CONGENITAL
ADRENAL
HYPERPLASIA
FAMILY CONFERENCE
SUNDAY 16TH MAY 1999

Transcripts prepared by Neil Cockburn
DTP by Melissa Cull

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GUEST SPEAKERS:

Dr Patricia Smith: Consultant Paediatrician & Paediatric Endocrinologist, City General Hospital, Stoke on Trent

Mr Adrian Bianchi: Consultant Paediatric Urologist, Manchester Children’s Hospital, Manchester

Dr Trevor Cole: Clinical Geneticist, West Midlands Regional Genetics, Women’s Hospital, Birmingham

Prof. Melissa Hines: Consultant Psychologist, UCLH, London

Mrs Kathryn May: Clinical Sexual Psychologist & Senior Lecturer, University of Central Lancashire, Preston

The CAH Support Group of CLIMB would like to thank all of the speakers referred to in this document for their participation and valuable contribution to the Stoke-on-Trent conference.

Please Note: This document is a summary of notes taken at the CAH conference at Stoke-on-Trent on 16th June 1999. Each section has been checked for accuracy by the relevant speaker and is correct at the time of printing. (Not withstanding typographical errors).
Dr Patricia Smith
Consultant Paediatrician & Paediatric Endocrinologist
(City General Hospital, Stoke on Trent)

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Transcript prepared by Neil Cockburn & checked for accuracy by Dr Smith

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"Nature may display her normal laws and secret mysteries through the study of rare forms of disease" William Harvey
1657

Management of CAH requires a multi-disciplinary approach; medical, surgical and psychological.
We already know a great deal and research is continuing.
Management of medication is about suppressing the hormones we don’t want and maintaining the levels of hormones wanted.

The problem facing parents is confusion of sex at birth - is the child a girl or a boy, parents naturally want to know definitively there and then. The question is "why can't we have an answer straight away" - it causes stress and turmoil not to have the answer immediately.

Parents need to know what the problem is and are frustrated by not being able to know; they want to know about the treatment, they want to know what to tell friends and family and just how to tell them. If the baby is different and is on an ordinary ward at the hospital it will draw unnecessary and unwanted attention, which brings further stress in itself for the parents.
Dr smith's recommendation would be to have a special mother and baby unit attached to the neonatal unit where the nursing staff and environment is better set up for support in cases like this.

**Some History !**

1865 Professor Luigi de Crecchio, an anatomist, did a post mortem on a Joseph Marzo. Joseph was considered female at birth but from age 4 conducted life as a male. The post mortem revealed masculinisation of the external genitalia 1st degree Hypospadias, normal internal female genitalia, cryptorchidism and adrenal hyperplasia. It was also quoted as saying it was of great importance to "determine the habits, tendencies, passions and general character of this individual". This may have been the first anatomist to describe behaviour and psychosexual orientation.

1887 Phillips, Study of 4 children born as hermaphrodites who died in early infancy with a wasting disease. It was quoted as fortunate for society that these "creatures do not survive, usually wasting and dying of inanition (exhaustion, as from lack of nourishment) shortly after birth.

1950 The first paper published detailing treatment with cortisone acetate.

**Ambiguity Types ~Disorders of Intersex = abnormalities of fetal sexual differentiation.**

- Female Pseudo-hermaphroditism - female fetus, XX (female) chromosomes, normal ovaries, abnormal virilisation.
- Male Pseudo-hermaphroditism - male fetus, XY (male) chromosomes, well differentiated testis, disturbance genital development; impaired virilisation at puberty.

**Sex of Individual determined by several different types**

- Genetic (chromosomes)
- Gonadal (ovaries/testes)
- Phenotypic (appearance)
- Sex of rearing
- Behavioural
- Secondary sexual development coinciding with adult gonadal function

One way to help the family in diagnosis is to do a chromosome test but if you do a pelvic ultrasound by a very well trained radiologist rather than a radiographer they should be able to see an endometrial echo on the uterus so that we can try to indicate that it is a baby with CAH, but we still have to wait for the blood tests. The hormones from the placenta(which was fed by the mother) still affect the baby 72 hours after birth, hence any blood tests need to be delayed by 72 hours to have any meaningful result. We have to think - What are the chromosomes, do we have ovaries or testes, what does the patient look like, because depending on the disorder, not CAH, but some of the other disorders we might have to have sex of rearing which is different from the chromosomes. From a practical point of view though , CAH is a group of disorders of adrenal sterodigenesis; an inherited deficiency in 1of 5 enzymes necessary for the conversion, in the adrenal cortex, of cholesterol to cortisol and aldosterone. At least 90% of cases are the 21 Hydroxylase deficiency. The adrenal glands sit on top of the kidneys and are under the control of the hypothalamus and the pituitary which is a little pea sized gland which sits at the base of the brain about an inch between the eyes. There are many hormones which are produced in the adrenal glands but they end up as cortisol sex steroids, aldosterone which controls the blood pressure.
and how much salt you retain, and cortisol which is what we need to fight infections and keep us generally well and healthy. When you have CAH you have a block, usually complete or partially complete, to the production of the aldosterone and the cortisol, all that the brain knows is that "hang on, I'm not producing enough of this product" and so it produces more and more of these other hormones to try and make the adrenal gland do its job. The consequence of that is to produce more ACTH. This comes from a long molecule which gets chopped in half, the other half is melanocorticotrophin - a melanocite (which in our skin causes sun tanning). The adrenal gland starting point is cholesterol and the end points are aldosterone, cortisol, androgens and oestrogens. If there is a break in the production of these because of a lack of a particular enzyme/hormone, then in CAH more testosterone is produced which gives little girls the ambiguity. It is an autosomal disorder. The prevalence in the UK is about 1:15,000 cf. Eskimo's where it is around 1:700.

Diagram to show the Control Loop for Adrenal Cortex stimulation

Cholesterol is the starting point in the adrenal cortex for conversion to the three main steroids as shown above: - Aldosterone (mineralocorticoid), Cortisol (Glucocorticoid) and Sex Hormones (androgens and oestrogens). A tanned appearance or easily tanned skin can be a symptom of CAH especially in boys. CAH is an auto recessive inheritance (see genetics ref Dr Cole later in these notes).
Chart to show different effects of CAH types on male and females

<table>
<thead>
<tr>
<th>ENZYME DEFICIENCY</th>
<th>XX Fetus</th>
<th>Girl</th>
<th>XY Fetus</th>
<th>Boy</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 HYDROXYLASE (most common &gt; 90%)</td>
<td>VIRILISATION</td>
<td>NORMAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 Beta HYDROXYLASE</td>
<td>VIRILISATION</td>
<td>NORMAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Beta HYDROXYSTEROID DEHYDROGENASE</td>
<td>MILD VIRILISATION</td>
<td>INCOMPLETE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17 Alpha HYDROXYLASE</td>
<td>NORMAL</td>
<td>INCOMPLETE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20.22 DESMOLASE</td>
<td>NORMAL</td>
<td>INCOMPLETE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Most children will need hydrocortisone and Fludrocortisone. What happens in practice is that some will have some ambiguity which is very severe or mild and this is described in 5 stages where stage 1 is completely female and stage 5 is completely male, with stages 2,3 and 4 being in between (!).

If babies present very ill it is important they have medical management straightaway. So if it is a little boy who has been vomiting it is very important that a drip with salt and glucose and steroids is given intravenously. It is important to get the diagnosis right and to get appropriate hormone replacement started.

**CLINICAL RECOGNITION**

**NEWBORN**

- ambiguous genitalia
- complete
- isolated clitoromegaly
- isolated labial fusion
- Cryptorchid, hypospadic "male"
- Salt wasting

**NEONATAL URGENT**

- chromosome test
- plasma 17 OHP (hydroxyprogesterone)

**IDENTIFIABLE CASES of NEWBORN CAH**

- All affected females
- Salt losers
- Cryptorchidism with Hypospadias
- Previous family history of CAH
- Positive prenatal diagnosis

**CLINICAL PRESENTATION**

Some children do not present in the neonatal period, but in childhood or Adulthood. It depends on the enzyme deficiency and if there is salt loss.
Through Childhood and Beyond

- **Pseudoprecocious puberty** (young boy who looks like he's going into puberty has a large penis but small testes because the hormones which produce puberty are not coming from the testes, they are coming from the adrenal glands. Normally boys penile development does not start until around 11 years old)
- **Isolated pubarche** (pubic hair)
- **Isolated clitoromegaly** (prominent clitoris)
- **Inappropriate rapid growth**
- **Hirsuitism** (hairiness)
- **Menstrual disorders**
- **Infertility**
- **Cryptic cases**

The growth hormone axis can be affected either directly by CAH or by hydrocortisone replacement therapy; growth consequently can be affected. It is therefore important to keep thinking all the time treatment is being given and growth is being monitored.

SCREENING

**Criteria for screening a (any) disorder at birth**

- Severe morbidity/mortality if undetected
- Effective treatment available
- Improved prognosis with early treatment
- Clinical screening unreliable
- Incidence of the disorder relatively high
- Cost of screening justifiable
- Screening is: simple, safe, reliable, rapid.

**Potential avoidable clinical problems**

- Salt wasting crisis
- Inappropriate diagnosis and treatment of pyloric stenosis
- Inappropriate gender assignment
- Precocious puberty
- Short stature
- Sudden unexplained death

TREATMENT

How to treat it - sufficient medication to replace the cortisol the patient is not making but not too much to give side effects, to replace salt retaining hormone because if you don't give sufficient salt retaining hormone you can't get the situation under control. The balance between the two is important to get the right control on growth.

- Correct sex assignment!
- Replace hormones - glucocorticoids (cortisone acetate, hydrocortisone) and mineralocorticoids (Fludrocortisone)
- Aim to suppress the ACTH drive.
Some typical treatment dosage levels

- Cortisone acetate 22-30 mg/m²/day
- Hydrocortisone  20-25 mg/m²/day
- Prednisolone   2-4  mg/m²/day (this most commonly started when puberty is reached and growth height has stopped)
- Dexamethasone  2-3  ug/kg/day
- Mineralocorticoid 100  ug/m²/day

- Growth data needs to be matched to the family profile not necessarily at the 50th centile. Growth rate should run parallel to the charted standard data.
- Parents and patients usually know best, especially when to give extra medication. In illness extra hydrocortisone either 2 or 3 times normal dose or intramuscularly as this could be lifesaving treatment before going to hospital. **It is vital that you insist with GP's and the like, when you believe it necessary to give additional medication!**
- You should have the courage to vary hydrocortisone up OR down to get optimum control and management of the condition.

EFFECTS OF INCORRECT TREATMENT DOSAGE

<table>
<thead>
<tr>
<th>UNDER TREATMENT</th>
<th>OVER TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excessive growth</td>
<td>Growth too slow</td>
</tr>
<tr>
<td>Further virilisation</td>
<td>Obesity (Cushing syndrome)</td>
</tr>
<tr>
<td>Advancing bone age</td>
<td>Blood pressure problems</td>
</tr>
<tr>
<td>Shorter adult height</td>
<td>Short as adults</td>
</tr>
</tbody>
</table>

TREATMENT SUCCESS INDICES

CLINICAL INDICES

- GROWTH
- BONE AGE
- pubertal deviation

CLINICAL AND BIOCHEMICAL INDICES

- PLASMA RENIN activity, potassium level
- Plasma ACTH
- Plasma 17 OHP, capillary 17 OHP
- Androstendione, venous, capillary, salivary
- Testosterone - age and sex dependant
- Urine steroid metabolites
- Growth velocity
- Bone age
- Blood pressure.
MANAGEMENT

AT BIRTH

- Urgent karyotype (chromosomal identification of gender)
- Antenatal diagnosis and/or female with genital ambiguity
- 17 OHP at 72 hours and timed urine
- Hydrocortisone 20mg/m2/day divided 8 hourly.
- Fludrocortisone 100 ug/m2/day
- Salt (NaCl) 5mmols/kg/day
- DO NOT WAIT FOR HYPONATRAEMIA / COLLAPSE.

AT PRESENTATION NaCl CRISIS / ILLNESS / SURGERY

- AIMS - Replace cortisol insufficiency and to correct hypoglycaemia
  a) hydrocortisone 25mg for 3-10kg in weight or 1mg/hour
     50mg for 10-20kg in weight or 2mg/hour
     100mg for >20kg in weight or 3mg/hour
  b) Correct hypoglycaemia then :- 10% dextrose (4-6mg/kg/hour)
  c) 0.9% saline 30ml/kg over 1-3 hours depending on dehydration and electrolytes
- for all of the above - until oral fluids and drugs can be tolerated.
- Rarely can be managed orally.
- DO NOT give heroic (large) doses of hydrocortisone especially to neonates (newly born).

UNDERGOING SURGERY

- **Short Procedure**
  (e.g. EUA - examination under anaesthetic) - give hydrocortisone, maintain double dose for two days.

- **Procedure Requiring Surgery**
  Hydrocortisone infusion until eating and drinking or hydrocortisone
  50 - 75mg/m2/day, Dextrose and saline to avoid hypoglycaemia and hyponatraemia. Restart Fludrocortisone with oral fluids.
  Increased Hydrocortisone for a further 2 -3 days

- **DURING ILLNESS**
  Double the morning dose of hydrocortisone for 2-3 days. If vomiting, drowsy or lethargic give Intra-muscular hydrocortisone and bring to hospital (especially infants).
### SUMMARY CHART TO SHOW DIFFERENT TREATMENT REGIMENS IN SEVERAL UNITS

#### CHART TO SHOW DIFFERING TREATMENT REGIMENS

<table>
<thead>
<tr>
<th>TREATMENT CHARACTERISTIC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DRUG TYPE</strong></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>76</td>
</tr>
<tr>
<td>Cortisone acetate</td>
<td>17</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>7</td>
</tr>
<tr>
<td>Fludrocortisone:</td>
<td></td>
</tr>
<tr>
<td>a) only on Salt Losers or patients with raised Plasma Renin activity</td>
<td>85</td>
</tr>
<tr>
<td>b) on all salt losers and non salt losers</td>
<td>15</td>
</tr>
<tr>
<td><strong>ADMINISTRATION SCHEDULE OF HYDROCORTISONE</strong></td>
<td></td>
</tr>
<tr>
<td>3 times a day</td>
<td>66</td>
</tr>
<tr>
<td>2 times a day</td>
<td>34</td>
</tr>
<tr>
<td>1 time a day</td>
<td>0</td>
</tr>
<tr>
<td><strong>DRUG DISTRIBUTION</strong></td>
<td></td>
</tr>
<tr>
<td>Evenly over the day</td>
<td>52</td>
</tr>
<tr>
<td>Larger dose in evening</td>
<td>30</td>
</tr>
<tr>
<td>Larger dose in morning</td>
<td>18</td>
</tr>
<tr>
<td><strong>DOSE OF HYDROCORTISONE USED</strong></td>
<td></td>
</tr>
<tr>
<td>5-10 mg/m2/day</td>
<td>1</td>
</tr>
<tr>
<td>10-20 mg/m2/day</td>
<td>63</td>
</tr>
<tr>
<td>20-30 mg/m2/day</td>
<td>36</td>
</tr>
</tbody>
</table>

### CONCLUSIONS

- It is a common disorder for which prenatal diagnosis is possible.
- Prevention of gender ambiguity
- Neonatal screening is possible
- Early treatment is important in preventing needless deaths and salt losing crisis.
- Continuing search for the “ideal” treatment regimen which will suppress excess adrenal androgen secretion but allow normal growth and maturation.
- Compromised final height is inevitable (?)
- Adult treatment is important in both sexes.
QUESTIONS TO DR SMITH

Q1. Is it best to give hydrocortisone 2 times or three times per day?

Answer 1. In theory, most patients need it in 3 doses spread over the course of a day. In practice that is not always the case. A pragmatic view needs to be taken. Some won't need it 3 times per day, however the more complete the deficiency the more likely it should be given in 3 doses. In any event the regimen has to be tailored to the individual.

Q2. I'm surprised that you put so much emphasis on giving 3x daily dose intramuscularly in cases of illness, why is that?

Answer 2. Perhaps over-zealous bias BUT it is important to know what to do in the event of acute illness. If there is a mild enzyme shortage the body can cope BUT if the shortage is severe the body can become hypoglycaemic and very stressed, even to get to a hospital it is an important consideration (no harm can be done by giving single high doses of intramuscular hydrocortisone - it is by far better to do this and minimise the risk; it could mean the difference in extremis between life and death). It is therefore a good idea to know how to give an intramuscular injection and have the kit to do it!

(COMMENT FROM PARENT in the audience) “From personal experience it is good not only to have the equipment and medication but also to practice so that in the real event it is an easier thing to do, and at least now with the ready mixed solution in a sealed glass phial it is a lot easier”.

Q3. In the case of a general anaesthetic I understand a need for giving additional hydrocortisone, but what about local anaesthetics, is it also necessary for then?

Answer 3. If in doubt give a double daily dose is a safe guide. For a full (general) anaesthetic it is necessary to have an intravenous injection; it is a medically proven factual requirement. This is followed by a hydrocortisone infusion to maintain the correct levels.

Q4. I have a son who is 2yrs old and weighs 28 lbs, his medication is 15mg split into 3 doses; I know a boy of 11 yrs old who is on the same dose, how can that be?

Answer 4. Are there any side effects on height or weight? "No, he is very hyperactive " If growth is normal it is probably ok. it is the cortisol depletion which is being treated
Glossary of terms

ACTH  Adrenocorticotropic hormone, which is produced by the anterior part of the pituitary gland and stimulates the adrenal cortex to release various corticosteroid hormones. (ACTH is also necessary for the maintenance and growth of the cells of the adrenal cortex.) ACTH production is partly controlled by the hypothalamus - an area in the centre of the brain - and partly by the level of hydrocortisone in the blood. When ACTH levels are high, the production of hydrocortisone is increased (in a normal adrenal cortex unaffected by CAH); this, in turn, suppresses the release of ACTH from the pituitary gland. If ACTH levels are low, hydrocortisone production falls and the hypothalamus releases factors that stimulate the pituitary to increase ACTH production. ACTH levels increase in response to stress, emotion, injury, infection, burns, surgery, and a decrease in blood pressure. The level of ACTH naturally fluctuates in a diurnal (24 hour) pattern.

ALDOSTERONE  A hormone secreted by the adrenal cortex and plays an important role in the control of blood pressure, and in the regulation of sodium and potassium concentrations in the blood and tissues.

ANDROGEN  A hormone (type) that causes virilisation, development of male characteristics, such as the growth of facial hair, deepening of the voice, enlargement of the penis and increase of muscle bulk. Adrenal androgens, which include testosterone, have smaller virilizing effects than those produced in the testes unless they are produced in excess. In adult males, excess androgens accentuate male physical characteristics. In boys, they cause premature sexual development. Initially they increase bone growth but adult height is reduced because they cause the long bones to stop growing.

CLITOROMEGALY  Enlargement of the clitoris.

CORTISOL  Another name for hydrocortisone, an important corticosteroid hormone produced by the drenal cortex which controls the body's use of nutrients and the excretion of salts and water in the urine. The level of cortisol in the blood is used to measure the function of the pituitary gland and the adrenal glands.

CRYPTORCHIDISM  (also cryptorchism) the condition in which the testes fail to descend into the scrotum at puberty.

CRF  Corticotrophin Releasing Factor.

HYPONATRAEMIA  Low Sodium.

HYPOSPADIAS  A congenital defect of the penis in which the opening of the urethra is situated on the underside of the penis. The urethral opening may be on the glans (head) or shaft of the penis. In some cases the penis curves downwards. In severe forms of hypospadias the urethral opening lies well back along the penis towards the scrotum. The scrotum may be small, and the testes are undescended. In such cases the true sex of the child may be in doubt.

PSEUD / PSEUDO  Prefixes that mean "false".

PSEUDOHERMAPHRODITISM  A condition in which the gonads of only one sex are present, but the external genitalia may not be clearly male or female.

PUBARCHE  Pubic hair.

PYLORIC STENOSIS  Narrowing of the pylorus (the lower outlet from the stomach) that obstructs the passage of food into the duodenum (the first part of the small intestine). Pyloric stenosis occurs in babies and adults.
MR ADRIAN BIANCHI
CONSULTANT PAEDIATRIC UROLOGIST
(Manchester Children’s Hospital, Manchester)

Contents:

CAH – A Surgical Perspective

Questions from the Audience

Transcript prepared by Neil Cockburn & checked for accuracy by Mr Bianchi

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CAH - A SURGICAL PERSPECTIVE

Embryologically both sexes start life with the same non-committed genital state, with the external genital structures being essentially of female form. The internal genitalia are represented by both the male (Wolffian Ducts) and the female (Mullerian Ducts) structures. The Mullerian ducts give rise to the major part of the vagina, the uterus and the fallopian tubes. The external genitalia consist of a clitoral-type phallus and a urogenital sinus, both of which are enclosed by labioscrotal folds. The primordial gonads are also as yet uncommitted containing both testicular and ovarian precursors. The Y (male) chromosome, through the sex determining genes, codes for instruction proteins that convey the male message such that the gonads develop into testes and commence production of testosterone. This male hormone circulates in the blood and is converted in external genital skin by the 5-alpha reductase enzyme, into the active dihydrotestosterone. Receptors on the cell membrane bind active hormone, which is conveyed to the nucleus to stimulate the “Virilization Process” leading to female to male conversion. The testes also produce a second hormone called Mullerian Inhibiting Substance (MIS), which diffuses locally on each side and acts to stop Mullerian duct development. This results in loss of the upper vagina, the uterus and the fallopian tubes.

The virilization process converts the clitoral-type phallus into a penis. There is a marked increase in length and size, and an alteration in position and direction. The penis is freed from the vulva and is able to erect freely to become the counterpart of the female vagina. Tubularisation of the ventral surface of the penis leads to the formation of the urethral tube, which opens at the tip of the penile head. The distal vagina regresses and the labia fuse from a proximal to distal direction in “zip-up” fashion to form the scrotum and the skin on the undersurface of the penis. Failure of the virilization process leads to incomplete conversion from basic female to male, and is represented by the various degrees of Hypospadias. Severely affected boys may be indistinguishable from virilized females. In similar fashion girls who are exposed to male hormones (androgens) at the crucial stage of external genital plasticity between the 6th and 19th week of gestation, will progress along masculinization pathway and may be difficult to distinguish from a poorly developed male. The most common cause of virilization in the female is Congenital Adrenal Hyperplasia (CAH) where an enzyme deficiency results in failure to produce hydrocortisone with consequent enlargement of the adrenal glands and a vast of androgenic (male type) hormones. Thus the clitoris enlarges and releases from within the vulva, the distal vagina regresses and becomes stenotic and the labia commence the Zip-up midline fusion to resemble a scrotum. It is relevant to note that androgens also influence brain development, priming the female brain to male orientation. Should there already be a family history of CAH, management commences with antenatal counselling and a consideration of feto-maternal therapy with Dexamethasone to provide hydrocortisone to the fetus and thus inhibit excess androgen production from the adrenal glands during the crucial genital plasticity phase between the 6th and 19th week of pregnancy. Chorio villus placental biopsy will confirm the diagnosis and allow for termination. It is clearly evident that management of CAH is multidisciplinary team effort, which includes the geneticist, the feto-maternal therapist, the endocrinologist and the “intersex” surgeon amongst others. Once the baby is born with a large phallus, labial fusion and the absence of gonads in the pseudo-scrotum it is important NOT to assign a sex or to register the child’s birth until the matter has been clarified by chromosomal analysis, 5OH Progesterone levels and expert endoscopic evaluation. Treatment is commenced with hydrocortisone also to inhibit the adrenal drive and androgenic output. Salt loss is often integral to the condition and requires correction of the “salt-losing state” with Fludrocortisone.

The indications for surgery are Psychoaesthetic in the early years but also Functional subsequently, and affect both the parents and the child. It is particularly relevant to normal parent-child bonding that the baby should have a defined sex and the appropriate genital appearance. It is relevant immediately to the parents and is crucial eventually to the child’s “gender identity” and acceptance of self. In time CAH females will seek to be sexually able, in all respects equivalent to the normal female. Surgery should be undertaken by agreement with and at the instigation of the parents, thus taking account of their psychological needs, during the early weeks or months of life once the child’s hormonal status is stabilised. The enlarged clitoris is reduced in size and positioned within the vulva at the normal site. Blood and sensation (sensitivity) are carefully preserved. The fused labia are separated or “Unzipped” to expose the stenotic vagina and to achieve a female appearance. Actual vaginal reconstruction only becomes relevant to allow intercourse at or after puberty, and is best undertaken after natural oestrogens from the ovaries have developed the vaginal tissue. Surgery is therefore in two phases with psychoaesthetic indications relevant to the parents and the child in the first early phase, and functional indications in the second phase at puberty.

At all stages parents and eventually children are offered psychological support, explanation and counselling with the aim of achieving a “bonded” family and a psychologically normal functional female. Of particular relevance at puberty, and subsequently, is a consideration of the emotional status and sexual orientation of the CAH female. Androgenic brain priming towards male during the crucial phase of “cortical sexual plasticity”, impacts heavily on the behaviour, gender acceptance and sexual orientation of CAH girls and may lead to major confusion and distress. The CAH Team together with the parents must therefore not only consider the physical needs of the CAH female, but must also be particularly sensitive to the emotional needs, sexual orientation and confusion which affects the androgenized CAH girl.

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QUESTIONS TO MR BIANCHI

Q1. Can you give an idea of the %age success rate for surgery?

Answer 1. Should be 100%; it depends on what is left to work with. If too much has been removed the success rate will be commensurately reduced. If the clitoris is too big that's ok something can be done. A tight vagina can be opened. Repositioning of the vagina can be done. It is very individual; you must know what you want. It can be done at any age, age is not relevant.

Q2. If the clitoris is not enlarged too much, is it better to leave opening the vagina until a later date?

Answer 2. It is entirely the choice of the parents and child. The question is “What do YOU want?”

Q3. Is there any advantage in leaving operations until later because of scar tissue preventing success later (had an operation been done while young)? And is there less scar tissue if the operation is done later?

Answer 3. You should never consider it as a one off operation; there may be less scar tissue if the operation is done later but you need to consider the child and the future. Compare it to a cleft lip which is very visible; it is not good enough to say that it (clitoris) won’t be seen, think of the child - SHE will see it!

Q4. How does a child cope psychologically with for instance menstrual difficulty?

Answer 4. As a baby there is no problem (obviously) but later as she grows up it is different; at 10 years old they don’t speak, they are shy. You have to talk freely and openly to them, take them into your confidence. Don't expect an answer though! After speaking to them and leaving things for a while all of a sudden I will get an answer by phone or by letter saying they want the surgery immediately! I once put it to one girl, look do you want to be a nun or lead a normal active life. A couple of days later she popped her head around the door of my surgery and quickly called out “I don’t want to be a nun” and then disappeared as quickly as she had appeared.

It is a sensitive zone a sensitive area; do nothing before the child understands. You need to build this understanding well before the time of the surgery not only for the lead up but also for after the surgery.

Q5. When is it appropriate to speak about surgery?

Answer 5. From the first moment the questions start like “Why do I have to go to hospital?” Always answer at a level equal to the child’s understanding. Details will grow in the questions; gauge the answer to what the child wants. Use the support group to help you.

Q6. How would you be sure that the surgeon is capable?

Answer 6. More often than not the whole thing is a team approach in a specialised centre, so have a chat with the endocrinologist and seek their counsel.

Q7. Can you ask for any surgeon anywhere?

Answer 7. Yes, a GP can send you anywhere that he or she thinks treatment will be best. You have the right.

Q8. What about dilation after surgery using dilators to expand the vagina?

Answer 8. When a round join is made, nature tightens it; scar tissue is a healing tissue, it tightens and shortens. Any tightness needs to be counteracted after the first six months, however dilating is not necessary at an early age - there is no need to, it serves no useful purpose (it only becomes useful in preparation if necessary for intercourse). At age 10 - 14 the mental state needs to be accounted for in considering the use of dilators. Dilators may be considered around the age when sexual activity is expected so that when intercourse does happen it is not an uncomfortable unpleasant experience putting either of the couple off sex.
Contents:

Genetics

The Genetic Helix

Autosomal Recessive (hidden) Inheritance

CAH in the UK

Familial Possibility of Being Affected

Tests in Pregnancy

Dexamethasone Treatment

Clinical & Molecular Genetics
It is important to say that the management of the condition is a team approach. Parents can say who should be in the team and how they want things to go.

**Diagram 1** to illustrate the process of hormonal change. Gene “1” produces enzyme “1” which acts as a catalyst to change hormone “A” into hormone “B”. An enzyme is a protein which enables hormonal change.

If a gene is missing the enzyme will not exist and a process of changing one hormone to another will not take place

**Diagram 2**

In diagram 2 there is a BLOCK in the line from hormone “C” to hormone “D”. This block represents a gene defect in not producing the enzyme which catalyses the change from “C” to “D” and as such is representative of what happens in CAB. In this case Genes 1 and 2 producing enzymes “1” and “2” work harder because hormone “D” is not produced. As Hormone “C” cannot be changed into “D” it has to go somewhere else. It finds a new path and produces hormone “F” instead.

So what we are talking about in CAH is a series of reactions. One hormone will go through a series of changes to convert to other hormones – reactions, which are stimulated by enzymes. An enzyme is a protein in the body, which allows this process to happen. Enzymes are made by genes. There are thousands and thousands of pathways converting one hormone to another. The adrenal is only one of them and a critical one. What happens in CAH is things start off ok but one gene is missing, therefore a critical enzyme is missing so a conversion process cannot happen.
THE GENETIC HELIX

A double helix made up of phosphates and sugars. Between the double helix are base pairs of ‘nucleotides’ giving the genetic coding. There are about 100,000 genes. Amino acids make proteins; there are 20 amino acids. There are 23 pairs of chromosomes. Changing a base pair can change the whole construction; as a simple means to demonstrate this look at the construction of the following 3 letter word sentence -

“GET THE CAT OFF THE MAT”
then change it by taking one letter away but maintain 3 letter combinations:

“GET THE CAO FFT HEM ATG” (the T on CAT has been removed and the letters moved to still form sets of three. This illustrates what can happen if a single nucleotide in a gene is missing)
In CAB it is chromosome 6 that carries the CAH gene, 21 Hydroxylase.

AUTOSOMAL RECESSIVE (hidden) INHERITANCE

The diagram shows that if both parents are carriers of the genetic defect then there is a 1:4 chance that the offspring will be fully affected. (1:2 of being a carrier and 1:4 of being unaffected are not a carrier). Autosomal meaning on one of the non sex chromosomes i.e. not for X or Y and recessive meaning hidden away. Recessive genes are important - we all have them. Because we all have altered recessive genes, (genes which aren’t working,) occasionally partners will have the same problem, if it happens to be the same recessive gene we may see manifestations of that gene. In effect, when we pass our genes on, we can’t pass them all on, so every time we create an egg or sperm we only pass on one chromosome of each pair and that is a totally random process. It is therefore a 50:50 chance that the altered copy will be passed on therefore a 1:4 risk of any child having CAH if both parents carry an altered copy.

CAH IN THE UK

- MAX Occurrence is 1:5000 and minimum is 1:15000
- Carrier occurrence is at a max 1:35 and minimum 1:61
- 5 mutations account for 80% of carriers.

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FAMILIAL POSSIBILITY OF BEING AFFECTED

- Offspring of an affected child
  $1 \times 1/50 \times 1/2 = 1/100 (1\%)$
- Offspring of a sibling of affected child
  $2/3 \times 1/50 \times 1/4 = 1/300 (0.3\%)$
- Uncle or Aunt of affected child
  $1/2 \times 1/50 \times 1/4 = 1/400 (0.25\%)$

TESTS IN PREGNANCY
The placenta and baby are from the same egg so it is possible to take sample from the placenta, known as a chorion biopsy.
Alternatively an amniocentesis can be done which samples the amniotic fluid surrounding the baby. The Chorion biopsy is happening more and more but is very operator dependant. The chance of miscarriage is 1:75 (However! 1:50 miscarriage anyway at 12 weeks without any test intervention). With an amniocentesis the chance of miscarriage as a consequence is ~1:150.

**Direct** - look for exact gene mutation if known but not always possible.

**Indirect** - Look for subtle changes very close to the gene identity if baby inherited the 2 number 6 chromosomes with the mutation. There is a small error rate with this testing from chromosomes ‘swapping’ pieces with each other – known as recombination.

CHORION VILLUS BIOPSY

**ADVANTAGE**
- Reassurance NO CAH
- Chromosomes Normal

**DISADVANTAGE**
- Miscarriage
- Baby is affected or a carrier found
- Chromosome abnormality found

For these last two maybe the parents would not want to know (psychological effect on parents and eventually the child)

DEXAMETHASONE TREATMENT

- Needs to be done on the mother as soon as possible if it is going to be done. The decision tree then looks like this

CHORION VILLUS BIOPSY

- Shows up a Boy - stop Dexamethasone
- Shows up a girl - unaffected - stop dexamethasone
- Shows up a girl - affected - continue dexamethasone.
FOETAL CONCERNS WITH DEXAMETHASONE TREATMENT

- (Speculative - no proof):
  
  **IMMEDIATE**
  
  - Not 100% effective
  - High doses - reduced birth size
  - Foetal loss on sudden withdrawal
  - Diabetes
  - Behavioural pattern

  **LONG TERM**
  
  - Cardiovascular disease

POSSIBLE MATERNAL CONCERNS WITH DEXAMETHASONE TREATMENT

- Hypertension
- Diabetes
- Proteinuria and headaches
- Weight gain and possibly cushingoid faces
- Oedema and Striae
- Mood fluctuations

DEXAMETHASONE THERAPY - Dr Maria New 1995 (8 years experience)

Test survey results

- 239 Prenatal tests carried out
- 37 Affected pregnancies
- 21 of the 37 were female
- 13 out of the 21 females were treated with Dexamethasone.
- In the treated cases babies were either not virilised or less virilised.

CLINICAL & MOLECULAR GENETICS

What are the aims?

- To understand the condition and know more about it
- To help make decisions
PROFESSOR MELISSA HINES
CONSULTANT PSYCHOLOGIST
(UCLH, London)

Contents:

The Psychological Development of People

Prenatel Androgen & IQ

Toys Used in Preference Task

Results of Preference Task Tests

Questions from Audience

Transcript prepared by Neil Cockburn & checked for accuracy by Professor Hines

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Androgens are male hormones (produced by all of us) e.g. testosterone, dihydrotestosterone, and are produced by the gonads (testes) and the adrenal glands. They determine male physical development, penile formation and growth and development of secondary sexual characteristics at puberty.

The idea that androgen exposure might influence psychological development is based in part on research in other species. Experiments have been done with monkeys in which androgens have been introduced to see if psychological development has been affected.

These actions to steroid hormones, like androgens, can be split into two fundamental types

Activational Influences

- These are transient, for instance in men, if they lose their source of testosterone as adults their sexual urges can be reduced, but if the testosterone is given back their sexual interest is raised.

Organizational influences

- Permanent modifications. There are critical periods of brain development occurring prenatally and neonatally. Even though the hormone is only there for a while it’s effect persists across the individuals’ lifespan.

Rough and Tumble Play Behaviour

- Is seen in juvenile animals, more common in males. It is in female rats and rhesus monkeys, increased exposure to testosterone during critical periods increasing rough and tumble play.

Brain Sensitivity

- (hypothalamus) testosterone treatment changes the female brain to be similar to the males in the hypothalamus (cells in this region do not die off as they would have done).

Prenatal Androgen Treatment (in Rats) affects the following

- Sexual behaviours
- Aggression
- Scent marking
- Feeding and body weight Lateral preferences
- Rough and tumble play
- Activity levels
- Maze performance

Other animals also show similar behavioral change (dog, ferret, sheep, marmoset monkeys, hamsters, mice), which raises the question whether or not human development would be similarly affected by testosterone. We cannot assume that it does because we are quite different, although being mammals, but our brains are quite different from other animals; the Associational region in the cerebral cortex of the brain is much larger by comparison in humans. So, although work on animals can give some indication of what might be you really need to look at people for accuracy.
**Human Psychological Sex Differences**

In animals not all behaviours are influenced by hormones, but the ones that are influenced are those that show sex differences (meaning that they differ on the average for males and females). There has been great debate over the years as to which human behaviours show sex differences, but there is general agreement that the ones on the following list do. (To put them in context the sex difference in height is familiar, it’s an average difference between men and women, men are taller on average than women but some women are taller than some men). The sex difference in height is two to ten times as large as behavioural sex differences.

- Core gender identity (basic sense of being male or female)
- Orientation (opposite versus same sex attraction for example)
- Juvenile play behaviour (toys, activities)
- Cognitive patterns (visuospatial abilities, verbal fluency)
- Hemisphere asymmetries (hand preferences, language lateralisation)

People have inconsistent reports in most of these areas about CAH however (in Melissa Hines opinion) we don’t have enough information on any of them other than on juvenile play activity. Several studies have been done which suggest common findings for play behaviour. In other areas, more work needs to be done on a larger population over a longer timeframe. Current study results are based on observations of small numbers.

**Prenatal Androgen and IQ**

Another problem is that if you’re looking at people with CAH and you’re trying to decide if there are changes in behaviour, one problem is that you’re not doing an experiment; people come to the clinic where there is a research project going on and some people say yes to becoming involved and others say no for various reasons, so you don’t really get the entire group and you have to be very careful about what that might mean. The history of research on CAH and intelligence illustrates this. In the 1950’s when people with CAH were reported to be more intelligent than would be expected based on population norms. However when control comparisons were made:

1. Hormone exposed patients had IQ higher than population norms
2. Hormone exposed patients had IQ similar to their unaffected relatives
3. Hormone exposed patients had IQ similar to controls matched for demographics

It is therefore best to compare studies with relatives as controls.

CAH girls **tend** to be tomboys.

**Tomboy characteristics**

- Boys toys, play with boys
- Liking rough outside activities
- Preference for more comfortable clothes than dresses - boyish clothes

Information from questionnaires gives this kind of information, and several studies worldwide have shown similar results. In order to verify (or otherwise) these results in actual practice an observation check was devised. Also the question of a more precise definition for tomboy needed to be established. So each child was brought into a playroom where he or she was surrounded by a lot of different toys; some of these toys had been classified as masculine and some as feminine and some as neutral. These classifications were based on prior research. The study had 26 girls with CAH, 11 boys with CAH, all of them between 3 and 8 years old, and the controls were 15 unaffected sisters or female first cousins and 18 male unaffected brothers or first cousins. The first thing that was done was look at the sex differences in the toy choices. The results can only be an average and there is a lot of variability from one child to another in behaviour, even within each sex, but as a group the children did show the predicted sex differences in toy preferences.
TOYS USED IN PREFERENCE TASK

- Masculine cars, helicopters, fire engine, constructional toys.
- Feminine ~ dolls, kitchen supplies, telephone
- Neutral Books, board games, crayon and paper.

RESULTS OF PREFERENCE TASK TESTS

Results of this observational study were similar to those based on questionnaires.

- CAH girls showed more masculine – typical toy choices.
- Boys with CAH did not differ from male relative controls.

The final thing, which was looked at, was Rough and Tumble play. There was particular interest in this because of the studies with rats and rhesus monkeys where rough and tumble play was increased in females exposed prenatally to high levels of androgen. CAH girls are about the same as the control girls in play. Unexpectedly boys with CAH showed less rough and tumble play. This seemed to relate to the amount of hospitalisation they experienced during the first to years of life.

A different issue which might make you curious about psychological development and CAH - does having this medical problem and things associated with it cause unusual levels of psychological distress or psychological problems than would otherwise be the case, and this is separate to the issue of whether androgens change behaviour in certain ways. But do things like hospitalisations, and surgeries and having to take tablets every day have an impact on the child’s psychological development. Surprisingly, we don’t know much about this, but one recent study from the Netherlands included 18 girls with CAH and they were among 59 children with various intersex disorders that were being studied. They found that 5 of the 18 girls with CAH suffered a serious psychological problem between the ages of 6 and 16 years old. The problems weren’t of one sort but they were about different types of things. One of them, mental retardation, had nothing to do with CAH. It was just a coincidence that a child had CAH as well as mental retardation. The other problems might also but they did not have a control group to say how many you would expect to have a serious psychological problem but what they observed in one girl with selective (…ism is that she wouldn’t talk - one was an anxiety disorder, some sort of phobia - an exaggerated fear, oppositional defiance disorder in one girl…

What we can say is that we don’t know enough about psychological development and people with CAH for various reasons. This is partly because we just don’t have enough information. People have not done enough studies of the sort that need to be done on large groups of people carefully controlled. Also, we know even less about psychological development in boys with CAH than we do about girls. In regard to girls, it does seem that they have more interest in boy typical activities as children and from what I’ve heard from people who have been in our studies this comes as no surprise to you as parents.
QUESTIONS TO PROFESSOR HINES

Q1. I have a daughter with CAH and I certainly back up your theories on the toys thing, she is totally boy orientated. What I wasn’t clear about was what your current study was trying to find, what it is you are trying to pinpoint, what aspect of those behaviours you are looking at?

Answer 1. We are doing a couple of things; one thing we want to see is how do people develop - there are theories relating toy choices to activities in later life. The idea is that playing with certain toys teaches skills. One thing we are looking at in older patients and relatives is cognitive patterns, which we don’t have enough information on. In the children with CAH we are looking at a finer study of the types of toys that they are interested in and also a bigger sample so that we can start to look at other factors like having siblings and other background factors that are thought to relate to toy choices.

Q2. Do you feel that there is support on the psychological side for children that are going up through puberty to adulthood with CAH or others in the family?

Answer 2. I think we could do more in that realm. There should be a psychologist present from diagnosis to help with the kinds of feelings that come up and to help explain what it might mean and to deal with problems that can come up in the children.

Q3. Does having CAH cause higher than normal psychological stress (because of hospital visits, tablets, operations etc)?

Answer 3. In Holland, a study of 18 girls ages in the range 5 to 16 years old, 5 suffered psychological problems (sexual, anxiety, selective mutation, oppositional defiant disorder). Other intersex children had a similar rate of psychological problems. With psychological intervention the outcome was good; it is treatable successfully. There is less known about boys because of the lack of studies.

Q4. With respect to “rough and tumble play” my son, who is physically big for his age, plays with older and stronger children with equal strength, can you comment on that?

(Audience member response) My 2 year old loves kitchen things in fact he’s almost obsessive about it.

Answer 4. There is a lot of variability in general independent of how CAH patients might behave.

(Dr Smith comment) I displayed tomboy behaviour as a young girl, I was always up trees; you must be careful therefore in making judgements.

(Female audience member comment) My eldest daughter, 8 years old, has CAH; she has a younger sister aged 5 and a brother aged 3 neither of whom have CAH. My boy is fanatical about wearing dresses and my shoes He is very much influenced by his older sisters.

Q5. Is there any psychological support for adolescent CAH patients?

Answer 5. We could and should do more.
Q6. Pen and paper are not classed, as girl’s toys in the preference task list are they?

Answer 6. No, they should be assigned to the neutral listing.

Q7. Are computer toys and games male or female?

Answer 7. It depends on the nature of the game.

Q8. Will the studies that you are conducting currently on children and siblings be carried through to adulthood?

Answer 8. Funding dependant, yes, I would like to do that.

Q9. My daughter’s (who is 5 years old) favourite “toy” is a bag of tools, she plays with boys and she is a tomboy. Would she have been anyway?

Answer 9. It is impossible to know for sure. CAH is associated with more boyish play, but some girls without CAH are boyish too. Yes, could be.

(Audience comment) My 14-year-old daughter with CAH was a tomboy when she was younger but now she is a typical female teenager!

Q10. My 7 year old daughter is a tomboy and it has an effect on her friends in the playground; she tends to be isolated. Should I be concerned or ignore it?

Answer 10. What are you concerned about?

(Reply) Her relationship with other children.

(Melissa Hines) How does she feel? Is it a problem to her?

(Reply) She tends to be aggressive. Talking makes no difference.

(Melissa Hines) I think you need to talk more to her and try to get to understand her better. It’s difficult to say more than that with the information to go on now.

(Audience commentary) I am 40+ and have CAH. Being a tomboy can have a positive effect. I have been more career oriented, it does not affect sex, it has helped my career. At a young age it is not a problem. Children must not be labelled, labelling is a problem.

Q1. I have a 38-year-old daughter, she was a tomboy. Androgens can affect the brain as you have said but if cortisone dosage was wrong at an early age and suppression of the androgens insufficient could that have been the cause?

Answer 1. Prenatally and up to 6 months old are the critical periods of development; once they are over it is unlikely to have had such an effect.
MRS KATHRYN MAY
Clinical Sexual Psychologist & Senior Lecturer
(University of Central Lancashire, Preston)

Contents:

Tailoring Skilled Service to Treat Problems

Sexual Development

Private / Public

Sexual Confidence

Passivity & Learned Helplessness

Preparation & Provision

Ways Forward

Transcript prepared by Neil Cockburn & checked for accuracy by Mrs May

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TAILORING SKILLED SERVICE TO TREAT PROBLEMS

The clinical work that I am normally involved in is psychosexual therapy work. Some is in a clinical base and some is actually training people to be psychosexual therapists. What I shall talk about is the sort of service provision that some of us who are already providing psychosexual services might be able to provide and tailor to the needs of people with CAH and their parents, who are obviously a crucial part of the equation. What we are about to do is find out a bit more about what these needs might be in terms of problems with psychosexual development adjustment. Obviously there may be people with CAH and no problem whatsoever and we don’t want to anticipate any where there are none but we would like to start looking at developing a skilled and specific service for parts of the country where that does not exist, to support people in some of the changes we have seen today and some of the medical and surgical interventions which might cause people some problems and logically will cause periods of adjustments to be necessary to people.

SEXUAL DEVELOPMENT

- A problem for all (potentially). If we think back to our own sexual development and crucial points within that it was very often through a process of trial and error that we made our way through critical points in sexual development and made successful relationships with people that perhaps later became sexual.

- Medical and social norms (powerful in how people see themselves). One of the first questions asked by people coming for psychosexual help is this big anxiety about whether they are normal, whether it’s ok for them to be there, whether somebody is going to label them as being abnormal.

- Medicalisation ~ double impact i.e. Response of child and response of parents. If you are actually medicalised and perhaps there is intervention into your sexual anatomy at a very early age, that medicalisation has a double impact because there is the child’s response to what’s going on and the ways in which they are actually going through that system and there is also the parental response to that, which complicates what is going on within that family.

- The other thing about medicalisation is some of the research papers on CAH show how effectively that can actually mask other important psychological aspects of adjustments, which may or may not be CAH related. But the questions about whether everything is functioning normally, or as well as can possibly be expected, can actually cover some of the other aspects of development which may be equally important and in order to function ok sexually both things are important; you need an intact neurological system you need an intact hormonal system, both things need to be functioning. On top of that, you need to be able to negotiate the world as a sexual person with sexual confidence and we all know what that can be like and how difficult that can be. There are layers relating to sexual functioning and you have to keep them all somewhere juggling in the background.

PRIVATE / PUBLIC

In relation to all of our sexual development there is this switch between what is private and what is public; what aspect of ourselves as sexual people and our bodies are for public consumption and what are private to us. Some of the messages we give to small children and certainly to adolescents are all around what it is appropriate for other people to see and observe and what isn’t. For a child with CAH who has had some of the early surgical intervention and is maybe looking forward to the adolescent surgery there may be lots of questions about ‘My body I Whose body’?

- Genitalia, procedures and anxiety (management involving anxiety links closely to development of your body and sexual development). Some of the literature identifies that unwanted surgical interventions, however necessary they are, can seriously knock sexual confidence. Therefore, talking to young people about the boundaries and how important it is to let certain people in to help, but still give them the confidence that those boundaries they can negotiate with other people within their private sexual life may be quite important. The other thing that comes out of literature and talking to people is that if the way you have been managed in terms of surgery and other management of CAH has involved anxiety for you and your parents then that can become very closely linked to the development of your body and the development of you as a sexual person.

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• Sexual need, satisfaction and pleasure when positive stimuli is greater than negative stimuli, this leads to good sexual motivation when positive stimuli is less than negative stimuli, this leads to anxiety and sexual inertia.

We know from general research into sexuality and other psychosexual difficulties that the balance between your body as a source of pleasure, your body as a source of sexual satisfaction, balanced against the things that can go wrong with that, is a really important balance. Some people see it as some sort of algebraic equation which is that basically, if the positive associations with your body and the sexual bits of your body are greater than the worries, the anxiety and the bad experiences, then there is high sexual motivation for you to engage with other people in a sexual way. However, if the positive feelings are less or lower than the worries and anxieties and the problems that there have been, then there may well be sexual inertia or just an anxiety about engaging with people because you don’t know, as none of us know, what might crop up in those sexual situations - the sorts of questions somebody might ask you, or how are you going to deal with that. If we accept that for people with CAH, or some people with CAH, there may well be anxieties and worries, then it seems important to create environments where they can work those out and explore them, in time to give themselves good chance to still have positive sexual relationships with other people.

SEXUAL CONFIDENCE

• Sexual Confidence is Key to sexual relationships. For any of us that have had negative sexual experiences or negative experiences relating to our sexuality then that fear of failure is intensified. It’s there for all of us in going into any sexual situation. The anxiety about things not working, things not going well, is a big factor whether you feel confident or not to go into that situation. The fear of failure and the fear of rejection is there for all of us. But if there have been some reasons why maybe you identify yourself as different sexually then that may be heightened.

• Impact of difference on the confidence of others.

• Early sexual situations - difficult for others to cope with your problem (a challenge for the other person, especially if they are young too and have fears of their own!)

If you think back to your teens or early twenties and being in early sexual situations you can also identify with how difficult it is for the other person perhaps to cope with you being different, if you need to say “look, I’m worried about intercourse because I’ve had some surgery and I’m worried about whether that’s going to go ok or not “then you’re also giving a challenge to the other person to be able to cope with that too. Very often it might be the case that the other person who may also be young and inexperienced and their own fear of sexual failure is high- that situation may be too much for them to cope with, but their withdrawal from the situation may be seen as rejection of you personally.

• Concept of sexual relationships and especially intercourse represents a hurdle to get over which leads to

• Anxiety and sensitiveness, and;

• Reflects other psychosexual problems and poor intimacy.

Reading through the literature on CAH and sexual relationships there is reference to the fact that both parents and adults with CAH see the idea of sexual relationships as a sort of challenge or a problem and particularly sexual intercourse as a hurdle to be got over. The anticipation of problems is well documented generally in people with sexual problems, obviously and quite understandably this can lead to people being a bit defensive. If you are going into a situation and you are worried about it, you are already slightly on edge and that then can lead on to problems in developing intimate relationships because intimacy depends on self-disclosure and people being able to move closer together. If you are going in a bit worried about what might happen in this situation, you may be a bit defensive and that may then mean that it is more difficult for you to form good intimate relationships, which in the long run makes some of the problems more difficult.

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PASSIVITY & LEARNED HELPLESSNESS

- Waiting for all to be well.

- Literature also indicates, and in particular for women with CAH, what it calls “passivity and learned helplessness”. Some of Brenda May’s work refers to this. It seems to be compounded by parents suggesting to girls that they need to wait until everything seems to be all right. If there seems to be problems in sexual relationships maybe that’s not the best person to be developing a sexual relationship with.

- Develop other aspects first

- Also, perhaps an encouragement to develop other aspects of personality and skills before the sexual bit. As a parent myself, with children coming into puberty, I think that we all want to protect our children from difficult experiences, unhappy sexual and relationship experiences, so if there are additional factors, the complexity of surgery for women related to CAH and the different points of intervention for example, and how they might tie in with what relationships you want at this point, is this a point at which you want a relationship which might involve intercourse? So it is very understandable that parents try to delay a while and try to defer things until later, until that person is more robust, older, perhaps feeling that they know more, it’s important to recognise that that is quite tempting and understandable, but may not be what young person wants.

- “Mr Right” as a panacea - why should this happen for CAH patients - it doesn’t happen for others!

- The idea of a “Mr Right” as a panacea, as an answer to all your problems, appealing as it might be. It doesn’t happen to generally, so why should it happen in this situation or for people with CAH? Waiting for “Mr Right” may mean not developing relationships which could work well.

- Parental dilemmas

- These questions and these issues do lead to some parental dilemmas the likes of which might at least be important for parents to have the chance to think through and to talk through before they are a reality in their lives.

PREPARATION & PROVISION

- Preparation of the child/young person is critically important; there are choices to be made, about surgery for example. This must be thought through before choices are given. As psychosexual practitioners and people involved in psychosexual services, that is something we already do so in relationship to some of the discussion earlier about vaginal dilators or trainers, we are really used to working with those with young women and talking about them and introducing them in ways where it’s a positive experience to be faced with a set of vaginal trainers, rather than a frightening or negative one. The idea of being able to prepare someone for some of the decisions or some of the questions they might need to answer is one that may be is being taken on board in some centres, but perhaps we need to do something that’s more available to all and easier to access.

- Parents need to be well placed to prepare and talk to the child but may not want to.

- Parents are really well placed to do some of this work in talking to their child or the young person or young adult, but sometimes they might not want to. That is well-reflected in things like sex education, where the biology teacher might know a lot about biology, but might not particularly want to talk to groups of young people about being sexual or having sexual relationships.

- Parents have their own support needs and perhaps an important one of those is the opportunity for a rehearsal, that there is a person they can phone or service they can go to where they can actually talk through what they
want to talk through with their child because you want to get it right first time. The subject may be upsetting, some of these things in an ideal world maybe we didn’t want to discuss with our child at all, so it’s important that we look at support services for parents and young people in tandem and getting continuity between those is important, so that parents can start to do some of that discussion with young people, but if they don’t feel they are the best person to continue or they don’t want to continue, or the young person wants to talk to someone who isn’t their mum or dad, that there is provision for that.

- Not forcing people to have problems - don’t have to have a label to get a service.

- If we provide a specific service which acknowledges that people with CAH, both young women and young men, are logically going to have different challenges from other people in the population, and we create and show that we are prepared to create a service to address that, then we are not forcing people to have problems in order to come and get support. We are saying “it’s here, you don’t have to be labeled as having a problem in order to have access to a service.

WAYS FORWARD

- Continuity of service provision - sensitivity issues. In all areas of sexual help continuity is important because if people are going to go along to somebody they have never met before and talk about some of the most sensitive and private bits of their lives, they don’t want to have to go back a little while later and do all that again with somebody else. Usually; they want to go back and pick up from where they left off - and maybe that is also true for parents too. The other idea is that this service should be generally available, and we don’t know how much is available to people in different parts of the country at this moment, and to what extent the teams of people working with CAH are able to give time and anticipate some of these things and discuss them with young people before they become issues that has to have requiring decision-making.

- Opt in / Opt out. How much time and service is available before decision/choices are presented.

- If people have to opt out of that, rather than opt in to it, it’s a bit more like their right in the first place, rather than something they have to go and seek when there is a crisis.

- Early positive promotion, people with CAH, just as much as anybody else, have the right to enjoy their bodies and the right to be sexual in a confident way and perhaps that means they have specific needs which need to be met before they are in situations where that is critical.

- ‘Creation of opportunity and choices which are not such a struggle. People with CAH tend to be less sexually explorative with themselves and have fewer relationships. Need to know own body and experience your body to give opportunity to lead normal sexual lives.
QUESTIONS TO DR PATRICIA SMITH, MR ADRIAN BIANCHI, DR TREVOR COLE, PROF. MELISSA HINES, MRS KATHRYN MAY

Contents:

Questions from the Audience

Transcript prepared by Neil Cockburn & checked for accuracy by Dr Patricia Smith, Mr Adrian Bianchi, Dr Trevor Cole, Prof. Melissa Hines, Mrs Kathryn May

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GROUP FORUM QUESTION & ANSWER SESSION

Q1. I have an 11 year old son with CAH whose bone age is 5; because he is coming into the age of puberty and he will obviously be late starting it they are talking about giving him testosterone next year when he is 12, have you any patients on that, what are your views? Puberty has started later than I would expect, is this because of excessive suppression of testosterone?

Answer 1. Is it a familial problem? Bone age is only a guide and depends on the person who is reading it. Bone age should not be used prescriptively. The dilemma is should additional testosterone be given or just back-off on control (suppression). Sometimes it is difficult to regain control. It could be growth hormone deficiency.

Q1a. Yes, but if it’s growth hormone deficiency, would there be any growth at all?

Answer 1a. Is he within parental norm 7 Puberty is not considered late until 14 years old.

Q2. Is there any research to support that gene therapy will be available in future?

Answer 2. No. It is a long way off. What, is gene therapy? Can you replace with a good gene? It is a long way off, treatment by putting cells in place with normal working chemicals like a transplant of a group of cells which work in the same way is probably more feasible in the shorter term. Most commonly research is done on more common conditions. The spin-off is techniques learnt which may be applicable to other diseases or conditions.

Q3. When my 8 year old daughter asks about the facts of life there are books which can help to explain relatively simply; couldn’t you do a paper for parents to explain about sexual problems?

Answer 3. Yes it’s possible, it would be good for parents to use to focus their minds before trying to explain to the child - like a rehearsal. The support service will hopefully be better in the future. It would only be guidelines of what’s important to think about. Commonly you start to explain things then need diagrams to help complete the explanation, it would be difficult to cover all aspects in this way.

Q4. I want somehow for my daughter to be able to come and tell me about her sex life when she needs to or should do, how can I ensure that?

Answer 4. Create the environment by talking to her about issues early on so that she feels able to do it quite naturally or get another person with whom such confidence can be created. (someone at school possibly or another adult with whom she has a good relationship).
Q5. Adrenalectomy used to be a standard treatment and is now being encouraged by some doctors; is this, the right thing to do?

Answer 5. In cases where the condition renders the patient very poorly or where it is difficult to control either from a patients compliance perspective or from the condition itself then maybe it could be an option. It should be very selective; you still need the adrenals for other normal development. It may be a small percentage relevant but only as a last resort on a difficult patient (and after puberty). You would still need Hydrocortisone and Fludrocortisone. It may even create more problems.

Q5a. My daughter had an adrenalectomy at 33 years old and appears to be relatively normal.

Q5b. After puberty would it be easier?

Answer 5b. Yes, but again only as a final option.

Q6. Are you treating anyone late diagnosed with Prostap?

Answer 6. No.

Q7. Is there any connection between CAH and Talapees (positioning of the foot)?

Answer 7. I can’t see how there should be or could be. Positional Talapees is common in the womb.

Q8. I have heard conflicting reports on the benefits of some research currently being carried out which takes 4 days to complete for each child studied, what is your view?

Answer 8. I don’t know the specifics of the research but as parents don’t feel obligated to participate. If you think it is inappropriate either in timescale (4 days in hospital seems a long time) or because of the bloodletting involved then you should not feel inclined to go along with it.

Q8a. Is the aim good though, is it worth while?

Answer 8a. It depends on whether it is looking at diurnal effects on hormones or not; it depends on the answer they are looking for. Don’t feel obligated to participate if it is not right for you as a family.

Q9. Is there a time release capsule for medication (Hydrocortisone)?

Answer 9. Not that I’m aware of.

Q10. Is vitamin supplement required?

Answer 10. No. They are a normal person!

Q11. Is Prednisolone only given to adults?

Answer 11. Prednisolone has a growth suppressing effect and other side effects. Normally we stick to Hydrocortisone until growth is complete. When the patient has completed growth changing to Prednisolone can be done.

Q12. What psychological (psychosexual) services are available now?
**Answer 12.** We are trying to do a need’s assessment now with parents and CAH patients. We are looking to set up a clinic at our psychosexual unit. We want to act as a link to refer to more local facilities. It is early days yet to provide what we think is needed throughout the country. However, skilled and experienced people are available on the phone initially. The availability of such services varies tremendously across the country.

**Q13.** Is there any plan to have newborn screening for CAH like PKU and other tests?

**Answer 13.** The question is What is best for ourselves and our children versus what can the NHS reasonably provide? What would the benefit be? In a population producing 5 0-60 CAH babies per annum of which 25-30 are boys (and therefore less obvious at birth) and only a few of which would present in crisis - of 600,000 births is there a test which is reliable and cheap enough? It is difficult to justify and I can’t see a resolution to it at present.

**Q14.** I have a 2 year old son who is very well managed and is very well. Is it naive to assume this will always be the case?

**Answer 14.** No. Normal life, normal lifespan - well controlled! Be optimistic!

**Q15.** I have a son who is 7. Last year at age 6 he had a bone age of 10; he is on a low dose of Hydrocortisone. He is still at average height.

**Answer 15.** If he is going through centiles on the growth chart he is being under-treated - not enough medication.

**Q16.** We are supporting Melissa Hines’ research; would it be possible and reasonable to have some progress update reports for our newsletter?

**Answer 16.** Yes.

**Q17.** I have a late (4 years old) diagnosed child who is now on treatment for CAH, he is now 9 but has a bone age of 14 and he is almost not growing at all now; should Growth Hormone Treatment be given?

**Answer 17.** Yes, it should be investigated.

**Q18.** Children going through puberty have excess weight gain; what percentage suffer this problem?

**Answer 18.** In puberty you need to let the child grow quickly as a natural growth spurt and not confuse it as wrong management of drug therapy. It would probably be as per the normal population in terms of a percentage figure.

**Q19.** My daughter urinates frequently, it also smells quite strongly. What can we do about it?

**Answer 19.** Pelvic floor may be weaker dependant on the degree of “unzipping”. You should have it investigated urologically.
CAH Support Group of CLIMB

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CONGENITAL ADRENAL HYPERPLASIA

Brief explanation and the aims of our support group

Congenital Adrenal Hyperplasia (CAH) is a metabolic condition which affects the production of steroids from the adrenal glands. The 3 main types of steroids are, cortisol (which is the stress hormone), aldosterone (salt retaining steroid) and androgens (male hormones). Both boys and girls with the condition are exposed to an excess of androgens whilst in the womb and although this has no visual effect on male babies, the females are usually, to some extent, virilised and should therefore be identified at birth. These girls obviously have female chromosomes (XX) and have a normal uterus, vagina and ovaries internally. However, they often require surgery to correct the appearance of their external genitalia.

Boys are more difficult to identify. In CAH there are salt losers and non-salt losers. Salt losers generally become ill within the first 2 weeks of life (they suffer what is known as an adrenal crisis). Hopefully, they then receive the appropriate tests and are put on the replacement steroids required. If not, unfortunately, this is a potentially fatal condition. Non-salt losing boys are usually identified by tall stature and signs of precocious puberty between the ages of 2-6 years. These tall boys will have an advanced bone age, which will have affected their final height potential and they will therefore be quite short adults.

All parents expect their children to be healthy and most are devastated to learn that their child has a chronic life threatening disorder, which will require life-long treatment. The CAH Support Group was set up to help families with CAH sufferers and was formed approximately 8 years ago. It is a sub group of the CLIMB (Children Living with Inherited MetaBolic diseases) which is a registered charity. Both the CLIMB and the CAH Support Group exist to:-

a) Give support to families and sufferers
b) To increase awareness of the condition(s) to the public and to the medical profession
c) To raise funds to support research

The support group committee is made up entirely of volunteers and our current membership stands at approximately 370 families and 120 professionals. We hold conferences at regular intervals and our key to success is getting information to where it is needed as soon as possible after the need is recognised; i.e. at diagnosis. Also support at this time is crucial. We believe that the existence of support groups is very reassuring and the work they do is vital in helping to cope and come to terms with the future.

Fortunately, the treatment for Congenital Adrenal Hyperplasia has improved dramatically over the years and the outlook for those affected is extremely encouraging.

Thank you for you reading, we hope this conference booklet has been of some help to you.

If you would like further information on the work of the support group please contact any of the committee listed on the back of this booklet.

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