Ms. Thomas

Load Ms. Thomas (Ms Thomas.ICS) using the **File / Load Initial Conditions** main menu selection.

Is Ms. Thomas OK? Actually, the thumbnail sketch on the  Charts panel suggests that she is not OK. She is confused – maybe worse.

To get a rough idea of Ms. Thomas’s condition, advance the solution in 1 hour intervals for a total of 3 hours, collecting data at the start and at the end of each interval. Check Ms. Thomas’s blood pressure, heart rate, temperature and respiration using the  Monitor panel.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variable | 12:00 | 1:00 | 2:00 | 3:00 |
| Systolic Blood Pressure (mmHg) |  |  |  |  |
| Diastolic Blood Pressure (mmHg) |  |  |  |  |
| Heart Rate (/Min) |  |  |  |  |
| Temperature  (deg F) |  |  |  |  |
| Respiration Rate  (/Min) |  |  |  |  |

The initial values look pretty good, but trouble soon develops. What does the pulse pressure and heart rate data suggest?

Click main menu selection Restart to restart the solution.

Attend to Ms. Thomas. Be prepared to discuss the following points.

1. What is the matter with Ms. Thomas?
2. What interventions are possible? Which do you recommend? Can you describe a beneficial course of action?
3. What physiological and pathophysiological mechanisms are causing Ms. Thomas’s condition?
4. What physiological mechanisms, if any, are actually beneficial to Ms. Thomas condition?
5. Summarize Ms. Thomas’s acid/base status?
6. What is Ms. Thomas’s fluid volume status?
7. What is Ms. Thomas’s renal excretory status?
8. Specifically, what are the neurological, endocrine and metabolic components of Ms. Thomas’s condition?

Ms. Thomas – Notes

Ms. Thomas has untreated Type I diabetes mellitus or insulin dependent diabetes mellitus (IDDM).

The key word here is *untreated*. Ms. Thomas has had little or no insulin therapy and is at extreme risk of falling into a coma caused either by hyperglycemia or ketoacidosis.

Creating Ms. Thomas

Ms. Thomas was created by simulating nearly complete loss of pancreatic beta cells. Specifically, pancreatic insulin secretion was clamped at 1 mU/Min compared to a typical secretion of 10 mU/Min.

The new parameters values are:

“Insulin Secretion, Clamp Level” = 1.0

“Insulin Secretion, Clamp Switch” = 1.0 // On

Then the solution was advanced for 18 hours (1080 minutes). Hyperglycemia and ketoacidosis quickly developed.

Interventions

Ms. Thomas’s condition is initially not very clear. So go to the  Blood Chemistry panel.

Several values jump out. Ms. Thomas has a blood glucose concentration of 1200 mG/dL compared to a normal of around 100 mG/dL. This increase is enough to produce a hyperglycemic coma.

There is also a severe acidosis. It is metabolic since blood pCO2 values are normal to low.

Blood ketoacids concentration is very high, causing a large anion gap and a small strong ion difference.

This looks like IDDM with inadequate insulin replacement. You could check the plasma insulin levels just to make sure.

The proper intervention is to inject insulin to bring the blood glucose concentrations down. I injected 20 U, but ended up with ventricular fibrillation due to hypokalemia.

So there are some additional issues during treatment that I should look into. Ms. Thomas is excreting 11 mL/Min urine vs. a normal flow of 1 mL/Min. She has become dehydrated and the dehydration is intracellular, with a cell water of 23 L vs. a normal volume of 28 L. Plasma [K+] is increased and this has stimulated aldosterone secretion.

I’ll look into this further. With a shot of insulin, the osmolarity falls and water rushes into the cells. Apparently K+ rushes in also, lowering plasma [K+] to lethal levels.

Apparently, an aggressive drip must accompany the insulin. At minimum, careful management is needed.

Some useful panels are

 Glucose

 Insulin

 Glucagon

 pH

References

I’m looking for some suitable references now.

Ms. Thomas – Instructors Notes

Ms. Thomas has Type I diabetes mellitus (IDDM).

She has had little or no insulin therapy and is at extreme risk of falling into a coma caused either by hyperglycemia or ketoacidosis.

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 *Amer. 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. *Amer. 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. *Amer. J. Kid. Dis.* 8:81-87, 1986.