“In memory of Thomas Addison M.D. Son of Joseph and Sarah Addison. Died June 29th 1860 aged 66 years. For 36 years physician to Guy’s Hospital London”.
Adrenal insufficiency & Sick Day Rules

• Case history
• Adrenal insufficiency
  – Clinical outcomes with steroid replacement
  – Adrenal crisis
  – Importance of education
• KTPH initiative
• Conclusions
Case 1

• 53M
• NPC 2003 – extensive XRT
• SCC palate Aug 2013 – surgery
**Case 1**

**Admission 1**

- Micturition syncope
- ± SIADH/1° polydipsia
- Hypopit considered
- fT4 8.8 (TSH 1.3)
- Testo 8.3 (FSH 4, LH 2)
- IgF-1 58 (99-295)
- Cortisol 321 (random)
- SST 222, 647, 838

Patient recovered 133
Case 1

Admission 1
Micturition syncope + SIADH/1° polydipsia
Hypopit considered
fT4 8.8 (TSH 1.3)
Testo 8.3 (FSH 4, LH 2)
IgF-1 58 (99-295)
Cortisol 321 (random)
SST 222, 647, 838
Patient recovered 133

Admission 2
Aspiration pneumonia
Antibiotics & hydration
Hypopit re-considered
fT4 9.5
Testo 7.8
IgF-1 61
Cortisol 968 (pre or post HC in A&E?)
Patient recovered 132

Sodium graph
Case 1

Admission 1
Micturition syncope + SIADH/1° polydipsia
Hypopit considered
fT4 8.8 (TSH 1.3)
Testo 8.3 (FSH 4, LH 2)
IgF-1 58 (99-295)
Cortisol 321 (random)
SST 222, 647, 838
Patient recovered 133

Admission 2
Aspiration pneumonia
Antibiotics & hydration
Hypopit re-considered
fT4 9.5
Testo 7.8
IgF-1 61
Cortisol 968 (pre or post HC in A&E?)
Patient recovered 132

Admission 3
Osteoradionecrosis
Antibiotics & hydration
Hypopit treated
HC 10 & 5
NaCl 2tab/d
T4 25

Sodium

Admission 1: Micturition syncope + SIADH/1° polydipsia
- fT4 8.8 (TSH 1.3)
- Testo 8.3 (FSH 4, LH 2)
- IgF-1 58 (99-295)
- Cortisol 321 (random)
- SST 222, 647, 838
- Patient recovered 133

Admission 2: Aspiration pneumonia
- Antibiotics & hydration
- Hypopit re-considered
- fT4 9.5
- Testo 7.8
- IgF-1 61
- Cortisol 968 (pre or post HC in A&E?)
- Patient recovered 132

Admission 3: Osteoradionecrosis
- Antibiotics & hydration
- Hypopit treated
- HC 10 & 5
- NaCl 2tab/d
- T4 25
Case 1

**Admission 1**
Micturition syncope + SIADH/1° polydipsia
Hypopit considered
fT4 8.8 (TSH 1.3)
Testo 8.3 (FSH 4, LH 2)
IgF-1 58 (99-295)
Cortisol 321 (random)
SST 222, 647, 838
Patient recovered 133

**Admission 2**
Aspiration pneumonia
Antibiotics & hydration
Hypopit re-considered
fT4 9.5
Testo 7.8
IgF-1 61
Cortisol 968 (pre or post HC in A&E?)
Patient recovered 132

**Admission 3**
Osteoradionecrosis
Antibiotics & hydration
Hypopit treated
HC 10 & 5
NaCl 2tab/d
T4 25

Endocrine f/up since
Off NaCl
Stable HC 15 & 10 (doubled during illness or surgery)
T4 50
SST 207, 342, 400
Case 1 - Lessons

• XRT for NPC is associated with hypopituitarism
NPC – XRT - Hypopituitarism

- N=50, median f/up 8y (3-21y)

Fig. 1 Prevalence of HP dysfunction according to number of hormonal axis involvement, post NPC irradiation

Fig. 2 Frequency of each anterior pituitary hormone dysfunction post irradiation for NPC

Ratnasingam et al, Pituitary 2014
NPC – XRT - Hypopituitarism

• N=50, median f/up 8y (3-21y)

Ratnasingam et al, Pituitary 2014
Case 1 - Lessons

• XRT for NPC is associated with hypopituitarism
• Inadequate steroid reserve may manifest during inter-current illnesses early on
• Synacthen test is strictly not a pituitary function test*
0900 h Cortisol
89% Sensitive, 100% specific for a cut-off of 100 nmol/l after pituitary surgery (Courtney et al. 2000)

Standard short Synacthen test
(SST; 250 μg)
57–100% Sensitive, 90–100% specific for a 30’ cut-off of 500 nmol/l (Shankar et al. 1997, Abdu et al. 1999, Rose et al. 1999a, Dorin et al. 2003, Schmiegelow et al. 2003a,b)

Low-dose short Synacthen test
(LDSST; 1 μg)
100% Sensitive, 68% specific for a cut-off of 550 nmol/l (Rose et al. 1999a)
LDDST diagnostic area under the curve (AUC) 0.94, superior to SST (AUC 0.85; Kazlauskaite et al. 2008)

Insulin tolerance test (ITT;
Considered gold standard. Cut-off:
500 nmol/l (Lindholm 2001)
Some authors advocate higher cut-offs of 550 nmol/l (Stewart et al. 1998, Tuchelt et al. 2000) or 580 nmol/l (Mukherjee et al. 1997)
Rare cases may be missed by the ITT (Tsatsoulis et al. 1988). Clinical judgement should decide on further testing

Glucagon test
Cortisol peak >500 nmol/l is commonly accepted as cut-off (Rao & Spadis 1987)
Other authors advocate 580 nmol/l (Orme et al. 1998)

Serum cortisol <138 nmol/l after last metyrapone dose confirms adequate blockade
Serum 11-deoxycortisol 210–660 nmol/l or more shows normal ACTH reserve
If insufficient 11-deoxycortisol response, ACTH <200 pg/ml (2–44 pmol/l) suggests secondary adrenal insufficiency
Case 2 – you do know...right?

- 61M
- Acute GE (holiday to Morocco)
- Dehydration, AKI (Cr 180)
- Overnight IVF, empirical IV antibiotics, isolated
Case 2 – you do know...right?

- 61M
- Acute GE (holiday to Morocco)
- Dehydration, AKI (Cr 180)
- Overnight IVF, empirical IV antibiotics, isolated
- 6AM – found drowsy in soiled bed, urgent bloods sent and fluid resus. amplified
- Post take round – drowsy, hypotensive, lab alert (K 6.5, Cr 500)
- ICU transfer
- Family update....
Case 2 – you do know...right?

- Patient on Hydrocortisone, Thyroxine, Testosterone
- Previous NFA with surgery & XRT
Case 2 – you do know...right?

• Patient on Hydrocortisone, Thyroxine, Testosterone
• Previous NFA with surgery & XRT
• Details available on paramedic sheet...regrettably not transferred to A&E or medical clerking...patient exhausted...
• Subsequent aggressive care in ICU (including temporary HD and IV steroids) led to near full recovery
Case 2 - Lessons

• Inter-current illness (AGE especially) amongst steroid users can be devastating
• Crucial to beware of medications (steroid use especially)
• Paramedic sheet one of the most useful information tool
• Sick day rules for steroid is not theory
AI outcomes with current steroid replacement

• 1849 – first description - ‘remarkable anemia’ from disease of ‘supra-renal capsules’

• 2y and 5y mortality of 80% & 100%

• 1938 – first synthetic mineralocorticoid

• 1948 – hydrocortisone arrived

Johannsson et al, Clin Endo 2015
AI outcomes with current steroid replacement

- How much steroid does one need?
- How best to administer?
- How best to monitor?
AI outcomes with current steroid replacement

• How much steroid does one need?
• How best to administer?
• How best to monitor?
AI outcomes with current steroid replacement

• How much steroid does one need?
  – Early radioisotope studies 30mg of HC/d
  – Recent studies (more stable isotope and deconvolution analysis) estimate much lower requirements (10-20mg/d)

Johannsson et al, Clin Endo 2015
AI outcomes with current steroid replacement

• How much steroid does one need?
• How best to administer?
• How best to monitor?

Johannsson et al, Clin Endo 2015
AI outcomes with current steroid replacement

- How much steroid does one need?
- How best to administer?
- How best to monitor?
AI outcomes with current steroid replacement

• How much steroid does one need?
• How best to administer?
• How best to monitor?
AI outcomes with current steroid replacement

• How much steroid does one need?
• How best to administer?
• How best to monitor?
  – Cortisol day curves (0, 1, 2, 5, 9h with TID HC)
  – UFC
  – ACTH
  – Salivary cortisol

Johannsson et al, Clin Endo 2015
AI outcomes with current steroid replacement

• How much steroid does one need?
• How best to administer?
• How best to monitor?
  – Cortisol day curves (0, 1, 2, 5, 9h with TID HC)
  – UFC
  – ACTH
  – Salivary cortisol
  – Clinical well being & monitoring for over treatment

Johannsson et al, Clin Endo 2015
AI outcomes – Mortality
Table 2. Summary of studies investigating mortality in patients with primary adrenal insufficiency

<table>
<thead>
<tr>
<th>Reference</th>
<th>Total number of deaths</th>
<th>Mortality findings</th>
<th>Number of events</th>
<th>RR/SMR/SIR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bergthorsdottir et al.</td>
<td>507</td>
<td>All-cause mortality</td>
<td>208</td>
<td>2.19 (1.91–2.51)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR men</td>
<td>299</td>
<td>2.86 (2.54–3.20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR women</td>
<td>103</td>
<td>1.97 (1.61–2.39)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cardiovascular mortality</td>
<td>136</td>
<td>2.31 (1.94–2.74)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR men</td>
<td>36</td>
<td>1.61 (1.13–2.23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR women</td>
<td>37</td>
<td>1.47 (1.03–2.02)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Death from neoplastic disorder</td>
<td>15</td>
<td>1.74 (0.97–2.87)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR men</td>
<td>30</td>
<td>3.74 (2.52–5.34)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Death from infectious disorder</td>
<td>6</td>
<td>6.57 (2.56–15.17)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR men</td>
<td>6</td>
<td>5.57 (2.04–12.13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Death from respiratory disorder</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR men</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR women</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Death in patients with concomitant DM compared with those without DM</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR men</td>
<td>NR</td>
<td>1.82 (1.29–2.60)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR women</td>
<td>NR</td>
<td>1.52 (1.11–2.07)</td>
</tr>
<tr>
<td>Bensing et al.</td>
<td>1621</td>
<td>Overall mortality</td>
<td>1621</td>
<td>2.7 (2.6–2.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SMR all</td>
<td>653</td>
<td>2.5 (2.3–2.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SMR men</td>
<td>968</td>
<td>2.9 (2.7–3.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SMR women</td>
<td>1333</td>
<td>2.8 (2.6–2.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SMR no APS</td>
<td>55</td>
<td>4.6 (3.5–6.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SMR APS1</td>
<td>233</td>
<td>2.1 (1.9–2.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SMR APS2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SIR all</td>
<td>333</td>
<td>1.3 (1.2–1.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SIR no APS</td>
<td>275</td>
<td>1.4 (1.2–1.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SIR APS1</td>
<td>13</td>
<td>2.3 (1.2–3.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SIR APS2</td>
<td>45</td>
<td>0.9 (0.6–1.2)</td>
</tr>
<tr>
<td>Erichsen et al.</td>
<td>132</td>
<td>Overall mortality</td>
<td>132</td>
<td>1.15 (0.96–1.35)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SMR all</td>
<td>35</td>
<td>1.18 (0.92–1.44)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SMR men</td>
<td>77</td>
<td>1.10 (0.80–1.39)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SMR women</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SMR diagnosis before 40 years of age (all)</td>
<td>NR</td>
<td>1.50 (1.09–2.01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SMR diagnosis before 40 years of age (men)</td>
<td>23</td>
<td>2.03 (1.19–2.86)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SMR diagnosis before 40 years of age (women)</td>
<td>NR</td>
<td>1.23 (0.70–1.76)</td>
</tr>
</tbody>
</table>

APS, autoimmune polyendocrine syndrome; CI, confidence interval; DM, diabetes mellitus; NR, not reported; RR, risk ratio; SIR, standardized incidence ratio; SMR, standardized mortality ratio.
*Estimated based on other data in the publication.
AI outcomes – Mortality

Primary AI

• Observational 2x mortality risk
  – Those with DM had greater risk
  – CV, neoplastic and infectious fatalities
  – Acute adrenal failure contributing to 15% of deaths

Johannsson et al, Clin Endo 2015
AI outcomes – Mortality

Primary AI
• Observational 2x mortality risk
  – Those with DM had greater risk
  – CV, neoplastic and infectious fatalities
  – Acute adrenal failure contributing to 15% of deaths

Secondary AI
• Risk of premature death and pituitary failure established
  – Difficult to tease out contributors
  – 5-6 SMR for infectious fatalities (ACTH def. in 82-100% and half considered to be in adrenal crisis)

Johannsson et al, Clin Endo 2015
AI outcomes – Bone metabolism

• Steroids reduces bone remodeling
• BMD data \textit{(on steroid REPLACEMENT patients)}
  – No reduction vs. post menopausal reduction vs. women only reduction
  – Inverse correlation between BMD and steroid dose per Kg weight
• Fracture data
  – Hip # HR 1.8 (vs. age and sex matched controls)
  – 784 vs. 434/100000 person-years in controls

Johannsson et al, Clin Endo 2015
AI outcomes – BP & vascular health

• Hypertension risk from steroid replacement
  – Permissive effect on other vasoactive agents
  – Direct effect of Hydrocortisone (MR effect)
• Atheroma progression with high dose steroids
  – RR 2.56 for CV event (68781 patients vs. 82202 non steroid users)
• Atherosclerosis prevalence in hypopituitariarism (but more related to untreated GH deficiency)

Johannsson et al, Clin Endo 2015
AI outcomes – Glucose & Lipid

- Dose related metabolic syndrome risk in hypopituitarism
- Increased co-incidence of type 1 diabetes and double whammy effect

Johannsson et al, Clin Endo 2015
AI outcomes – Body composition

- Dose & potency related BMI, waist circumference & waist:hip risk in hypopituitarism (n=717)
- 7.1kg reduction in body fat with reduction of steroid dose by 50% (no change in weight)
- Conventional vs. novel hydrocortisone replacement impacting on weight?

Johannsson et al, Clin Endo 2015
AI outcomes – QoL

• Norwegian population study (989 PAI or SAI)
  – 2.68 x affective & 2.12 x depressive disorders
• 18-25% out of work or on benefits (vs. 4.1% general population)
• Worldwide survey (1245 patients with AI)
  – 64% report compromised health
  – 40% report absence from school or work (3m before)
  – 76% concerned about future health
  – 38% hospitalized in the previous year
• Dose related reduction in QoL scores

Johannsson et al, Clin Endo 2015
Adrenal insufficiency outcomes – Adrenal crisis
Adrenal insufficiency outcomes – Adrenal crisis

Definition:
(A): Major impairment of general health with at least two of the following signs/symptoms
   Hypotension (systolic blood pressure < 100 mmHg)
   Nausea or vomiting
   Severe fatigue
   Fever
   Somnolence
   Hyponatraemia (≤132 mmol/l) or hyperkalaemia
   Hypoglycaemia
(B): Parenteral glucocorticoid (hydrocortisone) administration followed by clinical improvement

Grading:
Grade 1: outpatient care only
Grade 2: hospital care (general ward)
Grade 3: admission to intensive care unit
Grade 4: death from adrenal crisis (with or without parenteral glucocorticoid administration)
Adrenal insufficiency outcomes – Adrenal crisis

• Incidence
  – 5-10 per 100 patient years in patients on standard replacement
  – Prospective data: 64 crises in 767.5 patient years (8.3/100 pt years)
  – Mortality rate from crisis: 0.5/100 pt years

Johannsson et al, Clin Endo 2015
Allolio B, E J Endo 2015
Causes of adrenal emergencies

- 8% of Addisonian patients per year

- Vomiting 37%
- Diarrhoea 24%
- ‘Flu 10%
- Major infection 7%
- Blackout/Unconscious 6%
- Surgical recovery 6%
- Flu-like illness 4%
- Injury/Severe pain 3%
- Shock 2%
- Don’t know 1%
- Other

UK survey results 2003 N = 432

White & Arlt Eur J Endo 2010
Adrenal crisis - pathophysiology

- Permissive (cardiovascular responsiveness) versus suppressive influence of steroids at times of stress

Euadrenal

Hypoadrenal

Allolio B, E J Endo 2015
Pathophysiology of adrenal crisis

- Salt depletion: mineralocorticoid effect
  - Hypotension, postural
  - Tachycardia (bradycardia)
  - Electrolyte disturbance: back pain, muscle spasm

- Glucocorticoid deficiency
  - Vomiting, diarrhoea
  - Loss of appetite, weight loss, hypoglycaemia
Tips in diagnosis

• Some patients adapt very well to salt loss
  – Ask about salt cravings/ dietary habits

• Patients who have been vomiting may not be hyperkalaemic or acidotic

• Raised TSH, calcium may be a giveaway
Adrenal crisis - treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose/procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>100 mg bolus given immediately followed by 200 mg/day as continuous infusion or frequent i.v. (or i.m.) boluses (50 mg) every 6 h</td>
</tr>
<tr>
<td>Intravenous substitution of fluids</td>
<td>1000 ml of 0.9% sodium chloride during the first 60 min, further fluid administration (0.9% sodium chloride) guided by individual patient needs as assessed clinically or by central venous pressure; frequent haemodynamic monitoring to avoid fluid overload; measurement of serum electrolytes</td>
</tr>
<tr>
<td>Depending on the severity of the crisis and on the intercurrent illness</td>
<td>Admission to the intensive care or high-dependency unit; low-dose heparin; antibiotic treatment</td>
</tr>
</tbody>
</table>
Ongoing management

• Despite salt-depletion fludrocortisone isn’t necessary in first instance
  – Doses of Hydrocortisone >50mg daily act on mineralocorticoid receptor

• Many patients may be safely discharged once taking oral medication, often 36 or 48hrs after admission

• Review with the patient the opportunities to avert the crisis or admission

• ? Frequent crisis patient ?
Adrenal crisis - prevention

- Use of stress steroid doses reduced incidence of hospitalization to 27% (from 48%)
- Non adherence to sick day rules contributed to majority of adrenal crisis
Adrenal crisis – prevention (medics)

Sick day rules for elective procedures

**Table 3** Hydrocortisone adjustments for medical procedures (modified from (49)).

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Preoperative needs</th>
<th>Postoperative needs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major surgery</td>
<td>Start hydrocortisone infusion (100 mg over 12 h) just before anaesthesia</td>
<td>Continue hydrocortisone infusion (100 mg over 12 h) until able to eat and drink. Then double oral dose for 48 + h, then taper to normal dose</td>
</tr>
<tr>
<td>Labour and vaginal birth</td>
<td>Start hydrocortisone infusion (100 mg hydrocortisone over 12 h) at onset of labour</td>
<td>Continue hydrocortisone infusion until delivery (100 mg over 12 h). Double oral dose for 24–48 h after delivery, then taper to normal dose</td>
</tr>
<tr>
<td>Minor surgery and major dental surgery</td>
<td>100 mg hydrocortisone before anaesthesia given as a bolus intramuscularly or subcutaneously or as hydrocortisone infusion for the duration of surgery</td>
<td>Double oral dose for 24 h, then return to normal dose</td>
</tr>
<tr>
<td>Invasive bowel procedures requiring laxatives</td>
<td>Hospital admission overnight with 100 mg hydrocortisone intramuscularly or subcutaneously and fluid (isotonic saline), repeat dose before start of procedure</td>
<td>Double oral dose for 24 h, then return to normal dose</td>
</tr>
<tr>
<td>Dental procedure</td>
<td>Extra morning dose 1 h before surgery</td>
<td>Double oral dose for 24 h, then return to normal dose</td>
</tr>
<tr>
<td>Minor procedure</td>
<td>Usually not required</td>
<td>Double oral dose for 24 h, then return to normal dose Extra dose (e.g. 20 mg hydrocortisone) if symptoms persist</td>
</tr>
</tbody>
</table>

Allolio B, E J Endo 2015
Adrenal crisis – prevention (patient)

- Education, Education, Education

- Sick day rules for inter-current illness
  - BE AWARE THAT ONE IS ON STEROIDS
  - NEVER OMIT
  - IF UNWELL, DOUBLE THE ORAL DOSE FOR THE DURATION OF ILLNESS
  - IF VOMITTED OUT, TRY RE-DOSING AND IF STILL CANT KEEP IT DOWN, GET TO THE NEAREST A&E FOR IM/IV DOSAGE
  - REMIND ANY CLINICIAN ABOUT BEING ON STEROIDS
Adrenal crisis – prevention (patient)

- Education, education, education
- Sick day rules for inter-current illness
  - Pragmatic
  - Better to over estimate than under
  - Better to focus on chronic over-replacement
  - Early parenteral top up especially with GE
- Well informed patient guiding the busy clinician

Allolio B, E J Endo 2015
Steroid Card KTPH Initiative
INSTRUCTIONS

1. **ALWAYS CARRY THIS CARD** with you and show it to any medical practitioner you consult.

2. **DO NOT STOP** taking your steroid replacement without consulting your doctor.

3. If you accidentally miss a dose, take it as soon as you remember.

4. When you are not well (infections of moderate severity, dental procedures, surgery), you need more steroids and as a minimum you must **double your dosage** for the duration of these illnesses.

5. If you are unable to take the steroids by mouth (vomiting or unable to swallow), please go to the nearest emergency department to have it given as an injection.

---

**I am a patient on STEROID REPLACEMENT**

My Steroid Replacement is:

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For Condition: ____________________________

Patient’s Label

Drug Allergy: ____________________________
**ARAHAN**

1. **SENTIASA BAWA KAD INI** bersama anda dan tunjukkan kepada sebarang pengambilan perubatan yang anda temui.

2. **JANGAN BERHENTI** mengambil pengganti steroid anda tanpa mendapatkan nasihat doktor.


4. Apabila anda tidak sihat (jangkitan yang sederhana berat, prosedur perigian, pembedahan), anda menerapkan lebih banyak steroid dan secara minimum anda mesti menggandakan dos anda sepanjang tempoh penyakit tersebut.

5. Jika anda tidak dapat mengambil steroid melalui mulut (mentah atau tidak boleh menelan), sila pergi ke jabatan kecemasan yang terdekat untuk mendapatkannya melalui suntikan.

Untuk Keadalan:

Label Pesakit

Alahakah kepada Dadah: 

**ัญญิต้า**

1. ถ้าคุณเกิดปฏิกิริยาอันไม่คาดคิดหรือไม่เหมาะสมจากยาที่คุณได้รับ, ปรึกษาแพทย์เพื่อให้รับการดูแลที่เหมาะสมกับคุณ

2. คุณต้องมั่นใจว่าการใช้ยาสามารถทำได้โดยสมบูรณ์。

3. ยาเหล่านี้สำหรับคนที่มีการไม่สม่ำเสมอในระบบทางเดินหายใจ, สามารถทำให้เกิดการไม่สม่ำเสมอในระบบทางเดินหายใจได้

4. ยาเหล่านี้สำหรับคนที่มีการไม่สม่ำเสมอในระบบทางเดินหายใจ, สามารถทำให้เกิดการไม่สม่ำเสมอในระบบทางเดินหายใจได้

5. ยาเหล่านี้สำหรับคนที่มีการไม่สม่ำเสมอในระบบทางเดินหายใจ, สามารถทำให้เกิดการไม่สม่ำเสมอในระบบทางเดินหายใจได้

Patient’s Label
Conclusions

• Steroid replacement in AI is life saving
• Conventional therapy is associated with
  – Reduced life expectancy
  – Increased morbidity
  – Reduced QoL
  – Has not eliminated risk of adrenal crisis
• Continued challenges largely from
  – Lack of patient education
  – Failure to individualize treatment
  – Failure to provide adequate treatment at times of stress
• Need for continued research on alternative methods of steroid replacement
Adrenal Steroidogenesis after B Lymphocyte Depletion Therapy in New-Onset Addison’s Disease

Simon H. S. Pearce, Anna L. Mitchell, Stuart Bennett, Phil King, Sukesh Chandran, Sath Nag, Shu Chen, Bernard Rees Smith, John D. Isaacs, and Bijay Vaidya

October 2012 JCEM

- 6 patients recruited within 28 days of diagnosis
- Treated with B lymphocyte depletion
  - Rituximab 1g twice
- All measurements 36-40hrs off medication
## Demographics & baseline data

<table>
<thead>
<tr>
<th>Sex</th>
<th>Duration of illness</th>
<th>Serum Na / K at diagnosis (mmol/l)</th>
<th>Peak serum cortisol (nmol/l)</th>
<th>Plasma ACTH (ng/l)</th>
<th>Adrenal cell Ab *</th>
<th>21-hydroxylase Ab (U/ml) †</th>
</tr>
</thead>
<tbody>
<tr>
<td>F 44</td>
<td>6 mo</td>
<td>132/ 5.2</td>
<td>209</td>
<td>&gt;1250</td>
<td>Neg</td>
<td>0.68</td>
</tr>
<tr>
<td>F 19</td>
<td>4 mo</td>
<td>130/ 5.3</td>
<td>111</td>
<td>&gt;1250</td>
<td>Pos</td>
<td>345</td>
</tr>
<tr>
<td>F 38</td>
<td>12 mo</td>
<td>132/ 4.4</td>
<td>80</td>
<td>ND</td>
<td>Pos</td>
<td>1669</td>
</tr>
<tr>
<td>M 25</td>
<td>1.5 mo</td>
<td>116/ 5.4</td>
<td>145</td>
<td>430</td>
<td>Neg</td>
<td>1.29</td>
</tr>
<tr>
<td>F 17</td>
<td>6 mo</td>
<td>118/ 4.9</td>
<td>235</td>
<td>629</td>
<td>Pos</td>
<td>19200</td>
</tr>
<tr>
<td>M 47</td>
<td>4 mo</td>
<td>130/ 5.0</td>
<td>70</td>
<td>&gt;1250</td>
<td>Neg</td>
<td>6.3</td>
</tr>
</tbody>
</table>
Peak serum cortisol (post SST)

Replacement Rx stopped

Months

Diagnosis

Peak serum cortisol (nmol/l)
21-hydroxylase antibody levels

Serum 21-hydroxylase antibodies (% of baseline)

Months

0 3 6 9 12
THANK YOU