

## REVIEW

# Doctors, teach your adrenal insufficiency patients well: provide them with a European Emergency Card!

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## Abstract

Adrenal insufficiency is a life-threatening condition requiring chronic glucocorticoid replacement therapy, as well as stress adaptation to prevent adrenal crises. To increase patients' self-sustainability, education on how to tackle an adrenal crisis is crucial. All patients should carry the European Emergency Card.

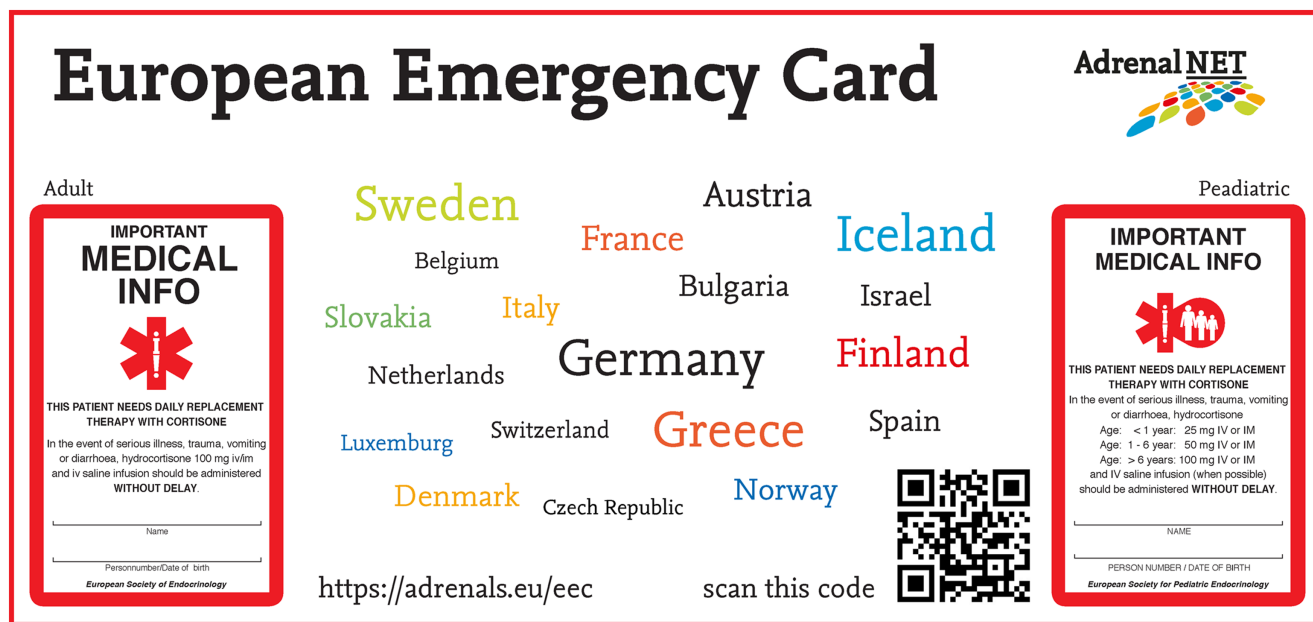
## Key Words

- ▶ adrenal insufficiency
- ▶ patient education
- ▶ medical alert card

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The number of individuals in Europe with primary and secondary adrenal insufficiency (AI) is estimated to be 20–50 per 100,000 (1). AI is characterised by a deficit in synthesis and release of cortisol, with symptoms including tiredness, weakness, loss of energy, weight loss, nausea, vomiting, abdominal pain, and muscle and joint pain. Patients with primary AI typically also crave for salt and are hyperpigmented, due to concurrent deficiency of aldosterone and increased adrenocorticotropic hormone. Once diagnosed, chronic, daily replacement with glucocorticoids is essential. An adequate hormone replacement dose is considered to be a total of 15–25 mg hydrocortisone (or cortisone acetate 20–35 mg per day) in adults in two to three daily doses, and 8 mg/m<sup>2</sup> body surface/day in children divided over three to four doses (2). Patients

with primary AI typically also require fludrocortisone, 0.05–0.2 mg daily. However, in situations of illness or severe stress, the ordinary replacement doses do not suffice. Therefore, patients with AI should be empowered by regular education on the use of sick day rules and emergency equipment. To avoid an adrenal crisis in situations of severe stress and/or illness, sick day rules include doubling or tripling the ordinary daily glucocorticoid dose, distributed evenly over the day (1). In addition, in the event of an adrenal crisis, patients have to be treated without delay with i.v. or i.m. hydrocortisone and, equally important, with i.v. physiological salt solution (3). A patient with adrenal insufficiency needs to be vigilant in case of food poisoning or any gastrointestinal upset since gastroenteritis is the most common cause of adrenal crisis (3).



**Figure 1**  
The European Emergency Card is now available in 18 European countries.

**Box 1**

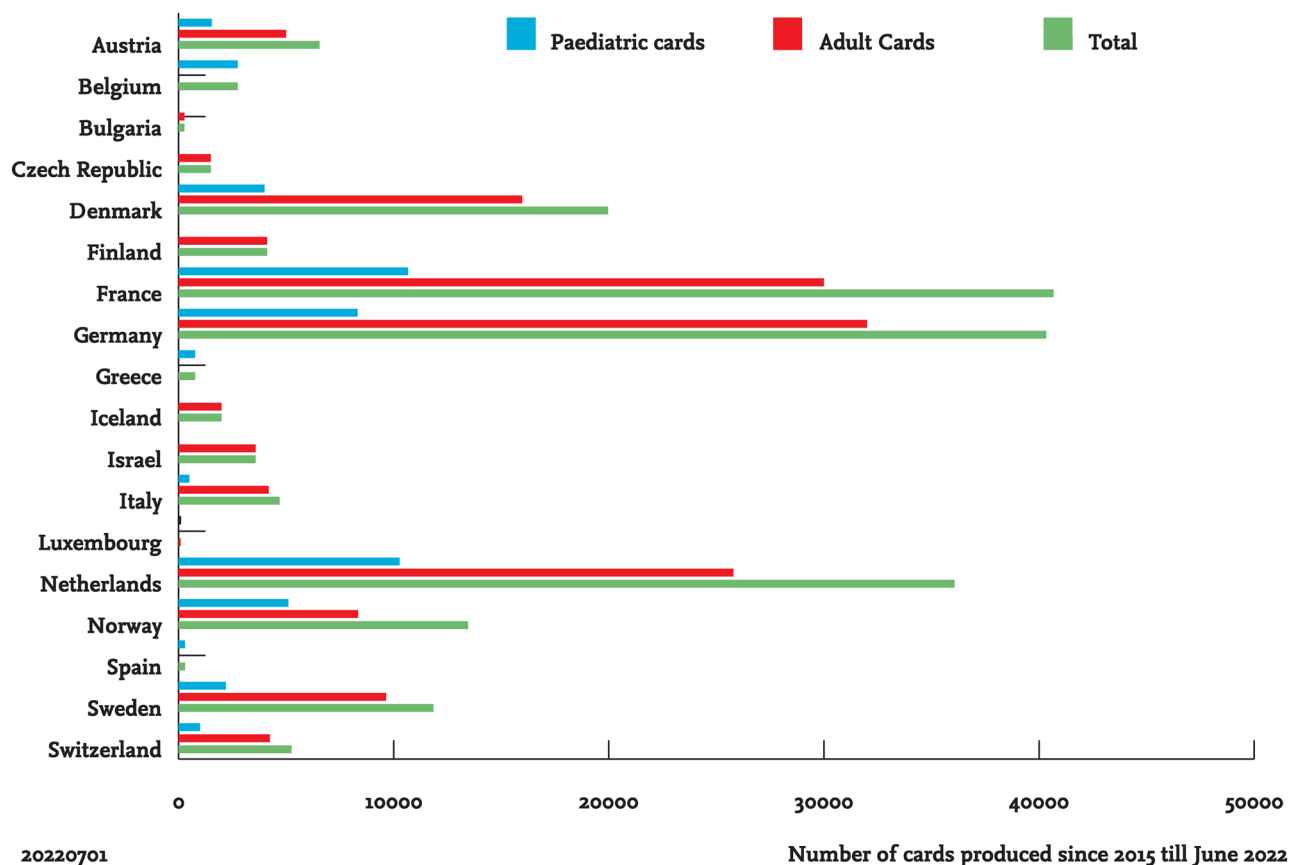
The European Emergency Card was based on an idea by Per Dahlqvist and Olle Kämpe, i.e. a uniform, well-designed, credit card-size plastic emergency card, with short and clear instructions in native language and English, intended to be well-recognised anywhere. Until then all hospitals and all countries had their own elaborate card, often in paper, which was not suited for an adrenal crisis emergency situation. The new card was designed by Johan Dahlqvist and implemented as standard national cards in Sweden in 2011 and in Norway in 2012.

In a 2014 meeting in Bergen of the European Patient Support Groups for Addison’s disease, Eystein Husebye recommended that the organisations promote the card in their individual countries, in order to create a standard emergency card in all of Europe. The Danish/Dutch Addison organisations thereafter made contact with Pia Burman, chair of the European Society of Endocrinology (ESE) Clinical Committee. A uniform emergency card, based on the Swedish version, was developed and made available for all European patients suffering from adrenal insufficiency. The project was endorsed by ESE and ECAS (the European Council of Affiliated Societies), and the card disseminated across many European countries (Fig. 1 and 2). The first publication of the European Emergency Card was in 2015 (6). Inquiries and interest in adopting the card have been made from endocrinologists and patient support groups in several countries outside Europe, and we believe a global uniform emergency card would increase recognisability even further; this is a long-term goal of the project.

The European Emergency Card – one version for adults and one version for children – is credit card-sized and provides instructions in English on one side and in the national language on the other side. These instructions describe how bystanders should act if a patient shows this card (Fig. 3 and 4). The message on the card is clear: treat this patient immediately with i.v. hydrocortisone and saline, independent of the underlying cause. There is, to our knowledge, no formal scientific evidence demonstrating that a uniform emergency card like this reduces adrenal crises with poor outcome; however, current guidelines recommend that all patients with AI are equipped with an emergency card, based on expert opinion and best practice statements (2).

The European Emergency Card is currently supplied by AdrenalNET – <https://adrenals.eu/emergency-card/>

## Historical information on the distribution of the EEC (=European Emergency Cards)



**Figure 2**

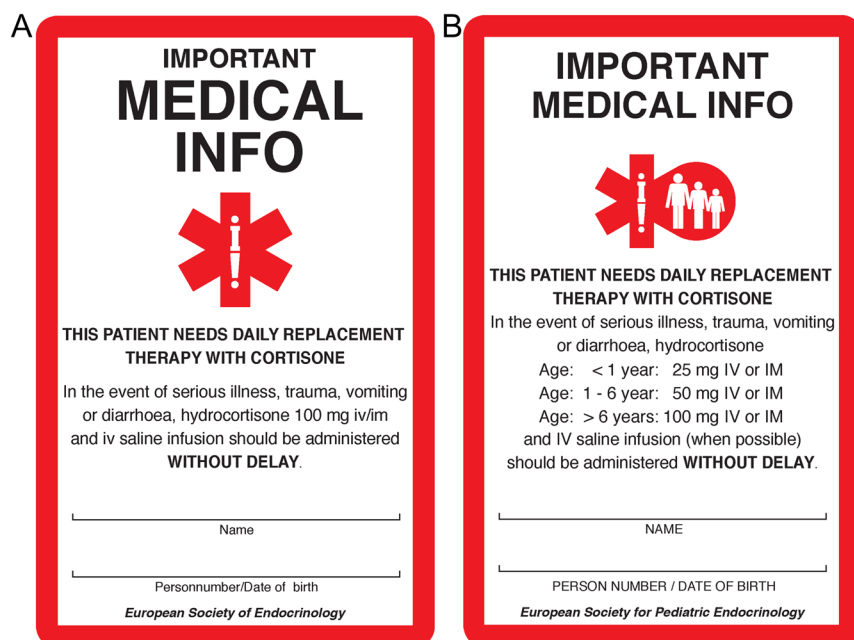
Since 2015, 150,000 adult cards and 50,000 paediatric cards have been distributed in 18 European countries.

For the patient to feel safe and to be able to prevent an adrenal crisis, education is essential. Patients should be provided with equipment for self-injection of hydrocortisone, and a medical alert card/European Emergency Card to inform physicians and other health professionals of the patient's condition and how to manage an acute adrenal crisis. Furthermore, the patients' families, perhaps also neighbours, friends and colleagues at work, should be familiar with the disease and how to act in the event of an emergency. Besides the patient's endocrinologist, endocrine nurses are invaluable resources for providing patient education.

In recent years, several important steps have been taken to improve self-management. In 2016, the Dutch AdrenalNET (network for adrenal gland patients, carers and healthcare practitioners) published stress instructions to prevent adrenal crises, which were later adopted by the European Society of Endocrinology and the European Reference Network on rare endocrine

conditions (Endo-ERN) (4). In addition, emergency injection 'kits' have been made available for patients (5) and a uniform European Emergency Card was developed (6) (Box 1, Fig. 3). AdrenalNET also developed e-learning courses for nurses. Currently, these courses are available in Dutch, English and Danish at <https://screenlearning.net/en/>. Translation to other languages is ongoing. Other countries have developed courses for physicians (Germany) and education groups for patients and relatives (The Netherlands, Germany, Norway and Sweden) (7).

Nonetheless, in a prospective study of more than 400 adult patients with AI, a prevalence of 8.3 adrenal crises per 100 patient-years was observed, with a mortality rate of 0.5 per 100 patient-years (8). A national study showed that adrenal crises were a major cause of premature death in patients with secondary hypocortisolism due to pituitary disease (9). A recent study observed one death due to an adrenal crisis per 300 patient-years in



**Figure 3** European Emergency Card (credit card size); (A) adult edition, (B) paediatric edition.

children and young adults with AI (10). Thus, there are still unmet needs in education and self-management. This is emphasised by results from a recent survey in 24 European countries (11), revealing that only 48% of the responders ( $n=183$ ) had access to guidelines on management of an adrenal crisis in their own language. Injectable hydrocortisone and emergency cards are still not available in all European countries (Box 2, Fig. 5). So, there is still work to be done. In our view, education has to start as soon as the patient is diagnosed. Patients have to be informed on how to adapt glucocorticoid doses in stressful situations.

Moreover, it is important to convince the patient that an adrenal crisis is potentially life-threatening, and

that the patient should not hesitate to use emergency injections or contact a physician. If necessary, this information has to be repeated over and over again. In addition, it also appears to be important to inform some doctors that a well-educated and well instructed patient will not misuse the emergency injection. Thus, continued efforts are needed to provide easily accessible and correct information to enhance awareness of AI and crisis management, for example, in social media and periodic courses to healthcare providers. We recommend that all patients with AI always carry the European Emergency Card. A well-known medical alert card increases the chances of the patient's medical



**Figure 4** Emergency Keycard (54 × 28.5 mm); (A) adult edition, (B) paediatric edition.



**Figure 5** Injectible hydrocortisone.

## Box 2

Injectable hydrocortisone is available in only 85% of responding European countries (alternative names Hydrocortisone, Solucortef, Flebocortid, Actocortina, Corhydron). A few countries have methylprednisolone instead (e.g. Bulgaria and Spain).

INJECTABLE HYDROCORTISONE IS NOT AVAILABLE IN 15% OF RESPONDING EUROPEAN COUNTRIES (11).

condition being recognised. Hopefully, these measures should help the patient to get adequate treatment fast and avoid preventable deaths from adrenal crises.

### Declaration of interest

None of the authors have any conflict of interest that could be perceived as prejudicing the impartiality of this work.

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## References

- Nowotny H, Ahmed SF, Bensing S, Beun JG, Brösamle M, Chifu I, van der Grinten HC, Clemente M, Falhammar H, Haner S, *et al.* Therapy options for adrenal insufficiency and recommendations for the management of adrenal crisis. *Endocrine* 2021 **71** 586–594. (<https://doi.org/10.1007/s12020-021-02649-6>)
- Bornstein SR, Allolio B, Arlt W, Barthel A, Don-Wauchope A, Hammer GD, Husebye ES, Merke DP, Murad MH, Strataski CA, *et al.* Diagnosis and treatment of primary adrenal insufficiency: an Endocrine Society clinical practice guideline. *Journal of Clinical Endocrinology and Metabolism* 2016 **101** 364–389. (<https://doi.org/10.1210/jc.2015-1710>)
- Husebye ES, Pearce SH, Krone NP & Kampe O. Adrenal insufficiency. *Lancet* 2021 **397** 613–629. ([https://doi.org/10.1016/S0140-6736\(21\)00136-7](https://doi.org/10.1016/S0140-6736(21)00136-7))
- Endo-ERN. Guidelines on taking hydrocortisone to prevent an Addison's crisis. Amsterdam, Netherlands: Endo-ERN, 2019. (available at: <https://endo-ern.eu/wp-content/uploads/2019/03/20190312-Stressinstructie-addisoncrisis-hydrocortison-ENG-Endo-ERN-approved.pdf>)
- BijnierNET/AdrenalNET. Short instruction: emergency injection in an adrenal crisis. (available at: <https://adrenals.eu/stress-instructions/emergency-injection/>)
- Quinkler M, Dahlqvist P, Husebye ES & Kampe O. A European Emergency Card for adrenal insufficiency can save lives. *European Journal of Internal Medicine* 2015 **26** 75–76. (<https://doi.org/10.1016/j.ejim.2014.11.006>)
- Repping-Wuys HJ, Stikkelbroeck NM, Noordzij A, Kerstens M & Hermus AR. A glucocorticoid education group meeting: an effective strategy for improving self-management to prevent adrenal crisis. *European Journal of Endocrinology* 2013 **169** 17–22. (<https://doi.org/10.1530/EJE-12-1094>)
- Hahner S, Ross RJ, Arlt W, Bancos I, Burger-Stritt S, Torpy DJ, Husebye ES & Quinkler M. Adrenal insufficiency. *Nature Reviews. Disease Primers* 2021 **7** 19. (<https://doi.org/10.1038/s41572-021-00252-7>)
- Burman P, Mattsson AF, Johannsson G, Hoybye C, Holmer H, Dahlqvist P, Berinder K, Engström BE, Ekman B, Erfurth EM, *et al.* Deaths among adult patients with hypopituitarism: hypocortisolism during acute stress, and de novo malignant brain tumors contribute to an increased mortality. *Journal of Clinical Endocrinology and Metabolism* 2013 **98** 1466–1475. (<https://doi.org/10.1210/jc.2012-4059>)
- Worth C, Vyas A, Banerjee I, Lin W, Jones J, Stokes H, Komlosy N, Ball S & Clayton P. Acute illness and death in children with adrenal insufficiency. *Frontiers in Endocrinology (Lausanne)* 2021 **12** 757566. (<https://doi.org/10.3389/fendo.2021.757566>)
- Van't Westeinde A, Noordzij A, Beun JG, Kristensen J, Brösamle M, Dal Maso G, Lazzarini A, Reisch N & Lajic S. *Access to Medical Treatment for Adrenal Insufficiency in Europe*. Presented at the European Congress of Endocrinology 2022, Milan, Italy. 2022.

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