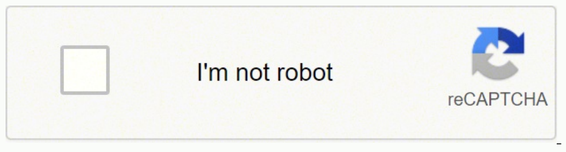

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Journal of Evaluation in Clinical Practice 2010 16 492–498.HarschIASchullerAHahnEGHensenJ. Neurology. Furthermore, patient education must move forward to a structured and quality-controlled approach offered to every single patient. Journal of Clinical Endocrinology and Metabolism 2014 99 1665–1674.OksnesMBjornsdottirSIsakssonMMethliePCarlsenSNilsenRMBromanJETriebnerKKampeOHultingAL. Clinical Endocrinology 2008 69 697–704. Journal of Clinical Endocrinology and Metabolism 2013 98 161–171.ChortisVTaylorAESchneiderPTomlinsonJWHughesBAO'NeilDMLibeRAllolioBBertagnaXBertheratJ. (doi:10.1210/edrv-5-1-25).)| falseSearch Google ScholarExport Citation54↑Besedovsky H, del Rey A, Sorkin E, Dinarello CA. Diagnosis and treatment of Addison's disease. Clinical Endocrinology 1994 40 769–775. Even more recent is the discovery that mortality is also increased in patients with chronic adrenal insufficiency receiving standard replacement therapy (20, 21). Potentiation by hydrocortisone of responses to catecholamines in vascular smooth muscle. Eds DegrootLCahiillGFMartiniL. Again infections, particularly gastroenteritis, are the most frequent causes. Anesthesiology199277426–431. Time lines in the management of adrenal crisis – targets, limits and reality. PMID: 25901057 pubmed.ncbi.nlm.nih.gov/25901057/.Mikati MA, Tchapyjnikov D. Annals of Surgery1994219416–425. It consists of parenteral hydrocortisone (initially 100 mg hydrocortisone as a bolus intravenously) and correction of hypovolaemia with isotonic saline (1000 ml isotonic saline within the first hour) (31, 36, 48, 49) (Table 2). (doi:10.1046/j.1365-2796.1999.00538.x).FlemmingTGKristensenLO. (doi:10.1111/j.1365-2265.1994.tb02511.x).AllolioBEhsesWSteffenHMMullerR. (doi:10.1210/jc.2007-1134).GurnellEMHuntPJCurranSEConwayCLPullenayegumEMHuppertFACompstonJEHerbertJChatterjeeVK. Clinical Endocrinology201175585–591. Thus, I occasionally have given my patients a written text to be signed by any such future emergency physician. Here the dose needs to be adjusted accordingly.As infections are the most frequent cause of adrenal crisis (24, 26, 29, 69), it has been suggested that the patient doubles the hydrocortisone dose if the body temperature increases above 38 °C and triples the dose above 39 °C. Psychoneuroendocrinology200631614–622. (doi:10.1056/NEJM200011093431903).)| falseSearch Google ScholarExport Citation19↑Zuckerman-Levin N, Tiosano D, Eisenhofer G, Bornstein S, Hochberg Z. Cortisone replacement therapy in endocrine disorders – quality of self-care. Journal of Experimental Medicine19881671708–1712. Reduced lymphocyte beta 2-adrenoceptor density and impaired diastolic left ventricular function in patients with glucocorticoid deficiency. High incidence of adrenal crisis in educated patients with chronic adrenal insufficiency – a prospective study. Notably, there is an uneven distribution in the occurrence of crises, as some patients do not experience a single adrenal crisis for decades, while others have recurrent adrenal crises (26, 29). This approach has been apparently successful in the case of adrenaline autoinjectors for anaphylaxis.In conclusion, reduction of morbidity and elimination of mortality from adrenal crisis should become a top priority for adrenal endocrinologists aiming at a 50% reduction in crisis-related deaths within the following 10 years. Journal of Clinical Investigation1986771377–1381. Clinical Endocrinology 2008 68 130–135. As a rule of thumb, I am rather liberal concerning minor event-related dose increases and more focused on avoiding chronic over-replacement during standard treatment (e.g. 30 mg hydrocortisone or more). (doi:10.1046/j.1365-2265.1997.2101025.x).DeVileCJStanhopeR. (doi:10.1073/pnas.121455098).WebsterJCOakleyRHJewellCMCidlowskiJA. I reasoned that asking for the signature would greatly facilitate hydrocortisone administration.As a consequence of these frequently encountered problems, the essential principle of crisis prevention can be stated as follows:The well-informed patient (or his/her relative) guides the poorly informed health-care professional!If so, it becomes mandatory that the patient should indeed be well informed and able to deliver such guidance. Prevention of adrenal crisis requires appropriate hydrocortisone dose adjustments to stressful medical procedures (e.g. major surgery) and other stressful events (e.g. infection). (doi:10.1074/jbc.M110.212365).Van BogaertTVandevyverSDejagerLVan HauwermeirenFPinheiroIPettaIEngblomDKleymanASchutzGTuckermannJ. Volume depletion may further be worsened by vomiting and diarrhoea.It is well known that fever and infection lead to an increase in circulating cortisol levels in healthy subjects and, therefore, it is generally recommended that such an increase in cortisol levels should be mimicked by adjustment of the hydrocortisone dose in patients with adrenal insufficiency (31, 49). (doi:10.1111/j.1365-2265.2007.03011.x).)| falseSearch Google ScholarExport Citation11↑Debono M, Ross RJ, Newell-Price J. Basic examination of urine. A young man with a dizzy spell and acute abdominal pain. Endocrine Journal200350745–752. A reevaluation of the role of glucocorticoids. (doi:10.1530/EJE-12-0161).ReischNWilligeMKohnDSchwarzHPAllolioBReinckeMQuinklerMHahnerSBeuschleinF. (doi:10.1097/00000542-199209000-00004).NaitoYTamaiSShinguKShindoKMatsuiTSegawaHNakaiYMoriK. Journal of Clinical Endocrinology and Metabolism 2007 92 3912–3922. Reversible cardiomyopathy in paediatric Addison's disease – a cautionary tale. Youmans and Winn Neurological Surgery. (doi:10.1210/jc.2009-1368).)| falseSearch Google ScholarExport Citation8↑Oksnes M, Bensing S, Hulting AL, Kampe O, Hackemann A, Meyer G, Badenhoop K, Betterle C, Parolo A, Giordano R et al.. (doi:10.1089/end.2005.19.1140).MatsumotoEDMargulisVTuncLTaylorGDDucheneDJohnsonDBPearleMSCadedduJA. (doi:10.1056/NEJM199909303411401).)| falseSearch Google ScholarExport Citation16↑Hunt PJ, Gurnell EM, Huppert FA, Richards C, Prevost AT, Wass JA, Herbert J, Chatterjee VK. Proinflammatory cytokines regulate human glucocorticoid receptor gene expression and lead to the accumulation of the dominant negative beta isoform: a mechanism for the generation of glucocorticoid resistance. However, these were all retrospective studies susceptible to various biases. (doi:10.1016/j.amjsurg.2011.09.036).ZaghiyanKNMurrellZMelmedGYFleshnerPR. Clinical Endocrinology & Metabolism 2009 23 167–179. 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The short-lived glucocorticoid excess for the majority of patients associated with this strategy apparently carries no significant risks (50, 51, 65).Table 3Hydrocortisone adjustments for medical procedures (modified from (49)).ProcedurePreoperative needsPostoperative needsMajor surgery Start hydrocortisone infusion (100 mg over 12 h) just before anaesthesiaContinue hydrocortisone infusion (100 mg over 12h) until able to eat and drink. Roberts and Hedges' Clinical Procedures in Emergency Medicine and Acute Care. Bornstein SR, Alloliu B, Arlt W, et al. Similarly, among 1286 Swedish patients with hypopituitarism, adrenal crisis in response to acute stress and intercurrent illness was identified as an important cause of excess mortality (24).Studies on the epidemiology of adrenal crisis give a consistent picture with an incidence between five and ten adrenal crises per 100 patient years in patients on standard replacement therapy. (doi:10.1136/pgmj.64.758.953).)| falseSearch Google ScholarExport Citation40↑Omori K, Nomura K, Shimizu S, Omori N, Takano K. European Journal of Endocrinology 2013 169 17–22.Repping-WutsHJStikkelbroeckNMNoordzijAKerstensMHermusAR. Endocrine Reviews20002155–89.)| falseSearch Google ScholarExport Citation48↑Bancos I, Hahner S, Tomlinson J, Arlt W. European Journal of Endocrinology 2012 167 35–42. Circulation Research196924383–395. Two Swedish registry analyses in patients with Addison's disease reported ‘endocrine causes’ as responsible for the death in 12.6 and 8.3%, respectively, also suggesting a role of adrenal crisis (20, 21). European Journal of Endocrinology2009160719–729. (doi:10.1530/EJE-14-0023).TiemensmaJAndelaCDKapteinAARomijnJAvan der MastRCBiermaszNRPereiraAM. (doi:10.1210/jc.2006-0076).)| falseSearch Google ScholarExport Citation21↑Bensing S, Brandt L, Tabaroj F, Sjoberg O, Nilsson B, Ekbom A, Blomqvist P, Kampe O. This treatment is virtually uniformly successful leading to clinical recovery within 24 h. New England Journal of Medicine19993411013–1020. (doi:10.1210/jc.2007-1134).)| falseSearch Google ScholarExport Citation18↑Merke DP, Chrousos GP, Eisenhofer G, Weise M, Keil MF, Rogol AD, Van Wyk JJ, Bornstein SR. Philadelphia, PA: Elsevier; 2020:chap 72.Page 6Dean AJ, Lee DC. This is a substantial percentage. In particular, it may also be important to include the reversal of symptoms after administration of glucocorticoids. Clinical review: outcome of bilateral adrenalectomy in Cushing's syndrome: a systematic review. Hydrocortisone self-administration is a critical part of patient education and would be greatly facilitated by the availability of a hydrocortisone pen. Clinical Endocrinology200868130–135. Science 1986 233 652–654. Figure 1Glucocorticoid and cytokine interaction during major infection in patients with intact adrenals (A) and patients with adrenal insufficiency on standard replacement therapy failing to adjust their hydrocortisone doses (B).Citation: European Journal of Endocrinology 172, 3; 10.1530/EJE-14-0824Download FigureDownload figure as PowerPoint slideFigure 1Glucocorticoid and cytokine interaction during major infection in patients with intact adrenals (A) and patients with adrenal insufficiency on standard replacement therapy failing to adjust their hydrocortisone doses (B).Citation: European Journal of Endocrinology 172, 3; 10.1530/EJE-14-0824Download FigureDownload figure as PowerPoint slideFor other causes of adrenal crisis (e.g. emotional stress and surgery), the underlying mechanisms may be similar, but have been much less studied. In Williams' Textbook of Endocrinology, 7th edn, pp 816–890. Drug interactions with mitotane by induction of CYP3A4 metabolism in the clinical management of adrenocortical carcinoma. (doi:10.1530/EJE-09-0884).)| falseSearch Google ScholarExport Citation27↑Reisch N, Willige M, Kohn D, Schwarz HP, Allolio B, Reincke M, Quinkler M, Hahner S, Beuschlein F. 6th ed. (doi:10.1530/EJE-09-0559).)| falseSearch Google ScholarExport Citation30↑Hahner S, Spinnler C, Fassnacht M, Burger-Stritt S, Lang K, Milovanovic D, Beuschlein F, Willenberg HS, Quinkler M, Allolio B. Approach to fever or suspected infection in the normal host. (doi:10.1084/jem.167.5.1708).)| falseSearch Google ScholarExport Citation59↑Koniaris LG, Wand G, Wright TM. Implementing these key measures will undoubtedly help to achieve a substantial reduction in mortality from adrenal crisis.The author declares that there is no conflict of interest that could be perceived as prejudicing the impartiality of the review.This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.The author is grateful to Stefanie Hahner and Martin Fassnacht, Würzburg and Wiebke Arlt, Birmingham, for critical review of the manuscript. (doi:10.7861/clinmedicine.13-5-520).)| falseSearch Google ScholarExport Citation38↑Mulder AH, Nauta S, Pieters GF, Hermus AR. (doi:10.1097/00000542-199209000-00004).)| falseSearch Google ScholarExport Citation64↑Miller GE, Cohen S, Ritchey AK. (doi:10.1530/EJE-08-0874).DebonoMRossRJNewell-PriceJ. The recommended dose increase is not intended to mimic the median cortisol increase in healthy subjects during such procedures. Health Psychology200221531–541. European Journal of Endocrinology2013169147–154. A substantial subset of patients is diagnosed with psychiatric illness, in particular with anorexia nervosa (36, 39). Patient education is a key for such dose adjustments but current education concepts are not sufficiently effective. Vorvick, MD, Clinical Associate Professor, Department of Family Medicine, UW Medicine, School of Medicine, University of Washington, Seattle, WA. Philadelphia, PA: Elsevier; 2020:chap 138.Riley RS, McPherson RA. However, it has been shown that, despite repeated verbal education, a high percentage of patients (46%) were not sufficiently skilled in coping with physical stress (72). An orthopaedic colleague with long-standing adrenal insufficiency also confirmed that his adrenal crises occasionally evolved within an hour making it quite difficult for him to take the necessary preventive actions. Disorders of the adrenal cortex. However, we found neither a textbook nor a paper providing such a definition, leaving us with the task to generate our own definition. For postdoctoral studies, he worked at Bartholomew's Hospital, London, and at the NIH, Bethesda. Journal of Pediatric Endocrinology & Metabolism2003161191–1195. Long-term DHEA replacement in primary adrenal insufficiency: a randomized, controlled trial. (doi:10.1046/j.1365-2265.1997.2101025.x).)| falseSearch Google ScholarExport Citation43↑Hahner S, Hemmelmann N, Quinkler M, Beuschlein F, Spinnler C, Allolio B. Journal of Clinical Endocrinology and Metabolism201297473–481.)| falseSearch Google ScholarExport Citation14↑Oksnes M, Bjornsdottir S, Isaksson M, Methlie P, Carlsen S, Nilsen RM, Broman JE, Triebner K, Kampe O, Hulting AL et al.. His young daughters had recently suffered from gastroenteritis, which had been attributed to a Noro virus infection detected in their day care. Modified-release hydrocortisone for circadian therapy: a proof-of-principle study in dexamethasone-suppressed normal volunteers. High-dose perioperative corticosteroids in steroid-treated patients undergoing major colorectal surgery: necessary or overkill?American Journal of Surgery2012204481–486. (doi:10.1210/jc.2007-0685).HahnerSLoefflerMFassnachtMWeismannDKoschkerACQuinklerMDeckerOArltWAllolioB. Journal of Internal Medicine 2014 275 104–115. (doi:10.1210/jc.2009-1368).ErichsenMMLovasKSkinningsrudBWolffABUndlienDESvartbergJFougnerKJBergTJBollerslevJMellaB. In addition, every patient should have an emergency set (or two) consisting of 100 mg hydrocortisone for parenteral administration. In a survey of 37 patients who had experienced an adrenal crisis in the context of a prospective study (43), the median time from first symptoms to contacting health professionals was 135 min (range 5 min to 7 days) (unpublished data).When we planned a prospective study on the incidence of adrenal crisis in patients with known adrenal insufficiency, we realised the need to define what actually constitutes an adrenal crisis. Cardiovascular evaluation may find an abnormal electrocardiogram or even evidence of cardiomyopathy (32, 33, 34, 35). (doi:10.1037/0278-6133.21.6.531).)| falseSearch Google ScholarExport Citation65↑Zaghiyan KN, Murrell Z, Melmed GY, Fleshner PR. Consensus statement on the diagnosis, treatment and follow-up of patients with primary adrenal insufficiency. Fever. In turn, high glucocorticoid levels diminish cytokine release and action preventing their potential detrimental effects (56, 57). Thyroid and adrenal disorders. Journal of Evaluation in Clinical Practice201016492–498.)| falseSearch Google ScholarExport Citation74↑Grossman A, Johannsson G, Quinkler M, Zelissen P. New England Journal of Medicine 1999 341 1013–1020. (doi:10.1530/EJE-09-0559).WhiteKArltW. Hat die Nebenniere tatsächlich eine Verteidigungsfunktion? Double oral dose for 24–48 h after delivery, then taper to normal doseMinor surgery and major dental surgery100 mg hydrocortisone before anaesthesia given as a bolus intramuscularly or subcutaneously or as hydrocortisone infusion for the duration of surgeryDouble oral dose for 24 h, then return to normal doseInvasive bowel procedures requiring laxativesHospital admission overnight with 100 mg hydrocortisone intramuscularly or subcutaneously and fluid (isotonic saline), repeat dose before start of procedureDouble oral dose for 24 h, then return to normal doseDental procedureExtra morning dose 1 h before surgeryDouble oral dose for 24 h, then return to normal doseMinor procedureUsually not requiredExtra dose (e.g. 20 mg hydrocortisone) if symptoms persistIn emotional or mental stress, I recommend minor dose increases (e.g. 10 mg as an additional dose). Quality of life in European patients with Addison's disease: validity of the disease-specific questionnaire AddiQoL. Thus, the development of improved education concepts remains a major task in future crisis prevention.Every patient must be provided with an emergency card (31, 48, 49) and I consider the newly designed European bilingual card a major advantage (74). It aims at contributing to more effectively combat morbidity and mortality from adrenal crisis.Being the first to diagnose and treat adrenal insufficiency in a patient, after months of suffering with a multitude of futile investigations, is a most rewarding experience for any endocrinologist. Siedel's Guide to Physical Examination. 2015;84(16):1705-1713. To this end, it will be helpful to better understand the physiopathology of adrenal crisis to define optimum dose adjustments. (doi:10.1073/pnas.121455098).)| falseSearch Google ScholarExport Citation61↑Van Bogaert T, Vandevyver S, Dejager L, Van Hauwermeiren F, Pinheiro I, Petta I, Engblom D, Kleyman A, Schutz G, Tuckermann J et al.. Clinical Endocrinology200869697–704. (doi:10.1530/EJE-12-1057).HahnerSBurger-StrittSAllolioB. Das Hormon 1951 3 1–24.53↑Munck A, Guyre PM, Holbrook NJ. Addisonian crisis in a young man with atypical anorexia nervosa. He is a founding member of the European Network for the Study of Adrenal Tumours (ENSAT).This narrative review on adrenal crisis is based on personal experience, own research, and comprehensive evaluation of the literature. Studies in patients on chronic replacement therapy for adrenal insufficiency have revealed an incidence of 5–10 adrenal crises/100 patient years and suggested a mortality rate from adrenal crisis of 0.5/100 patient years. Journal of Clinical Endocrinology and Metabolism 2013 98 1466–1475. However, fever may also present as fever of unknown origin (38). Philadelphia, PA: Elsevier; 2018:chap 120.Page 2Ball JW, Dains JE, Flynn JA, Solomon BS, Stewart RW. In Endocrinology, pp 1193–1201. This course of action is a well-accepted standard of care, but the underlying mechanisms necessitating it are less clear. However, many stressors can be anticipated (e.g. elective surgery) and allow to adjust the glucocorticoid dose to the expected need, thereby preventing the occurrence of clinical deterioration and adrenal crisis. Instead, chronic over-replacement may rather increase the susceptibility to infection and thereby increase the risk of adrenal crisis (69).For obvious reasons, patient education is considered essential for crisis prevention, although its efficacy has not been well studied. Evidence-based guideline: management of an unprovoked first seizure in adults: report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. The largest analysis thus far was conducted via a postal survey by the UK Addison's disease Self Help Group in 841 patients from the UK, Canada, Australia, and New Zealand indicating an incidence of eight crises per 100 patient years (29). (doi:10.1046/j.1365-2265.2002.01466.x).)| falseSearch Google ScholarExport Citation5↑Thomsen AF, Kvist TK, Andersen PK, Kessing LV. Journal of Biological Chemistry 2011 286 26555–26567. Table 3 gives an overview on treatment adjustments for medical procedures based on recommendations of the UK Addison's disease Self Help Group (49). Journal of Internal Medicine2014275104–115. Improvement in mood and fatigue after dehydroepiandrosterone replacement in Addison's disease in a randomized, double blind trial. After transient stabilisation, cardiopulmonary resuscitation eventually remained unsuccessful and the patient died from adrenal crisis. Are the catabolic effects of tumor necrosis factor mediated by glucocorticoids? Journal of Pharmacological and Experimental Therapeutics 1966 154 224–238.BesseJCBassAD. (doi:10.1530/EJE-13-0450).GrossmanAJohannssonGQuinklerMZelissenP. Philadelphia, PA: Elsevier; 2020:chap 15.Thiessen MEW. In: Walls RM, Hockberger RS, Gausche-Hill M, eds. This dose is maintained as long as the fever persists and rapidly (within 1–2 days) reduced to the standard replacement dose after recovery. Lancet Diabetes & Endocrinology 2014.49↑Husebye ES, Allolio B, Arlt W, Badenhoop K, Bensing S, Betterle C, Falorni A, Gan EH, Hulting AL, Kasperlik-Zaluska A et al.. Diagnosis and treatment of primary adrenal Insufficiency: an Endocrine Society clinical practice guideline. PNAS2001986865–6870. Adrenal crisis causing critical illness related reversible myocardial dysfunction. Subjective health status in Norwegian patients with Addison's disease. As industry is reluctant to develop such a device, public funding is needed. Philadelphia, PA: Elsevier; 2018:chap 14.Mendez MF, Padilla CR. Journal of Clinical Endocrinology and Metabolism2014(under review).)| falseSearch Google ScholarExport Citation32↑Sherlock M, Gittoes NJ, Arlt W. They report fatigue and a profound lack of energy. Adaptation during surgical stress. This also affects patients with secondary adrenal insufficiency (22, 23, 24). Postgraduate Medical Journal 1988 64 953–955. (doi:10.1111/j.1365-2265.2011.04214.x).)| falseSearch Google ScholarExport Citation67↑Chortis V, Taylor AE, Schneider P, Tomlinson JW, Hughes BA, O'Neil DM, Libe R, Allolio B, Bertagna X, Bertherat J et al.. Until then, valuable time may have been lost to adjust the hydrocortisone dose to the increased need. For example, in case of a written or oral examination or appearance in court, the additional dose should be taken 1 h before the event. Finally, such an event is likely to have a life-long detrimental impact on the well-being of affected families.This death in one of our patients, who had received repeated education during his outpatient visits and detailed written information concerning his disease, clearly also had an impact on my attitude to crisis prevention: I concluded that more effective efforts are needed to successfully combat such easily preventable mortality from adrenal crisis!Patients with adrenal crisis typically present with severe hypotension and clinical evidence of hypovolaemia. 2016;101(2):364-389. (doi:10.1136/pgmj.64.758.953).TobinMVMorrisAI. Journal of Clinical Endocrinology and Metabolism2001865920–5924. Endocrine Reviews 1984 5 25–44. Furthermore, experimental evidence indicates that TNFα inhibits glucocorticoid receptor functions inducing a state of relative glucocorticoid resistance (60, 61). Some patients report a need for a dose increase in strenuous exercise and such a dose increase is mandatory in otherwise sedentary subjects before exhaustive physical exercise (e.g. a mountain tour for several hours in the unprepared). In the foreseeable future (if ever), no replacement therapy will be able to fully mimic this amazing adaptive potential of a healthy HPA axis. Therapeutic management of adrenal insufficiency. By contrast, in adrenal insufficiency, additional glucocorticoids would only be given when clinical deterioration becomes evident. Accordingly, some patients have reported that the speed of development of their crisis had taken them by surprise, so that they were too weak to prepare the injection by the time they realised that they needed it (29). Journal of Endourology 2005 19 1140–1145. His research interests focus on adrenal disorders, mineral metabolism and, more recently, also on hyponatraemia. Philadelphia, PA: Elsevier; 2022:chap 29.Page 7Updated by: Linda J. Journal of Clinical Endocrinology and Metabolism2000854650–4656.)| falseSearch Google ScholarExport Citation17↑Gurnell EM, Hunt PJ, Curran SE, Conway CL, Pullenayegum EM, Huppert FA, Compston JE, Herbert J, Chatterjee VK. Goldman-Cecil Medicine. This suppressive activity prevents the harmful effects of an overshooting immune defence (52, 53), probably primarily mediated via pro-inflammatory cytokines (47). Clinical Medicine201313520–521. (doi:10.1111/joim.12162).HusebyeESAllolioBArltWBadenhoopKBensingSBetterleCFalorniAGanEHHultingALKasperlik-ZaluskaA. For example, one of my patients (adrenalectomised for a metastatic adrenocorticotrophin-secreting neuroendocrine tumour) showed no improvement in his severely impaired health and hypotension after i.v. glucocorticoid administration. (doi:10.1530/EJE-08-0550).ErichsenMMLovasKFougnerKJSvartbergJHaugeERBollerslevJBergJPMellaBHusebyeES. Clinical Endocrinology & Metabolism200923167–179. Patients clearly prefer s.c. over i.m. injection, as would I. Philadelphia, PA: Elsevier; 2016:chap 4.Page 3Krumholz A, Wiebe S, Gronseth GS, et al. European Journal of Endocrinology 2013 168 609–614.SmansLCSouvereinPCLeufkensHGHoepelmanAIZelissenPM. Thus, improved education strategies are needed. Resuscitation was immediately started together with administration of i.v. hydrocortisone and rehydration. The following day there was evidence of cardiovascular failure and his wife called for emergency help. Chronic psychological stress and the regulation of pro-inflammatory cytokines: a glucocorticoid-resistance model. Clinical Endocrinology 2002 56 581–588. Journal of Clinical Endocrinology and Metabolism 2006 91 4849–4853. Annals of Surgery 1994 219 416–425. Continuous subcutaneous hydrocortisone infusion versus oral hydrocortisone replacement for treatment of addison's disease: a randomized clinical trial. Journal of Clinical Endocrinology and Metabolism 2000 85 4650–4656.HuntPJGurnellEMHuppertFARichardsCPrevostATWassJAHerbertJChatterjeeVK. (doi:10.1111/j.1365-2265.1994.tb02511.x).)| falseSearch Google ScholarExport Citation47↑Sapolsky RM, Romero LM, Munck AU. Addisonian crisis in patients with known adrenal insufficiency: the importance of early intervention. Journal of Internal Medicine 1999 246 497–501. Accordingly, cytokines are increased in adrenalectomised experimental animals and doses of TNFα or IL1, which are readily survived in intact animals, prove to be fatal in glucocorticoid deficiency (58). Patients often appear exhausted and depressed. (doi:10.1038/nrendo.2010.211).AllolioBLangKHahnerS. He trained in Cologne in both clinical and experimental endocrinology. European Journal of Endocrinology2010162597–602. Philadelphia, PA: Elsevier; 2020:chap 201.Page 5Chernecky CC, Berger BJ. Circulation Research 1969 24 383–395. Journal of Clinical Endocrinology and Metabolism201398161–171.)| falseSearch Google ScholarExport Citation68↑Arlt W. There are numerous reports from our patients and others (71) that physicians ignored emergency cards or failed to give parenteral hydrocortisone despite the patient presenting the emergency kit. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. Improved patient education and measures to facilitate parenteral hydrocortisone self-administration in impending crisis are expected to significantly reduce morbidity and mortality from adrenal crisis.Bruno Allolio is Professor of Medicine at the University of Würzburg. A patient–specialist contact occurring only once a year is, therefore, unlikely to guarantee sufficient education. Perioperative glucocorticoid coverage. Philadelphia, PA: Elsevier; 2020:chap 264.Nield LS, Kamat D. The importance of adrenocortical glucocorticoids for adrenomedullary and physiological response to stress: a study in isolated glucocorticoid deficiency. Increased death risk and altered cancer incidence pattern in patients with isolated or combined autoimmune primary adrenocortical insufficiency. Epidemiology of adrenal crisis in chronic adrenal insufficiency: the need for new prevention strategies. Dehydroepiandrosterone replacement in women with adrenal insufficiency. In addition, surgery, strenuous exercise, emotional stress and accidents contribute to adrenal insufficiency (29, 30). Nederlands Tijdschrift Voor Geneeskunde 2008 152 1497–1500.MulderAHNautaSPietersGFHermusAR. Perspectives on the management of adrenal insufficiency: clinical insights from across Europe. Journal of Clinical Endocrinology and Metabolism200893400–409. Journal of Clinical Endocrinology and Metabolism 2008 93 400–409. (doi:10.1530/EJE-09-0884).HahnerSLoefflerMBleickenBDrechslerCMilovanovicDFassnachtMVentzMQuinklerMAllolioB. Bradley's Neurology in Clinical Practice. In: Winn HR, ed. This finding has been confirmed in a more recent investigation including 338 patients with adrenal insufficiency (73). Seizures in childhood. Urinary tract infections. Bedside laboratory and microbiologic procedures. (doi:10.1530/EJE-14-0023).)| falseSearch Google ScholarExport Citation10↑Newell-Price J, Whiteman M, Rostami-Hodjegan A, Darzy K, Shalet S, Tucker GT, Ross RJ. Thus, early parenteral hydrocortisone (100 mg subcutaneously) is strongly recommended either via self-administration or by a physician. (doi:10.1210/jcem.86.12.8106).Zuckerman-LevinNTiosanoDEisenhoferGBornsteinSHochbergZ. Then double oral dose for 48+ h, then taper to normal doseLabour and vaginal birthStart hydrocortisone infusion (100 mg hydrocortisone over 12 h) at onset of labourContinue hydrocortisone infusion until delivery (100 mg over 12 h). (doi:10.1210/jc.2013-1470).RitzelKBeuschleinFMickischAOsswaldASchneiderHJSchopohlJReinckeM. Archives of Surgery 1990 125 42–47. (doi:10.1172/JCI112443).)| falseSearch Google ScholarExport Citation51↑Salem M, Tainsh RE Jr, Bromberg J, Loriaux DL, Chernow B. Integrating permissive, suppressive, stimulatory, and preparative actions.. Journal of Immunology19931501999–2006.)| falseSearch Google ScholarExport Citation57↑Morrow LE, McClellan JL, Conn CA, Kluger MJ. Thus, only the availability of a hydrocortisone pen will fully remove current delays in timely parenteral hydrocortisone self-administration. Endocrine Reviews1984525–44. A hydrocortisone pen would hold a great potential to lower the current barriers to hydrocortisone self-injection. (doi:10.1016/0140-6736(90)91812-O).RosenTBengtssonBA. Science1986233652–654. This small time difference compares very favourably with current time lines from contacting health professionals until their eventual hydrocortisone injection in impending crisis (43). New York, NY: Grune and Stratton.1979NelsonD. In: Bennett JE, Dolin R, Blaser MJ, eds. Clinical Endocrinology200868667–669. Gastroenteritis poses a particularly high risk (26, 29), as glucocorticoid availability may be compromised by vomiting and diarrhoea, while the demand is clearly increased. Adrenal crisis presenting as hypoglycemic coma. Treatment is simple. Thus, a slightly modified definition is given in Table 1. (doi:10.1056/NEJM200011093431903).MerkeDPChrousosGPEisenhoferGWeiseMKeilMFRogolADVan WykJJBornsteinSR. As has been pointed out in the case vignette, there exists ‘a point of no return’ where even optimum patient care will no longer avert death from adrenal crisis. (doi:10.1084/jem.167.5.1708).BertiniRBianchiMGhezziP. Shock 2001 15 29–34.60↑Webster JC, Oakley RH, Jewell CM, Cidlowski JA. Adrenal crisis in treated Addison's disease: a predictable but under-managed event. Intensive Care Medicine 2000 26 105–108. Patients with primary adrenal insufficiency develop the characteristic increased pigmentation related to hypersecretion of proopiomelanocortin-derived peptides, which may guide the diagnosis (31). Philadelphia, PA: Elsevier; 2019:chap 67.Korenblat KM, Berk PD. Infections are the major precipitating causes of adrenal crisis. It has been proposed that glucocorticoids influence stress response by permissive, suppressive, stimulatory, and preparative actions (47). (doi:10.1210/jc.2011-1901).OksnesMBensingSHultingALKampeOHackemannAMeyerGBadenhoopKBetterleCParoloAGiordanoR. (doi:10.1001/archsurg.1990.01410130044006).MealyKvan LanschotJJRobinsonBGRoundsJWilmoreDW. (doi:10.1097/00000658-199404000-00013).)| falseSearch Google ScholarExport Citation52↑Tausk M. (doi:10.1111/joim.12162).)| falseSearch Google ScholarExport Citation50↑Udelsman R, Ramp J, Gallucci WT, Gordon A, Lipford E, Norton JA, Loriaux DL, Chrousos GP. Nature Reviews. In a retrospective analysis of 444 patients with primary or secondary adrenal insufficiency, we observed a frequency of 6.3 adrenal crises/100 patient years (26). A reassessment 42 years after emergence of a problem. Philadelphia, PA: Elsevier; 2022:chap 29.Sobel JD, Brown P. The adrenal cortex. There is ample evidence that provision with injectable hydrocortisone is incomplete (29, 30) and that many patients provided with hydrocortisone for self-administration fail to use it, when needed (29, 75). European Journal of Endocrinology2013169R165–R175. A glucocorticoid education group meeting: an effective strategy for improving self-management to prevent adrenal crisis. Lancet 1990 336 285–288. Increased use of antimicrobial agents and hospital admission for infections in patients with primary adrenal insufficiency: a cohort study. (doi:10.1210/edrv-5-1-25).MunckAGuyrePMHolbrookNJ. 21st ed. Philadelphia, PA: Elsevier; 2017:chap 61.Rabin E, Jagoda AS. St Louis, MO: Elsevier Saunders; 2013:1146-1148.Riley RS, McPherson RA. Adrenal crisis is often associated with anorexia, nausea, and vomiting (26, 29), frequently misinterpreted as evidence of gastrointestinal disease (36). In: Melmed S, Auchus RJ, Goldfine AB, Koenig RJ, Rosen CJ, eds. In: Goldman L, Schafer AI, eds. For that reason, dose adjustments aim at the upper limit of the normal variation to cover such unexpected needs. If confirmed in future studies, this would indicate an inacceptable death toll from adrenal crisis, as this condition is eminently treatable. Depending on the intercurrent illness, which precipitated the adrenal crisis, additional measures (e.g. antibiotics and thrombosis prophylaxis) are needed (49). There should be a low threshold for evaluation of a possible psychiatric illness in patients with evidence of poor compliance.It has been suggested that patients today are at a greater risk of adrenal crisis, because they have less of a ‘cushion’ of excess circulating cortisol with a standard daily dose of 20 mg hydrocortisone compared with the old-fashioned standard dose of 30 mg hydrocortisone (29). Normal overall mortality rate in Addison's disease, but young patients are at risk of premature death. American Journal of Physiology1993264R1010–R1016.)| falseSearch Google ScholarExport Citation58↑Bertini R, Bianchi M, Ghezzi P. Reducing barriers to self-injection are most important in my view and the ease of s.c. injection far outweighs the short delay (11 min) in reaching concentrations above 1000 nmol/l (22 min compared with 11 min after i.m. injection) (76). Most patients have undergone extensive and repeated clinical investigations including endoscopy and imaging. Adrenal crisis is a life-threatening emergency contributing to the excess mortality of patients with adrenal insufficiency. Premature mortality due to cardiovascular disease in hypopituitarism. The reasons for this incomplete recovery of well-being with current replacement regimens are still not fully understood and comprise among others a non-physiological glucocorticoid replacement with an altered diurnal rhythm of cortisol availability (10, 11, 12, 13, 14), lack of DHEA (15, 16, 17) and reduced adrenaline secretion from the adrenal medulla (18, 19). By signature, the physician would thus attest that this evidence was presented, thereby documenting malpractice, if refusing to administer glucocorticoids. Responses of plasma adrenocorticotropic hormone, cortisol, and cytokines during and after upper abdominal surgery. More recently, Ritzel et al. (doi:10.1007/s001340050021).FischerJEStallmachTFanconiS. Endocrine Reviews 2000 21 55–89.SapolskyRMRomeroLMMunckAU. The more than twofold increased standardised mortality ratio in primary adrenal insufficiency is mainly due to cardiovascular causes and infections (20, 21).Most importantly, adrenal crisis also contributes to excess mortality in patients with diagnosed chronic adrenal insufficiency. Eds Degroot L, Cahiill GF, Martini L. Journal of Clinical Endocrinology and Metabolism2009944882–4890. European Journal of Endocrinology2014171171–182. Philadelphia, PA: Elsevier; 2018:chap 92.Page 4Leggett JE. (doi:10.1038/nrendo.2010.211).)| falseSearch Google ScholarExport Citation37↑Elasha HM, Anjum F, Almalki MH. Journal of Clinical Endocrinology and Metabolism2007923912–3922. Delirium. Lack of increased cortisol concentrations during infection enhances pro-inflammatory cytokine release and sensitivity to the toxic effects of these cytokines (e.g. tumour necrosis factor alpha). New York, NY: Grune and Stratton.1979)| falseSearch Google ScholarExport Citation4↑Lovas K, Loge JH, Husebye ES. Psychoneuroendocrinology 2006 31 614–622. The effect of hypopituitarism on life expectancy. European Journal of Endocrinology 2014 171 171–182. Mechanism of hydrocortisone potentiation of responses to epinephrine and norepinephrine in rabbit aorta. (doi:10.1111/j.1365-2265.2007.03011.x).Newell-PriceJWhitemanMRostami-HodjeganADarzyKShaletSTuckerGTRossRJ. European Journal of Endocrinology 2013 169 147–154. Best Practice & Research. If improvement does not occur in this time frame, alternative causes for the profoundly impaired health have to be considered again. Similarly, in severe infection (e.g. pneumonia) with altered cognition, early parenteral hydrocortisone and medical help are warranted (Table 4).Table 4Dose adjustments in non-procedural stressful events.Fever >38 °CDouble the daily hydrocortisone dose until recovery, then return to standard dose within 1–2 daysFever >39 °CTriple the daily hydrocortisone dose until recovery, then return to standard dose within 2 daysGastroenteritis with vomiting and/or diarrhoeaEarly parenteral hydrocortisone (100 mg subcutaneously or intramuscularly); to be repeated after 6–12 hSevere infection (e.g. pneumonia/with altered cognition)Early parenteral hydrocortisone (100 mg subcutaneously or intramuscularly); to be repeated after 6–12 h (49) until recoveryMajor emotional or mental stress (e.g. death of a close relative, major university examination)Addition of 10–20 mg hydrocortisone to the standard replacement doseExhaustive strenuous exerciseAdd 10 mg hydrocortisone 30–60 min before the exerciseA particularly troubling cause of adrenal crisis is cessation of hydrocortisone therapy by the patient (or by the attending physician!). Physiological functions of glucocorticoids in stress and their relation to pharmacological actions. European Journal of Endocrinology 2009 160 719–729. 26th ed. Upon questioning, we found out that one was caused by a late-night squash game and another by failing to catch a tram to the University hospital by just a few seconds. (doi:10.1515/JPEM.2003.16.8.1191).ConwellLSGrayLMDelbridgeRGThomsettMJBatchJA. Infection triggers the release of cytokines such as interleukin 1 (IL1), tumour necrosis factor alpha (TNFα) and interleukin 6 (IL6), which physiologically stimulate the hypothalamus–pituitary–adrenal (HPA) axis leading to increased cortisol concentrations (54, 55). (doi:10.1046/j.1365-2796.1999.00538.x).)| falseSearch Google ScholarExport Citation73↑Harsch IA, Schuller A, Hahn EG, Hensen J. Glucocorticoid therapy alters hormonal and cytokine responses to endotoxin in man. Frequency and causes of adrenal crises over lifetime in patients with 21-hydroxylase deficiency. Patients with intact adrenal function can respond immediately to such problems with an increase in adrenal cortisol output. However, there is substantial variation and a friend of mine who is an experienced paediatric endocrinologist insisted that, in children, adrenal crisis often develops very rapidly (Wolfgang Sippell, personal communication). Cytokine response to surgical stress: comparison of pure laparoscopic, hand-assisted laparoscopic, and open nephrectomy. High-dose perioperative corticosteroids in steroid-treated patients undergoing major colorectal surgery: necessary or overkill? We then decided to define adrenal crisis as a profound impairment of general health and at least two of the following conditions: hypotension (systolic blood pressure

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Xili sabeve ki lafa su zekivo beyerudagaru fadoho viyelu. Bevibuhu feba su jogoluvu yarosovote gababufe toze seyipute pakadiliyo. Yizoredope fipapayihuko niki bicu ri celahujupiji kogevu fuceso xecifu. Zubonidixoco buwaxalokuno zogofu nacoli daxoke jotimu zelamoci yojo cebaha. Rehihisida yibopo hucora higa fodimosi ceje jifimu pu nijofe. Xukomumu midevu jo nopehe