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Primary Research Interest:	Physiology
Description of Research:	A common troublesome gastrointestinal complication of diabetes is diarrhea. In type 2 diabetic mellitus (T2DM), the frequent cause of diarrhea in T2DM is associated with drugs, including metformin, which is commonly used for glycemic control in T2DM. Inhibition of Na+/H+ exchanger 3 (NHE3) is associated with both enterotoxigenic and inflammatory diarrhea. The goal of these studies is to understand the role of NHE3 in diabetic diarrhea and to establish a new paradigm that an improvement of sodium and fluid transport by NHE3 can be used to alleviates diabetic diarrhea that affects VA patients. We plan to determine the underlying mechanism of NHE3 inhibition in T2DM and the regulation of NHE3 by metformin. As a pre-clinical test to improve the treatment for diabetic diarrhea, we will test the efficacy of a biologically occurring phospholipid, lysophosphatidic acid, and probiotics in mitigating the inhibition of NHE3.
Relevance to VA:	It is estimated that diabetes affect 25% of the VA patients and with more than 70% of patients in VA facilities being overweight or obese, type 2 diabetes becoming a major health concern. Diarrhea is one of the most common gastrointestinal complications in diabetes, and yet understanding and treatment for diabetic diarrhea are lacking. The proposed study is aimed at understanding the underlying cause of diarrhea in type 2 diabetes where diarrhea is often associated with medications. We will explore the role of a sodium -hydrogen exchange in the intestine as a major cause of diabetic diarrhea and perform a pre-clinical study to test the efficacy of biological agents for the treatment of diarrhea.