- IV drip including protein

Note that steroids are not available.

Select View | Basic Physiology to put the basic physiology group of panels on the toolbar.

- Pressures and flows.



- Volumes.

- Pulmonary edema.

Select View | Orthostasis to put the orthostasis group of panels on the toolbar. These panels show regional interstitial fluid volume, protein concentration and lymph flow.

Select View | Nephron Details to put the nephron group of panels on the toolbar. The click on Glomerulus to view the cause to the nephrotic syndrome. Click Urine to see what is being excreted.

Sodium Retention In Nephrotic Syndrome

Here is the classic picture of nephrotic syndrome. Albumin is lost into the urine. Plasma colloid pressure falls and water shifts from the plasma to the interstitium. Sodium retaining mechanisms are activated by the decreased plasma volume and sodium is retained. The retained sodium leaks into the interstitium and edema forms.

But Dorhout Mees noted in 1979 that the typical nephrotic syndrome patient does not show signs of plasma volume contraction and activation of sodium retaining mechanisms. In fact, the opposite is seen.

The best evidence comes from serial studies in patients that have episodes of nephrotic syndrome followed by spontaneous remission or favorable response to steroids.

In the new picture of nephrotic syndrome, plasma volume and blood volume are expanded, plasma renin activity and aldosterone concentration are normal or decreased (Dorhout Mees *et.al.*, Shapiro *et.al.*). Glomerular filtration is decreased. Dorhout Mees reported one patient that had a creatinine clearance of 34 mL/Min during nephrotic syndrome and 127 mL/Min during recovery. A water load is excreted slowly during nephrotic syndrome (Shapiro *et.al.*). Arterial pressure tends to be elevated.



The glomerular membrane is a complex tissue, but it appears that protein permeability is increased in nephrotic syndrome while sodium permeability is decreased. Note that albumin is an anion while sodium is a cation and the glomerular membrane is normally loaded with negative charges.

Experimental Nephrotic Syndrome.

In rats. Puromycin aminonucleoside (PAN) will produce a very good model of nephrotic syndrome in rats following close or systemic infusion.

These rats dump albumin and other small proteins as expected.

These animals also retain sodium. The whole kidney and single nephron glomerular filtration rates are decreased (Ichikawa *et.al.*). Sodium excretion as a function of renal perfusion pressure is greatly reduced (Firth *et.al.*). Firth has a great graph.

There is also some evidence for increased distal sodium reabsorption, although the reason is not clear. I need to look into this a bit more.

COP And Na⁺ Excretion In Normal Kidneys

Christine Bayliss, Thomas Maack and other have investigated the effect of colloid osmotic pressure on sodium excretion in normal kidneys. Usually using rats.

Decreased colloid osmotic pressure increases glomerular filtration and decreases tubular reabsorption. This two factors combine to net a big increase in sodium excretion, which is basically the opposite of what is seen in nephrotic syndrome.



Bayliss *Am er. J. Physiol.* 232:F58-F64, 1977 has some nice data.

Some other potentially useful references are:

AJP 226:426-430, 1974.

AJP 226:512-517, 1974.

Pflugers 301:7-15, 1968.

Circ. Res. 61:531-538, 1987.

Pfluger 306:92-102, 1969.

JCI 82:1757-1768, 1988.

Kid. Int. 34:220-223, 1988.

Physiological Compensations

There may be many important physiological compensations that help to keep the nephrotic syndrome patient alive. I don't have a big list at this time.

Falling plasma protein concentration slows the flux of protein from plasma to interstitium and this helps to keep available protein in the plasma.

Falling plasma protein concentration increases the Starling pressure gradient across the capillary wall. This increases the flux of water from plasma to interstitium. Interstitial pressure increases (Noddeland *et.al.*). Lymph flow increases and washes interstitial protein back into the plasma. Interstitial protein concentration can fall to a very low level (Noddeland *et.al.*, Koomans *et.al.*) Koomans has a very nice graph..

These responses in total keep as much of the available protein as possible in the plasma



(where it is needed) and not in the interstitium.

References

- Dorhout Mees, E.J., J.C. Roos, R. Boer, O.H. Yoe and T.A. Simatupang. Observations on edema formation in the nephrotic syndrome in adults with minimal lesions. *Am er. J. Med.* 67:378-384, 1979,
- Firth, J.D., A.E.G. Raine and J.G.G. Leddingham. Abnormal sodium handling occurs in the isolated perfused kidney of the nephrotic rat. *Clin. Sci.* 76:387-395, 1989.
- Ichikawa, I., H.G. Renke, J.R. Hoyer, K.F. Badr, N. Schor, J.L. Troy, C.P. Lechene and B.M Brenner. Role for intrarenal mechanisms in the impaired salt excretion of experimental nephrotic syndrome. *J. Clin. Invest.* 71:91-103, 1983.
- Koomans, H.A., W. Kortlandt, A.B. Geers and E.J. Dorhout Mees. Lowered protein content of tissue fluid in patients with nephrotic syndrome: observations during disease and recovery. *Nephron* 40:391-395, 1985.
- Joles, J.A., T.J. Rabelink, B. Braam and H.A. Koomans. Plasma volume regulation: Defences against edema formation (with special emphasis on hypoproteinemia). *Am . J. Nephrol.* 13:399-412, 1993.
- Noddeland, H., S.M. Riisnes and H.O. Fadnes. Interstitial fluid colloid osmotic and hydrostatic pressures in subcutaneous tissue of patents with nephrotic syndrome. *Scand. J. Clin. Lab. Invest.* 42:139-146, 1982.
- Shapiro, M.D., K.M. Nicholls, B.M. Groves and R.W. Schrier. Role of glomerular filtration rate in the impaired sodium and water excretion of patients with the nephrotic syndrome. *Am er. J. Kid. Dis.* 8:81-87, 1986.



