

Nephrotic Syndrome



Nephrotic syndrome is characterized by

- Loss of protein in the urine.
- Depletion of vascular and extravascular protein.
- Loss of water across capillary walls to form interstitial edema.
- Renal retention of large amounts of salt and water used in creating the edema.

A primary cause of nephrotic syndrome is increased permeability to plasma protein, namely albumin, at the glomerular membrane.

Protein loss leads to decreased protein concentration in the plasma and, consequently, decreased plasma colloid osmotic pressure. This alters the Starling forces at the systemic and pulmonary capillaries to increase ultrafiltration. We would also expect decreased colloid pressure to increase glomerular filtration, enhancing sodium excretion. This last response is not observed, leading to the notion that nephrotic syndrome has at least two importance causal components, both involving the glomerular membrane.

- Increased protein permeability at the glomerular membrane.



- Decreased filtration coefficient at the glomerular membrane.



We'll investigate both of these defects in this laboratory exercise, first separately and then combined.

Note that increased sodium reabsorption in the distal tubule and/or collecting has also been implicated in nephrotic syndrome; this possibility will not be explored in this exercise.

Use the **View** main menu selection to place  the Nephron Details button on the toolbar.


Protein Loss

Click **Restart** to establish initial conditions.

Go to the Glomerular Filtrate box in the  Glomerulus panel and slide protein permeability up from none to severe. Go to  Urine to observe urinary protein loss. Advance the solution 1 week.

Physical units for urinary protein loss are G/Min. Calculate daily loss.

_____ G/Min x 1440 = _____ G/Day

Go to  Circulating Protein and note the changes in vascular and interstitial protein.




Plasma Protein	Normal	Now
Mass (G)	208	
Concentration (G/dL)	6.9	
Colloid Pressure (mmHg)	28	

Interstitial Protein	Normal	Now
Mass (G)	235	
Concentration (G/dL)	2.0	
Colloid Pressure (mmHg)	7	

Go to  Interstitium and note the distribution and movement of extravascular water.

	Normal	Now
Plasma Volume (L)	3.0	
Interstitial Volume (L)	12.0	
Capillary Filtrate (mL/Min)	1.4	
Lymph Flow (mL/Min)	1.0	





Go to  Glomerulus and note the change in glomerular filtration rate that helped to prevent edema formation.

In summary, protein loss has caused some important changes in the body fluids, but it didn't cause significant edema. Keep in mind that rapid edema formation requires a lot of salt and water retention.

Note that extreme protein loss is fatal. What do think will be the cause of death?

Sodium Retention

Click **Restart** again to establish initial conditions.


Go to the GFR Determinants box in the  Glomerulus panel and slide permeability down from 20 to 4. Notice the immediate effect on glomerular filtration rate. Go to  Urine to observe urinary sodium excretion. Advance the solution 1 week.

Go to  Interstitium and note the distribution and movement of extravascular water.

	Normal	Now
Plasma Volume (L)	3.0	
Interstitial Volume (L)	12.0	
Capillary Filtrate (mL/Min)	1.4	









Lymph Flow (mL/Min)	1.0	
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Go to  Na⁺ and note the change in extracellular sodium mass. Sodium balance has been reestablished after a modest increase in extracellular sodium.

Extracellular Sodium	Normal	Now
Mass (G)	2170	

Over this week, several mechanisms were quietly working to offset the decrease in glomerular membrane permeability. Check on

- Arterial pressure at  Pressure
- Glomerular pressure at  Glomerulus
- Plasma renin activity at  Angiotensin
- Atrial natriuretic peptide at  Atrial Natriuretic Peptide
- Aldosterone at  Aldosterone
- Renal nerve activity at  Autonomic Efferents

	Normal	Now
Arterial Pressure (mmHg)	97	






Glomerular Pressure (mmHg)	60	
Plasma Renin Activity	2.0	
Atrial Natriuretic Peptide (Art)	26	
Aldosterone	300	
Renal Nerve Activity	1.5	

Nephrotic Syndrome

We will now combine protein loss with sodium retention to create a model of nephrotic syndrome.

Click **Restart** again to establish initial conditions.

Go to the Glomerular Filtrate box in the  Glomerulus panel and slide protein permeability up from none to severe. Then slide glomerular membrane permeability down from 20 to 4 in the GFR Determinants box. Go to  Urine to observe urinary sodium excretion and protein loss. Advance the solution 1 month to capture the full effect.

Go to  Circulating Protein and note the changes in vascular and interstitial protein.

Plasma Protein	Normal	Now
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Mass (G)	208	
Concentration (G/dL)	6.9	
Colloid Pressure (mmHg)	28	

Interstitial Protein	Normal	Now
Mass (G)	235	
Concentration (G/dL)	2.0	
Colloid Pressure (mmHg)	7	

Go to  Interstitium and note the distribution and movement of extravascular water.

	Normal	Now
Plasma Volume (L)	3.0	
Interstitial Volume (L)	12.0	
Capillary Filtrate (mL/Min)	1.4	
Lymph Flow (mL/Min)	1.0	

Go to  Na⁺ and note the change in extracellular sodium mass. Again, sodium balance



has been reestablished

Extracellular Sodium	Normal	Now
Mass (G)	2170	

Wrap up by revisiting the determinants of sodium excretion explored in the previous section.

	Normal	Now
Arterial Pressure (mmHg)	97	
Glomerular Pressure (mmHg)	60	
Plasma Renin Activity	2.0	
Atrial Natriuretic Peptide (Art)	26	
Aldosterone	300	
Renal Nerve Activity	1.5	

In summary, the nephrotic syndrome can show a variety of clinical faces, but the most typical elements are

- Protein loss by the kidney that lowers plasma colloid osmotic pressure and allows loss of salt and water into the interstitium.



- Renal salt and water retention to furnish the interstitial edema fluid.

References

Palmer, B.F. and R.J. Alpern. Pathogenesis of edema formation in the nephrotic syndrome. *Kidney Int. Suppl.* 59:S21-S27, 1997.

