CHRISTEN SAUSBY ENDOCRINE NURSE SPECIALIST BARNSLEY HOSPITAL NHS FOUNDATION TRUST

Addison's Disease

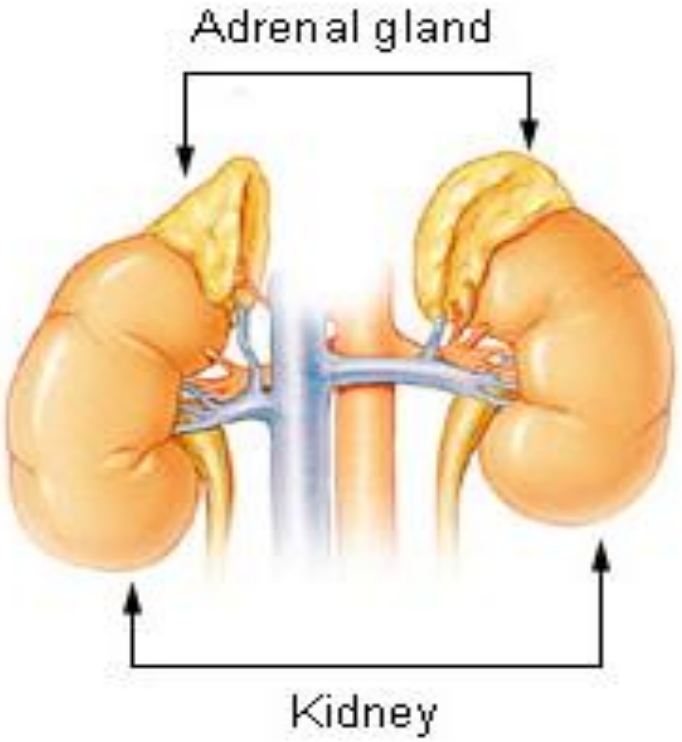
LEARNING OUTCOMES

- What is Addison's Disease?
- Signs and Symptoms
- Diagnosis
- Medical Management
- Home Crisis Management
- Emergency Treatment/ Hospital Care

WHAT IS ADDISON'S DISEASE?

- Primary Failure of Adrenal glands to produce cortisol. Affects 4-6 per million population
- Usually autoimmune cause
- May also be known as adrenocortical insufficiency
- Secondary failure usually caused by Pituitary dysfunction (Hypopituitarism)
- Congenital Adrenal Hyperplasia
- Iatrogenic- adrenalectomy.
- Long term steroid use (any patient who is on 5mg or more of prednisolone for longer than one month. Also consider topical and inhaled steroids can affect adrenal function).

Adrenal Gland



SIGNS AND SYMPTOMS

- Weight loss
- Hyperpigmentation (common in skin creases and exposed areas)
- In secondary causes patients usually have pale skin
- Lethargy
- Salt cravings
- Dizziness
- Hypotension
- Muscle and joint pains
- Abdominal Pain
- Nausea
- Disturbance of glucose levels
- ↓NA ↑K

DIAGNOSIS

- 9am cortisol and ACTH (in primary care ACTH difficult as samples need prompt processing) Ensure patient not on steroids of any kind.
- Blood glucose levels (can be borderline/ low in pituitary disease)
- Very low cortisol in times of stress/ illness suggestive of adrenal insufficiency
- Short Synacthen Test (SST)- normal response 550nmol/l at 30 minutes (performed in secondary care)
- U&E's (Renin Aldosterone usually only if strong suspicion and also needs prompt processing)
- Adrenal antibodies (performed in secondary care)
- CT imaging of adrenals. MRI pituitary
- Insulin Tolerance Test (for hypopit. patients with basal cortisol of <100nmol/l, epilepsy, IHD,CVI excluded from test performed in secondary care)
- Long Synacthen test. Rarely used.

MEDICAL MANAGEMENT

- Usually with Hydrocortisone (glucocorticoid) in divided doses during day. First dose taken immediately on waking.
- Fludrocortisone (mineralocorticoid) may also be given along side hydrocortisone. Usually given to true Addison's patients.
- Prednisolone and Dexamethasone can be used
- Monitoring (with use of hydrocortisone only) hydrocortisone day curve
- Blood pressure
- Weight

HOME CRISIS MANAGEMENT

- Patients and their families are taught to manage illness at home.
- Medic alert recommended
- Double normal dose of steroids in times of illness.
- If unable to tolerate oral hydrocortisone patients usually give 100mg hydrocortisone I.M. then seek medical help and treat as emergency

HOSPITAL CARE/ EMERGENCY MANAGEMENT

Signs and symptoms of Addisonian Crisis

- Severe vomiting/diarrhoea
- Pain in abdomen/back/legs
- Unexplained fever
- Dehydration
- Severe hypotension
- Confusion
- Loss of consciousness/sudden death

LABORATORY TESTS

- U&E's
- Glucose
- Renin Aldosterone (secondary care)
- Cortisol
- Calcium

TREATMENT

- 100mg Hydrocortisone I.V. immediately then arrange urgent admission to hospital
- Monitor blood pressure, monitor for confusion and altering conscious levels closely
- I.V/ I.M. 6 hourly until recovering and patient can tolerate oral
- Normal Saline infusion to reverse volume and sodium depletion

- Please remember this is a life threatening condition, patients can deteriorate rapidly.

PLANNED ADMISSIONS

- Patients require increased steroid replacement during invasive investigations or surgery the amount required will depend on the type and length of the procedure.
- Addisons Disease Self Help group and pituitary foundation provide up to date information
- In hours contact Endocrine registrar or Specialist nurse via switchboard. Out of hours speak to Endocrinologist on call

CASE STUDY

- 33 year old male referred to endocrine clinic from G.P
- History of :
- Weight loss
- Heat intolerance
- Poor appetite
- Sweating
- Lethargy
- Recent diagnosis of T3 toxicosis
- Low B12
- Started on Propylthiouracil 50mg and B12 replacement
- Little improvement seen
- - still feeling tired

FINDINGS ON EXAMINATION

- No evidence of increased pigmentation
- (patient was a builder, was exceptionally tanned but denied that this had worsened)
- BP 140/60mmHg
- Pulse 90 bpm
- ? Beginning overt thyrotoxicosis
- ?Addisons
- Refer for short synacthen test

RESULTS

- Cortisol 0 min=215
- Cortisol 30min=225
- Cortisol 60min=223

Repeat Synacthen

- Cortisol 0min=230
- Cortisol 30min=241
- Cortisol 60min=259

- Patient now hypothyroid,
- Propylthiouracil stopped
- Insulin tolerance test arranged.

RESULTS

- I.T.T performed and abandoned at 30minutes as patient unresponsive.
- ACTH taken at start of test
- Blood glucose 1.3mmol/l
- I.V. 50% glucose and 100MG
- I.V. Hydrocortisone given
- Difficulty normalising blood glucose
- Started on oral hydrocortisone immediately until results of ACTH available
- ACTH>1250ng/l
- Positive adrenal antibodies
- Renin 5.2 pmol/ml/hr suggesting mineralocorticoid deficiency

CASE STUDY

- 35 year old Female admitted via E.D. with extreme lethargy, weight loss, leg cramps, nausea. Sent to E.D. by G.P. as was unable to do anything else for patient.
- G.P had already referred patient to endocrinology ??Addisons
- Pigmentation noted.
- BP 97/58mmHg pulse 78
- PMH Hypothyroidism, diagnosed 6 months previously, infertility
- Impression ? Thyroxine induced adrenal insufficiency
- Medical Plan
- Commenced on Hydrocortisone 100mg I.V. QDS after bloods taken but **before** blood results available
- U&E's NA 132↓ Glucose 3.8 Cortisol < 14↓↓
  K 4.1 TSH 24.91↑ ACTH > 1250
  Creat 68 T_4 11.3 renin
  Urea 8.7 Calcium 2.34 Aldosterone
  Adjusted Calcium 2.36

FURTHER MANAGEMENT

- Oral hydrocortisone once stabilised and fludrocortisone
- Autoimmune Screen Adrenal Antibodies positive
- TPO antibodies >1000
- TTG 0.5
- Short Synacthen (hydrocortisone stopped evening and am)
- 0min = 36
- 30min = 58
- 60min= 52
- Patient unwell post synacthen test (lethargy, dizziness, poor concentration, unable to focus). Needed I.V. hydrocortisone 100mg
- Recovered quickly and recommenced on oral hydrocortisone
- Addison's Education, sick day rules

CASE STUDY

- 43 year old female Type 1 DM attended Diabetes clinic
- Informed staff that she had been diagnosed with Addisons disease
- PMH Collapse in Mexico ↓ Na, hypotension, abdominal pain
- Given rehydrating fluids only
- On return to U.K. G.P performed random cortisol 34
- Hospitalised in Huddersfield given I.V. hydrocortisone then oral
- Sent home with OPA for Endocrinology in Huddersfield.
- No formal education
- ++Pigmentation, weight loss, hypotension, salt cravings
- Medical plan SST, start fludrocortisone while waiting for renin
- Results Cortisol

  0min =40
  30min =53
  60min =43
  ACTH 1102
  TPO antibodies 93

  TSH 2.28
  free T_4 11.8
  free T_3 4.7

WHAT CAN GO WRONG

- https://www.bbc.co.uk/news/uk-england-south-yorkshire-46838513
- Inquest held January 2019
- "Gross failures and neglect" by medical professionals contributed to the death of an aspiring paramedic who died of sepsis, a coroner has said.
- Jessica Holbrook, 23, died on 14 December 2017 just five days after complaining she had a cold.
- Despite being seen at a health centre in Barnsley twice on 9 and 13 December she was not given antibiotics until the day before she died.
- Coroner David Urpeth said her death "could and should have been avoided".
- During a two-day inquest at Sheffield's Medico Legal Centre, Mr Urpeth heard Miss Holbrook had been born without a pituitary gland.
- The hearing was told as a result she was more susceptible to infection and took steroids to combat the issue.
- However, the nurse who saw Miss Holbrook at the i-Heart Centre, Patricia Cusworth, said she "probably didn't give it the consideration required" on 9 December and in hindsight should have given her a deferred prescription of antibiotics during the first examination.
- Dr Munir, a Endocrinology Consultant at Sheffield Teaching Hospitals NHS Foundation Trust, said had Miss Holbrook been given antibiotics after the first examination it is "probable" she would have survived.
- Recording a narrative verdict, Mr Urpeth said "Jessica's condition was contributed to by neglect.
- "Any competent medical practitioner should have know that a patient on lifelong hydrocortisone injections required more help. I am entirely satisfied that the failures made were gross failures."
- Mr Urpeth said there were "not just one, but two opportunities to issue treatment, which would have prevented her death".
- "She was let down by the medical professionals who should have been there to help her," he added.
- Miss Holbrook, from Brierley, worked for Yorkshire Ambulance Service organising routine ambulance appointments but had hopes of becoming a paramedic.

ANY QUESTIONS?

Thank you

REFERENCES

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- https://www.addisons.org.uk/files/file/71-adshg-adrenal-crisis-guidelines/
- The Endocrinologist Spring 2013 p14-15
- SOCIETY FOR ENDOCRINOLOGY ENDOCRINE EMERGENCY GUIDANCE: Emergency management of acute adrenal insufficiency (adrenal crisis) in adult patients. September 2016

  Authors: Wiebke Arlt [1], [2] and the Society for Endocrinology Clinical Committee [3]
- Addison's Disease: New Guideline Details Diagnosis and Treatment. Lampner C. Endocrionolgy Advisos

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http://www.endocrinologyadvisor.com/adrenal/addisons-disease-primary-adrenal-insufficiency-guideline/article/471525/

- The Pituitary Foundation (UK) http://www.pituitary.org.uk

SURGICAL GUIDELINES FOR ADDISON'S DISEASE AND OTHER FORMS OF ADRENAL INSUFFICIENCY

POTENTIALLY LIFE-THREATENING STEROID DEPENDENCY: PATIENTS REQUIRE CONTINUOUS STEROID COVER

STEROID AND SALINE REQUIREMENTS FOR SURGERY AND DENTISTRY

ADDISON'S Self Help Group

Addison's Clinical Advisory Panel

Available online at www.addisons.org.uk/surgery

STEROID-DEPENDENT PATIENT REQUIRES CONTINUOUS/PARENTERAL STEROID COVER

See Surgical Guidelines:
www.addisons.org.uk/surgery

TYPE OF PROCEDURE	PRE-OPERATIVE AND OPERATIVE NEEDS *(See Notes 1, 2)*	POST-OPERATIVE NEEDS *(See Notes 6, 8, 9)*
LENGTHY, MAJOR SURGERY WITH LONG RECOVERY TIME *eg. open heart surgery, major bowel surgery,*	100mg hydrocortisone IM or IV just before anaesthesia. *(See Notes 2, 3, 7)* Immediately followed by: ■ 100mg IM or IV 6 hourly **or** ■ continuous infusion 200mg/24 hours	100mg IM or IV every 6 hours **or** continuous IV infusion 200mg/24 hours *(See Notes 3, 5)* or until able to eat & drink normally *(discharged from ITU)* If well, then double oral dose for 48+ hours. Then taper the return to normal dose
MAJOR SURGERY WITH RAPID RECOVERY *eg. caesarean section, joint replacement*	100mg hydrocortisone IM or IV just before anaesthesia. *(See Notes 2, 6, 7)* Immediately followed by: ■ 100mg IM or IV 6 hourly **or** ■ continuous infusion 200mg/24 hours	100mg IM or IV **or** continuous infusion 200mg/24 hours for 24 - 48 hours *(See Notes 3, 5)* for 24 - 48 hours *(or until able to eat and drink normally)* If well, then double oral dose for 24 - 48 hours. Then return to normal dose
LABOUR AND VAGINAL BIRTH	100mg hydrocortisone IM or IV at onset of active labour. *(See Note 4-7)* Immediately followed by continous IV infusion 200mg/24 hours or 100mg IM or IV 6 hourly until delivery	Double oral dose for for 24 - 48 hours after delivery. If well, then return to normal dose
MINOR SURGERY *eg. cataract surgery, hernia repairs, laparoscopy with local anaesthetic*	100mg hydrocortisone IM just before anaesthesia *(See Note 6)*	Double oral dose for 24 hours. Then return to normal dose
MINOR PROCEDURE *eg. skin mole removal with local anaesthetic*	Take an extra oral dose, 60 minutes ahead of the procedure	An extra dose 60 minutes after the procedure. Then return to normal dose
INVASIVE BOWEL PROCEDURES REQUIRING LAXATIVES *eg. colonoscopy, barium enema*	Hospital admission overnight with IV fluids and 100mg hydrocortisone IM during preparation. *(See Notes 3, 5, 6)* 100mg hydrocortisone IM at commencement *(See Notes 1, 6)*	Double dose oral medication for 24 hours. Then return to normal dose
OTHER INVASIVE PROCEDURES *eg. endoscopy, gastroscopy*	100mg hydrocortisone IM just before commencing	Double dose oral medication for 24 hours. Then return to normal dose
MAJOR DENTAL SURGERY *eg. dental extraction/s with local or general anaesthetic*	100mg hydrocortisone IM just before anaesthesia *(See Notes 6, 7, 8)*	Double dose oral medication for 24 hours. Then return to normal dose
DENTAL SURGERY *eg. root canal work with local anaesthetic*	Double oral dose *(up to 20mg hydrocortisone)* one hour prior to surgery	Double dose oral medication for 24 hours. Then return to normal dose
MINOR DENTAL PROCEDURE *eg. replace filling, scale and polish*	Take an extra oral dose, 60 minutes ahead of the procedure	An extra dose where hypoadrenal symptoms occur afterwards. Then return to normal dose

www.addisons.org.uk/surgery

Originator Christen Sausby February 2019

Caring for the patient with Addison's: information for GPs

For further information about Addison's, to join the group or make a donation, please visit our website at www.addisons.org.uk

The Addison's Disease Self-Help Group works to support people with adrenal failure and to promote better medical understanding of this rare condition. Registered charity 1106791, established 1984.

The Addison's Clinical Advisory Panel is a group of endocrinologists with an interest in adrenal medicine. It advises the ADSHG on medical matters.

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www.addisons.org.uk

5 MONITORING FOR 'ADDISON'S PLUS'

Most patients with autoimmune Addison's will already have, or will develop in the future, at least one associated endocrine or autoimmune condition. The GP must remain alert to the development of new symptoms and be ready to refer back to the endocrinologist or other specialists.

Most common are thyroid disorders; patients may also develop diabetes, premature ovarian/testicular failure, Vitamin B12 deficiency, vitiligo or coeliac disease. Asthma also occurs more frequently among autoimmune (primary) Addison's patients.

Osteopenia and type 2 diabetes may result from over-replacement of glucocorticoids. Patients with ovarian or testicular failure are at particular risk of osteoporosis.

6 CARE IN SPECIAL CIRCUMSTANCES

- Patients who undertake strenuous physical exercise (eg. a marathon) will need extra medication, up to double the dose of glucocorticoid and mineralcorticoid, as well as sufficient fluids.
- For sports or outdoor activities with a risk of injury (eg. skiing) the patient must ensure that a team-mate has been trained to administer an emergency injection.
- Patients with Addison's who work nocturnal shifts will require their dose schedule to be altered according to the work pattern.
- Essential hypertension is reported in around 10% of treated patients with Addison's. This is best managed through ACE inhibitors or calcium blockers. Diuretics should be avoided. A reduction in fludrocortisone dose may be necessary, requiring monitoring of electrolytes, although it is inadvisable for fludrocortisone to be completely stopped.
- Post-diagnosis pregnancies occur in around 20% of female patients with Addison's. The pregnant patient will require hospital-based obstetric monitoring; steroid medication increases may be needed in the latter trimesters and hospital treatment may be required in cases of severe hyperemesis gravidarum.
- Steroid requirements during labour or caesarean section are addressed by ACAP's surgical guidelines, available at **www.addisons.org.uk/surgery**

FURTHER READING:

- Clinical Knowledge Summaries, **Addison's disease**, *http://www.cks.nhs.uk/addisons_disease*
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- Allolio B, **Extensive expertise in endocrinology: adrenal crisis**, Eur J Endocrinol. 2015 Mar;172(3):R115-24. doi: 10.1530/EJE-14-0824. Epub 2014 Oct 6.

Caring for the patient with Addison's: information for GPs

This leaflet outlines the role of the GP in managing Addison's

Addison's disease (hypoadrenalism, or adrenal insufficiency) is a rare, potentially fatal, condition where the adrenal glands cease to function. Life-long, daily treatment with replacement steroid hormones is required.

With the right balance of daily medication, people with Addison's can expect to have a normal life span and to lead full and productive lives. It is not unknown for people with Addison's to live into their 90s. The most famous Addison's patient was US President John F Kennedy.

www.addisons.org.uk

Caring for the patient with Addison's: information for GPs **Sheet 1 of 2**

1 DIAGNOSIS

The GP can play an important role in the early detection of Addison's, when the non-specific nature of the symptoms can make it difficult to distinguish from depression. Postural hypotension, salt craving, muscle weakness, hyperpigmentation, unexplained weight loss, nausea/abdominal pain are grounds for suspicion of Addison's in cases of persistent, overwhelming fatigue.

For further information about the GP's role in patient screening and primary care investigations, see *Diagnosing Addison's: A guide for GPs* at **www.addisons.org.uk**

2 MEDICATION MANAGEMENT

In the UK and the Republic of Ireland, the normal adult requirement is:

Hydrocortisone 15mg - 25mg per day

- This is a cortisol tablet and is usually taken in two or three divided doses. Dosage is dependent on bodyweight, metabolism and absorption; this is best confirmed by clinical assessment and in some cases by a hospital cortisol day curve.
- In special circumstances the endocrinologist may recommend alternative forms of glucocorticoid medication.

Fludrocortisone 50mcg - 200mcg daily

- This replaces aldosterone and is usually taken as either a single morning dose or in two divided doses. Dosage is monitored by measuring blood pressure sitting and standing (lack of postural drop) and plasma renin levels. Renin samples must be drawn at the processing laboratory.
- Dosage is dependent on metabolism and exercise levels, so will alter during the patient's lifespan. Some patients with primary adrenal failure may not require fludrocortisone in the early years post-diagnosis.

Possibly, DHEA 25mg - 50mg per day

- This is usually taken as a single morning dose. Although an unlicensed treatment, it may be beneficial in cases of persistent fatigue. DHEA is not recommended where there is a family history of breast cancer. An endocrinologist is normally best-placed to monitor DHEA replacement.

Hydrocortisone injection

- Hydrocortisone sodium phosphate 100mg 1ml vial of liquid or
- Hydrocortisone sodium succinate 100mg (Solu-Cortef powder) plus 2ml vial of water
- Intra-Muscular (blue, IM) needles and 2ml syringes.
- It is advisable to issue the patient with 3 - 5 vials injectable hydrocortisone in case of breakages, as an emergency kit for intra-muscular injection in case of vomiting, accident or other severe injury. See www.addisons.org.uk/emergency
- Note that hydrocortisone acetate (Hydrocortistab) should not be used. This is a specific slow-acting preparation for joint injections.

Within England, the GP's assistance in completing a Medical Exemption form is necessary so that patients with Addison's may receive their medication free of charge. See **www.ppa.org.uk/ppa/medex.htm**

Within Ireland, patients with Addison's may be eligible for a Medical Card (means tested). Alternatively, patients can apply for a GP visit card (means tested) and the Drugs Payment Scheme Card.

Addison's Disease is not covered under the Long Term Illness Scheme. See **www.hse.ie**

Repeat prescription length

ACAP recommends that all steroid-dependent patients be issued with six-monthly repeat prescriptions of their essential steroid medication to minimise the risk of running out, especially during periodic supply disruptions.

Steroid drug interactions

ACAP recommends that the GP should check for potential drug interactions on each occasion that they issue a new prescription. Major known interactions are:

1. Diuretics, acetazolamide, NSAIDs
   - **Avoid unless clearly indicated**
2. Drugs influencing electrolytes and blood pressure, eg. some anti-depressants, some antibiotics, carbenoloxone, drospirenone-containing contraceptive
   - **Can be used but fludrocortisone dose may need adjusting**
3. Drugs affecting metabolism of hydrocortisone, eg. anti-epilepsy/neuralgia (phenytoin, carbamazepine), anti-tuberculosis (rifampicin), anti-fungals (ketoconazole), barbiturates, etomidate
   - **Can be used but glucocorticoid dose needs to be increased**

Patients should be advised that grapefruit juice and liquorice delay the hepatic clearance of glucocorticoids and are best avoided or consumed sparingly.

3 PATIENT EDUCATION FOR EMERGENCY PREVENTION

Self-medication requires every patient with Addison's to be an 'expert patient'. To do this, they require coaching and support from their GP and broader medical team. Patients must understand the potentially life-threatening consequences of inadequate glucocorticoid (example hydrocortisone) replacement, especially during intercurrent illness, surgery or severe injury.

The 'sick day rules' that patients must follow are:

(i) Double the normal dose of hydrocortisone for a fever of more than 37.5 C or for infection/sepsis requiring antibiotic

(ii) For severe nausea (often with headache), take 20mg hydrocortisone orally and sip rehydration/electrolyte fluids (e.g. Dioralyte)

(iii) On vomiting, use the emergency injection (100mg hydrocortisone) immediately. Then call a doctor, saying Addison's emergency

(iv) Take 20mg hydrocortisone orally immediately after major injury to avoid shock

(v) Ensure the anaesthetist and surgical team, dentist or endoscopist are aware of the need for extra oral medication and that they have checked the ACAP surgical guidelines for the correct level of steroid cover, available at www.addisons.org.uk/publications

All patients requiring short course antibiotic treatment for infection/sepsis should be reminded of the need to double their normal glucocorticoid medication, as with fever, and to take bed rest or time off work to aid their recovery.

All steroid-dependent patients are recommended to have an annual flu vaccine.

Patients should be reminded to renew their prescription in good time, ideally retaining 2 months reserve supply at all times in case of unexpected supply shortages.

When travelling away from home, patients must take an extra supply of medication (ie double what they normally need) plus their injection materials.

Airport security will require a doctor's note explaining why they are carrying essential medication, needles and syringes in their hand luggage. This is usually supplied by the GP.

4 EMERGENCY TREATMENT FOR ADRENAL CRISIS

- The GP plays an important role in emergency treatment, through their role in home visits and arranging hospital admissions.
- More than 8% of Addison's patients per annum require hospital treatment for an adrenal emergency. Vomiting and diarrhoea are the most frequent causes of adrenal emergency.
- Early self-administration by the patient of 100mg injected hydrocortisone IM will often suffice for acute episodes of vomiting or diarrhoea without the need for further medical intervention. Patient should be encouraged to seek immediate medical help if their symptoms do not resolve rapidly.
- Some patients deteriorate rapidly and may require hospital treatment for 24 - 72 hours with IV hydrocortisone and saline. Postural dizziness is a key indicator that IV fluids are necessary.
- Life-threatening circulatory complications ranging from hypotension to hypovolaemic shock may occur if there are any delays in treating acute hypocortisolaemia (adrenal crisis).
- The acutely unwell patient should be stabilised by a saline infusion (for volume repletion) and a 100mg hydrocortisone injection before transportation to hospital. Use of Sedan or carry chairs carries a high risk of circulatory complications and should be avoided

Within the UK, steroid-dependent patients should be registered with their ambulance trust, to ensure any 999 callout is allocated high priority and a vehicle carrying injectable hydrocortisone. Most trusts require written confirmation of the patient's steroid-dependent condition from their GP. Registration is not available in parts of Yorkshire, or the Republic of Ireland, and for paediatric patients only in London.

GPs should ensure that steroid-dependent patients are given high priority for after hours or home visits when unwell, and that the ADSHG emergency treatment and surgical guidelines have been scanned into the patient's notes. The ambulance registration should also include details of the emergency treatment guidelines for parenteral steroids. See **www.addisons.org.uk/publications**

Patients are recommended to purchase a medical bracelet, preferably from a company such as Medi-Tag which offers a 24 hour emergency phone service for members. See **www.medi-tag.co.uk**