

There has been increasing evidence to indicate that coated vesicles and MVBs may mimic viral particles.<sup>3,S2,S3</sup> However, it is known that the budding of enveloped viruses (to which SARS-CoV-2 belongs) from the plasma membrane, or the limiting membrane of the endosome, resembles the formation of intraluminal vesicles inside MVBs. Moreover, the 2 processes share some components of the same protein machinery.<sup>4,S4</sup> Indeed, we detected intraluminal vesicles budding from discontinued limiting membrane of the vacuole in lung endothelial cells with positive SARS-CoV-2 RNA (Figure 1a). This finding strongly suggests that this structure is not MVBs but rather a cluster of viral particles with some of budding virions. Indisputable evidence of virions would thus be provided only by immunoelectron microscopy. In addition, coated vesicles might also faintly resemble viral particles, but it is necessary to be cautious about the intracellular location of coated vesicles. Specifically, coated vesicles are transient and are therefore mostly found in close vicinity to the membrane from which they bud, because they shed their coat within seconds after their formation.

To conclude, although TEM may serve as a useful diagnostic method for the detection of viral infection, caution should be exercised when confirmation of viral invasion relies only on TEM. Additional convincing methods, including immunoelectron microscopy, immunohistochemistry, and viral genetic material analysis, are needed for indisputable proof of viral invasion in organs.

## SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary References.

1. Su H, Yang M, Wan C, et al. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. *Kidney Int.* 2020;98:219–227.
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Maja Frelj<sup>1</sup>, Andreja Erman<sup>2</sup>,  
Karmen Wechtersbach<sup>1</sup>, Jerica Pleško<sup>1</sup>,  
Tatjana Avšič-Županc<sup>3</sup> and Nika Kojc<sup>1</sup>

<sup>1</sup>Institute of Pathology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia; <sup>2</sup>Institute of Cell Biology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia; and

<sup>3</sup>Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

**Correspondence:** Maja Frelj, Institute of Pathology, Faculty of Medicine, University of Ljubljana, 1000 Ljubljana, Slovenia. E-mail: [maja.frelj@mf.uni-lj.si](mailto:maja.frelj@mf.uni-lj.si)

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## Transient Renal Tubular Syndromes Associated With Acute COVID-19 Disease



**To the Editor:** We report 2 transient renal tubular syndromes associated with coronavirus disease 2019 (COVID-19).

A 47-year-old patient in a neurorehabilitation unit was diagnosed with COVID-19 following onset of respiratory symptoms and pyrexia, confirmed by reverse transcriptase polymerase chain reaction. Ten days later, he developed hypernatremia with an acute kidney injury. He was exclusively fed by percutaneous endoscopic gastrostomy tube.

Investigations (Table 1) supported a diagnosis of nephrogenic diabetes insipidus. He was managed with increased enteral water intake via the percutaneous endoscopic gastrostomy and intravenous 5% dextrose over 24 hours. Biochemistry improved progressively, with serum sodium renal function returning to baseline by day 23.

A 52-year-old woman with diabetic nephropathy and a kidney-pancreas transplant was recovering from a below-knee amputation. She developed fever and a cough; reverse transcriptase polymerase chain reaction confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Three days later, she developed a severe metabolic acidosis associated with profound hypophosphatemia, hyperphosphaturia, and low molecular weight proteinuria, diagnostic of the renal Fanconi syndrome (Table 1). She required aggressive i.v. potassium, bicarbonate, and phosphate supplementation; she was weaned off all supplementation by day 18.

Kidney disease is widely recognized in COVID-19; there is evidence of direct viral invasion of the

**Table 1.** Serum and urine biochemistry

	Patient 1	Patient 2
Age, yr	47	52
Gender	Male	Female
Past medical history	Traumatic head injury 2018, PEG-fed	Diabetic nephropathy, kidney/pancreas transplant 2011
Drug therapy	Meropenem	Tacrolimus, mycophenolate (suspended), meropenem
Date of COVID-19 diagnosis	April 3, 2020	March 26, 2020
Onset of syndrome, days after COVID diagnosis	10	3
Resolution of syndrome, d	21	18
Serum sodium, mmol/l	152	138
Serum potassium, mmol/l	3.6	2.9
Serum creatinine, $\mu\text{mol/l}$	154	90
Baseline serum creatinine, $\mu\text{mol/l}$	60	62
Serum bicarbonate, mmol/l	30	4
Serum corrected calcium, mmol/l	2.56	2.41
Serum phosphate, mmol/l	1.83	0.18
Serum magnesium, mmol/l	1.03	0.56
Serum osmolality, mosmol/l	321	ND
CRP, mg/l	74	100
Urinary $\text{FE}_{\text{PO}_4}$ , %	ND	70
Urinary retinol binding protein/creatinine ratio	ND	1540
Urinary osmolality, mosmol/l	264	ND

CRP, C-reactive protein; ND, not done; PEG, percutaneous endoscopic gastrostomy.

tubular epithelium.<sup>1,2</sup> Angiotensin-converting enzyme 2 (ACE2), the ligand for viral cell invasion, is expressed on both proximal and distal tubular cells.<sup>3</sup> The first patient had a distal lesion (nephrogenic diabetes insipidus); the second had proximal tubular dysfunction.

These renal tubular syndromes support a direct toxic effect of the virus on the tubular epithelium. The prevalence and consequences of tubular dysfunction in COVID-19 is worthy of further study.

1. Su H, Yang M, Wan C, et al. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. *Kidney Int.* 2020;98:219–227.
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Elizabeth R. Wan<sup>1</sup>, Robin G. Woolfson<sup>1</sup>,  
Richard Greenwood<sup>2</sup> and Stephen B. Walsh<sup>1</sup>

<sup>1</sup>University College London Department of Renal Medicine, Royal Free Hospital, University College London, London, UK; and <sup>2</sup>Acute Brain Injury Unit, National Hospital for Neurology and Neurosurgery, Queen's Square, London, UK

**Correspondence:** Stephen B. Walsh, University College London Department of Renal Medicine, Royal Free Hospital, London NW3 2QG, UK. E-mail: [Stephen.walsh@ucl.ac.uk](mailto:Stephen.walsh@ucl.ac.uk)

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## Serum Albumin Still of Interest to Predict Outcomes in Membranous Nephropathy in the Era of Phospholipase A2 Receptor



**To the Editor:** In a recent retrospective study, Lee *et al.*<sup>1</sup> demonstrated the interest of serum albumin (sAlb) as a prognostic marker of outcome in primary membranous nephropathy. The most significant limitation of their study was the absence of information about patients' phospholipase A2 receptor (PLA2R) status. Indeed, during the past decade, accumulating evidence suggested that clinical remission is preceded by immunological remission<sup>2,3</sup> and PLA2R serology has become an essential tool for primary membranous nephropathy monitoring. Whether sAlb remains a useful marker in the era of PLA2R is unknown. To investigate this question, we retrospectively analyzed 46 cases of PLA2R-related primary membranous nephropathy. Forty-one patients reached immunological remission after rituximab therapy with a median delay of 4.8 months. The evolution of patients with immunological remission and normal sAlb (>3.5 g/dl) was compared with that of patients with immunological remission and low sAlb (Table 1). The outcome of patients with immunological remission and normal sAlb was better than that of patients with low sAlb, that is, higher sAlb and lower proteinuria at 12 months and at last follow-up. Moreover, patients with normal sAlb had a higher probability to reach complete remission (log-rank test  $P < 0.001$ ) (Figure 1).

In conclusion, in 2017, the GEMRITUX trial suggested that sAlb appeared to be an earlier predictor of remission of nephrotic syndrome than proteinuria.<sup>4</sup> Recently, Lee *et al.*<sup>1</sup> confirmed that sAlb was an interesting and probably underestimated prognostic