Insights into MAnaging Growth for Endocrine Nurses

12-13 October 2017, Toulouse, France

An Independent Medical Education Event for Paediatric Nurses

CAH presenting as DSD

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Introduction

- Reminder of CAH
- How 46XX CAH sits within the Disorders of Sex Development (DSD) service
- Case study
- Clinical Nurse Specialist roles
- Conclusion

CAH – reminder of key points

- An adrenal enzyme defect
- Classical 21-hydroxylase deficiency is the most common
  - 1 in 15,000 births in the UK
- Results in glucocorticoid and mineralocorticoid deficiency
  - ↑ ACTH secretion by the anterior pituitary
  - Accumulation of steroid precursors prior to the enzyme defect
  - ↑ androgens production

Diagnosis in Boys

- Can have hyperpigmented scrotum and genitalia at birth, but usually look ‘normal’
- Presentation
  - Day 5
  - Second week of life
    - Poor feeding, weight loss, failure to thrive
  - If CAH not recognised
    - Salt losing crisis
      - Due to the aldosterone loss

Diagnosis in Girls

- Genitalia are usually virilized due to excess testosterone
  - Allows earlier diagnosis
- Mild clitoromegaly to full masculinisation
  - Prader staging
- DSD service

Diagnosis

- Confirmed by a raised 17OHP level after day 3 of life
- Salt wasting confirmed by:
  - Low plasma sodium
  - High potassium
  - Increased urinary sodium excretion
  - Virilised girls
    - Chromosome analysis
    - Pelvic ultrasound

Biochemical investigations

- Short synacthen test

Time	Cortisol	17-OHP	11-DOC	A4	ACTH	Renin
0	√	√	√	√	√	√
30	√	√	√	√		
60	√	√	√	√		

- Synacthen given IM or IV
  - 0 – 6 months: 62.5mg
- Urine
  - Steroid analysis to confirm the 21-hydroxylase deficiency defect

Medical management

- Hydrocortisone 10mg tablets
  - 10 – 15 mg/m2/day
  - Total dose spread 3 – 4 times throughout the day
- Fludrocortisone 100 mcg tablets
  - 150 mcg / m2/ day
- Salt supplements
  - Oral salt supplements (until one year of age) in the 5mmol/ml 30% Sodium Chloride solution – 5mmols/kg/day, in 4 divided doses = …….mls per dose four times a day
  - Can stop when fully weaned

Classification of DSD

- 46,XY DSD (under virilised genetic male)
  - Disorders of testicular development
    - Ovotesticular DSD
  - Disorders of androgen synthesis / action
    - CAIS
  - Others
    - Hypospadias
- 46,XX DSD (over virilised genetic female)
  - Disorders of ovarian development
    - Ovotesticular DSD
  - *Androgen excess*
    - *CAH*

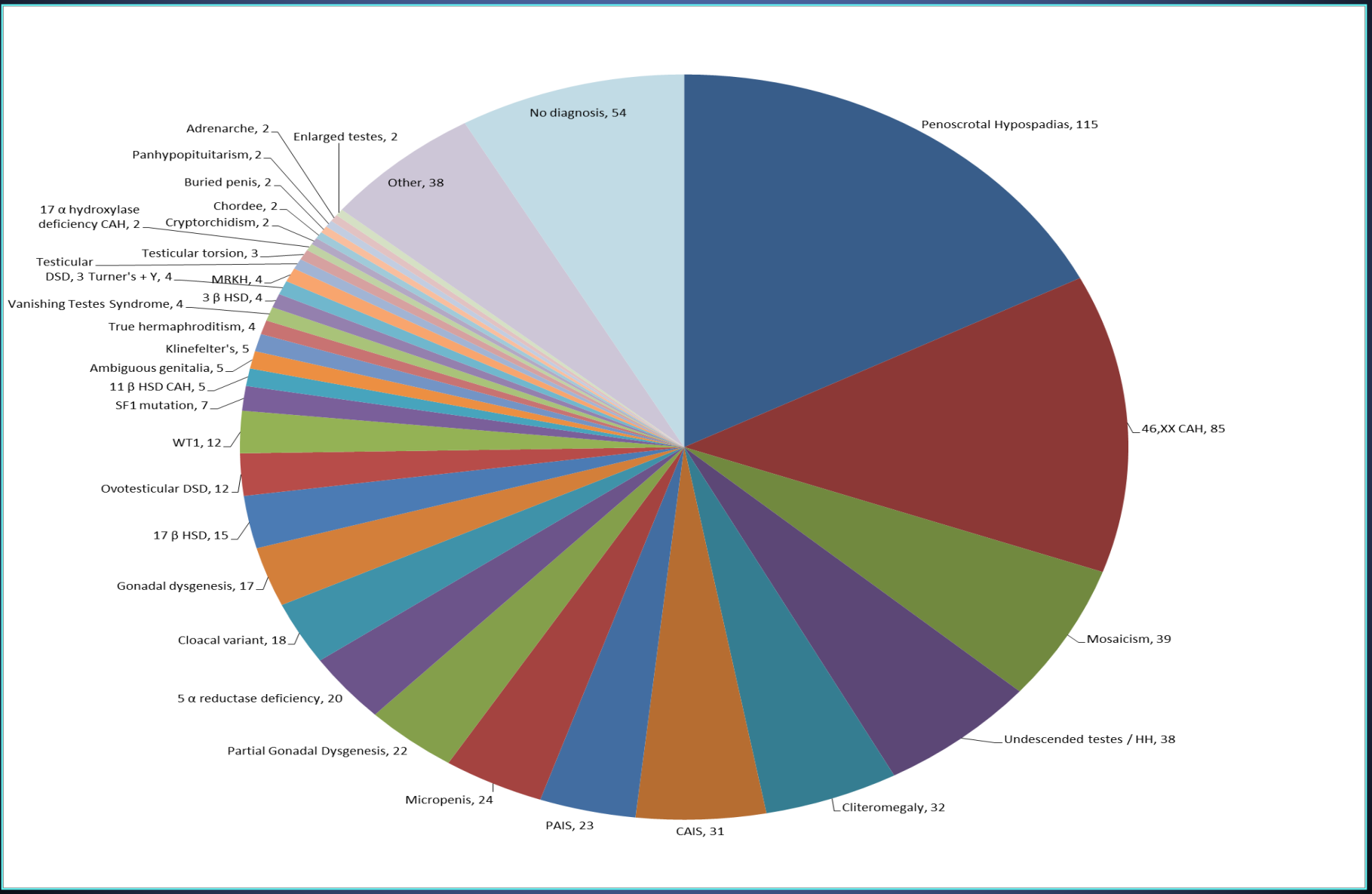
- Sex chromosome DSD (variable)
  - Turner's syndrome
  - Klinefelter's syndrome
  - Mixed gonadal dysgenesis

Lee et al (2006)
Consensus Statement on Management of Intersex Disorders

46XX CAH in DSD service

- Ambiguous genitalia
  - More than half of all infants born with AG are 46XX
    - Due to in utero exposure of androgens
    - Source may be adrenal (CAH) or testicular
- Complex congenital malformations
  - Cloacal extrophy, or bladder extrophy
- Gradual clitoris enlargements during childhood
  - Non classical CAH
- Abnormal developments at puberty
  - Primary amenorrhoea
    - No breast or pubic hair development (46XX gonadal dysgenesis or steroid biosynthetic defects) OR
    - Normal breast and pubic hair development (Mullerian duct agenesis)
    - Normal breast development but little or no pubic hair (CAIS)

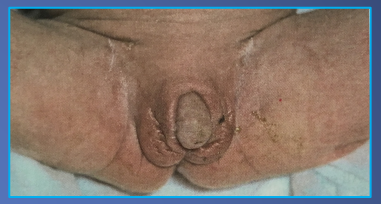
GOSH DSD data over 21 years N= 657



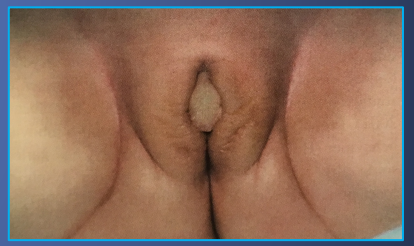
46XX CAH

- Baby will have been exposed to excess male hormone in-utero
- The genitalia will look like a boy's:
  - Labia will fuse to look like a scrotum
  - Clitoris enlarges and looks like a penis
- Can sometimes be so severe, sex assignment is difficult
  - Need karyotype
  - Will still have normal internal structures
  - Surgery may be needed to correct outer appearance
    - CONTROVERSIAL

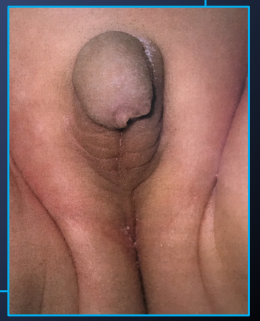
- Exposure to prenatal androgens and Prader III virilisation at birth



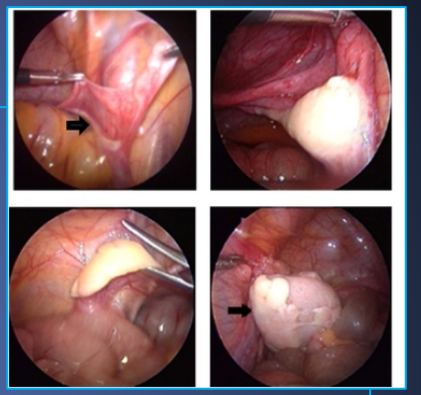
- Same baby at age 8 weeks at the time of genital reconstruction, showing some regression of virilisation after starting steroid treatment



- Another baby girl with a more severe form of 21OHD, leading to more severe virilisation (Prader IV)



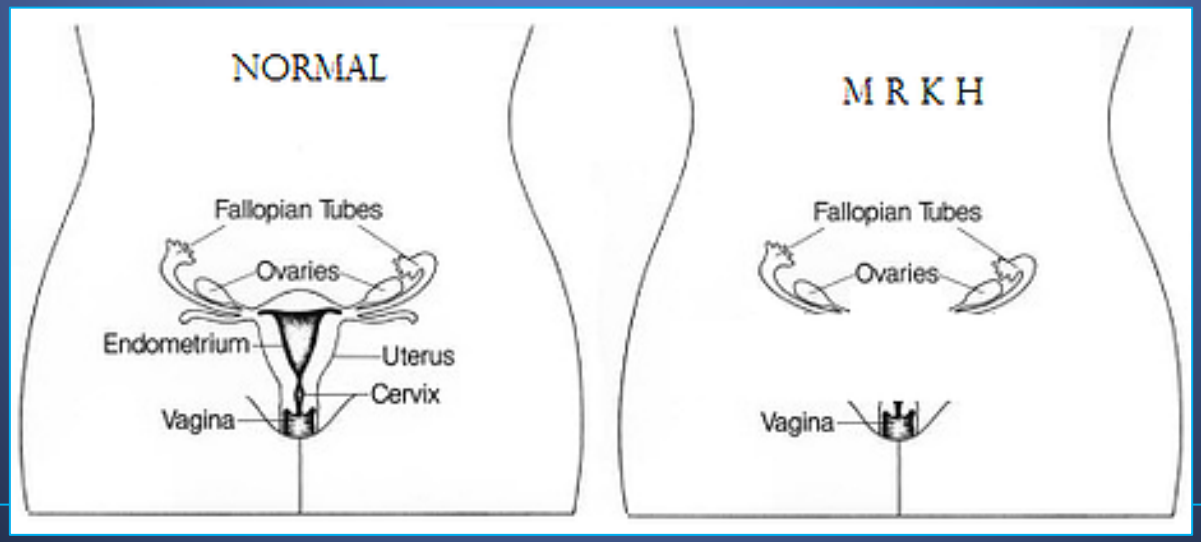
46XX Gonadal Dysgenesis



- Mutations in FSH receptor gene has been identified
- ‘Pure’ without features of Turner Syndrome
- Streak gonads are present due to germ cells not forming properly
  - Mostly composed of fibrous tissue
- Characterised by primary amenorrhoea with or without secondary sexual characteristics

46XX Mullerian Duct Agenesis

- Vaginal agenesis usually associated with an absent uterus and fallopian tubes but with normal ovarian development
  - Mayer–Rokitansky–Küster–Hauser syndrome



Case study

- 3/52 baby girl
  - 2nd opinion
  - ? Future management
- Born at term
- Weight 4.53kg
- Non-consanguineous parents
- No family history of any DSD

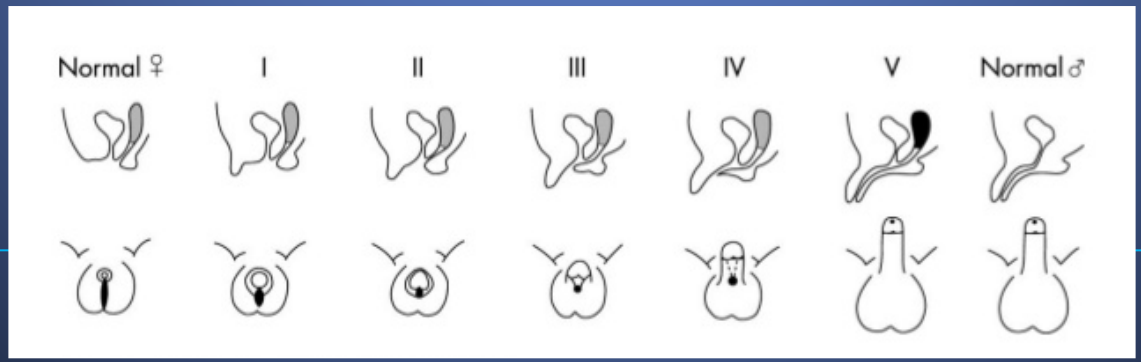
Case study

- Ante-natal USS
  - Boy
- Baby born
  - Male sex of rearing assigned
  - Given a male name
- Post natal check
  - No testes in scrotum
- Urgent USS..

- Normal bladder and kidneys
- No testes or ovaries
- Chromosomes
  - 46XX
- Bloods
  - ↑ 17OHP
  - 101.9 nmol/L (normal range 0– 5 nmol/L)
- Local Paediatrician
  - 21OHD CAH
  - Hydrocortisone and Fludrocortisone

Referral

- Parents very anxious
  - Genital reconstructive surgery
  - Father very angry
- Referral into the DSD MDT
- On examination
  - Prader V in Prader scoring system



Further investigations

- Repeat Pelvic USS
  - No testes
  - Ovaries seen

- Review of management, including intensive support and input from CNS

Change from hydrocortisone suspension to tablets

Medication review

- Stay on same dose of Fludrocortisone
- Hydrocortisone suspension three times a day
  - 2/2/3mg
- Changed to hydrocortisone 10mg tablets
    - 1.25mg four times a day
    - Guidance given on crushing and mixing with water breast milk
    - Dosage titrated against BSA calculations
      - Side effects of underdosing → androgenisation
      - Side effects of overdosing → Cushings
      - Regular bloods
- Intensive emergency management training
  - x 3 emergency hydcrocortisone packs prescribed and administered

CNS relationship with family

- Advanced knowledge on prescribing
  - Builds strong, trusting relationship with family
  - ? Increased compliance
  - Key team liaison
    - Any concerns
    - Difficulties with prescription
  - Liaison with Primary Care
    - GP
    - Health Visitors
      - School
  - ? Reduce unnecessary trips to GP / Hospital for specialised repeat prescriptions

Why tablets?

- Hydrocortisone suspension not bioequivalent to Hydrocortisone tablets (Merke, 2001)
- Instructions given:
  - Cutting and crushing tablets

Suspension v tablets

- ↑ need for higher hydrocortisone doses in children on liquid hydrocortisone
  - Inadequate control of androgens
  - Signs and symptoms of Cushing's syndrome
  - Endocrine Society Clinical Practice Guideline (2010)

Instructions for Hospital Doctor

Dear Doctor,

If this patient is brought to hospital as an emergency the following management is advised:

1) Insert an IV cannula
2) Take blood for U&Es, glucose, and perform any other appropriate tests (e.g. urine culture)
3) Check capillary blood glucose level
4) Give 100 mg hydrocortisone intravenously as bolus (unnecessary if patient has already been given IM hydrocortisone)
5) Commence IV infusion of 0.45% sodium chloride and 5% glucose at maintenance rate (extra if patient is dehydrated). Add potassium depending on electrolyte
6) Commence hydrocortisone infusion (50 mg hydrocortisone in 50ml 0.9% sodium chloride via syringe pump)
7) Monitor for at least twelve hours before discharge

IMPORTANT! If blood glucose is < 2.5 mmol/l, give bolus of 2 ml/kg of 10% glucose

If patient is drowsy, hypotensive and peripherally shut down with poor capillary return give 20ml/kg of 0.9% sodium chloride stat.

If in any doubt about this patient's management, please contact the urgent advice numbers

Useful Contact Numbers:

GOSH Switchboard
Tel: 020 7405 9200

For Urgent Advice:
Tel: 020 7405 9200 and ask to be put through to the endocrine registrar on call

University College Hospital Switchboard
Tel: 0845 155 5000

For Urgent Advice:
Tel: 0845 155 5000 and ask to be put through to the endocrine registrar on call.

Great Ormond Street Hospital for Children NHS Trust and University College London Hospitals NHS Foundation Trust

CORTISOL DEFICENCY

THE OWNER OF THIS CARD IS ON CORTISOL REPLACEMENT THERAPY

Name
Address
Tel
Mobile:
Date of Birth ___/___/___
Hospital No
Consultant
Hospital
Address
Tel Fax
General Practitioner
Address
Tel Fax

Affix photo here

Great Ormond Street Hospital for Children NHS Trust and University College London Hospitals NHS Foundation Trust

3. Draw up 2mls of cooled, boiled water into a 2ml syringe
4. Mix the crushed ¼ of a tablet with the 2mls of cooled boiled water
5. Then draw up 1ml of the mixture to give 1.25mg
6. Give by mouth as shown by ward nurses

Great Ormond Street Hospital for Children NHS Trust

Great Ormond Street Hospital for Children NHS Trust

Great Ormond Street
London WC1N 3JH

Tel: 020 7405 9200

Gastroenterology, Endocrinology, Metabolic & Adolescent Medicine (GEMA)
Direct Line: 0207-813-8214

cortisone (oral)
cortisone (oral)
supplements 5mmol/ml 30% solution:
ospital Doctor

nts cortisol deficiency, if this patient is brought to hospital as an emergency, gement is advised:

wsy and unresponsive give IM hydrocortisone in the following doses (0-1yr – 25mgs; 1-5 yrs – 50mgs; > 5yrs – 100mgs) if patient has not already ocortisone administered by ambulance crew or parents.

for U&Es, glucose and osmolality

ose is < 2.5 mmol, give bolus of 2mg/kg 10% dextrose

- If patient is drowsy, hypotensive and peripherally shut down, give 20ml/kg of nor insert an IV cannula and then continue with usual dextrose saline infusion
- Continue with bolus IV hydrocortisone at 2mg/kg every 4 hours until patient is to oral fluids and then swap to double usual oral Hydrocortisone doses until patient recovered and back to normal self (usually 2-3 days on double usual hydrocortis doses).
- Important: Please admit for a minimum of 12 hours

If there is ar a Great Street Hosp on Call)

for Children NHS Foundation Trust: Information for Families

Congenital adrenal hyperplasia (CAH)

reat Ormond Street Hospital
dical condition congenital
what to expect when your
sment and treatment.

Congenital adrenal hyperplasia is

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Great Ormond Street Hospital for Children NHS Trust

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London WC1N 3JH

Tel: 020 7405 9200

Gastroenterology, Endocrinology, Metabolic & Adolescent Medicine (GEMA)
Direct Line: 0207-813-8214

Date:
Reference:

Dr
Paediatric Consultant

Dear Dr

RE:

……is a …. year old ……under the care of …… at Great Ormond Street Hospital. He is a boy/girl with ……, he/she was referred with ……and we have since found he also has cortisol deficiency.

He/She has been commenced on Hydrocortisone at a dose of 2.5mg mane, 2.5mg at lunchtime, and 2.5mg nocte. ……'s mum has had education in his/her management during times of illness and has been trained in giving IM hydrocortisone should the need arise.

I would be extremely grateful if you could arrange for …… to have fast track access at the …… should he/she require emergency IM hydrocortisone. Please let us know on the number below.

Please do not hesitate to contact me should you require more information on 0207 813 8214.

Many thanks,

Yours sincerely

……
Clinical Nurse Specialist

Great Ormond Street Hospital for Childre

Cortisol deficiency steroid replacement the

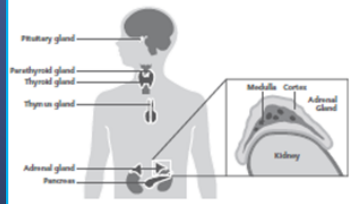
This leaflet explains about cortisol deficiency and how it is treated. It also contains information about how to deal with illnesses, accidents and other stressful events in children on cortisol replacement.

Where are the adrenal glands and what do they do?

The adrenal glands rest on the tops of the kidneys. They are part of the endocrine system, which organises the release of hormones within the body. Hormones are chemical messengers that switch on and off processes within the body.

The adrenal glands consist of two parts:

- the medulla (inner section) which makes the hormone 'adrenaline' which is part of the 'fight or flight' response a person has when stressed.
- the cortex (outer section) which releases several hormones.



●●●○○ O2-UK 22:02 100%

Great Ormond Street Hospital for Children NHS Foundation Trust

My Cortisol

London Ambulance Service NHS Trust

Patient Specific Protocol
PSP Paediatric Steroid Dependent Crisis

PSP

This protocol has been specifically prepared for STEROID DEPENDENT CRISIS patients and details the treatment to be given in specified circumstances.

Patient's Name: **Date of Birth:**

NHS Number:

Address:

School:-

Local hospital:

Reason for protocol: Administration of IM hydrocortisone in possible adrenal crisis

Specific Treatment / Instructions: Patient may have an adrenal crisis if IM hydrocortisone not administered in an emergency situation

In the event that this child is involved in an accident or develops diarrhoea or vomiting and presents with any symptoms of a steroid dependent crisis whilst at **Home or at School** they are to be administered IM hydrocortisone as detailed over leaf.

Note:- The IM hydrocortisone (Efcortesol) is kept both by the parents and by the school in an emergency pack.

Please transport this child to the above local hospital if possible, otherwise to the nearest paediatric A&E unit.

All other aspects of clinical care remain unchanged.

For further advice if necessary please contact the Endocrine Registrar on call via switchboard at Great Ormond Street Hospital on 020 7405 9200

1. Efcortesol 1ml ampoule (Hydrocortisone 100mg/ml - as sodium phosphate)

Dose: Age 0-1 years 25 mg IM
Age 1-5 years 50mg IM
Age 5+ years 100mg IM

2. Please also administer Glucogel (Hypostop) 25 gram tube, required dose in an emergency - up to 1/3 tube if not already previously administered by carers.

Following administration of the hydrocortisone remove to hospital with full monitoring and oxygen therapy as required.

All other aspects of clinical care remain unchanged.

If required contact EOC and ask for the Clinical Support Desk

PTO for further general info on Steroid Dependent Crisis

How to give an emergency injection of Efcortesol®

Information for families

Great Ormond Street Hospital for Children NHS Trust
University College London Hospitals NHS Trust

GP letter on discharge

GP details

Date

Dear Dr

RE:

Diagnosis: Congenital Adrenal Hyperplasia

…… was referred to us on …… from…… Hospital, and a diagnosis of Congenital Adrenal Hyperplasia has been made, and s/he has cortisol deficiency.

She/he has been commenced on the following medication and we would be very grateful if you could commence a repeat prescription for:

Hydrocortisone …… mg (as Hydrocortisone 10mg tablets, **NOT** suspension)
Fludrocortisone …… mcg daily
Oral salt supplements (until one year of age) in the 5mmol/ml 30% Sodium Chloride solution – 5mmols/kg/day, in 4 divided doses = ……mls per dose four times a day

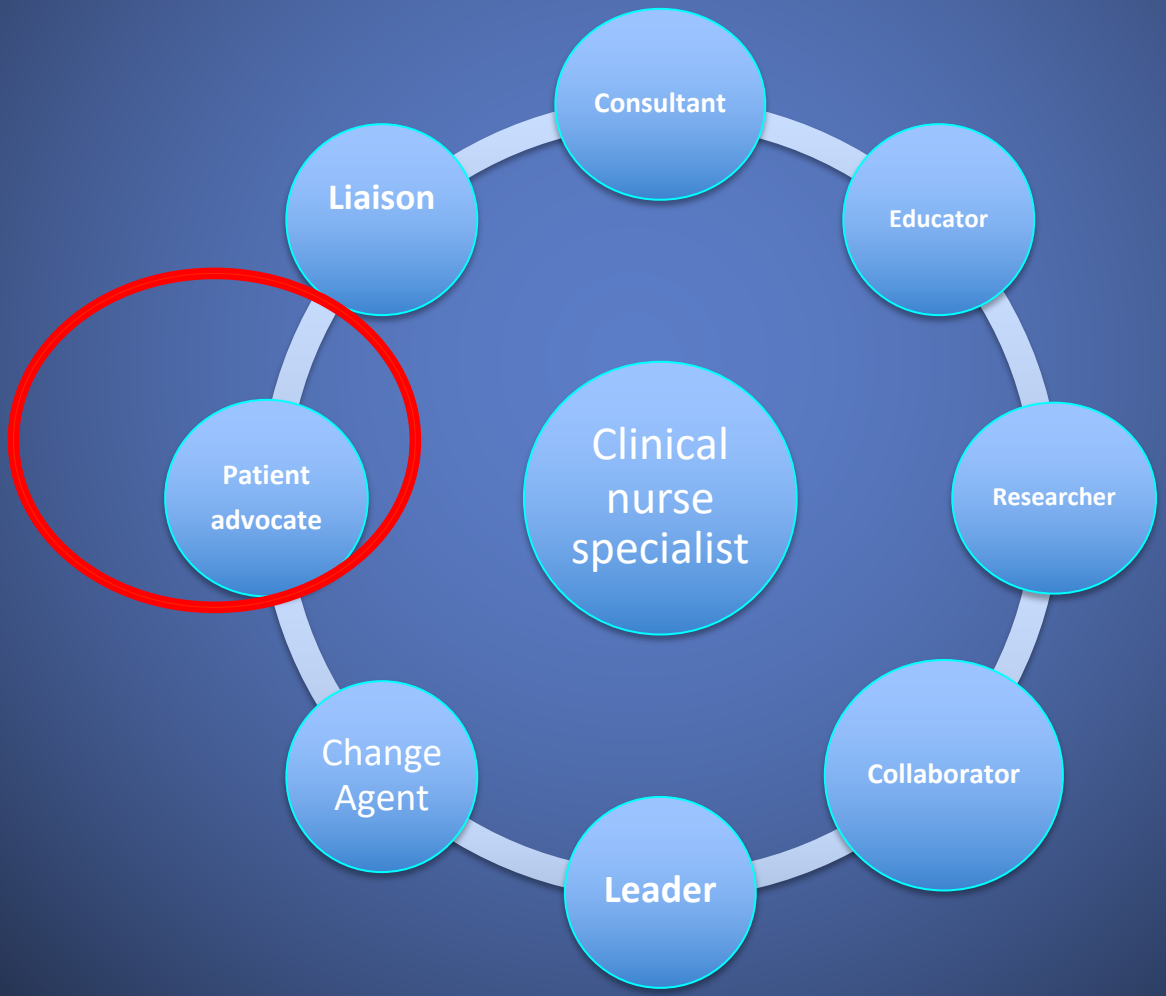
Also to be included on his/her prescription:
Hydrocortisone Emergency Pack to be renewed yearly:
Efcortesol 100mg vials, 25/50/100mg to be given IM in an emergency.
Glucose Gel 25g tube, 1/3 tube orally to be given in an emergency.

We have given ……'s parents a tablet cutter and a tablet crusher, and have educated them in how to prepare and administer their medication. ……'s parents have had education in his/her management during times of illness and they have been trained in giving IM hydrocortisone, 25/50/100mg, should the need arise, along with oral glucose gel. A steroid card has been given, and also information about Medic Alert jewellery to start wearing as soon as possible.

We have arranged with the local hospital and the local Paediatrician (……) to have fast track access should he/she require emergency IM hydrocortisone. We have also set up an arrangement with ……Ambulance Service to ensure a red alert system is in place.

- Medication onto repeat prescription system
- Tablets not suspension
- Also highlights that the baby can have all of their usual childhood immunisations

Clinical nurse specialist roles



CNS advocate role – at diagnosis

- Ensure referring team has parents admission leaflet
- Liaising with the MDT
  - From the referring team and also the team being referred to
  - Is the baby well / hospitalised
  - Are they requiring transport / nurse escort / will that nurse stay with patient
- Liaising with the ward
  - Ensure GnRH, Synacthen and HCG in stock on ward if need be
- Liaising with the parents!
- Prepare information packs for parents
  - DSD families leaflet
  - Cortisol deficiency booklets
  - CAH information
  - CNS contact details

- How is the baby feeding
  - Breast pump, bottles, quiet area available
  - Bottle feeding – enough milk
- Ensure parents bring
  - Phone chargers, nappies, wipes, books etc, lists of questions
  - Maternity notes, child health care notes, referral letters
  - Money for parking
- Can they speak English
  - Arrange interpreter, prepare translated information

CNS advocate role - ongoing

- Key liaison and support for family
- Involvement in support groups / support group days
- Be knowledgeable in specific condition and long term implications
  - Prepared for discussions on puberty and adolescence and beyond
- Liaise with adult DSD / gynaecology teams
- Patient and family empowerment

Conclusion

- Complexity of 46XX CAH discussed
- DSD service
- Management
  - Medical
  - Nursing
    - Focus on nursing roles
    - Optimise patient care

Thank you