Table 1. Adrenal gland (mal-)adaptation and its systemic impact during sepsis, obesity and regeneration. Adrenal gland function and structure is influenced by obesity and sepsis. Advances and challenges in regeneration or restoration of adrenal gland function.

SEPSIS	OBESITY	REGENERATION
Adrenal Gland (Mal-) Adaptation	**Adrenal Gland (Mal-) Adaptation**	**Advances**
Increased production of CAs and GCs	Adrenal hyperplasia	Increased survival of transplants with decellularized ECM
Increased adrenal gland size and blood flow	Increased expression of steroidogenic enzymes. Enhanced secretion of GCs and aldosterone	Transplantation of mixed cultures of adrenal cells, including capsular progenitors, improves aldosterone secretion
Chronic exposure to cytokines and neutrophil-derived anti-microbial agents (NETs, ROS, Enzymes)	Decreased storage and secretion of epinephrine. Decreased adrenal medullary responsiveness	Reprogramming of own patients stem cells by Sf1 overexpression
Adrenal exhaustion: decreased cholesterol content, expression of key steroidogenic enzymes and GC response to ACTH	HPA-axis dysregulation	Use of devices with semipermeable membranes for immune protection
Systemic Response to Adrenal Hormones	**Systemic Response to Adrenal Hormones**	**Challenges**
Protection against cardiovascular collapse, overt inflammation and mobilization of glucose	Visceral obesity, glucose intolerance, hypertension, dyslipidaemia, cardiovascular diseases	Low aldosterone and too high testosterone levels
Induction of immune paralysis and increase in risk of secondary infections	Elevation in TG, cholesterol, VLDL and LDL	Lack of circadian secretion of GCs
	Differentiation of pre-adipocytes to adipocytes	Too low GCs levels to provide protein during extensive stress
	Alteration of SAS activity	Immune rejection
	GCs-output from Adipocytes (11β-HSD1)	