

Uremic toxins by class and linkage with clinical symptoms and outcomes

Classification of Molecules ¹	Representative Molecules ^{1,7,13}	Relevant Clinical Effects and Symptoms	Dialytic Clearance ¹		
Small Molecules <0.5 kDa	● Urea (60 Da)	General Uremic Toxicity ^{2,3}	Removed by Low-Flux HD	Removed by High-Flux HD	Removed by HDF
	● Phosphate (95 Da)	Vascular Calcification ⁴ Chronic Kidney Disease-Mineral and Bone Disorder ⁵			
Small-middle Molecules 0.5-15 kDa	● PTH (9.2 kDa)	Chronic Kidney Disease-Mineral and Bone Disorder ⁵	Removed by High-Flux HD	Removed by HDF	Removed by HDx therapy
	● Beta 2 microglobulin (12 kDa)	Amyloidosis/Carpal Tunnel Syndrome ^{2,3}			
Medium-middle Molecules >15-25 kDa	● Myoglobin (17 kDa)	Oxidative Stress & Mitochondrial Dysfunction ³	Removed by High-Flux HD	Removed by HDF	Removed by HDx therapy
	● Kappa free-light-chains (23 kDa)	Multiple Toxicity ^{3,6}			
	● Complement factor D (24 kDa)	Contributor to Proinflammatory Status of Uremia ⁷			
	● Interleukin-6 (25 kDa)	Pruritus ⁸ , Recovery Time ⁹ , Chronic Inflammation ¹⁰ , CV Disease ¹⁰ , Protein-Energy Wasting in CKD ¹⁰			
Large-middle Molecules >25-45 kDa	● TNF-alpha (26 kDa)	Sepsis ³ , Chronic Inflammation ¹⁰ , CV Disease ¹⁰ , Protein-Energy Wasting in CKD ¹⁰	Removed by High-Flux HD	Removed by HDF	Removed by HDx therapy
	● FGF-23 (32 kDa)	Secondary Immunodeficiency, CV Disease ¹⁰			
	● Alpha 1 microglobulin (33 kDa)	Restless Legs Syndrome (RLS) ^{4,11}			
	● YKL-40 (40 kDa)	Inflammation ¹²			
	● Lambda free-light-chains (45 kDa)	Chronic Inflammation, Secondary Immunodeficiency ³			
Large Molecules [>58 kDa]	● Albumin (69 kDa)	Toxin Binding ³	Removed by High-Flux HD	Removed by HDF	Removed by HDx therapy

Kidney

1. Rosner MH, et al. Classification of Uremic Toxins and Their Role in Kidney Failure. *Clin J Am Soc Nephrol*. 2021;16(12):1918-1928. 2. Ronco C, La Manna G. Expanded Hemodialysis: A New Therapy for a New Class of Membranes. *Contrib Nephrol*. 2017;190:124-133. 3. Ronco C, et al. Expanded Haemodialysis: from operational mechanism to clinical results. *Nephrol Dial Transplant*. 2018;33(suppl_3):iii41-iii47. 4. Ronco C. Editor. Expanded Hemodialysis: Innovative Clinical Approach in Dialysis. Karger Medical and Scientific Publishers. 2017. 5. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease - Mineral and Bone Disorder (CKD-MBD). *Kidney Int Suppl*. (2011). 2017;7(1):1-59. 6. Desjardins L, et al. Association between Free Light Chain Levels, and Disease Progression and Mortality in Chronic Kidney Disease. *Toxins (Basel)*. 2013;5(11):2058-2073. 7. Vanholder R, et al. Biochemical and Clinical Impact of Organic Uremic Retention Solutes: A Comprehensive Update. *Toxins (Basel)*. 2018;10(1):33. 8. Kimmel M, et al. The role of micro-inflammation in the pathogenesis of uraemic pruritus in haemodialysis patients. *Nephrol Dial Transplant*. 2006;21(3):749-755. 9. Bossola M, et al. Recovery Time after Hemodialysis Is Inversely Associated with the Ultrafiltration Rate. *Blood Purif*. 2019;47:45-51. 10. Wolley M, et al. Exploring the Clinical Relevance of Providing Increased Removal of Large Middle Molecules. *Clin J Am Soc Nephrol*. 2018;13 (5):805-814. 11. Sakurai K. Biomarkers for Evaluation of Clinical Outcomes of Hemodiafiltration. *Blood Purif*. 2013;35(Suppl 1):64-68. 12. Lorenz G, et al. Mortality prediction in stable hemodialysis patients is refined by YKL-40, a 40-kDa glycoprotein associated with inflammation. *Kidney Int*. 2018;93(1):221-230. 13. EUTOX Uremic Solutes Database. June 2022. Uremic-toxins.org