

## Critical Illness-Related Corticosteroid Insufficiency (CIRCI)

Annane, Djillali; Pastores, Stephen; Arlt, Wiebke; Balk, Robert ; Beishuizen, Albertus; Briegel, Josef; Carcillo, Joseph; Christ-Crain, Mirjam; Cooper, Mark S; Marik, Paul; Umberto Meduri, Gianfranco; Olsen, Keith; Rochweg, Bram; Rodgers, Sophia; Russell, James; Van den Berghe, Greet

DOI:

[10.1007/s00134-017-4914-x](https://doi.org/10.1007/s00134-017-4914-x)

License:

Other (please specify with Rights Statement)

*Document Version*

Peer reviewed version

*Citation for published version (Harvard):*

Annane, D, Pastores, S, Arlt, W, Balk, R, Beishuizen, A, Briegel, J, Carcillo, J, Christ-Crain, M, Cooper, MS, Marik, P, Umberto Meduri, G, Olsen, K, Rochweg, B, Rodgers, S, Russell, J & Van den Berghe, G 2017, 'Critical Illness-Related Corticosteroid Insufficiency (CIRCI): A Narrative Review from a Multispecialty Task Force of the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM)', *Intensive Care Medicine*, vol. 43, no. 12, pp. 1781-1792. <https://doi.org/10.1007/s00134-017-4914-x>

[Link to publication on Research at Birmingham portal](#)

**Publisher Rights Statement:**

The final publication is available at Springer via [http://dx.doi.org/\[insert DOI\]](http://dx.doi.org/[insert DOI])

**General rights**

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

**Take down policy**

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact [UBIRA@lists.bham.ac.uk](mailto:UBIRA@lists.bham.ac.uk) providing details and we will remove access to the work immediately and investigate.

## **Figure 2. Glucocorticoid Synthesis and Signaling**

Glucocorticoids (e.g., cortisol) are synthesized from cholesterol in the mitochondria by two P450-type enzymes, CYP11B1 and CYPB11B2 and may exert genomic and non-genomic effects. Glucocorticoids diffuse through cell membranes and bind with glucocorticoid receptors (GR, classic GR and MR, mineralocorticoid receptor). Glucocorticoid receptors reside in the cytoplasm in a multiprotein complex with chaperone proteins, heat shock proteins and immunophilins. The classic GR (specifically GR- $\alpha$ ) is the major receptor involved in mediating the glucocorticoid responses to stress and inflammation. Upon binding of cortisol, the GR undergoes a conformational change that allows it to dissociate from the chaperone proteins and translocate into the nucleus and the mitochondria where it binds to glucocorticoid response elements (GRE) to activate (transactivation) or repress (cis-repression) pro-inflammatory gene expression of various transcription factors (TFs) such as nuclear factor-kappa B (NF-KB) and activator protein-1 (AP-1).