Electronic Supplementary Information (ESI) available

The following individual analysis of representative subjects demonstrates the BDV correlation to the severity of the catabolic inflammatory APR and evolving clinical condition.

Subject 4 (Figure S1) a 14-year-old male was admitted to the PICU following severe traumatic brain injury, grade 2 splenic laceration, fracture of his left clavicle, and laceration of his right brow sustained in an airplane crash. Initial chest radiographs (CXR) showed no lung infiltrates. He had a temperature of 39ºC on day 2 of the study at 02:00 hours that was deemed attributable to inflammation secondary to trauma. Temperature normalized until day 4 of the study at 2000 when it rose to 39.4ºC. A sputum culture was obtained. His initially elevated white blood cell count (WBC) secondary to trauma normalized on day 2 of the study but decreased below the normal range for age on day 4. Daily CXRs were monitored while on mechanical ventilation. On day 5 of hospitalization bilateral lung infiltrates were noted on CXR and the sputum culture was positive for *Serratia marcescens*. The BDV was -22.95‰ at enrollment and remained stable for the first 36 hours of study participation. On Day 3 of the study the BDV decreased from -22.5 to a minimum value of -24.61‰ over a 16 to 24 hour period.

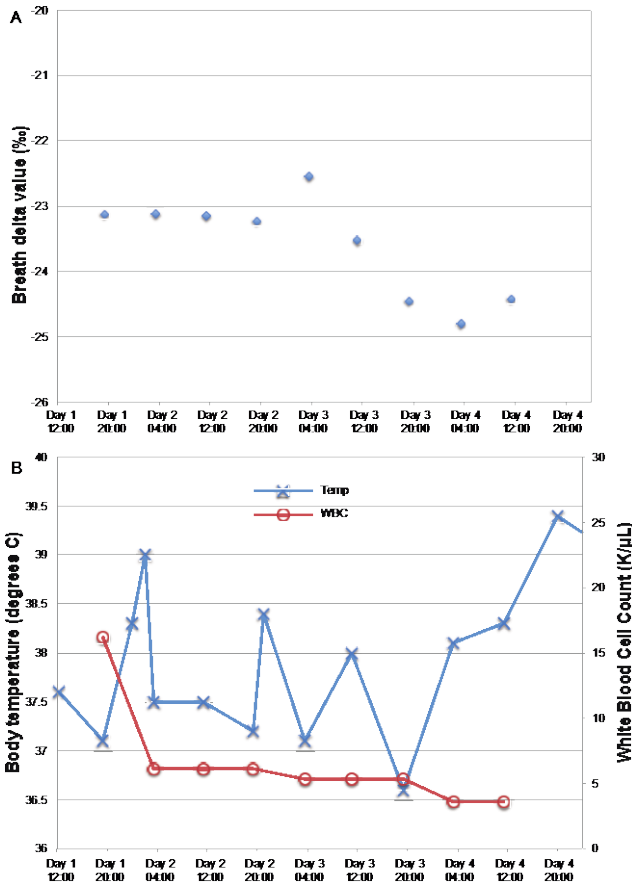

Figure S1: Subject 4 is an example of a trauma patient who develops respiratory infection during hospitalization.

Subject 15 (Figure S2) a 15-year old male was found unresponsive in his bed. Drug screen was notable for methadone ingestion. Magnetic resonance imaging (MRI) demonstrated changes consistent with hypoxic-ischemic/ toxic brain injury secondary to methadone toxicity and hypoventilation for an extended period of time. He had high fever during the first seven days of PICU hospitalization. The highest temperature was 39.4ºC at 0200 on day 1 of the study. The WBC peaked at 26.1 K/µL on day 2 of the study and then trended down gradually normalizing on day 3 of the study with a count of 9.4 K/µL. Initial high temperature and WBC were thought to be secondary to multisystem organ ischemia. This patient was initially started on prophylactic antibiotics. However, antibiotics were discontinued on day 3 when all initial cultures were negative. Sputum cultures grew *Staphylococcus aureus* on hospital days 4 through 7 and he continued spiking fevers. Accordingly, he was started on a seven-day course of oxacillin to treat respiratory bacterial infection. For the first 16 hours of study participation the BDV was approximately -21‰. Beginning on sample period 3 the BDV trended down over a 16 to 24 hour period of time to a minimum value of -23.21‰ on hospital day 5. The BDV remained below -22‰ beginning with sample 4.

Subject 7 (Figure S3) a 17-year-old male with type II diabetes was admitted to the PICU with altered mental status secondary diabetic ketoacidosis and staphylococcal septic shock. His clinical status improved quickly following fluid resuscitation, vasopressor, and antibiotic therapy. The BDV was -23.15‰ at enrollment. Over the course of study participation the BDV trended in a positive direction to a maximum value of -21.37‰ from the last sample. The temperature curve improved after day 2 of the study.

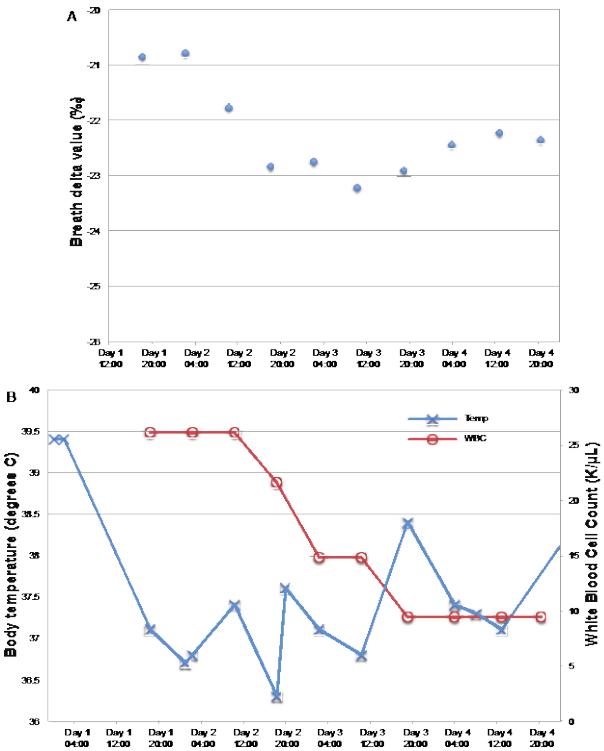

Figure S2: Subject 15 is an example of an unresponsive patient who develops a respiratory infection during hospitalization.

Subject 1 (Figure S4) a 2-year-old male with history of partially resected hepatoblastoma was admitted to the PICU for respiratory distress syndrome secondary to fungal sepsis. He was placed on extracorporeal

life support because of refractory septic shock and eventually died before completing the study. On his first day of participation the BDV was -25.15‰. The BDV rapidly increased over the next 24 hours to a final value of -16.87‰.

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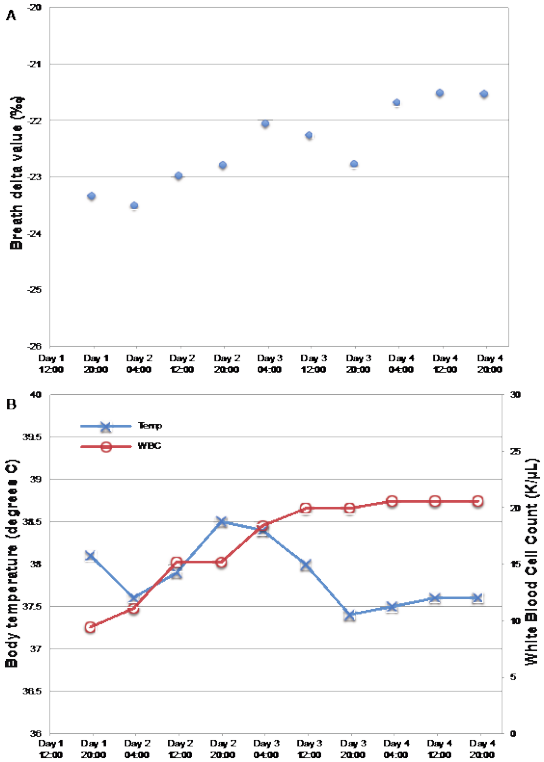

Figure S3: Subject 7 is an example of a septic patient successfully treated with fluids, vasopressor, and antibiotic therapy

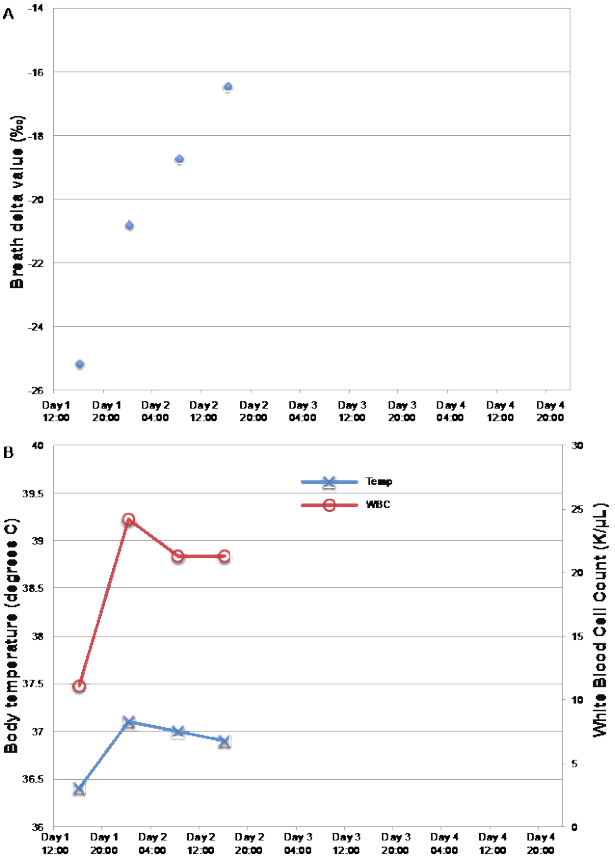

Figure S4: Subject 1 is an example of sepsis progressing to septic shock, multisystem organ failure, and death.

Supplementary table 1: Primary diagnosis and relevant demographic and clinical parameters for individual subjects

Subject (M/F)	Age (m/y)	Weight (kg)	Race	Diagnosis at enrollment	Nutrition	WBC count (K/μL)	Abnormal temperature (Y/N)	SIRS (Y/N)	Inflamation category	BDV (‰)
1 (M)	2.9 y	15.1	White	Hepatoblastoma, active funcal sepsis	TPN	19.8	N	Y	Active sepsis	-25.17
2 (F)	1.1 y	12.4	White	Methylmalonic acidemia; post-op day 4; hepatic transplant	TPN + enteral tube foods	7.4	N	N	No-ITS	-17.25
3 (M)	4.7 y	15.1	White	Spinal muscular atrophy; post-op day 8; tracheostomy placement and bilateral orchiectomy	Enteral tube foods	N/T	N	N	No-ITS	-19.56
4 (M)	14.6 y	68.5	White	Polytrauma day 1	NPO, IVFs	16.2	N	Y	Trauma/ post-op	-23.13
5 (M)	1.1 y	8	DNR	Adominal trauma day 1	NPO, IVFs	8	Y	Y	Trauma/ post-op	-23.36
6 (M)	7.7 y	17	White	Chronic Granulomatous disease; bone marrow transplant; ARDS	TPN + enteral tube foods	4.5	N	N	No-ITS	-19.52
7 (M)	17.5 y	116	DNR	Diabetic ketoacidosis; active sepsis	IVFs	9.4	Y	Y	Active sepsis	-23.34
8 (F)	6.1 y	23.3	Black	Guillain-Barre syndrome; respiratory failure	Enteral tube foods	10.5	N	N	No-ITS	-21.06
9 (F)	1 m	3.4	White	Congenital Surfactant deficiency; respiratory failure	IVFs + enteral tube foods	N/T	N	N	No-ITS	-22.30
10 (F)	3 m	6.7	White	Neuroblastoma, respitratory failure	TPN	7.5	Y	Y	No-ITS	-18.36
11 (M)	11.1 y	65	White	Trauma day 5	IVFs	7.7	N	N	Trauma/ post-op	-22.85
12 (F)	9 m	4.3	White	Post-op day 1; cauterization of subglottic cysts and dilation of subglottic stenosis	IVFs	12.7	N	N	Trauma/ post-op	-24.39
13 (F)	5 m	4.1	White	Post-op day 2; patent ductus arteriosus lication; respiratory failure	IVFs + enteral tube foods	7.6	N	N	Trauma/ post-op	-21.56
14 (M)	16.7 y	108.8	American Indian	Wegener's granulomatosis; ARDS; active sepsis	IVFs	32.2	N	Y	Active sepsis	-20.54
15 (M)	12.8 y	64	White	Toxic encephalopathy, shock	IVFs	26.1	Y	Y	Shock	-20.85
16 (F)	6.2 y	22.9	DNR	Post-op day 22; Gastrostomy tube, Nissen and septic shock	TPN + enteral tube foods	18.2	Y	Y	Shock	-16.99
17 (M)	16.7 y	35.6	White	Neurodegenerative disorder; septic shock	IVFs	12.7	N	Y	Shock	-19.42

WBC = white blood cell; SIRS = systemic inflammatory response syndrome; BDV = breath delta value; ARDS = acute respiratory distress syndrome; DNR = did not report; TPN = total parenteral nutrition; NPO = fasted; IVFs = intravenous fluids; N/T = not tested; No-ITS = No-infection, trauma or surgery

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