Mr. Johnson

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

Is Mr. Johnson OK? Actually, the thumbnail sketch on the  Charts panel suggests that he is not OK. He has a lot to complain about including lower body swelling and dyspnea.

To get a rough idea of Mr. Johnson’s condition, advance the solution 1 day at a time for a couple of days. Check Mr. Johnson’s blood pressure, heart rate, temperature and respiration using the Monitor  panel.

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

Click main menu selection Restart to restart the solution.

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

1. What is the matter with Mr. Johnson?
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 Mr. Johnson’s condition?
4. What physiological mechanisms are actually beneficial to Mr. Johnson’s condition?
5. What is Starling’s law of the capillary and how might this apply to Mr. Johnson?
6. What are the determinants of lymph flow and how might this apply to Mr. Johnson?
7. What are some causes of abnormal amounts and distributions of body fluids and how might this apply to Mr. Johnson?

Mr. Johnson – Notes

Mr. Johnson has nephrotic syndrome.

It’s severe. If you advance the solution for a couple of days with no intervention, Mr. Johnson develops a fatal case of pulmonary edema.

Creating Mr. Johnson

Mr. Johnson was created simply by increasing glomerular membrane protein permeability and letting a suitable amount of time go by.

The variable “Glomerulus, Protein Permeability” was increased from 0 (Normal) to 0.5 (Severe) and the solution was advanced 2 weeks. Then permeability was increased to 1.0 (Very Severe) and the solution was advanced 2 more weeks. Finally, permeability was set to 2.0 (Extreme) with 2 more weeks. At this point, Mr. Johnson is starting to develop pulmonary edema.

I could have added some impaired sodium excretion (see discussion below) but, as you can see, it really isn’t necessary.

Useful Displays

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.

Edema Formation

Edema can be severe in nephrotic syndrome, with extracellular fluid volume increasing to two or more times normal (Koomans *et.al.* 1986). Check Mr. Johnson’s body weight at the  Charts panel.

It takes a lot of renal salt and water retention to generate the large amounts of edema fluid filling the interstitium.

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 are many important physiological compensations that help to keep the nephrotic syndrome patient alive.

Blood volume tends to be elevated slightly and in proportion to the extracellular fluid volume expansion.

Decreased plasma colloid pressure leads to increased capillary ultrafiltration. But 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 fluid pressure increases (Noddeland *et.al.* 1982). Lymph flow increases and washes interstitial protein back into the plasma. Interstitial protein concentration can fall to a very low level (Noddeland *et.al.* 1982, Koomans *et.al.* 1985) Koomans has a very nice graph..

Protein washout moves the available protein to the plasma where it is needed. But also, protein washout and the resultant decrease in interstitial colloid pressure (Koomans *et.al.* 1985) modifies the capillary Starling forces, opposing the increased capillary ultrafiltration.

These responses in total keep as much of the available protein as possible in the plasma and not in the interstitium, but the price, of course, is that severe edema develops.

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.

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Mr. Johnson – Instructors Notes

Mr. Johnson has nephrotic syndrome.

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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.

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